Position Paper of Helmholtz Association of German Research Centres on Health Aspects in Horzion 2020

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HELMHOLTZ ASSOCIATION

The Helmholtz Association of German Research Centres with its almost 33,000 employees and an annual budget of 3.3 billion euros is Germany's largest research organisation and one of the largest in Europe. The Helmholtz Association participates in many European projects – often in a coordinating role – and benefits considerably from the established instruments of the Framework Programme of the European Union for Research and Technological Development. The instruments and actions of the Framework Programme contribute significantly towards supporting networking and collaboration between the scientists of the Helmholtz Association and researchers throughout Europe. They facilitate as well activities which cannot be realised at the national level or which provide added value in the form of collaborations at the European level.

Preamble

The Helmholtz Association welcomes the stronger focus of EU funding programmes on societal challenges which raise complex scientific and technological questions. Supplementing the position papers of the Helmholtz Association of German Research Centres on the 8th Framework programme of February 2010[1] and May 2011[2], this position paper aims to contribute to the discussion on defining different challenges within Horizon 2020.

According to the ongoing consultation and discussion process on "Horizon 2020 – The Framework Programme for Research and Innovation", the following issues have been identified as major societal challenges:

- Health, Demographic Change and Well-being
- Food, Security and Sustainable Bio-resources
- Secure, Clean and Efficient Energy
- Smart, Green and Integrated Transport
- Climate Action and Resource Efficiency
- Inclusive, Innovative and Secure Societies
- Future and Emerging Technologies
- …

To address these issues efficiently, concerted efforts by different stakeholders across Europe should be made. European aims and strategies should be formulated and implemented in collaboration with all relevant partners. The European Commission has already initiated the discussion process by organizing thematic workshops with stakeholder groups. We recommend continuing this approach in a more open, inclusive and transparent manner than has been previously been the case.

Furthermore, the above-mentioned list of topics needs to be continuously reviewed and expanded as necessary. It is likely that some issues which have not yet been included or might emerge in the future could have a comparable and equally significant impact on society. There should be provisions for including such emerging issues in Horizon 2020.

The Helmholtz Association sees collaborative research as the most appropriate instrument to achieve these goals. Collaborative projects should therefore continue to be the backbone of all EU programmes for funding RTD and should be complemented by strategic partnerships bringing together European research organizations and institutes. Research infrastructures are another essential enabling platform in the innovation chain and should receive substantially more funding from the EU.

1 Position paper of Helmholtz Association on the 8th EU Framework Programme (2014-2020), www.helmholtz.de/frp8-2010-en

2 Position paper of Helmholtz Association on the Communication of the European Commission "From Challenges to Opportunities: Towards a Common Strategic Framework for EU Research and Innovation" COM (2011) 48, www.helmholtz.de/greenpaper-2011-en

Global Change – Challenges for the Research and the Health System[3]

As a result of increasing life expectancies, the population of the EU is growing steadily older, and this demographic evolution presents a growing challenge to European society and European health systems.

The increased life expectancy in the EU has come about through improved hygiene, healthier lifestyles and medical progress. However, the ageing process itself has not been significantly affected in the last hundred years. Thus, chronic, age-related diseases such as neurodegenerative diseases, cancer, cardiovascular and metabolic diseases like diabetes, as well as pulmonary diseases and related infections of immune-deficient patients are becoming increasingly important. Changes in lifestyle characterised by supernutrition and lack of physical activity, smoking and environmental stress have led to a strong increase in metabolic and pulmonary diseases, especially in the Western countries. Furthermore, global mobility facilitates the emergence of new infectious diseases as well as the resurgence of those thought to be eradicated. The complex interaction of individual genetic disposition, lifestyle and environmental factors and their role in the development of disease is becoming an increasingly important focus of research. For example, the connection between metabolic syndrome, the result of a complex metabolic failure, and widespread diseases like diabetes mellitus and cardiovascular and neuropsychiatric disorders is becoming more and more apparent.

The maintenance and promotion of good health in European citizens as well as the prevention and targeted treatment of diseases also represent major societal challenges. Since every person has a unique genetic disposition and reacts differently to environmental and lifestyle factors, personalised medicine is the only way to provide diagnostic methods and therapies that are safer and more effective and economical than conventional therapies.

