The Future of Health Care: deep data, smart sensors, virtual patients and the Internet-of-Humans

About you

What is your background? Are you submitting this proposal as an individual, or do you represent a community or institution?

Prof. Dr. Hans Lehrach

Professor Hans Lehrach is director (em.) of the Max Planck Institute for Molecular Genetics in Berlin. He has held positions at Harvard University (USA), EMBL (Germany) and the Imperial Cancer Research Fund, UK. Prof. Lehrach is author of more than 1000 publications and 24 patents, is a fellow of the AAAS, and holds the Ján Jessenius SAS Medal of Honour (2003), the Karl Heinz Beckurts Award (2004) and the Gusi Prize (2015) in recognition of his achievements in medical sciences. He was co-ordinator of ‘ITFoM: IT Future of Medicine’ (www.itfom.eu), a finalist of the FET Flagship Call, which has established a strong technological roadmap and network of partners from 33 countries. In this current initiative, Prof. Lehrach represents a growing network of research institutions, industry representatives, scientists and patient groups that share a long-term vision for sustainable health care (www.heathcarecompactforeurope.eu).

Prof. Adrian M. Ionescu

Adrian M. Ionescu is a Professor of Nanoelectronics at the Swiss Federal Institute of Technology, Lausanne, Switzerland. He has held staff and/or visiting positions at LETI-CEA, Grenoble, France, LPCS-ENSERG, Grenoble, France and Stanford University, USA, in 1998 and 1999. He is director of the Laboratory of Micro/Nanoelectronic Devices (NANOLAB). Dr. Ionescu has published more than 400 articles in international journals and conferences. He received the Annual Award of the Technical Section of the Romanian Academy of Sciences in 1994 and the Blondel Medal in 2009, the IBM Faculty Award in Engineering in 2013, the Outstanding Service Award of the Swiss Academy of Technical Sciences in 2015 and an Advanced Grants ERC Recipient in 2016. He has been, together with Prof. Hierold of ETH Zürich, the coordinator of the FET Flagship Pilot ‘Guardian Angels for a Smarter Life’ (www.ga-project.eu), a finalist of the FET Flagship Call.

The proposal is strongly supported by a large network of universities, research institutes, industries and individual leaders, including:

- **CEA, France**: Nora Benhabiles, Professor. Director, External Collaborations and Industrial Partnerships at CEA.
- **Consorzio Interuniversitario Risonanze Magnetiche di Metallo Proteine (CIRMMP), Italy**: Claudio Luchinat, Professor of Chemistry.
- **ETH Zürich, Switzerland**: Christofer Hierold, Professor, Chair in Micro and Nanosystems, Lothar Thiele, Professor, Chair Computer Engineering and Networks.
- **Medical University Graz, Austria**: Kurt Zatloukal, Professor of Pathology.
- **University College London, UK**: Stefan Beck, Professor of Medical Genomics.
- **Kings College London, UK**: Tony Ng, Richard Dimbleby Professor of Cancer Research, King’s College London and Professor of Molecular Oncology at UCL-Cancer Institute, University College London.
- **Infineon Technologies AG Munich, Germany**: Knut Hufeld, Director, Research & Development Funding, Infineon Technologies AG; Reinhard Pufall, Dr.
- **Centre of Systems Biology (SYSBIO), Italy**: Lilia Alberghina, Professor, Director.
- **CEA-LETI, Grenoble, France**: Marie-Noelle Semeria, Director; Thomas Ernst, Chief Scientist.
What is the challenge and the vision?

What is the grand S&T challenge and its underlying vision and what are the main objectives your initiative would address?

Our individual existence and well-being depend primarily on remaining healthy and during ill health, receiving the individualised, optimal therapy. The continuing ‘health’ of our societies is, in contrast, increasingly threatened by the enormous cost of providing appropriate healthcare (currently 4 billion euros PER DAY in Europe alone) in the rapidly ageing societies of Europe. When faced with similar challenges with harmful and/or expensive consequences in other areas we have followed a very simple principle: mistakes are unavoidable in dealing with highly complex processes. While we cannot avoid making these mistakes, we can avoid most or all of their consequences by making these mistakes in-silico. This change of strategy has been implemented in most areas of our existence, increasing efficiency, saving lives and reducing costs.

