
The event gathered about 1,000 participants from around the world, who are key players and specialists in nanotechnology applied to health, to present and discuss the European developments in nanosciences and nanotechnologies for medical applications, thus bringing together many different disciplines with a focus on healthcare.

The information gathered in these Proceedings provides an overview of the state-of-the-art in the multidisciplinary field of nanomedicine (including: tissue engineering, drug delivery, cellular function, congenital/degenerative diseases, nanoimaging, implants, and diagnostic tools), as well as of the related cross-cutting topics such as risk assessment, communication, ethics, societal aspects, commercialization, and understanding and addressing the specific requirements of the developing world.

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EuroNanoForum 2005
Nanotechnology and the Health of the EU Citizen in 2020

European and International Forum on Nanotechnology

Edited by
Michael Mason
Sophia Fantechi
Renzo Tomellini

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1. A CDROM of these proceedings is available that also includes many of the presentations. Where presentations or updated presentations are available this is noted at the end of the paper.

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3. The views expressed in the papers included in this publication are the sole responsibility of the various authors and do not necessarily reflect the views of either the Institute of Nanotechnology or the European Commission.

4. Some of the sessions have an introductory report by the Chair or Co-Chair where this was provided. These texts do not commit either the editors of these Proceedings or the Speakers of the sessions.

The Editors

Michael Mason (IoN)  Sophia Fantechi (EC)  Renzo Tomellini (EC)
Europe has recognized the importance of nanosciences and nanotechnologies early on, building upon its already established strong position in material sciences. We must now further build on these strengths to maintain the leading position we have reached in the field and suitably exploit the potential of nanotechnology.

Following the successful EuroNanoForum 2003, the European Commission has defined the key elements for a strategy aiming at an integrated, safe and responsible approach for nanotechnology research and applications. The Member States welcomed this strategy and asked the Commission for an action plan to implement it. This action plan, which we presented in spring 2005, sets out the concrete steps that Europe should take in the years 2005-2009.

Nanosciences and nanotechnologies is a highly promising area for research and innovation, not only to boost the competitiveness of Europe’s industry but also to create new products that will make positive changes in the lives of our citizens. This is why, with €370 million in 2004 and more than €460 million in 2005, the European Community is the most important funding source for nanotechnology research in Europe.

This is also why, under the 6th Research Framework Programme, nanosciences and nanotechnologies are a priority for European Community research and why the Commission has proposed that nano remains a priority in the 7th Framework Programme, now on the table for discussion and decision by the European Parliament and Council.

Because nanotechnology is particularly promising for successful and useful applications in health care, EuroNanoForum 2005, organized in the context of the British Presidency of the European Union, was dedicated to the nanomedicine field.

Nanomedicine represents an extraordinary field of research and innovation, providing European citizens with new and improved solutions for health care and quality of life, as well as supporting the competitiveness of our industry, thus contributing to the fulfilment of the Lisbon goals.

I am particularly pleased that, during EuroNanoForum 2005, a group of industries and specialized centres and organizations announced the creation of the European Technology Platform on nanomedicine.

To them and to all the researchers engaged in research, development and innovation in nanomedicine go my best wishes for a successful and fruitful work.

Janez Potočnik
European Commissioner for Science and Research
Research Framework
Programme 7: 2007 - 2013

- Cooperation – Collaborative research
- Ideas – Frontier Research: European Research Council
- People – Human Potential: Marie Curie Fellowships
- Capacities – Research Capacity

According to the Commission proposal, a doubling of the budget from about 5 billion € per year to about 10 billion € foreseen.

Octavi Quintana Trias
OPENING SESSION

Towards a Europe of Knowledge: Commission Proposal for Framework Programme 7

Octavi Quintana Trias, MD, MPH
Director Health, DG Research, European Commission

The EC 7th RTD Community Framework Programme Proposal

The European Commission proposal for the 7th Community Research Framework Programme (2007 – 2013) is organized along four main Specific Programmes:

- **Cooperation** – dedicated to Collaborative research, a longstanding feature of the Community RTD Programmes
- **Ideas** – dedicated to Frontier Research: European Research Council
- **People** – dedicated to the Human Potential: Marie Curie Fellowships
- **Capacities** – dedicated to developing the research Capacity of the EU

The Commission proposes to double the Community Research budget, from about €5 billion per year to about €10 billion. This significant increase would follow regular increases since the €3.3 billion of the 1st Community Research Framework Programme in the 1980s.

The Cooperation Programme

Health-related research will be significantly featured under Themes 1, 2, 3, 4, and 6 of the Cooperation Specific Programme:

<table>
<thead>
<tr>
<th>1. Cooperation</th>
<th>Budget € million (2004 constant prices)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Health</td>
<td>7 325</td>
</tr>
<tr>
<td>2. Biotechnology, food, and agriculture</td>
<td>2 163</td>
</tr>
<tr>
<td>3. Information Society</td>
<td>11 159</td>
</tr>
<tr>
<td>4. Nanotechnologies, materials, and production</td>
<td>4 256</td>
</tr>
<tr>
<td>5. Energy</td>
<td>2 581</td>
</tr>
<tr>
<td>6. Environment</td>
<td>2 232</td>
</tr>
<tr>
<td>7. Transport</td>
<td>5 232</td>
</tr>
<tr>
<td>8. Socio-economic research</td>
<td>698</td>
</tr>
<tr>
<td>9. Security and space</td>
<td>3 488</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>39 134</strong></td>
</tr>
</tbody>
</table>

* Not including non-nuclear activities of the Joint Research Centre: €1 617m
Under each theme, there will be sufficient flexibility to address both Emerging needs and Unforeseen policy needs. Also, dissemination of knowledge and transfer of results will be supported in all thematic areas. Support will be implemented across all themes through

- Collaborative research (including the already existing modalities such Collaborative projects; Networks of Excellence; Coordination/support actions)
- Joint Technology Initiatives
- Coordination activities of national research programmes (via the ERA-NET, ERA-NET+, and Article 169 schemes)
- International Cooperation actions

**The Health Theme**

The sequencing of the human genome and the recent advances in post-genomics have revolutionized research into human health and diseases. Integrating the vast amounts of data and understanding underlying biological processes requires bringing together critical masses of various expertises and resources that are not available at a national level. Significant advances in translational health research, which is essential to ensure that biomedical research provides practical benefits, also requires multidisciplinary and pan-European approaches involving different stakeholders. Such approaches allow Europe to contribute more effectively to international efforts to combat diseases of global importance.

Clinical research on many diseases relies on international multi-centre trials to achieve the required number of patients in a short time-frame. Epidemiological research requires a large diversity of populations and international networks to achieve significant conclusions. Developing new diagnostics and treatments for rare disorders also require multi-country approaches to increase the number of patients for each study. And performing health policy-driven research at the European level enables comparisons of the models, systems, data, and patient material held in national databases and biobanks.

A strong EU-based biomedical research will help strengthen the competitiveness of the European healthcare biotechnology, medical technology and pharmaceutical industries. The EU also has to play an active role in creating an environment conducive to innovation in the pharmaceutical sector, in particular to maximize the success of clinical research. Research-based SMEs are the main economic drivers of the healthcare biotechnology and medical technology industries. Although Europe now has more Biotechnology companies than US, most of them are small and less mature than their competitors. Public-private research efforts at the EU level will facilitate their development. EU research will also contribute to the development of new norms and standards to set up an appropriate legislative framework for new medical technologies.
The main objectives of the Health theme will be, therefore, to improve the health of European citizens; to increase the competitiveness of European health-related industries and businesses and to address global health issues including emerging epidemics. Emphasis will be put on translational research (translation of basic discoveries in clinical applications), the development and validation of new therapies, methods for health promotion and prevention, diagnostic tools and technologies, as well as sustainable and efficient healthcare systems.

The main research theme priorities will be organized along three main action lines:

- **Biotechnology, generic tools and technologies for human health** (High-throughput research; detection, diagnosis and monitoring; predicting suitability, safety and efficacy of therapies (including alternatives to animal testing); innovative therapeutic approaches and interventions)

- **Translating research for human health** (Integrating biological data and processes: large-scale data gathering, systems biology; research on the brain and related diseases, human development and ageing; Translational research in infectious diseases; translational research in major diseases: cancer, cardiovascular disease, diabetes/obesity; rare diseases; and other chronic diseases)

- **Optimizing the delivery of healthcare to European citizens** (Translating clinical research into clinical practice, including better use of medicines; quality, solidarity and sustainability of health systems including transitional health systems; enhanced disease prevention)

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)
EuroNanoForum 2005 Introduction

Ottilia Saxl
Institute of Nanotechnology, UK

EuroNanoForum 2005 was the second of a series of international nanotechnology conferences organized by the country holding the Presidency of the European Union. The Institute of Nanotechnology was pleased to be the organizers of this conference, held during the UK Presidency of the EU.

The theme we chose to build the event around was ‘Nanotechnology and the Health of the EU Citizen 2020’, an exciting and important one, where the potential social and economic benefits of nanotechnology could be explored in detail. Also exciting for us as organizers of the Conference was the fact that the newly created ‘European Technology Platform in Nanomedicine’ chose Edinburgh, and this event for its launch and the publication of its Vision paper on Nanomedicine.

I think it is in order to explain in more detail some of the reasons why this conference on nanotechnology had the future of health and healthcare as its theme.

In the main, the focus of many debates and discussions has been the potential risks of nanotechnology. It was strongly felt there needs to be a balance of information, and although EuroNanoForum 2005 did not neglect the important issue of possible risks, most of time was devoted to exploring the potential benefits of nanotechnology for healthcare. These included: nanotechnology-enabled diagnostics to detect disease at an earlier stage, targeted therapies, personalized medicine, techniques enabling the regeneration of tissues and organs, and implants that perform better and are more body friendly.

As mentioned, the conference addressed the possible risks nanotechnology might pose, how they may be minimized, and what regulation might be required to ensure public safety and confidence.

Also addressed in the conference was how the application of nanotechnology might provide a better quality of life for the ageing population, and what nanotechnology might offer for treating or preventing the diseases of the developing world.

Apart from the health benefits, other issues which should be addressed by any nanotechnology conference - such as ethical questions, which are perhaps more serious than ever – were not neglected. Delegates debated on what nanotechnology might mean for improving human performance, especially in the spheres of military and sport applications.

The conference also explored how scientists can engage with the public, to better inform them of what nanotechnology might mean for society, so everyone can offer more reasoned and reasonable opinions as a consequence.
Finally, the need to raise the awareness of school pupils to nanotechnology and its implications was not neglected, and schoolchildren from around Scotland were treated to a visual exciting afternoon on ‘What is Nanotechnology?’ which included an actress playing the part of a citizen in 2020, discussing with them the effects of nanotechnology on lifestyles of the future.

All of this and more can be found in the ensuing Proceedings, which I hope will provide a deeper insight into what I have only touched upon here, namely the very exciting potential nanotechnology has for health and the many interesting issues surrounding this topic.

Finally, a few words about the Institute of Nanotechnology itself. The Institute has been active in promoting nanotechnology since 1997. It leads arguably the most important European nanotechnology information network, NanoForum www.nanoforum.org; holds regular events on nanotechnology for business sectors, on topics such as nanotechnology and smart textiles, nanotechnology and crime prevention, nanotechnology and food, and has launched a nanomedicine network for researchers, practitioners, and industry, as an output from this conference. For further details on all of the above, visit our site at www.nano.org.uk. I hope readers of these proceedings will attend our other events and perhaps enrol for our nanomedicine network.

Finally, I would like to thank the sponsors that made this event possible, the DTI and the European Commission in particular. I would like to especially mention Renzo Tomellini, Sophia Fantechi, Uta Faure, and Julie Deacon for their active participation and assistance.
Convergent Nanotechnologies in Healthcare

Dr Leonard Fass
Director, Academic Relations, GE Healthcare, USA

Nano sized objects have interesting physical properties, that have great potential for the development of materials with a very broad spectrum of applications. The nanotechnology market is already a global but very inhomogeneous market. The processes to bring new products to market are immature with a high risk of failure. It will be key to demonstrate value to replace existing technologies and to make the jump from technologies to systems. Close collaboration with systems manufacturers will be vital. The barriers to exploiting new technologies and the factors that impact negatively on commercializing nanotechnologies need to be addressed.

Healthcare Systems of the future will be a major user of nanomaterials and devices with multiple uses such as:

- MEMS devices for ultrasound transducers and circuitry
- High resolution displays using field emitters
- Nanocomposites for X Ray tube anodes
- Carbon nanotube field emitters for X Ray tube cathodes
- Targeted Nanoparticles for MRI and magnetically activated thermal therapy.
- Targeted Nanoparticles for Ultrasound imaging and therapy
- Quantum dots for Optical molecular imaging
- Nano Bio -Sensors for monitoring body functions incorporating telemetry
- Body Sensor Networks
- Power Management devices
- Electronic High Density Packaging and interconnect for miniaturization of compact systems
- Wireless Communication systems incorporated into portable and implantable devices
- Nanomaterials used for tissue engineering and organ replacement therapy.
- Nanocontainers and nanotubes for drug delivery

Complete systems will have several applications of nanotechnology.

Point of Decision Healthcare could utilize:

- In Vitro Analysis using protein targeting fluorescent nanoparticles, Lab on a Chip
- Medical Imaging devices incorporating MEMS and Nano Systems
- Local drug delivery using activation through nanotechnology based ultrasound and magnetic systems
- Communication Satellites with 3D, thin, low power, high density packaging electronics
- Mobile Communications with miniature, high performance systems

(The presentation made at the conference is available on the Proceedings CDROM)
From Science to Business in 15 Years

Dr Andreas Jordan
Managing Director, MagForce Nanotechnologies AG, Berlin, Germany

We developed the first tumour-specific cancer therapy, a nanoparticle-based method, over more than 15 years of R&D since 1985. The principle of the nanocancer-therapy is to use an externally applied AC magnetic field to warm up regional deposited or accumulated tumour-specific nano-particles of iron oxide. The heating performance of nano iron oxide is considerably higher than with most other interstitial methods as a result of the relaxation processes of those particles in an AC magnetic field. Due to the strong magnetic coupling between the particles and the externally applied magnetic field, almost every temperature can be obtained in almost every region of the body. Further heat-driven effects are available only on nanoscale, like the behaviour in vivo regarding the warmth based infiltration of the Interstitium of tumours with large amounts of particles but not into normal tissue. Complete remissions have been observed in different animal tumour models. The further-evolution of the nano-particles with new coating-structures made a differential endocytosis possible, i.e. up to eight- to tenfold higher and faster particle uptake in malign cells compared with normal cells of the same tissue-type (e.g. glioblastoma versus glia-cells). Differential heating between tumour and normal tissue as the consequence of differential uptake of tumour-specific nano-particles is a new way to introduce a ‘real’ biological specificity into thermal treatments leaving normal tissue undamaged. This nanotechnology driven innovation far exceeds the well-known thermal effects, because targeting of drugs, isotopes and anti-cancer effective molecules is also applicable with the MagForce® nanoparticles. In this place, the methods of nanotechnology lead to decisive evolution of particles, because the homogenous and highly controllable synthesis of those nanoparticle-surfaces is the key to the differential uptake into tumour cells and additional developments of further biotechnological evolution as well.

During one completed and four still ongoing clinical trials at the Charité for glioblastoma patients, for local residual disease tumours of different entities, for prostate carcinoma and oesophageal cancer patients the MagForce® nanoparticles have been applied directly into the tumour by interstitial application i.e. stereotactically navigation-based (brain tumours) or by CT-guided conventional interventional methods. The first world wide clinical therapy system (AC magnetic field applicator MagForce® MFH®-300F), has been approved for patient treatment. Analogous to the results of all the animal-tests, the MagForce® nano particles also approved for clinical evaluation, have been deposited well in GBM tumours as well as in other tumours with an excellent tolerability, effective temperatures and clear signs of local tumour control in all cases treated so far. The clinical prove-of-concept was highly successful.
1 – ORAL PRESENTATIONS

SESSION 1 - STRATEGY AND CURRENT ACTIVITIES AT EUROPEAN LEVEL

A European Strategy for Nanotechnology

Dr Renzo Tomellini
Head of Nanosciences and Nanotechnologies Unit, Industrial Technologies Directorate,
DG Research, European Commission

Nanotechnology is an area which has highly promising prospects for turning fundamental research into successful innovations. It has the potential to boost the competitiveness of our industry as well as creating new useful products that will make positive changes to the lives of our citizens in a wide range of sectors such as medicine, electronics, and the environment. The importance of nanotechnologies has been recognized early in Europe. The Commission has also recently proposed an integrated and responsible strategy which has been endorsed by the Council. This presentation outlines how the implementation of this strategy is progressing.

Worldwide investment in nanotechnology has surged in recent years to around €8 billion in 2004 and we find ourselves at an important juncture where levels of private funding are overtaking public funding. This reflects the fact that nanotechnologies are increasingly making the transition from the laboratory to the market. Europe should ensure that it takes the opportunity to capitalize upon its scientific excellence in terms of innovation, economic growth, and jobs, avoiding a repeat of the European ‘paradox’ that has been witnessed for other technologies. Within Europe, around €1.3 billion of public funding was devoted to support nanotechnology R&D in 2004 with €370 million via the Sixth Framework Programme (FP6). The proposed doubling of the budget for nanotechnologies in the Seventh Framework Programme (FP7), if approved by the Council and the European Parliament, would boost EU R&D in this important area. At the same time, it is important that steps are taking to increase the impact of funding at European, national and regional level by reducing fragmentation and duplication.

Infrastructure is recognized to play a pivotal role in the development of nanotechnologies given the often large capital investment that is required and the long time-to-market. There is an increasing need to pool resources at European to obtain the maximum impact from existing infrastructure in areas such as nanobiotechnology, nano(eco)toxicology and metrology as well as possibility developing new infrastructure. The interdisciplinary nature of nanotechnology is also placing new demands on the traditional models for education and training. Europe is very active in this respect with around ninety different courses at graduate and post-graduate level. Within FP6, around 15% of funding for nanotechnology was devoted to researcher training. An international workshop was held earlier this year on the subject and the main results will also be presented.
Societal issues should be fully integrated to ensure the responsible development of nanotechnologies. A recent survey of public opinion from thirty two European countries published by the Commission reveals that half of the respondents believe that nanotechnology will have a positive effect in 20 years time. It is important that we have an effective communication and dialogue with the public to better understand and take into account expectations and concerns. The European Commission has initiated several new projects in this area, including this conference, as well as exploring the possibility of defining a set of shared principles for the responsible development of nanotechnologies at global level.

Note that this paper represents the views of the author and not necessarily those of the European Commission and does not commit the European Commission in any way.

(The presentation made at the conference is available on the Proceedings CDROM)
Launch of The European Technology Platform on NanoMedicine

Dr Jouko Karvinen
President and CEO, Philips Medical Systems, The Netherlands

Dr Karl-Jurgen Schmitt
President and CEO, Siemens AG Medical Solutions, Germany

A team of people from a number of companies and research institutes with support from the European Commission have drafted a vision for NanoMedicine. The document is being launched at this conference.

This is my short version of the vision; it is not about incremental improvements in healthcare technology or procedure; it is about redefining the practice of Medicine altogether.

When my grandchild is born, which may be 15 years away! – The child will be checked for genetical predisposition for a range of diseases, allergies, or deficiencies in the immune system. During his or her lifetime, periodic in vitro tests will be performed to check on early warning signals of developing diseases; to be followed by in vivo imaging to visualize, identify and quantify the extent of the disease process, and then targeted in situ delivery of potent agents which will deal with the transformed cells before organs are actually affected in any noticeable way. Many diseases as we know them now will be avoidable - amongst them many cardiovascular ailments and cancer.

There was $9bn spent worldwide in 2004 on R&D. Europe and the USA appear to invest equal amount of money, ahead of Japan and the rest of the world. Forget for a moment that in Europe there is less private investments than in the US and Japan. What is more important is that 49% of the patents are in the USA, 25% in Japan, and only 18% in larger Europe! Europe’s output in terms of IPR appears to lag behind....

When we look at industrial activity, the situation is even more skewed. The are now 330 companies in the USA, vs. only 130 in Europe and 51 in Asia shows the same ratios; 55% of the start-ups are in the USA and 29% in Europe.

It is clear, it all starts with the technology, but it certainly does stop after that!

In the vision, three areas have been selected as focus areas:

- Diagnostics, both outside and inside the body. This will not come as any surprise, as the whole paradigm and vision of Nano and personalized Medicine is based on early and accurate diagnosis. Diagnostics are also needed to monitor the effectiveness of the therapy, and to follow the development of the treatment process.
Once you know the problem, it needs to be healed. Systemic – i.e. injecting in the blood stream- administration has many disadvantages, which can only be overcome if we can bring the drug or the therapy to the places where they are needed: the diseased cells in the body. That calls for a completely new approach to drug delivery and transfer into the targeted cells.

Finally regenerative medicine, this is about restoring the capabilities of a diseased organ, not just diseased cells. Often, the disease process can be stopped but the damage is done. Can we develop smart and long living implants to support the organ, as for congestive heart failure? Or even better, can we restore the organ by growing or seeding new cells which will take the role of the diseased cells?

Those are the areas where we believe nanomedicine has unique contributions to make.

Already in the last century researchers at Philips asked themselves, how much of a compound should you be able see to get real early diagnosis? It turns out such biosensors need to be orders of magnitude more sensitive than today to detect disease early, e.g. an early stage tumour. That is when they started to work on some novel nano diagnostic technologies. One of the most promising ones is the invention of a magnetic detection method that promises the required sensitivity to measure as many as a single molecule! Philips is also working with a number of leading medical universities to develop nanoimaging procedures.

In a long-standing research cooperation with Washington University of St Louis, MO, we have been asking whether you could measure vulnerable plaque in arteries, or very early tumours with MR.

Aggressive tumours grow new arteries fast, angiogenesis. The same appears to happen in vulnerable plaque. To detect these new arteries researchers at Washington University made stable and body friendly nanoparticles of liquid emulsions that carry a molecule which binds to the inner surface of new arteries. These particles can also carry a huge load of Gadolinium atoms, which can be made visible with MRI. This makes the particles very sensitive to MR, and just a couple of particles lead to a visible signal. Early diagnosis, in vivo.

Such solutions will lead to new care cycles, shorter, faster, and cheaper than we know today. Today there is worldwide a huge industry in technology to make the care cycle work. We think of Care Cycle as the sequence of steps that a patient goes through to get healed from a disease. Whether it is cancer, heart disease or any other disease, there exists a care cycle for it today. The challenge in NanoMedicine is not to optimize one or more of these steps, it is to define new care cycles, which are superior to the existing one in every way: patient benefits, time, and costs.

The best and brightest people are needed for the job – race for the best talents worldwide, starting with the researchers at universities.

Technology should not only work; proof is required.
IPR; how to manoeuvre safely through the impressive volume of patents already generated. How to deal with IPR in cross boundary projects; how to license in and out efficiently.

We talked about start-ups before; is there enough venture capital to support the entrepreneur?

Current lengthy and very expensive clinical trials would kill most if not all of the targeted solutions. How can we adapt the approval processes to the new realities?

How to best get the new procedures started? Could the reimbursement systems be optimized to stimulate fast adoption?

Physician adoption curves tend to be very long – on average 15 years until majority accepted; (Porter, HBR 2004). How can we shorten that time frame?

And finally, could there be opposition from within society, based on religious or unfamiliarity with the concepts?

So we praise ourselves very lucky that such a reputable and diverse group of companies and institutes are coming together to make it happen!

First step is to call a meeting for the stakeholder group, i.e. participants and EU representatives. At that meeting, the rules of engagement will be agreed upon, role and members of the steering group will be established and the Workgroup mission and tasks will be agreed upon. Also on the agenda will be a review of new applicants, and the process to get to the deliverable, the Strategic Research Agenda.

Just a word on the mirror group and the advisory board, which the stakeholders may like to include in the structure of the European Technology Platform. The mirror group should represent the member states (and may include, for States with a strong federal political system, representatives of important regions) - it might consist of people already working in liaison with the EC or entirely 'new faces'. The advisory board has proven to be most practical, if the members of the platform would like to get in touch with people who could not, or are preferred not to, be members of their own (industry leaders from non-European States, representatives of groups with political clout, etc.).

This is about inventing the new medicine. The challenges are huge, as are the benefits to mankind when we are successful. It brings many disciplines together that each by itself would make interesting progress without changing medicine. That is why we need to bring all these disciplines together, and build up the knowledge and proof that NanoMedicine works. We are counting on all of you to contribute.

**Dr Jouko Karvinen, President and CEO, Philips Medical Systems**

(The presentations made at the conference are available on the Proceedings CDROM)
Delegates at the Poster Session
SESSION 2A - TISSUE ENGINEERING, NANOSCAFFOLDS, AND INTERFACES

Overview
Science is moving from transplanted organs to implanting of substitute or artificial organs to stimulating the body to do its own repairs. Tissue regeneration is about enabling the body to ultimately regenerate its own diseased or failed organs. The market worldwide for tissue engineered products already worth $18bn, and many hundreds of thousands of people are awaiting transplants worldwide. This has led to an illegal market in donor organs from the poor to the rich, so the development of effective regeneration techniques offers a multitude of benefits.

So how does Tissue Regeneration Work?
Instead of being surgically repaired, transplanted, or even fixed using prosthetics, tissue or organ failure could be solved by implanting natural tissue and organ mimics which can be fully functional from the start, or grow into the required functionality. Nanotechnology helps to recruit the body’s natural healthy cells to promote the regeneration of tissue on or around a damaged area. It can also act as a ‘scaffold’ to provide a framework for developing tissues to latch onto and penetrate.

This application of nanotechnology will result in reconstructed tissue and wound treatments that are superior, longer lasting and more acceptable to everyone involved, most notably the patient.

The beauty of the process is that it is arguably the most natural way of healing, as it is the body’s own healthy cells which are regenerating - as they were meant to do - albeit with a small push to get started.

Tissue regeneration would be almost unthinkable without development in nanoscience and nanotechnology. It underpins the design of scaffolds on which the cells are grown, which are composed of special nanocomposite materials that contain cell growth stimulants, and have nanoscale, cell-friendly surface topographies. There is even the potential for whole organs to be grown to replace those that have failed through disease or old age.

Tissue regeneration offers a revolution in healthcare, with huge benefits for doctors who will be using the technology, to the government who will save money, and most importantly to the patients who are the ultimate beneficiaries.
Session Report

Professor Mike Eaton
Section Head – Medicinal Chemistry, Celltech Therapeutics Limited, UK

Through the development of new materials and the realization that both the physical and chemical properties of materials directly affect the manner by which they interact with living tissue, the efficient repair or replacement of damaged tissues within the body, (bone, connective tissue or even organs) is now possible. These include: traditional materials such as hydroxyapatite, which has been manufactured with nanoscale surface modifications (such as pits and pillars) to allow selective adherence to different cell-types; and new materials including silicon and biodegradable polymers.

This session on Regenerative medicine was opened by Dr Alessandra Pavesio (Director of Research & Development, Fidia Advanced Polymers, Italy).

The technology described was the reconstruction of synthetic tissue on a polymer scaffold (Hyaluronate) using cells expanded in vitro. The cells are sourced from bone stem cells, autologous or allogeneic and grown in a special, albeit relatively expensive, facility. To succeed one needs to understand the mechanisms for endogenous stem cell recruitment, activation, control and homing. Dr Pavesio outlined the multitude of low molecular weight regulators that are known to control stem cell fate and discussed reversine, which allows cells to de-differentiate into ‘stem cells’. In addition there are many biological molecules, which trigger regenerative processes, not all of which are known as yet. These various factors can be bound to or incorporated into the polymer lattice to produce a bioactive polymer coating.

The polymer design must consider the:

- Geometry (3D structure, porosity and nano architecture…)
- Biocompatibility (coating, mimesis, composite chemistry….)
- Chemical properties (degradation rate, time, products)
- Mechanical properties (strength, flexibility, viscosity…)
- Tissue inductivity (cell proliferation, organogenesis, vascularization, innervation…)

In the future it may be possible to design materials which respond to their environment by triggering cell recruitment and mimicking tissues in different parts of the body.

The beneficiaries of such therapies are likely to be the elderly with diseases such as CNS disorders, cardiovascular disorders, diabetes, and osteoarthritis, the therapeutic focus. The time scale will be comparatively long and the regulatory hurdles are largely unknown.

Dr David Hulmes (Institut de Biologie et Chimie des Protéines, CNRS, Lyon, France) discussed the complex subject of the reconstruction of the human cornea after scarring following accidents. Additionally this is an area impacting six million globally due to infection.
The shortage of human cornea makes tissue construction an interesting alternative. The goal is to reconstruct an artificial cornea using nanostructured extracellular matrix and adult stem-cell derived epithelial, stromal and endothelial cells with properties resembling natural cornea. The technique uses limbal stem cells from an undamaged eye. These cells are cultured to grow a corneal epithelial cell sheet which is surgically positioned over the eye and allowed to attach to the undamaged region. The result is a significant improvement in clarity of the cornea. These sheets are in clinical trials but also being researched are the following eye tissues, replacement of which required significant biophysical input.

- Epithelial cell sheets - clinical trials
- Hemi-corneas (epithelium + stroma) for pharmacotoxicity testing
- Hemi-corneas (epithelium + stroma) for lamellar keratoplasty
- Full depth corneas (epithelium, stroma, endothelium) for penetrating keratoplasty

**Dr Günter R Fuhr** (Fraunhofer Institute for Biomedical Engineering, Germany) gave a talk which outlined the problems with handling cells in time-scales which are normally deployed in the lab. The requirements are trypsin free cell detachment, surface-supported cell differentiation, gentle cell characterization, and pair fusion of adherent cells. Cellular processes are inherently slow and this must be mimicked by robots working on this time-scale. Using such micro-manipulation it is possible to produce cells with no nucleus or two nuclei! Equally it is possible to pick up individual cells without damage. Cells typically move round a very slowly moving needle without lysis.

**Dr Francesco Curcio** (University Centre for Regenerative Medicine, University of Udine Medical School, Italy) noted that the starting point for this research is the fact that 50% of patients waiting for a transplant die within the year. Very many surgical procedures are carried out each year to mend bone and articular cartilage some of these procedures are heroic and demand much steel reinforcing. The use of synthetic bone may replace some of these procedures. A problem is there is no EU regulatory framework for human tissue engineering. The tissues of interest are:

- Islets of Langerhans
- Heart and Liver
- Valves
- Olfactory neurons
- Bone Marrow stem cells transplantation

The culture of bone takes in differentiation but the morphology can be quite good with many proteins correctly expressed. There is a need for specialized minibioreactors for the in-vitro production of tissue-substitutes and good GMP clean rooms to house them. The state of the art...
is the manufacture of the growth scaffolding by stereophotolithography. Life Sciences research in Italy is underpinned by an extensive network of dedicated centres, some of them internationally renowned so with relatively low costs i.e. it is a good place to do this research.

Professor Jöns Hilborn (Lars-Magnus Bjursten, Thomas Engstrand, Björn Atthoff, The Angstrom Laboratory, Uppsala University, Sweden) noted that typically major cranial reconstructive surgery is carried out using patients bone implanted in the skull. Bone regrowth only occurs within a centimetre of this bone. The talk concentrated on the use of a patient’ muscle treated with BMP2s as a scaffold to build new bone using the patient’s own blood supply. The resulting vascularized bone whilst not perfect is a great improvement. Mechanics at interfaces is a key factor determining amount of fibrotic capsule formation (i.e. ‘tissue biocompatibility’). Stress of regenerated tissues may be required to produce normal organs and architecture, rather than simple masses of the correct type of cells.

Professor Minoru Ueda (Nagoya University, Graduate School of Medicine, Department of Oral and Maxillofacial Surgery, University of Tokyo, Institute of Medical Science) described how Japan has an aging population with tooth loss a major issue. To provide adequate viable bone for dental implants, many kinds of graft materials has been investigated and introduced for clinical use. Among them, autogenous bone grafting is the most predictable and well-documented surgical approach. The limitation of previous methods for bone regeneration has led to the development of tissue engineering, which uses basic principles from material science and biology. According to the concept, the human body can be regenerated by using stem cells, scaffolding, and signalling molecules. Among the medical fields, dentistry is the most progressive field for clinical use of regenerative surgery. Nanotechnology is one of the most important technologies for tissue engineering, especially for the morphological change, proliferation, and orientation of the cells using scaffold materials. Recently we have developed an injectable bone using culture-expanded marrow mesenchymal stem cell (MSC) and platelet-rich plasma (PRP). The injectable bone is a good method for bone regeneration with the advantages of minimum invasiveness and to infill the defect. MSCs have been thought to be multi-potent cells that can replicate as undifferentiated cells and that have the potential to differentiate into various mesenchymal tissue including bone, teeth, skin, muscle and so on. On the other hand, PRP contain the high concentration of growth factors such as TGF-β family, which are the universal initiators for all healing pathway. By using these multiple growth factors in platelets, we tried to accelerate the bone regeneration. Before the clinical use of the injectable bone, we performed a series of experiments to confirm:

- The osseointegration between implant and regenerated bone
- The mechanical properties of regenerated bone
Following dog studies, evaluation was done from 6 month to 3 years after the first surgery in nine patients. Twenty-five fixtures were installed with injectable bone in maxilla and all implants succeeded to osseointegration clinically. Radiographic evaluation showed that the mean increase in mineralized tissue was 8.7mm. Dr Ueda concluded by saying, “injectable bone is truly a new type of graft material. By using this, patients can be free from any damage due to bone grafting. I think this is a revolution in the field of implant surgery”.

**Dr Robert Brown** (University College London, UK) described the generation of natural biomimetic tissues using collagen in which cells are seeded. The water is removed to produce a structure with remarkably natural architecture. The shrinkage can be up to two orders of magnitude.
Nanotechnology in Regenerative Medicine - an Industrial Perspective

Dr Alessandra Pavesio

Director of Research and Development, Fidia Advanced Biopolymers (FAB), Italy

Current efforts in the field of Regenerative Medicine are based on the understanding that we have reached a limit to our current medical paradigm that emphasizes replacement of tissues or on the use of small molecule therapy to alleviate symptoms of disabling diseases - it is time to consider a shift towards a biomimetic philosophy, i.e. towards more biologically based strategies for the regeneration of pathological tissues, that will trigger the body’s self repair capabilities and allow it, ultimately, to heal itself. If this biomimetic philosophy is condensed to its basic elements, three become evident. Firstly, there is the requirement for intelligent biomaterials to act as scaffolds enabling tissue regeneration to take place. Secondly bioactive signal molecules must be released from these matrices to initiate and direct the regenerative process. The third element of the biomimetic paradigm is the cellular component - of huge impact would also be the ability to implant cell-free intelligent bioactive materials that would effectively provide signalling to leverage the self-healing potential of the patient’s own progenitor cells.

Access to nanotechnology has offered a completely new perspective to the material scientists aiming to mimic the different types of extra-cellular matrices present in tissues. Techniques are now available which can clearly produce macromolecular structures of nanometres size with a finely controlled atomic composition and architecture. These can be further improved by designing bioactive materials and encoding biological signals able to trigger biological events and in situ progenitor cell recruitment. Nano-assisted technologies could therefore be exploited for the development of cost effective biomimetic treatments of chronic disabilities that mostly affect the elderly, such as diabetes, osteoarthritis, cardiovascular and central nervous system degenerative disorders. These complex challenges can be addressed only in an interdisciplinary approach with specialists who are spread all over Europe and the world and with both an academic and an industrial background. This will require enlarging the number of laboratories in Europe with nanotechnological expertise and facilities. It will be essential to set up multi disciplinary research groups with expertise in diversified technical backgrounds as well as to ensure an adequate balance of academic and industrial researchers.

To ensure that nano-assisted cost-effective therapies are developed in a timely manner, guidance from industry is advocated. Of equal importance for the success of such novel therapies will be the ability for the regulatory bodies of the European Union to proactively respond to innovation by providing uniform and clear guidance for the development and registration of nanomedicinal products. If these challenges are met, nanoassisted technologies will represent a significant opportunity for advancing European leadership in life sciences.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)
Reconstruction of Human Corneas by Tissue Engineering

Dr David J S Hulmes
Project Coordinator CORNEA ENGINEERING, Institut de Biologie et Chimie des Protéines, CNRS, Lyon, France. www.cornea-engineering.org

Abstract

The CORNEA ENGINEERING project aims to reconstruct human corneas (partial or full thickness) both to replace donor tissue in human grafts and also to provide a non-animal alternative for use in pharmacotoxicity testing. The cornea is a remarkable tissue which is both the main focussing component of the eye as well as being mechanically strong to resist high intraocular pressure. It is composed of three cell layers, the epithelium, the stroma and the endothelium, where the central stromal region accounts both the optical and mechanical properties of the tissue, being composed of a dense extracellular matrix populated by stromal cells (keratocytes).

The project aims to reconstruct the cornea layer by layer using adult stem cell derived sources and nano-engineered scaffolds. Members of the consortium have already developed procedures for the repair of damaged epithelia in which epithelial cell sheets are amplified in vitro from autologous stem cells isolated from the limbus and then transferred to patients resulting in restored vision. The challenge is to reconstruct hemi-corneas (epithelium plus stroma) for pharmacotoxicity testing or lamellar keratoplasty (partial thickness grafts) or full depth corneas (including the endothelial cell layer) for penetrating keratoplasty (full thickness grafts). This requires identification and optimization of stem cell sources for keratocytes and endothelial cells, the ability to produce a cell scaffold that provides optimum conditions for cell growth and maintenance, as well as having the required optical and biomechanical properties.

The project combines fourteen partners in nine countries, including academic researchers, ophthalmologists and industrial partners, and is funded by the European Commission Framework 6 Programme.

Aims

The ultimate aim of the project is to reconstruct a human cornea in vitro, for use both in corneal grafting and as an alternative to animal models for pharmacotoxicity testing. The project responds to the urgent need to develop new forms of corneal replacements as alternatives to the use of donor corneas, in view of the world-wide shortage of donors, the increasing risk of transmissible diseases, the widespread use of corrective surgery which renders corneas unsuitable for grafting, and the severe limitations of currently available synthetic polymer-based artificial corneas. It also responds to EU legislation banning the marketing of cosmetic products that have been tested on animals, using procedures such as the Draize rabbit eye irritation test.
**Strategy**

As the principal refractive element of the eye, the cornea consists of three distinct cell layers (Figure 1): the outer epithelium (composed of keratinocytes), the inner endothelium and the central stroma (composed of keratocytes embedded in a dense, highly organized extracellular matrix of collagen fibrils and proteoglycans). Between these layers are specialized extracellular structures called Bowman’s and Descemet’s membranes. Nano-patterned scaffolds are being developed to support growth of the different cell types found in the cornea, derived from human adult stem cell pools.

**Figure 1. Structure of the Cornea**

**Specific Objectives**

- Production of recombinant proteins and construction of cell scaffolds resembling the normal human corneal stroma
- Identification of optimal conditions for epithelial, endothelial and stromal cell growth
- Multi-centric clinical evaluation of a new procedure for repairing damaged epithelial cell layers using cell sheets expanded *in vitro* from patient-derived stem cells
- Reconstruction of hemi-corneas (consisting of epithelial and stromal layers) as alternatives to animal models for pharmacotoxicity testing
- Reconstruction of hemi-corneas (epithelial and stromal layers) for use in partial thickness corneal grafting (lamellar keratoplasty)
- Reconstruction of full depth corneas for corneal grafting (penetrating keratoplasty)
Impact
Blindness caused by damage to or destruction of the cornea, either by accident or disease, is accompanied by reduced quality of life, disability and social isolation. The most effective methods of treatment are lamellar or penetrating keratoplasty, where either the outer layer or the entire depth of the cornea is replaced with donor tissue, of which approximately 25 000 such operations are carried out each year in Europe.

On a worldwide scale, there are an estimated 10 million people who are blind as a result of corneal damage or disease. Due to public health problems, the onslaught of new diseases (HIV, Creutzfeld-Jacob, hepatitis C), the lack of sufficient donors, and the increasing use of corrective surgery (LASIK treatment) which renders corneas unsuitable for grafting, there is an urgent need to develop viable alternatives to the use of donor tissue. The development of viable artificial human corneas will meet this important Community societal objective and improve the quality of life for thousands of blind or partially sighted individuals. In addition, it will relieve family anxieties at the time of bereavement when confronted with decisions about organ donation.

The project also addresses the need to develop alternatives to the use of animals in pharmacotoxicity testing, in view of EU legislation banning the marketing of cosmetic products that have been tested on animals. At the moment, the Draize eye irritation test, in which substances to be tested are placed directly on the rabbit cornea to assess toxicity, continues to be widely used in Europe for toxicity testing, thereby exposing thousands of animals to unnecessary suffering. The development of tissue engineered human corneas will provide a valuable alternative, having the double advantage of alleviating animal suffering and providing a tissue for toxicity testing closer to the natural human tissue.

At present, no validated alternative methods have been recognized or accepted by European regulation, which presents a major dilemma for cosmetic companies, not knowing which technique to use for safety evaluation of new ingredients or cosmetic formulations.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)
Gentle Handling of Individual and Groups of Animal and Human Cells

Dr Günter R Fuhr
Coordinator CellPROM (Cell Programming by Nanoscaled Devices), Fraunhofer-Institute for Biomedical Engineering, Germany

Gentle cell handling in vitro is a key problem of biotechnology and regenerative medicine. There are two general cases:

- Manipulation of cells in solution avoiding any surface contact
- Manipulation of cells adherently growing on biocompatible surfaces

In relation to the IP-CellPROM, the first solutions are explained and demonstrated. A key problem in cell manipulation is the molecular adhesion and slow migration velocity of higher animal cells. These cytoskeletonally controlled processes occur in minutes or hours. These times clash with the current technical trend of making all cell separation and manipulation procedures as fast as possible. With selected examples, the uses and advantages of extremely slow instrument motion to manipulate cells in an automated way are presented and discussed.

Tissue Engineering, a Lead User Perspective

Dr Francesco Curcio
Associate Professor of Molecular Pathology, Dipartimento di Patologia e Medicina Sperimentale e Clinica, Università degli Studi di Udine - School of Medicine, Italy

From a Physician point of view and ‘Lead User’ perspective, Tissue Engineering represents both a hope and a challenge. The hope lies in the opportunity of improving treatment possibilities, enhancing the Patients’ Quality of Life and, ultimately, overcoming the chronic shortage of organs available for transplantation. New techniques allow production of tissues for several recipients from a single donor through heterologous grafting procedure. Furthermore, appropriate proliferation conditions enable to grow cells from the recipient himself and make available autologous material. In addition, new tools, tissue-equivalents, and tissue-substitutes can be produced in vitro for research applications. This will change medical practice profoundly. The challenge, on the other hand, lies in the need to carry out multidisciplinary and integrated research encompassing medicine, materials science, biology, engineering, and process automation.

True innovation is always born at the intersection between invention and market needs: the leading involvement of Physicians is thus determinant for its adoption and ultimate success. As ‘lead users’ physicians help identifying critical issues and play a key role in advising Patients to accept new technologies. Safety and regulatory framework, as well as ethical concerns, are primary issues – as well as cost-effectiveness, functionality and reliability.
A complete integrated and seamless process of automated and computer operated protocols is needed, from Basic and early Clinical research stages to the Patient’s bed and to the industrial certification and exploitation. When Laboratory Researchers are also Medical Doctors, high quality research drives technology efforts providing key inputs to innovations through joint development with industry, by means of testing of advanced equipment and devices e.g. mini-clean rooms, scaffolds, micro-bioreactors. This is a distinctive feature of Italy, where thirty-six Integrated Clinical-Molecular Medicine Centres operate conducting more than 600 clinical trials per year. A case example in point is the development of small bone implants for maxillo-facial surgery and dentistry which we aim to make available as routine, safe, cost-effective treatment for many Patients.

(The presentation made at the conference is available on the Proceedings CDROM)

**Scaffolds for Tissue Engineering**  
**Professor Jöns Hilborn**  
*President, European Tissue Engineering Society, Uppsala University, Sweden*

Tissue Engineering is a technique which has the potential to assist in organ repair or create tissues and organs de novo and thereby offers a compelling new approach to major clinical problems such as treatment of skin burns, arthritis, major bone defects, liver pancreas, heart, Parkinson’s, stroke etc. Typically a small sample of healthy cells is taken from the patient. These cells are expanded in the laboratory to a much larger number and then seeded onto a cell carrier allowing implantation into the patient. Once in place the tissue is remodelled to form the desired organ and the biodegradable cell carrier disappears leaving nothing but the new tissue behind. Other strategies use only cells, the cell-carrying scaffold or even factors that stimulate certain cell types to grow faster in-vivo. In many cases, however, severe cell death and also scar formation occurs. These phenomena are believed to be related to the lack of nutrient supply and excessive mechanical stress on tissue caused by the scaffold. This presentation will discuss the underlying mechanisms, give experimental evidence, and also suggest methods and materials design criteria in attempts to overcome this.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)
Novel ‘Injectable Bone’ Technology for Implant Placement

Professor Minoru Ueda, DDS, PhD

President, Asian Society of Tissue Engineering, Nagoya University, School of Medicine, Japan

This paper relates to a Human Study of Injectable Bone Applied for Ridge Augmentation and Dental Implant Placement. In the field of implant surgery, alveolar bone availability is the key to successful placement of endosseous implants in the posterior maxilla and mandible. Various bone grafting materials have been used for alveolar augmentation including autogenous grafts, freeze-dried bone allograft, hydroxyapatite and xenografts. Although the results of these investigations indicate that augmentation is clinically successful for various graft materials, it is questionable whether these materials, except for autogenous bone, have been osteogenic potential and biomechanical properties. On the other hand, autogenous bone, which currently remains the material of choice, is available for bone reconstructive procedures. However its use is limited due to donor site morbidity and limited amounts of graft material available for harvesting.

Due to these circumstances, we attempted to regenerate bone in a significant osseous defect with minimal invasiveness and good plasticity, and to provide a clinical alternative to the previously mentioned graft materials.

The new technology which we developed is called ‘injectable bone’\(^{[1,2,3]}\), and involves the morphogenesis of new tissue using constructs formed from isolated cells with biocompatible scaffolds and growth factors, which had been established via a tissue engineering concept.

![Diagram of protocol of tissue engineered bone](image)

**Figure 1.** Protocol of Tissue Engineered Bone
**Materials and Methods**

Injectable bone preparation: One month before the operation, MSCs were isolated from the patient’s iliac crest marrow aspirates (10ml) according to the reported method. The MSCs were expanded and inducted to osteoblast. PRP was extracted 1 day prior to surgery. The blood was first centrifuged for 10 minutes at 1 100 rpm. A second centrifugation at (2 500rpm for 5 minutes) was performed to combine the platelets into a single pellet and the plasma supernatant. PRP (3.5 ml), MSCs (1.0×107 cell/ml), and 0.5ml of air were aspirated into a 5ml sterile syringe. In a second 2.5ml syringe, 500µl of the thrombin/calcium chloride mixture was aspirated. The cells were resuspended directly into the PRP and mixed in the syringe with other supplements.

**Patient**

The subjects were seventeen cases aged from 44-74 years (mean age 55.3 years). Nine patients with partially or totally edentulous were scheduled for sinus floor grafting and eight patient underwent concurrent onlay plasty.

**Results**

In case of sinus floor augmentation, evaluation was done from 6 month to 3 years after the first surgery. Twenty-five fixtures were installed with injectable bone. The clinical observation was carried out on the grafted area. Cumulative survival and success rates for fixtures placed in conjunction injectable bone were 100%. Postoperative radiographic findings were consistent with integration between the implant and the regenerated bone (no bone loss or peri-implant radiolucency). Pre- and postoperative radiographic evaluation showed the increasing in mineralized tissue which was 8.7mm. (Table 1).

<table>
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<th>No.</th>
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<th>Sex</th>
<th>Site</th>
<th>Bone height pre-op (mm)</th>
<th>Bone height Post-op (mm)</th>
<th>Increase in mineralized tissue (mm)</th>
<th>Number of implant</th>
<th>Success rate %</th>
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**Average 8.7**  **25**

* membrane perforation

Table 1. Sinus Lift
Table 2 describes the vertical ridge augmentation procedure for each patient and the survival data for implants available at re-examination. Also the clinical conditions associated with the thirty four remaining fixtures placed in conjunction with ridge augmentation using injectable bone are presented in the table.

<table>
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<th>No.</th>
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<th>Site</th>
<th>Vol. of TEB* ml</th>
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<th>Increase In Mineralized Tissue(mm)</th>
<th>Number of implant</th>
<th>Success rate %</th>
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* TEB: Tissue Engineered Bone

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<th>AVERAGE 5.0</th>
<th>** wound separation</th>
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Table 2. Vertical Ridge Augmentation

At the second surgery, which was performed after a mean healing period of 5.5 months, the mucosal flap was elevated relatively widely to observe the grafted site.

**Discussion and Conclusion**

This study showed that injectable bone induced bone in this anatomic site in 100% of the patients. The results also indicate that it might be possible to achieve the osseointegration of simultaneous implants placement with injectable bone grafts. It may be possible that the injectable bone can shorten the period of implant treatment and reduce the patient’s burden.

The potential for injectable bone in general and in particular is exciting for both patients and dental practitioners. The release of for general clinical use seems very near, although they have not yet been approved for use by the Japanese Food and Drug Administration.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)

References


Biomimetic Engineering of Cell Scaffolds for Tissue Templates

Professor Robert A Brown, Showan Nazhat, Umber Cheema, Cher-Bing Chuo, Mike Wiseman, Mary Morgan, and Vivek Mudera

Director, UCL Tissue Repair and Engineering Centre, UK
Coordinator of London Network and the British Tissue Engineering Network (BRITEnet), UK

Tissue repair and tissue engineering are, at present, heavily dependent our ability to control cell function, inside and out of the body. Bio-control of cell function (notoriously complex and difficult) is required at two levels: (a) tissue quantity and composition and (b) functional nano-micro (i.e. meso-scale) 3D architecture. However, we already know from ‘scar biology’ that (b), 3D organization, is the critical problem in musculo-skeletal tissues. Work with 3D tissue engineering scaffolds (topography, cytomechanics, durotaxis etc) now shows that the most effective approaches start by presenting cells with biomimetic cues, built into the scaffold. Two points are evident: (i) cues must be appropriate to the resident cells, particularly scale and locality (ii) 3D stromal cells with minimal scaffold structure do not spontaneously produce functional structures. The problem, then, is one of biomimetic engineering of cell scaffolds with heterogeneous, tissue-like architecture (e.g. fibre anisotropy, scaffold stiffness, layering, zoning). However, fabrication of meso-scale structures is notoriously slow and difficult, especially under cell-friendly conditions or in 3D cell culture.

We have recently developed a key shift in concept, towards engineering of biomimetic structure (with cells as passengers). This prefabrication uses a novel adaptation of plastic compression (PC), based on the remarkable properties of native collagen gels. Gel fluid is rapidly expelled from cell-seeded gels producing strong, biomimetic scaffolds in minutes. These can be given complex spatial organization at the gross level and then shrunk by >2 orders of magnitude to produce hierarchical meso-structures. PC biomimetic fabrication uses surface embossing, strain induced alignment, internal lamination, and 3D layering / zoning to produce complex structures around resident cells.

The fabrication is cell-independent, avoiding limitations of poor spatial control, perfusion and slow assembly. Constructs have excellent in-vivo properties as putative tissue templates and bio-artificial grafts. In summary, biomimetic engineering by PC fabrication presents a new platform technology for rapid, high fidelity production of the next generation of meso-structured tissues and biomaterials.

Supported by the UK research Councils (BBSRC & EPSRC) and technical assistance of the late Mike Kayser.
SESSION 2B - DRUG DELIVERY AND PHARMACEUTICAL DEVELOPMENT

Overview
Nanotechnology offers new tools and mechanisms for drug delivery. Nanoparticles, buckyballs, dendrimers, and nanocapsules have been developed that can be functionalized with targeting motifs to direct the drug to target tissues, while at the same time offering protection from the body’s defences.

The discovery of new drugs is increasingly based both on what we know of disease processes and, thanks to the human genome project and advances in genomics and proteomics, what we can determine from DNA sequence analysis, transcription and translation profiling between different cells as to the function of genes and the likely cellular role of their encoded proteins.

One of the bottlenecks of drug discovery is the screening of many thousands of candidate drugs for efficacy against the target macromolecule in a disease state. Nanotechnologies, through advances in microarray platforms, dip-pen nanolithography and new detection methods (including label-free), are now allowing researchers to investigate the effects of candidate drugs on target macromolecules with unprecedented speed.

A long standing issue for pharmaceutical companies is to deliver the right amount of drug to the site of disease. The inability to achieve this has means that drugs need to be administered in excessively high doses, increasing the likelihood that patients may suffer from toxic side effects.

So how can Nanotechnology Help?
Nanotechnology enables drugs to be targeted more effectively to the site of the disease, and activated ‘on arrival’. Drug can be prepared in such a way that they can cross epithelial barriers, and differentiate between healthy cells and diseased ones. Very small drug particles (nanoparticles) are coated with special molecules and travel round the body until they reach the disease site. Once there, the molecules ‘decorating’ the drug particles recognize the disease site, bind to it, and the drug is then activated.

This targeting means the drug will work efficiently and more effectively, and side-effects dramatically decrease. For example, chemotherapy in cancer usually means healthy cells are also killed off during the attempt to kill the cancerous cells. Targeted drug delivery circumvents this, and offers the potential for a quicker recovery.

Further Benefits
Nanotechnology has other benefits for therapy. In nanoparticulate form, drugs are less prone to degradation, meaning they will have a longer shelf-life. Nanoparticulate drugs can be coated to delay their activation, resulting in the drug remaining in the body longer, reducing the frequency of dosage required.
Some drugs may be linked to particles which fluoresce when they reach diseased cells. These is a special technique known as find, fight and follow, and is leading to early detection and treatment. The area of disease can be identified by imaging the fluorescent particles, which then deliver their payload of drugs, and the effectiveness of the drugs can be then monitored.

In essence, the application of nanotechnology to drug targeting and delivery offers more effective treatments, lower toxicity and side-effects and reduced cost from reduced dosage. Drug delivery and targeting are areas which are already offering real patient benefits.

**Session Report**

**Dr Uta Faure**

* Nanosciences and Nanotechnologies, Industrial Technologies Directorate, Research Directorate-General, European Commission

The Chair, Dr Andreas Jordan, welcomed all participants to the session and introduced the first speaker, **Professor Costas Kiparissides**, Director of the Department of Chemical Engineering and Chemical Process Engineering Research Institute, Aristotle University of Thessaloniki, Greece, who spoke about Recent Developments in Targeted Drug Delivery Systems.

Drug delivery is a rapidly developing and evolving discipline that is represented and practiced in most biomedical research facilities and institutions throughout the world. Typically, the principles underpinning drug delivery are intrinsically related to the development of new chemical entities and are inherently involved in many aspects of basic and applied medical and biotechnology research. The very slow progress in the efficacy of the treatment of severe diseases, e.g., cancer, with low molecular-weight drugs has suggested a growing need for a multidisciplinary approach to the delivery of therapeutics to targets in tissues. From this, new ideas on controlling the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, biorecognition, and efficacy of drugs were generated. These new strategies, often called drug delivery systems (DDS), are based on interdisciplinary approaches that combine polymer science, pharmaceutics, bioconjugate chemistry, and molecular biology. The combination of drugs with macromolecules created a new class of macromolecular therapeutics.

Directly afterwards the Chair introduced the next speaker, **Professor Ruth Duncan**, director of the Centre for Polymer Therapeutics, Welsh School of Pharmacy, Cardiff University, UK, who spoke about Polymer Therapeutics: Nanomedicines in Routine Clinical Use.

The descriptor ‘polymer therapeutics’ is an umbrella term that was coined to describe polymeric drugs, polymer-drug conjugates, polymer-protein conjugates, polymeric micelles to which drug is covalently bound, and multi-component polyplexes being developed as non-viral vectors.
From the industrial standpoint, these hybrid nanosized medicines are new chemical entities rather than 'drug delivery systems or formulations' that simply entrap, solubilize or control drug release without resorting to chemical conjugation. Conceptually, polymer therapeutics share many features with other macromolecular drugs (proteins, antibodies, oligonucleotides) and macromolecular prodrugs including immunoconjugates. A bonus, however, is the versatility of synthetic chemistry, which allows tailoring of molecular weight, addition of biomimetic features to the man-made construct and even the possibility to include bioresponsive elements. Over the last decade a growing number of polymerprotein conjugates have been transferred to market (including PEG-asparaginase, and PEGGCSF) and fourteen polymer-anticancer drug conjugates have progressed into clinical development.

Then the Chair introduced **Dr Barry D Moore**, Chief Scientist of XstalBio, UK, who spoke about Biomolecule Coated Microcrystals – Nanostructured Particles for Delivery of Therapeutic Biomolecules.

Administration of therapeutic biomolecules to the patient is currently almost exclusively via injection. With the rapidly increasing number of biological molecules in the clinic (NBE) there is considerable interest in alternative drug delivery routes that can replace or reduce the frequency of injections. This presentation will describe a novel method of formulating biomolecules such as peptides, proteins, and nucleic acids in the form of nanostructured particles applicable to alternative administration routes such as inhalation.

The second part of the session was chaired by the Co-Chair, Dr Uta Faure who introduced **Dr Laurent Levy**, CEO of Nanobiotix, France, who spoke about Nanobiodrugs Applications for Cancer Therapy.

Nanotechnologies have provided a wide range of applications during the past decade in the field of electronic, micro-device, computing, and materials. Health related applications are the most recent progress induced by nanotechnologies. Nanobiotix is developing targeted nanoparticles that can be activated by an external field (MRI, X-ray, Laser) and generate physical/chemical therapeutic effect. Such tools can provide new modalities for therapeutic and/or diagnosis of cancers. This talk covers the following subject areas: overview of current and potential application on targeted nanoBiodrugs, manufacturing process and best practices, toxicology.

Then the Co-Chair introduced **Dr Peter Venturini**, director of the National Institute of Chemistry in Slovenia, who spoke about Protein Drug Delivery Systems.

Drug delivery is becoming more important as more potent and specific drugs become available with the knowledge about diseases available from the human genome project. Recent advances in the field of proteomics have allowed us to better understand the role and function of several peptides and proteins. As a result many new peptide or protein-based drugs are being discovered every day and offer new ways to treat diseases.
Proteins play an increasingly important role as therapeutic agents. At present they represent around 10% of the global drug sales and are expected to increase in the next years as a large number of protein drugs are already undergoing clinical trials. The use of these potentially beneficial compounds as drugs for cancer and other diseases may, however be severely limited by their poor permeability through biological membranes, fragile structure of the biomolecules and the body's ability to rapidly remove them from the blood stream. At present protein drugs are usually administered by parenteral route, which is connected to inconvenient and painful injections as well as fluctuations of blood drug concentration. Optimum delivery of therapeutically important macromolecules to their site of action at the desired rate is despite the significant progress still a great challenge.

Directly afterwards the Co-Chair introduced Professor Leigh Canham, Chief Scientific Officer of pSivida, Australia, who spoke about Drug Delivery Using Nanostructured Semiconductored Technology: Intratumoural Therapy.

BioSilicon™ is a novel nanostructured, porous form of semiconductor silicon which is biocompatible and biodegradable. The clinical use of non-systemic intratumoural chemotherapy is still limited, even for those high mortality cancers which are characterized by well defined primary lesions, such as breast, colorectum, lung, prostate and skin. In recent years, much effort has been invested into developing 'localized' therapeutic regimens. In particular, radio-seeds (radioactive rice-sized implants) have been produced for injection directly into tumours (brachytherapy). However, the delivery of anticancer drugs and drug carriers at concentrations required for effective tumour therapy and low systemic toxicity remains a challenge.

The Co-Chair introduced the last speaker of the session, Professor Helmuth Möhwald, director of the Max-Planck-Institute of Colloids and Interfaces, Germany, who spoke about Intelligent Organic and Hybrid Nanocapsules for Controlled Drug Encapsulation and Release.

The last two decades have experienced tremendous progress in preparing and characterizing polymeric surfaces and thin films by means of self-assembly. These techniques have recently been adapted to coat colloidal particles yielding systems with a high specific surface area. Hence one can make use of well-defined surfaces in basic science, e.g. to apply techniques requiring much surface, as well as in applications. This contribution will concentrate on coating of colloids by consecutive adsorption of polyelectrolyte multilayers. Later alternatives like coating consecutively lipids and proteins and grafting polymers on inorganic templates will be considered. After dissolution of the colloidal core one then obtains hollow capsules with wall defined with nm precision as previously proved for planar films.

The session was closed with questions of the audience to the four speakers.
Recent Developments in Targeted Drug Delivery Systems

Professor Costas Kiparissides, S Alexandridou, K Kotti, S Chaitidou, and O Kammona
Director, Chemical Process Engineering Research Institute, Aristotle University of Thessaloniki, P.O. Box 472, 54124 Thessaloniki, Greece

Introduction
The very slow progress in the efficacy of the treatment of severe diseases, has suggested a growing need for a multidisciplinary approach to the delivery of therapeutics to targets in tissues. According to the above, drug delivery systems (DDS), based on interdisciplinary approaches that combine polymer science, pharmaceutics, bioconjugate chemistry, and molecular biology have been developed in order to control the pharmacokinetics, pharmacodynamics, toxicity, immunogenicity, biorecognition, and efficacy of drugs, to minimize drug degradation and loss, to prevent harmful side-effects and to increase drug bioavailability and the fraction of the drug accumulated in the required zone.

The drug carriers can be made slowly degradable, stimuli-reactive (e.g., pH- or temperature-sensitive), and even targeted (e.g., by conjugating them with specific antibodies). Targeting is the ability to direct the drug-loaded system to the site of interest. Two major mechanisms can be distinguished for addressing the desired sites for drug release: (i) passive targeting (i.e. preferential accumulation of chemotherapeutic agents in solid tumours as a result of the enhanced vascular permeability of tumour tissues compared with healthy tissues) and (ii) active targeting (i.e., surface functionalization of carriers with ligands that are selectively recognized by receptors on the surface of the cells of interest).

Controlled drug release and subsequent biodegradation are important for developing successful formulations. Potential release mechanisms involve: (i) desorption of surface-bound /adsorbed drugs, (ii) diffusion through the carrier matrix/wall, (iv) matrix erosion and (v) combined erosion /diffusion. Sustained drug release involves polymers that release the drug at a controlled rate due to diffusion and/or polymer degradation over time. On the other hand, pulsatile release involves polymeric carriers that respond to specific stimuli. Other approaches to drug delivery are focused on crossing particular physical barriers, such as the blood brain barrier (BBB), in order to better target the drug and improve its effectiveness, or on finding alternative routes for the delivery of protein drugs other than via the gastro-intestinal tract, where degradation can occur.

Drug Delivery Systems
The global market for advanced DDS was more than €37.9bn in 2000 and is estimated to grow and reach €75bn by 2005. Developments within this market are continuing at a rapid pace, as drug formulations seek to cash in on the €6.2bn worldwide market for genetically engineered protein and peptide drugs and other biological therapeutics.
**Drug Delivery Carriers**

Colloidal drug carrier systems such as micellar solutions, vesicle, liquid crystal, and nanoparticle dispersions show great promise as DDS. When developing these formulations, the goal is to obtain systems with optimized drug loading and release properties, long shelf-life, and low toxicity.

Micelles formed by self-assembly of amphiphilic block copolymers (5-50nm) in aqueous solutions are of great interest as DDS. The size and morphology of the micelles can be controlled by varying the chemical composition, molecular weight, and block length ratios of the copolymers. The drugs can be physically entrapped in the core of the micelles where they are effectively protected against hydrolysis and enzymatic degradation by a tight shell formed around the micellar core as a result of the formation of hydrogen bonds between the hydrophilic blocks and the aqueous surroundings. Functionalization of block copolymers with cross-linkable groups can increase the stability of the corresponding micelles and conjugation with specific ligands can lead to a much higher selectivity.

Liposomes are a form of vesicles that consist of phospholipid bilayers. Polar drug molecules can be encapsulated in the liposomal core whereas amphiphilic and lipophilic molecules can be solubilized within the phospholipid bilayer. Channel proteins can be incorporated without loss of their activity within the hydrophobic domain of vesicle membranes, acting as a size-selective filter, only allowing passive diffusion of small solutes such as ions, nutrients, and antibiotics. Thus, drugs that are encapsulated in a nanocage-functionalized with channel proteins are effectively protected from premature degradation by proteolytic enzymes. The drug molecule, however, can diffuse through the channel, driven by the concentration difference between the interior and the exterior of the nanocage.

Dendrimers are nanometre-sized, highly branched, monodisperse macromolecules with symmetrical architecture. They consist of a central core, branching units, and terminal functional groups. Targeting effectiveness is affected by attaching targeting ligands at the external surface of dendrimers, while their stability and protection from the Mononuclear Phagocyte System (MPS) is being achieved by functionalization of the dendrimers with polyethylene glycol chains (PEG).

