Scientific Challenges in European Health

A conference initiated by the Bavarian Universities

Brussels 20.10.2010

General Introduction

In order to ensure Europe's excellence in health care and medical science it is crucial to identify major international trends at the very frontline of research. Only by duly addressing future health challenges the long-term well-being of European citizens can be assured while innovation and competitiveness of European health-related industries and services are simultaneously fostered.

So which are the pivotal topics of tomorrow's medical research?

The overall objective of the conference "Scientific Challenges in European Health" is to provide a platform for discussing key challenges, goals and new directions in medical sciences with international stakeholders from science, industry and EU research policy-makers. This event contributes to the preparatory discussions addressing the "Innovation Union".

In presentations based on common positions with international partners, leading scientists from renowned research centres point out relevant future trends within four major themes:

- Neurosciences
- Bioimaging
- Degenerative Diseases
- Biosystems Research

"Scientific Challenges in European Health" is the third international conference of a series started in 2009. Initiated by Bavarian universities these conferences aim at contributing to the development of the European Research Area, encouraging participation in the Framework Programme, demonstrating scientific expertise and enforcing international and public-private networks. They promote new ideas issued from excellent scientific work to be developed on the European level.
For further information: www.bavarian-research-for-europe.eu

A conference initiated by the Bavarian Universities:
Universität Augsburg; Otto-Friedrich-Universität Bamberg; Universität Bayreuth; Friedrich-Alexander-Universität Erlangen-Nürnberg; Universität der Bundeswehr München; Ludwig-Maximilians-Universität München; Technische Universität München; Universität Passau; Universität Regensburg; Universität Würzburg

In cooperation with:
Bavarian Research Alliance; Bayerische Forschungsstiftung

Kindly hosted by the Representation of the Free State of Bavaria to the European Union

Content

Agenda: October 20, 2010

17.00 Welcome Address

Dr. Angelika Schlunck
Director of the Representation of the Free State of Bavaria to the European Union

Moderation

Ingrid Zwoch
NCP Life Sciences, Germany

Dr. Claudia Eggert
Deputy Director, European Liaison Office of the German Research Organisations, Brussels

17.15 Neurosciences – Perspectives of Adult Neural Stem Cells

Prof. Dr. Jürgen Winkler
Friedrich-Alexander University Erlangen-Nuremberg

17.45 Bioimaging – A Core Discipline of Tomorrow's Biology and Medicine

Prof. Dr. Vasilis Ntziachristos
Technische Universität München and Helmholtz Center Munich

18.15 Discussion

18.30 Musculoskeletal Regeneration – Innovative Therapies for Our Ageing Society

Prof. Dr. Matthias Schieker
Ludwig-Maximilians-Universität München

Prof. Dr. F. Jakob
University of Würzburg

19.00 Molecular Biosystems in Health and Disease

Prof. Dr. Patrick Cramer
Ludwig-Maximilians-Universität München

Dr. Michela Bertero
Center for Genomic Regulation, Barcelona

19.30 Discussion

19.45 Buffet and Poster Session

Neurosciences – Perspectives of Adult Neural Stem Cells

***ForNeuroCell* - Bavarian Science Consortium for "Adult neural stem cells"**

Presenter: Prof. Dr. Jürgen Winkler
Division of Molecular Neurology, University Hospital Erlangen
Friedrich-Alexander University of Erlangen-Nuremberg, Germany

European Partners: Prof. Ludwig Aigner, Institut für Molekulare Regenerative Medizin, Salzburg, Austria
Prof. Patrick Brundin, Wallenberg Neuroscience Center, Lund, Sweden
Prof. Pierre-Marie Lledo, Institut Pasteur, Paris, France
Prof. Stefano Pluchino, Institute of Experimental Neurology, Milan, Italy
Prof. Francis Szele, Department of Physiology, St Anne's College, UK

Neurological disorders cause long-term and severe impairment affecting the professional as well the daily life of patients. Acute disorders of the brain like cerebral ischemia, head trauma or spinal cord injury, age related chronic neurodegenerative diseases like Parkinson's (PD) and Alzheimer's disease (AD) as well as psychiatric disorders like depression are the major epidemiological challenges for western societies, not only for basic science and the medical community, but more importantly also for the European health care system. Furthermore, due to an increased life expectancy the number of people with age related cognitive decline and/or neurodegenerative diseases increases dramatically. There are existing estimates that frequency of disorders like PD increases within the next 25 years by 50-150%. During the last decades there is a tremendous development in regard of the understanding and the diagnosis for the most frequent acute as well as chronic neurological disorders. Despite large efforts of the European community in developing a causal therapy for these diseases, the translation into the clinic is not yet successful since the majority of the present clinical studies obtained by novel small molecules or immunotherapy were rather disappointing or associated with severe and significant side effects. To overcome these challenges of an ageing population, the development of innovative and long lasting **cell based therapies** are an urgent need for the affected individuals, the primary care givers and society.

Background
One of the most exciting findings in neuroscience over the last decades was the identification of neural stem and precursor cells in the adult brain (adult neural stem cells – aNSC's).
Adult stem and precursor cells of the mammalian brain

- exist in two regions of the adult central nervous system (CNS), the hippocampus and along the lateral ventricle within the subventricular zone.
- maintain the exceptional capacity during the entire life expectancy to divide and to mature into all cells of the CNS such as neurons, astrocytes and oligodendrocytes
- integrate into existing neural circuitries
- are non-immunogenic and -tumorigenic

These aNSCs are an endogenous, lifelong and powerful cellular resource within the brain enabling us to develop new strategies for the regeneration of damaged neural circuitries. Adult NSCs are able to replace damaged or lost neurons ultimately improving neural functioning.

Numerous *in vitro* and *in vivo* analyses of non-human models provided a detailed structural and molecular characterization of adult neurogenesis (=capacity to generate new neurons) and linked this phenomenon to processes such as learning, memory, mood and olfaction. In addition, targeted migration allows aNSCs to promote regenerative processes in damaged regions within the CNS. Taken these findings together aNSCs based strategies will generate novel means to induce regenerative processes for multiple CNS diseases.

Vision

There is an urgent need **to explore the potential of adult neural stem cells** in the **human CNS** in order to translate our knowledge toward novel therapeutic strategies in patients since current concepts are based almost exclusively in non-human models. Furthermore prevention strategies for age dependent neurodegenerative disorders will be an important issue for the quality of life of the individual as well as of the society.