To meet these challenges successfully, substantial research efforts coordinated at the European level are required. One starting point is the understanding of molecular causes and pathogenetic mechanisms underlying diseases prevalent to modern civilisation, including the analysis of cell-specific pathways based on excellent fundamental, hypothesis-driven biomedical research as well as systems biology approaches analysing data and modelling pathological processes in biological systems.

At the same time, new methods in research and development as well as the translation of results into clinical practice need to be developed further. This should proceed in two directions: Clinical experience should have an impact on research in the laboratory and vice versa.

3 The recommendations in this document are based on internal discussions currently ongoing among in the Helmholtz Centres active in health research.

Translational research is needed to accelerate the transfer of research results into clinical therapies for the benefit of the patient and to realise the potential arising out of fundamental research through the development of clinical applications. Innovative medicine requires a long-term commitment of public fundamental research, market analyses, preclinical research, including research on animals, studies involving clinical partners and a long-term focus on attracting and integrating the pharmaceutical and medical devices industries in order to achieve the commercialisation of results.

To unlock the enormous potential of scientific insights for the benefit of the patient, a concerted action of both national and European actors is vital.

In the view of the Helmholtz Association, the following diseases of civilisation represent important research themes at the European level, including ageing processes and the ageing population as major cross-cutting themes relating to all other areas:

- Cancer
- Cardiovascular and metabolic diseases
- Neurological diseases
- Metabolic syndrome, especially diabetes mellitus
- Infectious diseases
- Lung diseases and allergies

Prevention is a key issue that needs to be improved in order to ensure the financial stability of our health care systems over the long term. Insights gained from epidemiological studies can provide the basis for better prevention, diagnosis and therapy. In the view of the Helmholtz Association, studies based on prospective and population-based cohorts and the implementation of biomaterial banks provide an important foundation for research in the above-mentioned areas.

Disease-related topics

Cancer

The Helmholtz Association is convinced that development of new approaches to cancer diagnosis and treatment can be improved by innovative strategies based on research and development at the molecular, cellular and immunological level. Therefore, research in these areas needs to be strengthened. Medical technologies such as development of new imaging methods and strategies for radiotherapy, which make possible early detection and prevention, play an important role as well. Therefore, the main topics in cancer research should include:

- Signaling and proteomics in cancer cells
- Cancer induction
- Metabolic syndrome and cancer
- Health economy in the context of oncological diseases
- Personalised radio-oncology and ion therapy
- Radiopharmacy and molecular imaging
- Precision of radiotherapy

Cardiovascular and metabolic diseases

Cardiovascular diseases represent the most frequent cause of death in the Western industrial countries, with a steady upward trend. The main risk factors are high blood pressure, metabolic syndrome, in particular diabetes mellitus, increased levels of blood lipids, adiposity and tobacco consumption.

To achieve a significant, steady decrease in the incidence of these diseases and to counteract the consequences of demographic change, there must be large-scale efforts to elucidate the causes of these diseases. New approaches relating to the prevention, diagnosis and treatment of cardiovascular and metabolic diseases are required which should be based on a variety of methodological approaches in genetics, genomic research and systems biology, cell biology and epidemiology. Along these lines, important research topics include:

- Immune system and cardiovascular diseases
- Non-coding RNAs
- Role of metabolism for the prediction, prevention and course of disease
- New animal models for diseases and development of adequate methods for phenotyping
- Cardiac development and congenital heart defects
- Cardio-metabolic diseases and multimorbidity in old age
- Drug research
- Health economics in the context of cardiovascular diseases

Neurological diseases

With increasing age, the risk of neurological and psychiatric diseases increases. The main risk factors are age and chronic diseases such as diabetes, depression and cardiovascular diseases. Genetic analysis and epigenetic studies help to clarify the link between risk factors and neurodegenerative processes. Epilepsies, brain tumours or cognitive impairments following strokes also play an important role. Research into their causes, diagnosis, treatment and prevention is therefore essential.

In this context, a better understanding of molecular, cellular and systemic mechanisms and structures in the human brain is required. For successful implementation, transgenic animal models as well as research in genetics, cell biology, neurophysiology, neuroanatomy and high-performance

scientific computing are necessary. Moreover, methodological approaches such as structural and functional imaging, brain mapping and the "virtual brain" should be supported.