The liquid crystals combine the properties of both liquid and solid states. They can be made to form different geometries, with alternative polar and non-polar layers where aqueous drug solutions can be included.

Nanoparticles (i.e., nanospheres and nanocapsules of size 10-200nm) are able to adsorb and/or encapsulate a drug, thus protecting it against chemical and enzymatic degradation. Nanocapsules are vesicular systems in which the drug is confined to a cavity surrounded by a unique polymer membrane, while nanospheres are matrix systems in which the drug is physically and uniformly dispersed.
In recent years, biodegradable polymeric nanoparticles have attracted considerable attention as potential DDS in view of their applications in the controlled release of drugs, in targeting particular organs / tissues and in their ability to deliver proteins and peptides through the peroral route.

Hydrogels are three-dimensional, hydrophilic, polymeric networks capable of imbibing large amounts of water or biological fluids and modulating release in response to external stimuli. In these systems, release can be designed to occur within specific areas of the body (e.g., within a certain pH of the digestive tract) or also via specific sites (e.g., adhesive or cell-receptor specific gels). Hydrogels as DDS can be very promising materials if combined with the technique of molecular imprinting.

Molecular imprinting involves forming a pre-polymerization complex between the template molecule and functional monomers with specific chemical structures designed to interact with the template either by covalent or non-covalent chemistry. Once the pre-polymerization complex is formed, the polymerization reaction occurs in the presence of a cross-linking monomer and an appropriate solvent, which controls the overall polymer morphology and macroporous structure. After the removal of the template, the product is a heteropolymer matrix with specific recognition elements for the template molecule.

Examples of MIP-based DDS involve: (i) rate-programmed drug delivery, where drug diffusion from the system has to follow a specific rate profile, (ii) activation-modulated drug delivery, where the release is activated by some physical, chemical or biochemical processes and (iii) feedback-regulated drug delivery, where the rate of drug release is regulated by the concentration of a triggering agent, such as a biochemical substance, the concentration of which is dependent on the drug concentration in the body.
Figure 2. (a) Volume phase transition of a hydrogel induced by external stimuli, and (b) feedback-regulated drug delivery: (A) induced swelling and (B) loss of effective cross-links.

Conjugation of bioactive peptides/proteins and synthetic polymers is an efficient means to improve control over nanoscale structure formation of synthetic polymeric materials that can be used as DDS, to reduce toxicity, prevent immunogenic or antigenic side reactions, enhance blood circulation times and improve solubility. Modification of synthetic polymers or polymer therapeutics with suitable oligopeptide sequences, on the other hand, can prevent random distribution of drugs throughout a patient’s body and allow active targeting.

Figure 3. (a) Bioconjugates and (b) pharmaceutical carriers

Liquid formulations generating a (semi-)solid depot after subcutaneous injection (i.e. in-situ forming implants) are an attractive delivery system for parenteral application because; they are less invasive and painful compared to implants. Localized or systemic drug delivery can be achieved for prolonged periods of time, typically ranging from one to several months.

The ultimate goal in controlled release is the development of a micro-fabricated device with the ability to store and release multiple chemical substances on demand. Recent advances in micro-electro-mechanical systems (MEMS) have provided a unique opportunity to fabricate miniature biomedical devices for a variety of applications ranging from implantable DDS to lab-on-a-chip devices.
Administration Routes
The choice of a delivery route is driven by patient acceptability, drug properties, access to a disease location, or effectiveness in dealing with the specific disease. The most important drug delivery route is the peroral route which, despite the barriers that exist in the gastrointestinal tract, offers advantages of convenient administration, and potential manufacturing cost savings.

An increasing number of drugs are protein and peptide-based. They offer the greatest potential for more effective therapeutics, but they do not easily cross mucosal surfaces and biological membranes, they are easily denatured or degraded, prone to rapid clearance in the liver and other body tissues and require precise dosing. At present, protein drugs are usually administered by injection, but this route is less pleasant and also poses problems of oscillating blood drug concentrations.

Pulmonary delivery is also important and is effected in a variety of ways - via aerosols, metered dose inhaler systems (MDIs), dry powder inhalers, and nebulizers, all of which may contain nanostructures such as liposomes, micelles, nanoparticles and dendrimers. Research into lung delivery is driven by the potential for successful treatment of respiratory diseases by protein and peptide drug delivery and by the need to replace chlorofluorocarbon propellants in MDIs. However, the pulmonary delivery of proteins suffers by proteases in the lung, which reduce the overall bioavailability, and by the barrier between capillary blood and alveolar air (air-blood barrier).

Transdermal drug delivery avoids problems such as gastrointestinal irritation, metabolism, variations in delivery rates and interference due to the presence of food. The technique is generally non-invasive and aesthetically acceptable, and can be used to provide local delivery over several days. Limitations include slow penetration rates, lack of dosage flexibility and / or precision, and a restriction to relatively low dosage drugs.

Parenteral routes (intravenous, intramuscular, subcutaneous) are very important. For example, liposomes, the only nanosystems available in the market are administered intravenously. Nanoscale drug carriers have a great potential for improving the delivery of drugs through nasal and sublingual routes, both of which avoid first-pass metabolism and for difficult-access ocular, brain and intra-articular cavities.

Trans-tissue and local delivery systems require to be tightly fixed to resected tissues during surgery. The aim is to produce an elevated pharmacological effect, while minimizing systemic, administration-associated toxicity. Trans-tissue systems include drug-loaded gelatinous gels, which are formed in-situ and adhere to resected tissues, releasing drugs, proteins, cell-based delivery and device-directed delivery.
Future Opportunities and Challenges
Nanoparticles and nanoformulations have already been applied as DDS with great success and nanoparticulate DDS have still greater potential for many applications, including cancer and AIDS therapy, radiotherapy, protein delivery, antibiotics, vaccines and as vesicles to cross the BBB.

Nanoparticles provide massive advantages regarding drug targeting, delivery and release and, with their additional potential to combine diagnosis and therapy, emerge as one of the major tools in nanomedicine. The main goals are to improve their stability in the biological environment, to mediate the bio-distribution of active compounds, improve drug loading, targeting, transport, release, and interaction with biological barriers. The cytotoxicity of nanoparticles or their degradation products remains a major problem, and improvements in biocompatibility obviously are a main concern of future research.

Some of the technological challenges to be met in nanomedicine are the following: (i) Biocompatible and biodegradable nano-DDS that deliver large but highly localized quantities of drugs and biopharmaceutics to specific areas to be released in controlled ways, (ii) biomimetic polymers, (iii) virus-like systems for intracellular delivery, (iv) combined therapy and medical imaging (e.g. thermotherapy with magnetic particles), (v) universal formulation schemes that can be used as intravenous, intramuscular or peroral drugs, (vi) user-friendly lab-on-a-chip devices for point-of-care and disease prevention and control at home, (vii) better disease markers in terms of sensitivity and specificity, etc..

References

Polymer Therapeutics: Nanomedicines in Routine Clinical Use
Professor Ruth Duncan
Director, Centre for Polymer Therapeutics, Welsh School of Pharmacy, University of Cardiff, UK

The descriptor ‘polymer therapeutics’ is an umbrella term that was coined to describe polymeric drugs, polymer-drug conjugates, polymer-protein conjugates, polymeric micelles to which drug is covalently bound, and multi-component polyplexes being developed as non-viral vectors. From the industrial standpoint, these hybrid nanosized medicines are new chemical entities rather than 'drug delivery systems or formulations' that simply entrap, solubilize, or control drug release without resorting to chemical conjugation. Conceptually, polymer therapeutics share many features with other macromolecular drugs (proteins, antibodies, oligonucleotides) and macromolecular prodrugs including immunoconjugates.
A bonus, however, is the versatility of synthetic chemistry, which allows tailoring of molecular weight, addition of biomimetic features to the man-made construct and even the possibility to include bioresponsive elements. Over the last decade a growing number of polymerprotein conjugates have been transferred to market (including PEG-asparaginase, and PEGGCSF) and fourteen polymer-anticancer drug conjugates have progressed into clinical development.

Initially the anticancer drug conjugates incorporated well-known chemotherapeutic agents such as doxorubicin, paclitaxel and camptothecins, and the clinically most successful have been rationally designed in respect of their molecular weight, drug content and most importantly the polymer drug linker. Now that clinical proof of concept is established we are trying to develop more sophisticated second generation systems that will exploit either tumour, or tumour vasculature – specific targeting, improved delivery of novel natural product anticancer agents and also polymer-drug combinations. Novel polymer architectures (e.g. dendrimers), biodegradable polymeric carriers incorporating the drug via pendant linkage or as a component of the polymer main-chain are being explored. Whilst the first generation polymer-drug conjugates used lysosomotropic delivery as the route of intracellular delivery, bioresponsive, endosomolytic polymers provide an opportunity for intracytoplasmic delivery of proteins (e.g. non permanent toxins).

(The presentation made at the conference is available on the Proceedings CDROM)

References


Biomolecule Coated Microcrystals – Nanostructured Particles for Delivery of Therapeutic Biomolecules

Dr Barry D Moore
Chief Scientist, XstalBio, UK

Administration of therapeutic biomolecules to the patient is currently almost exclusively via injection. With the rapidly increasing number of biological molecules in the clinic (NBE) there is considerable interest in alternative drug delivery routes that can replace or reduce the frequency of injections. This presentation will describe a novel method of formulating biomolecules such as peptides, proteins, and nucleic acids in the form of nanostructured particles applicable to alternative administration routes such as inhalation.

(The presentation made at the conference is available on the Proceedings CDROM)
**Nanobiodrugs - Applications for Cancer Therapy**  
**Dr Laurent Levy**  
*CEO, Nanobiotix, France*

Nanotechnologies have provided a wide range of applications during the past decade in the field of electronic, micro-device, computing and material. Health related applications are the most recent progress induced by nanotechnologies. Nanobiotix is developing targeted nanoparticles that can be activated by an external field (MRI, x-ray, laser) and generate physical/chemical therapeutic effect. Such tools can provide new modalities for therapeutic and/or diagnosis of cancers. This talk covers the following subject areas: overview of current and potential application on targeted nanobiodrugs, manufacturing process and best practices, toxicology.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)

**Protein Drug Delivery Systems**  
**Dr Peter Venturini**  
*Director, National Institute of Chemistry, Slovenia*

Drug delivery is becoming more important as more potent and specific drugs become available with the knowledge about diseases available from the human genome project. Recent advances in the field of proteomics have allowed us to better understand the role and function of several peptides and proteins. As a result many new peptide or protein-based drugs are being discovered every day and offer new ways to treat diseases.

Proteins play an increasingly important role as therapeutic agents. At present they represent around 10% of the global drug sales and are expected to increase in the next years as a large number of protein drugs are already undergoing clinical trials. The use of these potentially beneficial compounds as drugs for cancer and other diseases may, however be severely limited by their poor permeability through biological membranes, fragile structure of the biomolecules and the body's ability to rapidly remove them from the blood stream. At present protein drugs are usually administered by parenteral route, which is connected to inconvenient and painful injections as well as fluctuations of blood drug concentration.

Optimum delivery of therapeutically important macromolecules to their site of action at the desired rate is despite the significant progress still a great challenge. Significant effort has been devoted to develop nanotechnology for drug delivery of proteins. Nanotechnology focuses on formulating therapeutic agents in biocompatible nanocomposites such as nanoparticles, nanocapsules, micellar systems, and conjugates. The nanometre size-ranges of these delivery systems offer certain distinct advantages for drug delivery.
These systems can improve the timed release of drug molecules, provide targeted delivery, improve poor bioavailability, and improve the stability against enzymatic degradation. Because of their versatility for formulation, sustained release properties, sub-cellular size and biocompatibility with tissue and cells they appear to be a promising system to achieve important objectives in delivery of therapeutically important biomolecules.

(The presentation made at the conference is available on the Proceedings CDROM)

**Nanostructured Semiconductor Technology for Drug Delivery**

**Professor Leigh Canham**  
*Chief Scientific Officer, pSivida, Australia*

**R Saffie-Siebert, C H Lau, D Drage, N Torabi-Pour, M Totolici, and L T Canham**  
pSiMedica Limited

**Z Kai, R Ng, and P Chow**  
*Singapore General Hospital*

**T Morris and S Watson**  
*Unit of Cancer Studies, University of Nottingham, UK*

BioSilicon™ is a novel nanostructured, porous form of semiconductor silicon which is biocompatible and biodegradable. The clinical use of non-systemic intratumoural chemotherapy is still limited, even for those high mortality cancers which are characterized by well defined primary lesions, such as breast, colorectum, lung, prostate and skin. In recent years, much effort has been invested into developing ‘localized’ therapeutic regimens. In particular, radio-seeds (radioactive rice-sized implants) have been produced for injection directly into tumours (brachytherapy). However, the delivery of anticancer drugs and drug carriers at concentrations required for effective tumour therapy and low systemic toxicity remains a challenge. Here we present evidence for the potential use of BioSilicon™ as a drug delivery system for intratumoural applications, which could open a new avenue for the use of BioSilicon™ in the medical field.

We measured the effect of our formulation on the efficacy/toxicity ratio of each treatment in tumour models. Cytotoxic agents, including Chlorambucil or Paclitaxel, delivered by BioSilicon™ and injected directly into the tumour significantly decreased the size of the tumour and increased the survival rate compared to the control mice, with 99% of the animals surviving long term. Based on the excellent efficacy and toxicology data, BioSilicon™ is being developed as a means of drug delivery in intratumoural therapy. BioSilicon™ can be designed so that it will slowly dissolve; thereby releasing the active cytotoxic material and allowing prolonged exposure to the tumour. This therapy has the potential to give better clinical results, increase patient compliance and have lower side effects than conventional cancer therapies.
Intelligent Nanocapsules for Controlled Drug Encapsulation and Release

Professor Dr Helumuth Möhwald
Director, Max-Planck-Institute of Colloids and Interfaces, Germany

The last two decades have experienced tremendous progress in preparing and characterizing polymeric surfaces and thin films by means of self-assembly. These techniques have recently been adapted to coat colloidal particles yielding systems with a high specific surface area. Hence one can make use of well-defined surfaces in basic science, e.g. to apply techniques requiring much surface, as well as in applications. This contribution will concentrate on coating of colloids by consecutive adsorption of polyelectrolyte multilayers. Later alternatives like coating consecutively lipids and proteins and grafting polymers on inorganic templates will be considered. After dissolution of the colloidal core one then obtains hollow capsules with wall defined with nm precision as previously proved for planar films. These capsules are distinguished by:

- Diameter 20 nm - 20 µm
- Wall thickness 10 nm – 100 nm
- Wall composition selectable from polymeric to inorganic and biomatter
- Composition variable across the wall

These unique features enable the construction of tailor made containers with tuneable permeability and mechanical properties. In special the permeability for proteins and drugs can be reversibly switched via pH, ionic milieu or solvent, irreversibly via temperature, light or via other remote control. This can be made use of to encapsulate enzymes or other catalysts to perform reactions in confined volume.

In special it can be shown that the stability of a reaction can be increased by protecting an enzyme against high molecular weight inhibitors and by creating an optimized local environment.

By external stimuli (light, micro-, acoustic waves) the capsules can be destroyed to achieve local drug release or, using the prodrug concept, to locally synthesize a drug.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)
SESSION 2C - CELL STRUCTURE AND FUNCTION

Overview
Humans are essentially a collection of cells! The better we understand how cells work, the more likely it is we can create effective cures, understand the cause of disease better and produce better drugs. Nanotechnology is enabling this understanding. This session is concerned with understanding of cell structure and function and how a cell manifests disease, and the new tools that are being developed to identify early signs of disease at the cellular level, monitor of healthy and diseased cells and the progress of therapy, and measure the effects of different drugs.

Monitoring Cell Activity and Diagnosing Disease
Once we know the signals that a cell gives when it is diseased we can look for that signal. Hand-in-hand with the growing understanding of cell function is the technology for measuring and identifying changes that indicate disease. The development of ‘lab-on-a-chip’ is one such technology which has many applications in disease identification. These include enabling cells to be studied independently of the body, the speedy screening patients for infection, and the analysis of the hereditary propensity to disease.

A lab-on-a-chip is a miniature laboratory that uses techniques developed from the electronics industry that offers speed, sensitivity, accuracy and portability, compared with more traditional techniques, which are slow, expensive resource intensive and may be inaccurate as samples deteriorate with time. In the future, this technology is leading to patient-centred medicine, with patients conducting tests in at their own homes, and downloading the results via their computer to a medical monitoring centre. Lab-on-a-chip technology also has important applications in being able to quickly screen a large population for disease or potentially killer infections, such as avian flu.

Lab-on-a-chip techniques and a knowledge of the human genome is leading to pre-symptomatic disease treatment through identify the individual genetic propensities say to breast or colon cancer or heart disease, so appropriate preventative action can be taken. This technology is also important for the developing world specifically in some African countries where disease is at epidemic rates. In areas where very little money, or even healthcare is available, the provision of cheap, fast-acting LOCs could offer early identification of disease, and enable more appropriate effective and cheaper treatment options. The cost effectiveness of what is basically a tiny microchip is another selling point; it can be mass produced incredibly cheaply.

Picture courtesy of Caliper Life Sciences
Nanosensors for Genomics, Proteomics, Cell Screening, and Diagnostics

Professor Jonathon Cooper
Chair of Bioelectronics Research Centre, University of Glasgow, UK

The growing need for sensitive, accurate and fast methods of analysis in the post genome era has generated considerable interest in the development of new analytical platforms. In this respect, we have developed a variety of new single cell technologies based upon the concept of the Lab-on-a-Chip and involving either thermal (sub-mK resolution), electrochemical, optical or electrophysiological techniques. One particular interest has been to use these new methods to study models for heart failure in the myocyte. Most recently, we have adapted these Lab-on-a-Chip methodologies with advances in nanoscale science and technology to improve both the quality and the context of the biological information.
Mastering the Nanoscale with Visible Focused Light

Professor Stefan W Hell

Director, Department of NanoBiophotonics, Max-Planck-Institute for Biophysical Chemistry Göttingen, Germany

We discuss and demonstrate a principle of fundamentally breaking the diffraction barrier through reversible saturable optical (fluorescence) transitions (RESOLFT). This principle was first put forward in far-field fluorescence microscopy in the form of Stimulated Emission Depletion (STED)\cite{1,3} and Ground State Depletion (GSD) microscopy\cite{2,3}. In these concepts, the diffraction barrier is broken by a saturated optical transition (depletion) between two states of a marker, whereby the transition is effected with an intensity distribution featuring one or more intensity minima (zero). The saturation level defines the size of the ultrasharp focal spot and/or the concomitantly enlarged bandwidth of the optical transfer function (OTF). We show that in a RESOLFT concept the resolution can be approximated by:

$$\Delta \alpha \approx \frac{\lambda}{2 n \sin \alpha \sqrt{1 + I/I_{\text{sat}}}}$$

which can be regarded as an extension of Abbe’s resolution equation\cite{4,7,8}. $I_{\text{SAT}}$ is the intensity required for saturating the transition, and $I$ is the intensity applied\cite{6}. $n \sin \alpha$ denotes the numerical aperture. The diffraction-unlimited nature of the RESOLFT family of concepts is reflected by the fact that the minimal resolvable distance can be continuously decreased by increasing $\zeta = I/I_{\text{sat}}$\cite{1-6}.

We give evidence of STED-microscopy displaying PSF of 10-20 nm FWHM, corresponding to a 15-fold increase over Abbe’s barrier\cite{8}. The reduction in fluorescence spot size provided by STED also allows fluorescence fluctuation (correlation) spectroscopy with sub-diffraction probing volumes\cite{9}. With suitable compounds the concept should also allow the diffraction unlimited writing of structures of any (nano)size and any density and pattern\cite{7}.

(The presentation made at the conference is available on the Proceedings CDROM)

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Nano Analysis and Detection of Gastrointestinal Tumour Cells

Dr Jürgen Schnekenburger
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Gastric cancers as pancreatic cancers are among the most severe diseases in western countries. The only effective therapy is an early resection of the tumours. Those cancers are detected by expensive diagnostic imaging methods at a late stage with a poor prognosis and a high lethality. The most important factor determining the outcome is an early detection of tumours at a resectable stage (Schneider et al 2005). The diagnosis of gastric tumours is often impaired by low amount of available material for molecular in vitro diagnostics and the limited applicability of novel technologies for in vivo diagnosis. These obstacles can be overcome by the application of nanoscale surface analysis technologies in the measurement of morphological and physical properties of cellular systems. Single cell based diagnostics and a marker free in vivo measurement of cell surface properties are future nanotechnology based solutions in early cancer diagnosis and classification.

Cancer cell function is mainly characterized by protein expression analysis. Whether cell surface properties are useful for the analysis of tumour state and progression is yet not known. We address this question by surface analysis of pancreatic tumour cell lines with different metastatic and migration potential by application of scanning electron microscopy (SEM), atomic force microscopy (AFM), digital holography and TOF SIMS analysis.

Pancreatic cancer is a rapid growing highly metastatic tumour. Due to the lack of a specific therapy more than 90% of the patients die within 6 months after diagnosis which makes pancreatic cancer the 4th most cause of cancer deaths in western countries (Jemal et al 2005; Lockhart et al 2005). We have generated genetically modified pancreatic tumour cell lines which were altered in the expression of the epithelial tumour suppressor gene E-cadherin. E-cadherin regulates cell-cell contacts and is frequently downregulated during tumour metastasis (Schnekenburger et al 2005). E-cadherin connects neighbouring cells and is intracellularly linked via catenins to the actin cytoskeleton. Actin filaments are major structural elements of eukaryotic cells and influence cell morphology and elasticity, cell surface structures and cell motility (Handschuh et al 1999). We recently identified the E-cadherin binding cell-cell contact protein p120 Catenin as a growth promoting factor in pancreatic tumours (Mayerle et al 2003). These data connect proteins determining cell surface properties with tumour progression and support the concept of cell surface analysis for tumour diagnostics.

E-Cadherin reexpression in metastatic pancreatic cancer cell lines resulted in an increased capacity of colony formation, reestablishment of cell-cell contacts and an inhibition of the metastatic potential. Most interestingly SEM analysis of E-Cadherin reexpressing cell lines revealed an altered morphology, the cells showed a flattened phenotype indicating a rearrangement of the actin cytoskeleton.
Atomic force microscopy and digital holography on living cells demonstrated a decrease in cell height of more than 60%. Using gene chip analysis we identified an E-cadherin dependent differential expression of three actin binding proteins, which may be responsible for the altered cell morphology.

Additional measurements using digital holography addressed physical cell properties as surface elasticity and dynamic cell surface processes as cell-cell contact formation and migration. E-cadherin expressing tumour cells could be differentiated from highly dedifferentiated E-cadherin deficient tumour cells by an altered cell migration and cell-cell contact dynamics (Carl et al 2004). The application of the label free and non invasive digital holography to isolated tumour samples was recently demonstrated to detect malignant tumour lesions by surface elasticity upon ultrasound stimulation (Avenhaus et al 2001; Avenhaus et al 2005).

The presented results demonstrate that in principle the correlation of protein expression data, biological cell features and cell surface properties can generate knowledge for the determination of pathophysiological cell features directly from cell surface analysis. Single cell surface analysis will be a tool in in-vitro diagnostics and drug development. The future application of marker free and partly non invasive nanoscale analysis methods like digital holography offers novel endoscopical in vivo diagnostics for the identification of malignant lesions based on physical cell properties.

References


Protection Mechanisms in Biomembranes

Dr Květoslava Burda
Institute of Physics, Jagiellonian University, Poland

All living cells and many eukaryotes organelles are surrounded by biological membranes, which are selectively permeable, compartmental barriers essential for their survivals. Biomembranes are active structures composed of lipids, proteins, and carbohydrates but proportion of each varies depending on the membrane. Lipids in the membranes act as an organic solvent for many biologically active compounds, which participate in various protective processes of the living organisms. For example carotenoids, which are fat soluble compounds, are efficient scavengers of singlet oxygen and free radicals.

Carotenoids similarly to tocopherols are essential micronutrients in animal and human nutrition due to their function as lipophilic antioxidants. Green tissues of photosynthetic organisms and in particular, dark yellow/orange vegetables and fruits are the sources of dietary carotenoids. The functions of carotenoids in plant tissues generating reactive oxygen species is far more complex and less understood than in animal and human tissues. The action of the natural pigments and directions of their possible applications in biotechnology and pharmacology will be presented.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)
Real Time Study of Membrane Binding Events

Dr Electra Gizeli

Department of Biology, University of Crete, & Institute of Biology and Biotechnology, FORTH, Greece

The membranes of living cells have a lipid bilayer matrix with associated proteins and carbohydrates. Membranes comprise the external boundary of all cells thus providing the medium by which cells communicate with the surrounding environment; eukaryotic cells also have a complex system of internal membranes that divide cells into separate compartments. Events such as the binding of peptides or other small molecules to cell membranes can affect cell processes; this can occur as a normal part of cellular signalling and also when the ligand comes from an external source such as an infectious agent or a therapeutic drug.

The majority of protein targets of therapeutic drugs are membrane proteins, making membrane binding events a subject of importance for the pharmaceutical industry.

Characterization of membrane binding events with model systems requires both a detection method and a model that reflects the reality of the membrane. The detection method employed here is a sensor based on piezoelectric acoustic devices analogous to those found in mobile telephones\footnote{1}. During sensor applications, an acoustic wave is generated at one end of the device by application of an alternating current to suitably placed interdigitated electrodes. The acoustic wave travels across the device before being converted back into an electrical signal by a second set of electrodes. The applied and output electrical signals can be compared to determine the speed and efficiency of transmission of the acoustic wave across the surface of the device; changes in these parameters will reflect changes in the density and viscosity of the medium adjacent to the device surface in the region between the electrodes. If a model membrane is deposited on the acoustic device in this area, then membrane binding events that result in a change in adsorbed mass or membrane mechanical properties can be detected by monitoring the output electrical signal from the device.

Supported lipid bilayers (SLBs), which have been employed widely as membrane models, can be deposited on the surface of acoustic devices for the study of membrane binding events\footnote{2}. The SLBs can provide a medium for supporting membrane proteins in their native environment or can be used by themselves to characterize interactions that occur directly with the lipids.

The initial step when characterizing binding events on model membranes is to determine the nature of the lipid layer that is acting as the model membrane. For SLBs deposited on the surface of an acoustic device by vesicle fusion, acoustic sensors can distinguish between adsorbed vesicle layers and adsorbed bilayers so that the bilayer presence can be confirmed prior to subsequent additions of analytes. If the lipid composition is systematically varied, then the range over which SLBs can be formed by vesicle fusion can be readily determined\footnote{3}.
Acoustic measurements with SLBs or supported vesicle layers (SVLs) will provide an average value for binding interactions over the area of the sensor surface. If there are localized variations in the binding due to lateral imhomogeneities in the lipid layer, then it will not be possible to detect these variations directly. The lateral heterogeneity of the lipid layers should therefore be considered when interpreting studies of membrane binding.

The lipid bilayers of cell membranes show lateral phase separation into nanometre-scale domains such as the gel phase lipid rafts that are rich in sphingomyelin and cholesterol. Phase separation will occur for lipid bilayers prepared with a wide range of lipid compositions. One example of a simple system that will separate into liquid ordered and liquid disordered domains is the 1-oleoyl-2-palmitoyl-sn-glycero-3-phosphocholine (POPC) and cholesterol system: at sufficiently low cholesterol concentrations, bilayers will be all in the liquid disordered (ld) state; at higher cholesterol concentrations, liquid disordered and liquid ordered (lo) states will both be present, and at sufficiently high cholesterol concentrations, the bilayer will only be in the lo state. One area of current research with the acoustic sensors described here is to determine the phase diagrams for different combinations of cholesterol with other lipids. This is done by measuring the change in the acoustic signal as cholesterol is removed from lipid layers with β-cyclodextrin; the initial rate of removal is plotted as a function of the lipid composition and the break points in this curve are used to identify the lipid composition at the phase transition points.

Acoustic sensors have also been employed to characterize the mode of bilayer disruption by the pore-forming cytolytic toxin CytB from *Bacillus thuringiensis*[^4]. Supported lipid bilayers deposited on the surface of the acoustic sensor remained stable in the presence of high concentrations of associated CytB. This supported the model of membrane disruption by the formation of pores rather than by a detergent-like action, an alternative mechanism that has been suggested for a closely related protein due to the high protein to lipid ratio required for disruption of liposomes. Research has continued in the subject of membrane disruption mechanisms, with a current focus on the mechanisms of action of the human antibiotic peptides called defensins.

References

Investigation of Cellular and Molecular Activity by AFM

Professor Manfred Radmacher

Institute of Biophysics, University of Bremen, Germany

We have used the AFM to follow biological processes under physiological conditions. At the cellular level the AFM allows the measurement of local mechanical properties of the cytoskeleton and thus gives new insights in processes like cellular locomotion or cell division. The cytoskeleton consists mainly of filamentous Actin and Actin binding proteins. Actin binding proteins are responsible for the degree of cross-linking and the architecture of the network. For instance, the motor molecule Myosin will create internal tension in the network (so called cortical tension). This can be observed during cell division in the cleavage furrow formed between the two daughter cells. When disabling Myosin biochemically with suitable drugs a softening of the cell will be observed.

On the molecular scale, we can demonstrate that the AFM allows the study of conformational changes of enzyme molecules during their activity. By watching fluctuations in the molecules’ height under different buffer conditions, e.g. in the presence of substrate or inhibitors, we could clearly detect the dynamics of single molecules by AFM. Recently, we have employed single enzyme molecules, which are immobilized to the very apex of an AFM tip, to modify locally suitable samples. Thus we have demonstrated for the first time a new surface modification technique, which we called enzyme assisted nano-lithography.

![AFM image of two fibroblast cells after cell division has occurred](image1)

*Figure 1. AFM image of two fibroblast cells after cell division has occurred*

![Features written by single enzyme molecules immobilized onto the tip of an AFM](image2)

*Figure 2. Features written by single enzyme molecules immobilized onto the tip of an AFM*
Probing Protein Trafficking and Interactions using Optical Nanotechnologies

Dr Mauro Giacca
Director, International Centre for Genetic Engineering and Biotechnology (ICGEB), Italy

Most of the biological events taking place inside a eukaryotic cell depend on the coordinated assembly of multi-component biological machineries. In particular, all DNA transactions in the cell's nucleus (replication, recombination, repair, and transcription) are carried out by multi-molecular protein and nucleic acid complexes that assemble in a timely, regulated manner in specific subnuclear locations. Recent advances in live imaging microscopy and the possibility of tagging biological molecules with fluorescent probes or quantum dots now permits the visualization of these events inside the living cells and in real time. Among several available techniques, fluorescence resonance energy transfer (FRET) permits the visualization of direct protein-protein interactions; fluorescence recovery after photobleaching (FRAP) monitors protein trafficking inside different subcellular compartments; fluorescence correlation spectroscopy (FCS) studies the diffusion of molecules inside biological microenvironments. A key tool that has paved the way to several of these studies is the utilization of the green fluorescent protein (GFP), originally cloned from the jellyfish Aequorea victoria, and of its several variants with different spectral properties and improved biological characteristics, such as resistance to wide pH range, specific sub-cellular localization, and susceptibility to photoreactivation after bleaching. In this presentation, I will review our experience on the study of several proteins involved in the control of gene expression of the human immunodeficiency virus-1 (HIV-1) using the above-described optical nanotechnologies. In particular, I will highlight the role that the HIV-1 Tat protein plays in the process of transcriptional activation of the viral genome and will describe its interaction with different proteins of the host cell’s transcriptional machinery, including factors that phosphorylate RNA polymerase II or are involved in the control of chromatin conformation at the site of proviral integration. Special emphasis will be given to the possibility of exploiting FRET and molecular dynamic techniques as tools for the identification of novel drugs that block HIV-1 infection by interfering with some of these newly discovered interactions.

(The presentation made at the conference is available on the Proceedings CDROM)
SESSION 3 – THE PROMISE OF NANOMEDICINE

Overview
Nanomedicine offers a huge spectrum of benefits for the better treatment of disease – from early diagnosis to better therapies to eventually preventative medicine; from stimulating the body to regenerate its own diseased tissues to the targeting and activating drugs at the site of disease. It also offers the possibility of developing better drugs, faster, which have fewer side effects, and are customized to the patient’s own genome.

This session examines three particular areas where nanotechnology will have a major impact: in relation to cancer; in relation to reducing animal testing, and in the commercial impact of new nano-based therapies.

Cancer treatment is the past has suffered from a lack of understanding the mechanisms of the disease at the cellular level, late diagnosis, and treatments based on attacking the whole body rather than the disease site. Nanotechnology is offering a totally new approach; from a better understanding of the root causes of disease, to quicker diagnosis and science-base treatments. Today, to quote Dr Mauro Ferrari, “we are seeing the tip of the iceberg” in terms of the potential nanotechnology offers for cancer treatment.

Another area where we are using a hammer to crack a nut is in the area of animal experiments for the validation of drugs. This has obviously produced some benefits in the past, but these are relatively small in relation to the large body of research (and cost) as many apparently good results could not be adequately replicated in humans, or produced unexpected side effects.

With a better knowledge of individual responses to chemicals, nanotechnology is leading to a refinement of techniques for drug discovery that are accurate and meaningful for the individual patient, based on the use of living cells.
The session concludes with a compelling economic argument. Because nanotechnology is leading to better treatments based on our knowledge of proteomics and genomics, this is leading to a win-win situation for drug companies and patients as well as huge economic benefits for those countries where the State provides healthcare. Drugs are becoming more efficient as they are increasingly designed to treat specific diseases, patients are cured more rapidly, less care is needed to counteract reactions (the fourth largest cause of death in the western world is adverse reaction to pharmaceutical drugs).

**General Applications of Nanotechnology in Medicine**

Nanotechnology is leading to faster diagnosis and more effective treatment, the early signs of disease, and its exact location. One such application uses quantum dots to locate the disease site. Quantum dots are semiconductor nanoparticles which can glow very brightly under certain criteria. The quantum dots can be attached to chemicals which link to diseased cells. When the link is made, the quantum dots glow. This allows the sites of disease to be accurately pinpointed, and also malignant and non-malignant tumours can be differentiated.

Quantum dots may help in identifying cells which may develop problems in the future. By recognizing certain indicators that cannot be detected using conventional technologies, quantum dots can call attention to potential disease sites, leading to the ideal of disease prevention.

Improved drug targeting and delivery is another highly promising area of nanomedicine, which is actually happening now. Coated drugs in nanoparticulate form can be delivered directly to the diseased cells. This means smaller or less frequent doses are required, and toxicity is reduced as the targeted drug works more effectively. Therefore nanomedicine is leading to the reduction of undesirable and costly side-effects of drugs, as the customisation and targeting of treatment would allow for more control over where the drug goes and what it affects in the body.

Nanotechnology is set to revolutionize healthcare through moving us towards preventative, or pre-emptive medicine, with many health and cost benefits, both to the State and the patient. Impacts are especially envisioned for the ageing and other hitherto disadvantaged populations.
Nanotechnology and New Cancer Research in the US
Dr Mauro Ferrari
National Cancer Institute, USA

Nanotechnology is the art and science of making functioning devices and their components on a dimensional scale that is normally populated by atoms and molecules - not human artefacts. The advent of nanotech-based approaches to medical research, clinical diagnostic and therapy is relatively recent, but has already produced a transformational impact. Early examples of small-scale technologies in medicine include microarrays, proteomic profiling substrates, micro/nanofluidic systems, liposomes, and imaging contrast agents. These are just the proverbial tip of the iceberg. Advances in all sectors of medicine may be envisioned, that will require a profound integration of nanotechnology and the established domains and methods of medicine. In particular, biomedical nanotech is being vigorously explored for applications to disease prevention, early detection, evolutionary diagnostics, multifunctional and personalized therapeutics, and symptom management. In this presentation, an overview of opportunities and frontiers will be presented, with emphasis on cancer, and applications to other braches of medicine.
Whole Cell Biosensors: Chip Canaries for Health Protection

Dr Shimshon Belkin

Director, Environmental Sciences and Technology Management, Hebrew University of Jerusalem, Israel

At the heart of every biosensor is a biological entity, the purpose of which is to react with the target analyte(s) and generate a readily quantifiable signal. Traditional biosensors are based on the unique specificity of enzymes to their substrates, antibodies to antigens or that of nucleic acids to their complementary sequences. In recent years we have promoted the use of a different concept, that of whole cell biosensors: natural or genetically engineered live cells that respond to pre-determined classes of chemicals.

While some of the specificity characterizing molecule-based biosensors may be lost, it is more than compensated for by the fact that by using live cells we are able to detect, by very simple means, very complex series of reactions that can exist only in an intact, functioning cell. Only a sensor of this type can report on the “well being” of a system, on the toxicity of a sample, the genotoxicity of a chemical or the bioavailability of a pollutant. No molecular recognition or chemical analysis can provide this type of information.

In order to turn such sensor cells into ‘real’ biosensors, they need to be immobilized onto a solid platform and coupled into a signal transduction apparatus. This complex nanotechnological challenge, requiring the cooperation of engineers, biologists, chemists and computer scientists, is recently being addressed by various research groups, attempting to incorporate different kinds of live cells into various types of biochips.
Nanomedicines - A Significant Share of the Non-Generic Market by 2020

Professor Michael A W Eaton
Section Head - Medicinal Chemistry, Celltech Therapeutics Limited, UK

The difficulty of discovering and registering new NCE drugs at the end of the 20th century has coincided with the start of sales of biologicals coming from the biotech revolution, a decade or so before. When the growing generic sector is removed, nanomedicines become a significant growth area, an opportunity that has not on the whole been missed by major pharma.

Two examples will be illustrated, Mylotarg® (gemtuzumab ozogamicin), the first antibody drug conjugate (ADC) to get FDA approval and CDP 870, an antibody polymer conjugate currently in phase III.

Mylotarg® illustrates many of the issues with drug conjugates[1], its success also rekindled worldwide the antibody magic bullet approaches, popular over a decade before. Much effort is now going into improving what at the time of Mylotarg was state of the art technology, with the primary target remaining oncology. The talk will describe many of the barriers that were overcome in bringing together one of the most toxic molecules known and providing a non-immunogenic delivery vehicle targeting the CD33 positive cells[2,3], responsible for acute myeloid leukaemia. Although the concept of targeting goes back to Ehrlich, its lack of demonstration in the clinic has proved to be a major barrier to commercialization. Much of the work done in academia has lacked the robustness that is required to convert it into a manufacturable product. Solid tumours present problems to most if not all therapeutic approaches; these will have to be understood and overcome if this class of nanomedicine is to be clinically and commercially successful. Antibodies are extremely good targeting and internalizing agents giving them an entrée to opportunities that NCEs will not be able to achieve. CDP870 can be described as a polymer therapeutic, it has an effector molecule: the antibody fragment, the other end of the block copolymer being polyethylene glycol. The role of the PEG is to increase the half-life of the fragment, such that a monthly injection in man is possible. The advantages of this type of polymer therapeutics will be discussed.

(The presentation made at the conference is available on the Proceedings CDROM)

References


SESSION 4A – CONVERGING TECHNOLOGIES FOR MEDICINE AND HEALTHCARE

Overview

Limits and barriers on medical research are being rapidly broken down by the convergence of many disciplines, such as nanotechnology, molecular biology with physics, information technology and even, at last, the humanities! Together, this is resulting in rapid advances in new techniques, processes and tools which are completely changing the way we have approached healthcare in the past.

It is not only researchers from different disciplines that are working together. Networks like Nano2Life are bringing private firms, scientists and research institutes together to solve the problems of treating disease. Strong partnerships are being formed that are providing a range of skills across the board, generating disruptive technologies and completely innovative solutions to old problems. These could include non-invasive diagnostics (who likes biopsies?), individual-specific drugs, identifying disease at the cellular level, faster validation of new drugs, and stimulating the patient’s own body to regenerate diseased or failed organs.

This session examines convergence and its benefits on a European level. It is case study-based, describing networks and their component organizations, and the benefits that have accrued to industry from EU-supported partnerships and initiatives that connect complementary skills from a wide range of disciplines.
Multifunctional Polymer Systems Designed for Biomedical Applications

Dr Steffen Kelch on behalf of Professor Andreas Lendlein, Director
Institute of Chemistry, GKSS Research Centre, Germany

Most polymers used in medical applications today are materials that were not developed originally for this application area. Different biomedical applications demand different specifications (i.e. mechanical properties) and the functionality of the biomaterials. Today polymer systems are developed which allow a tailoring of properties by varying the molecular parameters including a functionalization with regard to their application. Biofunctionality, degradability, and shape-memory functionality are counted among the required functionalities. The actual trend is the design of materials which show multifunctionality meaning and unexpected combination of different functionalities. Degradable implant materials for minimally invasive surgery or scaffold materials that temporarily replace the function of the extracellular matrix temporarily are examples for applications of such multifunctional materials.

The introduction of biodegradable implant materials as well as minimal invasive surgical procedures in medicine has significantly improved health care within the last decades. In this context multifunctional materials are biodegradable, showing a certain biofunctionality, and in addition the shape-memory functionality.

Shape-memory polymers can be fixed in a temporary, new shape and only recover to the original, permanent shape, when exposed to an external stimulus. The shape-memory effect results from the polymer structure and morphology in combination with a certain processing and programming technology[1,2]. The implants based on such materials could be inserted into the human body in a compressed (temporary) shape through a small incision and obtain their shape relevant for the specific application after warming up to body temperature. Because of the hydrolytic degradability a subsequent surgery to remove the implant is not necessary[3,4,5].

In general, Regenerative Medicine deals with the regeneration of degenerated cells, tissues, and organs. Tissue engineering is one of the technological approaches, where porous scaffold materials based on biodegradable materials are used to cultivate functional tissue for transplantation. Once a sufficient number of functional cells is available, the engineered tissue can be implanted in the patient to regenerate missing or damaged tissue. Another possibility is the development of alloplastic scaffolds that can be implanted directly and subsequently populated with the corresponding cell types in situ. The materials used for scaffold production are supposed to be degradable in a physiological environment, cell and tissue-compatible and should guide the tissue formation.

The material design of multifunctional polymer systems for medical application is at its very beginning. Extensive innovations have to be anticipated because of the interesting economical prospects for applications in the biomedical area.
A New Landmark in European Nanobiotech: Nano2Life

Dr Patrick Boisseau

Coordinator, Nano2Life, CEA-Léti, France

Nano2Life is a European network of excellence in nanobiotech
- Its research programme highlights nine strategic research areas
- Education and training on nanobiotech is a key activity
- Industrial cooperation is strongly supported, with the participation of high tech SMEs
- Ethics in nanobiotech is particularly addressed by the Ethics Board

Since 2004, Nano2Life – N2L - is the first European network of excellence in nanobiotech supported by the European Commission. More than two hundred scientists from twenty three research organizations in twelve countries regularly meet to implement a comprehensive programme of joint activities covering key aspects of the development of nanobiotech.

Nano2Life runs a scientific programme focused on nine strategic research areas, considered as key areas for the future development of innovative nanobio-devices. Successful joint research projects are initiated relying on an efficient mobility programme. Applications areas such as drug delivery, drug screening, diagnostics, and environment monitoring are addressed.

Education and training in nanobiotech is the second focus of Nano2Life. Students, young scientific as well as senior researchers are regularly trained on the latest technologies and disciplines with tutorials, summer schools, or workshops.

Nano2Life has initiated the first European road-mapping exercise in nanobiotech to prioritize expected application areas. A unique state of the art in nanobiotech has been performed, jointly with prospective workshops associating private companies.

Industrial cooperation is intensively developed. More than thirty five companies, mainly SME are associated to the network for easing and making technology transfer faster.

Ethics in nanobiotech is also monitored and studied by the Ethical, Legal, and Societal Aspects board of Nano2Life.

References
Nano2Life is a unique initiative under FP6 to connect and match complementary skills, expertise, and tools for accelerating the development of European nanobiotech and keep Europe as a leader in the field.

(The presentation made at the conference is available on the Proceedings CDROM)

**Biomimetic Approaches to Soft Nanotechnology**

**Professor Richard A L Jones**

_Head of Department, Department of Physics and Astronomy, University of Sheffield, UK_

The most effective nanotechnology we know about is cell biology. Rather than the scaled-down mechanical engineering, complete with cogs and gears, invoked in the futuristic visions of advanced nanotechnology, cell biology’s nano-machines are made from soft, responsive materials that flex and change shape. Physics looks different at the nanoscale, and this ‘soft’ approach to designing nano-machines exploits those differences. We should try and copy this approach; in the future much advanced nanotechnology will have more in common with biology than conventional engineering, and will exploit principles of self-assembly and molecular shape change to make functional nanoscale devices.
Medical Devices and Converging Technologies

Professor Patricia Connolly

Vice Dean Research, Department of Bioengineering, University of Strathclyde, UK

Major challenges exist in the field of medical devices that need to be met by converging technologies and medicine for healthcare. Many of these should utilize developments in nanotechnology but there are still fundamental problems in materials, physiology and engineering for human healthcare applications that need to be addressed. This situation reduces the chances of success for new medical devices, particularly those that must remain implanted in the body over long periods of time. There are three critical areas where medical devices need new developments or improvements:

- Monitoring / diagnostics
- Biocompatibility
- Rapid assessment and test programmes (Design, Clinical & Regulatory)

For example, many implantable devices are difficult to monitor in situ. The growth in the ageing population in the developed world means that there will be requirements to find ways of economically monitoring and reviewing performance of implanted devices in healthcare sectors such as cardiovascular surgery and orthopaedics.

The need to provide quality life and independence for this ageing population will extend the need for home monitoring of key parameters of wellbeing and drug regime compliance.

In terms of biocompatibility many fundamental challenges exist that need novel approaches which must draw together our current medical, biological and engineering knowledge in useful multidisciplinary projects. In 2005 we still cannot implant hip joints that are guaranteed to last an adult lifetime. In the cardiovascular sector, having a mechanical heart valve or any other implanted device such as a left ventricle assist pump means a lifetime’s commitment to warfarin. Blood biocompatibility of materials remains a major challenge to all sectors of medical devices and technology.

Screening and testing of new devices, particularly materials, is a lengthy and expensive process. Many new devices fail at this stage through lack of funding or lack of foresight at the design stage. Again convergence of expertise across the sector is required to provide the database from which new devices could be developed.

These challenges will be discussed in the presentations and some examples of projects that recognize and utilize the need for convergence will be used as an illustration of how teams in this field can build and go forward.

(The presentation made at the conference is available on the Proceedings CDROM)
Session 4B Panel Discussion
SESSION 4B – NANO FOR CONGENITAL / DEGENERATIVE DISEASES

Overview
Nanotechnology is expected to play an increasing role in the battle against congenital and degenerative diseases. As we live longer, many more diseases become manifest over a larger proportion of the population, such as Alzheimer’s and Parkinson’s. We are also experiencing an epidemic of lifestyle diseases, from diabetes to cancer to heart and vascular disease.

Firstly, early diagnosis is critical to many of these diseases, which is enabled by the miniaturization, user-friendliness, cheapness and wide availability of diagnostic techniques to such an extent that patients can monitor their own symptoms. Examples include self-testing for diabetes and cholesterol levels. The spectrum of possibilities will expand dramatically; test results can be transmitted to a central health bureau, and therapies prescribed remotely.

Working at the nanoscale has produced new hope for disease of the brain, for example. If the therapy is drug-based, drugs in nanoparticulate form can now cross the blood-brain barrier. If the therapy requires regeneration of diseased tissue, new research is enabling the growth of the patient’s own cells on nano-inspired scaffolds that can be then implanted into the brain.

Other areas where Nanotechnology offers hope is in the delivery of drugs in a way that emulated the body’s own systems. For example, in diabetes, insulin is required by the body at irregular intervals. Using techniques derived from the electronics industry, this need can be monitored using a small, silicon chip-based implant, and insulin delivered only as required.

Electronics combined with nanotechnology is also the basis of better retinal and cochlear implants. Today, new retinal implants have been developed that enable people previously classified as blind (through disease, such as macular degeneration) to be reclassified as sighted. Present cochlear implants are crude, difficult to insert, awkward to wear and give poor performance. Future implants will use nanocomposite materials, be small and easy to insert and be cheap to produce. This also has very promising implications for the poor.
Thermotherapy using Magnetic Nanoparticles: Principles and Clinical Application of Nanotherapy

Dr Andreas Jordan
Managing Director, Magforce Nanotechnologies, Germany

The MagForce Nanotherapy also termed ‘thermotherapy using magnetic nanoparticles’ is a new cancer therapy, in which iron oxide nanoparticles in aqueous solution (magnetic fluid) are directly injected into a tumour and subsequently heated in an alternating magnetic field. The magnetic fluid and the therapy system are described as well as results of preclinical studies and clinical trials.

Introduction
Thermotherapy using magnetic nanoparticles has been developed by our group in more than 15 years of research at the Charité - University Medicine Berlin[1,2] and is one of the first applications of nanotechnology in medicine.

The MagForce Nanotherapy, formerly designated ‘Magnetic Fluid Hyperthermia (MFH)’, is basically a thermotherapy, which is based on a defined energy transfer to biocompatible, superparamagnetic nanoparticles. The new technique, in which iron oxide particles (magnetic fluid) are directly injected into a tumour and subsequently excited in an alternating magnetic field, allows very precise heating of almost every part of the body.

The biological effectiveness of heat in treating cancer is known for decades and many of the corresponding molecular mechanisms are understood. Elevation of tissue temperature to above 40-41°C is termed hyperthermia. It alters the function of many structural and enzymatic proteins within cells as a function of time and temperature, which in turn alters cell growth and differentiation and can induce apoptosis[3,4]. Treatment with tissue temperatures above 46°C is termed thermoablation and has direct cytotoxic effects.

Thermotherapy is a physical therapy with fewer side-effects than chemotherapy or radiotherapy and is typically being used in combination with both of these therapies[5,6].

Although many successful clinical trials have been conducted, hyperthermia is not yet well established in clinical routine. It seems likely that this discrepancy rather derives from the limitations of technical and biological selectiveness of heat distribution in the depth of the human body than from a general lack of biological effectiveness. Common thermotherapy-techniques use different energy sources for generating heat in body tissue: Electromagnetic waves radiated by antennas (e.g. radiofrequency- or microwave-hyperthermia), ultrasound, magnetically excited thermoseeds as well as tubes with hot water[7,8].
The major problem of all conventional thermotherapy systems used these days is to achieve homogenous heat distribution and deep regional therapeutic temperatures in the treated tumour tissue. A failure may either lead to insufficient temperature rise in parts of the tumour, resulting in further tumour growth, or to negative effects on neighbouring tissue by too high temperatures.

The MagForce Nanotherapy particularly faces these problems.

**Components of the MagForce Nanotherapy System**

The magnetic fluid MFL AS consists of superparamagnetic iron-oxide nanoparticles in aqueous solution with an iron concentration of 112mg/ml. The iron-oxide core (diameter 15nm) is covered by an aminosilane type shell (Figure 1). The particles generate heat in an alternating magnetic field by Brownian and Neel relaxation processes.

Thermotherapy is performed in the therapy system MFH 300F®, generating an alternating magnetic field of 100kHz and variable field strengths of 0-18kA/m (Figure 1). The applicator, which has been specially developed for this type of therapy, meets the safety and practicability criteria for medical use imposed by the respective European authorities. Due to its universal design, it can be used for treatment of malignancies in every location of the human body.

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**Preclinical Studies on MagForce Nanotherapy**

MagForce Nanotherapy is a new type of local thermotherapy with the advantage of selective heat deposition to tumour cells. The nanotechnological construction of the shell enables differential intracellular ingestion, preferentially in proliferating cells like tumour cells[9].
In 1996, we firstly described in vivo experiments on thermotherapy using dextran-coated nanoparticles on intramuscularly implanted mammary carcinoma of mice. The study demonstrated local tumour control in many of the treated animals within 30 days after therapy\[^{10}\].

In a rat model of prostate carcinoma we obtained intratumoural temperatures of up to 70°C. A significant inhibition of prostate cancer growth of about 50% over controls could be demonstrated in the thermotherapy group. More than 80% of the injected dose of iron could still be detected 10 days after instillation into the tumour\[^{11}\]. Further experimental studies using this tumour model investigated the effect of combined magnetic nanoparticle thermotherapy and external irradiation. Mean maximal and minimal intratumoural temperatures obtained in these experiments were 59°C (centrally) and 43°C (peripherally) during the first thermotherapy and 55°C and 42°C, respectively, during the second of two treatment sessions. Combined thermotherapy and radiation reduced tumour growth by 88% versus controls\[^{12}\].

In a rat model of glioblastoma multiforme we could demonstrate the high efficacy of our new technique leading to an up to 4.5-fold prolongation of survival\[^{13}\]. The animals received two thermotherapy treatments within 48 hours after a single stereotactic injection of the magnetic fluid into the tumour. Intratumoural treatment temperatures between 43°C and 47°C could be correlated with prolonged survival. The application of the aminosilane-coated nanoparticles led to the formation of stable deposits, thus allowing for repeated magnetic field treatments without repeated applications of the particles.

**First Clinical Experience**

From March 2003 to June 2004 we performed the world’s first phase-I trial on MagForce Nanotherapy with fourteen glioblastoma multiforme patients\[^{14}\]. Glioblastoma multiforme is the most malignant brain tumour where median overall survival after first-line therapy does not exceed 12-15 months. No significant increase of survival has been achieved over the last decade.

All patients of this trial received stereotactic injection of the magnetic fluid into the tumour. Before starting thermotherapy, the position of the instilled nanoparticles was determined by computed tomography (CT). These data were matched to pre-surgical MR images by a specially designed software (MagForce NanoPlan®), thus allowing the calculation of the expected heat distribution within the treatment area in dependence on the magnetic field strength\[^{15}\].

Another feasibility study enrolled twenty one patients with local relapses of different other tumour entities (e.g. cancer of the rectum-, ovarian-, prostate-, cervix-carcinoma and sarcoma). All of these patients received thermotherapy in combination with radio- or chemotherapy\[^{16}\].
Since December 2004 a feasibility-study with ten patients with pre-treated prostate carcinoma is being performed, another main focus in the clinical use of thermotherapy using magnetic nanoparticles. The nanoparticles are injected transperineally into the prostate under transrectal ultrasound guidance and fluoroscopy\(^{[17]}\).

According to the experiences in these first clinical trials, the MagForce Nanotherapy is effective and can be applied without complications. The heat treatments were tolerated well without or with only minor side effects depending on the tumour location.

The follow-up showed encouraging results for severe oncological diseases and there are several strategies available to further improve the effectiveness of the treatment, for example to elevate the H-field (after modification of the applicator) or to increase the amount of magnetic fluid in the target area.

A Phase II study is in progress to evaluate the efficacy of our new approach on sixty five patients with recurrences of glioblastoma multiforme or anaplastic astrocytoma (started January 2005) focusing on the European wide approval of the MagForce\textsuperscript{®} products in 2007.

**Advantages of the MagForce Nanotherapy:**

- The magnetic fluid can be distributed in very small portions and therefore almost continuously within the targeted area
- With the help of the known power absorption capacities of the nanoparticles and density patterns gained from computed tomography a 3-dimensional analysis and planning of the expected temperature distribution is possible by means of specially designed software
- A collapse of tissue barriers during repeated heatings leads to improved diffusion of the magnetic fluid, resulting in a spreading of the nanoparticles within the target area
- The local stability of the particle deposits and the externally induced activation allow consecutive treatments without additional trauma
- For the first time, this new technique enables physicians to freely choose the treatment temperatures, even after a single injection of the magnetic fluid

**References**


**Nanostructure Biomaterials in Implants and Insulin Delivery**

**Dr Jackie Y Ying**

*Executive Director, Institute of Bioengineering and Nanotechnology, Singapore*

Nanostructured materials are of interest for a variety of applications. This talk describes the synthesis and properties of nanostructured materials that are made up of crystallites or particles of ~10nm. They may be generated by various physical and chemical approaches with ultrahigh surface reactivity. Through controlled synthesis in reverse microemulsions, my laboratory has achieved polymeric nanoparticles for the glucose-sensitive delivery of insulin. These stimuli responsive materials allow for the appropriate insulin delivery to diabetic patients only when their blood sugar levels are high, without the need for external blood sugar monitoring. We have also generated calcium-doped silicate nanoparticles via chemical precipitation as gene delivery vectors. This novel gene delivery system possesses excellent transfection efficiency and selectivity for osteoblasts, and is non-cytotoxic.

We have also employed nanocomposite processing to achieve hydroxyapatite-based orthopaedic implants. With an ultrahigh dispersion of hydroxyapatite and zirconia nanocrystals, this nanocomposite system demonstrates superior mechanical strength and bioactivity compared to conventional bioceramic systems. We have further derived organic inorganic nanocomposites as bone grafts that provide for similar microstructure and chemistry as natural bone.
This system allows for tuneable mechanical property and degradation rate, and exhibit excellent bioactivity as a bone graft material. Lastly, we have developed apatite-polymer nanocomposites for the sustained, zero-order delivery of protein therapeutics. By adsorbing valuable bone morphogenetic proteins on carbonated apatite nanocrystals that were then encapsulated within biodegradable polymeric microparticles, we are able to achieve controlled release of this growth factor for the bone healing process over an extended period of time.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)

**Dendrimers as Drugs and Carriers: A Unique Pharmacokinetics?**

Professor Ruth Duncan, N Malik, R Wiwattanapatapee, M Xyloyiannis, O L Padilla de Jesús†, J M J Fréchet‡, M Manunta, L Izzo, and A Jones

Centre for Polymer Therapeutics, Welsh School of Pharmacy, Cardiff University

† Department of Chemistry, University of California Berkeley

No paper available.

(The presentation made at the conference is available on the Proceedings CDROM)

**Biocompatibility – from Proteins to Tissue**

Professor Morten Foss, Mogens Duch, Kristian Rechendorff, Jeanette Justesen, Mads B Hougaard, Mathias H Bünger, Finn Skou Pedersen, and Flemming Besenbacher

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**Biocompatibility - From Proteins to Tissue**

In the interdisciplinary area of nanoscience and nanotechnology, the interaction between surfaces and biological systems have attracted much attention due to the potential applications in a range of different fields including biocompatible materials for implants. At the interdisciplinary Nanoscience Centre (iNANO) in Aarhus, a range of different techniques including quartz crystal microbalance with dissipation, atomic force microscopy and cell assays has been applied to follow the protein adsorption and cellular behaviour on well-defined topographically structured surfaces.

On a higher hierarchical level, bone is a composite consisting of both an organic and an inorganic phase. By Small-Angle X-ray Scattering the bone-implant interface has been studied.
Adsorption of Fibrinogen and BSA on Tantalum Films with Well-controlled Nanoroughness

Using quartz crystal microbalance, we have studied the adsorption of fibrinogen and bovine serum albumin on tantalum-coated quartz films (the surface of such film is in the oxide state) with well characterized surface roughness varying from 2 to 33nm. The saturation uptake is found to increase with increasing roughness. The effect is appreciable for fibrinogen and modest for bovine serum albumin. Monte Carlo simulations show that the results obtained can be quantitatively explained taking into account that the shape of the proteins is strongly anisotropic and nearly spherical, respectively.

Mineralization on Well-defined Topographically Structured Surface

A large number of squares with different structures have been produced on a single wafer for a comparative study of different cellular responses to all these structures. Here, mineralization on the topographic structures by a murine preosteoblastic cell-line is reported. The cellular response of embryonic fibroblasts and the murine preosteoblasts on the structure that mineralizes the most has furthermore been examined by cytoskeletal staining.

The Bone-implant Interface

The understanding of the interaction between bone and orthopaedic implants is important for the development of biomaterials with improved biocompatibility. The SAXS technique has previously been applied to offer structural information on mean crystal thickness, predominant orientation, and degree of orientation of mineral particles in bone. Therefore, one application of SAXS is to investigate the ultrastructure of bone in connection with ingrowth on implants, which is not possible with conventional optical techniques. The mineral particles in the trabecular bone were aligned along the trabeculae and tended to be aligned along the implant surfaces. Within the individual bone samples, a large variation in mean particle thickness and particle orientation was observed depending on the bone position relative to the implant.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)
SESSION 4C – NANOIMAGING AND FUNCTIONALIZED NANOPARTICLES

Overview
Medical imaging has advanced from a marginal role in healthcare to becoming an essential tool of diagnostics over the last 25 years. Molecular imaging and image-guided therapy is now a basic tool for monitoring disease and in developing almost all the applications of in-vivo nanomedicine. Originally, imaging techniques could only detect changes in the appearance of tissues when the symptoms were relatively advanced.

Later, contrast agents were introduced to more easily identify and map the locus of disease. Today, through the application of nanotechnology, both imaging tools and marker / contrast agents are being dramatically refined towards the end goals of detecting disease as early as possible, eventually at the level of a single cell, and monitoring the effectiveness of therapy.

The convergence of nanotechnology and medical imaging opens the doors to a revolution in molecular imaging (also called nanoimaging\(^1\)), leading eventually to the detection of a single molecule or a single cell in a complex biological environment.

Diagnostics is possibly the area where nanotechnology advances are having the most immediate impact. This encompasses enhanced imaging techniques for early in situ characterization of injury and disease in patients; and array platforms for screening biomolecules to determine cellular differences between normal and diseased tissues.

One of the most exciting developments has been the incorporation of AFMs into array diagnostics. This allows direct detection of biomolecular interaction without a requirement for fluorescent labels and also increases information density some 10,000 fold over existing microarray technologies. In addition, with future generations of AFM based arrays there will be parallel detection through the use of multiple AFM tips in a single instrument. Advances in this area are not just restricted to two dimensions e.g. bar-coded nanoparticles and quantum dots offer solution based diagnostic systems. Many different types of nanoparticle have potential uses for enhanced imaging. For example fullerenes are being developed as contrast agents for MRI and X-rays, while perfluorocarbon nanoparticles are being developed for ultrasound.

For the number one killers, cancer and cardiovascular disease - earlier and more sensitive screening, novel, and more effective treatments will be available.

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\(^1\) This image represents nanoparticle formation in a TiCl\(_4\) combustion simulation. Spot sizes and colour on the heated-object scale represent the mean diameter of particles at a given point in space, while the diversity of sizes of these spots in a given area relates to the standard deviation of spot sizes. Photograph: Patrick Coleman Saunders, Sean C. Garrick, and Victoria Interrante, University of Minnesota.
Session Report

Olivier Le Dour

Assistant to the Director, Health Directorate, Directorate General for Research, European Commission

I co-chaired the ‘Nanoimaging and functionalized nanoparticles’, session, attended by ca. 100 participants. I informed the participants that, in this particular field, it is likely that funding for collaborative projects be available for FP7 under the Health, IST and Nanotech priorities. I also indicated under which headings or sub-headings they would probably have to apply.

Some interesting trends and some hurdles. The clustering process, at nanoparticle scale, and the coating process of these clusters seem to be, today, sufficiently mastered to ensure a good specificity and selectivity of the contrast agents or therapeutical agents (i.e. for targeted drug-delivery or localized radiotherapy). Both are sometimes combined, to significant advantage, into a single ‘theranostic’ agent. The main hurdles seem to remain in the safety/toxicology area and in terms of costs.

Another element of interest noted is the advantage of the nano-scale for some purely mechanical applications. Professor Uli Aebi, from University of Basel, illustrated this with the case of elasticity measurements on cartilage that make it possible, working at the 10nm scale, to show evidence of osteoarthritical degenerescence, whereas similar measurements using mere microscopic tools would not enable the differentiation between healthy or non-healthy cartilages at such an early stage.
NanoMedicine - Moving from the Bench to the Patient

Professor Ueli Aebi, Martin Stolz, and Peter Burkhard
Director, M E Müller Institute, Biozentrum, University of Basel, Switzerland

Now that nanotechnology has grown out of its infancy, its armamentarium of tools, methods and materials is ready for almost unlimited applications in biology and medicine[1]. Tools based on, for example, the scanning force microscope (SFM) are not just limited to improved imaging of living matter in its physiological environment, but they can also be customized to measure and manipulate matter at the level of single molecules, organelles and cells. Moreover, the SFM tip can be functionalized so as to serve as a biosensor for a broad range of molecular targets without having to amplify and/or label these.

Nanotubes, nanocontainers and other rationally designed nanostructures may be used for local, minimally invasive diagnostic and therapeutic interventions, or they may serve as the building blocks for novel implants and tissue repair materials exhibiting improved mechanical properties and biocompatibility.

As a first example, we will show how indentation-type (IT) SFM can evaluate the mechanical properties - e.g. the stiffness - of soft tissue such as, for example, articular cartilage[2]. Most significantly, we found that cartilage compressive stiffness is typically 100-fold lower at the nanometre scale compared to the overall structural stiffness measured at the micrometer or millimetre scale[3]. The prospects of these findings for developing an arthroscopic SFM for minimally invasive diagnostic interventions will be discussed[2].