To achieve this goal the European Union should strongly support the clinical and structural research to characterize **adult neurogenesis in humans**. In particular, the underlying biological mechanisms such as proliferation, migration, differentiation, survival of aNSCs in the human brain have to be characterized. In addition, it will be necessary to delineate the regulatory pathways and receptors on human aNSCs as potential targets for pharmacological interventions. Finally, the development of novel imaging tools for visualization of aNSCs in humans will be one one of the major prerequisites to establish pro-neurogenic therapies in the clinic. Other cell based strategies (embryonic or inducible stem cell research) will complement these approaches.

Future achievements

To characterize adult neurogenesis in humans will help to use this endogenous resource for repair strategies in the brain. Pro-neurogenic interventional strategies will result in functional restoration in patients with CNS disorders thus improving important measures of quality of life. Over all, this will significantly reduce health care and economic costs throughout Europe.

Established methods and results within *ForNeuroCell*

Stem cell based therapy for the treatment of CNS diseases can be distinguished in two approaches to functionally replace dying neurons ultimately with the goal to halt or reverse the course of the CNS disease:

a) replacement through transplantation of stem cell derived neurons
b) neuronal replacement through recruitment of endogenous neural stem cell

Due to this fact, that aNSCs exist in the human brain and have the capacity to generate new neurons, the Bavarian Consortium **ForNeuroCell** tries to develop along this finding **stem cells based therapies based on aNSCs,** but still using predominantly non-human cells and tissues. By combining the expertise of basic neuroscience, neurology, neuropathology, neuroimaging as well as neurophysiology, it is the ultimate goal of **ForNeuroCell** via modulation and targeted differentiation of aNSCs to induce regenerative processes in the CNS in order to functionally restore deficits associated with these diseases.

The following mature topics are pursued:

1. Identification of signalling pathways to modulate and maintain aNSCs
2. Reprogramming and targeted differentiation of endogenously present aNSCs
3. Preclinical testing of aNSCs in acute and chronic disease models
4. Development of imaging technologies to detect endogenous and transplanted stem cells in the living mammalian brain
5. Translation of stem cell technology to human stem cells

The Bavarian Network **ForNeuroCell** consists of 10 projects of the following Bavarian Universities: Friedrich-Alexander-University Erlangen-Nuremberg, Ludwig-Maximilians-

Universität München, Technische Universität München, University Regensburg, Julius-Maximilans-University Wuerzburg, and the Helmholtz Centre Munich.

Within the Bavarian Consortium **ForNeuroCell** the following technical platforms have been established:

a) Modern molecular biology
b) Innovative cell biology
c) Preclinical animal models
d) High end novel imaging technologies

The Bavarian consortium ***ForNeuroCell*** and the expertise of these academic centres are combined, and together with European partners we envision aNSCs based therapies for patients with the CNS disorders like PD and AD in the future. The scientifical and clinical challenges to use this technology for the human brain will lead to novel translational approaches to the benefit of thousands of patients within Europe.

In Europe there are several networks focussing on cell-based strategies with special emphasis on embryonic, fetal or inducible pluripotent stems cells for neural repair (for more information see http://www.eurostemcell.org/). The present approach **of focusing on adult neural stem and precursor cells of human origin** will broaden this effort also in order to overcome the current setbacks in the development for therapeutic approaches and to achieve a successful translation into patients.

Bioimaging – A Core Discipline of Tomorrow's Biology and Medicine

Presenter: Prof. Dr. Vasilis Ntziachristos, Chair for Biological Imaging,
Technische Universität München

Contributors: Prof. Dr. Vasilis Ntziachristos, Chair for Biological Imaging,
Technische Universität München
Prof. Dr. Silvio Aime, University of Torino
Prof. Dr. Gooitzen M. van Dam, University Medical Center Groningen
Prof. Dr. Farouc Jaffer, Massachusetts General Hospital,
Harvard University
Prof. Clemens W.G.M. Löwik, Leiden University Medical Center
Prof. Dr. Franz Magerl, Hochschule Amberg
Prof. Dr. Maximilian Reiser, Klinikum der Universität München,
Ludwig-Maximilians-Universität München
Prof. Dr. Markus Rudin, Universität Zürich &
Eidgenössische Technische Hochschule Zürich
Prof. Dr. Markus Schwaiger, Klinikum rechts der Isar,
Technische Universität München
Dr. Herbert Stepp , Klinikum der Universität München,
Ludwig-Maximilians-Universität München
Prof. Dr. Bertrand Tavitian, CEA – Commissariat à l'Energie
Atomique et aux Energies Alternatives
Dr. Juan Vaquero, Fudacion para la Investigacion Biomedica del Hospital,
Madrid

Summary

Imaging plays a vital role in biomedical research and healthcare. There have been remarkable developments over the last decades leading to advanced microscopy methods and tomographic methods for biological and non-invasive animal and human imaging. Yet significant limitations remain. Microscopy only penetrates at depths of a few microns. Radiological modalities often lack required specificity on biomarkers. Entire segments of medicine, such as endoscopy or surgery, are still primarily based on human vision which significantly limits detection sensitivity and specificity. Through innovation and application development in the post-genome era imaging is expected to play an increasingly important role in advancing knowledge, enhancing discovery and improving detection and therapeutic outcomes. This will be achieved by exploiting new physical interactions, developing new technology, engineering disease targeting strategies and identifying informative biomarkers.

Europe has been a leading innovator and developer in the imaging field. Retaining and enhancing this leadership is of high strategic interest. From a socioeconomic standpoint imaging is a vibrant market that drives a need for components, systems, agents and services while clinical imaging has been a strongly developing area with direct impact on healthcare. Novel imaging tools bring a competitive advantage in multiple areas of biology, medicine and biotechnology and large industrial sectors in Europe are heavily invested in microscopy and clinical imaging. Importantly, leadership in imaging is directly linked with the quality and efficiency of today's ability to prevent, diagnose early or treat disease on a personalized level and to reduce healthcare costs.

Imaging growth

Imaging is a fundamental tool of biological discovery and medicine. There would be little ability for biological research or clinical diagnosis in the absence of methods that can look into the structure, function and molecular composition of tissues, cells and sub-cellular components. Originating with microscopy more than three centuries ago, imaging has seen a remarkable development in recent times. Optical microscopy has evolved to a powerful method present in virtually every biological laboratory. Similarly, seminal discoveries in the last century, ranging from the discovery of X-rays to computed tomography, Magnetic Resonance Imaging or nuclear imaging and ultrasound, have revolutionized the way we look into living specimen and humans. More recently, coupling of advanced imaging methods with engineered targeting strategies of cellular and sub-cellular function has offered a new direction of growth by allowing the in-vivo and often non-invasive visualization of a wealth of information identified by post-genome biology. Advanced optical and nuclear imaging approaches and progress in other radiological imaging offers now an unprecedented potential for visualization of life and disease from the anatomical to the molecular levels.