All of these methods and approaches can form a basis for better health care delivery and prevention in this area. Therefore, key research topics should include:

- Neurodegeneration, neuroprotection and neuroregeneration
- Signal mechanisms
- Animal models for neurodegenerative diseases
- Risk factors: ageing and co-morbidity (e. g., metabolic syndrome)
- Translational, diagnostic and functional imaging
- Epidemiological and population studies
- Health care systems and delivery
- Clinical research and intervention studies

Infectious diseases

Infectious diseases are still the third most frequent cause of death worldwide and will continue to be a serious threat to humanity. Although antibiotics and vaccines have been developed and hygienic measures improved, we are constantly confronted with new or recurring pathogens that at one time appeared to be under control. The increasing resistances of pathogens to common antibiotics and the facilitation of transmission of infectious agents through factors such as globalisation and climate change in combination with an ageing population make prevention and therapy of infectious diseases a huge challenge. This becomes particularly obvious through epidemic outbreaks of previously unknown diseases like SARS, bird and swine flu.

In addition, well-known pathogens can become more aggressive as a result of mutations. This was the case with the recent EHEC/HUSEC epidemic in Germany. Therefore, the development of new methods for diagnosis, prevention and therapy of infectious diseases based on fundamental research into molecular processes like the interactions of between pathogens and infected hosts is essential to combat these threats. New anti-infection and immune therapies must be developed to counteract the problem of increasing resistance and the decreasing number of potent antibiotics. Therefore, the main issues to be addressed are:

- Research on new and emerging infectious diseases
- Identification of new active substances to overcome pathogen resistance
- Research on host-pathogen-interactions
- Infection and age
- Nosocomial infections
- Diagnostics for personalised therapies
- Sequelae of infectious diseases (cancer, metabolic dysfunction, neurodegeneration)
- Chronic infections
- Immune modulation and intervention to combat infectious diseases
- Functional and integrative genomic research combined with
- Systems biology for a better understanding of infection processes and drug functions

Health and environment with a particular focus on pulmonary diseases and diabetes

Chronic pulmonary diseases, diabetes, neuropsychiatric diseases, cardiovascular failures, allergies, and cancer are the result of a complex interplay of genetic factors, environment and personal life style. To develop strategies for personalised prevention, early detection and therapy, the interplay of body and environmental factors needs to be explored. In addition, their role in maintaining health, their influence on the development of diseases as well as on the effectiveness of therapeutic interventions also needs to be investigated. An important related issue involves the influence of climate change on health. The entire organism and the ensemble of complex internal interactions should be observed through the use of systemic approaches. Fundamental biomedical research can contribute towards elucidating issues relating to such widespread diseases as neuropsychiatric diseases, infectious diseases, cardiovascular diseases, allergies and cancer.

Priorities in translational research in these areas should comprise pulmonological and diabetes research. Pulmonary diseases represent the second most frequent cause of death worldwide, with smoking being one of the main causes along with other factors. The development of new approaches for prevention and diagnosis is urgently needed, as well as therapies tackling the cause and symptoms of the disease.

Research on diabetes should forge new paths comprising an integrative research approach that combines various scientific disciplines like genetics, epidemiology, immunology, stem cell research and many other subdisciplines. Only in this way can a comprehensive understanding of this complex disease be achieved that will result in completely new therapeutic, diagnostic and preventive approaches. Therefore, the main issues to be addressed are:

- Environmental factors and epigenetics
- Stress and environment as risk factors
- Systemic analysis of active substances
- Metabolism and the neuroendocrinological axis
- Human microbiome
- Health care delivery and health economics
- Interaction of ageing, environmental factors and the genome
- Multiple exposures in urban environments and chronic diseases
- Medical radiation research

- Pulmonary diseases (pathological mechanisms, signalling pathways, etc.)
- Allergy research

Cross-cutting topics and methods

Prevention and early detection

Prospective epidemiological studies are regarded as the gold standard in the identification of genetic and environmental risk factors, that determine the onset and progress of disease. Since many widespread diseases can be detected solely at the advanced stage, it is necessary to improve health care delivery through new approaches to early detection and prevention. By providing tangible benefits for patients, these approaches can provide considerable potential for economising in our health care system. Therefore, appropriate studies should be designed and implemented through a Europe-wide network to make such research possible.

Personalised Medicine

Often, medical therapies are not effective or cause serious side effects. Therapeutic decision-making does not sufficiently take into account certain characteristics of the respective disease, individual genetic constitution, gender, age and co-morbidity of the patient, although these factors considerably influence whether the therapy has a successful outcome or not. To make treatments more effective, safer and more economical, personalised medicine aims to develop new preventive and therapeutic strategies which can be adjusted to the requirements of the defined group of patients. The factors which influence therapeutic decision-making must be identified and further elucidated and developed through research. In this context, research on biomarkers and a speedy transfer into diagnostics and clinical application are essential.