As a second example, peptidic nanoparticles will be presented that self-assemble from de novo designed peptides into polyhedral capsids with diameters as small as 15nm. Their building blocks can be customized for antigen display, as radionuclide carriers, or for delivering substances, and they can be targeted to a receptor or cell surface marker.

(The presentation made at the conference is available on the Proceedings CDROM)

References
Radioactive Nanoclusters for Medical Applications

Professor Stéphane Lucas
LARN, University of Namur, Belgium

Nanotechnologies offer several opportunities for the synthesis of new carriers for effective drug delivery. During the last two decades, several research groups have explored the synthesis of nanoparticles linked to molecular vector with controlled rates of drug releases as well as specific affinity for cells in order to improve the therapeutic potential of drug delivery vehicles.

In connection with radioimmunotherapy (RAIT) and radioimmunodetection (RAID), research has been focused on bioconjugate including a radioactive nanoparticles chemically linked to a biological vector molecule. Radioactive beta-emitting isotopes of metal are often used in various modalities of RAIT and RAID in the form of conjugates with monoclonal antibodies. While widely and easily available, beta emitting radioisotopes like 32P or 90Y are not the best choice for therapeutic effectiveness: when the targeting vector is localized to the nucleus and is very close to the DNA, auger and alpha emitting radionuclide are the most appropriate. Indeed, because cancerous cells and tumour targeting are characteristically heterogeneous, the corresponding mono-radionuclide distribution produces heterogeneity in dose absorption.

This problem could be circumvented if several ‘radiation-different’ radionuclides could be chemically linked to the biological vectors. Therefore, short penetration and large penetration ionizing radiations may add their effects and improve the irradiation homogeneity. Attachment of the radioisotopes to the targeting molecule is probably the most important part of the preparation of the radioconjugate, but unfortunately little work has been conducted on the attachment of more than one type of radionuclides to the same molecule.

The on-going work is devoted to the synthesis of radioactive nanoclusters of few nanometres in diameter. These nanoclusters have a very high specific activity (they may content several hundreds of radioactive atoms) and may be coated with a biocompatible and functionalized material in order to be chemically bonded to a molecular vector (e.g. monoclonal antibody). When combined with vectors able to selectively target and interfere with neovascularization, it is useful in the diagnosis and treatment of angiogenesis related diseases like a large proportion of cancers.

The nanoparticles can be loaded with diagnostic radioisotopes, curative isotopes or magnetic material (all together) and improve the diagnostic and therapeutic effectiveness of RAIT or RAID. Indeed the proposed vehicles represent one of the few areas of pharmaceutical research in which the performance of a therapeutic strategy can be monitored at several stages of the development process.

The presentation developed the concept and presented the first results on the synthesis of such radioactive nanoclusters based on 103Pd for lung cancer applications.

(The presentation made at the conference is available on the Proceedings CDROM)
Microbubbles as Targeted Contrast Agents and Drug Delivery Systems  
Dr Andreas Briel  
Schering AG, Research Laboratories, Germany

One major challenge facing the pharmaceutical industry today is to develop contrast enhancing agents for molecular imaging. Classic contrast agents primarily document the anatomy. For pathophysiological examinations using differential diagnostic techniques, in other words, characterizing the development of a disease, they are only suitable to a limited degree. Molecular imaging selectively tracks down molecules and cell structures to be able to establish proof of diseases at a very early stage – and then to make decisions on a highly individual treatment.

The next straightforward vision of medical imaging quite clearly lies in the concept “Find, Fight and Follow.” In radiopharmaceuticals we are already pursuing the approach of a triad consisting of early diagnosis, therapy, and therapy control. Utilizing the nanotechnological concepts of colloid- and interface science imaging on a molecular level can also be achieved via diagnostic ultrasound using tiny gas-filled polymer particles coupled to target-specific ligands.[1,2,3].

Additionally, nanosized polymeric drug carriers for targeting and controlled release have been extensively studied in the past. Here, a nanoparticle or capsule acts like a container for a pharmacologically active agent. Passive and active targeting can be attained by carefully chosen size and surface modification of the carrier.

Drug release can be controlled via desorption of surface-bound drugs, diffusion through the particle matrix or the capsule wall or matrix erosion. Moreover, a ‘smart’ release can be achieved by using smart-polymers (pH- or temperature sensitive) or, more interestingly, by applying an external stress to the drug carrier. If the drug carrier is appropriately designed, release can be induced by diagnostic ultrasound[4].

Building a bridge between therapy and diagnosis opens the field of ‘Theranostics’. With a ‘Find, Fight and Follow’ strategy, the tissue of interest first can be imaged via target-specific ultrasound contrast particles. In a second step, the same particles, now filled with a pharmacologically active agent, can be used for therapy. Finally, monitoring of treatment effects is possible by sequential imaging.

This early approach demonstrates the success of a resolute implementation of nanotechnological concepts in a medical application and will be presented with special emphasis on polymer nanoparticle and microcapsule formation, the control of colloidal structure, surface modification and the resulting in-vitro properties as an ‘Ultrasound-Theranostic’. Investigations with different drugs and targeting sites demonstrate that the approach can serve as a platform technology. In-vivo results will be addressed briefly.
Nanoparticles in Future Medical Applications

Dr Werner Hoheisel

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In the detection of infectious diseases various methods of in-vitro diagnostics (IVD) are commonly applied for identifying antibodies or nucleic acid sequences. In order to improve parallelization and sensitivity of the detection procedures new technologies especially for biosensors or biochips are being developed and even self-confined lab-on-chip systems are currently in the pipelines of academic and industrial research groups.

Due to the small size of antibodies or nucleic acids, concepts based on nanotechnology are increasingly making sense in new developments. Applications in IVD are the first steps in establishing nanotechnology in medicine. Nanoparticles in in-vivo diagnostics as well as therapeutics will follow in all probability.

Detection systems often rely on fluorescent dyes as tags to specifically indicate the presence or absence of an antibody or virus in an extract of a patient’s blood sample. As a substitute for the commonly used organic dyes, fluorescent nanoparticle systems are being increasingly recognized as attractive due to their unbeatable light stability and multiplex capabilities. The latter is essential to parallelize diagnostic tests. Furthermore, fluorescent nanoparticles have the potential to revolutionize imaging applications since they allow multicolour imaging with long observation times.

Semiconductor nanocrystals (quantum dots), in which the emission wavelength can be controlled by adjusting the particle size, are favoured by many users due to their commercial availability and the experience many groups already have. Nevertheless, less toxic nanophosphors are gaining interest. These are nanoparticles doped with ions mostly of the lanthanides (e.g. Eu, Tb, Dy etc.) which serve as light emitters with a characteristic narrow banded emission pattern. The emission wavelengths do not depend on the particle size which simplifies the production allowing more cost-effective preparation procedures.

Nanoparticles are regarded as interesting labelling agents for many applications in diagnostics and therapy. However, whether the great expectations in nanoparticulate systems can be fulfilled has still to be demonstrated and most concepts have still to be put into practice.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)
Overview

Nanomedicine offers many benefits for healthcare in the future. It is a complex subject, and additionally suffers from many misconceptions about the potential of Nanotechnology for medicine, arising out of confusion between science fiction and fact, even amongst highly educated people. Considering governments and institutions the world over are spending many billions on nanotechnology research and development, a small amount of that funding would be beneficially channelled to wider public awareness and engagement.

Engaging the Public

As with any new technology, there are risks as well as benefits. Too frequently the downsides of an innovation are publicized, out of proportion to the benefits.

A survey carried out last year by researchers at the University of North Carolina established that the more people knew about nanotechnology, the more they thought the benefits would greatly outweigh the risks. The opposite was also true. This is a key point which indicates a well-informed public is likely to embrace nanotechnology and, whilst remaining wary of some of the risks, if they see it as bringing a major benefit to their lives.

This session aims at exploring how best to inform the public, so they can make reasoned and reasonable decisions, and what needs to be put in place to provide reassurance that potential risks are receiving the right level of attention and response.

Note: The UK Government is alive to the need for open debate, and commissioned the Royal Society and the Royal Academy of Engineering to investigate the potential benefits of Nanotechnology and the likely risks, and what if any actions should be taken regarding each.

A survey, commissioned as part of the above report, found that the public held both positive and negative views about nanotechnology. They were excited by the idea of new advances particularly in medicine and in the creation of new materials; they had a sense that the developments were part of natural progress; and had the hope that they would improve the quality of life. Concerns were expressed about financial implications; the impact on society; the reliability of new applications; long-term side effects and whether the technologies could be controlled. The issue of the governance of nanotechnologies was also raised, as to which institutions could be trusted to ensure that nanotechnologies would be socially beneficial. Comparisons were made with earlier issues with genetically modified organisms and nuclear power.
Based on the survey and a wide dialogue with many stakeholders, the RA / RAE report made several recommendations. These included a more sustained and extensive programme of research into public attitudes, a debate about the future of nanotechnologies should be undertaken now, to inform key decisions, and that there should be public dialogue around the development of nanotechnologies. It emphasized that governance would also be an appropriate subject for early dialogue.

The report is recommended to all who wish a wider understanding of the issues involved, an proposed action. It can be accessed at www.nanotech.org

At a recent ESF ‘Forward Look’ on Nanomedicine workshop in Strasbourg, communicating with the public was agreed to be the most significant activity, on which all others depended! Public perception can make or break the acceptance of a new technology, and is usually influenced by the mass media (the public do not have access to scientific publications to gain information first-hand). Newspapers make money out of sensational stories; and scientists are often guilty of under- or over-selling their research. Nanomedicine is a new concept for many people that requires care in communication. Benefits of nanomedicine need to be presented to the public, without over-hyping (smaller doses, targeted to the disease site etc.).

Session Report

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Background: the Risk Analysis Framework

Most reports and many published papers contain a glossary. This isn’t just to pad out the paper but it serves the vital purpose of ensuring that we are all using the same technical language. We cannot be like Humpty Dumpty in Lewis Carroll’s “Through the Looking Glass” (“When I use a word, it means just what I choose it to mean – neither more, nor less”). When a regulator or a scientist uses a word, it needs to be precisely defined and this definition has to be accepted by all stakeholders.

The Risk Labyrinth

The risk labyrinth has many overlapping components with strong feedback loops between them. The labyrinth of specializations includes assessment, management, communication, perception, and issue management. The components that we will focus on this afternoon are risk assessment, risk perception and risk communication. While these fields of study are clearly functionally distinct we must not forget that fact that they overlap and that there are feedback loops between them.
Risk Assessment

Risk is the chance that a particular Harm will result from a given exposure to a Hazard. Risk Assessment is the determination of the quantitative (or if necessary qualitative) relationship between exposure to a particular Hazard and the probability of realization of a particular Harm.

Uncertainty

What do we precisely mean by uncertainty in this context?

There are three basic types of uncertainty.

- The first being Uncertainty of Effect (remember Shakespeare’s King Richard III standing “the hazard of the die”). Will it happen or not when you throw the dice.

- The second type of uncertainty is the Uncertainty of Cause. In practice, there are a number of possible hazards that could result in a specified harm i.e. a number of [HH] pairs. Taking the example of smoking, there is no longer any serious argument against the link between lung cancer and smoking. However, it is (and it is likely to remain so) impossible to state with certainty that a particular case of lung cancer was caused by cigarette smoking (or by some other hazard or a combination of hazards). (Bayes’s theorem can be used to obtain the probabilities that Hz(i) is the most likely cause of the given harm.)

- The third type of uncertainty arises because we do not always have sufficient scientific knowledge about a postulated risk scenario or [HH] pair. It is epistemic uncertainty and is of particular concern to the regulator – giving rise to the Precautionary Principle. If we imagine the plane of all possible HH pairs this has three principle zones, namely, relationship known, relationship uncertain, and relationship unknown (or ignorance).

We should keep in mind that it may be impossible to test the hypothesis that there is a given HH relationship below certain hazard exposures (because of natural background exposure to the hazard under consideration, the large number of trials required to obtain statistically significant results, etc.).

Precautionary Principle (PP)

The facts that support the [HH] relationships will be uncertain to a greater or lesser degree. If the uncertainty is small, standard risk assessments are straightforward. Above a certain level of uncertainty, this becomes increasingly difficult. In these circumstances, the PP may be invoked in deciding on appropriate risk management actions. Thus the PP locks the RA and the RM together under uncertainty.

The problem is not so much the PP itself but the precautionary action (PA) which follows, i.e. the risk management decisions that ensue. The question of the possible misuse of the PP turns on whether or not the PA that entrains is appropriate for the given risk.
The Commission’s Communication on the PP sets out five principles by which all risk management actions should be judged including precautionary (risk management) actions:

- The PA should be proportional
- The PA should be non-discriminatory
- The PA should be consistent
- The PA should be based on an examination of the costs and benefits of action.

Thus, invoking the PP does not result in derogation from the general principles of risk management.

The fifth principle, namely that the PAs should be subject to review in the light of new scientific data, is the only principle that directly relates to the PP. It ensures that measures based on the PP should be maintained only so long as scientific information is incomplete or inconclusive. Thus the PA should include programmes to improve the science base.

Communicating this science base to all stakeholders, with all its attendant uncertainties, and how this science base feeds into the risk assessment and determines the risk management actions is a key responsibility for scientists and regulators.

**Discussion**

Communicating with the public is surely one of the most significant activities for nanotechnology, on which all others depend. This has been reiterated at other events (including the EC ‘Forum on Science in Society’). Several new EC-funded projects are investigating mechanisms for engaging the public and scientists including NanoDialogue and NanoLogue, and government initiatives (such as the Royal Society report commissioned by the UK government) have looked at public awareness of nanotechnologies.

Public perception can make or break the acceptance of a new technology, and is usually influenced by the mass media (the public do not have access to scientific publications to gain information first-hand). Newspapers make money out of sensational stories; and scientists are often guilty of under- or over-selling their research.

Nanomedicine is a new concept for many people that requires care in its communication. Benefits of nanomedicine need to be presented to the public, without over-hyping (smaller doses, targeted to the disease site etc.). The ENF2005 conference focuses on the near to mid-term benefits of nanotech and in addition to making the proceedings available to the wider public, the conference has held a public debate on day 1 and a session ‘NanoMedicine, Ethics, and Society’ on Day 4 devoted to engaging the wider community in the nanotechnology debate.
At least four important points arise from the papers that might stimulate further discussion:

- How do we inform/empower the public about the risks and benefits of advanced technologies such as nanomedicine without trivializing the issues?
- Where there is an asymmetry of risks and benefits (between research centres, companies and the public) how do you ensure good risk governance and avoid the so-called ‘GMO situation’?
- Where there is considerable hype in the media about the expected benefits, how do we manage the ethical debate?
- How to ensure that the uncertainties do not dominate the regulatory agenda and avoid the ‘zero risk’ regulatory distortion?

**The Debate**

- Communication with the public is very important, but is it possible to set some ‘limits’, i.e. how much shall we say before the general public ‘understands’ nanotechnology and the risks?

  There seems to be no way of having control on how a technology is perceived by the public, as it is very difficult to persuade the ‘average’ citizen with a new technology using scientific arguments, as the ‘average’ citizen shows different interests in general.

  On the other hand, it can also be very easy to manipulate the public and there are many ways for doing this. This can also be very dangerous.

  In particular, since it is the consumer who decides in the end, we should of course avoid repeating the case of the GMOs. There, as it is well known, the whole matter was clearly led by a small group of people which has led to a very unsatisfactory result.

- Would an ad-hoc legislation just solve the problem and would it inform the consumer whether a given ‘nano-product’ contains dangerous components or not? If so the consumer would be able to decide in an objective way.

  Apart from the fact that labelling is important and that there are already several nanotechnology products that we use in our daily life (such as skin creams containing nanoparticles), the majority of the consumers would probably not look at the labels.

  And apart from the fact that it would be again difficult to explain the meaning of a label stating “this product contains nanoparticles”, we should not forget that also several nanoscale processes themselves can indeed be dangerous, while many nanoparticles do result to be harmless.
Many of these processes have been used by chemists for ages. Such a ‘superficial’ labelling could result in errors and create confusion (as it has happened for some GMO products). In the specific case of nanotechnology, the labelling of products should be considered in a much deeper way if it is meant to help the consumer.

➢ In the controversial area of nanotechnology risk assessment, who can we trust?

One first thing to do is to gather information on risks and present such information considering all points of view. European studies such as NanoDialogue represent such an attempt and should enhance the dialogue at societal level.

➢ There are short-term risks and long-term risks. There is information on what could be a potential risk and what true risks are. We have to separate all these elements and inform the public accordingly.

➢ It is extremely important to communicate also the benefits of these new technologies, and not only concentrate all the effort on communicating risks. For instance, in the case of GMOs there were no perceived benefits, but nanotechnology will bring many benefits indeed.

➢ It is extremely important to take into account that there are several nanotechnologies, all different and just having in common the manipulation of matter at the nanoscale for different purposes. We should analyse separately these different technologies and the different processes involved (i.e. nanoparticles are only one aspect of nanotechnology). When talking about benefits and risks and communicating these, we should say which technology they refer to.

This conference has successfully attempted to address and communicate (in various ways and at different levels) both risks and benefits of nanomedicine.
Applied Nanoscience and Environmental Health and Safety

Professor David M Berube

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This paper reviews some of the major research in nano-toxicology and the environmental disposal of nanoparticles and the issues which remain to be resolved. It begins with a series of caveats and a brief summary of the relevance of toxicological research on natural and incidental nanoparticles to engineered nanoparticles, the relevance of research on small ultra-fine particles, esp. diesel exhaust on engineered nanoparticles, and the question of whether nanoparticles should characterized as new or existing for purposes of regulation. While concerns associated with the disposal of nanoparticles have received little attention, what research has been published is summarized as well (see Chapter 8, NANO-HYPE, (NY: Prometheus Books, 2005). A toxicological gap analysis is presented.

Principles of proof from a hard reading of the precautionary principles to laissez-faire are outlined. Regulatory regimes in the USA centre on three governmental agencies: the Environmental Protection Agency (EPA), the Food and Drug Administration (FDA) and the Occupational Safety and Health Administration (OSHA). Challenges confronting these agencies are detailed. Problems associated with public outrage and engendering public trust are reviewed against research findings. Heuristics and biases related to public communication of technical information are reviewed.

Finally, recommendations are offered regarding how to communicate nanoscience and nanotechnology risk information to a lay audience. The presentation concludes with a brief review of two research projects, intuitive toxicology and risk fatigue, both underway at USC’s NSF supported NSTS program.

(The presentation made at the conference is available on the Proceedings CDROM)

Innovation, Risk and Stakeholder Engagement: Framing Nanotechnology

Professor Joyce Tait and Robin Williams

Director, Innogen Centre, University of Edinburgh, UK

The explosive growth of interest in nanotechnology and its wide range of potential applications has highlighted its role as a potential ‘breakthrough’ technology, with the capacity to drive a cascade of changes in our scientific knowledge base, in industry structures and processes, and in outputs and how they are used, building on the previous breakthrough technologies, information technology and biotechnology. Advances in scientific understanding and technique are often conflated with applications and outcomes as if these were imminent and predictable.
A novel characteristic of these areas of innovation is the intense public interest generated at an early stage in their development and the attempt to exercise what we call compressed foresight (the attempt to look further into the future and map the technical and social outcomes in a higher level of detail than previously). Those developing the science and technology, and particularly those seeking funding to do so, tend towards utopian perspectives on the future while public potential ‘users’ of the technology often seek to oppose it, predicting apocalyptic risks.

The claim that “Nanotechnology will be the next GM” has focused attention on what we should learn from the GM crops experience in Europe that may be relevant to nanotechnology. This paper will question some of the resulting conclusions which seem to imply a rather simplistic understanding of the fundamental processes of innovation, risk analysis, and foresight, and their interaction with public and stakeholder perspectives:

- The expectation that we will be able to predict the losers in the technology race when we have so far spectacularly failed to predict the winners
- The idea that we can readily ‘read-off’ at the outset the technical outcomes and social implications of emerging technology developments despite experience that these are hard to predict and differ sharply from initial expectations
- The idea that nanotechnology represents a unitary set of technical capabilities with determinate technical and social consequences
- The assumption that there will be a unitary, uncontested public view
- The presumption that public and stakeholder engagement, the further upstream the better, can be expected to yield smoother and more rapid acceptance of new technology

We will also consider how social scientists contribute to these debates, in particular how discussions on the implications of emerging technologies are framed by and for policy makers and stakeholders, and the often hidden presumptions implied. It is common for a rather simplistic combination of so-called ethical, legal, and social impacts (ELSI) of technology to be an important part of this overall framing.

We will propose a new and more constructive approach for the social sciences in addressing both social and technical implications of nanotechnology, informed by historical experiences with earlier technologies including life science technologies.

(The presentation made at the conference is available on the Proceedings CDROM)
Nanologue: A Europe-Wide Dialogue on the Social, Ethical, and Legal Implications of Nanotechnologies

Dr Volker Türk
NanoLogue Project Co-ordinator, Wuppertal Institute, Germany

“Nanotechnology kills cancer cells” titles BBC News and goes on “Nanotechnology has been harnessed to kill cancer cells without harming healthy tissue”\(^1\). A second source claims that “Nanotechnology will have a significant impact on the future development of the German economy”\(^2\). Others seem to be more sceptical, asking if applying the merits of nanotechnologies in the food industry will be “the evolution of frankenfoods”\(^3\), or warning about the potential danger of nanoparticles by stripping at a high street with messages such as “expose the truth about nanotech” written on the bare back\(^4\).

The field of nanotechnologies has attracted widespread attention and funding in recent years. Estimate on the trade volume of NT-based products and applications vary widely, but are in the hundreds of billions of Dollars for the coming years\(^5\). Various products developed from multinational as well as small- and medium sized enterprises have already entered the market, and applications based on today’s basic research are expected by many to form the next industrial revolution. The unique properties of nanotechnological applications suggest potential to solve some of the worlds most pressing challenges, but they come with uncertainties and risks as all new technologies. Taking advantage of technological progress and preventing adverse side-effects and societal backlashes requires analysis, evaluation, and guidance to ensure technology is developed in ways that benefits the economy, wider society and the planet. Aiming at contributing to this goal, the Nanologue project has been set up.

The Nanologue Project

Nanologue brings together researchers, businesses, and civil society representatives from across Europe to support the dialogue on the societal implications of nanotechnologies. Funded by the European Commission, the project is driven by the need to understand ethical, legal and social aspects (ELSA), i.e. benefits and potential impacts, of nanotechnologies – and communicate this understanding by raising awareness and providing information to societal actors.

\(^1\) BBC News: Nanotechnology kills cancer cells. Available at: www.news.bbc.co.uk/1/hi/health/4734507.stm [2005, September 09]
\(^2\) Der Aktionär: Deutschland vor dem Aufschwung. 12 January 2005.
\(^3\) Alternet: The Evolution of Frankenfoods? Available at: www.alternet.org/envirohealth/23534/ [2005, September 09]
\(^4\) THONG. Available at: www.chicagothong.org/nanocommerce.html [2005, September 13].
Nanologue is led by the Wuppertal Institute (Germany) and conducted in cooperation with EMPA (Switzerland), Forum for the Future (UK) and triple innova (Germany). The project, which started in spring 2005 and will last until mid 2006, comprises three main phases, followed by an extensive dissemination phase:

- A mapping study on recent developments regarding selected nanotechnology applications and ELSA to lay a common ground for the subsequent discussions
- Moderated dialogue sessions for an inclusive and neutral platform for information and opinion exchange and discussion. Interviews with experts to substantiate findings and opinions
- Scenarios that translate the insights gained for easy communication on the potential implications of these emerging technologies

Results of the project will be disseminated by a variety of means, ranging from media workshops, a website and an online Nanotechnology Opportunities and Threats Checker, to a project pamphlet and conference attendances. So far (October 2005), the projects first phase has been finalized and phase two started. The following describes the approach taken and first project results.

**The Nanologue Approach**

From the outset, the Nanologue project intended to base the dialogue on specific nanotechnology applications rather than on ‘nanotechnology’ in general. In line with the European Commission’s strategy for nanotechnology, ‘Nanotechnology (NT)’ is understood as a collective term, encompassing the various branches of nanosciences and nanotechnologies.\(^1\) Instead of discussing the ethical, legal, or social aspects of such a broad area, a step-by-step approach has been chosen to narrow down the project’s scope.

At the beginning of the project, working definitions for nanotechnology, nanoscience\(^2\), and ELSA have been agreed on. It was decided not to focus on ELSA from a specific discipline’s approach, but to use ELSA as a proxy of all different kinds of opportunities and threats the applications of nanotechnologies can pose to society (see the next chapter for more details).

In a first step a mapping of current literature has been carried out to identify NT application areas of potential relevance for the project. The literature revealed a variety of categorization schemes for NT application areas, many of them with a smaller or larger overlap.

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With the aim of initiating a dialogue based on applications close to the market and with relevance to various ethical, legal and social aspects, the areas materials, medicine & life-sciences, electronics & ICT as well as energy were pre-selected as priority areas for the project. Within each NT application area, a multitude of specific NT applications was identified and listed.

In parallel, a first preliminary analysis of the ethical, legal, and social aspects of NT applications discussed in the literature was carried out. More than hundred nanoscience- and nanotechnologies-related publications (studies, project descriptions, articles and websites) were mapped in order to provide a first overview of the state of the art and the ongoing debate.

In a second step fifteen recently published overview reports related to NT were chosen for more detailed analysis. Aiming to get an overview of the current state of discussion as well as the different perceptions, views and positions held, a broad mix of reports was chosen. Finally, based on the findings and further in-depth research (desk research, expert interviews), three application areas for NT and a core set of the most relevant ELSA have been selected for more detailed investigation. The application areas selected are:

- Energy conversion and storage
- Food packaging
- Medical diagnostics

**Nanologue’s Understanding of ELSA**

As recent debates in the EU and elsewhere demonstrate developments in science and technology does not take place in a vacuum, uninfluenced by social and ethical concerns. On the contrary, various actors with different views are shaping the process. Broad discussions of issues such as reproductive technologies, agriculture biotechnology, and nuclear energy illustrate this point clearly. Against this background it seems very likely that some applications of NT will raise significant social, ethical, or legal concerns.

Whilst there is much excitement about the potential for NT to offer many benefits, such as increasing energy efficiency, better medical treatment, safer food, and lower costs for computing, some observers (stakeholders, scientists, media) have also expressed their concerns about possible risks associated with NT. This has resulted in a number of important questions about the future of the technology: What will society look like when nanotechnology becomes more mainstream? Will the products be profitable? Are there any negative environmental or health impacts? Who controls the use of NT? How to deal with liability? Whom will the technology benefit or harm? What are the ethical problems?
These ELSA related questions are not unique to NT. They have been discussed with varying levels of success in other areas of science-driven development of new technology (e.g. biotechnology, Human Genome Project). Having learned from these discussions, most NT exponents have realized that ELSA reflections should not be an adjunct to NT development, but an integral to it.1

But what exactly are the ethical, social, and legal aspects of NT? Engineers and scientists, social scientist, policy makers, regulators, business people, journalists, and science-fiction authors all seem to already have strong opinions about these aspects. Depending on the respective social group or scientific discipline engaged in the debate, different questions regarding the hopes and fears of NT are discussed.2 They vary from the “nanodivide” to human enhancement, from civil liberties to military use, from environmental and human impact to technological convergence.

Given this backdrop, the Nanologue consortium has decided not to focus on ELSA from a specific discipline approach, but to use ELSA as a proxy for all different kinds of opportunities and threats the applications of nanotechnologies can pose to the society. In an iterative procedure, based on literature analysis, expert interviews, and internal evaluations, the consortium partners selected a core set of seven ELSA as basis.

The selected ELSA are:

- Environmental performance
- Human health
- Privacy
- Access
- Acceptance
- Liability
- Regulation and control 3

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3 The consortium is aware of the ongoing debate on military usage of NT (dual-use), but it was considered that this is out of the scope for the project.
First Results
Where necessary, the three application areas selected for the project have been further narrowed down to specific applications. These are fuel cells, solar cells and batteries for the application area energy conversion and storage, and lab-on-a-chip as well as NT-based in-vivo cancer detection applications for medical diagnostics. For food packaging, several specific applications and materials have been looked at, amongst others self-cleaning surfaces, antimicrobial materials, and polymer nanocomposites.

Based on an extensive literature review and expert consultations, the relation between the application areas and the ELSA selected has been analysed. Some preliminary findings for the medical diagnostics area are presented in the following.

The health-sector is frequently mentioned as one of the most relevant and promising application areas for nanotechnologies. Regarding health aspects Farkas expects NT to be, “the key technology for the 21st century” and Wood et al claim that the “...medicine and health area of NT applications is seen as one of the most potentially valuable, with many expected benefits to humanity. Fields mentioned are implants and prosthetics, diagnostics and drug delivery.”

Within the medical field of medical diagnostics, methods and testing techniques for the analysis of molecular substances e.g. DNA and RNA are used to detect diseases or predispositions to diseases. There are several ways of analysing those substances with the aid of nanotechnologies. Lab-on-a-chip (LOC) has been chosen as example for the following discussion of ELSA.

Simply speaking, LOC represent a miniaturization of chemical instrumentation integrating a multitude of processes, e.g. sample preparation, verification of reaction data, and detection of reaction products on one device. Although LOC is currently largely a microfluidic device, it is commonly mentioned in connection with nanotechnologies, as nanoparticles are increasingly used for the detection of analyte molecules, and nanoscale structures can be found on the chip. Expectations for the future encompass further miniaturizations of the chip down to a nanoarray level.

The application of nanotechnologies in the health sector, in particular for diagnostic purpose, promises big potential to enhance human health, for example regarding hopes to extent life expectancy or to win the fight against cancer. Next, the opportunities for human health, other ethical, social or legal aspects are also discussed.

Concerns about the impact of new diagnostic devices on e.g. privacy may pose obstacles for the development of nanotechnologies. An overview on the potential ethical, legal, and social implications of NT-based diagnostic devices is a first step to take full advantage of the technology.

The following chart summarizes the main benefits and risks mentioned for LOC diagnostic devices. It needs to be stressed that the chart simply lists the most common risks and benefits found, which is why some might even contradict each other. As mentioned above, the listing is intended to serve as input for the next projects phases and is not a genuine result of the Nanologue project.

Next Steps
Results of the projects first phase described above are designed to prepare the ground for the subsequent interviews and workshops, which started in autumn 2005. The latest project results and further information can be found at www.nanologue.net

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)

Further information on the project’s first phase can be found at:
- Nanologue Mapping study. Summary of key findings from a literature study on ethical, legal, and social aspects of nanotechnologies. A joint publication of the Wuppertal Institute, EMPA, Forum for the Future and triple innova. Available at www.nanologue.net
- Nanologue Background Paper on selected nanotechnology applications and their ethical, legal and social implications. A joint publication of the Wuppertal Institute, EMPA, Forum for the Future and triple innova. Available at www.nanologue.net
Enhancing Dialogue on Nanotechnologies and Nanosciences in Society at the European Level: NanoDialogue

Dr Jennifer Palumbo
Science and Society Projects, Città della Scienza Science Centre Naples, Italy

- The project is coordinated by the Fondazione IDIS, an agile structure managing cultural and scientific projects and activities in Naples, Italy. The partners represent a wide European dimension and cover a variety of fields of activity (e.g. research, science communication, social participation)

- NanoDialogue aims to implement social dialogue between the research community, citizens and relevant social actors through the adaptation of participatory procedure methods to the project’s needs

- An exhibition module, a website and a rich program of activities for the public will be the means of spreading information on nanoscience research and applications, on one hand, and encouraging active participation and debate, on the other

- The first phase of the project, an ‘exhibition game’ based on methodologies for social participation, has been successfully carried out. Members of the partner institutions met with scientists, decision makers and relevant stakeholders to provide a thematic framework and a common communication strategy for the exhibition and connected activities

The NanoDialogue project, coordinated by the Fondazione IDIS, is carried out by a partner consortium representing a wide European dimension and including different organizations that cover a variety of fields of knowledge. NanoDialogue will establish an integrated process of communication and social debate on a European level in the field of nanosciences and nanotechnology, key issues in contemporary science with a potentially enormous impact on daily life, which are not yet well known to the public at large. The phases of the project include designing a website and an exhibition module with the aim of providing information and knowledge, while at the same time developing specific tools to collect feedback on citizens’ opinions and expectations.

The first step in the development of the project’s activities has already proven extremely successful: the basic vision for the exhibition modules, as well as the common communication strategy and a list of actual exhibits, was proposed in Naples during the ‘Exhibition Game Workshop’, where scientists, social scientists, science museum staff, designers and other experts exchanged their views by using a participatory procedure especially adapted from the Scenario Workshop methodology. The modules will be displayed in eight science centres across Europe (partners of the project), each of which will provide a rich program of debates, activities and workshops in order to engage the largest possible number of people in the discussion.
The following phases of the project include the actual design and production of the exhibition modules, the implementation of the website and tools to collect the public’s opinions and expectations on nanotechnology and nanosciences and a final conference bringing together top European experts in the field both of sciences and social sciences. Among the expected results of the NanoDialogue project are an improvement of communication and networking among experts and stakeholders and an enhancement of social learning and public debate in the general public and stakeholders. Furthermore, the analysis of data collected from the public’s views and expectations will lead to the production of a document of policy advice to be presented to European decision makers.

(The presentation made at the conference is available on the Proceedings CDROM)
SESSION 5B – AFFORDABLE CURES – ADDRESSING DISEASES OF THE DEVELOPING WORLD

Overview
Technological advances invariably exacerbate the divide between the rich and the poor. Can nanomedicine be the exception that proves the rule?

Malaria, HIV, and tuberculosis are the scourges of the less developed countries of the world. What hope does nanotechnology hold for early diagnosis and cheap and effective treatments for these pernicious diseases?

This session examines areas of opportunity where nanomedicine may make a real difference to the poor and disadvantaged in the developing world.

The Developing World
According to a study by the Canadian Program on Genomics and Global Health (CPGGH) at the University of Toronto Joint Centre for Bioethics (JCB) - a leading international medical ethics think-tank - nanotechnology may provide the means to help developing countries across a spectrum of areas including improvement in water quality, reduction in environmental and early diagnosis and treatment and even prevention of killer diseases such as malaria, tuberculosis and HIV/AIDS.

The Benefits of Nanotechnology to the Developing World
- Diagnosis of Disease
  About a quarter of all Africans are infected with AIDS. It kills millions each year and 95% of all new cases of AIDS occur in developing countries. Nano-based devices are leading to easy and fast analysis of a range of diseases that can be undertaken cheaply and easily

- Treatment of Disease
  Nanomedicine also has the potential to ensure longer shelf life for drugs, easier administration, and lower dosage requirements. New high throughput screening techniques are leading to cheaper drug discovery; and cell based assays should lead to faster introduction of these drugs into the population

- Sources of Disease
  Nanotechnology-enabled systems have application for water purification through membrane filters, which would have the knock-on effect of reducing infection

Apart from benefiting medicine directly, nanotechnology is also offering access to cheap renewable energy using new polymer based solar power collectors that are lightweight, cheap, and efficient.
Nanotechnology and the Developing World

Fabio Salamanca-Buentello, Deepa L Persad, Erin B Court, Douglas K Martin, Abdallah S Daar, and Peter A Singer

Canadian Program in Genomics and Global Health, University of Toronto Joint Centre for Bioethics, Canada. peter.singer@utoronto.ca

Nanotechnology can be harnessed to address some of the world’s most critical development problems. However, to our knowledge, there has been no systematic prioritization of applications of nanotechnology targeted toward these challenges faced by the 5 billion people living in the developing world. In this article, we aim to convey three key messages. First, we show that developing countries are already harnessing nanotechnology to address some of their most pressing needs. Second, we identify and rank the ten applications of nanotechnology most likely to benefit developing countries, and demonstrate that these applications can contribute to the attainment of the United Nations Millennium Development Goals (MDGs). Third, we propose a way for the international community to accelerate the use of these top nanotechnologies by less industrialized countries to meet critical sustainable development challenges.

Developing Countries Innovate in Nanotechnology

Several developing countries have launched nanotechnology initiatives in order to strengthen their capacity and sustain economic growth[1]. India’s Department of Science and Technology will invest $20m over the next 5 years (2004–2009) for their Nanomaterials Science and Technology Initiative[2].

Panacea Biotec (www.panacea-biotec.com/products/products.htm) (New Delhi, India) is conducting novel drug delivery research using mucoadhesive nanoparticles, and Dabur Research Foundation (Ghaziabad, India) is participating in Phase-1 clinical trials of nanoparticle delivery of the anti-cancer drug paclitaxel[3]. The number of nanotechnology patent applications from China ranks third in the world behind the United States and Japan[4]. In Brazil, the projected budget for nanoscience during the 2004–2007 period is about $25 million, and three institutes, four networks, and approximately 300 scientists are working in nanotechnology[5].

The South African Nanotechnology Initiative (www.sani.org.za) is a national network of academic researchers involved in areas such as nanophase catalysts, nanofiltration, nanowires, nanotubes, and quantum dots (Figure 1). Other developing countries, such as Thailand, the Philippines, Chile, Argentina, and Mexico, are also pursuing nanotechnology[1].

Figure 1. Quantum Dots for Disease Diagnostics
Quantum dots may be used for cheap, efficient handheld diagnostic devices available at point-of-care institutions in developing countries
Science and technology alone are not the answer to sustainable development challenges. Like any other science and technology waves, nanoscience and nanotechnology are not ‘silver bullets’ that will magically solve all the problems of developing countries; the social context of these countries must always be considered. Nevertheless, science and technology are a critical component of development[6]. The 2001 Human Development Report[7] of the UN Development Program clearly illustrates the important roles of science and technology in reducing mortality rates and improving life expectancy in the period 1960–1990, but it did not emphasize nanotechnology specifically. In a report released in early 2005[8], the UN Task Force on Science, Technology and Innovation (part of the process designed to assist UN agencies in achieving the UN MDGs) addresses the potential of nanotechnology for sustainable development.

**Top Ten Nanotechnologies Contributing to the MDGs**

In order to provide a systematic approach with which to address sustainable development issues in the developing world, we have identified and ranked the ten applications of nanotechnology most likely to benefit developing countries. We used a modified Delphi Method, as described in our Top Ten Biotechnologies report[9] to identify and prioritize the applications and to achieve consensus among the panellists.

We recruited an international panel of eighty five experts in nanotechnology who could provide the informed judgments that this study required, of which sixty three completed the project (Table S1). We selected the panellists based on contacts identified in our previous study on nanotechnology in developing countries[11]. A conscious effort was made to balance the panel with respect to gender, specialty areas within nanotechnology, and geographic distribution. Of the panellists, thirty eight (60%) were from developing countries and twenty five (40%) from developed countries; fifty one panellists (81%) were male and twelve (19%) were female.

We posed the following open-ended question: “Which do you think are the nanotechnologies most likely to benefit developing countries in the areas of water, agriculture, nutrition, health, energy, and the environment in the next 10 years?” These areas were identified in the 2002 UN Johannesburg Summit on Sustainable Development[10].

We asked the panellists to answer this question using the following criteria derived from our previous Top Ten Biotechnologies study.

- **Impact**
  
  How much difference will the technology make in improving water, agriculture, nutrition, health, energy, and the environment in developing countries?

- **Burden**
  
  Will it address the most pressing needs?
- Appropriateness
  Will it be affordable, robust, and adjustable to settings in developing countries, and will it be socially, culturally, and politically acceptable?

- Feasibility
  Can it realistically be developed and deployed in a time frame of ten years?

- Knowledge gap
  Does the technology advance quality of life by creating new knowledge?

- Indirect benefits
  Does it address issues such as capacity building and income generation that have indirect, positive effects on developing countries?

Three Delphi rounds were conducted using e-mail messages, faxes, and phone calls. In the first round, the panellists proposed examples of nanotechnologies in response to our study question. We analyzed and organized their answers according to common themes and generated a list of twenty distinct nanotechnology applications. This list was reviewed for face and content validity by two nanotechnologists external to the panel.

In the second Delphi round, the panellists ranked their top ten choices from the twenty applications provided and gave reasons for their choices. To analyze the data, we produced a summative point score for each application, ranked the list, and summarized the panellists’ reasons.

Then we redistributed the top thirteen applications, instead of the top ten, to generate a greater number of choices for increased accuracy in the last round. Thus, the highest score possible for an application was 819 (63 x 13).

The final Delphi round was devoted to consolidating consensus by re-ranking the top ten of the thirteen choices obtained in the previous round and to gathering concrete examples of each application from the panellists.

Our results, shown in Table 1, were compiled from January to July 2004. They display a high degree of consensus with regard to the top four applications: all of the panellists cited at least one of the top four applications in their personal top four rankings, with the majority citing at least three.
<table>
<thead>
<tr>
<th>Ranking (Score)</th>
<th>Applications of Nanotechnology</th>
<th>Examples</th>
<th>Comparison with the MDGs</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 (706)</td>
<td>Agricultural productivity enhancement</td>
<td>Nanoporous zeolites for slow-release and efficient dosage of water and fertilizers for plants, and of nutrients and drugs for livestock Nanocapsules for herbicide delivery Nanosensors for soil quality and for plant health monitoring Nanomagnets for removal of soil contaminants</td>
<td>I, IV, V, VII</td>
</tr>
<tr>
<td>3 (682)</td>
<td>Water treatment and remediation</td>
<td>Nanomembranes for water purification, desalination, and detoxification Nanosensors for the detection of contaminants and pathogens Nanoporous zeolites, nanoporous polymers, and attapulgite clays for water purification Magnetic nanoparticles for water treatment and remediation TiO2 nanoparticles for the catalytic degradation of water pollutants</td>
<td>I, IV, V, VII</td>
</tr>
<tr>
<td>4 (606)</td>
<td>Disease diagnosis and screening</td>
<td>Nanoliter systems (Lab-on-a-chip) Nanosensor arrays based on carbon nanotubes Quantum dots for disease diagnosis Magnetic nanoparticles as nanosensors Antibody-dendrimer conjugates for diagnosis of HIV-1 and cancer Nanowire and nanobelt nanosensors for disease diagnosis Nanoparticles as medical image enhancers</td>
<td>IV, V, VI</td>
</tr>
<tr>
<td>5 (558)</td>
<td>Drug delivery systems</td>
<td>Nanocapsules, liposomes, dendrimers, buckyballs, nanobiomagnets, and attapulgite clays for slow and sustained drug release systems</td>
<td>IV, V, VI</td>
</tr>
<tr>
<td>6 (472)</td>
<td>Food processing and storage</td>
<td>Nanocomposites for plastic film coatings used in food packaging Antimicrobial nanoemulsions for applications in decontamination of food equipment, packaging, or food Nanotechnology-based antigen detecting biosensors for identification of pathogen contamination</td>
<td>I, IV, V</td>
</tr>
<tr>
<td>7 (410)</td>
<td>Air pollution and remediation</td>
<td>TiO2 nanoparticle-based photocatalytic degradation of air pollutants in self-cleaning systems Nanocatalysts for more efficient, cheaper, and better-controlled catalytic converters Nanosensors for detection of toxic materials and leaks Gas separation nanodevices</td>
<td>IV, V, VII</td>
</tr>
<tr>
<td>8 (366)</td>
<td>Construction</td>
<td>Nanomolecular structures to make asphalt and concrete more robust to water seepage Heat-resistant nanomaterials to block ultraviolet and infrared radiation Nanomaterials for cheaper and durable housing, surfaces, coatings, glues, concrete, and heat and light exclusion Self-cleaning surfaces (e.g., windows, mirrors, toilets) with bioactive coatings</td>
<td>VII</td>
</tr>
<tr>
<td>9 (321)</td>
<td>Health monitoring</td>
<td>Nanotubes and nanoparticles for glucose, CO2, and cholesterol sensors and for in-situ monitoring of homeostasis</td>
<td>IV, V, VI</td>
</tr>
<tr>
<td>10 (258)</td>
<td>Vector and pest detection and control</td>
<td>Nanosensors for pest detection Nanoparticles for new pesticides, insecticides, and insect repellents</td>
<td>IV, V, VI</td>
</tr>
</tbody>
</table>

Table 1. Correlation between the Top Ten Applications of Nanotechnology for Developing Countries and the UN Millennium Development Goals

1 The maximum score an application could receive was 819.
To further assess the impact of nanotechnology on sustainable development, we have compared the top ten applications with the UN Millennium Development Goals (Table 1 and Figure 2). The MDGs are eight goals that aim to promote human development and encourage social and economic sustainability\(^\text{[11]}\). In 2000, all 189 member states of the UN committed to achieve the MDGs by 2015. The MDGs are:

(i) Eradicate extreme poverty and hunger
(ii) Achieve universal primary education
(iii) Promote gender equality and empower women
(iv) Reduce child mortality
(v) Improve maternal health
(vi) Combat HIV/AIDS, malaria, and other diseases
(vii) Ensure environmental sustainability
(viii) Develop a global partnership for development

As shown in Table 1 and Figure 2, the top ten nanotechnology applications can contribute to achieving the UN MDGs.

**Figure 2.** Comparison between the Millennium Development Goals and the Nanotechnologies most likely to Benefit Developing Countries in the 2004–2014 Period
**Addressing Global Challenges Using Nanotechnology**

What can the international community do to support the application of nanotechnology in developing countries? In 2002, the National Institutes of Health (NIH) conceptualized a roadmap for medical research to identify major opportunities and gaps in biomedical investigations. Nanomedicine is one of the areas of implementation that has been outlined to address this concern. Several of the applications of nanotechnology that we have identified in our study can aid the NIH in this process by targeting the areas of research that need to be addressed in order to combat some of the serious medical issues facing the developing world.

To expand on this idea, we propose an initiative, called “Addressing Global Challenges Using Nanotechnology,” to accelerate the use of nanotechnology to address critical sustainable development challenges. We model this proposal on the Foundation for the NIH/Bill and Melinda Gates Foundation’s Grand Challenges in Global Health\(^{12}\), which itself was based on Hilbert’s Grand Challenges in Mathematics.

A grand challenge is meant to direct investigators to seek a specific scientific or technological breakthrough that would overcome one or more bottlenecks in an imagined path to solving a significant development problem (or preferably, several)\(^{12}\). A scientific board similar to the one created for the Grand Challenges in Global Health, with strong representation of developing countries, will need to be established to provide guidance and oversee the program. The top ten nanotechnology applications identified in Table 1 area good starting point for defining the grand challenges.

The funding to address global challenges using nanotechnology could come from various sources, including national and international foundations, and from collaboration among nanotechnology initiatives in industrialized and developing countries. These funds could be significantly increased if industrialized nations adopted the target set in February 2004 by Paul Martin, Prime Minister of Canada: that 5% of Canada’s research and development investment be used to address developing world challenges\(^{13}\).

In parallel to the allocation of public funds, policies should provide incentives for the private sector to direct a portion of their research and development toward funding our initiative. The UN Commission on Private Sector and Development report *Unleashing Entrepreneurship: Making Business Work for the Poor*\(^{14}\) underscores the importance of partnerships with the private sector, especially the domestic private sectors in developing countries, in working to achieve the MDGs.

Perhaps most importantly, our results can provide guidance to the developing countries themselves to help target their growing initiatives in nanotechnology\(^{15}\). The goal is to use nanotechnology responsibly\(^{16}\) to generate real benefits for the five billion people in the developing world.

(The presentation made at the conference is available on the Proceedings CDROM)
Acknowledgments

We are grateful to our panellists for providing their expertise, and to W C W Chan and A Shik for help with our analysis of the nanotechnologies. Grant support was provided by the Canadian Program on Genomics and Global Health (supported by the Ontario Research and Development Challenge Fund, and by Genome Canada through the Ontario Genomics Institute (Toronto, Canada); matching partners can be found at www.geneticsethics.net ). EBC is supported by the Ontario Genomics Institute; DKM is supported by a Career Scientist award from the Ontario Ministry of Health and Long-Term Care; ASD is supported by the McLaughlin Centre for Molecular Medicine; PAS is supported by a Distinguished Investigator award from the Canadian Institutes of Health Research. The University of Toronto Joint Centre for Bioethics (Toronto, Canada) is a PAHO/ WHO Collaborating Centre for Bioethics.

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Citation


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Nanotechnologies: Delivering better Vaccines for Developing Countries?

Dr Thierry Coche
Associate Director, Head of New Technologies and Bioinformatics, GlaxoSmithKline Biologicals R&D, Belgium

Vaccines have proven to be one of the most efficient and cost-effective public health tools in our medical arsenal. Systematic vaccination has reduced the incidence and the burden of major diseases throughout the world.

In spite of this highly successful track record of vaccination, there is still much to be done: coverage of the human population is insufficient, particularly in developing countries, and new vaccines to protect against major killers such as AIDS, TB, and malaria are badly needed.

Developing vaccines for developing countries pose a number of specific challenges. People in these countries often have to travel long distances to be vaccinated and therefore reducing the number of doses required for immunization and ensuring long-term protection would be an advantage. Being able to vaccinate children just after they are born and when they are accessible to medical treatment would not only be more convenient but would also significantly improve their chances of survival. Maintaining the cold chain is difficult and costly in many of these countries, so vaccines that can be stored at room temperature are desirable. Delivery of vaccines by a convenient, needle-free system would reduce the need for specialized medical personnel and reduce the risk of infection and contamination. Finally, our ability to manufacture such vaccines at a competitive price would be essential for their success.

All these requirements pose formidable technological hurdles for vaccine development and manufacturing. Examples of how nanotechnologies can be envisaged to address some of the specific requirements imposed by vaccines for developing countries are presented.

(The presentation made at the conference is available on the Proceedings CDROM)
Evaluation of Nano Encapsulation Techniques in Different Polymeric System for the Delivery of Anti-Tuberculosis Drugs (ATD)

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TB is currently one of the leading causes of death in adults in South Africa. Annually approximately 250 000 new cases of tuberculosis (TB) occur in South Africa and it is ranked 8th amongst the top twenty two high burden countries of the world, which collectively accounts for over 80% of all TB cases[1]. A major reason for the escalation of the TB epidemic is the evolution of the AIDS epidemic.

It is estimated that approximately 85% of adult TB cases aged 15-49 years are HIV-infected. Approximately 1.7% of new cases are multi-drug resistant. It is predicted that there will be 3.5 million new cases of tuberculosis over the next decade, and at least 90 000 deaths. The World Health Organization Regional Committee for Africa has declared TB an emergency in the African region, at its 55th session in Maputo, Mozambique, in August 2005[2]. The epidemic has more than quadrupled the annual number of new TB cases in most African countries since 1990 and is continuing to rise across the continent, killing more than half a million people every year.

Despite the discovery of the TB bacillus in 1882, and that of anti-TB drugs since 1944, efforts to control TB globally have so far failed. Although an effective therapeutic regimen is available, patient non-compliance (because of the need of taking anti-TB drugs (ATD) daily or several times a week) results in treatment failure as well as the emergence of drug resistant strains of TB (MDR). This raises the cost of TB treatment 100 times more, and about 50% of these patients die.

The TB nano drug delivery study (TB NDDS) outlined in this report seeks to address patient non-compliance in TB control programmes through the development of a system whereby drugs can be administered in a single dose that maintains an active level of the drug (minimum inhibitory concentration – MIC) for a number of weeks. It is envisaged that this will be achieved by nano-encapsulating traditional TB drugs and new ones which have very poor bioavailability and some with higher toxicity, using biodegradable polymers that will allow slow, steady release of the drugs. Biodegradable polymeric nanoparticles have been intensively evaluated as delivery systems for pharmacologically active substances such as low molecular weight and macromolecular therapeutics.
Considered for oral, nasal, intravenous or pulmonary administration, they are capable of providing sustained and controlled release of the encapsulated material at a target site while protecting the encapsulated agent from degradation and physiological clearance by macrophages\cite{3-6}; hence they are being explored in this drug delivery approach.

Numerous studies have been carried out on the design of nano and microparticles loaded with anti-tuberculosis drugs (ATD). However, fewer findings relating to the incorporation of these drugs into the alginate/chitosan-based nanoparticles have been published\cite{7}. Pandey et al reported the successful formulation of ATD encapsulates in poly[D,L-lactic-co-glycolic acid] PLGA. A subset of TB infected mice were treated with the formulation which was administered orally every 10th day. No tubercle bacilli, was detected in these mice after five doses\cite{8}. These reports thus form the basis for the feasibility as well as efficacy of this polymeric drug delivery strategy. Alginate/chitosan system is very attractive as compared to PLGA system because it is cheaper, more muco-adhesive that PLGA and is a natural polymer\cite{9}.

The eventual objective of the TB nano drug delivery project is, therefore, to develop a polymeric TB nano drug delivery system in South Africa that will significantly contribute to the saving of lives, while simultaneously reducing the enormous pressures on scarce national healthcare resources.

The specific aim of the work presented here is to investigate and to compare the preparation of nanoparticles fabricated from two different biodegradable polymeric systems namely: PLGA (50:50) and the polyionic complex alginate-chitosan, as potential anti-tuberculosis drug carriers. For the PLGA system we investigated parameters, such as type of solvent, different concentration of surfactant and different equipment used for making the emulsion. In case of Alginate/chitosan system the parameters analysed were, CaCl$_2$: alginate and Chitosan: alginate ratios as well as the type of equipment used to prepare the emulsion. These parameters have been reported to have a profound effect on the physico-chemical properties of the synthesized nanoparticles\cite{9} and will therefore ultimately influence the size of the tablets, release profiles and shed light to understanding the mechanism of the TB NDD system.

**Methods**

The double emulsion water-in-oil-in-water (W/O/W) technique was used for formulating PLGA nanoparticles. The drug loading and the particle size of PLGA nanoparticles were optimized by varying the concentration (from 1 to 3%) of the emulsifier, PVA, in the external aqueous phase, the technique to prepare the emulsion (sonicator or high-speed homogenizer) as well as varying the type of solvent used.

The preparation of alginate-chitosan-based nanoparticles was performed by a two-step ionic gelation technique. Changing CaCl$_2$: alginate and Chitosan: alginate ratios keeping alginate constant. In both cases emulsification reactors (sonicator or high-speed homogenizer) allowed the modulation of the size of nanoparticles made with alginate-chitosan complex.
Results and Discussion
The size and the morphology of nanoparticles were easily affected by a variety of processing factors such as those indicated above for both PLGA and Chitosan/alginate systems. For the preparation of PLGA nanoparticles, the increase of the emulsifier concentration led to a decrease in the size of the particles. This fact was very pronounced when sonication was used as the emulsification mode, where the size dropped from 190 to 140nm upon an increase of the concentration of PVA.

The highest encapsulation efficiency achieved was only (33%) with the PLGA system. This may be due to the high solubility of the drug (INH) in water. The organic solvent ethyl acetate revealed its capacity to produce a smaller particle size with a very narrow size distribution while using either a high speed homogenizer or sonicator. In addition, the encapsulation efficiency of the drug was relatively high. While for the alginate/chitosan system, a minimum size of 392nm was observed corresponding to the Chitosan: alginate ratio of 0.08.

At this stage, the encapsulation efficiency of the alginate/chitosan system has not been determined. The sonication process yielded nanoparticles with smaller particle size (392nm) than the mechanical homogenization. Controlling the size of nanoparticles is very important since; size affects the degradation rate, loading capacity and initial burst release of nanoparticles and release profiles. In conclusion, we were able to synthesize nanoparticles for both systems as illustrated in Figure 1A and B.

Figure 1. SEM photos of nanoparticles loaded with anti-TB drug. A= PLGA, B = A chitosan-alginate
However, the natural polymers (chitosan-alginate) presented more challenges. Therefore, further work needs to be performed to ensure an acceptable yield from the precipitation of the chitosan/alginate system. Based on the results of this study it appears that the mode of emulsification and the concentration of the stabilizer have a non-negligible effect on the size and the encapsulation efficiency when loading a drug into polymeric nanoparticles.

This technology is not only limited to TB drug delivery but once optimized it can be used for any drugs. Our long-term objective is to deliver anti retrovirus for HIV/AIDS patients, antibiotics as well as anti malaria drugs with this technique. Since these infectious diseases have led to the high death rate observed in Africa, it is envisaged that economic and health relief will be obtained with the new drug delivery approach.

Nanotechnology for drug delivery offers a suitable means of delivering small molecular weight drug as well as macromolecules such as proteins peptides or gene. With Nanotechnology we are closer than ever in reaching the long cherished goal of precise delivery of drug to a specific compartment in the target cell via intracellular and para cellular delivery.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)

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References

A Review of Current Trends in Technological Development

Vladimir Kozharnovich
United Nations Industrial Development Organization, Uganda

Recent and continuing advances in the life sciences are making a reality of the prediction that this will be the century of biotechnology in convergence with nanotechnology and ICT. They will transform the way a whole host of products are designed, manufactured, and used. Such transformation of industry on the basis of continuing diffusion of nanotechnology, new materials, new applications of biotechnology and information technology, will be at the crest of the wave. Their application could provide significant opportunities for sustainable growth in both developed and developing countries.

While nanotechnology in the health sector promises to offer relatively cheap diagnostic and treatment or water filtration techniques it highlights a key issue of how the innovation agenda can be effectively shaped to meet the needs of the poorest sectors of society. Currently, a wide range of R&D activities are maturing at a remarkably rapid pace: healthcare technologies drawing on nano-processing technologies, genetics, genomics, and proteomics that promise better health outcomes and more sustainable and higher value-added food. The development and diffusion of new gene-engineered technologies and nanotechnologies in medicines and management practice are already revolutionizing the industrial landscape in the developed world and have practical application in the developing countries. Practically, medicine biotechnology creates conditions for the development and production of renewable substances and medicines vital for all mankind.

Indeed the main thrust of R&D in these emerging technologies was likely to focus on the development of gene-engineering and cell industrial technologies for production of medicines for human and veterinary needs; production of bioactive food additives; protection of plants and environmentally sound technologies for waste management. All these areas have impact on health. Some of the nanotechnology applications in this area will be inexpensive and rapid diagnostics, new methods of drug delivery, and faster development of new drugs.

Today, the majority of countries have made healthcare programmes a priority in their plans and strategies for socio-economic development, sustained growth and security of the health of a nation. Therefore, supporting emerging and developing country health challenges through applications of new technology is important. Recently, UNIDO has designed and implemented an initial project, related to the health sector, within the frame of its large programme on establishment and operation of International Technology Centres as a mechanism for promotion of technological advances and fostering international cooperation.
In particular, the pilot phase of the International Centre of Medicine Biotechnology (ICMB) has established an institutional framework, which would act as a global focal point for developing countries in the field of medicine biotechnology by tracking the latest worldwide developments in leading-edge technologies and bridging the gap between the emerging market demands for new medicines and the existing technology base. Its main objective was to transform the existing knowledge and expertise into concrete industrial products enabling to solve the health problems and build up relevant technological and human capacity. This concept has proven its value through implementation of concrete technology transfer projects.

Experience has shown that to work with bio(nano)materials and substances at the gene and molecular levels about 8-10 years are required for a specialist and technician to be well qualified for carrying out research and look after the production processes at the nano-scale. However there is serious lack of schools and training materials and standardized international certificates following the completion of training courses. Therefore there is an imperative need to support efforts for building in-house research and production capacities in the emerging and developing countries themselves.

Furthermore European countries could assist in a special way by contributing to evaluation of the new technologies and their applicability in the context of developing economies. Hence UNIDO proposes the establishment of an international framework that would allow the developing countries, to evaluate the benefits of new technologies, taking into account a balance between the risks and benefits of nanotechnology research and what it would take to engage in full production.

Finally, strong legal framework, including system of intellectual property rights (IPR), should be established in support of ongoing and future developments in the nanotechnology area and their transfer, commercialization and application in other countries. All these measures and support would enable the researchers and industry in the developing and emerging economies to better interact with their counterparts in the industrialized world and help achieve almost all of the Millennium Development Goals (MDGs), which many governments have committed themselves to achieving by 2015 in the area of health.

(The presentation made at the conference is available on the Proceedings CDROM)
SESSION 5C – IMPACTING SOCIETY – NEEDS OF THE AGEING POPULATION

Overview

Nanotechnology could finally mean that growing old does not necessarily mean loss of faculties and a rapid reduction in quality of life.

Nanotechnology is supporting the rehabilitation of the infirm and elderly through the development of intelligent learning prosthetic devices. These include retinal and cochlear implants. Through the development of nanocomposites, nanoelectronics, nanosensors, nanotransducers and biomaterials, the next generation of implants will be more effective, body friendly and less traumatic to insert. They will reinvigorate the faculties of patients whose hearing or sight has been affected by accident, disease, or age.

Organ replacement is increasingly common across the generations. Transplantation is fraught with dangers such as rejection and side effects from drugs. As discussed under Tissue Engineering, research is leading to the growth of new organs from a patient’s own tissues. The ultimate objective is to produce innovative scaffold materials which can be seeded with the patient’s own cells, which, when implanted will regenerate bone, cartilage and skin tissues in the most natural way possible. Medical textiles are an exciting field of innovation. ‘Smart clothes’ are being developed which will regulate temperature and even monitor the health of the wearer.

This remarkable new technology poses even more questions regarding ethics – the ethics of who should benefit, if there is a choice to be made, where the line should be drawn, if any, at enhancing human performance (especially in relation to military and sports applications), and whether new technology will lead to a further widening of the gap between rich and poor, advantaged and disadvantaged.

Many techniques for combating congenital and degenerative and lifestyle diseases such as cancer can be found throughout the programme. For example, nanotechnology is leading to new ways of approaching gene therapy through novel delivery mechanisms such as designer vectors that have potentially much fewer side effects. Stem cells are being grown to differentiate and replace diseased tissues and take over the function of atrophied glands. Nanotechnology is leading to implants which can monitor blood sugar levels and automatically respond to varying insulin needs during 24 hours, and can also aid in screening for possible appetite suppressants and other therapies for the obese.

Targeted drug delivery is important for the treatment of cancers, as well as some novel magnetic nanoparticulate therapies which lead to the non-toxic dissolution of cancers. Imaging is also key in identifying cancers at the earliest stage; the aim is at the level of only a few diseased cells.
New Highly Efficient Non-invasive Nanoparticulate Delivery Systems for the Treatment of Chronic Diseases

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Abstract
We herein report the overall goals of the joint research project ‘Nano-Health’, which was positive evaluated by international reviewers within the first call of the Austrian Nano Initiative. Furthermore, we report preliminary results of two subprojects within the joint research project Nano-Health.

Nano-Health, which consists of nine single projects, aims to develop new multifunctional nanoparticles for the non-invasive targeted delivery of active substances for the treatment of chronic diseases like morbus Alzheimer and diabetes by different application routes, e.g. nasal, oral, and pulmonary. Furthermore, nanoparticles for a targeted release of magnetic resonance imaging contrast media for use in clinical diagnostics and therapeutics will be developed.

Keywords: nanoparticle, drug delivery, targeted drug delivery, chronic diseases, MRI

Introduction
Significance of Nanoparticles for Drug Therapy
In recent years, significant effort has been devoted to develop nanotechnology for drug delivery since it offers a suitable means of delivering small molecular drugs, as well as macromolecules such as proteins, peptides, or genes by either localized or targeted delivery to the tissue of interest. Nanotechnology focuses on formulating therapeutics in biocompatible nanocomposites such as nanoparticles, nanocapsules, micellar systems, and conjugates.

Nanoparticles are submicron-sized polymeric colloidal particles with a therapeutic agent of interest encapsulated within their polymeric matrix or adsorbed or conjugated onto the surface. Since these systems are polymeric and submicron in size, they have multifaceted advantages in drug delivery. These systems in general can be used to provide targeted (cellular / tissue) delivery of drugs, to improve oral bioavailability, to sustain drug/gene effect in target tissue, to solubilize drugs for intravascular delivery, and to improve the stability of therapeutic agents against enzymatic degradation (nucleases and proteases), especially of protein, peptide, and nucleic acids drugs.

The size-ranges of these delivery systems offer certain distinct advantages for drug delivery. Due to their subcellular and sub-micron size, nanoparticles can penetrate deep into tissues through fine capillaries, cross the fenestration present in the lining (e.g. liver), and are generally taken efficiently by the cells. This allows efficient delivery of therapeutic agents to target sites in the body.
Also, by modulating polymer characteristics one can control the release of a therapeutic agent from nanoparticles to achieve the desired therapeutic level in the target tissue for required duration for optimal therapeutic efficacy.

Furthermore, nanoparticles can be delivered to distant target sites either by localized delivery using a catheter-based approach with a minimal invasive procedure or they can be conjugated to a biospecific ligand which could direct them to the target tissue or organ\(^{[1,2]}\).

**Nanoparticles Derived from Synthetic-Polymers**

Up to now nanoparticles have been manufactured from a huge variety of materials. Reviews upon this issue were published frequently\(^{[1,3-5]}\). A majority of preparations have dealt with the nanoparticles of polylactide, poly(lactic acid) PLA, poly(glycolide) PLG, poly(lactideco-glycolide), PLGA, and poly(alcyl-cyanoacrylate) PACA.