Innovation has been a major driver of imaging developments generating a multitude of Nobel prizes, scientific societies and organizations and in the process amounting to a m-billion worldwide business. Insightful applications' development around imaging methods has revolutionized our perception of disease micro-environments, the observation and characterization of biological phenomena and clinical procedures. Imaging crosses multiple scales; from identifying the structure of proteins or studying sub-cellular components and cellular interactions to revealing anatomy, physiology and molecular biology in animals and humans. European research has played a fundamental role in the development of imaging over the years whereas European SME's and larger industry have enabled commercialization in all fields associated with imaging, including systems, imaging agents, methods and services.

Areas of future investment

Despite the significant history, imaging is a strongly advancing scientific field driven by novel ideas and existing needs in medicine, biology and biotechnology. Super-resolution optical imaging techniques, opto-acoustic methods that allow penetrations that are significantly deeper than the ones available to optical microscopy, or phase-contrast X-ray CT are just a few examples of the novelty and the innovation drive that exists in the field, pointing to a new ability to deliver biological discover and medicine. In parallel, reporter technologies, targeting and delivery approaches and new reporter molecules and nano-particles all represent very active and highly necessary fields of imaging research.

In addition, there are several biomedical areas where new imaging developments can have a significant impact. For example, large segments of today's healthcare are still primarily executed based on the physician's vision – from surgical and interventional procedures to many endoscopies. This approach, although possibly enhanced with magnification through microscopy methods, does not attain high sensitivity and specificity due to the limitations of human vision regarding sensitivity and depth discrimination. Progress in technology and labeling capacity that address largely underserved areas of biological discovery and medicine can bring a new level of standard by improving the procedures and the outcome of such methods.

Similarly, the ability to diagnose several diseases earlier needs to become a major driver of imaging developments as it impacts therapeutic outcomes and minimize costs. Combined with the potential of in-vitro diagnostics and risk stratification, technological advancements of imaging capacities do therefore not only reflect an ethical need for improved healthcare quality, but are also closely associated with a strategic mandate to improve efficacy and reduce discovery and healthcare costs.

To sum up, impacting biomedical areas with imaging and retaining imaging excellence requires support of 1) innovation in imaging technology and its application, 2) the development of tools that can improve and accelerate discovery practices, 3) the advancement of imaging tools that identify disease earlier, leading to more efficient and less expensive treatments and 4) to increasingly enable personalized medicine and improved treatment design through the continuing identification of biomarkers and targeting disease strategies.

Musculoskeletal Regeneration – Innovative Therapies for Our Ageing Society

Presenters: Prof. Franz Jakob, University of Würzburg, Germany
Prof. Matthias Schieker, University Hospital of Munich, Ludwig-Maximilians-Universität München, Germany

Contributors: Prof. Franz Jakob, University of Würzburg, Germany
Prof. Matthias Schieker, University Hospital of Munich, Ludwig-Maximilians-Universität München, Germany
Prof. Eckhard Wolf, Ludwig-Maximilians-Universität München
Prof. David Marsh, Clinical Orthopaedics, Stanmore, UK
Prof. Reinhold Erben, University of Vienna, Austria
Prof. Moustapha Kassem, University Hospital of Odense, Denmark

Summary
Ageing is characterized by fundamental changes in gene expression patterns in both regenerative precursor cells and mature tissue cells, which propagate degenerative diseases. Important musculoskeletal diseases are osteoporosis, osteoarthritis, sarcopenia and tendon degeneration. Current treatment options are symptomatic and cannot restore regeneration. New strategies exploiting ex vivo or in situ manipulation of regenerative cells create the potential of treating such degenerative diseases to maintain patient independence and enhance quality of life thus reducing both the individual and the economic burden of disease. Here we propose that Europe should strongly support strategies of Regenerative Medicine in age associated degenerative diseases of the Musculoskeletal System with respect to the growing population of the elderly.

Introduction and relevance of the problem
Musculoskeletal disorders are second to respiratory disorders as a cause of short-term sickness absence and are the most common health-related cause for long-term absence. In addition the incidence and burden of musculoskeletal diseases in the elderly is steadily increasing. Osteoporosis, Osteoarthritis, Sarcopenia and degenerative tendon calcifications and ruptures are the main constituents of this remarkable individual and economic burden. A total of 9 Mio fractures per annum were estimated to occur worldwide and 34 % of these happen in Europe. The number of hip fractures per year in Europe is estimated to reach 500.000 by 2025 and the money required to cope with fragility fractures in Europe will surmount 50 billion € per annum by 2030. Fragility fractures cause 2 Mio of lost Disability adjusted life years (DALYS), while the overall loss of DALYS due to all musculoskeletal diseases in Europe amounts to € 5,4 Mio. The incidence of sarcopenia as a major contributing factor is more than 20 % in males and females over 65 and exceeds 80% in males in nursing homes. Sarcopenia is a major risk factor for falls and fractures. One of the most important lesions with calfiying tendinitis and ruptures is that of the rotator cuff of the shoulder joint. Lesions of tendons in general account for 3 % of all injuries in Europe. In a German report 26 % of the total number of the 59,957 shoulder operations reported, were rotator cuff repairs. Although the data are scarce, the impact of such lesions can be judged by data from Norway saying that about 20% of the sick leave days in Norway are attributable to shoulder problems. While the socioeconomic challenges associated with fractures and osteoporosis have been appreciated during the last decade, sarcopenia and degenerative tendon diseases as important contributors to disability, frailty, falls and fractures have not sufficiently been addressed and their molecular mechanisms need to be unraveled to find targets that allow for population-wide intervention programs.

Tissue Regeneration in aging Organisms

Cellular aging is associated with a reduced capacity of tissue resident stem cells to proliferate, to migrate to sites of injury and to give rise to differentiated daughter populations. A combination of intrinsic defects and organismal overproduction of inhibitors of regeneration precipitates in altered tissue function and atrophy. In addition other phenomena associated with aging contribute to cellular aging and senescence like accumulation of damage in DNA and proteins. Chronic inflammatory processes also propagate aging. In many organisms the capacity and the principles of regeneration are still present and can be reactivated by taking away the inhibitors, e.g. sclerostin and activin in case of osteoporosis and sarcopenia, which have already been targeted for bone regeneration and osteoporosis treatment. Other principles of regeneration still await to be unraveled and to be targeted for therapeutic strategies, which can be systemic approaches, cell and scaffold based like in tissue engineering, or locally driven regenerative processes in so called “in situ guided tissue regeneration”.

