‘Session 1: Nanotechnologies today and tomorrow

Health applications of nanoscience and nanotechnologies

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Head of the European Medical Research Councils (EMRC)
Plan

1. Medical Innovation: Paradigm shift and patients unmet needs
2. Nanomedicine: Convergence of nanosciences and systems biology
3. Health applications today: examples
4. Health applications tomorrow: challenges
Medical Innovation: Paradigm Shift

- Paradigm shift from large markets to personalized/individualized medicine and need for knowledge transfer across disciplines and research sectors (e.g., academia & industry)

- Patient centered process

- Patients unmet needs (WHO, 2004)
Medical Innovation: Paradigm Shift

Current process for the development and commercialization of drugs in Europe (EBC EFNA)

Stakeholder involvement and major milestones

Innovation phases

Time through phase (months)

www.esf.org
Patient Centered Process
Priority diseases for Europe (WHO, 2004)

EUROPE
• Tuberculosis
• Osteoarthritis
• Diabetes
• Alzheimer disease
• Cardiovascular diseases
• Acute stroke (cerebro-vascular accident)
• Alcohol dependence and alcoholic liver disease
• Antimicrobial resistance as it relates to infectious diseases
• Influenza (primarily related to vaccines to counter the pandemic threat)
• Depression
• Chronic Obstructive Pulmonary Disease
• HIV/AIDS
• Cancers

THE WORLD
• Malaria
• Postpartum Haemorrhage
• Neglected Diseases including Trypanosomiasis, Leichmaniasis and Buruli Ulcer

ESF - ZON-MW - WHO (Nov. 2004)
‘Priority medicines for the citizens of Europe’
Priority diseases for Europe (WHO, 2004)

17 priorities

• Diseases for which **basic and applied research is required**: cancer; acute stroke
• Diseases for which **biomarkers are absent**: Alzheimer disease; osteoarthritis
• Diseases for which **better formulations** are required: cardiovascular disease (secondary prevention); diabetes; postpartum haemorrhage; paediatric HIV/AIDS; depression in the elderly and adolescents
• **Neglected diseases** or areas: tuberculosis; malaria and other tropical infectious diseases such as trypanosomiasis, leishmaniasis and Buruli ulcer, HIV vaccine
• Diseases for which **prevention** is particularly effective: chronic obstructive pulmonary disease including smoking cessation; alcohol use disorders: alcoholic liver diseases and alcohol dependency
• **Future public health threats**: infections due to antibacterial resistance; pandemic influenza
Priority diseases for Europe

Special concerns

- Children
- Elderly (ageing population in Europe)
- Rare diseases
Nanomedicine: Convergence of nanosciences and systems biology

‘The field of Nanomedicine is the science and technology of diagnosing, treating and preventing disease and traumatic injury, of relieving pain and of preserving and improving human health, using molecular tools and molecular knowledge of the human body.’

ESF-EMRC
Forward Look Report
Nanomedicine
November 2005

ESF
Forward Look
Systems Biology
September 2007
Nanomedicine: Convergence of nanosciences and systems biology

The field of nanomedicine is perceived as embracing five main sub-disciplines:

- Nanomaterials and Devices
  - Analytical and Imaging Tools
  - Novel Therapeutics and Drug Delivery Systems
- Clinical Applications
- Safety and Toxicological Issues
  - Environmental, manufacturing and clinical use
Paradigm shift curative towards preventive and predictive medicine

Molecular Imaging Diagnostics (MDx): Impact on healthcare in the future

Genetic disposition | DNA mutations
---|---

Developing molecular signature | First symptoms | Progressing disease
---|---|---

Today
Earlier diagnosis, optimized workflow

Screening | Diagnosis & Staging | Treatment & Monitoring | Follow-up
---|---|---|---

• Unspecific markers
• POC imaging
• Mammography

• Diagnostic imaging
• Biopsies

• Surgery
• Cath-lab
• Radiation therapy
• Diagnostic imaging
• Unspecific markers

Future

Screening | Diagnosis & Staging | Treatment & Monitoring | Follow-up
---|---|---|---

• Specific markers (MDx)

• Molecular imaging: quantitative, whole-body
• CA Diagnosis

• Mini-invasive surgery
• Local/targeted drug delivery & tracing
• Tissue analysis (MDx)

• MI, MDx
• Non-invasive, Quantitative imaging
**Biological Applications:**

- Definition of target and pathway and network identification
  - Via multiple, co-assembled biomolecules

- Definition of mechanisms of signalling and signal transduction
  - Via artificial assemblies in vitro

**Medical Applications:**

- Drug targeting
  - Whole body, cellular, sub-cellular localisation of drugs, proteins and genes

- Drug discovery
  - High Throughput Screening technology with biomolecular or cellular read-outs
  - Novel bioactives, obtained through nanotechnology
  - Novel drug delivery systems

- Diagnostics and sensing
  - In vitro (multiple analyte detection) and in vivo

- Regenerative medicine
  - Materials to regulate cell signalling and differentiation, and also controlling morphogenesis thus helping to bring functional integration
Health applications today: examples

Nanomaterials and nanodevices

Medical devices and diagnostics: e.g., Biosensors (J. Deacon, UK MNT)

Regenerative medicine: bioresponsive materials for tissue engineering
(J.A. Hubbell, CH; J. Planell, IBEC, ES)
Role of biosensors
diagnostics vs drug discovery (AstraZeneca)

- An analytical tool consisting of a biologically active material used in close conjunction with a device that will convert a biochemical signal into a quantifiable physical signal (current, light etc.)