Other synthetic polymers such like polymethylmethacrylate (PMMA), poly(epsilon)caprolacton, polyamide, polyphthalamide, polystyrene were used less frequently. New polymers such as thiomers or thiolated acrylates are potential materials with increased mucoadhesive properties and will be interesting drug delivery carriers for the future\(^{[6,7]}\).

**Nanoparticles Derived from Biopolymers**

In addition to synthetic polymers which have several advantages in comparison to natural biopolymers, such as defined chemical structure and higher purity, biopolymers from natural sources are also attractive excipients for pharmaceutical preparation.

Nanoparticles have been prepared from a huge variety of biopolymers for about 30 years. Bovine serum albumin (BSA) and later the human serum albumin (HSA) are the oldest biopolymers used first for microparticles and later also for nanoparticles.

Gelatine, a widely used substance in food und drug industry, was also investigated for nanoparticle preparations. Sodium alginate was more often used for larger particles and for microcapsules. It has a very good biocompatibility leading to special applications such like the encapsulation of total cells. Chitosan, recently reviewed in a special issue of the European Journal of Pharmaceutics and Biopharmaceutics (Vol. 57,1), has a large potential in pharmaceutical industry. So far it was used as tableting excipient; however, newer applications focus on nanoparticles used for DNA and protein drug delivery\(^{[1,3,8-10]}\).

One of the oldest and most studied biopolymers for controlled drug release is protamine, a polycationic peptide with a mass of approximately 4,000–6,000 Dalton. Studies on protamine started in the year 1868 by Friedrich Mierscher\(^{[15]}\). A long period of research work was necessary to characterize this group of arginine rich, strongly basic, aliphatic peptides present in the sperm cell nuclei of fish. However, already in 1936 Hans Christian Hagedorn developed the first particulate slow release drug delivery system for insulin based on protamine. This NPH insulin particle suspension was optimized over the years and became the most frequently used long-term insulin.
Nanoparticles prepared from protamine were first invented by the group of Zimmer and will be part of the present grant application\cite{12,13}. These nanoparticles, so called proticles (Protamine-Oligonucleotide-Particles) are now applied from different groups to deliver oligonucleotides into mammalian cells\cite{14-19}. Recent developments have also shown the potential of these nanoparticles as drug delivery systems for proteins.

**Liposomal and Lipid-Based Nanoparticles**

The potential pharmaceutical use of liposomes as biocompatible and biodegradable carriers for small molecules, peptides, proteins, or DNA has been extensively studied over the past few decades. Improved pharmacological properties, enhanced safety, and increased efficacy have been achieved for liposomal carriers compared to conventional formulations, in particular for applications in cancer chemotherapy, antimicrobial therapy and vaccination. Only recently, several liposomal drug formulations have been approved for clinical use and are now on the market.

Liposomes, in general phospholipid vesicles, are self-assembling, nanoscopic arrangements of one or more lipid bilayers surrounding a hydrophilic environment. Vesicles can be made in different sizes, compositions, surface charges, or bilayer fluidities and can easily be manipulated.

In combination with co-additives, ligands or by surface coating vesicles offer attractive possibilities to entrap drugs of different lipophilicity, either in the hydrophilic core or in the lipophilic lipid shell, or alternatively, drugs or targeting ligands can be coupled to the surface. This enormous versatility enables a rational design of lipid-based nanoparticles (\textasciitilde{}50nm to 500nm diameter) with respect to the target and to the route of administration.

Due to the unique phospholipid shell structure providing a barrier, vesicles are efficient delivery vehicles for drugs, which would otherwise undergo proteolytic degradation in the biological milieu upon administration. Moreover, liposomal encapsulation reduces toxicity of drugs, while retaining or augmenting the therapeutical efficacy of the drug. In addition, by construction of tailor-made vesicles a sustained, slow drug release combined with a reduction of systemic side effects and target specificity can be achieved. Given the success of liposomal drug formulations currently available, more breakthroughs can be expected for the future\cite{20-23}. Further, lipid based nanoparticles are currently under development. Due to a high pharmaceutical stability solid lipid nanoparticles (SLN), which have similar properties compared to liposomes, are most promising. However, they exhibit a solid lipid core and therefore can not encapsulate a water compartment with dissolved hydrophilic drugs\cite{24, 25}.

The most sophisticated but also most complicated lipid based nanoparticles are lipoproteins such like LDL and HDL. These carriers, so far used only in experimental medicine, are one of the natural nanoparticles of our own body which deliver lipids, drugs and other substances to specific targets for receptor mediated uptake\cite{22}.
Joint Research Project ‘Nano-Health’

Goals
The main objective of this project is the development of new concepts in design and application of nanoparticles for drug, peptide, and protein delivery. The novelty of the approach relies on the encapsulation or trapping of modified therapeutic agents in nanoparticles, which are designed on the basis of current knowledge of formulation, but imply distinct variations in composition, surface charge, hydrophobicity, size, and shape. By the use of such ‘custom-made’ nanocarriers for peptide and protein delivery, a significant improvement in the efficiency of organ-specific targeting i.e. brain and lung by alternative administration routes i.e. nasal, pulmonary, and oral is aimed at. Depending on the therapeutical agent to be delivered, a reduction in degradation propensity, toxicity, application rate, or achievements concerning sustained release, enhanced efficiency and bioavailability are envisaged goals of the project.

The approach to design appropriate vesicular nanoparticles will be complemented by a comprehensive structural analysis of loaded and unloaded nanoparticles by different biophysical techniques, including light scattering, X-ray small angle scattering, MRI, zeta potential measurements, light microscopy, and calorimetry. Likewise, cell and tissue culture studies up to animal models on uptake, biological activity, distribution of and cellular response to the various drugs tested will be performed.

As a future perspective, the knowledge gained on the biophysical, biological, and cellular behaviour of special triggered drug formulations, might easily be transformed and adapted to other related substances.

Overall Approach
The development of potent formulations for non-invasive peptide delivery represents one of the main challenges in modern pharmaceutical technology. Today most of these extraordinary pharmacological potential therapeutic agents have to be administered via parenteral routes, which are inconvenient because of pain, fear and risks being associated with this type of application.

‘Injectable-to-non-invasive-conversions’ and in particular ‘injectable-to-oral-conversions’ are consequently highly in demand. In order to provide a sufficient high bioavailability with non-invasive peptide delivery systems, however, various hurdles have to be overcome. They include the diffusion barrier being based on the mucus gel layer covering mucosal membranes, which has to be passed by peptides in order to reach the absorption membrane[26], and the enzymatic barrier being represented by secreted and membrane bound peptidases[27]. Moreover, having reached the absorption membrane in intact form therapeutic peptides have to permeate this membrane barrier in order to reach the systemic circulation[28].
Pharmaceutical technological attempts to overcome these barriers include the use of enzyme inhibitors\cite{27}, permeation enhancers\cite{29} and multifunctional polymers ideally guaranteeing both enzyme inhibition and permeation enhancement\cite{30}.

In case of multifunctional polymers these effects, however, can only take place if a tight contact of the polymer with the mucosa is provided for the whole period of peptide drug release and absorption. Apart from enzyme inhibitory and permeation enhancing properties multifunctional polymers should therefore offer also strong mucoadhesive features.

The very slow progress in the efficacy of the treatment of severe diseases has suggested a growing need for a multidisciplinary approach to the delivery of therapeutics to targets in tissues. Chronic diseases like diabetes, Alzheimer’s disease, and chronic obstructive pulmonary disease are priority diseases to be addressed for the development of new treatments and drug delivery systems\cite{31}.

One way to improve the delivery of drugs are nanoparticles. The benefit of nanoparticles as highly potent drug delivery systems is generally accepted and documented in numerous multicenter randomized clinical trials. Today, however, the full potential of nanoparticles in drug delivery has not been reached by far.

By optimization of three different nanoparticle technologies (proticles, thiomers and lipo-based) and by combining them new innovative types of nanoparticles will be generated. These multifunctional nanoparticles will be used for the non-invasive administration of therapeutic and diagnostic agents via the nasal, oral and pulmonary route and as a depot formulation for the long term treatment of specific organs e.g. lung and brain.

These formulations will be tested in various biological models (cell and tissue culture, membrane and animal models and subsequently in humans).

These nanoparticles will be used for the delivery of insulin and calcitonin via the oral route, hGH and amyloid binding peptide via the nasal route and vasoactive intestinal peptide (VIP) via the pulmonary route. Nanoparticles delivering insulin and calcitonin will target the intestine by using the enhanced mucoadhesive and permeation properties of thiomer particles. The nasal route will be addressed by using small lipid based nanoparticles and thiomers. Pulmonary delivery will employ small unilamellar vesicles, proticles, and thiomer technologies to deliver VIP into the deep lung.

An overview of the envisaged concept of Nano-Health is given in Figure 1.
**Preliminary Results**

First results of this project already showed that the intestinal and nasal residence time of thiomers particles is significantly prolonged in comparison to state-of-the-art particles, as the thiol substructures of thiomers particles are capable of forming disulfide bonds with cysteine-rich subdomains of mucus glycoproteins. Due to this prolonged and intimate contact of thiomers with the mucosa a pharmacological efficacy of 7% could already be reached for orally administered insulin in diabetic mice and a relative bioavailability of 8% for nasally administered hGH in rats.

Vasoactive intestinal peptide is a potential new drug to treat severe lung diseases like primary pulmonary hypertension, (PPH) an orphan disease. PPH is a fatal disease causing progressive right heart failure within 3 years after diagnosis. Consequently, the substitution therapy with the hormone, administered three times per day as a single dose inhalation, results in substantial improvement of hemodynamic and prognostic parameters of the disease without side effects.

VIP has already passed phase I and II clinical trials for PPH. The main goal of this project is now to develop new and innovative depot formulations for the non-invasive pulmonary administration by use of nanoparticulate carriers to reach the deep lung for long term treatment with improved bioavailability and biostability.

(The presentation made at the conference is available on the Proceedings CDROM)
References

Deep Brain Stimulation for Movement Disorders and Pain

Professor Tipu Aziz

Nuffield Department of Surgery, University of Oxford, UK

Although as a concept deep brain stimulation was about in the 1960’s the technology did not mature until the mid 1980’s. It was established that implanting electrodes in the thalamus could control tremor by high frequency stimulation, thought to cause a depolarization block of the neurones. It has now been shown to be effective in Parkinson’s disease when implanted in the subthalamic nucleus; thalamic targets are effective for tremors and pain, and the periventricular area for pain. Pain stimulation parameters are different to those for movement disorders, being applied at a much lower frequency and presumably driving the region. More recently a new target, the Pedunculopontine nucleus, has been shown in primates to be effective in alleviating the slowness of drug-resistant Parkinsonism.

A drawback of the technology has been that continuous stimulation is part of the course in movement disorders and in some conditions very high voltages may be required. The batteries can run out in 12 months and require surgical replacement at phenomenal cost despite often miraculous effects. Thus deep brain stimulation is limited by what costs a health service can tolerate. We implant the deep brain electrodes and externalize them in our patients to confirm efficacy. This has given us a unique opportunity to record field potentials and correlate them with EMGs recorded from muscles.

We have found that there are significant changes in the field potential prior to bursts of tremor. We present these findings and speculate that an intelligent sensor could deliver pulses of current as required when changes predicting tremor are recorded. Thus stimulation frequencies could be dropped from 180Hz to 5-7Hz. This would reduce power consumption dramatically and would make such therapies economically viable.

(The presentation made at the conference is available on the Proceedings CDROM)

Bio-engineered Meniscus Substitute: Community Added Value

Dr Enrico Tognana

Fidia Advanced Biopolymers, Italy

Every year in Europe, about 400 000 people undergo treatment for injuries to the knee meniscus. Each knee has two menisci – fibro-cartilaginous pads resting side by side between the top of the larger lower leg bone (tibia) and the end of the thigh bone (femur). Providing cushioning and helping articulation of the knee joint, they are frequently damaged, especially by sports injuries. Although torn menisci can be repaired surgically and will be partially regenerated naturally by the body, recovery is limited and patients often suffer from osteoarthritis within a year or two.
Orthopaedic researchers in fact have shown that without the adequate protection and support provided by the meniscus, the knee joint can become unstable and the articular cartilage covering the femur and the tibia may begin to deteriorate or degenerate. Over time, the degenerative process can cause persistent and increasing knee pain and may lead to osteoarthritis and in some cases also to total knee replacement. Together with knee instability, this leads to a lower quality of life. Meniscus-Regeneration is the acronym for a Commission-funded project, coordinated by Fidia Advanced Biopolymers. The project aims to use tissue engineering to develop an artificial meniscus; it will take five years, ending in 2007, and involves a wide range of expertise from four different European countries. The presentation shows the state of the art of the project outlining its possible impact on quality of life and health of the citizens.

**Intelligent Scaffolds for Tissue Engineering of Bone, Skin, and Cartilage – ‘INTELLISCAF’**

*Dr Naseem Theilgaard*

*Project Coordinator INTELLISCAF, Danish Teknological Institute, Denmark*

With our ageing and more active population, there is an increasing demand for materials that can potentially replace, repair or even regenerate injured bone, cartilage and skin tissues. Present surgical or grafting procedures are only partly successful in restoring all functions of the damaged tissues. The work carried out in the ‘INTELLISCAF’ project is aimed at developing functional biomaterials and targeted at providing advanced nano-tailored materials via surface technologies and nanostructured particles.

_The objective is to produce innovative scaffold materials with characteristics tailored to regenerate bone, cartilage and skin tissues upon implantation._

During the course of this project, scaffolds will be developed that have the ability to both activating existing cells as well as to generate new cells, not only from bone, but from skin and cartilage as well. Such intelligent scaffolds would not only act as passive implant systems, but be active in repairing the tissue concerned, both by attracting and concentrating bioactive molecules (e.g. BMPs, cell-adhesion factors) and activating existing tissue cells. Surface modification of scaffolds by nano-technology is considered to be essential to achieving this goal.

(The presentation made at the conference is available on the Proceedings CDROM)
SESSION 5D – LAB TO THE CLINIC – COMMERCIALIZING NANOMEDICINE

Overview
Investment in nanoscale research has grown from around €1bn p.a. in 2000 and is expected to reach €10bn p.a. worldwide by 2006. The use of nanotechnology is accelerating, and a prediction made in the USA in 2000 that one trillion dollars in products worldwide would be affected by nanotechnology in 2015 has now been brought forward by five years to 2010.

Nanotechnology applied to medicine is a key area of economic potential, but in some areas suffers from a regulatory bottleneck, with a long lead in time from lab to application. This means huge costs of development, the possibility of financially catastrophic failure, and expensive products by the time the successful ones reach the market.

Taking NanoProducts to the Marketplace
Nanotechnology has already been commercialized in products ranging from anti-ageing creams to hearing aids to anti-scratch coatings to DVDs. In healthcare, silver nanoparticles are being incorporated in wound dressings to provide improved biocidal properties – the common everyday sticking plaster has now been vastly improved by the application of nanotechnology.

A major problem besetting nano innovators is that their technology may be generic, i.e. have more than one application. For example, Oxonica is a small company with expertise in creating and functionalizing nanoparticles. They have developed nanoparticles for imaging and diagnostic applications, as well as for sunscreens and as fuel additives. One problem for similar small companies is making the decision on which market to attack first, and how to effectively penetrate each one.

Another problem is dealing with a public backlash against nanotechnology; no matter how unreasonable that might be with regard to most products. Government may demand even more regulation that will further slow the progress of a Nanotechnology breakthrough to full commercialization.
Session Report

Del Stark

Institute of Nanotechnology, UK

This session was devised to encourage discussions around the development of nanotechnology related products for the healthcare market. Specifically the session was an ideal situation for researchers around the world to discuss success stories about bringing nanotechnology to the clinic.

The speakers were: Dr Kees Eijkel, Technical-Commercial Director, MESA+ Research Institute, University of Twente, The Netherlands, Dr Richard G Caro, CEO, TangibleFuture, Inc., USA, Dr J Malcolm Wilkinson, Managing Director, Technology for Industry Limited, UK, and Professor Luis R Mejia, Stanford University, USA.

Kees Eijkel opened the session discussing how miniaturization is a driving force in delivering healthcare to future generations. Speed, functionality, less energy use and portability will be key issues to personalized health with a need to shift treatment from curative to preventive. The ageing population will also need new ways in which to communicate to health professionals and options could be telemetrics, e-health and novel forms of imaging.

Eijkel noted that challenges will be the integration of nanotechnology to all disciplines and breakthroughs are to be expected where scientists truly integrate. There also needs to be common jargon between the NIH, the hierarchy of science, new networks and disciplinary environments and so on.

A variety of products and process were highlighted, but the final message was to link with multidisciplinary efforts while keeping the interface between business and science separate.

Richard Caro, followed with an excellent presentation on building a business based on new technology. Caro gave many examples on how a new technology company will fail. The main focus of the talk was to encourage smart business planning as the technology will not run the company. The session delegates found this presentation very useful.

Malcolm Wilkinson gave a good introduction to nanotechnology and its applications for health care. The main focus of this talk highlighted the time in which it takes to bring products to market. One product, the i-STAT which is a disposable blood analysis cartridge used in combination with a hand held instrument, took 12 years from concept to first production. The reasons for this were:

- Long development time because of lack of manufacturing experience in the University R&D team and the need for regulatory approval
- Slow take-up of the product because of need to change methods of blood analysis in hospitals
Dedicated manufacturing plant under-utilized due to slow take up, leading to high product cost and low profit margin

Company in weak financial situation, acquired by Abbott

Wilkinson ended suggesting that there are ways to speed a product to the market such as making sure there is a clear market need, make sure the science is proven and use technology suitable for volume manufacture possibly in collaboration with an experienced design team.

**Luis Mejia** was the last speaker of the session and his presentation looked at the university technology transfer dilemma in which only thirty inventions out of 5,000 produced over $1m. Some of the bottle necks include: evaluation, marketing, patenting plus:

- 4 years on average for US Patent
- Diagnostic products 3-5 years
- Therapeutic products 15-20 years
- 15 years for the university to break even

Mejia quoted Arthur Schawlow, Stanford Physicist, and Nobel Prize winner, “What I can imagine is rather dull, it’s what I cannot imagine that excites me”. In the future tech transfer needs to become a more efficient process with physicians and buyers getting over their reluctance of change.

The session ended with a discussion looking at time to market and when will many new medical applications become available to physicians. The message was positive in that in three to five years many new products will be available to patients and care providers.
Commercializing Issues around Health Applications

Dr Kees Eijkel

Technical-Commercial Director, MESA+ Research Institute, University of Twente, The Netherlands

Health applications have a natural link with nanotechnology: basically, living systems can be interpreted as very complex nanotechnology systems, built up through bottom-up processes. Being able to approach living systems on their relevant level of processes on the nanoscale or single molecule scale, is therefore tremendously important for progress in health. Innovations will include research on cellular and disease processes, diagnostics, drug delivery, tissue regeneration, imaging, therapeutics and many others. At the same time, an interesting field on the borderline between health and food appears where nanotechnology has tremendous added value: improvements in food safety, food quality, personalized diets, and food processing.

The highly regulated health sector has its own specific character, when commercialization is an issue. At the same time, regulation and certification are mostly defined on the national level. This contribution will focus on the specific issues of commercialization of health applications enabled by nano and microtechnology. Some issues of social implications, which are highly related to commercialization, will be touched upon.

(The presentation made at the conference is available on the Proceedings CDROM)
Applied Entrepreneuring: From Science to Profitable Business

Dr Richard G Caro
CEO, TangibleFuture, Inc., USA

Turning an idea for a novel medical device or drug into a product that is clinically effective, and becomes widely adopted, takes a long time, costs a lot of money, and involves a lot of hard work by many people. This is particularly true when the innovation is at the level of basic science - as is generally the case when nanotechnology is involved.

The journey from science project to profitable business is different in every case, but involves a series of generally applicable milestones, as well as all too common pitfalls and errors. Unfortunately, many entrepreneurs setting out on this journey do so without the benefit of a roadmap; unaware of the key milestones; and untrained in the skills useful for avoiding the pitfalls. All too often, the results are avoidable errors - leading at best to loss of time and momentum, and to unnecessary cost; and at worst to corporate death.

Over the last 20 years, Dr Caro has led or advised project teams trying to turn ideas into medical devices for applications in ophthalmology, cardiology, radiology, orthopaedics, general surgery, pulmonology, and anaesthesia. A number of these projects led to successful, widely used products, and created substantial shareholder value along the way.

Some ran up against scientific challenges that could not be solved with the time, people, and money available; while others led to clinically effective products, which were overtaken by cheaper, less complex technology before entering mainstream usage.

In this talk, Dr Caro draws on his experiences to discuss the process of creating a successful business from an idea for a medical device, and in particular:

- The key ingredients needed to create a successful new nanohealthcare product and business
- The key value creation milestones
- The most common errors and how to avoid them
Fast Track Incorporation of Nanotech in Medical Products

Dr J Malcolm Wilkinson, Dr George Adamson, and Kalyan Sarma
Managing Director, Technology for Industry Limited, UK

Nanotechnology is not just a technology for the future – it is being used now in many medical applications. This paper will review some fast track examples where the advantages of the technology are providing immediate product benefits. In addition, some general observations will be made about the business models being employed by the companies exploiting nanotechnology. Some companies are choosing a vertically integrated model, others a niche supplier position. Both can be profitable but offer very different growth prospects.

In wound care, silver nanoparticles are being incorporated in wound dressings to provide improved biocidal properties. Novel gels provide improved oxygen flow to wounds and microfluidic structures remove fluid. Artificial skin based on woven textile support incorporating the patient’s own cells reduces the chance of tissue rejection and speeds healing.

Drug delivery devices are being developed based on microfluidic structures such as needles and aerosol producing nozzles. Nanoparticles with specific coatings are being employed to delay release of drugs or target their release at specific organs or cell types.

Surgical tools are already in production using the enhanced mechanical properties of nanostructured alloys and extremely sharp edges produced in diamond films.

Coatings on cardiovascular stents can provide long term release of drugs preventing re-stenosis of arteries or improving biocompatibility. Coatings on artificial joints can make them longer lasting.

By analyzing some of the development problems encountered during the development of these and other micro and nanotechnology based products, some guidelines can be established to help speed up the development cycle for future products.

(The presentation made at the conference is available on the Proceedings CDROM)
Transferring Early Stage Nanotechnologies from the Lab to the Healthcare Marketplace

Professor Luis R Mejia
Stanford University, USA

Most inventions that are patented are directed to incremental and modest improvements over the existing art. But occasionally there is a convergence of technological innovations that produces a break-through technology. For example, at Stanford, we can point to but one invention out of 4000 that generated significant royalty income. To effectively transfer nanotechnologies from the lab to the healthcare marketplace, these realities must be considered.

The dearth of big hits notwithstanding, the adoption of new innovations can be brought forward effectively for public use and benefit by strategic use of technology transfer management. This is especially true where nanotechnology is concerned because it is such a broad field that achieving a specific commercialization focus for the healthcare industry can be particularly challenging. This presentation will provide an overview of technology transfer with a particular emphasis on transferring early stage nanotechnologies from the lab to the healthcare marketplace.

Overview of Technology Transfer

Integral to the mission of most major US research universities is the transfer of technology for public use and benefit while generating unrestricted income to support research and education. By any international standard, it is clear that US universities have become very effective at transferring new innovations to the commercial sector, having generated about $1.4bn in licensing income in 2003.

Technology Transfer has Discrete Forms

It is important to recognize that technology transfer can be manifested in several forms. The first is the graduation of students. This reality was put into perspective by Gordon Moore, co-founder of Fairchild Semiconductor and Intel, who believes that Stanford’s major contribution to Silicon Valley has been the several hundred graduating Master's degree students that each year adds to the Silicon Valley engineering talent pool. Secondly, the publication of research results in scientific journals, at conferences and on websites provide for an immense volume of knowledge transfer. Lastly, and certainly of considerable importance, the licensing of inventions provides a very direct and quantifiable form of technology transfer.
Technology Transfer has become more Important in a Global Economy

Global competition has intensified and governments are looking for strategic tools to help their economies compete. At the same time large companies are under pressure to justify the huge cost of maintaining their own basic research labs. While at the other end of the commercial spectrum, university generated innovations are seen as important for the creation of new business ventures.

Licensing Best Practices

There are many strategies to employ for successful technology transfer, but one important thing to recognize is that licensing early stage inventions requires patient capital. As an example, Stanford OTL took 15 years to generate income that exceeded its expenses.

Inventors are a key element of a successful licensing strategy; not only can they help to identify prospective licensees; they may also obtain research funding as a direct result of their interactions with those companies.

Another aspect of best practices is focused on the qualifications of licensing professionals: they should have technical backgrounds, relevant business experience and must be excellent communicators. Lastly, an effective licensor is a good business partner who is responsive to business needs and views deals as long-term relationships.

Challenges in Licensing Nanotechnology to the Healthcare Industry

Nanotechnology like any technology being transferred must have a marketable product that can be identified. For example, novel nano processes like the nanofoil developed at Lawrence Livermore National Lab and licensed to Reactive Nanotechnologies had many possible commercial applications but finding the right one on which to focus was not obvious – finding the killer app was elusive. At Stanford, thirty seven invention disclosures with ‘nano’ as a keyword have been evaluated and churned through the tech transfer process.

Over 1 100 marketing letters were mailed to industry, sixty patent applications filed, nearly $300 000 spent on patents – the results: one licensee. Adding to the challenges, healthcare markets are big and attractive, but are particularly cost sensitive and costly to penetrate.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)
SESSION 6A – NOVEL IMPLANTS AND DEVICES

Overview
Nanotechnology, new materials and nanoelectronics are the basis of novel retinal and cochlear implants. New retinal implants have been developed that enable people previously classified as blind (through disease, such as macular degeneration) to be reclassified as sighted. Present cochlear implants are crude, difficult to insert, awkward to wear and give poor performance, Future implants will use nanocomposite materials, be small and easy to insert and be cheap to produce. This also has very promising implications for the poor.

What can Nano do for Implants and Devices?
Implantable devices incorporate the latest advances in electronics and material sciences with improved biocompatibility and a more sensitive interchange allowing a more rapid response to (or detection of) physiological changes. For example, nanostructured electrodes can offer improved battery life, which in turn lengthens the replacement time of implants, while in other applications this increase in active surface area can improve the signal at the interface of living tissue (e.g. the retina) with the implant. Nanostructured coatings can help prevent infection at the site of the implant (e.g. nanosilver coatings) while both chemical and topographical changes to the implant’s surface can affect cell adhesion thus preventing it from occurring where required or helping to direct specific cell binding.

Over $30bn is spent on implants annually (hip, knee, dental etc.). Nanotechnology can help bring about better implants. For example, Proteins at the body-implant interface play a decisive role in the acceptance or rejection of the implant. Using nanotechnology we can produce ‘body-friendly’ coatings and also create topographies that cells like, to increase the likelihood of acceptance. These biocompatible coatings are even being used in devices like hearing aids, reducing the likelihood of irritation or skin reaction.

Around 1 000 000 hip and knee-joint replacements are carried out in the EU each year. However, the lifespan of the implants is only around 10 years, shorter if the patient is particularly active or overweight.

This poses both a quality of life problem, and a cost effectiveness issue.

Nanocomposites are also being developed that form ceramic implants which are stronger and longer-lasting, with potential life-spans of more than 30 years.
Nanocomposites for Biomedical Applications

Dr Ramón Torrecillas

INCAR-CSIC, Chemistry of Materials Department, Nanostructured Material Group, Spain

BIOKER Project


In modern surgery, a total hip replacement (THR) using prosthesis constitutes a state-of-the-art operation. Today, more than one million hip- and knee-joint replacements are fitted annually throughout the European Union. Such procedures are extremely successful in restoring mobility to sufferers from arthritic and other degenerative conditions. However, the average lifetime of a hip prosthesis, for example, is around 10 to 15 years – with active and heavyweight patients being particularly prone to premature failure. This clearly poses a quality-of-life problem for younger and other vulnerable recipients. Moreover, the cost of revisionary surgery is 70 to 100% additional (that is 170-200%) to the one of the original operation, adding around €520m a year to the EU’s medical costs.

Ceramic materials are now considered as an alternative to the common metal femoral heads articulating against an acetabular cup of polyethylene, or to metal-metal bearing devices. Because of their hardness, these materials appear to be ideally suited for joint prosthesis, which results in turn low wear rates and an excellent biocompatibility. In fact, abrasion in the artificial joint can lead to loosening of the implant due to the osteolysis caused by polyethylene wear particles. Thus, ceramic materials appear as the ideal candidates for joint prostheses. However, ceramic materials are known to be brittle and susceptible to slow crack growth (SCG). Biocompatible oxide ceramics are sensitive to SCG because adsorption of water can take place at the crack tip, leading to a strong decrease of the surface energy in humid (or air) conditions.

This so called ‘stress corrosion’ process was first reported for glass but is now accepted for all oxide ceramics. The sensitivity of ceramic oxides to SCG is one of their major drawbacks concerning demanding, long term applications, an example being orthopaedic implants.

In the three-year BIOKER project, funded under the European Commission’s GROWTH programme, a consortium of research institutes and industrial partners from three EU countries has investigated the use of alumina nanocomposites to form ceramic-ceramic implants with potential life-spans of more than 30 years. The specific nano-structure of ceramic oxides can lead to a SCG resistance never reached before, close to that of covalent ceramics. The compressive residual stress field caused by the presence of a small volume fraction of evenly distributed zirconia nano-particles is responsible for the drastic change in the overall resistance to Slow Crack Growth of the alumina-zirconia nanocomposite.
This result opens a new avenue of developing oxide ceramic based nanostructured composites for structural applications since they offer crack resistance similar to covalent materials without their major drawbacks associated to processing as well as machining.

Nanostructured powders can be made using the top-down approach from the macroscale to the nanoscale, or conversely, by assembly of atoms or particles using the bottom-up approach. The control of arrangement of atoms from the nanoscale to the macroscale is indeed the strength of materials chemistry and has been the preferred route in the BIOKER project. Concerning processing of bulk nanostructured composite materials, up to now only one approach was pursued: powder processing route, wherein nanoparticles of the material are first synthesized by some convenient chemical or physical method and then mechanically or wet mixed, and finally consolidated by pressure-less or pressure-assisted sintering. When it is sought to obtain a dense composite formed by a matrix and a homogeneous distribution of a nanosized second phase, many problems arise for two reasons. First, in conventional powder processing, it is essential to synthesize nanoparticles that have to be nonagglomerated and preferably monodispersed. Second, the obtention of a homogeneous distribution of second phases on the nanometric scale is quite complex.

Additionally hazard studies demonstrate that ultrafine or nanoparticles produce more potent adverse effects in the form of inflammation and subsequent tumours compared with larger sized particles of identical chemical composition at equivalent mass concentrations or intratracheally-instilled doses. Surface properties, such as surface chemistry and area, may play a significant role in nanoparticle particle toxicity. The very high size-specific deposition of nanoparticles when inhaled as singlet ultrafine particles rather than aggregated ones also contributes to their effect.

A new processing route was proposed in the BIOKER project resolving the above mentioned problems.
The surface of submicronic alumina particles in stable slurry in alcohol media are used as ‘support’ for hydrolysis reactions with different diluted alkoxydes. By controlling the surface state of the submicronic alumina particles (OH groups) in the stable suspensions, diluted alcoxides in alcohol media are added dropwise. Controlling the OH-groups present on the surface of the original powder, a hydrolysis reaction takes place on the surface of the particles being recovered by the alkoxyde. From this point, by controlling the processing parameters it is possible to control nucleation and growth on the surface (in situ formation of nanoparticles) in such a way that it is possible to synthesize the nanoparticles and densify the material in a single step with the purpose to obtain nanocomposites with a metallic and/or ceramic matrix avoiding nanoparticle handling.

Produced using the specially developed nanostructured powders and processing technology, the developed material contains numbers of zirconia nanoparticles distributed uniformly among the alumina grains. The distribution of nanoparticles at both grain boundaries and intragranular position can be tailored by using the adequate dopants with a homogeneous molecular distribution.

After evaluating many different processing variables and mechanically testing a variety of compositions, we eventually selected a formulation containing 1.7 vol% of zirconia. The nanostructured material has a much higher stress intensity threshold than that of either of its individual components. Another advantage is that we do not need to use the stabilizers required for pure zirconia ceramics. Due to reactions taking place in the human body, these were one of the sources of crack generation.

A complete study of the mechanical behaviour of the alumina nanocomposites developed in the project has been done. Both, static and dynamic fatigue tests corroborate the improved behaviour of nanocomposites compared to actually used materials.

Biocompatibility of alumina nanocomposites is a key point in this project. It has been shown that alumina-zirconia nanocomposite presents better biocompatibility than alumina. Further biological tests have shown the excellent promise of BIOKER materials.

Finally, a comparison with materials available on the market has shown the superiority of the materials developed in this project concerning mechanical resistance.

Wear test made on nanocomposite-nanocomposite couples (ball and cotile) have shown the excellent behaviour of this new family of nanostructured materials for biomedical applications.
Further years of development and clinical trials would be required before implants based on the BIOKER nanocomposite could enter regular medical service. Their eventual adoption would solve the current material supply problem. In addition, it would make it more feasible – and more affordable – for both, young and older European citizens, to benefit from what have already been shown to be highly life-enhancing interventions.

Towards Learning Retina Implants for the Blind

Professor Rolf Eckmiller

Head, Division of Neural Computation, Department of Computer Science, University of Bonn, Germany

 Shortly after photoreceptor cells degenerate in humans with Retinitis Pigmentosa (RP) or Age-related Macula Degeneration (AMD), the intra-retinal information processing breaks down, although about half the ganglion cells, which form the neural connection to the central visual system remains intact. The central visual system expects retinal ganglion cell activity from the epiretinal electrical stimulation of a retina implant as pre-processed and filtered visual information, similar to the receptive field processing of ganglion cells during normal vision. This electrode-location specific, expected spatiotemporal filtering and pre processing has to be tuned and adjusted for each blind subject individually, since it can not be predicted neither by the retina implant producer nor by the ophthalamic surgeon, who implants the epiretinal microcontact foil.

![Figure 1](image.png)

**Figure 1.** Schema of the retina implant with a retina encoder (RE) outside the eye and an implanted retina stimulator (RS). The structure within the photosensor array depicts a receptive field (RF) with centre and surround of a typical adaptive spatiotemporal filter (RF filter) similar to receptive field properties of a ganglion cell in the primate retina. RS will be epiretinally implanted, adjacent to the ganglion cell layer for example as ring-shaped, soft micro contact foil cantered about the fovea. The wireless signal- and energy transmission system (SE) with an external module and an implanted module provides the communication between RE and RS.
Consequently the major international efforts towards a visual prosthesis for this group of blind subjects to regain vision including a certain level of ‘Gestalt Perception’ attempt to bypass the defective retina by means of an implanted micro contact foil at the ‘output’ of the retina, e.g. adjacent to the ganglion cell layer. Accordingly, the intraretinal information processing has to be mimicked by a retina encoder (RE) with a sufficiently large number of spatiotemporal filters. Individual RE tuning is attempted in a perception-based dialog with the human subject.

Various types of micro contact structures have been successfully developed and tested in animals and partly in humans in conjunction with custom-designed microelectronic circuit chips for signal and energy (SE) communication, stimulus signal generation, and for photosensor arrays. Different versions of learning REs including dialog-based tuning by means of learning algorithms have been developed and successfully tested in subjects with normal vision.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)

**Genomic Nanoprocessors: A Platform for Future Healthcare?**

*Dr John Beattie*

*Chief Operating Officer, Scottish Centre for Genomic Technology and Informatics, UK*

Change in healthcare provision is being driven by three key technology trends. First medical practice is becoming increasingly information-intensive, with enhancements in IT enabling improved health monitoring, recording and analysis. Second, dramatically enhanced understanding of the molecular basis for disease following the sequencing of the human genome has opened up new potential for understanding, diagnosing and treating disease. Third, improvements in automation combined with increasing miniaturization of silicon chip technologies is driving towards faster, more sensitive instrumentation with a smaller physical footprint.

There is an opportunity to harness the convergence of these technologies at the nano scale to address applications in healthcare. A research programme at the University of Edinburgh is developing a novel concept in switchable biosensors. These are based on nano-scale biomolecules which can switch between two molecular conformations depending on a controllable ion flux. This conformation change can be enabled or disabled by the detection of target biomolecules and may be detected using optical or other techniques.

These nanoscale switchable biosensors potentially bring specific advantages. The switching action provides a means of enhancing signal:noise ratio of signals, and they can be used to optically detect biomolecules without sample labelling. If mounted on an electronic biochip they can be used to form addressable microarrays, using locationally-specific ion flux to control array spots.
These biosensors have potential applications in developing instrument-based devices for research and drug development, and for improved clinical diagnosis and treatment. There is also the future potential to use such elements to form more complex biological information processing devices, which could be used to monitor and treat diseases in-vivo. As with all diagnosis and treatment, careful regulated trials will be essential to ensure both efficacy and patient safety.

Developing novel convergent technologies demands highly multidisciplinary expertise. This programme involves combining capability from four diverse research centres in medical genomics, electronic engineering, electrochemistry, and physics. To achieve this, the team has applied a target-orientated approach, more often used in product development, to form a highly integrated programme of basic and applied research.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)

Integration of Bio, Micro, Nano, and Information Technology for Medical Diagnostic Systems: Challenges and Opportunities

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The convergence of micro and nano technology with biology and information technology (BioInfoMNT) promises tremendous advances and potential cost reductions for medical applications and healthcare in general. However, real advances that translate into real benefits for society, and in particular for individuals, will only come about when solutions become integrated into healthcare systems and impact on the provision and delivery of healthcare services and products. This is particularly the case for medical diagnostics, where expenditures for diagnosis represent generally less than 1% of the total health care expenditure¹.

This implies that an increase in the frequency of testing does not directly increase the costs of health care, but rather it can significantly contribute to the quality of health care delivery. The clear benefits of facilitating rapid and increased diagnostic testing include: earlier and more appropriate and therefore less costly treatment; assist in minimizing expensive treatments; reduce the costs of treatment due to complications; and potentially shortens the length of hospital stay by making therapies more effective and therefore more cost-effective.

¹ As was shown for in vitro diagnosis in European IVD Market Estimates 2003, European Diagnostic Manufacturers Association (EDMA), Brussels 2003, www.edma-icd.be
The integration of concepts, processes, and technologies across the enabling disciplines and dimensions of micro and nano technology will lead to the development of unique systems for personalized medicine and the next generation of Point-of-Care (POC) medical diagnostic instrumentation. Together with the advent of the ambient intelligent environment, where technology has become completely transparent, these advanced POC solutions must address the needs of the well informed consumer, who demands greater functionality, performance, connectivity, and value for money, especially concerning personal health and well-being issues. Solutions will rely on a combination of factors: the development of enabling technologies for the modular components (biorecognition elements, sensors, and microfluidics); the integration of key components into a useful system using novel, low cost manufacturing techniques; the interfacing of the system to the external environment and the informed understanding of system level requirements from the user community. To achieve this successfully (both technically and commercially) is a significant challenge.

However, access to developments in the exquisitely sensitive and specific biorecognition elements based on antibody and binding reagent scaffolds, combined with the ability to manipulate and position these elements in nanodimensional space provides the strong possibility of meeting the requirements of a small scale, immediate response portable process. Further requirements include smart but simple surface design for positioning and transduction processes and an understanding of the interfacial forces and chemistries which are absolutely key to the transfer (transduction) of the recognition event to a readout which is consistent with the needs of the user. Here the engineering and microfabrication capacities contribute significantly to the overall microfluidic control of the biorecognition reaction kinetics. Each of these elements contribute significantly to the success in developing devices which are; frugal in their requirements for sample and reagent volume, fast in their completion of sensing, and simple in their presentation of results to the end user. In bringing together the optimal version of each of the above elements, it is essential that the design of each is compatible with all elements of the process, and consistent with production of the recognition elements and manufacturing of the platforms and devices.

Addressing these issues, strategic development must be focused towards a system integration approach for the investigation design and manufacturing of the biosensor technology. A key factor relies on implementing new manufacturing strategies to advance initial developmental work into true manufacturing environments, particularly those focused towards the developing of low cost polymer replication platforms that integrate the key enabling technologies (including transducers, microfluidics, and bio-materials) to realize unique polymer based packaged solutions. This allows for the cheap manufacture of single use (disposable) devices that are important in health monitoring due to the contamination risk. On the short term, semi-polymer solutions that integrated both polymer and non-polymer components are being developed. These hybrid solutions integrate traditional materials for the transducers and electronics, and polymers for the fluidics, interconnections, and packaging.
On the longer term (i.e., 2015) entire polymer platforms will have both active and passive components fully integrated offering true low cost and novel solutions. These polymer based sensors need both active and passive components. Active components will evolve from the advances made in polymer electronics, but must go further to be able to exploit and mimic the more complex biological mechanisms pertinent to protein and cellular interactions. The integration of polymer based (or polymer compatible) chemistries for the functionalization of surfaces/structures is seen as a vitally important direction, and offer the possibility of increased (and new) detection capabilities via novel three dimensional structures (i.e., dendrimers, grafted and molecularly imprinted polymers). From a manufacturing perspective, the establishment of polymer replication platforms that include micro and nano moulding facilities and replication equipment that can accommodate the subsequent integration of the other key (polymer and traditional) sub-components is seen as a major priority.

Again with the longer term view of the further convergent technologies and reduction in scale, biodetection will move away from sampling fluids and tissues from the body for in vitro diagnostics to in vivo imaging and biodetection.

Currently in-vivo imaging requires large and complex scanning instrumentation, whereas solving the design of engineered and manufactured devices at the MNT level will enable their signals to be transmitted from the body, captured externally, and deconvoluted to produce results.

The presentation summarizes some of the key opportunities and challenges that face the development of MNT based diagnostic systems for the implementation of ‘affordable and available’ POC systems into healthcare environments. A case study of the developmental path and implementation plan for advanced cancer diagnostics is presented, highlighting the key functional components of the system level integration.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)
Tissue Engineering of Cartilage and Bone - State of the Art and Future Challenges

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### Tissue Engineering

The interest in modern biological technologies such as tissue engineering, which is an interdisciplinary field of physicians, engineers and scientists, has dramatically increased since it is feasible to isolate living, healthy cells from the body, expand them under cell culture conditions, combine them with biocompatible carrier materials and re-transplant them into patients.

Therefore, tissue engineering gives the opportunity to generate living substitutes for tissues and organs, which may overcome the drawbacks of classical tissue reconstruction: lacking quality and quantity of autologous grafts, immunogenicity of allogenic grafts and loosening of alloplastic implants. Common tissue engineering principles focus on: (a) healthy cells, which have to be nonimmunogenic, easy to isolate and highly responsive to distinct environmental cues, (b) suitable carriers for the *in vitro* cell differentiation and subsequent transplantation, and (c) a set of bioactive molecules driving the process of cell migration, differentiation and maturation (Ringe et al 2002, Naturwissenschaften). Thus key technologies, which are needed for regenerative medicine and which are established in the Berlin Tissue Engineering Laboratory, are for instance organotypic cell culture, cell delivery technologies, cell biomaterial interactions, the differentiation and recruitment of stem and progenitor cells, analysis of the molecular quality of transplants, different animal models, development of GMP-compatible protocols and the technology transfer.

### Biomaterials as Key Components for Tissue Engineering

Tissue engineering transplants are mainly composed of two components: (a) tissue specific cells or stem cells, and (b) a biocompatible carrier scaffold on which these cells can develop. The cells are important for the formation of new tissues through extracellular matrix synthesis and are responsible for the long-term stability of this matrix. Biomaterials provide short-term mechanical stability of the transplant and provide a template for spatial growth of the developing tissue (Sittinger et al 2004, Current Opinion Biotechnology). Several biomaterials have been used for skeletal tissue engineering: (a) gels and viscous suspensions like agarose, alginate, hyaluronic acid, fibrin and collagen, (b) sponge like, porous materials like coralline materials, preserved allogenic bones and porous polymers, (c) textile structures like resorbable fibres, and in the last years (d) advanced nanofibrous scaffolds like poly-caprolactone based scaffolds.
Nanotechnology based scaffolds are of special interest, since cells react on the micro- and nanoscale to the shape and chemistry of their surrounding environment. Nanoscale grooves no wider then cells can act as templates, organizing cells themselves. Thus, such scaffolds most probably will allow the engineering of tissues and organs.

As indicated above, biomaterials represent important tools for the delivery of tissue specific or stem cells. In this regard, the role of a delivery material is to ensure (a) a convenient cell and tissue handling, (b) an initial \textit{in vivo} stability, (c) an efficient local distribution of cells at sites of defects, (d) anchorage and integration of transplants, and (e) to allow a minimal invasive delivery. Important properties of such an delivery material are (a) a high interconnecting porosity, (b) a low material per volume ratio, (c) an appropriate mechanical stability, depending on the clinical application, (d) biocompatibility, and (e) if the aim is a clinical application, FDA or similar approval.

Regarding a commercial application of a tissue engineering product the latter point is of special importance and we claim that in next clinical tissue engineering applications rather available, approved and cheap delivery materials than “optimal” but not approved materials will be used. Of course, this is also important for new nanotechnology based delivery materials.

Different strategies have been applied for cell seeding into biomaterials. Most groups add their cells ‘on’ the polymer fibres of the scaffold. In consequence, this results in a non-optimal three-dimensional (3D) cell distribution. Even in the scaffold, the cells only show a surface growth then. Our group prefers another strategy. We first mix our cells with a gel structure like for example fibrinogen. This ensures an optimal 3D-distribution of cells in the gel. In the next step we add polymer fibres, such as PGLA, to stabilize the cells and to ensure a good tissue handling. This technology is used in the clinical applied products for cartilage and oral bone repair BioSeed\textsuperscript{®}-C and BioSeed\textsuperscript{®}-Oral bone.

**State of the Art in Cartilage and Bone Tissue Engineering**

Damaged or diseased articular cartilage frequently leads to progressive disability resulting in a marked decrease in the quality of life. Osteoarthritis (OA) as the most prevalent disorder of the musculoskeletal system is a consequence of mechanical and biological events destabilizing tissue homeostasis in articular joint tissues. Thus, it involves the disturbance in the normal balance of degradation and repair in articular cartilage, synovial membrane, and subchondral bone. Means for an efficient treatment are rather poor and are generally restricted to symptomatic measures, reconstructive surgery, or even endoprothetic replacement. The outcomes of conventional surgical procedures including joint resurfacing (abrasio, drilling, debridements, microfracture techniques, or arthroscopic shaving) or biological autografts are quite unsatisfactory in the long-term evaluation. This failure is due to an insufficient repair resulting in the formation of mechanically inadequate fibrocartilage.
Current technologies of tissue engineering offer new strategies for the treatment of such defects or diseases. In the first generation of cartilage tissue engineering products, as described by Brittberg et al in 1994, chondrocytes are harvested from small tissue biopsies, are extensive culture expanded and then transplanted as a cell suspension into small cartilage defects. To prevent a leakage of chondrocytes, the defects have to be covered by a periosteal flap. This technique, called Autologous Chondrocyte Transplantation (ACT), has been used to treat more than 15,000 patients with small cartilage defects. Second generation tissue engineering products base on composites of the already discussed bioresorbable delivery materials and cells like mesenchymal stem cells or differentiated chondrocytes/osteoblasts. Preformed 3D-cell/biomaterial constructs either can be transplanted directly into a cartilage or bone defect or can be cultured for some days in perfusion culture systems or other bioreactors prior transplantation.

BioSeed®-C, clinically applied to treat cartilage joint defects, developed by the Berlin Tissue Engineering Group and TransTissue Technologies Inc., and commercialized by BioTissue Technologies Inc., is one of the few second generation products already established (more than 500 patients) on the market (Figure 1, www.biotissue.de). To ensure a homogeneous distribution of chondrocytes, these cells first are mixed with fibrinogen and the suspension are soaked into polymer fleeces of PGLA. Then cells and fibrinogen are polymerized by the addition of thrombin. The transplants are fixed by a transosseous 4-point fixation.

Because of the fixation technique, BioSeed®-C also can be used to regenerate defects with no clear surface, e.g. in patients with early osteoarthritis. An arthroscopic implantation is possible. Compared to 1st generation products (ACT), the advantages of such engineered transplants are (a) that no chondral suturing is required, (b) a rapid fixation is possible, (c) a shorter operating time, (d) an arthroscopic transplantation is possible, (e) a robust transplant handling, and (f) a low risk for loss of transplanted cells and stable anchorage.
BioSeed®-Oral Bone, on the European market since 2001, also developed by the Berlin Tissue Engineering Group and TransTissue Technologies Inc., and commercialized by BioTissue Technologies Inc., is an engineered 3D-bone transplant for sinus lift bone regeneration (Figure 1, [www.biotissue.de](http://www.biotissue.de)). Moreover, to the best of our knowledge, it presents worldwide the only commercial available bone tissue engineering product (more than 700 patients) on the market. In case of a decreased oral bone thickness, sinus lift regeneration often represents the prerequisite for tooth implantation. For transplant preparation, patients own mandibular-derived periosteal progenitor cells are isolated, culture expanded, combined with fibrinogen and PGLA, cultivated in perfusion culture in medium containing patients own serum and bone formation stimulating factors.

**Next Generation of Tissue Engineering Products**

A prerequisite to produce cell-based products of the 1st and 2nd generation is to have access to an expensive health care clean room in which all the production steps have to be carried out under time and cost consuming GMP-conditions. Because of the high cell culture costs and to avoid the removal of biopsies from patients, we strongly believe that future (3rd) tissue engineering therapies will be based on an *in situ* treatment of tissue or organ defects.

In case of cartilage repair, we follow the hypothesis, that a tissue engineering approach using chemoattractant molecules will allow the *in situ* recruitment of mesenchymal stem cells (MSC) from bone marrow to sites of degenerated articular cartilage and their subsequent use for the directed generation of cartilaginous joint structures (Figure 2). An isolation of cells is not necessary then. The regenerative process comprises (a) chemoinductive substrates, (b) *in situ* recruitment of MSC from bone marrow, and (c) cell proliferation and differentiation.

![Figure 2. In situ tissue engineering of the joint](image-url)
Although the goal is to avoid MSC isolation, these cells have to be characterized meticulous *in vitro*. In contrast to bone marrow hematopoietic stem cells, MSC are CD34 negative bone marrow stem cells. They show a high proliferative activity *in vitro* and develop in different tissue such as bone and cartilage *in vitro* and *in vivo* (Pittenger et al 1999, Science). Therefore, they have been used in several animal models for 3D skeletal tissue engineering. Several data concerning the expression of a wide variety of markers and their receptors have been described so far. In two European projects of the 6th Framework Programme: “STEPS” and ‘GENOSTEM’ (www.genostem.org), MSC are under investigation using e.g. Genomics and Proteomics technologies, which represent the state of the art in marker screening. Moreover, we have performed chemotaxis and differentiation assays to investigate the migration and differentiation potential of these cells (Schmitt et al 2003, Differentiation).

More general, the 3rd tissue engineering generation, namely *in situ* tissue engineering, will depend on smart delivery concepts that make use of the regenerative potential of stem cells, migration and differentiation factors, and their controlled release, and biomimetic materials (Sittinger et al 2004, Current Opinion Biotechnology).

Biomimetic coatings may be useful to “activate” scaffolds with distinct molecules permitting stem cell migration, adhesion and differentiation to tissues and organs. In this regard, nanotechnology will play an important role, because scaffolds that have nanostructured features will allow control over interactions with biological entities like protein factors and cells. Furthermore nanotechnology will deliver new scaffolds, new biomimetic surface coatings with chemotactic, cell adherence, and growth and differentiation factors, and nanoscale methods to analyze scaffolds and coatings and unique controlled delivery systems for bioactive factors.

(The presentation made at the conference is available on the Proceedings CDROM)
SESSION 6B – NANO SENSORS AND DIAGNOSTICS

Overview
In nanodiagnostics, the ultimate goal is to identify disease at the earliest stage possible, ideally at the level of a single cell. When testing for disease, nanotechnology offers better sensitivity, specificity and reliability. Several steps from sample preparation to detection can be integrated into a single, tiny device. An important application is in cheap, reliable devices, based on nanotechnology that can be used at the ‘point of care’ in clinics by non-expert technicians, and eventually by individuals themselves.

Advances in in-vivo diagnostics will rely mainly on imaging. In molecular imaging, the goal is to create sensitive, reliable agents that can detect, deliver and monitor therapy. This is the “find, fight and follow” concept, sometimes also known as theranostics. The likely diseased tissue is firstly imaged, using target-specific contrast agents (quantum dots). These contrast agents can be combined with a drug; and the results of therapy can then be monitored, again using imaging techniques.

The advances in diagnostics have presented major opportunities for healthcare, including a plethora of new personalized treatments and early diagnosis for individuals suffering from a wide variety of illnesses such as cancer, diabetes, and heart disease.

Nanotechnology has even made a tiny ‘nano needle’ possible which can provide important information on disease at the level of a single cell. Other types of nanosensors include cantilevers which are sensitive, simple and cheap and able to accurately detect tiny biochemical changes.

Session Report

Dr Leonard Fass
Director Academic Relations, GE Healthcare, UK

The session was co-chaired by Dr Leonard Fass, Director Academic Relations at GE Healthcare and Dr Griet Van Caenegem, of the Micro and Nanosystems, Components and Systems Directorate, Information Society and Media Directorate-General, European Commission.

This session covered two different subjects. There were two papers on Biosensors to be used in remote patient monitoring and point of care diagnostics and three papers on Diagnostics that covered the application of nanotechnology to high throughput techniques searching for new leads in drug discovery. One paper was not presented.

There was a lively discussion and interest in commercial availability in the technology presented.
Professor Christopher Lowe, the Director of The Institute of Biotechnology at the University of Cambridge presented a paper on Recent Advances in Biosensors. His research programme covers biopharmaceuticals, microbial technology and biosensors and includes not only aspects of biochemistry, microbiology, chemistry, electrochemistry, physics, electronics, and chemical engineering, but also the entire range from pure science to strategic applied science.

He explained how during the past two decades there was a lot of optimism about the likely impact of biosensor technology on the diagnostics industry: Biosensors offered the promise of real time measurement of physiological data. Progress has been slow so far and the market size in 2003 was <2% of the global diagnostics market. The presentation looked at the needs and advantages of sensors and the technology that has been developed over the past two decades to address the perceived needs and the inherent problems with current approaches such as cost, ease of use, size, power requirements, reliability and repeatability. Sensors are used for measurements of signals such as heart rate, blood pressure, and blood analysis.

His talk focused on newer detection technologies such as holographic polymers, which can be used to test analytes by imaging the holographic pattern. These tests would be disposable and cost less than €1 per test. He suggested how they are likely to have a much more significant impact in the future, particularly in sectors such as point-of-care diagnostics, real-time monitoring, and e-medicine.

Professor Anja Boisen leads a team of fourteen researchers in the Department of Micro and Nanotechnology at the Technical University of Denmark. She described how a micrometer-sized cantilever can be used as a very sensitive, simple, and cheap biochemical sensor in ambient and aqueous environments. Detection of DNA hybridization as well as various types of protein recognition has for example been performed by this method.

Basically, a biochemical reaction at the cantilever surface can be monitored as a bending of the cantilever, due to a change in the surface stress. Furthermore, highly sensitive mass detection can be achieved by using resonating nanocantilevers. Her group has developed cantilever-based sensors with an integrated readout, which hold promise as fast and cheap ‘point of care’ devices. The detection technique involves no labelling of the molecules by fluorescent, magnetic or radioactive markers and bulky detection schemes like laser scans, CCD imaging or radiography are avoided.

For monitoring changes in surface stress they have developed various types of micromachined silicon based cantilever devices with integrated piezo resistive readout. Arrays of up to ten cantilevers have been integrated in micro-channels offering a method to develop compact biosensors with a simple read-out scheme. Recently we have realized cantilever sensors in the polymer SU-8, which is a negative resist with excellent mechanical, thermal and chemical properties. The use of the polymer makes the fabrication process simple, cheap fast and flexible. Moreover, the polymer technology opens up for completely new ways of detecting cantilever bending, which can increase the sensitivity significantly.
They are currently pursuing hybrid system integration, where the sensor unit is packaged for specific handheld sensor applications in diagnostics.

For mass detection they have realized silicon-based nanocantilevers with an integrated capacitive read-out and electrostatic actuations. Due to problems with high stray capacitances the sensor is monolithically integrated with a CMOS chip for on-chip amplification of the signal. The sensor has been used for detection of mass changes caused by controlled deposition of glycerine droplets and from these experiments a mass resolution of 3ag/Hz has been deduced.

Dr. Rolf Guenter the Chief Scientific Officer of Evotec Technologies described the development of very high-resolution cellular imaging systems. He explained how the spatial organization of cells and tissue delivers a wealth of information for the scientist.

Confocal fluorescence microscopy can reveal molecular interaction in the nanometre range.

Using various approaches, such as FIDA (Fluorescence Intensity Distribution Analysis) to look at single molecules), FRET (Foerster Resonance Energy Transfer) and other optical methods modern automated equipment for microscopy offers a throughput of 100 000 samples per day with extremely high resolution, enabling for systematic library approaches instead of single point measurements. Screening genome wide siRNA (Small Interference RNA) libraries are just the most prominent example of such an approach. The presentation addressed the requirements for and the benefits of both a high throughput and high resolution imaging strategy. Pharmaceutical companies use systems of this type in order to identify new drug targets in the search for new pharmaceuticals.

Professor Matt Trau the Director and Founder of the Centre for Nanotechnology and Biotechnology at the University of Queensland in Australia presented the Applications of Drug and Gene Nanoballs in Genomics, Proteomics, Diagnostics, and Personalized Medicine. He explained how the recent completion of the human genome project has heralded a new era of molecular and genetic based medicine.

Major opportunities include a whole range of new (personalized) treatments and early diagnoses for individuals suffering from a wide variety of illnesses such as cancer, diabetes, heart disease, autoimmune disease, as well as a wide range of infectious diseases such as SARS, West Nile Virus, Dengue Fever, and Bird Flu. A major stumbling block that inhibits the full utilization of genomic data generated from the human genome project is our current inability to conveniently and accurately read large amounts of biomolecular information, either intrinsically present within the cell (e.g., the DNA code), or continually produced by the cell (e.g., proteins, antibodies and other metabolites).

Specifically, there is a lack of bio-sensing techniques to rapidly and accurately read low concentrations of biological mixtures that contain large libraries of compounds such as DNA, proteins, antibodies, peptides, polysaccharides or drug leads.
Chip based technologies offer a possible solution, however they are currently limited by high cost, poor accuracy and the restricted number of compounds (<10^5) that may be displayed on the two-dimensional surface of the chip. He presented an alternative method, developed within his Centre1-8, of screening extremely large (>10^10) compound libraries on extremely cheap platforms: encoded colloidal suspensions. The colloidal suspensions are produced via combinatorial chemistry procedures, however are optically encoded for rapid and unique recognition of each individual compound. Once encoded, these particles may be screened at rates of 30,000 to 100,000 compounds per second on a conventional flow cytometer. Potential applications include High Throughput Screening in the areas of Genomics, Proteomics, Drug Discovery and Diagnostics.

Dr Ahmet Senoglu the CEO of Nanoxis presented Nanoscale Devices for Proteomics and Drug Discovery. Nanoxis is a spin-out from Chalmers University in Gothenburg and develops nanofluidic devices based on biomimetic materials and biological methods of operation.

He described methods to build geometrically and topologically complex nanotube-vesicle networks with compartmentalized chemistry. The networks are chemically programmable and have multiple-input multiple-output capabilities. It is possible to transport and route single nanoparticles in the networks. It is possible to make large scale network integration in nanofluidics. The networks can be interfaced with biology, microfluidics and micro-electronics. The networks are compatible with optical, electrochemical and biosensor based single molecule detection techniques.

Professor Jeremy Lakey the Scientific Director and Founder of Orla Protein Technologies was unable to attend but submitted an abstract on Interfacing Biology and Physical Science through Nanoscale Protein Engineering.

His abstract described how Molecular biology works at the nanoscale with most cellular processes depending on complexes of proteins, DNA, and membranes that have dimensions in the range 1-100nm.

In order to interface with biology any physical device should present biological components which are ordered on this scale. To achieve this control we must resort to bottom-up methods of manufacturing and this requires that the biological component displays self assembly.

All proteins self-assemble to form precise structures by the process of folding, but precise spatial arrangement needs additional control. Protein engineering can be applied to membrane proteins to create new tools for the formation of precise interfaces for biochips and cell culture. The use of membrane proteins to create self-assembling bio-interfaces has led to the establishment of a spin out company (Orla Protein Technologies). Orla technology provides unique expertise for addressing these challenges. Orla interfaces can present reproducible and precisely orientated molecules (for example enzymes, receptors, cell adhesion molecules) as single layers on surfaces by self assembly.
This provides a platform based on scaffold proteins capable of being engineered for any requirement. The technology also enables label-free translation of binding events into digital signals, giving flexibility in detection methods. The self-assembling protein layer was developed jointly by the groups of Prof Lakey and Prof Horst Vogel (of the L'Ecole Polytechnique Fédérale de Lausanne, EPFL) Lausanne, Switzerland. The combination of the robust bacterial proteins and the thiolipid technology developed by Professor Vogel creates a durable biomimetic layer.

**Recent Advances in Biosensors**

**Professor Christopher Lowe**

*Director, Institute of Biotechnology, University of Cambridge, UK*

Many extravagant claims have been made in the past two decades about the likely impact of sensor technology on the diagnostics industry: In reality, the market size in 2003 was <2% of the global diagnostics market. This presentation looks at the need for, and advantages of sensors, the technology that has been developed over the past two decades to address these perceived needs and the inherent problems with current approaches.

The talk will describe newer detection technologies, which may circumvent the problems, and suggests how they are likely to have a much more significant impact in the future, particularly in sectors such as point-of-care diagnostics, real-time monitoring, and emedicine.

**Cantilever-Based Sensing Devices for Diagnostics**

**Dr Anja Boisen**

*Assistant Research Professor, Department of Micro and Nanotechnology, Technical University of Denmark, Denmark*

A micrometer-sized cantilever can be used as a very sensitive, simple, and cheap biochemical sensor in ambient and aqueous environments. Detection of DNA hybridization as well as various types of protein recognition has for example been performed by this method. Basically, a biochemical reaction at the cantilever surface can be monitored as a bending of the cantilever, due to a change in the surface stress. Furthermore, highly sensitive mass detection can be achieved by using resonating nanocantilevers. We have developed cantilever-based sensors with integrated readout, which hold promises as fast and cheap ‘point of care’ devices. The detection technique involves no labelling of the molecules by fluorescent, magnetic, or radioactive markers and bulky detection schemes like laser scans, CCD imaging, or radiography are avoided.

For monitoring changes in surface stress we have developed various types of micromachined silicon based cantilever devices with integrated piezoresistive readout. Arrays of up to 10 cantilevers have been integrated in micro-channels offering a method to develop compact biosensors with a simple read-out scheme.
Recently we have realized cantilever sensors in the polymer SU-8, which is a negative resist with excellent mechanical, thermal and chemical properties. The use of polymer makes the fabrication process simple, cheap fast and flexible. Moreover, the polymer technology opens up for completely new ways of detecting cantilever bending, which can increase the sensitivity significantly. We are currently pursuing hybrid system integration, where the sensor unit is packaged for specific handheld sensor applications in diagnostics.

For mass detection we have realized silicon-based nanocantilevers with integrated capacitive read-out and electrostatic actuations. Due to problems with high stray capacitances the sensor is monolithically integrated with a CMOS chip for on-chip amplification of the signal. The sensor has been used for detection of mass changes caused by controlled deposition of glycerine droplets and from these experiments a mass resolution of 3 ag/Hz has been deduced.