Competence Networks in Bavaria and their European partners

During the last decade experts from various disciplines have founded Bavarian network research in key segments of regenerative medicine. We have successfully established an excellence cluster for stem cell biology, cellular aging, scaffold and material science, cell tracking, tissue engineering and small and large (transgenic) animal cloning. Translational efforts have governed the development of our interdisciplinary consortia consisting of basic scientists and clinicians to develop new targets and SOP for cell base regenerative procedures in the elderly.

The partners are already involved in the following network projects: ForZebRA, Bavarian research cooperation for cell based regeneration of the musculoskeletal system in old age (www.forzebra.de), DFG 793 Research Unit “Mechanisms of fracture healing and bone regeneration in osteoporosis” (www.biomechanics.de/dfg793), and the EU FP7 projects VascuBone (www.vascubone.fraunhofer.eu/index.html) and ADIPOA (http://first.aster.it/news/show_news.php?ID=22678). The latter are dealing with tissue engineering constructs for critical size bone defects and with the application of mesenchymal stem cells in the treatment of osteoarthritis. Future activities should involve both basic scientists and clinicians in close collaboration to unravel mechanisms of degeneration and regeneration in the elderly as discussed above and develop new therapeutic applications. Such activities would ideally be linked to existing initiatives like the “Survey of Health, Ageing and Retirement in Europe (SHARE)” program to integrate economics, medicine, and social sciences.

Scientific and economic impact

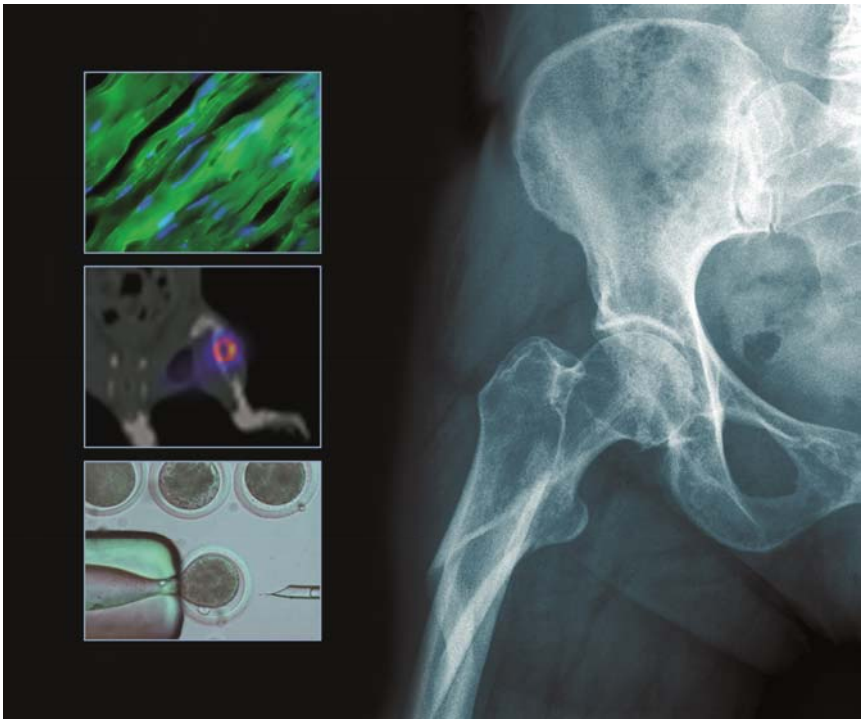
Aging societies need tools and programs to cope with this increasing population of elderly to maintain their independence and minimize their dependence on public health care and nursing care programs. Research in the mechanisms of aging and degeneration is an extremely competitive area worldwide. It is of utmost importance to support European scientists to keep up and develop cutting edge knowledge about such molecular processes of degeneration. Moreover we will also need knowledge about systems biology of regeneration and degeneration, which may be achieved by close cooperation with partners collaborating in the European Network of Excellence ENFIN (www.enfin.org/page.php).

We will see an overwhelming amount of new intervention strategies being developed within the next decade and this could contribute to a substantial expansion of the health care and medical technology sectors of European economies. Close cooperations with translational research and development organizations like Fraunhofer Gesellschaft (www.fraunhofer.de) appear to be very important and this is already established in our EU Network “Vascubone”. The economic impact of tools and programs will be enormous in terms of patenting new applications and fostering small and medium enterprises which care for translation into everyday life. Our scientific goals meet the visions of European network structures like EATRIS, the “European Advanced Translational Research InfraStructure in Medicine”, and also the European Network ELIXIR, a “European Life Science Infrastructure for Biological

Information" (www.elixir-europe.org/page.php). Hence support of research in regeneration and degeneration in the elderly will have consequences in terms of reduction of public expenditure in nursing care and at the same time for the development of employment. This scenario is complementary to the visions of the European Innovation Union (http://ec.europa.eu/research/innovation-union/) to head for "more jobs, improved lives and a better society".

The need for interdisciplinary research in Europe

In conclusion, due to the rapid increase of ageing populations both the clinical needs and the worldwide competition and technical achievements dramatically accelerate the pace in scientific development in this area. In order to further fast-track translation from basic knowledge into clinical applications we need interdisciplinary and international collaborations.



New innovative therapies for degenerative diseases of bone, cartilage and tendon.

Molecular Biosystems in Health and Disease

Presenters: Prof. Patrick Cramer, Director, Gene Center Munich, Ludwig-Maximilians-Universität München, Germany
Dr. Michela Bertero, Center for Genomic Regulation, Barcelona

Contributors: Prof. Patrick Cramer, Director, Gene Center Munich, Ludwig-Maximilians-Universität München, Germany
Dr. Michela Bertero/Prof. Luis Serrano, Center for Genomic Regulation, Barcelona, Spain
Prof. Susan Gasser, Director, Friedrich-Miescher-Institute, Basel, Switzerland
Prof. Frank Holstege, University of Utrecht, Netherlands
Prof. Angus Lamond, Director, Wellcome Trust Center, Dundee, UK
Prof. Renee Schroeder, University of Vienna, Austria

Summary
To accelerate progress towards new diagnostics and therapies, the European Union should strongly support the emerging discipline of molecular biosystems research. The future of the life sciences, biomedicine, and biotechnology will critically depend on our understanding of molecular biosystems and our capability to quantify, evaluate and manipulate molecular biosystems. The aim of molecular biosystems research is to understand biological responses at a system-wide level and in terms of the underlying molecular mechanisms, hence obtaining realistic, quantitative models of cellular behaviour. Research on molecular biosystems thus requires that two established disciplines, molecular biology and systems biology, will merge. At present, European science is very strong in both traditional molecular and structural biology on one hand and functional genomics and systems biology on the other hand. However, there is a great potential at the interface of these disciplines that promises a mechanistic understanding of biological systems, in particular gene regulatory systems, that is currently left largely unexplored. A concerted effort of the leading European institutions and research groups could however bridge this gap and position Europe as the leader in an emerging field that will transform biomedicine, biotechnology, and personalized health care.