- Most people associate the term biosensor with an integrated device (e.g. glucose sensor), but Pharma looking to stress in-situ transduction system and external detector (e.g. telemetry probe)

<table>
<thead>
<tr>
<th>in diagnostics</th>
<th>in drug discovery</th>
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<tbody>
<tr>
<td>usually for measuring single analyte e.g. glucose</td>
<td>usually for measuring multiple analytes e.g. RNA chips, SPR</td>
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<tr>
<td>ease of use</td>
<td>flexibility</td>
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<tr>
<td>simple, easy to interpret output</td>
<td>can accept more complex output</td>
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<tr>
<td>may be used for many years for same application</td>
<td>may be used in short campaigns e.g. 3 month HTS assay</td>
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THE NEW ERA OF REGENERATIVE MEDICINE

Dozens of biotech companies and university labs are developing ways to replace or regenerate failed body parts. Here are a few of the projects:

**BONE**
Bone growth factors or stem cells are inserted into a porous material cut to a specific shape, creating new jaws or limbs. A product that creates spine bones is in clinical trials.

**COMPANIES:** Creative Biomolecules, Orquest, Salford Orthopaedics Biologies, Genentech Institute, Osiris Therapeutics, Regenereon.

**SKIN**
ORGanogenesis Algurial, a human skin equivalent, is the first engineered body part to win FDA approval, initially for leg ulcers. Other skin types are in the works for foot ulcers and burns.

**COMPANIES:** ORGanogenesis, Avanced Tissue Sciences, Integra LifeSciences, LifeCell, Ortec International.

**LIVER**
A spongy membrane is built up and then seeded with liver cells. Organ size is small but a full-size liver could take 10 years due to its complexity.

**COMPANIES:** Advanced Tissue Sciences, Human Organ Sciences, Organogenesis.

**TEETH**
Enamel matrix proteins are used to fill cavities. It works in dogs; human trials are a few years away.

**COMPANIES:** Gore, Alax Laboratories, Creative BioMolecules.

**BREAST**
In preclinical studies, several companies have been able to create a cosmetic nipple by inserting a ball of cartilage. Researchers are now trying to grow a whole cosmetic breast.

**COMPANIES:** Reprogenesis, Integra LifeSciences.

**PANCREAS**
Insulin-manufacturing cells are harvested from pigs, encapsulated in membranes, and injected into the abdomen. The method has been tested in animals and could be in human trials in two years.

**COMPANIES:** Biomedical Technologies, Neocrin, Circe Biomedical.

**HEART VALVES, ARTERIES, AND VEINS**
A 10-year initiative to build a heart has just started. Genetically engineered proteins have been used to regenerate blood vessels.

**COMPANIES:** ORGanogenesis, Advanced Tissue Sciences, Genentech, LifeCell, Reprogenesis.

**SALIVA GLANDS**
Proteins called aquaporins allow cells to secrete water and used to recreate saliva glands damaged by disease or radiation. Glands are also being engineered to secrete healing drops. The technique has proven successful in mice.

**COMPANIES:** None yet.

**URINARY TRACT**
Cartilage cells are taken from the patient, packed into a tiny matrix, and injected into the weakened ureter, where they bulk up the tissue walls to prevent urinary back-up and incontinence. The method is in late-phase clinical trials.

**COMPANIES:** Reprogenesis, Integra LifeSciences.

**BLADDER**
Doctors at Children’s Hospital in Boston have grown bladders from skin cells and implanted them in sheep. They are about to try the same process on a patient.

**COMPANIES:** Reprogenesis.

**SPINAL CORD NERVES**
Scientists are in-seeding with nerve-growth factors, injecting them at the site of damage to encourage regeneration or seeding them along absorbable filaments and implanting them. Rats have been made to walk again.

**COMPANIES:** Acorda, Regenesis, SytoTherapeutics, Guildford Pharmaceuticals.
Candidates for bone repair and regeneration in minimally invasive surgery

Injectable Porous Calcium Phosphate Cements
(J. A. Planell, IBEC, Barcelona, ES)
Health applications today: examples

Molecular and Patient Imaging

Targeted therapeutics and molecular imaging in cancer

Figure 5: Radiation treatment planning (right) of head/neck cancer based on fusion of morphologic and functional information obtained with PET-CT (left) (courtesy of Prof. Liselotte Højgaard)
Imaging is crucial for the concept of personalised medicine

For treatment tailored to the individual patient’s disease biology and in the future combined with genetic make-up.