(The presentation made at the conference is available on the Proceedings CDROM)

**Requirements and Benefits of a High Resolution Imaging Strategy**

*Dr Karsten Kottig*

*Evotec Technologies, Germany*

The spatial organization of cells and tissue delivers a wealth of information of the scientist. Confocal fluorescence microscopy can reveal molecular interaction in the nanometre range by various approaches, such as FIDA, FRET, and others. Modern automated equipment for microscopy offers a throughput of 100 000 samples per day with extremely high resolution, enabling for systematic library approaches instead of single point measurements. Screening genome wide siRNA libraries are just the most prominent example of such an approach. The presentation addresses the requirements for and the benefits of a high throughput and high resolution imaging strategy.
Drug & Gene Nano-Balls: Applications in Genomics, Proteomics, Diagnostics and Personalized Medicine

Professor Matt Trau

Director, Centre for Nanotechnology & Biomaterials, University of Queensland
Nanomics BioSystems Pty Limited, Australia

The recent completion of the human genome project has heralded a new era of molecular and genetic based medicine. Major opportunities include a plethora of new (personalized) treatments and early diagnoses for individuals suffering from a wide variety of illnesses such as cancer, diabetes, heart disease, autoimmune disease, as well as a wide range of infectious diseases such as SARS, West Nile virus, Dengue Fever and Bird Flu. A major stumbling block that inhibits the full utilization of genomic data generated from the human genome project is our current inability to conveniently and accurately read large amounts of biomolecular information, either intrinsically present within the cell (e.g., the DNA code), or continually produced by the cell (e.g., proteins, antibodies and other metabolites). Specifically, there is a lack of bio-sensing techniques to rapidly and accurately read low concentrations of biological mixtures that contain large libraries of compounds such as DNA, proteins, antibodies, peptides, polysaccharides or drug leads. Chip based technologies offer a possible solution, however are currently limited by high cost, poor accuracy and the restricted number of compounds (<105) that may be displayed on the two-dimensional surface of the chip. We shall present an alternative method, developed within our Centre1-8, of screening extremely large (>1010) compound libraries on extremely cheap platforms: encoded colloidal suspensions. The colloidal suspensions are produced via combinatorial chemistry procedures, however are optically encoded for rapid and unique recognition of each individual compound. Once encoded, these particles may be screened at rates of 30 000 – 100 000 compounds per second on a conventional flow cytometer. Potential applications include High Throughput Screening in the areas of Genomics, Proteomics, Drug Discovery, and Diagnostics.

References
Interfacing Biology and Physical Science through Nanoscale Protein Engineering

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Molecular biology works at the nanoscale with most cellular processes depending on complexes of proteins, DNA and membranes that have dimensions in the range 1-100 nm. In order to interface with biology any physical device should present biological components which are ordered on this scale. To achieve this control we must resort to bottom-up methods of manufacturing and this requires that the biological component displays self-assembly. All proteins self-assemble to form precise structures by the process of folding, but precise spatial arrangement needs additional control. I will present data showing how protein engineering can be applied to membrane proteins to create new tools for the formation of precise interfaces for biochips and cell culture.

The use of membrane proteins to create self-assembling bio-interfaces has led to the establishment of a spin out company (Orla Protein Technologies). Orla technology provides unique expertise for addressing these challenges. Orla interfaces can present reproducible and precisely orientated molecules (for example enzymes, receptors, cell adhesion molecules) as single layers on surfaces by self-assembly. This provides a platform based on scaffold proteins capable of being engineered for any requirement. The technology also enables label-free translation of binding events into digital signals, giving flexibility in detection methods. The self-assembling protein layer was developed jointly by the groups of Professor Lakey and Professor Horst Vogel (of the L'Ecole Polytechnique Fédérale de Lausanne, EPFL) Lausanne, Switzerland. The combination of the robust bacterial proteins and the thiolipid technology developed by Professor Vogel creates a durable biomimetic layer.

The technologies which have changed lives most in recent years have been the micro-technologies which enable the electronics and information revolution. Although biotechnology has advanced in its scientific prowess, its main effects upon our daily life are probably yet to come. One way in which this will occur is when medical analysis is fully integrated into the world of microelectronics. Thus instead of a computer running a diagnostics machine, the computer will be the diagnostics device with biological tests built into and benefiting from small scale reactions and sensing.

This development will require that the biological sensing event takes place on a micro/nanotech device. Sensing of this form requires selectivity at the biological level which requires molecular recognition afforded by proteins. The important events take place in an interfacial zone which is nanoscale in its depth and which is generally ignored in descriptions of nanobio devices.
This is not just surface chemistry since the surface proteins are themselves flexible and fragile topological features which have three dimensional structures on the one to ten nanometre scale.

DNA array technology has revolutionized the analysis of genetic information but these generally rely upon interactions of surface bound and soluble single stranded DNA (both unfolded) which combine to form robust double helical strands. Hence there is no requirement to reserve a complex three dimensional structure. Protein interactions offer us the possibility of directly measuring the presence of active molecules in cell and tissue extracts. Proteins, the active molecules of life, show specific interactions with other proteins, drugs, hormones, sugars etc by virtue of complex interactions involving charge, hydrophobicity and surface complementarity. By bringing proteins to the nanoscale interface, between existing physical technologies and medicine, we can create a new mould breaking technology which will assist medical diagnosis, treatment and disease monitoring. The latter is important, diagnostics have been a great aid to disease state identification but with increasing emphasis upon disease management and age related infirmities low cost, rapid and IT integrated disease monitoring is likely to be a significant growth area in future.

![Figure 1. Membrane proteins (cyan) embedded in a 4nm thick bilayer of polar lipids](image)

Proteins are largely soluble molecules with about 30% being considered to be membrane bound and therefore water insoluble. However it is this minority that are designed to act at ‘the interface’ being held in a 5nm-thick self assembling layer of polar lipids, the membrane, which provide a hydrophobic interior that matches hydrophobic bands on the membrane proteins See Figure 1.

Thus the membrane provides a 2 dimensional lattice environment in which the proteins are inserted in a defined orientation. Thus membrane proteins are suited to being applied to the interface if the supporting lipids can be added as well. This has been solved in many cases and the methods are reviewed in [1]. The most effective method is to immobilize a layer of polar lipids onto a thin gold surface (20nm thick) by gold sulphur chemistry. Sulphur atoms are incorporated into the ends of these ‘thio-lipids’ and thus they assemble with their polar head
groups attached to the gold surface. Addition of membrane lipids will now form a biological like membrane by self assembly and if membrane proteins are added they will adopt their correct position by self assembly. This is true bottom up nanotechnological construction\[^{2}\]. The structures produced are biomimetic in their fluidity but this also leads to a limited stability since the forces that maintain it are largely hydrophobic and in the absence of full covalent attachment the bilayer can degrade, especially if surfactant molecules are present.

A robust use of sulphur gold chemistry has been developed by employing thioalkanes rather than thiolipids. The molecules are like the thiolipids but contain a single hydrophobic chain terminated at one end by a thiol. (-SH). They assemble at gold surfaces and pack tightly due to their repetitive simple shape, and large van der Waals/hydrophobic interactions. These structures being wholly bonded to the gold surface are robust and form dense layers that fully isolate the gold surface from the aqueous layer above. The exposed methyl end of the thioalkane can be made to bear a range of molecular groups such as carboxyl, hydroxyl, amine, ethoxyl, sugars, DNA, peptides. These self assembled monolayers thus enable nanoscale molecular engineering of surfaces and have been the subject of almost countless articles since their initial description by Bain and Whitesides\[^{3}\].

Figure 2. Schematic of a thioalkane self assembled monolayer

In searching for a method to present proteins at the interface we wished to satisfy a series of constraints, these include fixed orientation, self assembly, direct gene to surface method involving little or no chemical processing of the proteins, low non specific binding, easy scale up and easy manufacturability. The latter is important, we wish to allow high tech companies which have bio ambitions but no bio expertise to incorporate biological components in their devices with the minimum of effort and production line modification.

The crucial step towards this was the seminal discovery by researchers from Jeremy Lakey’s group at Newcastle University and Horst Vogel’s group at the EPFL, Lausanne, Switzerland that bacterial outer membrane proteins could be assembled on gold surfaces and when co assembled with thiolipids were greatly stabilized. Bacterial outer membrane proteins may seem an unusual choice but they provide what is known as a protein engineering scaffold which allows multiple new structures to be designed into or around them. The foundation of a generic method for protein interface design had been discovered\[^{4}\].
Since then the stability and behaviour of the immobilized membrane proteins have been investigated by many methods including AFM and neutron reflection. In all cases the layers are revealed to be of folded and robust arrays of oriented membrane proteins\cite{5}. We have also developed the method of circular dichroism to analyze protein monolayers and now for the first time the structure of proteins on gold surfaces can be directly determined in aqueous solution\cite{6}.

Using the bacterial outer membrane protein OmpA we have created a range of proteins which endow gold surfaces with exciting new properties. In one example Z domains from antibody binding protein A were added and the OmpA part enabled this protein to assemble stably and clearly on a gold surface. Antibodies could then be bound to the protein-thiolipid layer to create antibody arrays with defined orientation, density and with low non specific binding. The advantage of gold is that it can be used directly in surface plasmon resonance methods which can record the binding of molecules to the surface. Thus it is possible to monitor both the assembly of the layers and their subsequent interactions with specific ligands in real time. This powerful approach has lead to an exciting collaboration with Cambridge Consultants Limited who have developed a unique surface imaging surface plasmon interferometer. This can detect the spatial distribution of binding events on a protein modified gold surface and can thus be used to directly interrogate protein bio-arrays in a label free manner. The read out is simple since it simply records the binding of mass to particular spots on the surface and above all it is label free. Label free means that we do not have to either pre-label the binding partner as is the case with fluorescence readers or label the bound complex with antibodies as is the case with ELISA. In essence the system can replace 10-50 ELISA assays with a single test that can be directly linked to a data management system. A multivariate diagnosis could be performed remotely.

To achieve this the interface is crucial and thus what the Orla technology does in the 5nm nearest the surface is critical for the success of the whole project. Binding must be strong and specific. The first is helped by our ability to present the protein targets as folded and complex entities. By using recombinant methods we can bring complete and folded protein modules to the surface whereas synthetic peptide approaches can only present peptide epitopes. By the combination of thiolipid and protein we can ensure that only the desired protein domains are ‘visible’ by the interacting partner and that the rest of the surface is highly resistant to non specific binding by the complex mixtures of samples which may be applied to it. The self assembling methodology ensures that the whole surface is under the control of the designer and no part, even at the sub Angstrom level, remains uncovered. A simple example can illustrate the point. The protein A molecule was modified in two different ways to create a pair of engineered proteins. One of these binds to the gold and presents an antibody epitope (FLAG™ epitope) to the exposed surface. The second has an identical epitope which is, however, exposed to the gold surface. Before addition of thiolipid both proteins offer antibody binding sites. After self -assembly of the lipid, only the epitope designed to be exposed at the
upper surface reacts with the antibody. There is no other system which presents proteins at surfaces that can offer this quality of precise design.

**Figure 3.** Surface imaging SPR of antibody binding. Two forms of OmpA are assembled in separate regions of the biochip. Each has an antibody binding epitope (FLAG) inserted where the yellow cross is drawn on the cartoon. Antibody is added to the two areas but binding only occurs where the epitope is exposed above the self assembled membrane layer. The distance between the two sites is about 3nm and confirms the nano scale assembly accuracy of the Orla system.

Finally, such a simple design for protein surface manufacture has, clearly, many other applications. The other which we are actively pursuing with commercial and academic partners is the design of bespoke surfaces for cell culture, particularly for primary cell lines and stem cells where control of differentiation state and growth is much more challenging than with robust laboratory cell lines. We can produce surfaces which provide the correct signals which the cells might obtain from other cells or components of the extracellular matrix, furthermore we can guarantee what is on the surface and that there are no components of animal origin. Mixtures of precisely engineered Orla protein which show significant advantages for several cell lines are in development but the power can be demonstrated by the simple RGD motif. This peptide sequence can influence the growth of many cells and here the standard laboratory fibroblast cell line was used.
A thin gold surface (20nm and thin enough to transit light for microscopy) was treated with a sport of RGD modified OmpA protein. The surface was then covered with thiolipid which covers the free gold around and between the protein molecules. Fibroblasts were cultures for 24h and the resulting growth shown. Whilst similar results have been published for synthetic peptide based self assembling systems, the Orla system can equally well present folded protein domains at the interface.

In summary the Orla systems can provide answers to protein immobilization demands in a wide variety of applications and offers a precise and simple way to bring biology to the physical interface.

Orla Protein Technologies Limited was an award winner at the 2002 Bioscience Business Plan Competition.

(The presentation made at the conference is available on the Proceedings CDROM)

Acknowledgements
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References
Nanoscale Devices for Proteomics and Drug Discovery

Dr Ahmet Senoglu

CEO, Nanoxis AB, Sweden

Nanotechnology offers a very broad stage on which the research community can play. Among other breakthroughs, nanometre-scale physics and chemistry has lead to the development of the smallest and fastest transistors and the strongest and lightest materials available today.

Nanoxis R&D team has been working extensively in the area of soft nanofabrication technologies. In particular, the group focuses on the development of nanofluidic networks based on surfactant membrane technology. This work has resulted in groundbreaking innovations, which have already proven useful in robust production of nanoscale networks with unique capabilities to transport and perform controlled chemistry on single molecules. Nanoxis’ concept is integration of nanotechnology into biotechnology, physiology, and biology, using materials with unique biomimetic and biocompatible properties. The products being developed are easy and safe to use and adaptable to suit a particular application. Nanoxis develops tools that fully integrate with the biological system being studied, i.e. they are often designed to be a part of it and have the capability to actively interact with the biological system. This concept includes biochips, chip-based biosensors, and nanomaterials relevant to the biochip or sensor functions, especially signalling and material transport pathways.

Nanoxis is determined to provide generic and optimized analysis tools for membrane proteins. The main mission of the company is to develop and introduce these innovations to the global research community and industry, creating a high intellectual and scientific impact in the research area as well as commercially competitive applications. The overall goal with the techniques is to provide researchers and industry with reliable, cheap, smart, and fast equipment, and products in order to increase throughput, performance, and information content in areas such as protein analysis (structure and function), single-molecule synthesis and analysis, and sensor applications. In addition, ‘material science’ development of soft materials integrated to electronics and optics lies within this mission.

(The presentation made at the conference is available on the Proceedings CDROM)
SESSION 6C – NANOPARTICLE RISK ASSESSMENT

Overview
In nanomedicine, risks seem to be associated only with some nanoparticles. The risk factor is also the source of the medical opportunity! For example, research is presently excited by the possibility of using fluorescent nanoparticles, called quantum dots, as unique disease markers, helping differentiate between malignant and non-malignant growths, and also in the detection and treatment of disease at the very earliest stage. However, the toxicity of these nanoparticles is incompletely understood, and work is needed to determine how these particles can be safely used in achieving important diagnostic and therapeutic goals. Europe is fortunate in having notable strengths in this area, but new research is needed both into modelling nanoparticle behaviour, and cell, rather than animal-based testing, as a way forward.

Assessment of health risks arising from exposure to chemicals or other substances requires understanding of the intrinsic toxicity of the substance, the levels of exposure (by inhalation, by ingestion or through the skin) that may occur and any relationship between exposure and health effects. Concerns about the lack of knowledge and possible risks arising from exposure to nanoparticles led the UK Government to request advice from the Royal Society and Royal Academy of Engineering and to the formation of their Nanoscience and Nanotechnology Working Group. Their report, published in July 2004 (www.nanotec.org.uk), makes wide ranging recommendations about the need for more and better information and for a coherent approach to these concerns.

All applications of nanotechnology to medicine must comply with a high level of health and safety considerations for the patient. The benefits and the risks from nanoparticles both relate to the increased chemical activity of particles at the nanoscale. Many aspects of nanomedicine rely on new nanoparticles (cancer therapy, imaging, and targeted drug delivery). Risk analysis will look at currently available information, and identify new research. A high level of public health, safety, environmental and consumer protection requires:

- Identification of safety concerns (both real and perceived) and action at the earliest stage
- Toxicological and ecotoxicological data and evaluation of human/environmental exposure
- Adjustment, if necessary, of risk assessment procedures for issues of nanotechnology
- Integration of risk assessment at all stages of the life cycle of the technology

This session explored the potential risks of nanoparticles, including levels of exposure, where and the kind of data that exists already, and the conclusions that can be drawn from earlier research; and where more work needs to be undertaken.
An Introduction to the Toxicology and Risk Assessment of Particles

Professor Ken Donaldson
Scientific Director, Centre for Inflammation Research (CIR), University of Edinburgh, UK

This talk sets the scene for the main talks in the session by discussing the basics of toxicology and risk assessment of particles. Using well-known harmful particles as examples I described:

- The role and methodology of toxicology in measuring hazard
- The ways that particle exposure is measured
- The use of hazard and exposure to determine risk and how risk can be managed so that people can work safely with particles

(The presentation made at the conference is available on the Proceedings CDROM)

Translocation and Cardiovascular Effects of Nanoparticles

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Nanomaterials: A Look Beyond Translocation of Nanoparticles

Nanoscience and its emerging nanotechnologies are expected to bring a fundamental change in manufacturing in the next few years and will have an enormous impact on Life Sciences, including drug delivery, diagnostics, nutraceuticals, and production of biomaterials. At the same time materials are being produced with new dimensions and properties, which may also affect their environmental distribution and impose new health hazards. Nanotechnology offers an attractive escape from current economical competition with Eastern Europe and China. It creates a high-added value, needs little material and will contribute to sustainable production. However, Nano is not that new and its primary property is that of enabling other technologies such as biotechnology, computing, drug delivery and imaging. EU expects a lot from Nano in its race to become the world most powerful player in high technology (EU, 2005). One of the most attractive features of Nanoscience is its converging power. Understanding Nano or working in Nanoscience requires an open alchemistic mind to be able to cross the traditional barriers between and within chemistry, physics, and biology. As an example, viruses may be considered as little (20-50nm) nano machines able to copy through our genetic machinery, which also consists of proteins and DNA in the nanorange. A DNA-polymerase reading a single DNA-strand can also be considered as a little nanoball rolling over a DNA-surface its direction driven by friction and little regular holes. It takes some imagination and guts to look with different eyes at existing theories. This offers opportunities for education of young professionals and researchers that are needed in the future.
Cardiovascular Effects of PM: Relevant for Nanoparticles?

Another fact is that for most newly manufactured NP no toxicity data are available (Royal Society, 2004). Most of the experimental, toxicological work on NP has been generated with a small set of bulk nanoparticles, such as carbon black (CB), titanium dioxide (TiO₂), iron oxides and amorphous silica. These NP have been manufactured by the chemicals industry for some decades and are produced in many tons per year.

For hazard characterization, risk assessment and future regulation of newly engineered materials several crucial questions need to be answered. One of these questions is whether particle translocation is an effect that needs to be taken serious with respect to the risk of particles to other organs than the place of deposition. The issue has come up to explain for the increased cardiovascular mortality, which is associated to PM exposure in the environment.

Exposure to particulate matter, and more specifically that induced by traffic, is well known to be associated to increased mortality in patients with cardiovascular disease (Peters et al, 2004; Pope et al, 2002). A increasing body of literature is being generated that suggests that PM exerts these effects either on the electrical activity of the heart leading to arrhythmias or on the blood supply to the heart leading to ischemia (Figure 1).

![Figure 1. Schematic description of different theories to explain for the cardiovascular mortality associated to exposure to Particulate Matter (PM)](image-url)
The well-established cardiovascular effects of PM have not yet been linked to the NP component in human epidemiological studies. However, experimental animal studies with combustion derived NP do show that high exposures to diesel soot NP or other surrogate NP causes observable cardiovascular effects (Donaldson et al, 2005). However these are invariably seen in experimental animals given high doses, often by instillation into the lungs or the blood.

Several toxicological studies have demonstrated that combustion and model NPs can gain access to the blood following inhalation or instillation and can enhance experimental thrombosis. Diesel particles instilled into hamster lungs also enhance thrombosis but it is not clear whether this was an effect of pulmonary inflammation or particles translocated to the blood. High exposures to DEP by inhalation caused altered heart rate in hypertensive rats interpreted as a direct effect of DEP on the pacemaker activity of the heart. Inflammation in distal sites has long been associated with destabilization of atheromatous plaques and instilled high doses of PM in Watanabe rabbits or Apo E -/- mice cause morphological evidence of atheromatous plaque destabilization. Ultrafine carbon black and carbon nanotubes instilled into the blood have been reported to induce platelet aggregation and prothrombotic changes.

**Translocation to the Brain: a Link to Cardiovascular Effects?**

It has recently been reported that different types of NP (gold, carbonaceous, MnO₂) can translocate from the nasal cavity through the olfactory epithelium along the olfactory nerves to the central nervous system (CNS) (Oberdorster et al, 2004). Such a mechanism was first reported for the polio virus (30nm) moving into the olfactory bulb of various primates. This is a mechanism specific for NP and it remains to be established whether this uptake is also associated with a specific effect. Recent animal studies have suggested that uptake in the brain is associated to induction of pro-inflammatory mediators.

However, it remains to be determined whether this uptake-distribution phenomenon leads to functional changes in humans and thereby poses a new qualitative hazard/risk combination for inhaled nanoparticles. We have taken up this challenge and performed a study with volunteers exposed for 1 hr to 300ug/m³ diesel exhaust particles (DEP) to investigate whether DEP caused changes in information processing in the brain. Information processing in the brain was measured by qualitative changes in the EEG-spectrum and quantified as relative and absolute changes in discrete frequency bands (between 0.5 and 30Hz). Our hypothesis is illustrated in the Figure 2 and suggests that heart rate variability maybe indirectly affected by changed information processing in the brain, induced by nanoparticle translocation. Data will be available early 2006.
Inhalation UFP → Translocation of NP → Irritant receptors → VR → HRV

**Figure 2.** Hypothetical association between translocation of Nanoparticles to the brain and effects on autonomous activity in the heart, usually assessed by heart rate variability (HRV)

(The presentation made at the conference is available on the Proceedings CDROM)

References


Nanoparticle Exposure – Risk Relationship between Exposure and Health Effects

Dr Rob Aitken
Director of Research, Institute of Occupational Medicine, UK

Assessment of health risks arising from exposure to chemicals or other substances including nanoparticles requires understanding of the intrinsic toxicity of the substance, the levels of exposure (by inhalation, by ingestion or through the skin) that may occur and the relationship between exposure and health effects. While some studies concerning the toxicity of newly emerging nanomaterials are now being published, little information has been published about the levels of exposure experienced by those involved in the development, manufacture and use of these materials. A major difficulty in assessing the exposure to nanoparticles has been the lack of good methods for the measurement of biologically relevant metrics such as surface area and information about the relationship between these measures and more common metrics such as mass or number. Management of the potential risks requires an integrated approach in which all of these aspects are considered and addressed.

Percutaneous Uptake of Nanoparticles: The NANODERM Project

Professor Tilman Butz
University of Leipzig, Germany

Objectives

- For the penetration studies we introduced new techniques which allow spatially resolved quantitative analysis of concentrations of ultra-fine particulate matter after percutaneous uptake. We used a combination of three methods:
  - Ion microscopy with the following detection modes: Particle Induced X-ray Emission (µ-PIXE); Scanning Transmission Ion Microscopy (STIM); secondary electron morphological images
  - Electron microscopy and High-Resolution Transmission Electron Microscopy
  - Autoradiography with radiolabelled nanoparticles
- Choice of skin samples:
  We consider transverse and sagittal cryo-sections of skin indispensable. We started with domestic pig skin which resembles human skin closest and later switched to human skin. We shall include psoriatic skin in our studies.
- Choice of ultra-fine particulates and transporters:
  We selected micronized TiO\textsubscript{2} with particle sizes of about 20 nm and various formulations including commercially available sunscreens.
The health impact is studied by the following methods:

- Laser Modulated Mass Spectrometry (LMMS) and Static Secondary Ion Mass Spectrometry (S-SIMS)
- We performed in-situ analysis of the skin response. In-vivo immune activity assays, proliferation, differentiation, and apoptosis assays are used
- We investigated the cellular response in-vitro on a few important cell types using modern laser fluorescence techniques and various markers (permeability, structure and integrity, proliferation, differentiation, apoptosis, allergen-specific antibody production)

Results
In the first two years of this project several different formulations containing ultra-fine TiO$_2$ particles were applied according to a standardized protocol to healthy porcine skin, human skin transplanted to SCID-mice, and healthy human skin with a focus on short exposure times. Thin and ultra-thin cross-section from biopsies were analysed by various laboratories with focused ion beams and transmission electron microscopy. The results of the ultra-structural analyses indicate that TiO$_2$ particles do not penetrate beyond the *stratum corneum*. In these experiments individual particles of typically 20 nm diameter are visible and usually agglomerate. High-resolution scanning transmission ion microscopy on freeze dried samples indicates that the spacing between individual galleries in the *stratum corneum disjunctum* in the electron microscopy samples may be enlarged compared to the native architecture due to preparation. Elemental maps obtained by particle induced X-ray emission yielded both a clear-cut delineation between the *stratum corneum* and the *stratum spinosum*. In many cases Ti was found only on top of the *stratum corneum* and inside the *stratum corneum*; typical penetration depths were limited to less than the full *stratum corneum* thickness. In some cases, Ti was found in deeper strata, e.g. the *stratum granulosum* and *spinosum*; however, in several cases these spots could be unambiguously identified as contaminations. In none of these cases a typical diffusion pathway was observed. These observations were corroborated by autoradiography using radiolabelled TiO$_2$ nanoparticles and nuclear microemulsions.

All results show that penetration is a result of mechanical action and not a diffusive process. Therefore, penetration and clearance kinetic studies are obsolete. Surprisingly, TiO$_2$ nanoparticles were found as deep as 400 µm in hair follicles. The investigation on SiO$_2$ nanoparticles in household products is cancelled because we expect the same penetration depth due to mechanical action and the minimum detection limits would be less favourable than for TiO$_2$. TiO$_2$ nanoparticles differentially, yet substantially affect the cellular processes of cell populations of human skin.
Benefits and Beneficiaries
A tentative conclusion at the present stage would be that TiO₂ particles do not penetrate into viable tissue under our experimental conditions. This holds true for porcine as well as for human skin. The only penetration throughout the entire stratum corneum with possible contact with vital tissue which we observed was likely to be related to micro lesions.

Future Actions
In the third year, experiments with healthy human skin will be completed and experiments with psoriatic skin will be carried out. Experiments with radiolabelled TiO₂ on healthy human skin explants will be continued. First results of static SIMS as well as in-vivo skin response and in-vitro cellular response experiments indicate that they are indispensable for the risk assessment. Following the advice from a member of the International Advisory Board we shall include a few tests with pigmentary (pharmaceutical) grade TiO₂ in our studies. First, the mechanical action on larger particles could be different; second, there is little information on the particle size distribution on pigmentary grade material, especially in the nanometre regime.

(The presentation made at the conference is available on the Proceedings CDROM)
The Central Nervous System as a Target for Inhaled Nanoparticles

Professor Günter Oberdörster
Professor of Environmental Medicine, University of Rochester, USA

The propensity of NP to translocate across cells, along neuronal pathways and distribute to lymph and blood circulation makes them uniquely suitable for therapeutic and diagnostic uses. Thus, one aspect of nanomedicine is the targeting of specific organs by using NP. However, this very mechanism exposes target organs to potential adverse effects (oxidative stress) due to subcellular distribution in sensitive target organs such as the CNS. Translocation pathways in the respiratory tract for inhaled insoluble nano-sized particles (<100 nm) along sensory neurons will be discussed, with special emphasis on the upper respiratory tract and the potential of delivery of nanomaterials to the CNS.

The neuronal pathway is contrasted with CNS delivery of blood-borne substances, and examples of the importance of particle size and solubility will be presented. Implications of species differences in respiratory tract anatomy, breathing pattern, and brain anatomy for extrapolation to humans of NP effects observed in rodents need to be considered. Although there are anecdotal data indicating a causal relationship between long-term ultrafine particle exposures in ambient air (e.g., traffic related), at the workplace (e.g., metal fumes), and neurotoxic effects in humans, more studies, experimental and toxicological, are needed to test the hypothesis that inhaled nano-sized particles cause neurodegenerative effects.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)

A Global Strategy for Safe Production and Use of Nanoparticles: NanoSAFE 2

Dr Frédéric Schuster
CEA, France

No paper available.
SESSION 7 – NANOMEDICINE, ETHICS, AND SOCIETY

Overview
Nanotechnologies are said to offer great promise for medicine, but much of this lies in the future. Nanomedicine, like any other technological advance, will pose its own set of ethical questions. Who will choose who receives new treatments? Will nanomedicine exacerbate the rich-poor divide? What are the ethics regarding enhanced physical performance for military or sports application?

Converging technologies – nanotechnology, biotechnology, and information technology combined with the cognitive sciences offer many opportunities for healthcare, and also raise ethical questions. Where is the line drawn between ‘learning’ prosthetics for providing an enhanced quality of life for the disabled, and ‘learning’ prosthetics for creating super humans?

In this session questions will be asked and discussed regarding the uncharted future which nanotechnologies may offer medicine. How society seeks answers to these emergent technologies will be of crucial importance, so that the right benefits may be achieved for humankind.

Session Report
Simone Scholze
Chief, Division of Ethics of Science and Technology, UNESCO, France

Nanotechnology is one of the most rapidly developing fields of technology with many promising applications in manufacturing, communication, but above all medicine and human health. Like any new technology, it raises ethical issues. The possible benefits and harms are increasingly discussed, as well as its implications for international relations in science and technology policies.

An early, informed interdisciplinary and public debate is essential for nanotechnology in order to maximize the benefits that can be expected from it. The failure to have this debate is to a large extent the cause of the criticism and public defiance encountered in other scientific advancements, for example with genetically modified organisms. This perception is even more sensible by the manifest influence of science fiction in current debate and public hype about nanotechnology.

Although nanomedicine does not exhaust the range of ethical issues of the various fields of nanotechnology, it represents the most important due to the direct implications to human lives. Medical research advancements that are usually related to nanotechnology, such as biochemical sensors, targeted drug delivery, molecular biotechnology, genetic engineering, neurophysiology, tissue engineering must be properly addressed aiming at differentiating real ethical challenges from imaginary worries.
The opportunities and risks of nanotechnology in products and applications that involve human health or that may affect the environment must be well pondered even from the international point of view. In this perspective, many issues require in-depth ethical, and not only scientific, consideration, such as:

- Risk analysis and standardization
- Research and development policies
- Ethical research in connection with legal issues
- Nanotechnology implications for development
- International cooperation and sharing of benefits

References

Through the Ethics of Science and Technology Research Programme, UNESCO has been carrying out anticipatory studies regarding the ethical and social impacts of nanotechnology and its applications. This is in line with the emphasis on anticipatory identification of ethical dimensions of new and emerging technologies undertaken by the UNESCO World Commission on the Ethics of Scientific Knowledge and Technology (COMEST) that could have considerable impact on all countries and that will require appropriate policy responses.

A multidisciplinary ad-hoc expert group on ethics and nanotechnology was established in 2005 in order to map the ethical dimensions of nanotechnology from a global perspective and to explore the respective implications for UNESCO Member States. The expected outcomes of this activity are:

- The elaboration of a UNESCO Policy Document on Ethics of Nanotechnology, comprising four kinds of actions: awareness raising, education, research and policy. This document will propose international actions to be undertaken by UNESCO.
- The publication of a book "Nanotechnologies: science, ethics and policy issues", in the "Ethics of science and technology" series of UNESCO, that will be translated in the six working languages (English, French, Spanish, Arabic, Russian and Chinese).

Finally, in order to raise awareness concerning ethical issues of nanotechnology to the public at large, UNESCO will also publish an informative brochure on nanotechnology and ethical issues.
Nanotechnologies Today and Tomorrow: Ethical Aspects

Professor Göran Hermerén
President, European Group on Ethics in Science and New Technologies, Brussels, Belgium

No paper available.

Dreams, Hopes, and Uncertainties in the Nano Revolution

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People who confuse science with technology tend to become confused about limits, they imagine that new knowledge always means new know-how; some even imagine that knowing everything would let us do anything.

(E.Drexler, 1986, Engines of Creation. The Coming Era of Nanotechnology, Anchor Books)

Abstract
Nanotechnologies are among the major emerging research areas whose social and ethical implications policy makers, scientists and engineers are considering more closely. Realizing that public perception may be at a tipping point, industries and government agencies are funding sociologists, philosophers and ethicists to study the public perception of nano.

Yet nanotechnology is not at all new, at least in human mind. I shall argue that the roots of the nano-revolution have to be found in the baroque period. The dream of the nano-revolution is embodied in the baroque science and in its fascination towards wonders.

I am aware that in placing the baroque period at the centre of my argument I am challenging the traditional approach to ethical and social implications of nanotechnology. Yet, as a psychoanalyst who has worked for years in technology ethics, I have always been particularly intrigued by the claim that the technological revolution has posed totally new questions.

But is this true? And if it is, in what way? Some of the knots in current technology ethics depend on the answers to this question.

Introduction
As a psychoanalyst who has worked for years in technology ethics, I have always been particularly interested in a claim which is often repeated, that is that the technological revolution has posed totally new ethical questions. But is this true? And if it is, in what way? Some of the knots in current technology ethics depend on the answers to this question.
My central argument is that nanotechnology – obviously as an ideal project - is not at all new. I shall argue that the nano dream stems from the baroque age and from its fascination and fear towards wonder and infinity\(^1\). Wonder and infinity – I would like to suggest – are two key words to understand the wider social implications of the nano revolution. I am aware that in placing the baroque period at the centre of my argument I am challenging traditional approaches to ethical and social implications of nanotechnology. There are, however, several good papers devoted to ethical, legal and social aspects of nanotechnology and some of them are being presented in this very conference. As far as I am concerned I just aim to provide a number of suggestions and raise a number of questions. If I succeed in doing this, I shall have achieved my goal.

**Nano Tales**

Human beings, states Blaise Pascal, who was the paradigm of baroque scientists - are suspended between two infinities: the infinite large and the infinite small. We are attracted and repelled by both, because in them we divine our destiny, without knowing whether that destiny is a destiny of eternal life or eternal nothing.

It has long been a dream of human beings to explore and eventually to manipulate infinity. For centuries mathematics have done the job. In XX century scientists have started to tempt to construct microscopic machines – motors, valves, sensors and computers – down at the molecular scale. They could be implanted into larger structures where they would carry out their invisible function. Such devices are now a reality and scientists, policy makers, industry people, and journalists have called nanotechnology the foundation for the ‘next industrial revolution’.

Together with enthusiasm there is also a lot of hyperbole and anxiety over nanotechnology accompanied by an over-perception of risk. Of course, legitimate ethical social issues do exist as usual. These include, for instance, privacy concerns, health risks from nanoparticles in the environment, human enhancement, and alienation from technology by those who distrust it. Society may amplify the perception of risks to the extent the public mistrusts scientists and government officials and has doubts over who controls benefits and dangers\(^2\).

Scientists, engineers, and government officials must confront head-on the ethical and societal implications of nanoscience and nanotechnology in order to keep the field from falling victim to the obstacles that have hampered progress in biotechnology.

Yet solid scientific assessment of risks in not enough. There's a real obligation on the part of the scientific, industrial and political communities to go more in depth in their understanding of people anxiety about nanotech.
The ability of societies to master technology shapes their destiny\cite{2}. Modern sociology and history of technology have conducted a powerful critique against the view that technologies develop according to an irresistible, internal technical logic. In a long series of articles and books, scholars have dismantled the perception of technology as driven by technical necessity alone in certain, predictable directions. Actually technology is a cultural product and, in its turn, it is a producer of culture. Technology is a social practice that embodies the capacity of societies to transform themselves. Technology implies the capacity to create and manipulate symbols and culture of a society. In other words behind any technology there is one or more narratives, which are somehow its ‘unconscious’.

I argue that one of the main narratives behind nanotechnology is fairy tales. Nanotechnology fairy tales started from the very beginning when in his oft-cited ‘Engines of Creation’, nanotech pioneer K Eric Drexler warned that "replicating assemblers and thinking machines pose basic threats to people and life on Earth" - threatening to turn everything on the planet into an amorphous ‘grey goo’. In 2000, Bill Joy, co-founder of the computer giant Sun Microsystems, wrote a chilling and widely read article warning that self-replicating nanomachines could eventually overwhelm the human race. Then came Michael Crichton’s "Prey" - where nanomachines run amok - and since many others.

The roots of the nano tale may be traced back to old fairy tales such as “Puss in Boots” or “Blue Bird” – at least in their essential features. Philip\cite{3} defines fairies as all kinds of magical beings who can take a human form. The trope of little people, pixies, small folks and other magic – sometimes mischievous – creatures living in parallel worlds or anyway hidden is a common trope in fairy tales\cite{4}. Also magic objects which serve their master - a child, a young girl or a boy – are a trope of fairy tales\cite{3}. Nano tales thus merge these two tropes.

Fairy tales are a baroque literary genre. The earliest published collections of fairy stories, in Italy, France, Germany, and Denmark begin in the sixteenth century. Yet the first important collection of fairy tales was transcribed in Italy in Neapolitan dialect by Giambattista Basile (c.1575-1632). Published posthumously in 1637, “Lo cunto de li cunti” (The Pentamerone, or The Story of Stories) is based upon traditional folk tales women told their children. The Pentamerone is typical in its expression of the Baroque age: action is lively, dramatic, bloody and full of complicated intrigue and wit. Then came Charles Perrault (1628-1703), a member of the French Academy, who published “Contes du temps passé” (Tales of Long Ago).

Both Basile and Perrault sought curatives for modern life in the fairy lore of the people; their tales were a way to help people to deal with uncertainty and novelty, with the new era that the Baroque age was opening\cite{3}.
The Baroque period is stylistically complex, even contradictory. In general the desire to evoke emotional states by appealing to the senses, often in dramatic ways, underlies its manifestations. A key feature of the Baroque age is an obsession with wonder and novelty. Even the fascination for infinity – that can be easily traced in mathematics, philosophy, religions, art, music, science, literature – can be subsumed under the love for wonders\cite{1}, in a typical mixture between pleasure and fair, which is another distinctive feature of Baroque.

**Wonder and Science**

I’m not certainly the first who notes that there is a number of similarities between our time and the Baroque age. We live – one can even say – in new baroque period. In particular there are impressive similarities in the way in which post modernity – or late modernity as some prefer to call our time – and Baroque deal with science and technology.

The most important feature shared by Baroque and Post Modernity is the importance given to wonder in science. There is no need to be an expert in mass communication, to appreciate that the science communication is nowadays largely based on wonder. What shapes public opinion is more the way in which scientific discoveries are presented to the public than their actual essence. In turn, the way in which the public is formed affects scientific research, both by influencing funding agencies and exerting psychological pressures on researchers, thus establishing a circle that can be either virtuous or vicious. Similarly baroque scientists, philosophers, artists were meant to surprise the readers, hearers, and spectators and thus helped to convey the impression of total novelty and originality, which mirrored a totally new world picture. The Italian Baroque poet Giambattista Marino expressed this principle in a memorable couplet\cite{5}:

\begin{align*}
E \text{ del poeta il fin la meraviglia [...]}
\end{align*}

\begin{align*}
Chi non sa far stupar, vada alla striglia!
\end{align*}

The increasing enrolment of physicians as gatekeepers in assessing reports of miracles both in Protestant and Catholic countries is another example of the strict connections between science and wonders in the Baroque period. More generally, wonder was important in the education of the elite. Since the mid-16th century the Jesuit colleges had been among the main pedagogical institutions. Wonder as a passion was skilfully deployed in Jesuit pedagogy and propaganda, for example in their enormously influential theatre with its characteristic use of machinery and spectacular devices. And it is difficult to overestimate contemporary perception of the Jesuits as some of the major suppliers and collectors of natural and artificial wonders in the seventeenth century, as their Society struggled to incorporate all the novelties and curiosities of nature into the Aristotelian framework of their ratio studiorum.

The Collegium Romanum where Kircher manufactured automata and explained natural wonders was an influential site of education as well as a must for travellers touring Italy\cite{11}.
As shown by Daston and Park[6] in their history of wonder, wonders have been never neutral in political, social, and ethical terms. Wonder in Baroque age was the mainstay of political practices. As masses of urban people became increasingly visible and politically active, sophisticated forms of control and manipulation were designed and implemented by the establishment. Complex choreographic apparatus in political ceremonies, trompe l’oeil in church frescos, extraordinary automata and powerful new weapons were meant to stir the wonder of people. Celebrated for the ingenuity of their authors, these wonders entertained the elite while seducing, ruling and controlling urban multitudes.

Post modernity is confronted with revolutionary and accelerated changes in science and technology that challenge in different ways some basic implicit and explicit moral assumptions and legal norms[7]. Scientists, policy makers, ‘journalists’ must help people to elaborate the change of their worldviews. Wonder is a key instrument to convey a new world picture through scientific communication. Of course wonder may also be a powerful tool for social control by only inspiring feelings of respect, fear and fascination[8]. Yet by exciting curiosity wonder may also promote a true public understanding of new technologies.

Conclusions
I would like to conclude with two remarks and one final consideration. Both remarks concern research on ethics and wider social implications of nanotechnologies:

1. My first remark concerns the importance of studying the collective imaginary that surrounds nanotechnology. Impact studies are certainly important but we also need to understand the way in which people ‘metabolize’ information. Different narratives are used to process information. Some of them trace back to the origin of the mental life. Like the myth and the legend, the fairy tale touches the most primitive parts of the psyche[9].

2. My second remark concerns the importance of letting people to elaborate their impact with nanotechnology. In a study conducted in the spring of 2004 by North Carolina State University[10] on the public’s perceptions about nanotechnology, people who have read Crichton’s novel Prey surprisingly showed a more positive attitude towards nanotechnology than those who did not read the novel. Tales are an important element to allow people to deal with complex and contradictory novelties. They allow to handle fears and to overcome them.

My final consideration concerns ethics and nanotechnology. History teaches that worrying overmuch about technological change rarely stops it. If we are concerned about ethical and social implications of nanotechnology, we would do better to form a clearer picture of how scientists and policy makers should communicate with the public[11] and, above all, we should refuse any temptation to reject popular narratives as naïve and misleading.
On the contrary popular narratives can give us the key to understand what is going on in public’s mind and they can be an important instrument to help people to elaborate fears and hopes.

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)

References
Can Nanotechnologies Make Humans Better? - Ethical Issues in Nano-medicine

Dr Donald Bruce

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Nanotechnology suffers from the gap in expectations between basic science which is mostly in its exploratory and discovery phase and the well publicized futuristic claims for its potential. Reality is so far more modest. This paper examines what are the real ethical issues likely to be posed by nanobiotechnologies. It asks first what (and whose) values or even world views are shaping and driving today’s research directions and ultimately tomorrow’s applications. It discusses whether these reflect the values, and the more sceptical mood, of wider European societies to which nanotechnology promises benefits. Where are there potential points of synergy or of conflict?

It examines look at some nanobiotechnology examples which bring established medical issues into sharper focus, like genetic information. ‘Lab-on-a-chip’ nanotechnology is hoped to enable rapid genome analysis in a family doctor’s surgery. But these may provide the patient who came with a simple cough with more disturbing information than she expected. Suppose the read-out, which quickly tells the doctor the anti-biotic that is best for her genomic group, also shows she carries a breast cancer gene? Should she be told, and when? Whom else should know – her family, insurance company, employer ...? Large amounts of pre-symptomatic, probabilistic information may not always be a good thing. Indeed, if other nano-devices enable us to monitor a wide array of functions of the human body, what do we now mean by a ‘well’ person? Would the particular functions read by the nano-sensors rightly interpret the complexity of human health? Nanotechnology aims to target the individual cells with therapeutic agents. The same precision which may enable needs to be handled with great care, so that it has the intended effect and not some precise but adverse consequence.

The paper also examines human enhancement. The goal of ‘making people better’ in medical care and treatment is universally accepted. But should we also seek to make ‘better humans’ by non-medical interventions enabled by the convergence of nanotechnology, biotechnology, cognitive and other fields of science? The paper asks about our assumptions of the nature of a human being. Should we let technological possibility define our future, as the transhumanists believe, or are there basic values we should be careful not to lose? The paper argues that functional improvement is misguided as too limited a vision of our humanity, as well as raising problems of social justice. This raises a wider question of social justice. In a world of great global inequity should the proclaimed potential of nanotechnology be aiming less at sunscreen and super-abilities for a few rich people than for more basic needs for the world’s poor?

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)
Nanomedicines and Biotechnology Pharmaceutical Research, Regulatory, and Ethical Implications

Dr Rogerio Gaspar

Laboratory of Pharmaceutical Technology, Faculty of Pharmacy, University of Coimbra, Portugal

No paper available.

(The presentation made at the conference is available on the Proceedings CDROM)
SESSION 8 – WHAT CAN WE DO AT INTERNATIONAL LEVEL?

Overview
Many countries of the world are making important advances in the area of nanomedicine. This session, the final one of the conference, examines international strategies in Europe, India, South Africa, China, Japan, and Russia. The US approach to nanomedicine specifically in cancer research was presented by Dr Mauro Ferrari in Session 3.

The aim of this session is to become better acquainted with international activities in nanotechnology, with the aim of avoiding duplication, and of identifying potential areas of collaboration across national boundaries.

The Case for Multinational Research Infrastructures
Hervé Pero
Head of Unit, Research Infrastructures, Structuring the ERA Directorate, Research Directorate-General, European Commission

Summary
The ability of Europe’s research teams to remain at the forefront of all fields of science and technology depends on their being supported by state-of-the-art infrastructures. In addition Research Infrastructures are key elements of ‘capacity building’ in Europe, from knowledge to innovation, from skills to strategic position. FP7 will continue supporting the development of a European approach with regard to research infrastructures, including computing and communication based e-infrastructures and virtual infrastructures. The carrying out of activities in this area at Union level can make a significant contribution to boosting European research potential and its exploitation, in particular in emerging fields such as nanotechnologies.

Definition of Research Infrastructures
The term ‘Research Infrastructures’ in the context of the Framework Programme refers to facilities, resources or services that are needed by the research community to conduct research in all scientific and technological fields. This definition covers major equipment used for research purpose, knowledge based resources such as collections, archives or structured information used in scientific research, enabling Information & Communication Technology-based infrastructures or any other entity of a unique nature that is used for scientific research.
Community Support to Research Infrastructures
A Community policy to support research infrastructures has been developed with success over consecutive Framework Programmes by financing, notably, the access of researchers to research infrastructure, the networking of infrastructures, joint research projects to improve performance, design studies for new infrastructures and support to the construction. Yearly budget is today around €180m.

Towards FP7
Research infrastructures play an increasing role in the advancement of knowledge and technology and their exploitation. The importance of such infrastructures is already well established in areas such as energy, space and particle physics and is increasing in other areas.

For example, radiation sources, data banks in genomics and data banks in social science, observatories for environmental and space sciences, systems of imaging or clean rooms for the study and development of new materials or nano-electronics, are at the core of research. The main challenge is to continue developing RIs of European interest through the creation of a ‘real’ European policy on Research Infrastructures, allowing:

- Elaborating visions and roadmaps for the future
- Optimizing the networks and the use of current RIs
- Supporting the construction and operation of RIs of priority EU interest

While Member States’ role will remain central in the development and financing of infrastructures, the Community can and should play a catalysing and leveraging role by helping to ensure wider and more efficient access to, and use of, the infrastructures existing in the different Member States, by stimulating the development of these infrastructures, and their networking, in a coordinated way and by fostering the emergence of new research infrastructures of pan-European interest in the medium to long term. In this respect, the European Strategy Forum on Research Infrastructures (ESFRI) plays a key role in identifying needs and a roadmap for European research infrastructures.

The main activities under FP7 will be:

- For existing research infrastructures: (1) Transnational Access: to ensure effective use by researchers, of the best infrastructures existing in Europe; (2) Integrating Activities: to structure better, on a European scale, the way RIs operate, in a given field, and promote their coherent use and development; (3) ICT based e-infrastructures: to foster the development and evolution of high-capacity and high-performance communication and grid infrastructures
For new research infrastructures: (4) Design studies: to promote the creation of new research infrastructures by funding feasibility studies; (5) Construction of new infrastructures (or major upgrades of existing ones): to promote the creation of new research infrastructures

For support to policy making and international cooperation: (6) Support measures

Some activities will be implemented through ‘bottom-up’ calls for proposals open to all fields of sciences and technology, whereas targeted calls will be launched for priority domains in close cooperation with activities taking place in thematic areas such as the research for nanotechnologies.

The support to construction will be developed on the basis of the ESFRI roadmap, i.e. on a ‘top-down’ approach. In this context, an efficient coordination of the different financial instruments will be ensured for an effective implementation.

Financial plans would include, in variable proportions and variable stages, several sources and kinds of funding: private funding; national funding; support from the Framework Programme; contributions from other EU sources, such as the Structural Funds and the European Investment Bank (EIB).

(An updated version of the presentation made at the conference is available on the Proceedings CDROM)

**Nanoscience and Technology Initiatives in India**

*Professor Venkatesh Rao Aiyagari*

*Head, Science and Engineering Research Council, Department of Science and Technology, Government of India, India*

India needs trained professionals who are able to exploit emerging opportunities in the ‘omnipotent’ field of Nanotechnology. Introduced in Richard Feynman’s famous 1959 speech, in which the physicist suggested that machines could be developed with atomic precision, Nanotechnology is now creating waves in the sphere of scientific research and beyond. It is being talked about in superlative terms. Like any new thing, it is being touted as the technology of the future even as sceptics express their concern over the huge hype. But going by what researchers working in this area say, Nanotechnology has immense potential to create better products, new markets and more jobs. Multinational corporations including pharmaceutical companies are investing in Nanotechnology research. Countries like the US and Germany have reportedly committed millions of dollars towards Nanotechnology research.

India, too, is gearing up to face the challenge. Nanotechnology is an interdisciplinary area that includes the principles of Physics, Chemistry, Biology, as well as Engineering. In this, scientists view an object on the nano-scale at which the properties of the element change. Recently, the government announced the launch of the Nanomaterials Science & Technology Initiative.
The intent of introducing the scheme was not to miss the nanotech bus. The objective of the initiative was to "spread the base of research in Nanotechnology" in academic institutes and research organizations.

The programme is focused on the overall research and development in Nanoscience and Nanotechnology so that India can become a significant player in the area and contribute to the development of new technologies besides carrying out basic research. The government plans to fulfil its objectives through supporting scientists in their R&D projects. DST boasts of having sponsored more than seventy projects across various areas of Nanoscience and nanotechnology including nanofabrication, nanolithography, DNA chips, nanocomposites, and molecular electronics taken up in various national institutes, labs, universities, and colleges. Nanotechnology can have wide-ranging applications in various areas such as in medicine, chemicals, electronics, and Information Technology. It can be employed in drug delivery and manufacturing tinier chips, smaller and faster machines, amongst other things.

DST has established Centres of Excellence at IIT Kanpur, IIT Madras, the National Chemical Laboratory in Pune, the Indian Institute of Science in Bangalore, the Jawaharlal Nehru Centre for Advanced Scientific Research in Bangalore, the S N Bose National Centre for Basic Sciences in Kolkata, the Indian Association for the Cultivation of Science in Kolkata, the Banaras Hindu University and the University of Pune. These institutions will serve as core facilities which scientists from nearby areas can also use. In addition to these, research in Nanotechnology is going on at institutions like the DRDO labs, University of Hyderabad and Anna University.

Moreover, the country needs trained professionals who are able to exploit emerging opportunities in this ‘omnipotent field’. The country may have high calibre scientists who possess the know-how in the field of Nanoscience but the younger generation of researchers has to be trained.

The odyssey is yet to begin in India.

(The presentation made at the conference is available on the Proceedings CDROM)
Nanosciences and Nanotechnology in South Africa: Challenges and Opportunities

Dr Molefi Mokutu

General Manager, Research and Development, Mintek, Council for Mineral Technology, South Africa

The latest developments and strategies in Nanosciences & Nanotechnology and the possible impact of these initiatives on the socio-economic development of South Africa will be discussed, with emphasis on those activities in nanobio, medicine, and health. The opportunities and challenges facing South African nanosciences and nanotechnology community will also be discussed in a broader framework of the national science, engineering, and technology (SET) system.

With the advent of democracy, the new South African government was faced with many challenges; which included the delivery of services and improvement of the quality of life for ALL citizens, poverty alleviation and transformation, economic growth and wealth creation, and the establishment of new technology missions that were aligned with the new dispensation. Key and critical national economic and social objectives included interventions in the areas of health, water and sanitation, food security and agriculture, education, technology and energy. Mastery and integration of modern technologies, including nanosciences and nanotechnology, into the social and economic activities, education, governance, and delivery of basic and essential services such as health was recognized as paramount to the sustainability of the economy. However, technology diffusion to all sectors of the society as well as translating research and developments outputs into creation of new products, processes, and services is still a major challenge.

In addition to economic and social changes in the country, South Africa also witnessed a significant reduction in R&D investment and performance by the private sector. Globalization also exposed inadequacies in the protection of the intellectual property legislation and infrastructure, which resulted in inventions and innovations from publicly funded research and development not effectively being protected and managed. Small, medium and micro enterprises (SMME) have largely not being participating and benefiting from R&D activities and the emergence of new high-tech businesses has been slow in coming.

Human resources for science and technology, including nanosciences and nanotechnology, are not being adequately developed and renewed. There is a dire need to produce critical mass of scientists, engineers and technologies in nanosciences and nanotechnology-related fields. South Africa's current level of investment, about 0.81% of GDP, is significantly lower than it should be to ensure future national competitiveness. Increased competing priorities meant more money being directed by the new government towards other programs and less for scientific research and development.
By focusing basic science research activities, including nanosciences and nanotechnology, on areas that are directly relevant, critical as well as those that South Africa has a strategic natural and knowledge advantage has been rewarding. For example, to locally add value to the natural resources and leverage resource-based industries (mining and minerals, agriculture, energy production, fishing and forestry) as well as developing new knowledge based industries from them (i.e. mobilizing the power of existing sectors) has served the country well. Equally important, was to focus on areas such as health were the country is adversely affected.

(The presentation made at the conference is available on the Proceedings CDROM)
Chinese Approach – Nanotechnology in Regenerative Medicine: Tracking Transplanted Stem Cells in the Primate and Human Brain Using Superparamagnetic Nanoparticles

Professor Jianhong Zhu¹, Xing Wu², Xuhei Wu², Feng Ge², Jun Liu², Liang Gao², Daoyin Gen², Liangfu Zhou², and Helen L Zhang³

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Abstract

Regeneration of damaged brain tissue with neural stem cells (NSCs) is a promising strategy for reversing the neurological deficits. Investigations of the stem cell therapy have required non-invasive analysis of the fate and the migration of the implanted NSCs. Superparamagnetic iron oxide nanoparticles (SPIOs) have been used to label cells ex vivo, providing researchers with the ability to monitor the migration of these cells with magnetic resonance imaging (MRI)²,⁴,¹⁰. A 34-year-old male patient suffered with open brain trauma in left temporal lobe in February 2004. During emergency operation, exposed brain debris among the hair and cranial fracture bone were collected and transported immediately to a laboratory dedicated to the cultures of NSCs. The day before implantation, co-incubation of Feridex IV and Effectene in serum-free medium led the contrast agent infusion into the cells to label NSCs. After harvesting, cells were diluted in patient’s cerebrospinal fluid, and autologously implanted at four points around damaged region, each point contained 40ul volumes of cell suspensions (5×10⁴/ul) with MRI guided stereo tactic technique. Imaging was achieved in gradient reflection echo (GRE) with TR/TE 200 ms/20 ms and a flip angle of 20° at 24 hour later and each 7 days after transplantation. The SPIO labelling of NSCs led to a markedly susceptibility change with powerful signal damping in T2-weighted MRI. It thus produces a strong contrast against the normal tissue background. The injection sites were visible as circular dark tissue areas on the first day after implantation, where no pronounced hypointense signals were found in the injection sites before implantation. The hypointense signal in the injection points faded during the follow-ups. From the first week, the implanted cells had accumulated and extended around the lesion, which intensified during the second and third week. The implanted cells massively populated the border zone of the damaged brain tissue and were localized in the injured tissue around the traumatic lesion, suggesting that NSCs migrating away from the primary implantation sites and gathered around the lesion. The method opens a variety of field for clinical investigation of the therapeutic potential of stem cell transplantation strategies.
Background
To determine the fate of transplanted cells, including their migration in vivo, cells are currently labelled ex vivo using a vital dye (e.g., a fluorochrome), a thymidine analogue (e.g., bromodeoxyuridine, BrdU), or a transfected gene (e.g., LacZ or green fluorescent protein, GFP), for later visualization using immunohistochemical procedures following invasive and irreversible tissue removal. The use of progenitor and stem cells in clinical studies will require a technique that can monitor their fate non-invasively and repeatedly, so as to take a momentary 'snapshot' assessment of the cellular bio-distribution. Magnetic resonance imaging (MRI) has the capabilities of non-invasive whole body in vivo imaging, with a resolution of 25-50 microns, approaching the resolution of single cells. For transplanted cells to be detectable by MR imaging, they need to be labelled with an MR contrast agent.

The ability to localize or track specific cell populations in vivo via MRI has been pursued intensively over the past decade. A number of different contrast agents have been developed, all predicated on loading cells with paramagnetic or superparamagnetic compounds. Initial techniques to facilitate endogenous cellular uptake of superparamagnetic iron oxide particles included targeting to the transferrin receptor via monoclonal antibodies, linking small dextran-coated fluorescent iron oxide particles (USPIO) to tat peptide or liposomal coating and then membrane fusion, but neither resulted in efficient enough uptake for in vivo tracking, and there was significant cellular toxicity or impact on critical cellular characteristics\textsuperscript{[16,17]}. Most recently, Bulte and co-workers\textsuperscript{[9]} have utilized a new contrast agent termed a magneto-dendrimer, suspending iron oxide particles within a dendrimer matrix that is efficiently taken up into cells and optimized for favourable magnetic properties for imaging; 50 000 neural stem cells labelled with these particles could be detected in vivo following injection into the rat brain and used to track migration of the cells for up to 6 weeks. Finally, mixing ultra-small iron oxide particles with common lipofection agents has enabled efficient labelling of stem cells and in vivo tracking in the brain\textsuperscript{[11,14]}. Labelling of the cultured cells with superparamagnetic iron oxide nanoparticles and the use of (SPIO) provide a non-invasive method for studying the fate of transplanted cells in vivo\textsuperscript{[7-9,15]}. Superparamagnetic contrast agents are formed by a superparamagnetic core, which is represented by iron oxide crystalline structures described by the general formula Fe\textsubscript{x}O\textsubscript{y}Mn\textsubscript{z}O, where M is a divalent metal ion (M=Fe\textsuperscript{2+}, Mn\textsuperscript{2+}). For the synthesis of the contrast agents, small crystals of magnetite Fe\textsubscript{x}O\textsubscript{y}FeO are predominantly used. During the preparation of the contrast agent, the crystals are covered by a macromolecular shell, formed by dextran, starch and polyol derivatives. In an applied magnetic field, SPIO particles create extremely large microscopic field gradients for dephasing nearby protons\textsuperscript{[7,15]}. This, in turn, dramatically shortens the nuclear magnetic resonance T\textsubscript{2} relaxation time, over and far beyond the usual dipole-dipole relaxation mechanism that affects both T\textsubscript{1} and T\textsubscript{2}. Owing to the predominant T\textsubscript{2} effect, these 'T\textsubscript{2} agents' usually create hypointense contrast on conventional spin-echo MR sequences, in particular when agglomerated within cells.
On gradient-echo images, where T₂ effects dominate, these (intracellular) particles induce an even larger hypointense contrast effect. This in turn leads to a ‘blooming effect’, that is, an amplification of signal changes. Given the greater sensitivity of MR imaging for detecting superparamagnetic nanoparticles, these contrast agents are a natural choice for labelling cells. Since 1999, much effort has focused on exploring efficient techniques for incorporating the SPIO nanoparticles within cells. Using transfection agents to incorporate magnetic nanoparticles is a promising approach for labelling cells. Liposome agents, dendrimers, poly-L-lysine [PLL] and protamine sulfate all can efficiently incorporate the SPIO or USPIO into cells, and have no significant toxicity to labelled cells[1-3,6,10,13,18]. Moreover, the combination of two commercially available, FDA-approved agents, ferumoxides and protamine sulfate, are used to effectively label a variety of cells without short or long-term effects on cell viability, proliferation, and differentiation[5-6]. Clinical experience with use of both agents should allow translation of this method from the experimental setting to clinical trials. We reported the feasibility to labelling human NSCs with SPIO and tracking NSCs after clinical transplantation with 3.0 Tesla MR.

**Methods and Materials**

*Isolation procedure of NSCs*

About 5-20g exposed brain tissues, which were contused and mixed with hair and blood in the cranial fracture bone and/or among the hair, were collected directly into cold DMEM-F-12-N2 Medium (Gibco) containing 20% FBS (PD-FBS; Cocalico Biologicals, Reamstown, PA) and rinsed five times. Because debris of brain tissue had lose of normal architecture it was difficult to distinguish sub-cortical structure from cortical structure, and usually mixed together. But in some cases, we obtained large piece of brain tissues, from which we distinguished cortex from sub-cortical structure. After resection and removal of pia and arachnoid tissues, specimens were minced into 50–300µm pieces with sterile scalpel blades, incubated in pre-warmed papain/DNase I solution (11.4U/ml papain; 10U/ml DNase; Sigma) for 30 minutes at 37°C. The tissue was then collected by centrifuging at 200×g, and their pellets were collected and rinsed once with DMEM-F-12-N2 containing 20% FBS to stop the enzymatic dissociation.

The resulting crude tissue homogenate plated into uncoated T75 flask with complete medium. The complete medium we used for NSC culture was mixture of 44ml of Neurobasal (NB) medium (Gibco), 5ml of foetal calf serum, 0.04 ml of gentamicin (Cellgro) and 0.5 ml of glutamine, 0.5 ml of B27 (Gibco), and supplemented with epidermal growth factor (EGF) (20ng/ml; Sigma) and fibroblast growth factor-2 (FGF2)(20ng/ml; Sigma). After plating, 50% of the medium was replaced, three times weekly. Non-adherent cells and debris from the removed supernatant were pelleted by centrifugation and re-introduced into the cultures together with the fresh medium.
After 7 days in culture, plates were agitated by sharp rapping with a marking pen and 100% of the culture medium and non-adherent material was removed, while the removed medium was centrifuged to pellet cell debris and non-adherent cells and to recover complete medium as supernatant. The pellet, containing the non-adherent fraction, was re-suspended in complete medium, and then transferred to a flask. After one week, the procedure was repeated, except that the non-adherent fraction was discarded. In this way, an additional population of cells was recovered from the non-adherent fraction. All the cells were eventually combined to form a single population of cultured cells.

At near confluence, cultures were passaged by lifting with a solution of Cell Dissociation Buffer (GIBCO) supplemented with trypsin. The cells were washed twice with PBS and plated in complete medium into an uncoated T75 flask. Thereafter, and at approximately one week intervals, cells were lifted and similarly plated into twice the surface area from which they were removed. After the cells had reached a confluent surface area of 600cm², and these cells were cultured for two weeks before immunocytochemical analysis, or differentiation and immunocytochemical analysis.

Labelling MSCs with SPIO by Lipofection
Labelling of the cells was achieved with the magnetic resonance contrast agent Feridex IV (Advanced Mag. Co. USA) consisting of superparamagnetic iron-oxide particles (SPIO). For this purpose, the lipofection technique, generally used for the infusion of DNA into cell nuclei, was applied by using the lipofection reagent Effectene (Qiagen, Valencia, California US), which is a unique non-liposomal lipid formulation designed to achieve high transfer efficiencies. Coincubation of Feridex IV (125ug/ml Fe) and Effectene (25ug/ml) in 5ml serum-free DMEM for 60 min led to the encapsulation of the contrast agent by Effectene, consequently facilitating the contrast agent infusion into the cells. The required concentration conditions included incubation of the cells with Effectene and Feridex IV for 24 h in the corresponding medium. After 72 hours, all cells were washed in phosphate buffered saline to remove any excess iron particles from the cell surface. The rat MSCs were co-labelled with 5µM BrdU (Sigma) 24 hours prior to transplantation.

Neural Progenitor Cell Transplantation
Prior to implantation, 5ml cerebrospinal fluid was aspirated through lumbar puncture to wash the neural progenitor cells harvested from the expansion cultures. The final concentration of the cells, suspended in cerebrospinal fluid, was about 50 000/ul. During the operative procedure, using local anaesthesia and MRI stereo tactic neurosurgical technique, we slowly advanced a needle to the injured area and injected seven samples, each sample contained 15ul volumes of cell suspensions.

MRI of Labelled Cells
MR imaging of the brain was performed at 3.0 T (Signa, Echospeed; GE Medical Systems) by using a 3-inch receive only surface coil. Single sagittal, coronal, and transversal images were
obtained by a fast spin-echo sequence (repetition time msec/echo time msec, 3,000/45) for localizing, the subsequent T2-weighted transversal images measured by a multisection gradient echo sequence (200/20; flip angle, 20°). All images were obtained with a matrix size of 256×256 with two signals acquired, a section thickness of 1mm, and a 6–8cm field of view.

**Histology**

After incubation with Feridex-Effectene, cells were washed 3 times to remove excess Feridex-Effectene, trypsinized (adherent cells), and transferred to slides. Cells were fixed with 4% paraformaldehyde (PFA), washed, incubated for 20 to 30 minutes with 2% potassium ferrocyanide (Perl reagent for Prussian blue staining) in 3.7% hydrochloric acid, washed again, and counterstained with neutral red.