The future of the life sciences
Biological research has traditionally been centered on the analysis of individual genes and proteins and their immediate context. Emerging with the advent of genomic research and high throughput methodologies in recent years, research on molecular biosystems is a new field that aims to explicitly investigate the behavior of entire biological systems, but in a quantitative and dynamic rather than a descriptive way. In many ways, molecular biosystems research represents the major future direction of biology and offers the greatest potential for translation of research both medically and commercially. The principal questions asked are: 1) What are the components of a system (genes, proteins, metabolites); 2) How do the components interact with one another (transcription/translation control; protein-protein binding, enzymatic reaction); 3) How does the system behave as a whole, when left alone or when disrupted by intrinsic (mutation) or extrinsic (environment) perturbations? To address these questions, all components, interactions, and perturbations have to be analyzed in a quantitative fashion. Such detailed insights will support the development of new anti-cancer and anti-viral therapies, and contribute to efficient pharmaceutical applications.

The need for interdisciplinary collaboration
Due to the complexity and highly quantitative nature of the problem, a meaningful study of biological systems requires a close and sustained collaboration between biologists of various backgrounds, biochemists, computer scientists, physicists and mathematicians. This poses

a significant challenge, since these disciplines traditionally have had very distinct scientific approaches and outlooks, but much of the necessary innovation needs to occur precisely at the interface between them. For such research to be successful, it is necessary to found international networks in which scientists of the different disciplines share a common intellectual and scientific environment and collaborate on joint research projects. Integrating industrial partners to these networks at a very early stage will be required to accelerate new technological developments and their exploitation. The interdisciplinary approach is also crucial for educating the next generation of scientists, who need training that spans multiple fields, but will also be able to absorb the new interdisciplinary culture.

International scientific landscape

In comparison to the United States, research on molecular biosystems is only weakly developed in Europe, despite, for example, a long-standing interest in theoretical and systemic questions of biology (biokybernetics). The reasons for this situation are complex, but contributing factors are likely a relative late onset in the areas of genomics and high-throughput technologies, and an under-representation of genetic models (yeast, worm, fly) compared to traditional disciplines. In the US, these areas have been the driving force for almost all the existing systems biology initiatives. Many of the top universities in the US have systems biology programs, and a second wave of institutes are now being founded, financially supported by the currently very active scientific philanthropy, but also by strong public funding (NIH, NSF). In Europe, a limited number of systems biology initiatives have been launched, but a stronger effort is needed to get to the forefront at an international scale.

Resources, know-how, and networks in Europe

There are already several excellent centers that develop molecular biosystems research in Europe, with a particular emphasis on gene regulatory systems that underlie the expression of the genome. At the University of Munich, the Gene Center, a national center of excellence in research (CIPSM, 9 Mio Euro p.a.), a Humboldt-Professorship (5 million Euro), and nationally funded networks such as SFB646 and TR5 (each 7 million Euro p.a.), already provide many of the required technologies and address key questions on genomic regulation. Funding for a new building (29 million Euro) housing the Munich Center for Molecular Biosystems has been obtained.

At the Center for genomic regulation in Barcelona, molecular insights are used to specifically perturb signalling systems and to interpret genome data. At the Wellcome Trust Center in Dundee, proteomics and computational approaches are used to study the dynamics of cellular protein networks. At the University of Utrecht, high-throughput transcriptomics is used to uncover regulatory pathways. At the Max Perutz Labs of the University of Vienna, regulatory RNA molecules are discovered by new genomic selection procedures. At the Friedrich Miescher Institute in Basel, the temporal-spacial organization of gene activation and silencing is investigated on a cellular scale. These partners all interact with the private sector, have established national and international contacts, and participate in various research networks that will form the basis for a large, coordinated European effort that will shape the future of biology and medicine.

Europe can lead molecular biosystems research

The scientific communities in several institutions and companies in Europe have noticed that the future of biology and medicine lies to a large extent in our capability to describe biological systems on the level of the underlying molecular mechanisms. What is lacking in Europe is a strong network of leading institutions that have realized the current limitations and are now developing molecular systems biology on a national level with the aim of reaching a true mechanistic understanding of biological processes that is required to develop new tools in diagnostics, personalized medicine, and biotechnology. To guarantee European technological and economic progress, we suggest that the European Union supports these efforts that have been initiated in several leading European institutions, and sets the stage

for training the next generation of life scientists and bringing Europe to the forefront of an emerging discipline that will shape the life sciences and biomedicine in the future.

Short CVs of the presenters

Dr. Michela Bertero

Michela Bertero graduated with a PhD in Genetics and Molecular Biology from the University of Pavia (Italy) in 2000. As postdoctoral fellow, she did research at University of British Columbia (Vancouver, Canada) until 2004 and at the Gene Center (Munich, Germany) until 2006. Her main research interests focused on structural and functional characterization of large macromolecular cellular machines, such as respiratory complexes in bacteria and RNA polymerases in archaea. In 2006, she moved to the Center for Genomic Regulation in Barcelona as Scientific Officer of the CRG-EMBL Systems Biology Programme. Since March 2010, she is heading the CRG Office dedicated to International Collaboration & Sponsorship, directly supervised by the CRG Director, Prof. Miguel Beato.