This enormous progress has, as yet, reached neither our health care system nor the way we develop new drugs. Drug based therapy and prevention is still statistical, with many patients receiving drugs, which are ineffective or, even worse, harmful. Unavoidable errors in drug development still cause the cost per drug reaching the market to remain in the multi-billion euro range and endanger patients participating in large, non-stratified clinical trials. In addition, our ‘health’ care system is still far too much a ‘disease’ care system. The majority of our efforts are focused on treating rather than preventing diseases; or at least diagnosing diseases (or their progression) early enough to be able to react.
Changing this will require nothing less than a revolution, based on technical developments in two general areas, but intimately linked to many other aspects of the organisation of health care and its legal and regulatory basis (see also www.healthcarecompacteurope.eu):

We need to know much more about the patient (or the potential patient), based on advanced -omics (e.g. genomics, proteomics, metabolomics) analyses, imaging techniques, and information from sensors deployed in various form factors. We will draw primarily on concepts developed under two separate Flagship proposals (both of which had reached the final stage of the last competition): IT Future of Medicine (ITFoM: www.itfom.eu), with a very strong -omics component, and ‘Guardian Angels for a Smarter Life’ (www.ga-project.eu/), with a particular focus on the development of novel autonomous sensors/low energy computing. In addition, we plan to incorporate a similarly strong imaging component, from the level of individual cells up to the entire organism.

Data is however not everything. We also need concepts to integrate this information and to predict the effects and side effects of possible therapies (or preventive measures) on every individual. Towards this we will build on the concept of the ‘virtual patient/virtual individual’, proposed in ITFoM. Such a ‘virtual twin’, updated intermittently by medical/omics/imaging information, and essentially continuously by a multitude of sensors could, in theory, accompany every European through life as a true ‘Guardian Angel’. These ‘Guardian Angel’ models will, to a large extent, be based on modelling the biology of every patient and the diseases mechanistically, providing by far the best chance to translate complex data sets into accurate predictions, complemented by machine learning/statistical techniques, whenever mechanistic models cannot be established due to insufficient knowledge, e.g. on disease mechanisms. Development in these areas will however also help to accelerate and de-risk the development of new drugs, based e.g. on virtual ‘clinical trials’, starting shortly after (and maybe even before) the synthesis of new candidate compounds, in a ‘virtualisation’ of drug development matching the enormous positive effects that a similar virtualisation has had on e.g. the car industry.

Technology is however only a part of the solution. We will, in addition, have to reconsider many aspects of our health care system, its legal basis, regulations and reimbursement mechanisms, to draw maximal benefits from the significant progress in technologies allowing us to truly personalise medicine and prevention. We propose a vision of a truly individualised health care and disease prevention system in Europe, based on a detailed characterisation (e.g. clinical, molecular, imaging and sensor based) of the patient/individual and their wellness, health and disease course, exploiting the most advanced molecular, imaging, sensing, computing and communication technologies, through an internet-of-humans, for truly personalised and preventive medicine.

The main objectives are:

- To develop the technology, the required infrastructure, and the legal, regulatory and educational environment for a fully sustainable health care system that will offer truly personalised medicine, prevention and wellness for European citizens, providing a completely new Quality-of-Life.
- To develop novel -omics, imaging and multi-level advanced smart sensor technologies and big data/deep data analytics for problem solving in IoH/personalised health care.
- To address the full value chain of the virtual human at all multidisciplinary levels required, from -omics, imaging and sensor data to complex simulation models.

**Why is this a grand S&T challenge and what makes it a “game-changer”?**

Medicine and prevention have historically been statistical, treating individuals as members of (usually quite heterogeneous) groups. To switch focus from the statistically best therapy for billions to the individual, will ultimately require much more information on EVERY patient, than we had on the whole of human biology just a short time ago. We go from bytes to terabytes, from handwritten notes to a deep -omics characterisation, from a cursory check at irregular doctor visits to continuous monitoring of all relevant parameters throughout life. Our vision is a game changer, of a future in which no patient
will ever again receive harmful therapies, flagged by observing negative effects first on the in-silico model of the individual patient. This will:

- Directly address the enormous (and almost certainly irreducible) complexity of the biological differences between every patient and every disease by deep clinical, molecular and imaging analyses.
- Provide a new generation of frictionless autonomous smart sensors at all levels required by health care data collection: implantable, wearable, environmental. Develop new feedback-interfaces for life-style feedback loops and related diseases.
- Develop computer models of every patient and disease state that allow physicians to test the consequences of all possible therapies/preventative and life style measures in a virtual rather than the real patient, computational ‘Guardian Angels’ potentially guarding every European from before birth into old age.
- Acquire, store and redistribute the ever-accumulating amounts of data per patient required to fulfil this goal, within a strong governance framework which protects personal data from misuse and ensures privacy.