**Electron Microscopy**

One million cells were initially fixed with 1.25% glutaraldehyde in 0.1 M cacodylate buffer (containing 0.1 M sodium cacodylate trihydrate, 0.4mL hydrochloric acid, and 0.05%, calcium chloride at a pH of 7.4 for a total of 1 L) at 4°C overnight. After washing in Sabatini solution (0.1 M cacodylate buffer containing sucrose and calcium chloride) the cells were post-fixed in 1% osmium tetroxide, dehydrated through ascending alcohol and propylene oxide, and embedded in SCI Poxy 812 (Energy Beam Sciences, Agawam, MA). Ultra thin sections were cut with a Leica Ultracut UCT, stained with uranyl acetate and lead citrate, and examined with a JEOL 1200 EXII transmission electron microscope.

**Results and Discussion**

A 34-year-old male patient suffered with open brain trauma in left temporal lobe in February 2004. During emergency operation, exposed brain debris among the hair and cranial fracture bone were collected and transported immediately to a laboratory dedicated to the cultures of NSCs. The GCS of the patient was 11 before operation, had no evidence for malignant diseases, infections in the transplantation locus, a history of leucopoenia, thrombocytopenia, or hepatic or renal dysfunction, or unwillingness to participate. The ethics review board of the Huashan Hospital of the Fudan University of Shanghai, China, approved the protocol, and the study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from the patient.

The day before implantation, coincubation of Feridex IV (a contrast agent based on dextrancoated SPIO) and Effectene (a lipofection reagent) in serum free medium for 60 min led the contrast agent infusion into the cells to label NSCs. 24 hour and 7 day after labelling with SPIO, iron oxide nanoparticles labelled NSCs were stained blue to dark-blue dots by Prussian blue. Transmission electron microphotograph showing a cluster of iron nanoparticles located in the close vicinity of the Golgi apparatus nuclear and cell membrane, confirming the presence of iron inside the cell.
After harvesting, cells were diluted in patient’s cerebrospinal fluid, and autologously implanted at four points around damaged region, each point contained 40 ul volumes of cell suspensions (5x10^4/ul) with MRI guided stereotactic technique. Imaging was achieved in gradient reflection echo (GRE) with TR/TE 200 ms/20 ms and a flip angle of 20° at 24 hour later and each 7 days after transplantation, with a MR imager. The patient grafted SPIO labelled NSCs were examined weekly for a period of 3 weeks post-transplantation with an MR imager (Signa 3.0T, GE Medical Systems). The SPIO labelling of NPCs led to a markedly susceptibility change with powerful signal damping in T2-weighted MRI. It thus produces a strong contrast against the normal tissue background. The injection sites were visible as circular dark tissue areas, where no hypointense signals were found there before implantation. The hypointense signal in the injection points decreased during the follow-ups.

One week after implantation, the implanted cells massively populated the border zone of the damaged brain tissue and were localized in the injured tissue around the traumatic lesion, suggesting a migration from the injection sites toward the lesion. The pronounced migration was intensified during the second and third weeks. The recognizable hypo-intense signals in implantation points were detected 24 hours later in T2-weighted MRI. The hypo-intense signals in the injection sites faded during the follow-ups. From the first week after implantation, hypo-intense signals accumulated and extended in the damaged areas where only slight hypo-intense signals were found before implantation, which intensified during the second and third week. It suggested that NSCs migrating away from the primary implantation sites and gathered around the lesion.

Meanwhile, a 42-year-old male patient suffered with open brain trauma in right temporal lobe was implanted NSCs without SPIO labelling as a control case. No pronounced hypo-intense signals appeared around the lesion after NSCs implantation in the control patient, except from slight hypo-intense signals along the injection sites. During the observation period, the hypo-intense signals had no significant changes.

Feridex IV, dextran-coated SPIO nanoparticles, are MR contrast agents approved by the Food and Drug Administration (FDA) for use in hepatic reticuloendothelial cell imaging and in cancer imaging[12]. Our study first demonstrates that MRI techniques with 3 Tesla clinical scanner can be used to monitor the migration and viability of implanted NPCs in brain traumatic patient. NSCs can be labelled in vitro by Feridex and remain viable in culture. The MRI technique can thus provide information about the migration of the implanted cells. And it also provide information about the vitality of labelled cells because contrast released from lysed cells or freely injected into striatum led to rapidly dissipate MRI contrast with the contrast agent diffusing radially through the extracellular space.

Such a dynamic contrast pattern was not observed after implantation of labelled cells[14]. The SPIO-labelling NSCs implanted patient had no seizure, fever and deterioration of neurological function after progenitor cell implantation.
In addition, injection of progenitor cells did not induce an acute inflammatory response as measured by leukocyte blood count. Thus, the expansion and labelling of NSCs with SPIO followed by re-implantation appears to be safe for clinical application. The method opens a variety of field for clinical investigation of the therapeutic potential of cellular replacement strategies.

**Conclusions**

The MRI technique can provide information about the migration of the implanted cells. The method opens a variety of field for clinical investigation of the therapeutic potential of cellular replacement strategies.

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**References**


Nanobiotechnology and Nanomedicine in Japan
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Many Japanese scientists believe that nanotechnology is a key driving force of science in the 21st century. Nanotechnology is now expected to apply for the biology and medicine in Japan. In this presentation, the current topics of nano-biotechnology and nano-medicine in Japan were introduced. There are many studies for nano-biotechnology and nano-medicine in Japan. In this presentation, I focused on drug delivery system (DDS), nano-medicine, microfluidic based nano-bioanalysis, and cell sheet technology.

The Japanese government focuses on four fields, which are life science, Information & communication, Environment and nanotechnology & materials science. In 2002, budget for nanotechnology & materials science was about $713m, and in 2004, about $783m. Budget scale of life science is five times bigger that that of nanotechnology. Total Budget for nanotechnology and materials in Japan is almost same to that in USA. Total science budget of USA is ten times much bigger than Japan. That means the rate of budget for nanotechnology in Japan is much bigger than that of USA. However, number of papers from Japan is ten times less than USA and five times less than EU. The numbers of Japanese patents also are few in comparison with the United States and EU.

There are two big projects concerning with DDS in Japan, one of them, ‘Material development for innovative nano DDS’. Research groups of the National Institute for Materials Science are developing base materials for DDS utilizing material nano-technology in collaboration with universities including the University of Tokyo. The aims of the research are to establish innovative materials technology and to contribute to the progress of medical engineering, thereby realizing effective therapy for intractable diseases including diabetes, cancer and viral diseases. There are many big projects of nano-medicine in Japan such as ‘Development of artificial organs utilizing with nanotechnology and materials science’. In this project, the target is development of biocompatible materials and materials for artificial organs utilizing the outstanding from the fusion of nano- and bio-technologies.

Finally, I have introduced CREST project Nano-Tissue Engineering Toward Next Generation Biosensors. In this project, using polymer science, biotechnology, micro fabrication technology, and sensing technology, cellular arrays and microfluidic channels will be developed and then these technologies will apply for next generation biosensors for medical and pharmaceutical usage. The microfluidic based nano-bioanalysis and cell sheet technology have been introduced. We have developed sensor cells which transfected fusion plasmids of HSP70B’ gene promoter and luciferase or GFP genes to human and animal cell lines. These sensor cells could detect cellular stress, such as cytotoxicity of CdCl2. These sensor cells have significant advantages for the detection of cytotoxicity in terms of both speed and sensitivity. These sensor cells can be cultured in laminar flow, and detect cytotoxicity of CdCl2.
Nano(Bio)Technology for Medicine in Russia

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This paper deals with the state of the art of nanobiotechnology in Russia. The most perspective directions of medical nanobiotechnology based on the AFM molecular detectors as well as on the express optical and electrochemical detectors are analysed.

Introduction

In analyzing the perspective nanotechnological research directions, the following can possibly be highlighted as most important: nanomaterials, nanobiotechnology, and nanoelectronics. In Russia, special attention is given to nanobiotechnology, in particular, to its medically-oriented branch. At present, seven research directions dealing with medical nanotechnology may be singled out:

- Nanoanalytical proteomics: AFM as a tool for medical proteomics and diagnostics of infectious diseases and cancer
- Biosensor nano diagnostics
- Nanoparticles as containers for drug delivery
- Nanoparticles as drugs
- Nanorobots for medical applications
- DNA based synthetic genomes as self-multiplied systems
- Nanotechnology in regenerative medicine (tissue engineering)

Given below is a brief review of those directions that are being developed in the Institute of Biomedical Chemistry, RAMS (Moscow) – a leader in nanobiotechnological research in Russia.

Nanoanalytical Proteomics: AFM as a Tool for Medical Proteomics and Diagnostics of Infectious Diseases and Cancer

The major problem of the present-day proteomics lies in the lack of a reaction similar to PCR; hence the impossibility of multiplying various protein molecules, which in turn makes it impossible to enhance the concentrations of assayed biological material. Thus, there is a methodological barrier in proteomics: protein molecules with concentrations below 10^{-12} M cannot be identified in biological material\(^1\). Of note, the protein identification method based on a combination of 2D electrophoresis or chromatography with mass spectrometry has a sensitivity of 10^{-9}-10^{-12} M\(^1\). The sensitivity of immunoenzyme methods (ELISA, RIA) is 10^{-12}-10^{-15} M.
However, it is the concentration range starting from $10^{-15}$ M downwards that is most interesting from the biomedical viewpoint. Thus, for those tissue proteins, whose concentrations upon their leakage into plasma are lowered manifold, the required limit of diagnostic sensitivity lies in subfemtomolar concentrations. The latest nanotechnological achievements allow such problems to be effectively solved\[^2\]. Atomic force microscopy (AFM) appears to be one of the most perspective diagnostic tools. AFM enables not only to measure protein concentrations but also to literally count single proteins/viruses. Therefore the AFM-based nanotechnological methods have been adapted for use in medical proteomics and the AFM-biochips for disease diagnostics have been fabricated. The scanning AFM\[^3\] registers the force of interaction between the probe tip of the cantilever and the surface of the sample immobilized onto the atomically smooth support.

The commonly adopted measurement scheme is based on the monitoring of the cantilever’s deviation upon scanning the biomolecular surface with the probe tip of the microscope. The deviation is registered with the aid of an optical system including a position-sensitive photodiode. Interesting results were obtained in our AFM studies of the complicated water-soluble cytochrome P450cam monooxygenase system involving three proteins - cytochrome P450cam, putidaredoxin (Pd), and putidaredoxin reductase (PdR)\[^4\]. The AFM was demonstrated to reveal binary and ternary complexes of these partner proteins in multi-component systems and to distinguish, in these systems, the binary from the ternary complexes - the latter finding being especially important for proteomic researches. We have undertaken to study the microsomal membrane-bound cytochrome P452B4 monooxygenase system involving three membrane proteins: cytochrome P4502B4, cytochrome P450 reductase, and cytochrome b5, in the presence of the detergent Emulgen 913; as a result, the binary and ternary complexes of partner proteins were revealed based on the increase of imaged objects’ heights following complex formation\[^5\].

The unique ability of the AFM technique to recognize individual proteins and their complexes may be used in important areas of medical diagnostics such as immunoanalysis. The analytical procedure involved, at the first step, covalent immobilization onto the support of one protein molecule, e.g. the antibody or antigen molecule, for the fabrication of AFM-biochip. This support was then incubated in the biological fluid. With one of the partner proteins being immobilized, the formation of the antigen/antibody complex was registered.

In our study, the images of hepatitis C diagnostic markers (antibodies) to HCVcoreAg, anti-HCVcoreAg and to HCVcoreAg/anti-HCVcore complexes were taken. It was found that the heights of the complexes formed (3-4 nm) exceeded heights of the isolated antigen (1.5-2 nm) and antibody (2 nm) molecules (Figure 1). As was shown in our study, upon incubation of AFM-biochip (with immobilized anti-HCVcore) in serum, containing hepatitis C viruses, a number of new 10-35 nm objects emerged; these objects were lacking in the control negative serum in which the sizes of characteristic objects did not surpass 5 nm.
Figure 1. AFM images and cross sections for HCVcoreAg (A), anti-HCVcore (B) and for anti-HCVcore/HCVcoreAg complexes (C) on mica on air. AFM was a SOLVER P47H device (NT-MDT). Tapping mode. Experimental conditions: 1 µM (2µL) HCVcoreAg in PBS/T buffer (A), 1 µM (2µL) anti-HCVcore in PBS/T buffer (B) and the (1µM/1µM) anti-HCVcore/HCVcoreAg mixture in PBS/T (mixture volume, 2µL) (C), pH 7.4, were placed onto the AFM array, incubated for 2 min and rinsed in distilled water; t=25°C. The image area was 1x1 µm.

Analogously, by using the antibodies to HbsAg immobilized onto AFM-biochip, it became possible to fish out from serum the viral particles of hepatitis B with characteristic sizes 10-40nm.

Most promising for diagnostic purposes are nano arrays onto which in coordinate order various macromolecular probes for various diseases are deposited. The AFM nano arrays we have developed may be applied in immunoanalysis for the diagnostics of diseases accompanied by markers’ appearance – such as cancer, infections, and various disease states.
Biosensor Nanodiagnostics
Nanodiagnostics on the basis of optical and electrical biosensors are finding an increasing application. Two types of optical biosensors are presently used:

- Surface plasmon resonance biosensors and resonant mirror-based biosensors (SPR and RM biosensors, respectively). We have fabricated biochips to such biosensors- for use in the diagnostics of hepatitis B and C and of oncological diseases

- Compact disk-based biosensors; CDs are developed in the form of biochips and nano arrays

Two types of electrochemical detectors are presently used:

- Nanowire single-molecular detectors

- Electrochemical detectors containing nano gold particle-based cytochromes P-450

Let us describe the above devices in more detail.

**SPR and RM Biochips for the Diagnosis of Hepatitis and Cancer**
Optical biosensor (OB) techniques employing resonant nanostructures – surface plasmon resonance (SPR)[6] and resonant mirror (RM)[7] - take advantage, under total internal reflection conditions, of the evanescent wavelength as a probing element that registers refractive index changes occurring in the medium upon complex formation in the reaction zone located within several hundred nanometres from the sensor surface. Optical biosensor techniques enable complex formation of macromolecules to be registered with concentration sensitivity up to $10^{-12}$ M and with resolution time of about a few seconds, thereby providing the most convenient tools for studying macromolecules’ complex formation in real time, for measuring association/dissociation rate constants as well as for determination of thermodynamic parameters of protein-protein complex formation. Of note, the labelling of proteins is not required with application of OB technique, which is very important for solution of proteomic problems. The most commonly used commercial optical biosensors are the 4-channel SPR devices of the BIAcore type (Biosensor, Sweden) and the 2-channel RM biosensors of the IAsys+ type (Affinity Sensor, UK). Ligate, immobilized onto the biochip surface, is complementarily bound to its partner, e.g. protein. Increasing the surface concentration of a protein due to the ligand/ligate complex formation increases the refractive index in the sensitive layer adjacent to the sensor surface, which in turn leads to the change of the resonant angle position of the probing light. Such biosensors are capable of determining the surface concentration of the ligand bound to the sensor surface as a function of time.

It is accepted that a major problem of practical clinical medicine is one of optimum speed and precise diagnostics. It is by correct diagnosis that the effective treatment of patients (and even their life) is largely dependent. The biosensor fishing technique appears to be one of the most perspective diagnostic tools.
Based on this technique, we have created the biosensoric system of real-time registration of disease markers (e.g., the hepatitis B marker)\(^8\). Importantly, this system does not require special labelling of molecules. The hepatitis B (HB) marker in this system - HBsAg - was isolated from patient serum by use of a biochip. Employed as a biochip was the biosensor support with immobilized antibodies (anti-HBs). The association and dissociation rate constants for anti-HBs in this system had the following values: \(k_{on} = (6.3\pm1.5) \times 10^3 \text{ M}^{-1} \text{ c}^{-1}\), \(k_{off} = (0.20\pm0.16) \times 10^{-3} \text{ c}^{-1}\), and \(K_d = (3.2\pm2.6) \times 10^{-8} \text{ M}\). The HBsAg/anti-HBs complexes readily dissociated in 10mM HCl and thus the anti-HBs-containing biochips were re-usable. To test serum samples for the presence of HBsAg, the serum was loaded onto the OB biochip wherein the formation of complexes in the HBsAg-containing serum was registered by refractive index changes. For the registration of the complex dissociation, the serum was removed from the biochip and the standard phosphate buffer/Tween 20 (PBS/T) was added. Figure 2 presents typical curves of the biochip response to the addition of sera \(N^01\) and \(N^02\). One can see that the HBsAg/anti-HBs complexes were registered in serum \(N^01\) but not in serum \(N^02\). As was confirmed by ELISA, serum \(N^01\) contained HBsAg while serum \(N^02\) did not contain it. The advantage of the biosensor system as regards HBsAg revelation in sera lies in rapid (within 5-8 minutes) detection of the antigen and the repeated usage of the biochip.

![Figure 2. Detection of HBsAg in an IAsys optical biosensor aminosilane biochip. Anti-HBs is immobilized onto the biochip bottom. Serum S1 contains HBsAg while serum S2 does not contain HBsAg. The ordinate axis is the biosensor response which is proportional to the amount of bound HBsAg. The incubation mixture contained 54 µl PBS/T buffer, pH 7.4. T=25 C. Arrows indicate addition of 6 µl sera (S1 and S2) and replacement of the serum solution by PBS/T buffer.](image)

The same approach was taken by us in fabricating a biochip with immobilized HCVcoreAg. This biochip allowed us to detect anti- HCVcore in serum. Analogously, by using a biochip with immobilized antibodies to serum amiloid A (SAA), the presence of SAA in serum was registered (SAA is one of the markers for the early diagnosis of ovarian cancer\(^9\)).
In the course of our optical biosensor studies many protein pairs were investigated and kinetically characterized. Among such pairs are HBsAg/antibody, HCVcoreAg/antibody, insulin/antibody, alpha-fetoprotein/antibody, glycodeline/antibody, trypsin/inhibitor, chemotrypsin/inhibitor, and streptavidin/biotinilated oligonucleotide.

Compact Disk (CD) Biochips and Micro-or Nano Arrays

The devices termed ‘biosensors’ means those transforming the intermolecular interactions into the optical, electric, mechanical, and other signals. On compact disks biosensors the direct transformation of bimolecular interaction into the 2-bit code is carried out\textsuperscript{10}. The CD is read by measuring the change in reflection of a polarized infrared laser. As the laser beam travels through a CD, the binary system is generated by modulating the reflection of light according to its reflection from land or from lowered pits within an internal layer. When the beam hits a pit, the reflected light is destructively interfered by the incoming beam. The player reads 1 when the beam hits land - or 0 when the beam hits a pit (light is switched off by destructive interference). Standard writing onto a CD presupposes the availability of information allowing the CD-ROM to reveal and correct, by use of a special program, the numerous errors emerging upon contamination or damage of the disk surface. The CD-ROM performance makes it possible to estimate the state of the CD surface at any one of its points. The CD-ROM biosensor method is based on the analysis of errors made upon reading the information from the modified CD.

A standard CD-ROM reader to a PC with biochip disks serves as an analyzer. Biochip is a compact disk with a biomolecular monolayer immobilized onto it. Such a biolayer interferes with the optical transmission of the CD polycarbonate layer; as a result, first-level errors emerge upon reading by laser the digital data from the internal CD layer. By depositing onto the biochip of the sample containing partner biomolecules to the immobilized biolayer, the molecular complexes are formed, which leads to the increase in the number of reading errors due to the optical density changes occurring on the CD surface. The principle of complex revelation is based on registering these second-level errors. By comparing the distribution of second-level errors caused by complex formation with the distribution of first-level errors on the compact disk bearing an immobilized ligate protein, the number of complexes formed may be calculated. By using CD-ROM biosensor, successful registration of streptavidin/biotin complexes (Kd< 10\textsuperscript{-10} M) and of low-affinity concanavalin A/α-mannoside complexes (Kd = 10\textsuperscript{-4} M) was demonstrated\textsuperscript{10}.

Based on the CD-ROM biosensor we have developed a new diagnostic method. For this purpose the viral antibodies to viral antigens were immobilized onto the CD surface to fabricate CD-biochips for disease diagnostics. The biospecific fishing procedure based on reading of these standard CD-ROMs reveals specific virus particles in the biological sample by means of estimation of the increase in the number of errors that emerge upon formation of complexes with biolayers immobilized on the CD surface.
This nano diagnostic device has two major advantages: (a) it may be applied in very simple clinic-diagnostic laboratories without special equipment; (b) some of the diagnostic tests may be adapted so as to allow the user to make a home analysis.

**Electrochemical Biosensors - Nanowire Single-molecular Detectors**

In this device the changes in conductivity of semi conductive nanowires, modified by receptors upon receptor/ligand complex formation on the nanowire surface, are registered. The detectors have been created that feature a matrix of semi-conductive nanowires with receptors immobilized onto them – such as antigen or antibody probes\(^{[11]}\). Upon deposition onto a biochip of a biological fluid containing partner biomolecules, the specific biomolecular receptor/partner complexes are formed, and their formation changes the conductivity of nanowires. The registration of marker molecules is carried out in real time. The major advantage of such detection is the registration of formation of protein-protein and interoligonucleotide complexes in real time (without labelling of molecules) with high concentration sensitivity to single viral particles.

**Electrochemical Detectors Containing Nano Gold Particle-Based Cytochromes P-450**

Nanostructured electrochemical biosensor systems enable unique registration parameters to be achieved. The estimated limit of such systems, which were created in our institute, is 2-8 mM for aminopyrine and 0.1-1 mM for benzphetamine - with the sensitivity 0.01-0.5 \(\mu\text{A/mM}\). The estimated limit for cholesterol is 10-300 mM with the sensitivity 7-20 nA/\(\mu\text{M}\).

An electrochemical biosensor is a device of changeable type because its basic element is an electrode obtained by the print method supplied with a nanostructure support, containing an appropriate cytochrome P 450\(^{[12]}\). To facilitate the electronic transfer from the cathode to the enzyme's active centre gold nanoparticles were used. We have established the (bioreactor-generated) cholesterol concentration dependence of the current in this bioreactor, which was equipped with print electrodes in a combination with gold particles. The cholesterol concentration sensitivity of about 70 \(\mu\text{M}\) was attained\(^{[12]}\).

The multiplicity of cytochromes P450 allows us to plan the construction of nanostructured electrochemical biosensors for all classes of organic compounds - cytochrome P450 substrates. Taking into account that cytochromes P450 is a major enzyme of liver microsomes and that it performs the detoxicating function in the liver, the above-described enzyme electrodes may well replace the expensive animal studies on toxicity of new medicinal drugs; also, such electrodes may be used in pharmacokinetic investigations.

**Phospholipids as Nanoparticle Drugs and Drug Delivery Systems**

In the Institute of Biomedical Chemistry, RAMS, a new certified medicinal preparation Phosphogliv on the basis of phospholipid nanoparticles with the diameter < 50 nm has been created\(^{[13]}\). The phospholipid nanoparticles are formed by enlarging the phospholipid emulsion jet in the nozzle by use of a gas bomb with a pressure of 1 500 atm.
The preparation, designed for treatment of liver diseases of various aetiology, has successfully passed clinical tests and has shown high efficiency in treatment of patients with acute and chronic viral hepatitis A, B, and C and exists on Russian pharmaceutical market\[14\]. Upon clinical application, the phosphogliv preparation has produced an inhibitory effect on the replicative activity of hepatitis B and C viruses. Also, it has exerted a positive influence on immune interferon status due to the presence of glycyrrhizic acid in its composition. Phosphogliv has minimal toxicity, does not induce allergic reactions, and is stable in storage. The certified phospholipid nano system may be further used as a transport system for other medicinal drugs and gene constructs.

**Conclusion**

Thus, the priorities of medical nanobiotechnology in Russia involve:

- Elaboration of nano analytical proteomic technologies: AFM (that offers an ability to count single molecules/viruses) may be used as a tool for proteomics and for diagnostics of infectious diseases and cancer
- Creation of biosensor nanodiagnostics
- Usage of phospholipid nanoparticles as drugs and containers for drug delivery

These research areas are being intensively developed. The nano analytical proteomic technologies and biochips for disease diagnostics (i.e. the first two approaches) are at the stage of certification in Russia while the third approach, directly connected with treatment of patients, has been effectively realized in the form of commercially produced medicinal preparation Phosphogliv for use in treatment of liver diseases in Russia.

**Acknowledgements**

This work was supported by RFBR Grant #05-04-48690, by Scientific School Grant and by FASI contract 02 435 11 3010 on "Biosensor arrangement with direct detection for medical diagnostics".

**References**

2. THEMATIC WORKSHOPS

Workshop One - European Science Foundation (ESF) Forward Look

Monday 5 September 2005 11.00 – 13.30
Organized by Micro and Nanotechnology Network (MNT), UK
Chair: Professor Ruth Duncan
Co-chair: Julie Deacon (MNT Network)

The European Science Foundation prepared a foresight study on the topic of nanotechnology applied to medicine (Scientific Forward Look on Nanomedicine). The goal of this Forward Look was to exchange views on the current status of Nanomedicine between scientific experts and policy makers, and to reflect upon future developments, opportunities and challenges facing this important field in Europe and worldwide. Over 100 international experts from academia, industry, private foundations and governmental agencies supporting scientific research have contributed to this activity.

The ESF Forward Look on Nanomedicine has led to a definition of the current status of the field and debates on strategic policy issues. This workshop launched the full ESF Policy Paper, which summarizes recommendations from this Forward Look activity. Implementation of recommendations from the ESF Scientific Forward Look on Nanomedicine would strengthen Europe’s leading-edge research and ensure further development in Nanomedicine, resulting in reduced healthcare costs and the rapid realization of medical benefits for all European citizens. A summary of the outcome of this exercise can viewed in ESF Policy Briefing document No. 23 (2005) at www.esf.org

Workshop Programme

11:00 Introduction to ESF and NanoMedicine Forward Look
PROFESSOR CLEMENS SORG, Chair EMRC

11:15 Overview of ESF Nanomedicine Forward Look and Recommendations
PROFESSOR RUTH DUNCAN, Cardiff University, Steering Committee Chair ESF Forward Look on Nanomedicine

11:30 Analytical Techniques and Diagnostic Tools
DR JULIE DEACON, MNT Network

11:50 NanoImaging and Manipulation
DR ANDREAS BRIEL, Schering AG

12:10 Nanomaterials and Nanodevices
12:30  **Drug Delivery & Pharmaceutical Development**  
PROFESSOR RUTH DUNCAN, Cardiff University

12:50  **Clinical Applications and Toxicology**  
DR KEN DONALDSON, University of Edinburgh

13:10  Open Forum/Discussion  
All speakers

13:30  Closing Comments  
Networking Lunch

For further information contact Stephen Dennison at PERA, [steve.dennison@pera.com](mailto:steve.dennison@pera.com)
Workshop Two – Intellectual Property (IPR) Issues Affecting Nanoscience

Monday 5 September 2005 11.00 – 13.30

This workshop was uniquely jointly organized by three leading professional companies in the field of Intellectual Property:

- Hindle Lowther, Edinburgh
- Mewburn Ellis LLP, London
- WJM LLP, Glasgow

The workshop covered patent issues relevant to protecting nanotechnology inventions, with a particular focus of inventions with healthcare applications. Of interest to a wide audience, the presentation was directed in particular to start-up businesses and investors in such businesses as well as others interested to understand the role patents can play in supporting a nanotech business and the particular issues faced when seeking patents in this rapidly developing field.

Workshop Programme

11.00  Introduction and General Overview of the Roles Patents Play
Explaining the importance of patents to the nanotechnology & healthcare sectors and provide a summary of the roles patents can play. Also, a short overview of the key characteristics of patents and the requirements for obtaining them.

11.20  Patents in the Nanotechnology/Healthcare Space
Explaining what types of innovation can be protected in this space using patents, with practical examples to illustrate them. Also, looking at the special considerations when seeking to protect medical applications of nanotechnology.

12.00  Patent Strategy & Due Diligence
Addressing the importance of patents in this context and considering how best to match a patent strategy to the overall strategy of a business.

Whether an investor, a start-up business looking for investment or an established business looking to expand, it is important to understand the role patents play in supporting a developing business and to have strategies to get the most value from the available budget for patent protection.

12.40  Conclusions and Discussion

13.00  One-on-one clinics

13.30  Close
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Workshop Three - Royal Society and Royal Academy of Engineering Report, ‘Nanoscience and Nanotechnologies: Opportunities and Uncertainties’

Monday 5 September 2005 11.00 – 13.30
Organized by Micro and Nanotechnology Network (MNT), UK
Chair: Julie Deacon (MNT Network)
Co-chair: Stephen Dennison (MNT Network)

‘Nanoscience and nanotechnologies: opportunities and uncertainties’ - was published on 29 July 2004. The report illustrates the fact that nanotechnologies offer many benefits both now and in the future but that public debate is needed about their development. It also highlights the immediate need for research to address uncertainties about the health and environmental effects of nanoparticles – one small area of nanotechnologies.

The UK Government’s response to the joint Royal Society and Royal Academy of Engineering report was published on 25 February 2005. The response recognizes the importance of ensuring nanotechnologies are appropriately regulated and the Government has made an important commitment to a public dialogue on nanotechnologies which will inform both the direction of research and development and progress on regulation.

Workshop Programme

11:00  Introduction to Royal Society and Royal Academy of Engineering Report & its Recommendations
       JULIE DEACON, (MNT Network)

11:10  1. Current and Potential Uses of Nanoscience
       PROFESSOR JOHN RYAN

11:30  2. Health and Environmental Impacts
       PROFESSOR ANTHONY SEATON

11:50  The Government Response
       DR ADRIAN BUTT, OST

12:10  SNERK
       DR ROB AITKIN

12:30  Open Forum/Discussion
       Speakers and MNT Moderators

13:30  Closing Comments
       JULIE DEACON (MNT Network)

For further information please email: rs.MNT@pera.com
Workshop Four - Nanologue Project

Monday 5 September 2005 09.00 – 17.30
Organized by Nanologue, Germany

In its published Action Plan on Nanosciences and Nanotechnologies, the European Commission highlights the need to “respect ethical principles, integrate societal considerations into the R&D process at an early stage and encourage a dialogue with citizens.” (European Commission, 2005). The European Commission-funded project Nanologue addresses this demand. Led by the Wuppertal Institute, the Nanologue project brings together leading researchers, developers of NT-applications, businesses, and other stakeholders from across Europe to facilitate an international dialogue on the social, ethical and legal benefits as well as potential impacts of nanoscience and nanotechnologies (NT). Based on an intensive literature research and expert consultations, potential ethical, legal and social aspects (ELSA) have been identified on a general level as well as for three specific NT-application areas (energy, food, and medical diagnosis). Stakeholder workshops and interviews discussing these areas will contribute further to the positions identified and the outputs will be used to finally create three scenarios exploring future NT developments.

As well as informing the general public through media workshops, the Nanologue project aims to develop an easy to use and free-of-charge internet-based tool specifically addressing researchers and developers of NT-applications. The online-tool will facilitate the consideration of potentially critical ELSA for NT research and development projects at an early stage. For example, the tool is expected to help researchers applying for project funding to respond to requests for descriptions of societal implications of their projects and improve public acceptance of the research or development by considering ELSA right from the start. The findings of the project will also be used to inform political decision-makers, e.g. in the process of setting up research funds.

Following the literature analysis, the Nanologue project wished to identify the position of marketers, accommodators and users of nanotechnology with regard to social, ethical, and legal aspects (ELSA) of NT-applications by means of an individual telephone interview and a workshop. The interviews were held as part of the workshop and explored:

- The main findings of the Nanologue project so far
- The key ethical, legal and social aspects of nanotechnology applications
- Recommendations for the dialogue between Science, Civil Society, Business and the Consumer/Citizen

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Workshop Five - Intelligent eHealth Systems for Personalized Medical Care

Monday 5 September 2005 13.45 – 17.45
Organized by MyHeart Project & ICT for Health Directorate, Information Society and Media Directorate-General, European Commission
Chair: Dr Harald Reiter (Philips Research Laboratories, Aachen, Germany) Dr Loukianos Gatzoulis (DG INFSO, European Commission, Belgium)

Within the next few years, healthcare systems will start undergoing a fundamental change towards the provision of personalized care and the extension of care beyond hospitals and care institutes. The convergence of ICT, micro-, nano- and bio- technologies holds great promise for healthcare. Intelligent textiles and wearable monitoring systems, implantable micro- and nano-systems, neuro-stimulating implants, Lab-on-a-Chip, informatics and genomics are some of the key technologies in realizing the vision of personalized medical care.

The workshop focussed on the potential opportunities for healthcare arising from this convergence of ICT, bio- and nano- technologies. It included presentations from the EU-funded projects WEALTHY, MYHEART and HEALTHY AIMS, as well as additional presentations on multidisciplinary topics. The objective was to reflect upon, suggest and discuss visions for potential research directions in future research programmes.

Workshop Programme
13:45 Welcome by the Chair, Workshop Objectives
13:50 EU Current and Future Activities on Wearable eHealth Systems for Personalized Care
   DR LOUKIANOS GATZOULIS, DG Information Society and Media, European Commission, Belgium.
14:10 Biomedical Clothes for Vital Signs Monitoring (WEALTHY and MYHEART)
   DR RITA PARADISO, Smartex s.r.l., Italy
14:30 Fighting Cardiovascular Diseases By Prevention & Early Diagnosis (MYHEART)
   DR HARALD REITER, Philips Research Laboratories, Germany
14:50 Integration of Micro- and Nano-Technologies in Intelligent Textiles
   PROFESSOR ANNALISA BONFIGLIO, Dept. of Electrical and Electronic Engineering, University of Cagliari, Italy
15:10 Coffee break
15:25 Implantable Therapeutic Systems (HEALTHY AIMS)
   DR SUE DUNKERTON, TWI Limited, UK
15:45  **Pathway Biology And Genomic Nanoproceessors: Convergent Fields For Personalized Healthcare**
DR DEBORAH SPENCER, Scottish Centre for Genomic Technology & Informatics, University of Edinburgh, UK

16:05  **Role and Potential Impact of Nanotechnology in Personalized Care**
PROFESSOR PATRICK BOISSEAU, CEA-LETI, France

16:25  Discussion and Final Remarks

17:00  Demonstration of wearable health monitoring systems (WEALTHY and MYHEART)

17:45  Close

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Workshop Six - Exploitation of Nanomedicine

Organized by Micro and Nanotechnology Network (MNT), UK
Chair: Julie Deacon (MNT Network)
Co-chair: Stephen Dennison (MNT Network)

There have been significant advances in medicine arising from micro- and nanotechnology: novel approaches to discovery, diagnostics, drug delivery and tissue regeneration. The objective of this workshop was:

- To bring together the users and providers of nanotechnology to discuss the applications of nanotechnology in the broad medical field
- To identify the commercial needs of the pharmaceutical and medical equipment sector
- To highlight the solutions that exist and the developments required to address these needs
- To catalyse the exploitation of nanomedicine

Workshop Programme

13:30 Networking buffet lunch
14:30 Introduction
   JULIE DEACON, MNT Network
14:35 Micro & Nanofluidic Technologies for Drug Discovery
   BRIAN WARRINGTON, GlaxoSmithKline
14:50 Challenges for Targeted Drug Delivery
   DAVID HATRICK, PA Consulting
15:05 Commercialization Challenges for Nanotechnology in Regenerative Medicine
   CHRISTINA DOYLE, Xeno Medical
15:20 Tea & Coffee
15:45 Nano-chemical Approaches to Controlled and Targeted Drug Delivery
   MARIE-CLARE PARKER, XstalBio
16:00 Current Developments in Micro- and Nano-medical Diagnostics
   DAVID WILLIAMS, Unipath
16:15 Cardiac Risk Panel Diagnostics
   LINDY MURPHY, Oxford Biosensors
16:30  Open Forum/Discussion “**Exploiting Nano-Medicine: Technology Push or Demand Pull?**”
       Speakers

17:25  Closing Comments - followed by Tea & Coffee and opportunity for further networking
       JULIE DEACON, MNT Network

For further information contact Stephen Dennison at PERA, [steve.dennison@pera.com](mailto:steve.dennison@pera.com)
Workshop Seven - Commercialization of Medical Diagnostic and Other Devices

Monday 5 September 2005 14.00 – 17.15
Organized and sponsored by MANCEF (Micro and Nanotechnology Commercialization Education Foundation), UK
Chair: David Tolfree, Vice President Europe, MANCEF

Medical Diagnostics are inextricably linked to the future development of health care. The development of accurate and inexpensive measuring devices capable of delivering rapid results to the patient are in great demand and will have a massive market. Expert speakers presented and discussed the commercialization challenges which these present. Researchers, manufacturers, practitioners and end users were welcomed as part of the audience and also participated in a panel session when questions and issues were discussed.

Workshop Programme

14.00  Introduction
      DAVID TOLFREE, Vice President Europe, MANCEF

14.05  Commercialization Challenges in Medical Diagnostics
      DR ROBERT MEHALSO CEO, Microtec Associates

14.30  Supply Chain Partnerships for Success in Nanotechnology Commercialization
      DR MALCOLM WILKINSON, TFI Limited

15.00  Medical BioNano Roadmapping for Medicine
      PROFESSOR STEVE WALSH, Founder MANCEF

15.30  Strategies to link Public Research into the Commercialization Chain for Medical Devices
      DR KEES EIJKEL, President MANCEF

16.00  Break

16.15  Panel Discussion with audience participation
      All speakers and audience. Chaired by David Tolfree

17.15  Close

MANCEF is an organization with over 600 members that has a global mission to support the creation, exchange, and dissemination of knowledge vital to people, organizations, and governments interested in the commercialization of miniaturization technologies.

For further information please visit: www.mancef.org
Workshop Eight - South Africa / Europe Partnership in Nanotechnology, Materials, and Production

Monday 5 September 2005 11.00 – 13.00
Organized by ESASTAP (European South Africa Science and Technology Advancement Programme), South Africa
Chair: Pontsho Maruping, ESASTAP

The European Union (EU) is one of South Africa’s (SA) most strategic partners in international science and technology cooperation. This partnership has been significantly boosted with the announcement at the end of June 2005 of the launch of the European – South African Science and Technology Advancement Programme (ESASTAP).

Since the signing of a S&T cooperation agreement between SA and the EU in 1996, 160 South African partners have participated in the Fourth, Fifth and Sixth Framework Programmes. The aim of this workshop is to explore mechanisms for increasing collaboration between South African and European researchers in the area of nanotechnology, materials and production.

Workshop Programme

11.00  Introduction
       PONTSHO MARUPING

11.15  South African Research in Nanotechnology
       DR MOLEFI MOTUKU

12.00  ESASTAP
       MABATHO MPHOMANE

12:30  Common Areas of Interest
       PONTSHO MARUPING

13.00  Close
Workshop - British Association for Lung Research (BALR)

British Association for Lung Research – Summer 2005 Meeting Summary

In September 2005, the British Association for Lung Research (BALR) met in Edinburgh. It was organized by Professors Vicki Stone and Ken Donaldson.

The topic, Nanoparticles in the Lung, was run in conjunction with the EuroNanoForum 2005, a major European conference focusing on the healthcare applications of nanotechnology - an acknowledged area of strength in Europe.

The BALR event brought together an international audience of speakers and delegates where the participants were treated to an exciting programme of research with stimulating presentations from leading speakers from the USA, Europe and the UK. In addition, the meeting included a highly competitive Young Scientist competition and excellent poster presentations.

After welcoming the delegates, Professor Ken Donaldson (University of Edinburgh, UK) opened the meeting by briefly outlining his own thoughts and findings on the emerging field of nanotoxicology.

This was followed by an excellent presentation from Professor Günter Oberdorster (Rochester, NY, USA) with an historical introduction to nanoparticle (NP) toxicology. In particular, he showed the significance of the impact of NPs on the central nervous system focusing on the potential for translocation of NP to the brain via the olfactory bulb.

Professor Wolfgang Kreyling (Munich, Germany), described how NPs may have the ability to redistribute from the lung to the systemic circulation. In his presentation, Professor Kreyling focused on the importance of size on translocation, using either 1.5nm gold clusters consisting of a stable conformation of 55 atoms or 18nm gold colloids. By administering the NPs intratracheally or by injecting them directly into the circulation of rats, he was able to demonstrate that the size of the gold NPs clearly affected translocation kinetics across the alveolar air-blood barrier or vascular endothelium.

The study of the effects of diesel exhaust inhalation on vascular and endothelial function in humans was presented by Dr Nick Mills (Edinburgh, UK). His work purported that inhalation of dilute diesel exhaust (combustion-derived NPs) impairs two important and complementary aspects of vascular function in humans: the regulation of vascular tone and endogenous fibrinolysis.

Professor Vicki Stone (Napier University, Edinburgh, UK), discussed the molecular mechanisms driving particle-derived inflammation, describing how reactive oxygen species derived from low solubility NP can drive oxidative stress and calcium signalling leading to the up-regulation of pro-inflammatory cytokines.
Models for studying inhaled NPs were presented by Dr Jean-Paul Morin (Universite de Rouen, France). Here he reported a novel technique using biphasic cultures of rat lung slices for toxicological evaluation of NP. The importance of preserving both particulate matter size distribution and adsorbed pollutant bioavailability, which could not be ascertained using more classical in vitro approaches, was discussed and was put forward as a prerequisite for further developments of in vitro studies to model in vivo inhalation of complex atmospheres.

Finally, Professor Peter Gehr (University of Bern, Switzerland) completed the invited speaker session with an excellent presentation on the topic of particle interactions with lung lining liquid. In particular, Professor Gehr described a novel triple co-culture model of the human airway barrier designed to simulate the cellular part of the air-blood barrier of the respiratory tract represented by macrophages, epithelial cells, and dendritic cells. The interplay of epithelial cells with macrophages and dendritic cells during the uptake of polystyrene particles (1 micron in diameter) was investigated with confocal laser scanning and conventional transmission electron microscopy. Particles were found in all three cell types, even though dendritic cells were not directly exposed to the particles.

The meeting was then brought to a close by Dr Terry Tetley (London, UK), Chairman of the BALR, who thanked all the participants for their attendance and contributions, as well as the organizers, for their hard work in putting together yet another very successful BALR meeting.

The Young Scientist competition was, as ever, very competitive, encompassing six presentations from those just starting their research careers. This year the winner was Emma Ford from Imperial College, London who gave an excellent presentation entitled ‘Inhibition of mucin secretion from respiratory epithelial (A549) cells by a retargeted clostridial endopeptidase’. The prize was very kindly sponsored by The Colt Foundation and presented to Emily, on behalf of the Colt foundation, by Professor Tony Newman Taylor.

The cash poster prize was again sponsored by The Colt Foundation and was equally competitive. This year there were twenty-four entrants. The winning poster was by Barbara Rothen-Rutishauser from the University of Bern, Switzerland who presented a study entitled ‘Interaction of nanoparticles with cells of the airway epithelial barrier: a study with an in vitro model.’ Dr Kim Harrison, the incoming Chairman of the BALR, presented the prize for the Best Poster to Barbara.

The meeting was well-attended, very interactive, and enriched by excellent discussion sessions. We thank the local team in Edinburgh for their contribution, and finally we would like to thank our sponsors, The Colt Foundation, Oxonica, Taylor and Francis, and Scientific Laboratory Supplies.
For further information about up and coming BALR events, as well as information about the BALR itself, please visit our website at www.balr.org.uk or contact:

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UK
3. PUBLIC DEBATE

As an important part of EuroNanoForum a Public Debate was held on the potential benefits of NanoMedicine. It was publicized through the press to encourage the public to understand the near-term benefits and issues surround nanotechnology. Delegates to the conference were also encouraged to attend.

The debate was chaired by Susan Watts, Science Editor of BBC Newsnight. There was a panel of four experts from across disciplines who briefly presented the potential in their field followed by questions from the floor.

The questions from the audience followed two main themes:

- The way nanomedicine / technology is portrayed in the press
- Scientific questions on particular technologies

Some of the groups opposing nanotechnology were invited to attend but declined.

(As a result of the conference BBC Newsnight subsequently broadcast an item on NanoMedicine).
Some of the audience at the Schools Session
4. SCHOOLS SESSION

Overview

A schools session was organized as a key part of EuroNanoForum 2005.

The aims of this session were:

- To inform young people about nanotechnology and how it will affect future life
- To make them aware of the issues that must be discussed in the development of any new technologies
- To excite them about a career in science and technology in response to the declining numbers of students entering science degree courses

All Scottish schools were invited to send a delegation of 15-16 year old pupils interested in a career in science, together with their teachers.

Speakers whose subjects could engage the young people were selected and asked to aim their presentation at the S4-S6 level.

There were 208 in attendance overall with 185 pupils and 23 teachers. They represented nineteen schools from across Scotland, this included two independent schools.

The event was over an afternoon starting with an actor describing life in 2020, talks by invited speakers, and a special tour of the exhibition.

The pupils were each given a special delegate bag with two DVDs on nanotechnology and other material provided by the organizers and EC. Teachers were given further information that could be shared with other science groups at their schools.

The pupils were asked to complete a quiz, with shopping vouchers as prizes, and an evaluation form to provide input to future events. The feedback received was very positive from both teachers and pupils and included this comment from Karen McNish of George Heriots:

"I assume that this was the first time that such an event occurred and I was very impressed. The pitch was perfect, the speakers were interesting and varied and the quiz/discussion at the end was very appropriate."

This event was free to schools and was sponsored by the Scottish Executive.
Schools Session Programme

14.00   Registration

14.15   The impact of Nanotechnology on Daily Life in 2020
        ‘Citizen of 2020’
        Rose, our friendly citizen of 2020, talking through a normal day in her life. Without
        noticing nanotechnology applications have become integrated into her lifestyle even
        though she can remember when very few people in the general public even knew
        what nanotechnology was – see page 230.

14.30   What is Nanotechnology?
        DEL STARK, Institute of Nanotechnology, UK
        Nanotechnology is already all around and Del introduced the
        basics of nanotechnology and also some of its exciting
        applications which range from smart textiles to solar cells. From
        working with companies involved in nanotechnology
        development Del knows of numerous products we are already seeing in the high
        street.
14.45  **What the Nanotechnology Future Holds**  
IAN PEARSON, BT Futurist, BT, UK

Technology will soon bring smart environments, with tiny chips everywhere. In our gadgets, our clothes, our food, even on and in our skin. We will finally see augmented reality giving us useful data in our field of view, but it will also bring dual architectures, with virtual appearances as important as real ones. Similarly dual fashion, with digital bathroom mirrors, digital bubbles that interact with those of other people. The world will be a much more interesting place. Meanwhile, advances in AI are taking us quickly towards smart machines, which will be conscious and smarter than people.

15.00  Break

15.15  **What is so Different about Nanomedicine?**  
PROFESSOR DAVID CUMMING, University of Glasgow, UK

Medical diagnosis of illness in the gastro-intestinal tract often has to resort to expensive and invasive procedures that are unpleasant for the patient. An exciting new technology that alleviates these problems is the SmartPill. In this talk David presented some of the background to the technology and the state-of-the-art that is currently in use.

15.30  **Nanotechnology and the Developing World**  
ERIN COURT, University of Toronto Joint Centre for Bioethics

Nanotechnology has the potential to address some of the most pressing challenges faced by developing countries today, particularly with respect to health needs. The key role of science and technology in contributing to the realization of the eight United Nations Millennium Development Goals will be explored. The students gained insight into some of the nanotechnology activity presently occurring in developing countries, as well as the nanotechnology applications which hold the greatest promise for development. The take-home messages is that nanotechnology can be harnessed for development, and the responsible progression of this technology must take into account the 5 billion voices of people in the developing world.

15.45  Discussion and Quiz

16.10  Special Tour around Exhibition Hall – the exhibitors were asked to prepare special handouts on nanotechnology and employment potential.
Script for ‘Citizen of the Nanotechnology Future’

Our character is called Rose and lives in Edinburgh in 2020. She is around fifty years old (and speaks using some Scots dialect).

I wake up to the sound of a gentle alarm. Even though it is November in Edinburgh, the house is lovely and warm as it has been constructed from energy-efficient nanocomposite materials, specially designed to keep the atmosphere warm in winter and cool in summer. My windows have a special nanocoating that allows in filtered light but retains heat; it is also dirt repellent, so they never need washing.

I call out, “News, please” and one wall of my bedroom suddenly becomes illuminated, and shows scenes, with a commentary, on the latest happenings in the world. I call ‘weather in Edinburgh, please’ and the image changes to show a weather map, with the forecast for the day. I then say, “Fine, thanks”, and the screen reverts to wallpaper once again.

Then it is time for getting up, even nanotechnology cannot make that any better! I go into the bathroom where my water is constantly recycled, using nanofilters. I have a wash, and brush my teeth with toothpaste which incorporates nanoparticles which means my teeth are perfect, with no fillings or decay. Those painful dentist visits of the past are long gone as are old people waking up to their wallies in a glass of water by their bed.

It may be difficult to believe but I am not completely perfect. When I was ten I was involved in an accident and as a result my hearing was damaged; but thanks to nanotechnology, I now have a tiny cochlear implant that requires no external power source. I got it fitted several years ago, almost painlessly, and it only cost me around the price of a new pair of shoes. The quality of the sound means I can hear as well as anybody else. This technology is available cheaply, all across the world, as are many medical advances based on nanotechnology.

During the day, I am a busy executive, working for a well-known bank. I take care of my health, as I know that I have a genetic propensity for heart disease, like many other Scots, found by checking my genome at home using a cheap, palm-sized instrument. Therefore I make sure I monitor all my ‘vital’ systems every morning. In the bathroom, I grasp a small ‘handle’ for a few minutes, and in a few seconds, my pulse rate, blood pressure and cholesterol level are displayed on the bathroom mirror. If I want to know anything more such as my blood sugar level, I will need to wait a little longer; but he doesn’t bother. Everything seems to be fine and with all this monitoring technology it would be easy to become a hyperchondriac!

After a shower I put on my clothes, which are treated to stay fresh and clean, and crease-free. No more boring ironing sessions for me and it means less wasted energy and water on washing machines and tumble dryers.
My breakfast usually consists of fruit, bread, porridge, and yoghurt – these are ‘nutrigenomic’ foods; specially modified to provide the optimum kind of nutrition that keeps my heart in good order, and helps my general well-being.

Ahead is a busy day. I decide to start work. I could use his bedroom as an office, but prefer to move into another room. As I open the door, already I can see some of my colleagues are at work, in my virtual office. The closest person to me in my office actually lives 400km away. I know I have a series of meetings arranged for today with clients from across the world. Travel is not the norm any more, and it is simple to meet by means of virtual reality. The technology makes it so natural that people have been known to forget they are conversing with a hologram, and try to shake hands or pat each other on the back. As the day progresses I communicate with my work colleagues, who live in many different places, but we are all so comfortable with the technology we feel like we are actually are in the same room. We even eat a virtual lunch together!

I remember the days when people travelled by car or aeroplane, until droughts, fires, famines, floods and hurricanes became so frequent that the scientific evidence for an imminent, irreversible ecological global disaster could no longer be ignored. Governments had to then make some very hard-hitting decisions to ensure the survival of the planet, and the continuation of the human race. Travel was forbidden, except in emergency, new forms of energy use were enforced through legislation, such as the adoption of renewable energy technologies (mainly solar), and energy saving became like a habit rather than a chore.

The health of the population began to be monitored remotely, and most patients could be treated early, in their homes, saving energy and other resources. Technology enabled disease to be identified at the level of a few cells, and treated in situ. In extreme cases, patients could go to small, local surgical units that contained all the latest equipment. At this time, funding had been made available to implement long-awaited cures for the diseases of the less developed world (which had existed for some time, but had not been deemed economical by their developers). Industry, including the food industry, had been thrown into turmoil. Food had to be grown and consumed locally, so new flavours were created to provide variety in taste; and many foods were scientifically modified to provide health benefits and prevent the manifestation of genetically inherited diseases. These were specially grown in isolated units.

When I am on my own I occasionally reflect that life in 2025 is actually not too bad. My home is comfortable, I can communicate with all of my friends worldwide, and when I get bored, I can transform my surrounding environment, using a few spoken commands, into a beach paradise; only lacking the real sea. I do prefer, though, just to go for a walk outside, and marvel at the miracle of nature. The tarmac of many roads, drives and gardens had been torn up, and the underlying soil painstakingly nursed back to health – a desperate attempt to regenerate the precious bacteria, providers of a healthy atmosphere on which all life depends.
When I think back I am glad that some nations, especially Europe, had seen the wisdom twenty years ago, of encouraging new research and development in the technologies that people now needed. Surprisingly, also, the bank had done rather well out of the new world order. The use and development of these new technologies had been enforced by law, and this meant a new role for the bank in providing finance. By law also, banks today had to use a high proportion of their surplus to support projects in specified regions of the world at very low interest rates. Not popular to begin with, but the benefits were now apparent. However, it had been sad to see so many businesses such as those involved in import and export of out-of-season fruits, flowers and vegetable, and those needing a high energy input such as glass factories, go to the wall.

Life is generally good. Surprisingly, people understand that we have been saved from the brink of extinction - there is still a long way to go to be sure, and all the indicators of climate change are currently monitored, almost obsessively, using nanosensors. It was interesting to see, though, how attitudes to waste and recycling had changed; small plots of land were again being nurtured in the quest for good food; less travel had meant more social interaction, and the cheapness, ubiquity and user-friendliness of information and communications technology meant that education and entertainment were available on demand. Technology had certainly made this new era so much better than he’d ever hoped.

With the day over, I reach for a bottle of homemade wine my neighbour had recently given me. I open it. ‘Surprisingly good’, I thought; ‘a bit like life is just now’. I better be careful not to break the bottle, though; glass bottles and jars are extortionately expensive nowadays.
Outcome of Schools Session Evaluation

After the presentations 112 secondary pupils (aged between 14 and 18) completed a questionnaire on their opinions on nanosciences and nanotechnologies (N&N) and their career aspirations. All students were studying at least one science and technology subject. Their answers are summarized below:

- The majority had heard of N&N before, with school (58) and TV (50) cited most often as source of this information
- 98% believe that N&N will benefit society, mainly through improvements in health and medicine (63%)
- 74% believe that N&N also poses risks, which include societal effects, misuse, autonomous machines and inadequate testing
- Over 70% of students believe that career advisors, the internet and someone they know are effective methods in making career decisions
- The most important criterion for career choice by far is fulfilment (70%), followed by financial remuneration (20%)

The main outcomes are summarized in the following graphs:
The Glasgow Academy Pipe Band welcoming Delegates to the Conference Party and Poster Session
5. SPEAKER PROFILES

Professor Ueli AEBI
Director, M E Müller Institute, Biozentrum, University of Basel, Switzerland

Ueli Aebi earned a PhD in biophysics in 1977 from the University of Basel, Switzerland, where he dissected the structure, assembly and maturation of bacteriophage T4. He spent the next 10 years in the US, first at the University of California in Los Angeles and then at the Johns Hopkins University School of Medicine, where he held faculty appointments in the Departments of Cell Biology and Anatomy, and in Dermatology.

In 1986, he joined the Biozentrum, University of Basel, and has since built a world-class structural biology department that integrates X-ray crystallography, NMR spectroscopy, and light, electron and scanning-probe microscopy. At present, he is Professor and Director of the M.E. Mueller Institute for Structural Biology at the Biozentrum. He is also a member of the National Centre of Competence in Research ‘Nanoscale Science’ where he heads the project module ‘Nanomedicine’. His lab is pursuing a structure-based functional understanding of supramolecular assemblies that include the actin and intermediate filament cytoskeleton, nucleocytoplasmic transport, and fibrillogenesis of amyloid forming peptides. Also, his group is working on novel optical and mechanical nano-sensors and -actuators for local diagnosis and therapy by minimally invasive interventions.

In addition, Ueli Aebi has over 20 years of business experience. In 1981 he co-founded Protek, Inc. to develop, manufacture, and sell hip and knee prostheses in North America. Between 1986 and 1991 he also served on the Technical Board of Protek AG. Since 1996 he has been chairing the board of Gehring Cut that develops and manufactures surgical instruments and other precision mechanical components. In 2003 he co-founded Therapeomic, Inc. that focuses on novel protein drug formulations and growth factor enhanced tissue repair.

Dr Rob AITKEN
Director of Research Development, Institute of Occupational Medicine, UK

Dr Rob Aitken is Director of Research Development and Head of the Exposure Assessment Group at the Institute of Occupational Medicine (IOM). The IOM has been one of the leading research organizations concerned with the health effects of dust and particles since its formation in 1967. Rob’s principal research interests include exposure measurements and modelling, the effectiveness of control and the potential health effects of nanomaterials.
He is the co-ordinator of SnIRC, (www.snirc.org) the Safety of Nanomaterials Interdisciplinary Research Centre, a collaboration between the IOM, and the Universities of Edinburgh, Napier, and Aberdeen. SnIRC brings together leading UK and international experts in particle toxicology, exposure, eco-toxicology, and human studies/epidemiology to address nanoparticle risk issues.

Professor Venkatesh Rao AIYAGARI
Head, Science and Engineering Research Council, Department of Science and Technology, Government of India, India
Venkatesh Rao Aiyagari is the head of ‘Science and Engineering Research Council (SERC)’ which is responsible for promoting R&D in newly emerging and frontier areas of science and engineering. Rao has been working with the Department of Science and Technology for a number of years and has made significant and outstanding contributions to the various activities related to promotion of R&D in Science and Engineering and also to various issues related to formulation of policy statements on science and technology. He has greatly contributed to the Review of the Scientific Policies and in the preparation of the Technology Policy statement 1983 and more recently the new Science & Technology Policy 2003.

He has greatly contributed to the formulation of the science and technology plans in the country and also has considerable international exposure to the issues connected with science policy and management of R&D. He was responsible for modelling major National Programmes and Research Centres of Excellence in areas like Smart Materials for application, Carbon & Nanomaterials technology; Computational Fluid Dynamics; Laser Processing of Materials; Application of Lasers in Medical Science; Robotics and manufacturing Science, Fuel Cell Technology, Bio-medical resonance, Display technologies. He has also played an important role in developing a blue print for the S&T activities of the All India Council for Technical Education. He has also made significant contributions to the programmes of the United Nations System in the field of Science & Technology. He is also the author of various papers and books.

Professor Alexander I ARCHAKOV
Director, Research Institute of Biomedical Chemistry, Russian Academy of Medical Sciences (RAMS), Moscow, Russia. archak@imbc.msk.su www.ibmc.msk.su

Professor Archakov has been Director of the Research Institute of Biomedical Chemistry RAMS, a department of the Russian Academy of Medical Sciences since 1989. RAMS consists of more than 200 research associates, including two Academicians of RAMS, nine Professors, sixty five Candidates, and twenty six Doctors of Science.
Professor Archakov is laureate of the A N Bakh prize of the USSR Academy of Sciences, State Prizes of the USSR, RSFSR and Russian Federation.

He is a member of the International Organizing Committees on Microsomes & Drug Oxidation; Biophysics and Biochemistry of the Cytochrome P450; International Human Proteome Organization (HUPO), European Society of Biochemical Pharmacology and Biochemical Society of Great Britain, IUBMB and New York Academy of Science, editor of Journal "Biomedical chemistry".

He is one of 2 000 outstanding scientists of the 20th century mentioned by the International Biographic Centre of Cambridge, England and by “Who is Who in America”, Marquis, USA.

His interests include: microsomal oxidation, development of cytochromes P450 database, and computer-assisted analysis of protein structure and function.

**Professor Tipu AZIZ**

**Nuffield Department of Surgery, University of Oxford, UK**

Professor Aziz is a consultant neurosurgeon at the Radcliffe Hospital Oxford and Charing Cross Hospital London. He qualified in medicine in 1983 and subsequently pursued a career in neurosurgery to follow an interest in surgery for movement disorders. Towards this end his doctoral research established that lesioning the subthalamic nucleus alleviated Parkinsonism in the experimental primate. This work was central to establishing the STN as a target for Parkinson’s disease. He has also developed applications of deep brain stimulation for conditions such as tremor of Multiple Sclerosis and trauma, dystonia and neuropathic pain. He is also active in clinical neurophysiology and in the primate laboratory has recently established that the Pedunculopontine nucleus may be an effective target in alleviating drug resistant Parkinsonism.

**Dr John BEATTIE**

**Chief Operating Officer, Scottish Centre for Genomic Technology and Informatics UK**

John Beattie has a background in software engineering and new venture management based on nine years’ experience with Zeneca, including a founding role in the creation the world’s largest manufacturer of DNA for therapeutic use. He is currently the Chief Operating Officer at the Scottish Centre of Genomic Technology and Informatics, where he is applying his management experience to the growth of this postgenomic research centre within the University of Edinburgh Medical School.
In particular, he is responsible for managing integrated, interdisciplinary R&D programmes in biochips and bioinformatics. He has a degree in Engineering from the University of Cambridge, an MBA from the University of Edinburgh and is a Chartered Engineer. He also runs his own technology management consultancy.

Dr Shimshon BELKIN
Director, Environmental Sciences and Technology Management, Hebrew University of Jerusalem, Israel

Shimshon Belkin obtained his PhD from the Hebrew University of Jerusalem in 1983. He has been a guest investigator at the Woods Hole Oceanographic Institution (1983-4), at the University of California in Berkeley (1984-6) and at the Dupont Company Central R&D (1993-94). He has been a professor at the Ben Gurion University Desert Research Institute until 1996, and is now a full professor at the Institute of Life Sciences at the Hebrew University of Jerusalem. His research activities combine environmental microbiology and biosensor technology. He is an international authority on the genetic engineering of microbial cells for monitoring environmental conditions and their integration into whole-cell biosensors. He is past president of the Israel Society for Environmental Quality Sciences, and presently directs two teaching programs at the Hebrew University: Environmental Studies and Industrial Management.

Professor David M BERUBE
Communication Studies & Associate Director NanoSTS, USC NanoCenter, University of South Carolina, USA

David Berube is a Professor in Communication Studies at the University of South Carolina where he teaches courses in risk communication, heuristics, and biases, and the rhetoric of science and technology. In addition, he is the Associate Director of the NanoScience and Technology Studies Program and a member of the USC NanoCenter.

He is a co-principle investigator on a NSF NIRT grant to study societal implications of nanotechnology and is the proposed assoc. director of a NSEC on Nanotechnology in Society. In October 2006, Prometheus Books released his new book ‘Nanohype: The Truth about the Nanotechnology Buzz’. Currently, he is actively engaged in research on intuitive toxicology and risk fatigue.
Dr Anja BOISEN

Assistant Research Professor, Department of Micro and Nanotechnology, Technical University of Denmark, Denmark

Dr Anja Boisen received her MSc degree in physics in 1993 from the University of Roskilde and her industrial PhD in micromechanics in 1997 from MIC – institute of micro and nanotechnology and the company Danish Micro Engineering A/S.

Since 1997 she is an assistant research professor at MIC, and since January 1999 she is associate professor and project leader of the Bioprobe project. As of January 2005 Dr Boisen has been appointed full professor at MIC. She has a thorough knowledge on micromechanics and nanotechnology and has more than 10 years experience in microfabrication and cantilever-based sensing.

Anja is co-author of more than fifty scientific papers and five patent applications. Her group consists of 14 researchers and she is collaborating with European universities and Danish companies. In 1999 Anja achieved the competitive FREJA grant for female research leaders (acceptance rate of less than 3%) from the Danish Research Foundation to establish her group. Since then she has attracted external funding through several EU and Danish research programmes. Anja was awarded the AEG Electronics prize in 2000 for an extraordinary contribution to the electrotechnical field and is currently a member of the Danish research council on technology and production. Anja is co-founder of the company Cantion A/S, which was established in 2001.

Dr Patrick BOISSEAU

Coordinator, Nano2Life, CEA-Léti, France

Patrick Boisseau is the coordinator of Nano2Life, European network of Excellence in nanobiotech, since 2004. He took part to the initiation of the local centre for innovation in nanobiotech called NanoBio in Grenoble, France. Agronomist by training, Patrick Boisseau started his research for 7 years at CEA in Aixen-Provence, France, in plant biology. He then moved to strategy and foresight in life science and environment at CEA headquarters in Paris, France. Then, he came back to cellular and molecular biology as well as structural biology in Grenoble, France. He definitely moved to project and science management in 2002. He is also responsible for the section on nanobiotech at the European Federation of Biotech.
Professor Paul J A BORM  
Centre of Expertise in Life Sciences (CEL), The Netherlands  
Since 2003, Professor Dr Paul J A Borm has been with the Centre of Expertise in Life Sciences (CEL) in An Heerlen, The Netherlands. He earned his PhD in 1984 from the University of Utrecht in The Netherlands. From 1998-2003, he was head of section, Particle Research, Institute for Environmental and Medical Research, University of Düsseldorf, Germany, in 2001.