Prof. Dr. Patrick Cramer

Over the last ten years, Professor Cramer has given many internationally recognized contributions to the understanding of the mechanism of eukaryotic gene transcription using an integrated structural biology approach. As a postdoctoral fellow at Stanford University his work was instrumental for awarding the Nobel Prize in Chemistry to Roger Kornberg in 2006 for the “molecular basis of transcription”. In the recent past, Professor Cramer and his team showed that three-dimensional protein structures can be used to design mutations that lead to defined transcriptome responses. Gene transcription and its regulation underlie cell growth and differentiation, its deregulation causes diseases such as cancers and metabolic diseases. The present and future work contributes to a better understanding of complex diseases and also help to elucidate the cellular reprogramming of adult stem cells and may therefore become important for a future regenerative medicine and better cell therapies. As a leader of the Gene Center at the University of Munich, he initiated numerous interdisciplinary approaches as well as many successful interdisciplinary collaborations in academia and industry, which succeeded in 11 prizes, awards, and honours. These include the Gottfried-Wilhelm-Leibniz Award of the German Research Council (DFG), the highest research award in Germany.

Prof. Dr. Franz Jakob

Prof. Dr. Franz Jakob was trained in human medicine from 1975-1981 at the University of Wuerzburg, Germany. He specialised in internal medicine, endocrinology and diabetes and became an assistant professor of internal medicine in 1994. In addition he received a basic science training at the Max-Planck-Institute for Experimental Endocrinology in Hannover from 1/1986 to 6/1988. He headed research projects on the estrogen receptor in cells of the immune system, on estrogen and vitamin D metabolism and on vitamin D-regulated genes in bone cells. In 2001 he was appointed a full professor for experimental and clinical osteology at the Orthopaedic Department of Wuerzburg University. He is now heading research at the Orthopedic Center for Musculoskeletal Research and was recently appointed as Head of the interdisciplinary Musculoskeletal Center Wuerzburg MCW. His main research topics are presently mesenchymal stem cell biology, cellular ageing, metabolic bone diseases and tissue engineering.

Prof. Dr. Vasilis Ntziachristos

Prof. Dr. Vasilis Ntziachristos is an internationally recognized expert in optical and molecular imaging and has been in the field of the imaging sciences for more than 15 years. Prof.

Ntziachristos is a Professor of both, Medicine and Electrical Engineering, as well as the Chair for Biological Imaging at the Technische Universität München (TUM) and director of the Institute for Biological Imaging at the Helmholtz Zentrum München (HMGU). Prior to his appointment, he served as an assistant professor for 5 years at Harvard Medical School, where he where he pioneered fluorescence imaging and tomography. Prof. Ntziachristos has contributed to more than 100 peer-reviewed publications on imaging, he is an associated editor for IEEE Transactions on Medical Imaging and Optics Letters and serves as chair in many international imaging conferences. Among other distinctions he has been named one of the “world’s top young innovators who will shape the future” by the Massachusetts Institute of Technology (MIT) in 2004 and has been awarded from the EU by the distinguished ERC Advanced Grant in 2008.

Prof. Dr. Matthias Schieker

Matthias Schieker, MD, Surgeon, studied medicine in Munich, London and Boston. He started working on bone regeneration in 1996 during his thesis at the medical faculty of the LMU. In 2000 he founded the "Tissue Engineering of Bone"-group at the Department of Surgery – Downtown, LMU Munich. After having finished his training to become a certified surgeon in 2005, he became Head of Research at the Department of Surgery and founded the laboratory of Experimental surgery and regenerative Medicine (ExperiMed). Matthias Schieker is Professor of Regenerative Medicine with focus on muskuloskelettal tissues since February 2010 at the LMU Munich.
In addition to his research at the LMU, Matthias Schieker is Head of research and science at the Bavarian Research Foundation (since May 2008). Moreover Prof. Schieker is clinical consultant of osteoporosis and orthogeriatrics at the Department of Surgery (LMU) and is member of the steering committee of the interdisciplinary clinical osteoporosis center (LMU).
Info: www.experimed.de, www.alterstraumatologie.de, www.osz.kliniku.uni-muenchen.de

Prof. Dr. Jürgen Winkler

J. Winkler studied human medicine at the Universities of Freiburg and Strasbourg. After his residency in Neurology he obtained an assistant adjunct professorship in Neurosciences as National Fellow of the Brookdale Foundation at the University of California (San Diego). After his return to Germany he served as a Professor for Clinical Neurobiology and managing attending neurologist at the Department of Neurology of the University of Regensburg. In September 2008 he moved to the University Hospital Erlangen and became head of the division of Molecular Neurology (www.molekulare-neurologie.uk-erlangen.de/).
His research focuses on neurodegenerative diseases and especially on the development of neuroregenerative strategies for Parkinson’s disease. The main goal is to understand the biology of adult neural stem cells in the brain and to explore this potential as a source for cellular regeneration. In clinic, he heads the outpatient center for movement disorders.
At present he is also speaker of the Bavarian network “Adult neural stem cells – ForNeuroCell” and the Department of Neurosciences at the University Hospital Erlangen. In addition, he serves as an advisor for the German Parliament on ethics and technology of stem cells. His research is funded by the Federal Ministry of Education and Research and the Bavarian State Ministry of Sciences, Research and the Arts.

Contact Details

Prof. Dr. Ludwig Aigner
Institut für Molekulare Regenerative Medizin
Paracelsus Medizinische Privatuniversität
Phone: +43 662 44 2002 1281
Fax: +43 662 44 2002 1223
Email:ludwig.aigner@pmu.ac.at
Internet: www.pmu.ac.at

Prof. Dr. Silvio Aime
University of Torino
Phone: +39 11 670 6451
Fax: +39 11 670 7855
Email: silvio.aime@unito.it

Dr. Michaela Bertero
Center for Genomic Regulation CRG, Barcelona, Spain
Phone: +34 93 316 02 47
Fax: +34 93 396 99 83
Email: michela.bertero@crg.es

Patrick Brundin, Prof., MD, PhD
Neuronal Survival Unit
Department of Experimental Medical Science
Phone: +46 46 222 05 29
Fax: +46 46 222 05 31
Email patrik.brundin@med.lu.se

Prof. Dr. Patrick Cramer
Director of Gene Center,
Ludwig-Maximilians Universität München
Phone: +49 89 2180 76951
Fax: +49 89 2180 76999
Email: cramer@lmb.uni-muenchen.de

Prof. Reinhold Erben
Abteilung für Pathophysiologie,
Institutsvorstand/Institutsvorständin
Universität Wien
Email: Reinhold.Erben@vetmeduni.ac.at

Prof. Dr. Susan Gasser
Director, Friedrich-Miescher-Institute, Basel
Phone: +41 61 697 72 55
Fax: +41 61 697 3976
Email: susan.gasser@fmi.ch

Prof. Dr. Gooitzen M. van Dam
University Medical Center Groningen
Phone: +31503612283
Email: g.m.van.dam@chir.umcg.nl