Prof. Liselotte Højgaard, Chair of EMRC
Various types of nanopharmaceuticals

Novel therapeutics and Drug delivery systems (R&D)

- Liposomes
- Antibodies and their conjugates
- Viruses as viral vectors
- Polymer micelles
- Nanoparticles
- Polymer-protein conjugates
- Unimolecular polymer and dendrimer conjugates
Health applications today: examples

Novel therapeutics and Drug delivery systems (R&D)

- Mylotarg: an Antibody-Drug conjugate (M. Eaton, UCB, BE)
- Polymer conjugates: e.g., Paclitaxel Poliglumex (Xyotax) as therapeutic in NSCLC (J. Singer, Cell Therapeutics, USA); for delivery of combination therapy (endocrine and chemotherapy); PEG-protein conjugates as anticancer agents
- Gene therapy: gene delivery based on biodegradable polyesters (T. Kiessel, DE)
Health applications tomorrow: challenges

- **Safety and Toxicological Issues** (environmental, manufacturing and clinical use): proactive risk assessment (EuroNanoPar project)

- Categories and Design of Clinical Trials
- Regulatory and Legal issues, IPR and Data sharing
- Funding and Models of Partnerships
- Management and Logistics of Clinical Trials
- Education and Training, Career and Authorship
Health applications tomorrow: challenges

• **Regulatory and legal status**: was mainly targeted to address large Pharma R&D, need to support Academia and Biotech and to establish early dialog with Competent Authorities

  1/ Actual references in Europe for medicinal drug on human use: First in place at the international level (US, EU, JP) ICH E6 for GCP (1996)

    - EU Directives: 2001/20/EC (and guidelines) enforced by 1 May 2004 and completed by 2005/28/EC
    - 2003/94/EC for GMP
    - EU Directive for medical devices 93/42/EC
    - EU Directive for personal data 95/46/EC
    - EU Regulation for paediatrics and rare diseases and thoughts are given in US to develop specific regulation for women and ethnic groups
Health applications tomorrow: challenges

2/ Other guidelines incl. draft for specific cases and new situations:
   - Draft guideline on requirement for first-in-man clinical trials for potential high risk medicinal products (EMEA/CHMP/SWP/28367/2007): including chemical and biological medicinal products. It covers the first administration of a single dose of high-risk medicinal product and the initial single ascending dose phase of clinical development

To be developed?
   - Diagnosis
   - Theranostics
   - Population survey and biobanking
   - Physiology and physiopathology
   - Surgery
   - Socio-Economic Studies
It is necessary to create **true multi- and interdisciplinary research environments** where medical doctors, pharmacists, physicists, chemists, mathematicians, molecular biologists, computer scientists can work together.

**Long-term funding** of large research projects, collaboration between universities and major research centres.

**European coordination and collaboration.**
Synergies between BMS ESFRI Infrastructures: *Concerted approach*

Prof. C. Bréchet (Inserm CEO)
ECRI 6 June 2007
Hamburg (DE)
"The special case of medicine"

The University Hospitals produce the majority of research in health & lifesciences in Europe.

Need for GMP facilities
On the European level there is a need to develop, coordinate and adopt better systems for evidence-based medicine and health technology assessment for recommendations of standard practice in patient care.
In conclusion

**EMRC:** Clinical and Translational research should be strengthened in Europe

**NIH in USA:** Clinical and Translational research very important focus areas

**Launch in 2007 of the ESF-EMRC Forward Look on**

“Investigator-Driven Clinical Trials”

**Chair:** Prof. Jurgen Schölmerich (Vice-President DFG) in collaboration with NIH and FDA
**ESF - EMRC FL 07-01**

‘Investigator Driven Clinical Trials’ Time Line

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**FL 07-01: Investigator Driven Clinical Trials (IDCT)**

- Approval April, Launch July
- Management Committee

**Strategic Workshops cover:**
- Current Status
- Build Scenarios
- Make recommendation
- Dissemination

5 Strategic Workshops on:
- Categories and Design of Clinical Trials
- Regulatory and Legal issues, IPR and Data sharing
- Funding and Models of Partnerships
- Management and Logistics of IDCT
- Education and Training, Career and Authorship

**Consensus Conference**


**Final report**

**Dissemination**
This paper was produced for a meeting organized by Health & Consumer Protection DG and represents the views of its author on the subject. These views have not been adopted or in any way approved by the Commission and should not be relied upon as a statement of the Commission's or Health & Consumer Protection DG’s views. The European Commission does not guarantee the accuracy of the data included in this paper, nor does it accept responsibility for any use made thereof.