Previous positions include head of department, Toxicology of Particles & Fibres, Medical Institute of Environmental Hygiene, University of Düsseldorf, Germany (1998-2001), associate professor in Toxicology and Occupational Hygiene, University of Maastricht, Dept of Health Risk Analysis & Toxicology (1988-1998), and director of ABK, Maastricht Consultancies BV, Consultancy in Occupational Health (1989-1992). From 1991-1997, he was head of Toxicology Division; Nutrition, Toxicology and Environmental Research Institute, Maastricht, The Netherlands. From 1986-1988, he was secretary of the NWO-group ‘Health and Labour’, a Dutch national platform studying work-related health problems.

Professor Borm is a member of the German MAK-commission and of the Dutch Evaluation committee on Occupational Substances (DECOS), and the special board on risks and opportunities of Nanomaterials.

He has been an invited member of expert groups such as IARC (1996), ILSI (1998) and ECVAM (1997). He was the organizer of a large series of international meetings, including the Symposium "Health effects of Occupational exposure to inorganic dusts, the Symposium on Coal Dust Induced Respiratory disorders (1993), the International Workshop on Nasal Lavage (1996), the 7th International Meeting on Particle Toxicology, Maastricht (1999), and the DFG workshop on particle carcinogenicity, Munich (2000).

He is an editorial board member in Human Experimental Toxicology and Inhalation Toxicology and co-editor of Particle and Fibre Toxicology, and has done peer reviews for many journals.

Dr Andreas BRIEL  
Schering AG, Berlin, Germany  
Andreas Briel studied chemistry at Philipps-Universität in Marburg (Germany) with the main focus on physical-chemistry of polymers and has subsequently developed research interest in the field of structure control of polyions with different nano-architectures. He completed his PhD studies in 1996 at the Max-Planck-Institute of Colloids and Interfaces (studying the classical polyelectrolyte effects in polymeranalytics).
In 1997 he joined Schering AG in Berlin and worked 3 years in pharmaceutical development of Ultrasound Contrast Agents (supporting Phase I & II clinical trials, and research project leader for novel contrast agents), 2 years in the Drug Delivery Systems department, and 2 years in the CMC-Technology Office of Schering evaluating recent developments in drug delivery technologies.

Andreas is an expert in Nanotechnology, Target-specific in-vivo Diagnostics and Drug Delivery Systems. Currently, he is involved in Schering’s Corporate Research Business Area Diagnostics and Radiopharmaceuticals. Andreas is chairman of the Association of Colloids and Interfaces Berlin/Brandenburg founded in 2001 and since 2003 also lecturer for ‘Novel Technologies and Innovation’ at the University of Applied Sciences in Berlin.

Professor Robert A BROWN

Director, UCL Tissue Repair and Engineering Centre, Coordinator of London Network and the British Tissue Engineering Network (BRITEnet), UK

Professor Brown first graduated in Zoology (University of Newcastle), shifting for his PhD into medical Biochemistry and Rheumatology (Manchester), with particular focus on connective tissue and collagen function. This merged into his postdoctoral training in control mechanisms underlying angiogenesis (in joint disease and tumours). During this period he was involved in the description of novel collagen species and identification of collagenolysis as a key controlling element of new capillary invasion (angiogenesis). During a 4 year period in semi-commercial research and development (plasma protein fractionation) he worked extensively on fibronectin. Following his return to academic research, this led to his identification of a novel process for production of fibrous fibronectin guidance scaffolds for use as tissue engineering templates.

These have now been extensively developed as neural regeneration conduits and tissue engineering substrates, promoting peripheral nerve and spinal regrowth after injury. His work in scaffold-cell guidance and control mechanisms (in UCL plastic & reconstructive surgery scar control) linked naturally with cell-mechanics. This has become a major theme, in collaboration with mechanical and optical engineers, providing new insight into advanced 3D tissue growth in bioreactors, controlled through biomimetic substrate topography and cell-mechanics (with non-destructive optical monitoring). This platform tissue engineering (now based in UCL Orthopaedics) aims to understand generic mechanisms of 3D spatial control for functional tissue growth, applicable to many example tissues. It has increasingly focused on cell/matrix organization control by incorporating biomimetic cues at the nano-micro- (i.e. meso-scale) level into scaffold structure.
Dr Donald BRUCE

Director, Church of Scotland's Society Religion and Technology Project, UK

Dr Donald Bruce holds doctorates in chemistry and theology, and originally worked in nuclear energy research, risk assessment, and energy policy. In 1992 he became Director of the Church of Scotland’s Society, Religion, and Technology Project (SRT). This unique project was established in 1970 to address ethical and social issues of modern technology for Scotland’s national church, by engaging closely with the science and technology community. In this capacity, Dr Bruce has worked on a wide range of issues in biotechnology and on the environment. He co-edited the pioneering Engineering Genesis multi-disciplinary expert study on the ethics of GM crops and animals in the 1990’s and has played a major role in cloning and stem cell debates.

He is a member of the advisory board of the Institute of Nanotechnology and of the ethical board of the Nano2Life European Network of Excellence on NanoBioTechnology, for whom he recently wrote a scoping paper on the ethics of nanobiotechnology. He has been a member of the Scottish Science Advisory Committee and the public advisory group of the UK Biotechnology Research Council, and is an observer to the UNESCO International Bioethics Committee and the Council of Europe’s bioethics committee. He is a frequent speaker, writer, and broadcaster on bioethics.

The SRT Project is active in sustainable development and energy policy and promoting environmental action in local churches through the Eco-Congregation Programme.

Dr Květoslava BURDA

Institute of Physics, Jagiellonian University, Poland

Květoslava Burda received her M.Sc. degree in Physics (specialization of Medical Physics) from the Faculty of Physics, Mathematics, and Astronomy of the Jagiellonian University in Krakow (Poland) in 1988 for her work on pathological haemoglobins, in particular on sulfhemoglobin. The work was supervised by Professor J S Blicharski from the Institute of Physics and by Professor J Frendo from the Medical Academy in Krakow. She received her PhD in Physics from the Institute of Nuclear Physics Polish Academy of Sciences in Krakow in 1993 for research on porphyrins and cytochromes done under supervision of Professor J Stanek form the Institute of Physics and Professor K Strzalka from the Institute of Molecular Biology of the Jagiellonian University.
In 1993 she was appointed a position in the Institute of Nuclear Physics of Polish Academy of Science. In 2004, Dr Burda earned her habilitation degree in Biology with specialization in Biophysics from the Faculty of Biotechnology of the Jagiellonian University for investigations of the mechanisms of manganese redox chemistry in photosynthesis. She carried out her research in the group of Prof. G.H.Schmid at the Faculty of Biology of the University of Bielefeld, Germany. Since 2005 K.Burda holds a position of Associate Professor in the Department of Medical Physics at the Institute of Physics of the Jagiellonian University.

Květoslava received the following fellowships:

1993 European Fellowship Go-West Institute of Physics, University of Gent, Belgium
1994 Fellowship of the German Conference of Sciences, Faculty of Biology, University of Bielefeld
2001 DAAD Fellowship, Faculty of Biology, University of Bielefeld, Germany
2001-2002 Marie Curie Individual Fellowship, Faculty of Biology, University of Bielefeld, Germany

She obtained distinctions summa cum laude for her PhD and habilitation theses.

Her research interests span a wide range of disciplines concerning biochemical and biophysical processes of energy and ions transport in living matter on the molecular level. She works on structure and mechanism of metalloproteins participating in the proton and electron transport as well as protection mechanism occurring in biomembranes under stress conditions.

**Professor Tilman BUTZ**

**University of Leipzig, Germany**


1993 Professor of experimental physics at the University of Leipzig, 1993-1994 Head of Physics and Dean, 1994-1996 Vice-Dean.

1997-2000 Vice-Rector for Research.
Dr Andrew CAMPITELLI
MiniFAB Pty Limited, Australia
Dr Andrew Campitelli is Programme Director for Bio-micro and nano technology at MiniFAB (Aust) Pty Limited. Most recently (April - November 2004) he was Manager of Advanced Health Technologies, Office of Science and Technology, within the Victorian Stave Government, Melbourne, Australia, investigating strategic planning for the deployment of micro and nano technologies into healthcare systems.

Originally trained as an Engineer, and with a PhD specializing in microsystem-based biosensors, Andrew returned to Australia in April 2004 after 7 years in Europe. His last role was with IMEC (Europe's leading independent centre for microelectronics and nanotechnology) in Belgium as Group Leader of the Biosensor Group, which he co-established. Dr Campitelli actively contributed to the European bio-MNT arena (e.g. author of the NEXUS Roadmap for POC, published September 2003), and has acted as an expert reviewer to the EC for biosensors on numerous projects. Andrew has an excellent track record in European Community funded projects (5th Framework) having been involved as coordinator or partner in over six major projects (e.g. co-ordinator of the PAMELA project IST-1999-13478, 1999-2002, budget of over €2.5m that developed an integrated micro biosensor system for patient point-of-care monitoring).

Andrew is also a member of the Steering Committee for SmartHEALTH, a new EU 6th Framework Integrated Project that aims to develop the next generation intelligent medical diagnostic platforms, of which MiniFAB is a participant. Andrew’s new role at MiniFAB focuses on the technical and commercial development of new business opportunities in the healthcare sector based on the fusion of bio, micro, nano, and information technologies.

Professor Leigh CANHAM
Chief Scientific Officer, pSivida, Australia
Professor Leigh Canham has 25 years experience conducting research on widely differing aspects of silicon technology. Two key personal discoveries – that silicon can emit light efficiently (1990) and be rendered biodegradable (1995) have had academic and commercial impact worldwide. With over 6,000 citations on the ISI database, his work on the optoelectronic properties of nanostructured silicon are well known, and led to an Honorary Chair award at the University of Birmingham in 1999.
He is a scientist devoted to finding a range of novel properties and uses for the semiconductor that already pervades our everyday lives. Trained at University College (BSc Physics) and Kings College (PhD Solid State Physics) in London, Leigh then conducted research at QinetiQ (formerly, RSRE, DERA) in Malvern UK from 1986-2000. From 1995 onwards he became increasingly aware of the huge potential benefits of using biocompatible silicon technology in medical therapy. In December 2000 he co-founded with Dr Roger Aston, pSiMedica Limited, based upon the biodegradable BioSilicon™ technology platform invented in QinetiQ. The company, now part of the pSiVida Limited group (Australia) is conducting clinical trials in Singapore via its subsidiary company, pSiOncology Pte, where radioactive BrachySil™ is being assessed for the treatment of liver cancer via intratumoural brachytherapy. The drug delivery applications of the material are at the pre-clinical stage.

**Dr Richard G CARO**

**CEO, TangibleFuture Inc. USA**

Born in Australia, Dr Caro received a B.Sc. degree from the University of Melbourne, a D.Phil. in physics from Oxford University, where he was a Rhodes Scholar, and was an IBM postdoctoral fellow at Stanford University. Since 1982, he has lived in the USA, and has worked in industries ranging from life sciences to communications, and in roles that include CEO, CTO, management consultant, venture catalyst and angel investor.

Dr Caro has led and advised a number of teams engaged in trying to turn science projects into profitable businesses, leading to a variety of successful products, and substantial shareholder wealth creation. He has twenty one issued patents. Dr Caro is presently CEO & founder of TangibleFuture, Inc., where he helps entrepreneurs and managers create and grow high technology businesses.

**Dr Thierry COCHE**

**Associate Director, Head of New Technologies and Bioinformatics, GlaxoSmithKline Biologicals R&D, Belgium**


In 1988 Assistantship in the Laboratory of Quantitative Biology, FUNDP. Co-author of a project for the European Space Laboratory. In 1989 Post-doctoral research in the Laboratory of Molecular Genetics, FUNDP, Molecular Biology of the yeast PHO81 gene.

From 1997 until 2001 Thierry was Senior Scientist, GlaxoSmithKline Biologicals R&D. Cancer Vaccines Disease Area Program. Responsible for the Cancer Antigen Discovery Program then between 2002 and 2004 Associate Director, GlaxoSmithKline R&D. Head of Molecular Biology, Bioinformatics and Automation. Responsible for Molecular Biology, Bioinformatics and Automation activities throughout R&D projects.

From 2005 to present Thierry is Associate Director, GlaxoSmithKline R&D, Head of New Technologies and Bioinformatics. Responsible for establishing and reducing to practice long term vision of technology needs for future vaccine development.

**Professor Patricia CONNOLLY**

**Vice Dean Research, Department of Bioengineering, University of Strathclyde, UK**

After the completion of a BSc and PhD in Electrical and Electronic Engineering, Professor Connolly started her Initial career in high voltage engineering but changed direction immediately after her PhD to enter field of Bioelectronics. For seven years she worked in the medical diagnostics industry in Italy and Switzerland, directing industrial research and development projects and co-ordinating international project teams.

Patricia was appointed to the new Chair in Bioengineering at the University of Glasgow in April 1999. Current Research interests include Cell & Tissue Engineering Sensors, Point of Care Diagnostics, Non-invasive Diagnostics. She is currently the Director of the Medical Devices Doctoral training Centre at the University of Strathclyde, the only EngD centre for medical devices in the UK which is funded by EPSRC Life Sciences Interface Programme. She has a number of external industry appointments.
Professor Jonathon M Cooper
Chair of Bioelectronics Research Centre, University of Glasgow, UK

Jon's research focuses on miniaturization of micro and nano-sensors for the biological and biomedical sciences, including the development of new technologies in spectroscopy, microfluidics, and immobilization chemistry. His work on combining microfluidics with on chip sensors was central to the success of the UK's DTIForesight Lab-on-a-Chip Consortium, and is now being further developed as part of the IRC in Bionanotechnology. He is on the editorial board of Biosensors and Bioelectronics and is Editor in Chief of IEE Proceedings in Nano-Biotechnology. Last year he was elected to the Royal Academy of Engineering.

The academic highlights of his work over the last decade include: the development of the methods for high resolution (1-2 micron) photopatterning of proteins on sensors, producing high density proteomic arrays for immunoassays (Angewandte Chemie, 34 (1995) 91-93, et seq); performance of electrochemical measurements of metabolites from single cells in a Lab-on-a-Chip formats (Anal. Chem., 70 (1998) 1164 1170); and the implementation of the first proof of principle of the Lab-on-a-Pill concept with wireless transmission of chemical data (pH, conductivity, temperature and pO2) from a capsule (IEEE Transactions in Biology and Medicine, 2004), and finally, the implementation of multiplexed SERRS in a lab-on-a-chip format for DNA assays (Chem Commun, 2004).

Erin Court
Canadian Program in Genomics and Global Health, University of Toronto Joint Centre for Bioethics, Canada

Erin Court studies Bioethics at the University of Toronto. A research assistant in the Canadian Program in Genomics and Global Health, Erin has co-authored three papers on nanotechnology and the developing world: the first surveyed and categorized select developing countries according to their level of nanotechnology activity; the second was a commentary arguing that nanotechnology can and should be applied as a tool for development; and the third was a study that identified and ranked, for the first time, the ten applications of nanotechnology most likely to benefit developing countries. Erin is also a member of the Genomics and Nanotechnology Working Group of the United Nations Millennium Task Force on Science, Technology, and Innovation.
In addition to the implementation of science and technology for development, Erin’s research interests lie in public engagement on controversial emerging technologies. She co-developed an educational module on the science, ethics, and governance of stem-cell research that was distributed to all high schools in Canada, and is presently developing an engagement tool for youth to learn about nanotechnology in a development context.

Dr Francesco CURCIO

**Associate Professor of Molecular Pathology, Dipartimento di Patologia e Medicina Sperimentale e Clinica, Università degli Studi di Udine, School of Medicine, Italy**

Medical Degree from the University of Naples Medical School, ‘summa cum laude’, October 1981. Specialty Degree in “Biologia Clinica (Clinical Biology)”, July 1985

1992-to date: Associate Professor of Molecular Pathology, University of Udine Medical School. 1998-to date: Section Chief, Unit of Cellular and Molecular Diagnosis and Therapy, University of Udine Medical Centre, Udine, Italy. 1995 to date: Component of the Teaching Board of the Socrates/Erasmus supported International Annual Course in ‘Bioethics and the New Perspectives in Biomedicine’. 2000-to date: Director of the Cell Culture Service of the MATI Centre of Excellence of the Ministry of Education at the University of Udine. Vice Director of the ‘Centro di Medicina Rigenerativa’ of the University of Udine

2001-to date: Chief Scientific Officer, human somatic cell therapy, HCC, LLC, Sebago, Maine, USA

**Areas of Research:**

- Pathophysiology of diabetes: effects of insulin on splanchnic and peripheral glucose metabolism; effects of non-enzymatic glycosylation on the functions of several plasma proteins in diabetic patients and in opiate addicts and regulatory effects by drugs; effects of high glucose-generated oxidative stress on cardiovascular complications of diabetes

- Mechanisms of cell differentiation in culture: intra- and inter- specific hybridizations; obtainment, characterization and utilization of normal, continuous cell strains expressing tissue-specific functions in vitro, such as a rat parathyroid epithelial cell line, a rat parathyroid endothelial cell line, a bovine bone endothelial cell line and rat olfactory neuron cell lines; production of monoclonal antibodies to tissue specific proteins; in vitro tissue reconstruction; microenvironmental influence on the expression of tissue specific functions in culture; establishments of in vitro conditions to culture various human differentiated cells (Islet, liver, thyroid, parathyroid, parotid, muscle and endothelial cells)
Effects of space environment on cell differentiation: MASER 7 Campaign, MAP Project and MASER 9 Campaign

Regulatory issues: definition, testing, and application of cGMP protocols for preparing engineered tissues for human transplantation

Professor Ken DONALDSON

Scientific Director, Centre for Inflammation Research (CIR), University of Edinburgh, UK

Kenneth Donaldson is the Scientific Director of the ELEGI Colt Laboratory in the Medical School of the University of Edinburgh, where he is Professor of Respiratory Toxicology. Prior to this he was Professor of Pathobiology, Napier University and before that Head of the Toxicology Unit, Institute of Occupational Medicine, Edinburgh. Ken is recognized as an expert in the mechanisms of lung disease caused by particles and fibres and in this capacity has provided expert opinion and consultancy to the US Environmental Protection Agency (North Carolina), US Health Effects Institute (Massachusetts), World Health Organization, International Agency for Research on Cancer (Lyon France), WHO Air Quality and Health (Bonn, Germany), UK Medical Research Council, UK Health and Safety Executive, French Ministry of the Environment etc..

Professor Donaldson sits on two government committees pertaining to toxicology of air pollutants - Committee on the Medical Effects of Air Pollution (COMEAP) and Expert Panel on Air Quality Standards (EPAQS). Ken has given advice on the toxicology of fibres to the US EPA and UK HSE.

In relation to nanoparticles (NP) and nanotubes, he was one of the initial proponents of the NP theory of the toxicity of particulate air pollution and has acted as a consultant to various bodies on the risk from NPs such as European Science Foundation, Health and Safety Executive, ECETOC and the WHO. He has published over 250 scientific papers, reviews and book chapters, a large number of which concern nanoparticles and PM and he currently has a research programme into the adverse effects of PM/NP on the lungs and cardiovascular system. He is Editor-in-Chief of a recently-launched Open Access journal entitled ‘Particle and Fibre Toxicology’ to be launched soon.
Professor Ruth DUNCAN

**Director, Centre for Polymer Therapeutics, University of Cardiff, UK**

Ruth Duncan is Head of the Centre for Polymer Therapeutics and Professor of Cell Biology and Drug Delivery at the Welsh School of Pharmacy, Cardiff University. Professor Duncan was a founder member of the UK Association of Pharmaceutical Scientists, and is a past Chair of the UK and Ireland Controlled Release Society, the Gordon Conference on Drug Carriers in Biology and Medicine and the British Pharmaceutical Conference.

She is currently Chair of the European Science Foundation's Steering Committee undertaking a Forward Look on Nanomedicines. In recognition of her team's research, which transferred the first polymer-anticancer conjugates from laboratory to clinical trial, she has been recipient of a number of awards including the Pfizer Award, Royal Society of Chemistry’s Interdisciplinary Award, the Berlin-Brandenberg Academy of Sciences Monika Knutzner Award for Innovative Cancer Research, and the World Pharmaceutical Congress Millennium Award for Excellence in Pharmaceutical Science.

Professor Mike EATON

**Section Head, Medicinal Chemistry, Celltech Therapeutics Limited, UK**

Mike is currently a section head of Antibody Chemistry at Celltech’s Antibody Centre of Excellence in Slough and responsible for antibody drug conjugates and nanotech drugs. He has been at Celltech, now part of the UCB group, for 25 years and has seen the growth of a whole new industrial sector in that time. He has a PhD in Molecular Sciences from Warwick.

Professor Rolf ECKMILLER

**University of Bonn, Germany**

Rolf Eckmiller received his M.Eng. and Dr Eng. (with honours) degrees in electrical engineering from the Technical University of Berlin, in 1967 and 1971, respectively. Between 1967 and 1978, he worked in the fields of neurophysiology and neural net research at the Free University of Berlin, and received the habilitation for sensory and neurophysiology in 1976.

From 1972 to 1973 and from 1977 to 1978, he was a visiting scientist at the University of California at Berkeley and the Smith-Kettlewell Eye Research Foundation in San Francisco.
From 1979 to 1992, he was professor and head of the Division of Biocybernetics at the University of Düsseldorf. Since 1992, he has been professor and head of the Division of Neural Computation, Department of Computer Science at the University of Bonn.

His research interests include vision, eye- and arm movements in primates, neural nets for motor control in intelligent robots, and neurotechnology with emphasis on learning retina implants and motor implants. He developed a learning retina encoder, which can be tuned in perception-based dialog with the human subject.

Since 1987, he directed three international conferences on neural computers. Since 1991, he has participated in an international research initiative for neurotechnology (retina implant, functional electrical stimulation) to link pulse processing neural computers with the human nervous system. Since 1996, he advises research teams for the development of a learning retina implant. Dr Eckmiller is a member of various societies, including the International Neural Network Society, Society of Neuroscience, ARVO, and American Academy of Ophthalmology (AAO). He is a senior IEEE member. He holds several US patents in the area of learning neural prosthetic systems.

Dr Kees EIJKEL

Technical-Commercial Director, MESA+ Research Institute
University of Twente, The Netherlands

Dr Kees Eijkel holds the position of technical-commercial director at the MESA+ research institute at the University of Twente. Together with the CEO of MESA+ he is responsible for this Dutch institute in micro/nanotechnology with over 450 people and an integral turnover of over €50m. He has special attention for commercialization, which has resulted in a well-developed strategy and network which supported the formation of over twenty five start-ups over the past 15 years.

He is board member of two non-profit foundations supporting commercialization and education in micro/nano in the Twente region, and of the Dutch Association of Micro/Nano Companies MINACNed. He is CEO of MTF Limited, which develops offices and labs, focused on further development of the regional commercialization strength. Currently, he is president of the Micro and Nanotechnology Commercialization Education Foundation, MANCEF.

He is co-architect of the €250m Dutch Nanotechnology Initiative. He is responsible for the nano-chapter in the Dutch Foreign Trade Minister's trade mission to Silicon Valley in January 2004 and Boston in September 2005. He was speaker, keynote, and/or session chair in a large number of international conferences, with emphasis on conferences addressing the commercialization issues around scientific research.
Dr Leonard FASS

Director, Academic Relations, GE Healthcare, USA

Leonard Fass was born in London. He graduated in Electrical Engineering and was granted a PhD in Materials Science at the Imperial College London. After initially performing research into the optical and electronic properties of semiconductors he has spent the last 36 years in the field of medical technology in R&D and marketing roles.

He contributed to the development of the first rare earth phosphor based X-ray intensifying screens and solid-state image intensifiers for X-rays at the 3M Company. At EMI he helped develop the initial CT market in Italy. He has expertise in all medical imaging technologies and had responsibility for the European CT and MR business of GE Medical Systems as well as being country manager for Italy. He served as General Manager for Otsuka Electronics for Europe.

In his present position in GE Healthcare he has had responsibility for the development of the molecular imaging market in Europe and managing Academic Relations. He has advised institutions such as the Cambridge MIT Institute, the UK DTI, the European Patent Office, and the European Bioinformatics Institute. He has served on various congress steering committees including the Global Medical Forum, the International Workshop on Implantable Sensors, the NanoForum Congress and was Co-Chairman of the Bio-nanotechnology Patenting Congress.

Currently he is a member of the Business and Industry Advisory Committee to the OECD for New and Emerging Health Related Technologies and a member of the Advisory group for the DTI Beacon projects.

Dr Mauro FERRARI

National Cancer Institute, USA

Dr Ferrari is a founder of the field of biomedical micro/nanotechnology, especially as it pertains to drug delivery, cell transplantation, implantable bioreactors, and other innovative therapeutic modalities. In these fields, he has published more than 100 papers and two books. Dr Ferrari is the inventor of more than fifteen issued patents, with about thirty more pending in the United States and internationally. His contributions have received a variety of accolades, including the National Young Investigator Award of the National Science Foundation, a Shannon Director's Award of the National Institutes of Health, and the Wallace H. Coulter Award for Biomedical Innovation and Entrepreneurship.
Dr Ferrari earned his degree of Dottore in Matematica at the University of Padova, Italy (1985), and then completed M.S. (1987) and Ph.D. (1989) degrees in mechanical engineering at the University of California, Berkeley. He started his academic career at Berkeley, where he was awarded tenure as Associate Professor of Materials Science, Civil Engineering, and Bioengineering. He moved to the Ohio State University in 1999, where his current appointments include serving as Edgar Hendrickson Professor of Biomedical Engineering and Professor of Internal Medicine, Mechanical Engineering, and Materials Science. Dr Ferrari is also Associate Vice President, Health Science Technology and Communications, and Associate Director of the Dorothy M. Davis Heart and Lung Research Institute. He currently advises the National Cancer Institute as a Special Expert on Nanotechnology.

**Professor Morten FOSS**

*Associate Research Professor, Interdisciplinary Nanoscience Centre (iNANO), University of Aarhus, Denmark*

Surface Scientist. Research interests include biocompatibility of metal implants.

No profile provided.

**Dr Guenter FUHR**

*Coordinator CellPROM (Cell Programming by Nanoscaled Devices), Fraunhofer-Institute for Biomedical Engineering, Germany*

Studied at the Technical University Dresden, electronical engineering and semiconductor technologies obtaining a diploma (Thesis: Development of a thermal video imaging system for the diagnosis of tumours) in 1975.

From 1975-78 Guenter was technological manager of electronical camera production, Pentacon, Dresden. From 1978-81 Guenter undertook a research study in biophysics at the Humboldt-Universität zu Berlin then a doctoral level in biophysics (Dissertation: Spectroscopic examination of the photomorphogenesis of higher plants). In 1985 Habilitation in the field of cell biology and biophysics (postdoctoral thesis: On the rotation of dielectric bodies in rotating fields).
From 1991-95 Guenter was a member of the development group of the Federal Ministry of Education and Research to reorganize the Humboldt-University and the Museum of Natural History, Berlin.

In 1993 Guenter became C4-Professor at the Institute of Biology at the Humboldt-Universität zu Berlin and from 1994-96 Vice Dean of the Faculty of Mathematics and Natural Sciences I at Berlin.

Between 1994 and 2004 Guenter planned, executed, and led nine polar expeditions.

In 1997 Research study as visiting professor in Japan on invitation of the University of Nagoya; Foundation of a research group at the Institute of Biology, Department of Physiology of Membranes, funded by industrial partners; 2000 Foundation of the Centre of Biophysics and Bioinformatics at the Humboldt-Universität zu Berlin and first director of the Centre; 2000 Call on a chair at the Medical Faculty at the Universität des Saarlandes combined with the directorship of the Fraunhofer Institute for Biomedical Engineering (IBMT).

Since 2001 Guenter has been Head of the Fraunhofer Institute for Biomedical Engineering (IBMT) in St. Ingbert with branches in Shenzhen (Guandong, China), Sulzbach (Saarland), Potsdam (Brandenburg), Lübeck (Schleswig-Holstein) and Berlin.


Dr Rogerio GASPAR

Laboratory of Pharmaceutical Technology, Faculty of Pharmacy, University of Coimbra, Portugal

No profile provided.

Dr Mauro GIACCA

Director, International Centre for Genetic Engineering and Biotechnology, Italy

Dr Giacca obtained his degree in Medicine in 1984 from the University of Trieste, Italy and his PhD in Microbiology in 1989 from the University of Genova, Italy. Since 2004, he is the Director of the Trieste Component of the International Centre for Genetic Engineering and Biotechnology (ICGEB), where he has been the Group Leader of the Molecular Medicine Laboratory since 1995. From 2000 to 2005, he has been Associate Professor of Molecular Biology at the 'Scuola Normale Superiore' in Pisa, Italy and Director of the Molecular Biology Laboratory of the same Institution. Since April 2005 he is Full Professor of Molecular Biology at the University of Trieste.
Mauro’s research interests focus on two major topics in the field of Molecular Medicine. The first project concerns the development of viral vectors for human gene therapy, with special emphasis on vectors based on the adeno associated virus (AAV) and their application for gene therapy of cardiovascular disorders. The second project concerns several aspects of the molecular biology of HIV-1 infection with particular reference to the study of the interactions of some viral proteins (Tat, integrase) with cellular factors. He also maintains a long-standing interest in the study of the molecular mechanisms involved in initiation of DNA replication in mammalian cells.

Dr Giacca has published over 160 full papers in peer-reviewed international journals, among which, Science, the EMBO Journal, the Journal of Clinical Investigation, the Proceedings of the National Academy of Science of the USA, the Journal of Virology, Journal of Biological Chemistry, Gene Therapy and Molecular Therapy.

**Dr Electra GIZELI**

**Department of Biology, University of Crete, & Institute of Biology and Biotechnology, FORTH, Greece**

Dr Gizeli received a BSc in Chemistry at the University of Athens in Greece and a MSc in biotechnology at the University College London, U.K. Her PhD was on the development of novel acoustic devices for biological sensing applications and she obtained it in 1993 at the Institute of Biotechnology, University of Cambridge, UK.

Following post-doctoral work at the same department, in 1996 she was awarded a BBSRC Junior Research Fellowship and established her group on acoustic biosensors at the Institute of Biotechnology in the University of Cambridge. In 2003 she was elected Assistant Professor at the Department of Biology at the University of Crete, Greece and Group Leader at the Institute of Molecular Biology and Biotechnology-FORTH, Crete, Greece. Her research interests are the study of biomolecular interactions of biological and biotechnological significance by using a novel high frequency acoustic wave technology. Her research is carried out at the interface of biology, chemistry, physics, and engineering and can be applied to the areas of bioanalytical sciences, nanotechnology, drug screening and proteomics. Dr Gizeli’s work has been funded by many international and national funding bodies as well as industrial sponsors.
Professor Stefan W HELL

Director, Department of NanoBiophotonics, Max-Planck-Institute for Biophysical Chemistry Göttingen, Germany

Stefan W Hell (b. 1962) received his doctorate in physics from the University of Heidelberg, Germany in 1990. From 1991 to 1993 he worked at the European Molecular Biology Laboratory in Heidelberg, followed by a stay as a senior researcher at the University of Turku, Finland between 1993 and 1996, and as a visiting scientist at the University of Oxford, England (1994). In 1996 he received his habilitation in physics from Heidelberg, where he also teaches physics. In 1997 he was appointed to the Max Planck Institute for Biophysical Chemistry in Göttingen, where he built up his current research group dedicated to subdiffraction resolution microscopy.

In 2002, Stefan was elected Scientific Member of the Max Planck Society and a director at the Max Planck Institute for Biophysical Chemistry in Göttingen, where he established the Department of NanoBiophotonics.

Stefan Hell is also heading the High Resolution Optical Microscopy Division at the German Cancer Research Centre (DKFZ) in Heidelberg and is a member of the board of directors of the Laser-Laboratorium Göttingen. He has been appointed as an Adjunct Professor of Physics at the University of Heidelberg (2003) and as an Honorary Professor of Experimental Physics at the University of Göttingen (2004). Stefan Hell is credited with having found and validated the first viable concept for breaking Abbe’s diffraction resolution barrier in a focusing light microscope. He has published more than 100 original publications in refereed journals and has received several national and international awards, e.g. the Prize of the International Commission in Optics (2000) and the Carl Zeiss Research Award (2002).

Professor Göran HERMERÉN

President, European Group on Ethics in Science and New Technologies, Brussels, Belgium

- Chairman, advisory board, German Reference Centre for Ethics in the Life sciences, (Deutsches Referenzzentrum für Ethik in den Biowissenschaften), Bonn, Germany
- Member, The National Council on Medical Ethics in Sweden, (Statens Medicinsk-Etiska Råd), Stockholm, Sweden
- Chairman, Medical Research Council, Committee on Research Ethics (Medicinska forskningsrådets nämnd för forskningsetik), Stockholm, Sweden
- Member, European Steering Committee of the Encyclopaedia of Bioethics, Brussels, Belgium

Hermerén has also received grants from a number of Swedish research agencies like the Medical Research Council, the Vardal Foundation, and Forskningsrådsnämnden.

**Professor Jöns HILBORN**

*President, European Tissue Engineering Society, Uppsala University, Sweden*


Professional presentations have been made upon invitations to twenty six international conferences and hundred’s of national, international, and local presentations:

- Keynote Lecture at world tissue engineering conference 2002 in Kobe, Jpn: ‘Compliant scaffolds for engineering of soft tissue’
- Invited speaker to Polymers for Advanced technologies, Orlando 2002: “Protein Abhesive and Protein Adhesive Biodegradable Polymers by Surface Active Endgroups”
- Invites keynote speaker to 1st World Conference on Regenerative Medicine 2003 in Leipzig: ‘A new evolving paradigm for biocompatibility’
- Invited speaker to American Chemical Society Biomaterials Oct 2004
- Invited speaker to World Tissue Engineering Meeting Oct 2004 (keynote lecture)

**Research Areas:** Polymer photochemistry, High performance polymer synthesis, Macromolecular architectures and nanomaterials, Biodegradable polymers and gels, and Tissue engineering and biomaterials. Publications / Patents: 130 Publications and twelve patents
Dr Werner HOHEISEL  
**Bayer Technology Services GmbH, Leverkusen, Germany**

Dr Werner Hoheisel is a research scientist and project manager at the Competence Centre Biophysics at Bayer Technology Services GmbH, a subsidiary of the Bayer Group in Leverkusen, Germany. He has performed his research studies at the University of Heidelberg and received a degree in physics (PhD) in 1992. From 1992 to 1994 he worked as a postdoc at the Department of Chemistry at the University of California in Berkeley on semiconductor nanoparticles, quantum dots, which are well known as nonbleaching fluorescent markers for biomolecules today. Thereafter he was an assistant at the Department of Physics at the University of Kassel working on nanostructured surfaces before he went to the Philips Research Laboratories in Aachen and subsequently to the Central Research Department of the Bayer AG in Leverkusen 1995. There he evaluated the potential for upvaluing technical polymers with nanotechnological approaches and initiated corresponding projects. Among other things in 2001 he took over the responsibility for a consortium which has developed non-toxic and non-bleaching fluorescent nanophosphors for their general use in medical diagnostics and molecular biology.

Professor Shervanthis HOMER-VANNIASINKAM  
**Consultant Vascular Surgeon, General Infirmary of Leeds, UK**

Professor Shervanthi Homer-Vanniasinkam was appointed Consultant Vascular Surgeon at The General Infirmary at Leeds in October 1995 and was awarded a Personal Chair in Clinical and Experimental Vascular Research by the University of Bradford in June 1998. In addition to her clinical work as a full-time vascular surgeon, she is actively involved in a number of basic, applied, and translational research projects. Her research interests have focused on ischaemia-reperfusion injury in which she has published widely and has given a number of national and international presentations. She has successfully initiated, and been the principal investigator for, many clinical trials.

More recently, Professor Homer-Vanniasinkam has been associated with emerging technology projects and is keenly interested in the medical applications of these technologies. She currently holds a number of collaborative appointments in the UK and abroad.
Doctor David J S HULMES

Centre National de la Recherche Scientifique – Délégation Rhône Alpes, Institut de Biologie et Chimie de Protéines, France

David Hulmes obtained his PhD in Molecular Biophysics at the University of Oxford in 1975. Following postdoctoral work at the European Molecular Biology Laboratory (Grenoble) and Harvard Medical School (Boston) he then returned to the UK to the Department of Medical Biophysics at the University of Manchester, and then to the Department of Biochemistry at the University of Edinburgh. In 1996 he moved to France to become Research Director with the CNRS at the Institute for the Biology and Chemistry of Proteins (Lyon). He is the author of over seventy scientific publications in the area of connective tissue research and is currently co-ordinator of the FP6 STRP on cornea engineering.

Professor Richard A L JONES

Head of Department, Department of Physics and Astronomy, University of Sheffield, UK

Richard Jones is Professor of Physics at the University of Sheffield. His first degree and PhD in Physics both come from Cambridge University, and following postdoctoral work at Cornell University, U.S.A., he was an assistant lecturer, then a lecturer, at the University of Cambridge’s Cavendish Laboratory. In 1998 he moved to Sheffield. He is an experimental polymer physicist who specializes in elucidating the nanoscale structure and properties of polymers and biological macromolecules at interfaces.

He is the author of many research papers, a monograph, Polymers and Surfaces and Interfaces (with Randal W. Richards, CUP, 1999), and a textbook, Soft condensed matter (OUP, 2002). He was the co-author, with Alison Geldart and Professor Stephen Wood, of a report published by the UK’s Economic and Social Research Council, The Social and Economic Challenges of Nanotechnology (2003). His book on nanotechnology for the general reader, Soft Machines: nanotechnology and life, was published by Oxford University Press in 2004.

Dr Andreas JORDAN

Managing Director, Magforce Nanotechnologies GmbH, Germany

Dr Jordan, born in 1959, started his career with the biology course at the Freie Universität Berlin (Free University of Berlin) and a second course in biochemistry at the Technische Universität Berlin (Technical University of Berlin), chemistry faculty. His excellent appraised doctorate, completed in 1993, already attended to the production of nanoparticles and their use in the cancer therapy.
The paper was based on research projects, which were already started in 1985 – long before the topic nanotechnology reached international significance. Activities in the scientific project management for the Virchow-clinic of the FU (now Charité) as well as for the Schering subsidiary Institut für Diagnostikforschung GmbH (IDF) (Institute for Diagnostics Research) followed.

After further positive research results with the nanotechnology based cancer therapy, founded and developed by Dr Jordan, he founded the company for medical technology MFH Hyperthermiesysteme GmbH. From then on this company attended to the production and commercialization of a magnetic field applicator for the new nanotechnology-based cancer therapy. After further numerous discoveries in the field of coating of nanoparticles, Dr Jordan founded the MagForce Applications GmbH for the production and commercialization of tumour specific nanoparticles in the year 2000. In 2001 the foundation of the MFH Magnetic Fluid Hyperthermia GmbH, a financial holding for the mutual commercialization of the MFH and MagForce products, followed.

Since the nanotechnology-based cancer therapy had been started it found lively and very positive public interest, which leaded to numerous publications within the press with more than 800 articles in magazines as well as in books and in the Internet. Dr Jordan acted here as (co-)author.

Dr Jordan was already able to hold more than 500 scientific lectures concerning the nanotechnology-based cancer therapy. He wrote forty publications in peer reviewed journals and smoothed the way for altogether ten international patent families (partly licensed) for the companies.

Contacts to the NASA, the National Cancer Institute (NCI) and the Food & Drug Administration (FDA) as well as to famous US-clinics, like the University of California, San Francisco (UCSF), the Cleveland Clinic Foundation (CCF), Cleveland, Ohio as well as in Asia, most notably Singapore and China, reveal his world-wide commitment. The international distinguished conference “NanoMed – Biomedical Applications of Nanotechnology”, established by Dr Jordan, took place in October 2004 the fourth time with rapidly growing number of participants.

With the successful completion of a second round financing in July 2004 the both historical grown companies were united in a financial holding and renamed in MagForce Nanotechnologies GmbH, which will soon be converted to a public limited corporation. With this round the Nanostart Investments AG is the new investor and member of the company. It is planned to enter the market with the nanotechnology-based cancer therapy of MagForce Nanotechnologies in 2007.
Dr Jouko KARVINEN

President and CEO Philips Medical Systems

Jouko Karvinen is Chief Executive Officer of Philips Medical Systems and a member of the Group Management Committee. Before joining Philips, Mr Karvinen was responsible for the Automation Division of ABB Group Limited. and was a member of the ABB Group Executive Committee from 2000 to 2002. Jouko also served ABB Group in several international positions, with business responsibilities in marketing and sales, project management and operations across a global marketplace.

In June 2002, Jouko Karvinen joined Philips to manage its Medical Systems division, focusing in particular on the global healthcare imaging, monitoring, information, and services market.

Jouko Karvinen was appointed Chief Executive Officer of Philips Medical Systems and a member of the Group Management Committee on October 1, 2002.

Jouko Karvinen was born in Finland in 1957, and holds a Master of Science degree in Electronics and Industrial Economics from Tampere University of Technology in Finland. He is married, with two children.

Dr Steffen KELCH

Institute of Chemistry GKSS Research Centre, Germany

The department polymer chemistry develops polymers in particular for medical applications in the context of the HGF research programme Regenerative Medicine. Moreover, stimuli-sensitive polymers as functional polymer systems are developed within the scope of the HGF programme Advanced Engineering Materials. Besides material development an optimization of syntheses as well as an up-scaling of syntheses plays an important role.

Professor Costas KIPARISSIDES

Director, Chemical Process Engineering Research Institute, Aristotle University of Thessaloniki, Greece

Professor Costas Kiparissides is full time Professor of Chemical Engineering at the Aristotle University of Thessaloniki since 1985. He has performed his research studies in Canada (PhD - McMaster University - 1978), has been an assistant professor at the University of Alberta (1978-1980), an associate professor at the University of Alberta (1980-1983), and a visiting professor at Queens University (1987-1989). In May 2001, he was appointed Director of the Chemical Process Engineering Research Institute (CPERI) in Thessaloniki.
He has won several awards including Texaco Award for best Diploma Thesis, salary supplement award, University of Alberta, Canada, and ‘Golden Apple Award’, for best teacher, Queen's University, Canada. He is also a member of American Institute for Chemical Engineers (USA), Hellenic Association of Engineers, and Advisory Board of Chem. Proc. Engin. Res. Institute, Thessaloniki, Greece.

Costas is a reviewer for Scientific Journals: AIChE, J. Appl. Polym. Sci., Chem. Eng. Sci., etc. He is also a reviewer of BRITE/EURAM Research Proposals (EC), and NSF grant applications (USA). Costas also participated in twenty three EU programmes with a total budget 8m and in twenty industrial contracts with major EU polymer manufacturers with a total budget of €4m.

Dr Karsten KOTTIG
Evotec Technologies, Germany

Evotec Technologies is a spin out company formed to commercialize the technology platform.

No profile provided.

Vladimir KOZHARNOVICH
UNIDO - United Nations Industrial Development Organization
P.O. Box 300, A-1400 Vienna, Austria. Tel: + 43 1 260263720
V.Kozharnovich@unido.org

No profile provided.

Professor Jeremy LAKEY
Scientific Director and Founder, Orla Protein Technologies, UK

Jeremy Lakey is Professor of Structural Biochemistry in the Institute of Cell and Molecular Biosciences at the University of Newcastle-upon-Tyne, UK.

His research mainly involves biophysical studies on membrane and ion channel proteins and this work has been funded by research councils, charities, and government.

Prior his move to Newcastle in 1993 he was an EMBO fellow and later Staff Scientist in the research group of Franc Pattus at the European Molecular Biology Laboratory, Heidelberg, Germany (1987-93), NATO fellow in the group of Marius Ptak at the Centre de Biophysique Moleculaire, CNRS, Orleans France and post-doc in the group of Edward Lea at the University of East Anglia, Norwich UK where he also studied for his PhD in membrane biophysics. His first degree was in Zoology at the University of Liverpool, UK where he first realized the breadth of technological innovations waiting to be discovered in biology.
In 2000 Jeremy Lakey was a visiting Professor in the group of Horst Vogel at the Ecole Polytechnique Federale de Lausanne, Switzerland, and a BBSRC Research Development Fellow 2002-2005. He is Founding Scientist and non-executive director of Orla Protein Technologies Limited and is an Editor of the Biochemical Journal. His nanotechnology interests involve the use of membrane protein engineering in the design of novel interfaces and their analysis by a range of biophysical techniques.

Dr Laurent LEVY

**CEO, Nanobiotix, France**

Laurent has a thorough understanding of the technical and scientific market of nanotechnologies, since he has been working with these tools for almost 10 years. During his managerial experience with Altran, he participated in the implantation of these technologies with major health care industry accounts (Aventis, Guerbet, Rhodia, L’Oreal).

Laurent had first acquired his experience from doctoral studies in France and the United States. He is the author of thirty international publications and communications and several patents in this area. Laurent is bilingual French-English, Ph.D. in Physical Chemistry specialized in nanomaterials (UParisVI-CEA (Atomic Energy Agency) Saclay, France) and holder of a "DEA" (Advanced Studies Degree) in condensed matter at the ESPCI. He carried out his postdoctoral work at the Institute for Laser Photonics and Biophotonics (Professor P Prasad) at the State University of New York (SUNY), Buffalo.

Professor Chris R LOWE

**Director, Institute of Biotechnology, University of Cambridge, UK**

Christopher R Lowe received his BSc and PhD degrees in biochemistry from the University of Birmingham in 1967 and 1970 respectively. He has conducted post-doctoral research in Liverpool and Sweden and held a lectureship/senior lectureship at the University of Southampton. He is currently Director of the Institute of Biotechnology and Professor of Biotechnology at the University of Cambridge. He is a fellow of Trinity College.

The principal focus of his biotechnology research programme over the last 30 years has been the high value - low volume sectors of pharmaceuticals, fine chemicals, and diagnostics. The work not only covers aspects of biochemistry, microbiology, chemistry, electrochemistry, physics, electronics and chemical engineering, but also the entire range from pure science to strategic applied science, some of which has significant commercial applications and had led to the establishment of seven spin-out companies. He has 250 publications, seven monographs, and forty patents.
Professor Lowe is actively involved in many collaborations worldwide, is on the editorial boards of a number of academic journals, sits on a number of research council, grant awarding and government committees, and is active in various legal and entrepreneurial roles.

He has supervised over fifty PhD students and won a number of prizes over the last two decades: the Pierce Award for Outstanding Contributions to the Field of Affinity Chromatography and Related Techniques (1989); David Curnow Prize in Clinical Chemistry for work on Biosensors (1991); Schlumberger Stichting Prize (1994); The Queen's Award for Technological Achievement (1996); The Jubilee Medal of the Chromatographic Society (2002); Elected Russian Academy of Medical Sciences (2002).

Professor Stéphan LUCAS

University of Namur, Belgium

Stéphan Lucas is professor of Physics at the University of Namur (Belgium). His current research interest includes radioisotope production for medical application, novel fabrication methods of radioactive nanoparticles, internal dosimetry, and material science.

He received its PhD (1991) degree from the University of Namur – Belgium. After a post-doc at the University of Aarhus (DK), he has spent 6 years in the research centre of a steel industry (Arcelor) working on plasma coating of steel.

He joined the company Ion Beam Application (Belgium) where he developed cyclotrons for the production of radioisotopes. Before moving back to the University of Namur as a professor in 2003, he was General Manager of IBARadioisotopes, a company involved in the development of new radioactive medical devices for Brachytherapy. He is the holder of nine patents in related fields.

Professor Luis MEJIA

Stanford University, USA

Professor Mejia is a Senior Associate in the Office of Technology Licensing at Stanford University. In his position at Stanford, Luis manages a portfolio of technologies ranging from electronics to marine biology. He has negotiated over 200 licenses in his 17 years at Stanford OTL. Luis is a co-founder of two Stanford spin-off companies, most recently Paraform, Inc. a 3-D software modelling company which was acquired by Metris International.
Professor Mejia is a member of the Association of University Technology Managers and the Licensing Executives Society and has given talks on technology transfer in China, Japan, Australia, South Africa and Europe.

He frequently lectures to Stanford's Business and Engineering Schools on technology commercialization and is on the Business Development Advisory Board at Los Alamos National Laboratory.

Luis Mejia is a Board Member of the Stanford University OTL, LLC and is an intellectual property advisor for Neoconix, Inc. of Sunnyvale, CA. Prior to joining Stanford he held positions at PG&E and Honeywell. He holds a B.S. degree in Mechanical Engineering from Arizona State University.

Professor Helumuth MÖHWALD

**Director, Max-Planck-Institute of Colloids and Interfaces, Germany**

Dr Helumuth Mohwald is the Director and Scientific Member of Max Planck Institute of Colloids and Interfaces, Golm/Potsdam. After completing his PhD Dr Mohwald worked as a postdoc in IBM, scientific co-worker at Dornier-System, Friedrichshafen and as an Associate Professor in Experimental Physics (Biophysics at TU München). He is the Honorary Professor at University of Potsdam, he was also the Chair in Physical Chemistry, University of Mainz. Dr Mohwald was a guest professor at University of Pennsylvania, Weizmann Institute, Rehovot and currently at Zheijiang University, Hangzhou. Dr Mohwald has also won several awards including Physics Award of the German Physical Society, Raphael-Eduard-Liesegang Award of the German Colloid Society, Vannegard Lecture, Gothenburg, Lectureship Award of the Japanese Colloid Society, Sendai. His research interests include Biomimetic Systems, Chemistry and Physics in Confined Space, Dynamics at Interfaces, Supramolecular Interactions.

Dr Molefi MOKUTU

**General Manager, Research and Development, Mintek, Council for Mineral Technology, South Africa**

Molefi Motuku is the General Manager: Research & Development of the Council for Mineral Technology (Mintek), a research organization that specializes in mineral and metallurgical technology. Previously, he was the Manager of Physical Metallurgy Division, Mintek.

Molefi is the South African National Contact Point (NCP): Nanotechnologies and nanosciences, knowledge-based multifunctional materials and new production processes and devices for the Sixth Framework Program (FP6) of the
European Union. He started his professional career as an Assistant Professor of Materials & Mechanical Engineering and a Graduate Faculty Member at Tuskegee University, USA, were he founded and chaired the Annual Undergraduate Science and Engineering Conference (USEC). He then later moved to South Africa were he assumed the position of the Director of Fort Hare Institute of Technology (FHIT).

Molefi serves on different boards and committees, has been nominated for and has received many awards & honours, and has published extensively in peer-reviewed journals and proceedings of international conferences. He has a PhD & MSc in Materials Engineering from the University of Alabama at Birmingham (UAB), USA; and a BSc in Mechanical Engineering & Physics from Tuskegee University, USA.

Dr Barry D MOORE

Chief Scientist, XstalBio, UK

Dr Barry D Moore has a strong track record for carrying out innovative interdisciplinary research and has published over 60 papers and patents. He has made important contributions to the understanding of protein behaviour in low water media including methods for measuring and controlling enzyme protonation and hydration state, novel spectroscopic techniques, and development of ultrasensitive enzyme assays.

His invention with Dr Marie Claire Parker of protein coated microcrystals as a versatile method for stabilization and formulation of therapeutic biomolecules led to the spin-out of XstalBio Limited from the Universities of Strathclyde and Edinburgh.

Dr Moore is currently holder of an XstalBio Industrial Fellowship and responsible for the company’s science programme.

Dr Moore obtained a First Class Chemistry degree and PhD from the University of Nottingham and following post-doctoral periods in Strasbourg and Cambridge took up an academic position at the University of Strathclyde in 1990.

Professor Emilio MORDINI

Director, Centre for Science, Society, and Citizenship, Italy

Emilio is an MD from the University La Sapienza of Rome and MA in Philosophy from the Pontifical University S.Thoma. Emilio Mordini is a practicing psychoanalyst. He teaches Bioethics in the Medical School of the University of Rome ‘La Sapienza’, and since March 2002 he has been managing director of the Centre for Science, Society, and Citizenship (CSSC). Since 1996 Emilio Mordini has been member of the Bioethical Commission of the National Research Council (CNR) where he has served as scientific secretary from 2000 to 2004.

He is co-ordinator of the Psychiatric Network of the International Association of Bioethics, and member of the executive council of the Association for the Advancement of Psychiatry and Philosophy (AAPP).
Professor Mordini is past treasurer and past secretary of the European Association of Centres of Medical Ethics (EACME). He has also served as a member of the board of directors of the International Association of Bioethics (IAB).

Emilio is currently coordinating two EU funded projects in the area of Science & Society: BiG (Bioethical Implications of Globalization – www.bigproject.org ) and BITE (Biometric Identification Technology Ethics – www.biteproject.org ).

Emilio has been editor of six books, has published sixty four articles or chapters of book in reviewed publications, 160 articles in non-reviewed journals and newspapers.

Professor Günter OBERDÖRSTER

Professor of Environmental Medicine, University of Rochester, USA

Dr Oberdörster is Professor in the Department of Environmental Medicine and Head of the Division of Respiratory Biology & Toxicology at the University of Rochester and Director of the University of Rochester Ultrafine Particle Centre.

He is known for his research on the effects and underlying mechanisms of lung injury induced by inhaled nonfibrous and fibrous particles, including extrapolation modelling and risk assessment.

His studies with ultrafine particles influenced the field of inhalation toxicology, raising awareness of the unique biokinetics and toxicological potential of nano-sized particles.

He is a recipient of the 1982 Joseph von Fraunhofer Prize (Germany), the Society of Toxicology’s ISS 1996 Career Achievement Award, the Society of Toxicology’s ISS 1997 Paper of the Year Award; and the Thomas T. Mercer Prize: Outstanding contributions in the field of Aerosols in Medicine, 2003, awarded jointly by American Assoc. for Aerosol Research (AAAR) and Intl. Society of Aerosols in Medicine (ISAM).

He is on the editorial boards of Environmental Health Perspectives; the Journal of Aerosol Medicine, International J. Hygiene & Environmental Health; Particle & Fibre Toxicology; Nanotoxicology, and Associate Editor of Inhalation Toxicology.
Dr Jennifer PALUMBO  
**Science and Society Projects, Città della Scienza Science Centre, Naples, Italy**

Jennifer Palumbo collaborates with Città della Scienza as a project manager in a number of projects funded by the EC within the Science and Society framework, among which the ‘European Citizens’ Deliberation on Brain Science’ and ‘NanoDialogue’.

Dr Palumbo has a background in chemistry (University of Bologna) and a master's in Science Communication (International School for Advanced Studies, Trieste, Italy).

Dr Alessandra PAVESIO  
**Fidia Advanced Biopolymers, Italy**

Alessandra Pavesio holds a degree in pharmaceutical sciences, and has been in FAB (Fidia Advanced Biopolymers) since its inception. As a director of FAB’s research and development efforts, her focus is on the design, development and testing of novel biodegradable surgical specialties and in the exploitation of tissue engineered solutions for application in wound care and skeletal tissue repair.

As a founder of the company, she has contributed to a number of patented inventions and has managed the development of FAB’s entire CE and FDA approved products. Hyaluronan (HA) derivatives represent a novel alternative to currently available resorbable biomaterials. FAB’s proprietary esterification and cross-linking technologies have been employed to produce novel hyaluronan biopolymers with increased longevity in vivo, cell receptor interactivity and processability into stable three-dimensional configurations.

Keratinocytes, fibroblasts, chondrocytes, mesenchymal stem cells, adipocytes, endothelial cells, urethelial cells, and nerve cells have proven to efficiently proliferate on FAB’s proprietary three-dimensional HA scaffolds. Entirely biodegradable, based on a ubiquitous molecule such as HA, these scaffolds represent the most advanced and user friendly enabling technology for regenerative medicine currently available in clinical practice.

In virtue of its unique expertise in developing and bringing to the market tissue engineered constructs, FAB is a recognized leader worldwide in the emerging field of regenerative medicine.
Professor Manfred RADMACHER

Institute of Biophysics, University of Bremen, Germany

Manfred is a Professor in Biophysics at the University of Bremen. His studies include Diploma in Physics at the Technical University Munich, PhD in Physics at the Technical University Munich, Habilitation (Venia Legendi) at the Ludwig-Maximilians Universität Munich.

He worked as a Postdoctoral Researcher at the University of Santa Barbara, Physics Department, Research Associate at the University of Munich, Physics Department, Lecturer at the University of Munich, Physics Department, and Professor for Applied Physics at the University of Göttingen, Physics Department.

His research interest include Cellular Mechanics, properties of cytoskeleton, cell migration, protrusion forces single enzyme activity, enzymatic nanolithography, biological applications of AFM (Atomic Force Microscopy).

Dr Jochen RINGE

Department of Tissue Engineering, Charité University Medicine, Berlin, Germany

Jochen Ringe has six years of experience in the field of bone and cartilage tissue engineering. During his study of biotechnology (Technical University of Berlin), he joined the Tissue Engineering group of Michael Sittinger (University Hospital Charité, Humboldt-University of Berlin). Within the scope of his diploma thesis and doctoral thesis, he has established the ‘mesenchymal stem- and progenitor cell group’, which became an important and successful branch of the Tissue Engineering group.

Since 2003, he leads the stem cell group. Current research is focused on the next generation of tissue engineering products, namely the in situ regeneration of degenerated joint structures using smart delivery materials, differentiation factors, and chemotactic molecules recruiting mesenchymal stem cells from bone marrow to the defect site.

Since 2001, Jochen has also worked in the stem cell research & development department of TransTissue Technologies GmbH, a ‘spin-off’ company of the Charité Tissue Engineering group.
Ottilia SAXL

CEO, Institute of Nanotechnology, UK

Ottilia Saxl founded the Institute of Nanotechnology in January 1997, as a follow on from the centre for Nanotechnology, established by her in 1994. She has gathered a profound knowledge of nanotechnology over nearly 11 years of actively working in the field, and has close links with key academic and industrial players worldwide.

Ottilia has worked with the UK Government in formulation of its policy in nanotechnology and has organized fact finding missions to major nanotechnology centres across Europe and the USA.

Ottilia has been a member of several UK and EU nanotechnology panels, including the EU FP6 Advisory Group for Priority 3, the UK Government’s Basic Technologies Programme, and the EU expert group on New Wave Technologies.

Currently Ottilia serves on the EU’s ETP NanoMedicine Panel and is a member of the EU High Level Expert Group on Key Technologies.

Dr Jürgen SCHNEKENBURGER

Department of Medicine, University of Münster, Germany

Education at the Universities of Tuebingen, Munich, and Berlin. Diploma degree in Biochemistry and PhD at Max-Planck-Institute for Biochemistry, Martinsried, Department of Molecular Biology.

1997 – 2003 senior scientist at Department of Medicine B, University of Muenster, basic research programme in molecular pancreatolgy. Since 2003 head of the research unit, Gastroenterological Molecular Cell Biology at Department of Medicine B, University of Muenster.

Research focus:

- Analysis of the basic molecular mechanisms of pancreatic cancer cell migration and metastasis
- Function of cell-cell contact proteins of the Cadherin/Catenin complex and cell-matrix adhesion proteins of the integrin family in the organization of the actin cytoskeleton and cell migration
- Application of novel technologies as Digital Holography and TOF SIMS in cancer cell analysis and correlation of results with data from gene arrays and cell biological assays for new insights in cancer cell biology

Funding by DFG, BMBF, and EU programmes.
**Dr Frederic SCHUSTER**  
*CEA, France*  
No profile provided.

**Dr Ahmet SENOGLU**  
*CEO, Nanoxis AB, Sweden*  
Ahmet Senoglu is the founder and CEO of Nanoxis. Nanoxis is a nano-biotechnology company specializing in development and sales of advanced analytical devices such as chip platforms tailored for solving difficult bio-analysis problems for pharmaceutical and biotech companies.

Before Nanoxis, Ahmet Senoglu worked as a management consultant at McKinsey & Co. During his consulting career, he worked as an advisor to pharmaceutical, biotechnology and IT companies. Before McKinsey & Co., he worked as an investment banker on Wall Street.

Ahmet has Master of Science in Operations Research and Industrial Engineering, and MBA from Cornell University, USA.

**Dr Frank SINNER**  
*Head of Department for Proteomics, Institute of Medical Technologies and Health Management, Austria*  
Dr Frank Sinner is responsible for the department of bioanalytics and the laboratory at the Institute of Medical Technologies and Health Management, JOANNEUM RESEARCH. He joined JOANNEUM RESEARCH in 2001 after completing his PhD in macromolecular and analytical sciences at the University of Innsbruck, Austria. Frank studied technical chemistry at the University of Graz, Austria and “Chemie et Biologie Végétale Appliquée” at the University of Perpignan, France.

Main research activities fall into the following main domains: quantification of peptide, proteins, and lipids of medical importance starting from low human fluid sample.

The laboratory is specialized in the quantification of interstitial fluid with high sensitivity lying in the femtomol to attomol range by means of nano-HPLC combined with mass spectroscopy.

Furthermore, new monolithic separation phases for nano-liquid chromatography are developed within the department of bioanalytics, improving sensitivity and speed of analysis.
Furthermore, the laboratory is working according Good Laboratory Practise, performing analysis for clinical trials as well as applied research projects for industrial partners.

Dr Frank Sinner is the coordinator of the joint research project ‘Nano-Health – nano structured materials for drug targeting, release and imaging’ within the first Austrian Nano Initiative, having a total budget of €1.8m for the first two years. Within this project, new nano particles for targeted drug delivery for chronic diseases are investigated. He is also the CEO of the BioNanoNet, a platform in the development of new pharmaceutical development with a strong focus on bionanotechnology. This platform is transdisciplinary and nearly 20 academia and industrial members from all over Austria have joined the network, carrying out applied research projects as well as basic research projects founded by the national government, the European Union and national and international industries.

Dr Hulda SWAI

Senior Scientist, Centre for Polymer Technology, CSIR-Manufacturing and Materials Technology, South Africa

Dr Swai is currently a Senior Scientist at the Council for Scientific and Industrial Research (CSIR) in the Centre of Polymer Technology (CPT). For the past three years she has been working on encapsulation of living things e.g. bacteria, cell, vitamins and vaccine using supercritical carbon dioxide. This research is now going through preclinical trials.

Hulda’s current research interests are in the development of nano drug delivery systems, with emphasis on delivering Tuberculosis (TB), Malaria and HIV/AIDS drugs. These drugs are nano-encapsulated with biodegradable polymers using the double or triple emulsion method. She is also working on developing a nano-encapsulation technique using supercritical carbon dioxide, which is a superior method since it uses carbon dioxide as a solvent instead of organic solvents.

Other aspects of her current research involve designing appropriate in vitro studies to determine and optimize the drug release systems e.g. using FT-IR imaging and HPLC. Part of Dr Swai’s work in this regard involves the supervision of undergraduate and postgraduate students, as well as postdoctoral fellows in polymer science and analytical chemistry.

Prior to joining CSIR Dr Swai did her doctoral studies at the University of London (part time), where she also worked for nine years. The subject of Hulda’s PhD was Water Absorption and Drug Release from Methacrylate Polymers.
As an employee of University of London she was involved in the development of a slow release device for Candida infected HIV/AIDS patients. This device was approved by Medical Research Council in Britain. During Hulda’s time at the University of London, she was also involved in the development of a polymer composite for dental material.

**Professor Joyce TAIT**

**Director, Innogen Centre, University of Edinburgh, UK**

Joyce Tait is Director of the ESRC Innogen Centre (Centre for Social and Economic Research on Innovation in Genomics – see [www.innogen.ac.uk](http://www.innogen.ac.uk)). She is a Professor in the University of Edinburgh with an interdisciplinary background, covering natural and social sciences, particularly developments in life sciences, strategic and operational decision making in companies and public bodies; policy analysis; risk assessment and regulation; Foresight; and public attitudes and communication. She is a member of the Scientific and Technical Council of the International Risk Governance Council, the Scottish Science Advisory Committee, and the Office of Science and Technology Foresight Team working on Detection and Identification of Infectious Diseases.

**Dr Akiyoshi TANIGUCHI**

**Associate Director, Biomaterial Centre, National Institute for Materials Science, Japan**

Ph.D in Pharmaceutical Sciences, Toho University, 1991.

1991-2002 Associate Professor in Toho University, School of Pharmaceutical Sciences.

2002- Senior researcher of Bionic Materials technology Group, Biomaterials Centre, National Institute for Materials Science, Japan.

Research field: biomaterials, molecular biology, and cell biology.

**Dr Naseem THEILGAARD**

**Project Coordinator INTELLISCAF, Danish Technological Institute, Denmark**

Senior Consultant and Project Coordinator. BSc (Hons) Chemistry & Polymer Science & Technology, DIS MIDA.

5 years as quality control manager for a company producing insulating components for the wire & cable industry.

15 years R&D work in the field of injection moulding technical ceramics.