Prof. Dr. med. Jochen Herms
Zentrum für Neuropathologie und Prionforschung
Labor für ExperimenPhonele Neuropathologie
Ludwig-Maximilians Universität München
Phone: +49 89 2180 78010
Fax: +49 89 2180 78037
Email: jochen.herms@med.uni-muenchen.de

Prof. Dr. Frank Holstege
University of Utrecht
Phone: +31 88 755 5874
Fax: +31 88 756 8479
Email: f.c.p.holstege -at- umcutrecht.nl

Prof. Dr. Farouc Jaffer
Massachusetts General Hospital, Harvard University
Phone: +1 617 724 9353
Email: fjaffer@mgh.harvard.edu

Prof. Dr. F. Jakob
Orthopedic Center for Musculoskeletal Research
Experimental and Clinical Osteology
Orthopedic Department
University of Würzburg
Phone: +49 931 8031580
Fax: +49 931 8031599
Email: f-jakob.klh@uni-wuerzburg.de

Prof. Moustapha Kassem
Endocrinology and Metabolism &
Director Stem Cell Research and Treatment Center
University Hospital of Odense
Phone : +45 6550 4084
Fax : +45 65919663
Email: mkassem@health.sdu.dk

Prof. Dr. Angus Lamond
Director, Wellcome Trust Center, Dundee
Phone: +44 1382 385473
Fax: +44 1382 345695
Email: a.i.lamond@lifesci.dundee.ac.uk

Prof. Günter Lepperdinger
Austrian Academy of Sciences
Institute for Biomedical Aging Research
Phone: +43 512 5839 1940
Fax: +43 512 5839 198
Email: guenter.lepperdinger@oeaw.ac.at

Dr. Pierre-Marie Lledo
DR1 CNRS
Principal Investigator
Perception and Memory Laboratory
Institut Pasteur
Phone: +33 1 45 68 88 03
Fax: +33 1 45 68 83 69
Email : pierre-marie.lledo@pasteur.fr

Prof. Clemens W.G.M. Löwik
Leiden University Medical Center
Phone: +31 71 526 3075
Fax: +31 71 524 8136
Email: c.w.g.m.lowik@lumc.nl

Prof. Dr. Franz Magerl
Hochschule Amberg
Phone: +49 961 382 181
Fax: +49 961 382 138
Email: f.magerl@haw-aw.de

Prof. David Marsh
Professor of Clinical Orthopaedics
Institute of Orthopaedics and Musculoskeletal Science, UCL
R&D Director, Royal National Orthopaedic Hospital, Stanmore
International Ambassador for the Bone and Joint Decade
Email : d.marsh@ucl.ac.uk

Prof. Vasilis Ntziachristos
Chair for Biological Imaging, Technische Universität München
Helmholtz Zentrum München
Phone: +49 89 3187 3852
Fax: +49 89 3187 3017
Email: v.ntziachristos@tum.de

Stefano Pluchino, MD, PhD
CNS Repair
DIBIT II and Institute of Experimental Neurology
San Raffaele Scientific Institute
Phone: +39 2 2643 4353
Fax: +39 2 2643 4855
Email: pluchino.stefano@hsr.it

Prof. Dr. Maximilian Reiser
Institut für Klinische Radiologie
Klinikum der Universität München
Ludwig-Maximilians-Universität München
Phone: +49 89 7095 2750
Fax: + 49 89 7095 8895
EMail: maximilian.reiser@med.uni-muenchen.de

Prof. Dr. Markus Rudin
Universität Zürich & Eidgenössische Technische Hochschule Zürich
Phone: +41 446337604
Fax: +41 446331187
EMail: rudin@biomed.ee.ethz.ch

Univ.-Prof. Dr. med. Matthias Schieker
Professor of Regenerative Medicine at LMU, with a focus on the Musculoskeletal System
Clinic of Surgery – Downtown Medical Campus
University Hospital of Munich
Ludwig-Maximilians-Universität München
Fax: +49 89 5160 5482
Email: Matthias.Schieker@med.uni-muenchen.de

Prof. Dr. Renee Schroeder
Professur für RNA-Biochemie am Zentrum für Molekulare Biologie
Universität Wien
Phone: +43 1 4277 54690
Fax: +43 1 4277 9528
Email: renee.schroeder@univie.ac.at

Prof. Dr. Markus Schwaiger
Klinikum rechts der Isar,
Technische Universität München
Phone: + 49 89 4140 2971
Fax: +49 089 4140 4841
Email: m.schwaiger@lrz.tum.de

Dr. Herbert Stepp
Klinikum der Universität München
Ludwig-Maximilians-Universität München
Phone: +49 89 7095 4880
Fax: +49 89 7095 4864
Email: Herbert.Stepp@med.uni-muenchen.de

Francis Szele PhD
Department Department of Physiology
Anatomy and Genetics College
St Anne's College
Oxford, OX1 3QX
Phone: + 44 1865 282627
Fax: +44 1865 272420
Email: francis.szele@dpag.ox.ac.uk

Prof. Dr. Bertrand Tavitian
Comité à l'Energie Atomique et aux Energies Renouvelables
Phone: +33 1 69 86 78 67
Fax: +33 1 69 86 77 86
Email: bertrand.tavitian@cea.fr

Dr. Juan Vaquero
Fudacion para la Investigacion Biomedica del Hospital, Madrid
Phone: +34 914265067
Fax: +34 914265180
Email: juanjo@mce.hggm.es

Prof. Dr. Juergen Winkler
Head, Division of Molecular Neurology,
University Hospital Erlangen,
Friedrich-Alexander University Erlangen-Nuremberg
Phone: +49 9131 853 9323
Fax: +49 9131 853 6597
Email: juergen.winkler@uk-erlangen.de
www.molekulare-neurologie.uk-erlangen.de

Prof. Eckhard Wolf
Forzebra und DFG793 (MS, FJ)
Gene Center Munich
Institute of Molecular Animal Breeding and Biotechnology
Ludwig-Maximilians Universität München
Phone: +49 89 2180 76800
Fax: +49 89 2180 76849
Email: ewolf@lmb.uni-muenchen.de