What are the main technologies, including digital technologies, which your initiative will advance?

- Clinical/imaging/molecular survey (genome, epigenome, transcriptome, proteome, metabolome, immune status etc.) techniques to provide a detailed characterisation of individuals in health and disease.
- New self-powered families of revolutionary sensors for IoH/truly personalised health care based on energy efficient approaches and heterogeneous integration solutions in bio-compatible form factors to extend human senses and to support specific prevention strategies.
- Self-learning mechanistic/machine learning models translating this information into predictions on the future development of diseases (prevention) and the likely response to specific therapies and preventive measures.
- Data security and availability: hardware to software solutions specific for IoH/personalised medicine data. New human-machine interfaces for IoH/personalised medicine, personalised and capable of non-verbal interactions.

Why is it good for Europe?

Is your initiative relevant for the European industry and what is its innovation potential that would benefit Europe’s economy and/or society?

The health care ‘Internet-of-Things’ market segment is poised to hit $117 billion by 2020 (MarketResearch.com), with exponential increases in revenues predicted. The current Flagship initiative will progress beyond these projections, by generating unexpected and still unknown applications that are beyond the imagination of today’s Internet-of-Healthcare. Truly personalised prevention and therapy will provide much better health at a much lower cost. The technologies which will be developed within this project do however extend far beyond health applications and into the wellness/social interaction domain, which has already generated some of the largest companies worldwide.

Poised at the interface between medical sciences, math, computation and engineering, the initiative is intrinsically multidisciplinary, fueling innovation and driving change within the field of translational medicine. We foresee and advocate innovation via a multidisciplinary and holistic vision of convergent technologies designed by doctors, scientists, mathematicians and engineers, e.g. in the form of Technological Hospitals in Europe, as a unique environment to generate innovative ideas and new services for health care.
A data and computational model driven strategy in health and wellness will provide major benefits to the region’s citizens within one of the most important aspects of their lives – health care. Through the deployment of personalised medicine, prevention and wellness strategies proposed by this program and the incentives provided for European companies to form, develop and prosper as part of the new ecosystem created, there is huge potential to alleviate the suffering and improve the health and wellbeing of the EU’s 500 million citizens, whilst strengthening the economic outlook of Europe as a whole.

**Key Benefits for:**

- **EU citizens**, through a radical improvement of their health care and a new quality of life.
- **European economy**, through new job and employment opportunities. Formation of a new vibrant economic ecosystem bridging traditional engineering, computer sciences and health care.
- **European industry**, stimulating the life sciences, pharmaceutical, health care, sensor and IT sectors, providing a large potential for innovation that can be further exploited in translational medicine.
- **Public finances**, by curbing the uncontrolled increase in health care spending (potential savings of hundreds of billions of euros) through a data and model driven truly personalised health care, improving continuously in a self-learning system, duplicating, in a sense, human evolution.

**Are there existing international research initiatives linked to this proposal?**

The technological roadmaps and the networks of partners generated by the two Flagship pilots (ITFoM and Guardian Angels) create a unique opportunity for implementing a joint concept proposed here. The aims and goals also align with the Health Care Compact for Europe (www.healthcarecompactforeurope.eu), an international initiative that promotes the use of a data and computational model-driven approach to sustainable health care.

The project will also actively leverage synergies between similar initiatives worldwide, including the 100K Wellness Project (http://research.systemsbiology.net/100k/), the Personal Genomes Project (PGP, www.personalgenomes.org/), the new Precision Medicine Initiative (http://www.nih.gov/precisionmedicine/) by the US government; for smart sensing technology, road-mapping links for analytical techniques are forseen with the recent NEREID initiative (www.nereid-h2020.eu/) and with existing activities in the Joint Undertaking ECSEL (www.ecsel-ju.eu/).