16 years experience in European Commission funded projects including:

- Coordinator of the DTI activities in EU funded project: ‘Complex shaped advanced ceramics’
Overall co-ordination and project manager for B/E project. ‘Functionally Graded Ceramics for Biomedical Applications’

Overall project co-ordinator and project manager for B/E Project “Bioresorbable implants for minimal invasive surgery (BRIMAS)’

Overall co-ordinator and project manager for 5th Framework Project ‘PORELEASE’

Overall co-ordinator and project manager for 5th Framework Project ‘INTELLISCAF’

Chairman of the Scientific and Technical Committee for 6th Framework Project ‘AUTOBONE’

Dr Enrico TOGNANA

Fidia Advanced Biopolymers, s.r.l., Italy

Enrico Tognana is a cellular biologist and received his PhD in neuroscience in 1997 for his work on the development of the neuromuscular junction. Since then his research interests switched to tissue engineering applications. After a first period of studies in the field of epidermal and dermal tissue engineering from 2000 he is firmly dedicated to the resolution of osteochondral defects by means of tissue engineering strategies.

In 2001 he completed a master degree in ‘Biomaterials and Tissue Engineering’ His interest in the field of cartilage tissue engineering lead Dr Tognana to the Skeletal Research Centre at Case Western Reserve University in Cleveland where he investigated the possible role of mesenchymal stem cells in cartilage tissue engineering and their use for the restoration of cartilage defects when delivered via a hyaluronan-based scaffolds. He then moved to the Massachusetts Institute of Technology where he studied tissue engineered cartilage integration with native cartilage and bone.

At this point of his career Enrico Tognana is at Fidia Advanced Biopolymers s.r.l. (Abano Terme, Italy) in the R&D of tissue engineering as head of the preclinical unit.
Dr Renzo TOMELLINI

Head of Nanosciences and Nanotechnologies Unit, Research Directorate-General, European Commission

Born in 1960, Renzo graduated in chemistry ‘cum laude’ in Rome in 1986. After a period as visiting researcher in Germany and France, he worked in Italy as a researcher at the Centro Sviluppo Materiali. His further education included management and business administration, leadership and European law and regulations.

In 1991 Renzo joined the European Commission in Brussels, where was scientific/technical responsible for ECSC steel research projects. Between 1995 and 1999 he was managing the ECSC-Steel research and technological development programme. In 1999 he became the assistant to the director of ‘Industrial Technologies’ in the Research Directorate-general of the European Commission. Amongst others, he prepared for the provisions to bring to its end the ECSC Treaty and to launch the new research fund for coal and steel (see the Nice Treaty). Meanwhile, since 1999 he promoted initiatives in nanotechnology and in 2003 became the Head of the newly-created Unit ‘Nanosciences and Nanotechnologies’.

He deposited four patent applications (a new source for atomic spectroscopy and some innovative sensors), published fifty articles, drafted four standards on analysis and measurements, edited twelve books, created a newsletter and two web pages, and realized three films on science and research issues.

Dr Ramón TORRECILLAS

INCAR-CSIC, Chemistry of Materials Department, Nanostructured Material, Spain

The Nanostructured Materials Group started to work on materials with a nanometre-sized microstructure in 1995. The main research fields deal with the synthesis, characterization and processing of Nanostructured Materials, mainly in generation of materials with controlled microstructural characteristics, research on their processing into bulk materials with engineered properties and technological functions, and introduction of new device concepts and manufacturing methods.

The main application fields of our research are: biomedical (teeth, hip and knee implants), aeronautic/aerospace and automotive applications (Metallic Matrix Nanocomposites MMCs) and cutting tools (Ceramic Matrix Nanocomposites).

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1 Centre for development of materials
2 European Coal and Steel Community (historically, the first of the European Communities)
**Professor Matt TRAU**

**Director, Centre for Nanotechnology & Biomaterials, University of Queensland, Nanomics BioSystems Pty Limited, Australia**

Professor Matt Trau is currently an ARC Federation Fellow and the Director of the Centre for Nanotechnology and Biomaterials at the University of Queensland, Brisbane, Australia. Matt obtained his BSc (Hons) (1987) and PhD (1992) in Physical Chemistry from Sydney and Melbourne University respectively. Following completion of his PhD he was a Fulbright Research Fellow for 4 years at Princeton University in the Department of Chemical Engineering and the Princeton Materials Institute.

In 1997 he returned to Australia to take up a faculty position in the Chemistry Department at the University of Queensland. In 2001 he founded the Centre for Nanotechnology and Biomaterials (a cross faculty research Centre) which he now runs. Matt’s main research interests are in the area of Nanostructured Assembly and manipulation of matter in order to produce novel materials and devices. Applications of this work include novel devices for rapid DNA sequencing, diagnostics, drug screening, and novel biomaterials for human implants. His work in this general area has resulted in two *Nature* and two *Science* publications, as well as many follow-on publications and patents.

In the past 4 years, Matt has presented twenty six invited international seminars on his work, three of which were plenary lectures at major international conferences. Matt is the founder of Nanomics BioSystems Pty Limited, a company focused of commercializing a platform Nanotechnology applicable to high-throughput DNA sequencing and other forms of ‘biomolecular reading’.

**Dr Volker TÜRK**

**NanoLogue Project Co-ordinator, Wuppertal Institute, Germany**

Volker Türk studied Land Resources Management and Environmental Management and Policy in Germany and Sweden. Currently working as research fellow at the Wuppertal Institute for Climate, Energy and Environment (Germany), his focus area is the sustainability assessment of new technologies.

Volker has worked extensively on information and communication technologies and its applications, ranging from the assessment and improvement of products, life-cycle wide analysis of e-business applications to sectoral analysis.
Nanotechnologies, as new emerging technology, and technology assessment concepts have developed as subsequent area of interest.

Volker is the co-ordinator of an EU-funded project called Nanologue, a Europe-wide dialogue launched on benefits, risks and social, ethical, and legal implications of nanotechnologies. In addition he is member of several expert committees on the societal implications of Nanotechnologies.

A second competence field next to new technologies is tools and concepts for a sustainable development in enterprises.

**Professor Minoru UEDA**
**President, Asian Society of Tissue Engineering, Nagoya University, School of Medicine, Japan**

Professor Ueda started his career as a Research Associate at Department of Oral Surgery, Nagoya University School of Medicine in 1982 and become Assistant Professor in 1987. In 1990 he become the Associate Professor and working as the Professor and Chairman since 1994. He is also a professor at Department of Stem Cell Engineering, Institute of Medical Science, University of Tokyo. He is also a member and office bearer of various academic societies like, The Japanese Society of Tissue Engineering (Former President), Asian Society of Tissue Engineering (President), Tissue Engineering Society international (Vice President), Academy of Osseointegration (International committee).

**Dr Peter VENTURINI**
**Director, National Institute of Chemistry, Slovenia**

Education: PhD Chemistry (1996), University of Ljubljana, Slovenia. MBA (2000) The University of Kansas, Lawrence, USA. BSc Chemistry (1991), University of Ljubljana, Slovenia.


Memberships and Professional Activities:

- Slovenian Research Agency (Member of the Board 2004-)
- The Slovenian Science Foundation (Vice President of the Council, 2001-)
- Coordination of the Slovenian Research Institutions (Member 1999-, President 2003, Vice-president 2002, 2004)
- The House of Experiments, Slovenia (President of the Board, 2002-)
Dr J Malcolm WILKINSON

Managing Director, Technology for Industry Limited, UK

Malcolm is a strategic thinker with experience across all business functions in high technology industries in the UK, USA, and Europe. He has a track record of success in bringing new technology from R&D concept through to volume production in both large and small company environments. He is a skilled negotiator with international commercial experience.

Malcolm founded Technology for Industry in 1992 which is the leading UK consultancy focusing purely on micro and nanotechnology.

Malcolm’s analytical skills combined with his practical experience ensure that he has the exceptional ability to carry out in-depth strategic assessments and analysis. He was joint author of the DTI report on UK Microsystems strategy 2001 and regularly carries out strategic projects on behalf of the public sector.

Dr Jackie Y YING

Executive Director, Institute of Bioengineering and Nanotechnology, Singapore

As an AT&T Bell Laboratories Ph.D. Scholar at Princeton University, Professor Ying began research in materials chemistry, linking the importance of materials processing and microstructure with the tailoring of materials surface chemistry and energetics.

Professor Ying has been on the Chemical Engineering faculty at Massachusetts Institute of Technology since 1992, and was promoted to Associate Professor in 1996 and to Professor in 2001. She is currently the Executive Director of the Institute of Bioengineering and Nanotechnology.

Professor Ying’s research is interdisciplinary in nature, with a theme in the synthesis of advanced inorganic structures for catalytic, membrane, ceramic and biomaterial applications.
Her laboratory has been responsible for several novel wet-chemical and physical vapour synthesis approaches that create nanostructured materials with exceptional size-dependent characteristics. In particular, the engineering of surface reactivity, microstructure, and thermal stability for nanoparticulate, nanoporous, and nanocomposite systems has been the focus of her research. Professor Ying has authored 140 articles and presented over 140 invited lectures on this subject at international conferences.

Professor Ying has been recognized with a number of research awards, including the American Ceramic Society Ross C. Purdy Award 1993, David and Lucile Packard Fellowship, Office of Naval Research Young Investigator Award, National Science Foundation Young Investigator Award, Camille Dreyfus Teacher-Scholar Award, Royal Academy of Engineering ICI Faculty Fellowship, American Chemical Society Faculty Fellowship Award in Solid-State Chemistry, TR100 Innovator Award, American Institute of Chemical Engineers (AIChE) Allan P Colburn Award for excellence in publications, and World Economic Forum Global Young Leader.

**Professor Jianhong ZHU**

**Professor of Neurosurgery, Fudan University Huashan Hospital, Deputy Director of National Key Laboratory for Medical Neurobiology, Shanghai Medical College, Fudan University, China**

Dr Jianhong Zhu is the Professor of Neurosurgery at Fudan University Huashan Hospital and the Deputy Director of National Key Laboratory for Medical Neurobiology in Fudan University Shanghai Medical College. He received a doctor degree in medicine from Suzhou University School of Medicine, China and his Ph.D. degree in molecular cell biology from Berlin-Humboldt University, Germany.

His postdoctoral research was done at Nippen Medical School in Tokyo. He was a Kesley Welch Fellow at Brigham and Women’s Hospital and Children’s Hospital in Harvard Medical School, Boston. Dr Zhu is the recipient of a Young Neurosurgeon Award of the World Federation of Neurosurgical Societies (WFNS) and an Alexander von Humboldt fellowship of Humboldt Foundation (AvHS) and a Cheung Kong Professorship of National Education Minister.

He has been a visiting professor of neurosurgery at Benjamin Franklin-Medical Centre, Free-University Berlin. Dr Zhu serves on the executive committee as the current treasurer for Asia-Australasian Society of Neurological Surgery AANS.
6. SUMMARY REPORT OF EuroNanoForum 2005

EuroNanoForum 2005, the international Forum (conference, workshops, and exhibition) on 'Nanotechnology and the Health of the EU Citizen in 2020', was held over a week in Edinburgh at the Edinburgh International Conference Centre in September 2005 by the Institute of Nanotechnology with the support of the European Commission and UK DTI in the framework of the UK Presidency of the EU.

EuroNanoForum 2005 was the flagship technology event of the UK Presidency of the EU.

The event gathered about 1 000 participants from around the world - key players and specialists in nanotechnology applied to health, to present and discuss the European developments in nanosciences and nanotechnology for medical applications, thus bringing together many different disciplines with a focus on healthcare.

The event has provided an overview of the state-of-the art in the multidisciplinary field of nanomedicine (including: tissue engineering, drug delivery, cellular function, congenital / degenerative diseases, nanoimaging, implants, and diagnostic tools), as well as of the related cross-cutting topics such as risk assessment, communication, ethics, societal aspects, commercialization, and the specific requirements of developing world.

NanoMedicine: The Bigger Picture

Future techniques in medical diagnosis and treatment have often been the subject of science fiction literature and cinema. The approaches are surprisingly consistent. In Star Trek, for example, the diagnosis of illness and its treatment is generally non-invasive and mostly painless. In ‘The Six Million Dollar Man’, an individual who has undergone serious accidental damage was given replacement organs and tissues that function as well, or even better than the originals.

What was once the stuff of science fiction is now closer to becoming a reality. Nature operates at the nanoscale, and today we are acquiring an increasingly profound understanding of natural processes at this scale, enabled by a new generation of scientific instruments. From this knowledge, we are able to design devices that can either directly interact with, or influence, the behaviour of living cells.

Nanotechnology has a trump card to play when applied to medicine. At the nanometre scale, materials often exhibit surprisingly different physical, chemical, and biological properties when compared with the same material in bulk form. The properties of nanoparticles, such as increased chemical activity and the ability to cross tissue barriers, are leading to new drug targeting and delivery techniques.
In the future, it is within the realms of possibility that a nanoparticle may be designed to search for, find and destroy a single diseased cell, taking us even closer to realizing the ultimate goal of disease prevention.

Nanotechnology is also making possible other techniques, such as the stimulation of the body’s own mechanisms to successfully repair diseased or damaged tissues, replacing the need for transplants and artificial organs. In the foreseeable future, allied to advances in information and communication technologies, nanotechnology as applied to medicine, will lead to advances in remote monitoring and care, where a patient may be treated at home - a less expensive option, and one that is more conducive to a successful medical outcome than treatment in a surgery or hospital.

Continued research into disease processes at the molecular level is essential for the development of nanomedicine, and involves teams of scientists from across 'conventional' disciplines, such as physics, chemistry, surgery and mathematics, as well as those from the 'new' fields of genomics, proteomics, metabolomics, pharmacokinetic modelling and even microscope design. Challenges exist in training and managing these multidisciplinary teams and partnerships, and importantly, in finding new solutions to the intellectual property issues that presently hinder the speedy commercialization of new knowledge.

Research challenges also relate to understanding and modelling the toxicity of engineered nanoparticles, and require that toxicologists work alongside medical scientists wherever nanoparticles are involved in drug targeting and contrast agent development.

There are technological challenges, too, in the areas of molecular manufacturing, quality assurance and the eventual programmability of nanodevices. Nanomedicine will also bring its own set of new legal and ethical challenges to be resolved.

Cost benefit analyses are also critical. Where money can be best invested for the greatest social and economic benefit needs to be carefully decided. Should investment be made in prevention or treatment; in diseases of the poor or the rich; in long term hospitalization or costly drug development and deployment? Any strategy for nanomedicine must also be influenced by the facts that resources are finite and demands are great. Within these constraints the health needs of an ageing population need to be managed, cures found for major lifestyle ‘killer’ diseases, such as cancer, and for the diseases of the less-developed world, such as HIV / aids, malaria and tuberculosis.

In conclusion, nanosciences and nanotechnologies are leading to extraordinary new breakthroughs in medicine that were once the stuff of dreams. EuroNanoForum 2005 provided a small but representative snapshot of these exciting opportunities.
Participants
The total participant numbers were:

- Thematic Workshops: 120
- Delegates (inc. speakers): 444
- Journalists: 60
- Schools: 210
- Public Debate: 290
- **TOTAL**: 1,124

EuroNanoForum 2005 Event
The event consisted of a number of different elements:

- **Thematic Workshops**
  These were held over one full day of the conference with topics proposed by relevant organizations and groups. Several of these groups were EC project-based (e.g. Workshop 4), others looked at specific topics and were chaired by a particular organization (e.g. Workshop 7), some by the UK MNT Network (e.g. Workshops 1, 3, & 6), and one by a group of commercial lawyers and patent agents brought together by the IoN to jointly present a collaborative workshop (Workshop 2). In addition the British Association for Lung Research held their annual workshop as part of EuroNanoForum 2005.

  The workshop topics were:

  - Workshop One - European Science Foundation (ESF) Forward Look. Organized by the Micro and Nanotechnology Network (MNT), UK
  - Workshop Four - Nanologue Project. Organized by: Nanologue, Germany
  - Workshop Five - Intelligent eHealth Systems for Personalized Medical Care. Organized by: MyHeart Project & ICT for Health Directorate, Information Society and Media Directorate-General, European Commission
Workshop Six - Exploitation of Nanomedicine. Organized by Micro and Nanotechnology Network (MNT), UK

Workshop Seven - Commercialization of Medical Diagnostic and Other Devices. Organized by MANCEF (Micro and Nanotechnology Commercialization Education Foundation), UK

Workshop Eight - South Africa – Europe Partnership in Nanotechnology, Materials, and Production. Organized by ESASTAP (European South Africa Science and Technology Advancement Programme), South Africa

NanoForum - Not listed in the programme as a workshop but held as a parallel all-day event was a meeting of the NanoForum (European network of networks) partners

Workshop - British Association of Lung Research (BALR)
This workshop was held on the third day, as a parallel session. It formed the annual meeting of the BALR and allowed delegates from the two events to mix and attend the exhibition

- The formal launch of The European Technology Platform on NanoMedicine With presentations by Dr Jouko Karvinen, CEO of Philips Medical Systems and Dr Karl-Jürgen Schmitt, Corporate Communications Director of Siemens AG Medical Solutions

- A Public Debate on the potential benefits of NanoMedicine
Chaired by Susan Watts, Science Editor BBC Newsnight. There was a panel of four experts from across disciplines who briefly presented the potential in their field followed by questions from the floor. The questions followed two main themes: the way nanomedicine / technology is portrayed in the press and scientific questions on particular technologies. In addition to the public delegates from the conference attended. There was an opportunity to network over tea and coffee after the event

- Strategy and Current Activities at European Level
Strategy and current activities at European level in the fields of health, nanotechnology, and nanomedicine in particular, were described in the Opening Session and in a dedicated session (Session 1), as well as through two stands at the exhibition (Cordis and Industrial Technologies Programme). Several presentations were also made on current EC-funded projects covering different topics of the conference

- Presentation of Papers
Some ninety two speakers from over thirty countries made presentations in a combination of plenary and parallel sessions. The focus was science that would benefit the citizen of 2020. It was specifically not an academic conference - it mixed industry with leading academics and, most importantly, was multi-disciplinary. There were sessions devoted to issues of safety, ethics, and the issues of the developing world
Exhibition
Thirty eight companies and organizations exhibited at the event. Around half of these were UK SMEs looking to showcase their technology. The exhibition was open from Tuesday until Friday. One success was the combined exhibition, poster displays, and catering. This ensured a large footfall for exhibitors.

Poster Session
Ninety three posters were exhibited. A number of these were from sponsored students whose attendance had been fully funded. The poster session was divided into the themes of the conference sessions.

Schools Programme
All Scottish schools were invited to send a delegation of 15-16 year old pupils interested in a career in science, together with their teachers. The event was over an afternoon starting with an actor describing life in 2020 followed by invited speakers making presentations. The pupils were then given a special tour of the exhibition.

Press Programme
Separate presentations from key speakers were made to the sixty science journalists attending. This has led to numerous positive articles on both the technology presented, and the event itself.

Social Programme
A social programme was offered, providing an opportunity for networking in the evenings. This included a lively poster session and conference party and where Scotch whisky and Scottish cheeses were sampled. The formal events were a Civic Reception, Ceilidh, and Gala Dinner.

Networking
Leading to potential joint ventures between delegates, speakers, exhibitors, and sponsors to further focus on the event’s near-to-market theme.

Outcomes
These proceedings are available as an interactive CDROM and as a dedicated website at http://www.EuroNanoForum2005.org

and via Cordis at: http://cordis.europa.eu.int/nanotechnology

It is clear there were good outcomes in terms of science from a variety of disciplines looking at common health problems being shared between academia and industry.

The event achieved its aim of being a high-profile, and successful event to mark the UK’s Presidency of the EU.
Delegates at the Exhibition
7. EXHIBITORS

(Detailed profiles are available on the Proceedings CDROM or from the website).

**ABCR GmbH & Co**

ABCR® – A Better Choice for Research Chemicals – is a leading chemical supplier focused on speciality chemicals used in pharmaceutical and medicinal research. ABCR supplies over 48 000 metal-organics, organo-silanes, catalysts, fluorinated aromatics, heterocycles, and organic compounds.

ABCR GmbH & Co. KG, Im Schlehert 10, D-76187 Karlsruhe, Germany
Tel: +49 721 950610
info@abcr.de http://www.abcr.de

**Accelrys**

Accelrys is a scientific software and services company. Accelrys offers simulation, cheminformatics, and bioinformatics products that span drug discovery from target identification and candidate evaluation to compound management and development engineering, as well as materials simulation and informatics products that support product and process development in the chemicals and materials-based industries.

334 Cambridge Science Park, Cambridge, CB4 0WN, UK
Contact: Dr Gerhard Goldbeck-Wood. Tel: +44 (0)1223 228500
gerhard@accelrys.com www.accelrys.com

**AML – Applied MicroEngineering Limited**

AML was formed in 1992 to focus on and commercially exploit MEMS, or as it is now known MNT. The founders of AML have been involved in MEMS for over 20 years. AML’s history of expertise and capability in MEMS covers almost every aspect i.e. design and fabrication of MEMS devices, new process development and the design & manufacture of equipment used to produce MEMS devices, specifically Wafer Aligner-Bonders. AML now focuses on Wafer Bonding; by commercially supplying unique, in-situ wafer aligner-bonder machines, providing a wafer bonding service and developing new bonding processes.

173 Curie Avenue, Didcot, Oxon, OX11 0QG, UK
Contact: Robert Santilli, Tel: +44 (0)1235 833934
rob@aml.co.uk www.aml.co.uk
Bionanotechnology IRC
The Bionanotechnology IRC, based at Oxford University, is the UK's leading research centre for bionanoscience and technology. It is an interdisciplinary collaboration between Oxford University, the University of Glasgow and the National Institute for Medical Research (London). Its research programme includes self-assembled bionano structures, functional membrane proteins and biological molecular machines. The IRC is developing industrial R&D partnerships with leading international companies in areas including drug discovery and diagnostics, and is working with companies to develop analytical tools for bionanotechnology and nanomedicine.

Bionanotechnology IRC, Clarendon Laboratory, Oxford University, OX1 3PU, UK
Contact: Professor John Ryan. Tel: +44 (0) 186 527 2267
J.Ryan1@physics.ox.ac.uk

CENAMPS
CENAMPS is an international Centre of Excellence for Nanotechnology, Micro and Photonic Systems. Headquartered in the North East of England and with partners in major trading blocks worldwide, CENAMPS actively work with industry, academia and governments to create sustained technological capability via exploitation of nanotechnology, microsystems and photonics opportunities. CENAMPS are an independent and entrepreneurial organization developing and commercializing small-scale technologies and their services are focused on stimulating high-tech high-value-add new product innovation and manufacturing technologies in advanced functional materials, biotech, electronics & photonics.

CENAMPS, Fabriam Centre, Middle Engine Lane, Silverlink, Tyne & Wear, NE28 9NZ, UK
Contact: Shak Gohir, Tel: +44 (0) 1912804782
enquiries@cenamps.com

CORDIS
CORDIS is the information service that keeps you up-to-date with European Community activities and initiatives in the field of Research & Development (R&D) and Innovation. CORDIS is free of charge and offers a wide range of information about EU research and innovation policies, EU funding programmes, initiatives, potential partners, and previous and on-going projects. This service is a powerful knowledge and funding resource for both SMEs and big companies across Europe that wish to increase their innovative potential.

Contact: Laura Hernández-Saldaña, Tel: + 32 (0) 2 238 17 37
l.hernandez@cordis.lu http://cordis.europa.eu.int/
**Eminate**

Eminate is the name of the Micro- and Nanotechnology Centre which will be based at BioCity, Nottingham's bioscience innovation centre. Having gained DTi funding as a distinct node of the UK's MNT Network, Eminate will provide services and facilities to industrial customers in the healthcare and related sectors in order to facilitate the adoption of novel micro- and nanotechnologies. Eminate will also promote the commercialization of novel nanotechnologies emerging from the East Midlands' universities and facilitate partnerships between industry and academia.

_c/o The University of Nottingham, University Park, Nottingham, NG7 2RD, UK_
Contact: Dr Laurence Archibald, Tel: +44 (0)115 951 5995
laurence.archibald@nottingham.ac.uk www.nottingham.ac.uk/mnt/

**European Nanotechnology Trade Alliance (ENTA)**

Membership of ENTA is open to businesses and organizations for whom nanotechnology has or may have an impact.

ENTA offers:

- Membership of a trade body that interfaces with the public, the media, and government
- Networking opportunities
- Access to specially commissioned reports and studies
- Fast dissemination of news and hot topics
- Access to customers and new markets
- Opportunities to meet potential partners and financiers
- Discounts on attendance at leading edge events, conferences and exhibitions
- Social and Ethical Impact of Nanotechnology

_Del Stark, Weipers Centre, Garscube Technology Complex, Glasgow, G61 1QH, UK_
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del@euronanotrade.org www.euronanotrade.org
**Epigem**

Epigem is a professional partner of the ‘bionano’ industry bringing microfluidics technology to life. Our business philosophy is to enable our customers to meet their critical business objectives by providing solutions for the design, fabrication and assembly of integrated microfluidic components and modules through state of the art polymer microengineering services. Epigem’s expertise enables our customers to understand the nanoworld and to create products that employ nanotechnology or produce bionano products.

*Malmo Court, Kirkleatham Business Park, REDCAR, TS10 5SQ, UK*
*Contact: Tim Ryan, Tel: +44 (0)1642 49630*
*info@epigem.co.uk www.epigem.co.uk*

**Dr Frances Geesin – Artist in Residence**

Dr Frances Geesin from The London College of Fashion and The University of the Arts London is collaborating with Dr Andreas Briel of Schering AG in Berlin to produce artwork that relates to medical imaging. Frances’s collaboration with Schering AG in Berlin is only weeks old. Dr Briel supplied Frances with information and an image exposing in awesome detail blood vessels and capillaries in a foot which have been revealed through Magnetic Resonance Imaging (MRI). Frances has been exploring methods to capture that visual in textile and fibre which provided her beginning whilst trusting her intuition and familiarity of fibre and cloth to appreciate and connect the threads of ideas generated to create a three dimensional form.

*Headrest, Street End Lane, Broadoak, Heathfield, East Sussex, TN21 8TU, UK*
*Contact: Frances Geesin, Tel: +44 (0)1435 863994*
*frances@geesin.demon.co.uk*

**Imperial College London**

Imperial College London is consistently rated among the top three universities in the UK with a pioneering record among academia in commercialization and industry partnerships – it has the highest industry funded research income among all UK universities. Imperial College London has attracted major international funding in nanotechnology including £3.4 million last year from US investors in a bundle of seven commercially oriented nanotechnology projects.

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*p.cheema@imperial.ac.uk www.imperial.ac.uk*
INEX

INEX is one of the UK’s leading research & commercialization organizations in MEMS, microsystems and nanotechnology. INEX provides professional services to industry in four key areas:

- Design, modelling & simulation of MEMS/microsystems components, devices, and systems
- Development of new processes, products, devices, and prototypes
- Production of MEMS devices & products, manufacturing, Level 0/1 packaging, transfer to high volume operations.
- Business & Consultancy, financial support to UK-based spin-outs & companies, investment opportunities, microsystems/MEMS industry reports, market research, strategy & technology consultancy.

Herschel Annex, University of Newcastle, Newcastle upon Tyne, NE1 7RU, UK
Tel: +44 (0)191 222 3500
enquiries@inex.org.uk www.inex.org.uk

INNOS Limited

The Innos facility develops and manufactures devices using a wide range of technologies including top down and bottom up nanotechnology; microfluidics and MEMS; photonics; micro and nano electronics; bioelectronics and bioMEMS and is therefore uniquely placed to integrate the technologies required by the European healthcare market. The company operates a 1 000m² clean room containing a large suite of fabrication tools including the only Jeol 9300 direct write Ebeam system in the UK, which is capable of writing features as small as 10nm.

Mountbatten Building, Highfield, Southampton, SO17 1BJ, UK
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The Institute of Nanotechnology

Organizers of EuroNanoForum 2005

The Institute of Nanotechnology (originally the Centre for Nanotechnology founded by Ottilia Saxl in 1994) was one of the world's first nanotechnology information providers, and is now a global leader. The IoN works closely with governments, universities, researchers, and companies worldwide on developing and promoting all aspects of nanotechnology. It also serves as a key organizer of international
scientific events, conferences, and educational courses designed to raise awareness of nanotechnology implications, as well as stimulating interest in the less developed countries.

Technology Transfer Centre (TTC) - If you are interested in how nanotechnology will impact your market and are seeking relevant technologies and applications, then TTC can find the solutions. Utilizing the Institute of Nanotechnology’s (IoN) 45 000+ database of researchers and companies involved in micro and nanotechnologies, TTC can plug your company directly into relevant R&D, finding solutions to your technology needs. Based on these technology needs, TTC will match the relevant researchers and companies and facilitate collaborative activity. Contact Andy Garland, andy.garland@nano.org.uk

Overseas Links - The Institute’s activities are continuing on the European front, but it is extending its reach to new countries and continents in an effort to foster nanotechnology developments and partnerships all over the globe. A recent visit to Japan to attend Nanotech 2004 by Ms Saxl and her staff has resulted in a strong interest in working with Japanese companies and researchers, to provide them with information on activities in Europe that may lead to future collaborative projects. Many of the members of the Institute’s Advisory Group already have joint projects with Japanese organizations, and are keen to develop more.

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InvestInItaly
InvestInItaly is the newly established Italian organization for investment promotion created by Sviluppo Italia - the National Agency for Enterprise and Inward Investment Development, and the Italian Trade Commission (ITC), the Government Agency which promotes the internationalization of Italian companies.

InvestInItaly, Via Calabria, 46, 00187 Rome, Italy. Tel: +39 06 421601
info@investinitaly.it www.investinitaly.com

Kelvin Nanotechnology Limited
Kelvin Nanotechnology was created in 1997 to facilitate the commercialization of the world-class technology and expertise in the Department of Electronics and Electrical Engineering at the University of Glasgow. Kelvin Nanotechnology acts as a facilitator for industry and academia to gain cost effective access to state of the art nanofabrication facilities and expertise that exists within the James Watt Nanofabrication Centre at the University of Glasgow.

Kelvin Nanotechnology Limited, 70 Oakfield Avenue, Glasgow, G12 8QQ, UK
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brendan@kelvinnanotechnology.com www.kelvinnanotechnology.com
Lambda Photometrics

Lambda Photometrics is one of the UK’s leading suppliers of lasers, measurement systems, optical components, optical test equipment, micro-positioning products, machine vision products and fibre optic components and instrumentation. With over 27 years of experience, and an extensive range of products from leading companies world-wide.

Lambda House, Batford Mill, Harpenden, Herts, AL5 5BZ, UK
Contact: Dean Edwards, Tel: +44 (0)1582 764334
info@lambdaphoto.co.uk www.lambdaphoto.co.uk

Liquids Research Limited (LRL)

Liquids Research Limited (LRL) was founded in 1990 by Professor Kevin O’Grady and Dr Stuart W. Charles. LRL specialize in the preparation of colloidal dispersions of magnetic nanoparticles. At present the materials upon which we work fall broadly into four categories. These are: ferrofluids, employing ferrite and metal particles, with typical sizes of between 4 to 10nm for a broad range of engineering applications (e.g. loudspeaker performance enhancement, rotary vacuum seals), magneto-rheological dispersions of micron sized particles which exhibit dramatic viscosity changes under the influence of a magnetic field. Magnetic inks are produced, which is a new and rapidly developing area in which we produce specialist magnetic particles of a similar size to ferrofluids.

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London Centre for Nanotechnology

The London Centre for Nanotechnology is a multidisciplinary research institute that bridges the physical and biomedical nano-sciences. It focuses on technology creation and exploitation and is a joint venture between two world class institutions, namely University College London and Imperial College London. LCN combines the skills of eight disciplines, including medicine, chemistry, physics, electrical and electronic engineering, materials, earth science and business. The Centre is developing various technologies in three areas: Information Technology, Health Care and the Environment, and has international commercial links in each.

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lcn-director@ucl.ac.uk www.london-nano.ucl.ac.uk
Metal Nanopowders Limited (MNPL)

Metal Nanopowders Limited (MNPL), a spin-off from the University of Birmingham, is dedicated to the production of metal (e.g. Al, Fe, Zn, Cu, Mg, Ni, Ti, Ag etc.), ceramic (TiN, TiO2, ZnO, SnO, CuO etc.) and composite powders at the sub-100nm scale using novel and cost-effective patented process. Our facilities allow us to produce nanopowders with exceptional purity & physical properties. Our aim is to supply the increasing demand for nanopowders across industry and to develop nanopowders for specific applications.

Department of Metallurgy and Materials, University of Birmingham, Birmingham, B15 2TT, UK
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mnpl@metalnanopowders.com www.metalnanopowders.com

Nanoforum

Nanoforum is a pan-European nanotechnology network funded by the European Union under the Fifth Framework Programme (FP5) to provide information on European nanotechnology efforts and support to the European nanotechnology community. It is led by the Institute of Nanotechnology (UK) and partners include VDI-TZ (Germany), CEA-Leti (France), MTV (Netherlands), METU (Turkey), UNIPRESS (Poland), the Monte Carlo Group (Bulgaria), FFG (Austria), and NanoNed (Netherlands).

On the Nanoforum website (www.nanoforum.org), all users (whether they are members of the public, industry, R&D, government or business communities) can freely access and search a comprehensive database of European nanoscience and nanotechnology (N&N) organizations, and find out the latest on news, events and other relevant information (including education tools, further training, jobs, and other EU projects). In addition, Nanoforum publishes its own specially commissioned reports on nanotechnology and key market sectors, the economical and societal impacts of nanotechnology, as well as organizing events throughout the EU to inform, network and support European expertise.

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mark.morrison@nano.org.uk www.nanoforum.org
NanoMagnetics Limited

- Materials solutions provider driving developments in water purification, medical imaging and diagnostics and data storage
- Medical applications developments including: MRI Contrast Enhancement, Point-of-Care Diagnostics, Cellular Therapy and Cell Labelling, and Tracking
- Substantial base of pre-clinical in vivo work with the National Institutes of Health (NIH) indicating Magnetoferritin is a promising contrast agent for MRI
- Strongly supported by top-tier, international venture capital backers
- IP platform of thirty four international filings, with ten fully granted

NanoMagnetics Limited, University Gate East, Park Row, Bristol, BS1 5UB, UK
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okasyutich@nanomagnetics.com www.nanomagnetics.com

Nanomet Limited

Nanomet is a start-up company based in Kent University, Canterbury, associated with the Canterbury Enterprise Hub at Kent University. The company was founded in June 2005 with the aim of developing and producing instruments to measure and characterize nanoparticles.

5 Woodrough Copse, Bramley, Surrey, GU5 0HH, UK
Contact: Dr Robert Muir. Tel: +44 (0)1483 890597
robert.muir@innospan.co.uk

National Contact Points

The NCP network is the main provider of advice and individual assistance on all aspects of participation in the Sixth framework programme (FP6) for Member States and Associated States.

As the NCPs are national structures, the type and level of services offered may differ from country to country. In general, the following basic services will be available in accordance with the Guiding Principles agreed by all countries:

- Guidance on choosing thematic priorities and instruments
- Advice on administrative procedures and contractual issues
- Training and assistance on proposal writing
- Distribution of documentation (forms, guidelines, manuals etc.)
- Assistance in partner search
NMP

NMP is the acronym for the research priority ‘Nanotechnologies and nanosciences, knowledge-based multifunctional materials, and new production processes and devices’ in FP6. With a budget of more than €1 300m for 2002-2006, the NMP priority under the European Union's 6th Framework Programme is conceived to promote the transition towards knowledge-based products and services through breakthroughs in new applicable knowledge and long-term RTD. The NMP priority supports research projects in the area of Nanotechnology and nanosciences, knowledge-based multifunctional materials and new production processes and devices.

European Commission - DG Research, Directorate G - Industrial Technologies
NMP Info-desk: RTD-NMP@cec.eu.int
http://europa.eu.int/comm/research/industrial_technologies/index_en.html
http://cordis.europa.eu.int/nanotechnology

Orla Protein Technologies Limited

A need exists for technology that allows the direct interaction of materials and physical devices with biology. The interaction is best performed via a truly biomimetic interface; nature uses proteins and lipids to provide this function, but proteins are difficult to immobilize in a functional way. Orla Protein Technologies provides unique expertise for addressing these challenges. Orla surfaces can present reproducible and precisely orientated molecules (for example enzymes, receptors, cell adhesion molecules) as single layers on surfaces by self-assembly. Orla’s technology platform means that Orla can meet customer needs ranging from simple protein immobilization to complex biomimetic surfaces.

Nanotechnology Centre, Herschel Building, Newcastle Upon Tyne, NE1 7RU, UK
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dale.athey@orlaproteins.com www.orlaproteins.com
PA Consulting Group
PA Consulting Group is a leading management, systems and technology consulting firm. Operating worldwide in more than thirty five countries, PA draws on the knowledge and experience of 3 000 people, whose skills extend from the initial generation of ideas, insights, solutions and new technology all the way through to detailed implementation.

Cambridge Technology Centre, Back Lane, Melbourn, Royston, Hertfordshire, SG8 6DP, UK
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Photonix Limited
Photonix is an open-access, multi-user microstructures fabrication facility. It owns and operates a fully equipped 10 000 ft² clean-room, laboratory and serviced office capability. Photonix offers both serviced and unserviced access to the full range of microstructures technology deposition, fabrication, integration and characterization equipment. Its customers include companies and universities.

Kelvin Campus, West of Scotland Science Park, Maryhill Road, Glasgow G20 OTH, UK
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tooley@photonix.org.uk www.photonix.org.uk

Quantitech Limited
Quantitech Limited, based in Milton Keynes, provides sales and service support for analysers and monitors used to measure airborne pollutants. We employ ten people in sales, service and administration.

Since Quantitech was founded in 1983 we have represented instrument manufacturing companies from Europe, USA and Asia, selling their gas and particulate sampling and measuring equipment. These products have been applied for assessment of emissions and occupational exposure as well as in many areas of environmental research.

Unit 3, Old Wolverton Road, Milton Keynes, MK12 5NP, UK
Contact: Chris Tyrrell, Tel: +44 (0)1908 227722
tct@quantitech.co.uk
**Rondol Technology Limited**

There is considerable interest in the development of new materials which may contain nano materials and which can be moulded into medical devices or implants to regenerate human tissue in the form of bone, skin or even organs.

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**Scottish Development International**

Scottish Development International is the international economic development arm of the Government in Scotland and merges inward investment activities along with a range of international business development services to Scottish companies and institutions to help them develop their overseas business. Assistance varies from providing basic market information to detailed matching of business partners, as well as the organization of inward and outward missions and Scottish stands at key international exhibitions.

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david.j.smith@scotent.co.uk www.scottishdevelopmentinternational.com*

**Technēsium TC**

Founded on highly relevant and down-to-earth technological, business and legal know-how, Technēsium TC® is a consultancy firm dedicated to helping others develop and commercially exploit a wide variety of nanotechnologies.

Examples of some of the nanotech clientele to which Technēsium TC® makes its services available include: start-up and spin-out companies; R&D clusters; universities delving into nanoscience exploration; would-be nanobusiness investors; and corporates seeking nanotech applications.

*Technēsium TC® (Europe), 54 Hans Place, Suite 2, London, SW1X 0LA, UK
Technēsium TC® (North America), 118 West Streetsboro Street, Suite 237, Hudson, Ohio 44236, USA
Contact: Robert Bennett: info@technesiumtc.com www.technesiumtc.com*
8. PROGRAMME

Monday 5 September 2005

Thematic Workshops

11.00 – 13.30  Workshop One - European Science Foundation (ESF), NanoMedicine Forward Look
Organized by the Micro and Nanotechnology Network (MNT), UK

11.00 – 13.30  Workshop Two - Intellectual Property Issues Affecting Nanoscience
Jointly organized by Hindle Lowther – Edinburgh, Mewburn Ellis LLP – London, WJM LLP - Glasgow

Organized by the Micro and Nanotechnology Network (MNT), UK

09.00 – 17.30  Workshop Four - Nanologue Project
Organized by Nanologue, Germany

13.00 – 14.30  Lunch

13.45 – 17.45  Workshop Five - Intelligent eHealth Systems for Personalized Medical Care
Organized by MyHeart Project & ICT for Health Directorate, Information Society and Media Directorate-General, European Commission

14.30 – 17.30  Workshop Six - Exploitation of Nanomedicine
Organized by the Micro and Nanotechnology Network (MNT), UK

14.00 – 17.15  Workshop Seven – Commercialization of Medical Diagnostic and Other Devices
Organized by MANCEF (Micro and Nanotechnology Commercialization Education Foundation), UK

11.00 – 13.00  Workshop Eight – South Africa – Europe Partnership in Nanotechnology, Materials, and Production
Organized by ESASTAP (European South Africa Science and Technology Advancement Programme), South Africa

All the workshops were sponsored by the Micro and Nanotechnology Network (MNT), UK
Public Debate: Nanotechnology – Promising a Revolution in Healthcare

18.00 – 20.00

Chair: SUSAN WATTS, Science Editor, Newsnight BBC
Panel:

- PROFESSOR SHERVANSTHI HOMER-VANNIASINKAM, General Infirmary of Leeds, UK
- PROFESSOR ROLF ECKMILLER, University of Bonn, Germany
- DR ANDREW CAMPITELLI, MiniFAB Pty Limited, Australia
- DR ALESSANDRA PAVESIO, Fidia Advanced Biopolymers, Italy

Event Sponsored by Celltech, DTI, BBSRC, and EPSRC

Tuesday 6 September 2005

Opening Session
Moderator: OTTILIA SAXL, CEO Institute of Nanotechnology, UK

09.30 Welcome and Introduction
OTTILIA SAXL, CEO, Institute of Nanotechnology, UK

09.40 Introduction
DR OCTAVI QUINTANA I TRIAS, Director of Health, Research Directorate-General, European Commission

10.00 Convergent Nanotechnologies in Healthcare
DR LEONARD FASS, Director, Academic Relations, GE Healthcare, USA

10.30 From Science to Business in 15 Years
DR ANDREAS JORDAN, Managing Director, Magforce Nanotechnologies, Germany

11.00 Coffee

Session 1 – Strategy and Current Activities at European Level

Chair: DR OCTAVI QUINTANA I TRIAS, Director of Health, Research Directorate-General, European Commission

11.30 A European Strategy for Nanotechnology
DR RENZO TOMELLINI, Head of Nanosciences and Nanotechnologies Unit, Industrial Technologies Directorate, Research Directorate-General, European Commission

12.00 Launch of The European Technology Platform on NanoMedicine:
- DR JOUKO KARVINEN, President and CEO Philips Medical Systems, The Netherlands
- DR KARL-JÜRGEN SCHMITT, Corporate Communications Director, Siemens AG Medical Solutions, Germany

12.30 Drinks Party for Launch of ETP
12.50 Lunch

Session 2A – Tissue Engineering, Nanoscaffolds, and Interfaces

Chair: PROFESSOR SHERVANTHI HOMER-VANNIA SINKAM, Consultant Vascular Surgeon, The General Infirmary of Leeds, UK
Co-Chair: PROFESSOR MIKE EATON, Section Head – Medicinal Chemistry, Celltech Therapeutics Limited, UK

14.00 Nanotechnology in Regenerative Medicine: an Industrial Perspective
DR ALESSANDRA PAVESIO, Director of Research & Development, Fidia Advanced Biopolymers, Italy

14.20 Reconstruction of Human Corneas by Tissue Engineering
DR DAVID J S HULMES, Project Coordinator, Centre National de la Recherche Scientifique – Délégation Rhône Alpes, Institut de Biologie et Chimie des Protéines, France

14.40 Gentle Handling of Individual and Groups of Animal and Human Cells
DR GUENTER FUHR, Coordinator CellPROM (Cell Programming by Nanoscaled Devices), Fraunhofer-Institute for Biomedical Engineering, Germany

15.00 Discussion
15.20 Coffee

15.50 Tissue Engineering, a Lead User Perspective
DR FRANCESCO CURCIO, Associate Professor of Molecular Pathology, Dipartimento di Patologia e Medicina Sperimentale e Clinica, Università degli Studi di Udine – School of Medicine, Italy

16.10 Scaffolds for Tissue Engineering
PROFESSOR JONS HILBORN, President, European Tissue Engineering Society

16.30 Novel ‘Injectable Bone’ Technology for Implant Placement
PROFESSOR MINORU UEDA, President, Asian Society of Tissue Engineering, Nagoya University, School of Medicine, Japan

16.50 Biomimetic Engineering of Cell Scaffolds for Tissue Templates
PROFESSOR ROBERT BROWN, Director, UCL Tissue Repair and Engineering Centre, Coordinator of London Network and the British Tissue Engineering Network (BRITEnet), UK

17.10 Discussion

Session 2B – Drug Delivery and Pharmaceutical Development

Chair: DR ANDREAS JORDAN, Managing Director, Centre of Biomedical Nanotechnology (CBN), Magforce, Germany
Co-Chair: DR UTA FAURE, Nanosciences and Nanotechnologies, Industrial Technologies Directorate, Research Directorate-General, European Commission

14.00 Recent Developments in Targeted Drug Delivery Systems
PROFESSOR COSTAS KIPARISSIDES, Director, Chemical Process Engineering Research Institute, Aristotle University of Thessaloniki, Greece

14.20 Polymer Therapeutics: NanoMedicines in Routine Clinical Use
PROFESSOR RUTH DUNCAN, Director, Centre for Polymer Therapeutics, University of Cardiff, UK
14.40 Biomolecule Coated Microcrystals – Nanostructured Particles for Delivery of Therapeutics Biomolecules
DR BARRY D MOORE, Chief Scientist, XstalBio, UK

15.00 Discussion

15.20 Coffee

15.50 Nanobiodrugs – Applications for Cancer Therapy
DR LAURENT LEVY, CEO, Nanobiotix, France

16.10 Protein Drug Delivery Systems
DR PETER VENTURINI, Director, National Institute of Chemistry, Slovenia

16.30 Nanostructured Semiconductor Technology for Drug Delivery
PROFESSOR LEIGH CANHAM, Chief Scientific Officer, pSivida, Australia.

16.50 Intelligent Nanocapsules for Controlled Drug Encapsulation and Release
PROFESSOR DR HELUMUTH MÖHWALD, Director, Max-Planck-Institute of Colloids and Interfaces, Germany

17.10 Discussion

Session 2C – Cell Structure and Function
Chair: DR PATRICK BOISSEAU, Coordinator, Nano2Life, CEA-Léti, France
Co-Chair: DR DAVID RICKERBY, Institute for Environmental and Sustainability, Joint Research Centre, European Commission

14.00 Nanosensors for Genomics, Proteomics, Cell Screening, and Diagnostics
PROFESSOR JONATHAN M COOPER, Chair of Bioelectronics Research Centre, University of Glasgow, UK

14.20 Mastering the Nanoscale with Visible Focused Light
PROFESSOR STEFAN W HELL, Director, Department of NanoBiophotonics, Max-Planck-Institute for Biophysical Chemistry Göttingen, Germany

14.40 Nano Analysis and Detection of Gastrointestinal Tumour Cells
DR JÜRGEN SCHNEKENBURGER, Department of Medicine, University of Münster, Germany

15.00 Discussion

15.20 Coffee

15.50 Protection Mechanisms in Biomembranes
DR Kvetoslava BURDA, Institute of Physics, Jagiellonian University, Poland

16.10 Real Time Study of Membrane Binding Events
DR ELECTRA GIZELI, Department of Biology, University of Crete, & Institute of Biology and Biotechnology, FORTH, Greece

16.30 Investigation of Cellular and Molecular Activity by AFM
PROFESSOR MANFRED RADMACHER, Institute of Biophysics, University of Bremen, Germany

16.50 Probing Protein Trafficking and Interactions using Optical Nanotechnologies
DR MAURO GIACCA, Director, International Centre for Genetic Engineering and Biotechnology, Italy

17.10 Discussion

18.00 Poster Session
Sponsored by Scottish Enterprise
Wednesday 7 September 2005

SESSION 3 – The Promise of Nanomedicine
Chair: OTTILIA SAXL, CEO, Institute of Nanotechnology, UK
Co-Chair: DR RENZO TOMELLINI, Head of Nanosciences and Nanotechnologies Unit, Industrial Technologies Directorate, Research Directorate-General, European Commission

09.00 Nanotechnology and New Cancer Research in the USA
DR MAURO FERRARI, National Cancer Institute, USA
Discussion

09.40 Whole Cell Biosensors: Chip Canaries for Health Protection
DR SHIMSHON BELKIN, Director, Environmental Sciences and Technology Management, Hebrew University of Jerusalem, Israel
Discussion

10.20 NanoMedicines – A Significant Share of the Non-Generic Market by 2020
PROFESSOR MIKE EATON, Section Head – Medicinal Chemistry, Celltech Therapeutics Limited, UK
Discussion

12.30 Coffee

Session 4A – Converging Technologies for Medicine and Healthcare
Chair: DR ALESSANDRA PAVESIO, Fidia Advanced Biopolymers, Italy
Co-Chair: DR RAYMOND MONK, Nanosciences and Nanotechnologies Industrial Technologies Directorate, Research-General, European Commission

11.30 Multifunctional Polymer Systems designed for Biomedical Applications
PROFESSOR ANDREAS LENDLEIN, Director, Institute of Chemistry GKSS Research Centre, Germany represented by DR STEFFEN KELCH

11.50 A New Landmark in European Nanobiotech: Nano2Life
DR PATRICK BOISSEAU, Coordinator, Nano2Life, CEA-Léti, France

12.10 Biomimetic Approaches to Soft Nanotechnology
PROFESSOR RICHARD A L JONES, Head of Department, Department of Physics and Astronomy, University of Sheffield, UK

12.30 Medical Devices and Converging Technologies
PROFESSOR PATRICIA CONNOLLY, Vice Dean Research, Department of Bioengineering, University of Strathclyde, UK

12.50 Discussion
13.00 Lunch
Session 4B – Nano for Congenital / Degenerative Diseases

Chair: PROFESSOR RUTH DUNCAN, Centre for Polymer Therapeutics, University of Cardiff, UK

Co-Chair: DR BERNARD MULLIGAN, Head of Unit Fundamental Genomics, Health Directorate, Research Directorate-General, European Commission

11.30 Tumour Specific Iron Oxide Nanoparticles for Cancer Therapy
DR ANDREAS JORDAN, Managing Director, Magforce Nanotechnologies, Germany

11.50 Nanostructured Biomaterials in Implants and Insulin Delivery
DR JACKIE Y YING, Executive Director, Institute of Bioengineering and Nanotechnology, Singapore

12.10 Dendrimers as Drugs and Carriers: A unique pharmacokinetics?
PROFESSOR RUTH DUNCAN, Centre for Polymer Therapeutics, University of Cardiff, UK

12.30 Biocompatibility – from Proteins to Tissue
PROFESSOR MORTEN FOSS, Associate Research Professor, Interdisciplinary Nanoscience Centre (iNANO), University of Aarhus, Denmark

12.50 Discussion

13.00 Lunch

Session 4C – NanoImaging and Functionalized Nanoparticles

Chair: PROFESSOR DR HELUMUTH MÖHWALD, Director, Max Planck Institute of Colloids and Interfaces, Germany

Co-Chair: DR OLIVIER LE DOUR, Assistant to the Director, Health Directorate, Directorate-General for Research, European Commission

11.30 NanoMedicine – Moving from the Bench to the Patient
PROFESSOR UELI AEBI, Director, M E Müller Institute, Biozentrum, University of Basel, Switzerland

11.50 Radioactive Nanoclusters for Medical Applications
PROFESSOR STÉPHANE LUCAS, University of Namur, Belgium

12.10 Microbubbles as Targeted Contrast Agents and Drug Delivery Systems
DR ANDREAS BRIEL, Schering AG, Berlin, Germany

12.30 Nanoparticles in Future Medical Applications
DR WERNER HOHEISEL, Bayer Technology Services GmbH, Leverkusen, Germany

12.50 Discussion

13.00 Lunch

Session 5A – Engaging the Community – Views of Risk vs. Public Perception

Chair: DR MICHAEL ROGERS, Bureau of European Policy Advisers (BEPA), European Commission

Co-Chair: DR SOPHIA FANTECHI, Nanosciences and Nanotechnologies, Industrial Technologies Directorate, Research Directorate-General, European Commission

14.30 Applied Nanosciences and Environmental Health and Safety
PROFESSOR DAVID M BERUBE, Communication Studies & Assoc. Director NanoSTS, USC NanoCenter, University of South Carolina, USA
14.50 **Innovation, Risk and Stakeholder Engagement: Framing Nanotechnology**  
PROFESSOR JOYCE TAIT, Director, Innogen Centre, University of Edinburgh, UK

15.10 **Nanologue: A Europe-Wide Dialogue on the Social, Ethical and Legal Implications of Nanotechnologies**  
DR VOLKER TÜRК, NanoLogue Project Co-ordinator, Wuppertal Institute, Germany

15.30 **Enhancing Dialogue on Nanotechnologies and Nanosciences in Society at the European Level: NanoDialogue**  
DR JENNIFER PALUMBO, Science and Society Projects, Città della Scienza Science Centre Naples, Italy

15.50 Discussion

Session sponsored by the DTI

**Session 5B – Affordable Cures – Addressing Diseases of the Developing World**

Chair: PROFESSOR VENKATESH RAO AIYAGARI, Head, Science and Engineering Research Council, Department of Science and Technology, Government of India, India

Co-Chair: PROFESSOR GÖRAN HERMERÉN, President, European Group on Ethics in Science and New Technologies, Brussels, Belgium

14.30 **Nanotechnology and the Developing World**  
ERIN COURT, Canadian Program in Genomics and Global Health, University of Toronto Joint Centre for Bioethics, Canada

14.50 **Nanotechnologies Delivering better Vaccines for Developing Countries?**  
DR THIERRY COCHE, Associate Director, Head of New Technologies and Bioinformatics, GlaxoSmithKline Biologicals R&D, Belgium

15.10 **Evaluation of Nanoparticles Delivering Anti-Tuberculosis Drugs**  
DR HULDA SHAIDI SWAI, Senior Scientist, Centre for Polymer Technology, CSIR-Manufacturing and Materials Technology, South Africa

15.30 **A Review of Current Trends in Technological Development**  
DR ABEL JOHN JULIAN RWENDEIRE, United Nations Industrial Development Organization, Uganda, represented by VLADIMIR KOZHARNOVICH

15.50 Discussion

**Session 5C – Impacting Society – Needs of the Ageing Population**

Chair: PROFESSOR JIANHONG ZHU, Professor of Neurosurgery, Shanghai Medical College, Fudan University, China

Co-Chair: DR TORBJÖRN K INGEMANSSON, Biotechnology and Applied Genomics, Health Directorate, Directorate-General for Research, European Commission

14.30 **Non-invasive Nanoparticulate Delivery Systems for the Treatment of Chronic Diseases**  
DR FRANK SINNER, Head of Department for Proteomics, Institute of Medical Technologies and Health Management, Austria

14.50 **Deep Brain Stimulation for Movement Disorders and Pain**  
PROFESSOR TIPU AZIZ, Nuffield Department of Surgery, University of Oxford, UK

15.10 **Bio-engineered Meniscus Substitute: Community Added Value**  
DR ENRICO TOGNANA, Fidia Advanced Biopolymers, Italy
15.30 **Intelligent Scaffolds for Tissue Engineering of Bone, Skin and Cartilage: INTELLISCAF**  
DR NASEEM THEILGAARD, Project Coordinator INTELLISCAF, Danish Technological Institute, Denmark

15.50 Discussion  
Session sponsored by the DTI

**Session 5D – Lab to the Clinic – Commercializing Nanomedicine**

Chair: DEL STARK, Business Development Manager, Institute of Nanotechnology, UK  
Co-Chair: DR DIDIER BOUIS, Competitiveness in the Pharmaceuticals Industry and Biotechnology, Consumer Goods Directorate, Directorate-General for Enterprise and Industry, European Commission

14.30 **Commercializing Issues Around Health Applications**  
DR KEES EIJKEL, Technical-Commercial Director, MESA+ Research Institute University of Twente, The Netherlands

14.50 **Applied Entrepreneuring: From Science to Profitable Business**  
DR RICHARD G CARO, CEO, TangibleFuture Inc., USA

15.10 **Fast Track Incorporation of Nanotech in Medical Products**  
DR J MALCOLM WILKINSON, Managing Director, Technology for Industry Limited, UK

15.30 **Transferring Early Stage Nanotechnologies from the Lab to the Healthcare Marketplace**  
PROFESSOR LUIS MEJIA, Stanford University, USA

15.50 Discussion  
Session sponsored by the DTI

17.30 Civic Reception at Edinburgh City Chambers  
19.30 Ceilidh with Haggis, Neaps, and Tatties

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**Thursday 8 September 2005**

**Session 6A – Novel Implants and Devices**

Chair: DR MAURO GIACCA, Director, International Centre for Genetic Engineering and Biotechnology, Italy  
Co-Chair: PROFESSOR JONS HILBORN, President, European Tissue Engineering Society, Uppsala University, Sweden

09.00 **Nanocomposites for Biomedical Applications**  
DR RAMÓN TORRECILLAS, INCAR-CSIC, Chemistry of Materials Department, Nanostructured Material Group, Spain

09.30 **Towards Learning Retina Implants for the Blind**  
PROFESSOR ROLF ECKMILLER, Head, Division of Neural Computation, Department of Computer Science, University of Bonn, Germany

10.00 Coffee
10.30  **Genomic Nanoprocessors: A Platform for Future Healthcare?**  
DR JOHN BEATTIE, Chief Operating Officer, Scottish Centre for Genomic Technology and Informatics UK

10.50  **Integration of Bio, Micro, Nano, and Information Technology for Medical Diagnostic Systems: Challenges and Opportunities**  
DR ANDREW CAMPITELLI, Programme Director, Bio-Micro Nano Technology, MiniFAB Pty Limited, Australia

11.10  **Tissue Engineering of Cartilage and Bone – State of the Art and Future Challenges**  
DR JOCHEN RINGE, Department of Tissue Engineering, Charité, University Medicine, Berlin, Germany

11.30  Discussion

12.00  Lunch

**Session 6B – Nano Sensors and Diagnostics**

Chair: PROFESSOR LEONARD FASS, Director, Academic Relations, GE Healthcare, USA  
Co-Chair: DR GRIET VAN CAENEGEM, Micro- and Nanosystems, Components and Systems Directorate, Information Society and Media Directorate-General, European Commission

09.00  **Recent Advances in Biosensors**  
PROFESSOR CHRIS LOWE, Director, Institute of Biotechnology, University of Cambridge, UK

09.20  **Cantilever-Based Sensing Devices for Diagnostics**  
DR ANJA BOISEN, Assistant Research Professor, Department of Micro and Nanotechnology, Technical University of Denmark, Denmark

09.40  **Requirements and Benefits of a High Resolution Imaging Strategy**  
DR ROLF GUENTER, Chief Scientific Officer, Evotec Technologies, Germany represented by DR KARSTEN KOTTIG

10.00  Coffee

10.30  **Drug and Gene Nano-balls: Applications in Genomics, Proteomics, Diagnostics, and Personalized Medicine**  
PROFESSOR MATT TRAU, Director, Centre for Nanotechnology & Biomaterials, University of Queensland, Nanomics BioSystems Pty Limited, Australia

10.50  **Interfacing Biology and Physical Science through Nanoscale Protein Engineering**  
PROFESSOR JEREMY LAKEY, Scientific Director and Founder, Orla Protein Technologies, UK

11.10  **Nanoscale Devices for Proteomics and Drug Discovery**  
DR AHMET SENOGLU, CEO, Nanoxis AB, Sweden

11.30  Discussion

12.00  Lunch
Session 6C – Nanoparticle Risk Assessment

Chair: DR VICKI STONE, Reader in Toxicology, Co-director Biomedicine Research Group, Napier University, Edinburgh

Co-Chair: DR PHILIPPE MARTIN, Risk Assessment, Public Health and Risk Assessment Directorate, Consumer Protection Directorate-General, European Commission

09.00 An Introduction to the Toxicology and Risk Assessment of Particles
PROFESSOR KEN DONALDSON, Scientific Director, Centre for Inflammation Research (CIR), University of Edinburgh, UK

09.20 Translocation and Cardiovascular Effects of Nanoparticles
PROFESSOR PAUL J F BORM, Centre for Expert’s Assessment in Life Sciences (CEL), The Netherlands

09.40 Nanoparticle Exposure – Risk Relationship between Exposure and Health Effects
DR ROB AITKEN, Director of Research Development, Institute of Occupational Medicine, UK

10.00 Coffee

10.30 Percutaneous Uptake of Nanoparticles: The NANODERM Project
PROFESSOR TILMAN BUTZ, University of Leipzig, Germany

10.50 The Central Nervous System as a Target for Inhaled Nanoparticles
PROFESSOR GÜNTER OBERDÖRSTER, Professor of Environmental Medicine, University of Rochester, USA

11.10 A Global Strategy for Safe Production and Use of Nanoparticles: NanoSAFE 2
DR FREDERIC SCHUSTER, CEA, France

11.30 Discussion

12.00 Lunch

Session Sponsored by Degussa

Session 7 – NanoMedicine, Ethics, and Society

Chair: DR SIMONE SCHOLZE, Senior Programme Specialist, Division of Ethics of Science and Technology, UNESCO, FRANCE

Co-Chair: DR MAURIZIO SALVI, Ethics and Science, Science and Society Directorate, Research Directorate-General, European Commission

13.30 Nanotechnologies Today and Tomorrow: Ethical Aspects
PROFESSOR GÖRAN HERMERÈN, President, European Group on Ethics in Science and New Technologies, Brussels

13.45 Dreams, Hopes, and Uncertainties in the Nano Revolution
PROFESSOR EMILIO MORDINI, Director, Centre for Science, Society and Citizenship, Italy

14.00 Can Nanotechnologies Make Humans Better? – Ethical Issues in Nanomedicine
DR DONALD BRUCE, Director, Church of Scotland’s Society Religion and Technology Project, UK

14.15 Nanomedicines and Biotechnology Pharmaceutical Research, Regulatory and Ethical Implications
DR ROGERIO GASPAR, Laboratory of Pharmaceutical Technology, Faculty of Pharmacy, University of Coimbra, Portugal

14.30 Coffee
15.00  Discussion – NanoMedicine, Ethics, and Society
Session sponsored by the DTI

12.30  Gala Dinner

Friday 9 September 2005

Session 8 – What can we do at International Level?
Chair:  DR RENZO TOMELLINI, Head of Nanosciences and Nanotechnologies Unit, Industrial Technologies Directorate, Research Directorate-General, European Commission
Co-Chair: Julie Deacon, Assistant Director, Micro and Nanotechnology Network (MNT), UK

09.30  The Case for Multinational Research Infrastructures
HERVÉ PERO, Head of Research Infrastructures Unit, Structuring the ERA Directorate, Research Directorate-General, European Commission represented by DR RENZO TOMELLINI

10.00  Nanoscience and Technology Initiatives in India
PROFESSOR VENKATESH RAO AIYAGARI, Head, Science and Engineering Research Council, Department of Science and Technology, Government of India, India

10.30  Nanosciences & Nanotechnology in South Africa: Challenges and Opportunities
DR MOLEFI MOKUTU, General Manager, Research and Development, Mintek, Council for Mineral Technology, South Africa

11.00  Coffee

11.30  Chinese Approach – Nanotechnology in Regenerative Medicine
PROFESSOR JIANHONG ZHU, Professor of Neurosurgery, Fudan University Huashan Hospital, Deputy Director of National Key Laboratory for Medical Neurobiology, Shanghai Medical College, Fudan University, China

12.00  Nanobiotechnology and Nanomedicine in Japan
DR AKIYOSHI TANIGUCHI, Associate Director, Biomaterial Centre, National Institute for Materials Science, Japan

12.30  Nano(Bio)Technology for Medicine in Russia
PROFESSOR ALEKSANDRA I ARCHAKOV, Research Institute of Biomedical Chemistry, Russian Academy of Medical Sciences (RAMS), Moscow, Russia
Discussion and Conclusions

13.00  Lunch and Departure
The Venue for EuroNanoForum 2005: The Edinburgh International Conference Centre (EICC)
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EuroNanoForum 2005, the international Forum (conference, workshops, and exhibition) on ‘Nanotechnology and the Health of the EU Citizen in 2020’, was organized in September 2005 by the Institute of Nanotechnology and the European Commission in the framework of the UK Presidency of the Council of the European Union.

The event gathered about 1,000 participants from around the world, who are key players and specialists in nanotechnology applied to health, to present and discuss the European developments in nanosciences and nanotechnologies for medical applications, thus bringing together many different disciplines with a focus on healthcare.

The information gathered in these Proceedings provides an overview of the state-of-the-art in the multidisciplinary field of nanomedicine (including: tissue engineering, drug delivery, cellular function, congenital/degenerative diseases, nanoimaging, implants, and diagnostic tools), as well as of the related cross-cutting topics such as risk assessment, communication, ethics, societal aspects, commercialization, and understanding and addressing the specific requirements of the developing world.

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