Scientific Challenges for European Health - 20 October, 2010		
List of participants		
Ludwig	Aigner	Paracelsus Medizinische Privatuniversität - Austria
Ina	Andrees	Fraunhofer-IGB
Annabelle	Ascher	European Commission - RTD
Philip	Asherson	MRC Social Genetic Developmental Psychiatry - University of London
Andre	Berberich	KoWi
Michela	Bertero	Centre for Genomic Regulation - Barcelona
Jerome	Boehm	European Commission - SANCO
Patrick	Brundin	Wallenberg Neuroscience Center - Sweden
Jan	Buitelaar	Radboud University Nijmegen - Medical Centre - NL
Jiří	Buriánek	General Secretariat of the Council of the EU
Jeroen	Buters	Center for Allergy and Environment - Helmholtz Zentrum Munich – Technische Universität München
Patrizia	Campolongo	La Sapienza University of Rome
David	Collier	MRC Social Genetic Developmental Psychiatry - University of London
Mihai	Costea	mixcoach networx
Patrick	Cramer	Gene Center Munich, LMU Munich
Karima	Djabali	Technische Universität München
Rüdiger	Dohms	European Commission - COMP
Dieter	Dollase	KoWi
Tanja	Eberhardt	Fraunhofer Institute for Interfacial Engineering and Biotechnology
Claudia	Eggert	KoWi
Thomas	Eigner	Bavarian Research Alliance
Veronika	Erben	Helmholtz-Zentrum, Munich
Michael V.	Fedorov	LIFE-Zentrum - Klinikum der Universität München
Peter	Fisch	European Commision - RTD - A3
Kirstin	Folda	European Office of the Bavarian Local Authorities
Barbara	Franke	Radboud University Nijmegen - Medical Centre - NL
Wendelin	Freiherr von Gravenreuth	CEPF - Confederation of European Forest Owners
Stefan	Fuehring	European Commission
Carmen	Galan	University of Cordoba - Spain
Simone	Gautier	International Programmes - LMU Munich
Sonja	Gerlach	Vertretung des Landes Niedersachsen bei der EU
Babett	Glaeser	Saxony Liaison Office
Joachim	Grammer	Technische Universität München
Günther	Greiner	Technische Fakultät University Erlangen-Nürnberg
Aziza	Haas	European Commission
Jochen	Herms	LMU Munich
Arnd	Hoeveler	European Commission - RTD F5
Christoph	Hofbeck	European Commission
Frank	Holstege	University of Utrecht - NL
Philipp	Holzheid	Representation of the Free State of Bavaria to the European Union
Christina	Hübscher	University of Rostock
Andrés	Ingason	deCODE genetics, Reykjavik
Franz	Jakob	ForZebRA, University of Würzburg
Philippe	Jehenson	European Commission - RTD
Angelika	Joos	Merck Sharp & Dohme (Europe) Inc.
Elisabeth	Kaindl	European Office of the Bavarian Local Authorities
Ulrike	Kaltenhauser	Baygene - LMU Munich
Ines	Kaufmann	Department of Anaesthesia and Intensive Care - LMU Munich
Susan	Kentner	Helmholtz-Gemeinschaft, Büro Brüssel
Charles	Kessler	European Commission - RTD F5
Susanne	Kettler	Coca-Cola Services s.a.
Hanna	Kipp	Fraunhofer-Gesellschaft

Martin	Klingenspor	Technische Universität München
Matthias	Koepp	UCL Institute of Neurology
Rainer	Kollmar	Head of Stroke Unit - University Hospital Erlangen
Angus	Lamond	Wellcome Trust Center Dundee UK
Mark	Larance	University of Dundee
Anna	Lechner	European Research Council - Executive Agency
Dorothea	Leonhardt	Bavarian Research Foundation
Jerome	Lepeintre	European Commission - SANCO
Klaus-Peter	Lesch	University of Würzburg
Pierre-Marie	Lledo	DR1 CNRS, France
Kirsten	Look	Hanse-Office
Karin	Lukas-Eder	Bavarian Research Alliance
Jakob	Madsen	DANRO
Franz	Magerl	University of Applied Sciences Amberg-Weiden
Wolfgang	Mayer	IMMUMED GmbH, München
Judith	Millecker	GABO:mi
Kevin	Mitchell	Trinity College, Dublin
Andrea	Mogni	European Commission
Claudia	Moser	European Commission - GD JLS - E
Ursula	Mühle	Technische Universität München - GSISH
Constanze	Multerer	European Commission - RTD
Jörg	Nittscher	Vertretung des Landes Niedersachsen bei der EU
Vasilis	Ntziachristos	Chair for Biological Imaging - Technische Universität München
Andreas	Nüssler	Klinikum rechts der Isar, Technische Universität München
Christoph	Palm	University of Applied Sciences Regensburg
Cora	Pfafferott	European Commission
Jenny	Pick	ForTe, Technische Universität München
Tapani	Piha	European Commission - SANCO
Stefano	Pluchino	San Raffaele Scientific Institute - Italy
Heidrun	Potschka	LMU Munich
Siegfried	Praun	V&F Medical Development GmbH Austria
Alexander	Roediger	MSD (Europe), Inc.
Benno	Roozendaal	University of Groningen - NL
Dan	Rujescu	LMU Munich
Jürgen	Sautter	European Commission - RTD F5
Mircea	Sbarna	Permanent Representation of Romania to EU
Gustav	Schelling	LMU Munich
Anne-Marie	Schickel	European Commission
Katrin	Schiebel	University Erlangen-Nürnberg
Matthias	Schieker	ForZebRA, LMU Munich
Angelika	Schlunk	Director of the Representation of the Free State of Bavaria to the European Union
Cornelius	Schmaltz	European Commission RTD A6
Ulrich	Schmid	European Commission
Christian	Seitz	University Erlangen-Nuremberg
Laurent	Selles	European Commission
Daniel	Sheffer	Leibniz Association
Pawel	Sikorski	NTNU, Norway
Mirjam	Söderholm	European Commission
Kathrin	Staffler	ForTe, Technische Universität München
Herbert	Stepp	Laser-Forschungslabor University Hospital of Munich
Gianpietro	van de Goor	European Commission - RTD
Lukas	Van Oudenhove	University of Leuven, Belgium
Bruna	Vives Prat	Centre for Genomic Regulation, Barcelona
Herbert	von Bose	European Commission - RTD
Maria	von Stern	European Parliament
Wolfgang	Weidenhammer	Klinikum rechts der Isar - Technische Universität München

Sebastian	Weinzierl	European Commission
Brigitte	Weiss-Brummer	International Programmes - LMU Munich
Jürgen	Winkler	Molecular Neurology University Hospital Erlangen
Sebastian	Winkler	ERC Executive Agency
Meike	Ziegenmeier	Representation of Niedersachsen (Lower Saxony)
Ingrid	Zwoch	NCP Life Sciences