**How would this initiative position Europe with respect to other regions in the world?**

Europe has reached a crucial turning point and has put a range of measures in place to drive the development of digital health, moving forward with large-scale initiatives (see below), increasing investment and innovation support, and generating the political drive required to break down existing barriers. This initiative is more than timely and will position Europe at the edge of advancements in diagnostic techniques (-omics, imaging, autonomous sensors) as well as translational and personalised medicine. Within the field of Information and Communications Technology (ICT), Europe has an important role to play in Embedded Systems as part of future IoE and Cyberphysical systems. The health care, automobile and aeronautical industries are key for European leadership; however, the role of new smart sensing technologies for health care is seen as much more revolutionary due to the significant societal impact and through the direct connection to a more sustainable model for health care costs. It will therefore be important to further develop the fundamental infrastructure that will enable scientific discovery and progress, in tandem with the political mechanisms in Europe that will support the translation of innovation. This will not only ensure maximal benefits for European citizens through improvements in the health care system but also provide economic benefits due to the development of a vibrant economy that links medicine, diagnostics and IT.

**What would it take to do it?**
**What is the scale of the effort required to reach the objectives and how long will it take to do so?**

The scale of effort is of the order of 10-15 years, with ambitious but practical goals, which will be addressed in a series of ‘working prototypes’ until final rollout of a system ready to be implemented for multiple disease areas on large scale in European health care systems.

The effort is well balanced between: (i) deep -omics and imaging technologies, data analysis (ii) smart sensing technologies, energy efficient computing, big data analytics for IoH, (iii) data integration, virtual patient models and (iv) personalised medicine validations and field trials.

There are four major phases for development:

**Phase I: Initiation.**
Initial infrastructure development, development of improved pipelines for omics and imaging data integration in virtual patient models, implantable or wearable sensor solutions, pilot projects in oncology and life-style related diseases (e.g. Type II Diabetes).

**Phase II: Expansion and Consolidation.**
Development of virtual patient/virtual individual models for the vast majority of multi-factorial, non-infectious diseases, integrating -omics, imaging and sensor data.

**Phase III: Maturation and Innovation penetration.**
Scale out and clinical engagement across Europe by full adoption of the new methods and innovation by technology-health care interactions, -omics and all-scale imaging and sensing technologies, model validation and model improvements through feedback of treatment results.

**Phase IV: Full Implementation of paradigm shifts.**
Establishment and deployment in practicing health care systems, effect and impact of personalised and preventive medicine quantifiable.

Existing EU financing tools (e.g. Horizon2020, regional funds, Juncker Plan) will be leveraged, supplemented by private funding sources once the EU expresses its political will and creates the required legal environment. It is expected that in the later stages the private sector would top-up the EU funds at a ratio of minimally 1:5 (public/private).

**Why is Europe well positioned in terms of skills/expertise and capabilities, including industrial capabilities, to address the challenge and exploit the results? Which are the research communities to be involved?**

Europe is home to leading expertise and capabilities, combining world-class academic research with top industrial players in the life sciences, pharmaceutical, healthcare, sensor and IT sectors, providing a large potential for innovation that can be further exploited in translational medicine. Truly personalised prevention and therapy are logical next steps, translating technology and infrastructure improvements into improving the life of all Europeans, both individually, and as societies. European academics at the top of their fields, from geneticists and clinicians to systems biologists, engineers, chemists and mathematicians, pool their efforts in Future Health to provide the basic science underpinning the initiative to the technological breakthroughs making the vision reality.

**Are there existing national or European research initiatives linked to this proposal?**

Fruits are harvested from previous and on-going European (and global) research initiatives; technological possibilities are harnessed and new infrastructures created to enable the intelligent combination and exploitation of personal molecular data and health care data, e.g.:

- Lighthouse Initiative on Personalised Medicine - European Alliance for Personalised Medicine.
- Global Alliance for Genomics and Health (GA4GH): [https://genomicsandhealth.org](https://genomicsandhealth.org)
What is the added value for such an effort at the European level?

The proposed initiative will provide the technology, the required infrastructure, and the legal, regulatory and educational environment for a sustainable health care system that will offer truly personalised medicine, prevention and wellness for European citizens, combined with much more cost effective development of new drugs.

Public spending will be curbed using a data and computational model driven strategy that will continue to become more cost effective, driven by significant progress in computational and analytical techniques, and an exponentially increasing information base flowing back into an evolving, self-learning system. European talent and innovation will be harnessed to help European citizens witness a revolution in health care and wellness, with a radical improvement of their quality of life. New employment and job opportunities will be created through the formation of new vibrant economic ecosystem that merges traditional engineering, computer sciences and health care – an emerging economy that will provide unique opportunities for production in Europe.