New model systems for diseases and optimisation of pre-clinical research

To carry out a comprehensive analysis of systemic diseases such as cardiovascular and metabolic diseases, optimised model systems (complex cell culture systems, animal models) are still required because already existing models are often deficient with respect to predictability or because of side effects in humans. The development of adequate methods for phenotyping is also necessary to provide new insights. Along these lines, new transgenic techniques and new research methods should be established to optimise pre-clinical research.

Active substances and structural biology

Innovative approaches for the identification of small molecules with effects on biological systems are becoming increasingly important for biomedical research and form a basis for a targeted and quick development of secure and affordable pharmaceutical agents. To expedite the translation of active substances into applications, interdisciplinary approaches and shared chemical-biological platforms with relevant test procedures are needed. The basis for the strategic development of new therapeutic agents depends on generating and exchanging new knowledge among different areas like structural biology, in silico modeling, in vitro screening and in vitro design. This approach should be accompanied by the systematic analysis and optimisation of bioactivity in models and the development of clinical applications. New methods such as defining spatial structures of biomolecules in solution make it possible to observe dynamic effects and biological regulatory mechanisms and can help gain new insights into metabolic processing. Metabolomics and chemical biology establish new competencies that are helpful in developing close collaborations between research institutions and industry.

Imaging

Functional characterisation of tissue plays a major role in investigating complex systems as well as in the diagnosis and individualised treatment of cancer and other diseases such as cardiovascular, pulmonary, psychiatric and neurological diseases. Molecular imaging and methods for the analytical interpretation of images combined with high-throughput analysis should be developed further. This includes improvement of nuclear medicine imaging methods (especially PET), development of new approaches in magnetic resonance tomography, quantitative real-time multispectral optoacoustic tomography (MSOT) as well as the development and establishment of high-resolution optical methods like Stimulated Emission Depletion (STED)-microscopy and fluorescence tomography (FMT) associated with development of combined procedures (multimodal imaging). All of these include as well the development of molecular and nanoscale probes based on radiotracers, fluorescent markers and MR-contrast agents.

Health economics

Along with clinical efficacy, long-term cost effectiveness is a key success factor in innovative approaches in prevention, diagnosis and therapy. The possible economic implications of the innovative and individualised approaches require comprehensive analysis, and appropriate research in these areas should therefore be supported.

Research infrastructures

Research infrastructures (RI) represent an effective means of creating platforms for scientific collaboration and research networks. Moreover, as they provide methods and resources for research and development in biomedical research, RIs are essential for exploiting the full potential of translational research because they establish links between scientists carrying out fundamental and clinical research and physicians in clinical settings. (Laboratory → Clinic, Clinic → Laboratory). Moreover, RIs facilitate links between scientific research and the education and training of young researchers as well as their involvement in international research collaborations. Therefore, it is essential to provide support for the design, implementation and operation of RIs in Horizon 2020.

Transfer of research results into innovation

Successful transfer of research results into the pharmaceutical, biotechnological and medical device industries is a key indicator for effective translation. Chemical biology and drug research play an important role in transferring research results into the pharmaceutical industry by increasing the value of academic research and making it attractive for industry. Strategic partnerships between industry and academia, licensing or spin-offs can contribute to shortening the length of time needed to transfer innovative ideas for clinical application into the market and generating new impulses for innovation and growth in the health industry. Clinical applications based on new insights relating to e.g. new prognostic markers have an important impact because they provide immediate help to patients or to physicians making treatment decisions.

BRIEF PORTRAIT OF THE HELMHOLTZ ASSOCIATION

In the Helmholtz Association, 18 German research centres have joined forces to share their resources in strategically oriented programmes to investigate complex questions of societal, scientific and technological relevance.

They concentrate on six major research areas: energy; earth and environment; health; aeronautics, space and transport; key technologies and structure of matter. The scientists work closely together across the centres on these issues.

The Helmholtz Association provides the necessary resources, a framework for long-term planning, a high concentration of scientific competence and an outstanding scientific infrastructure with major projects, some of which are unique worldwide.

The research objectives of the Helmholtz Association are set by the funding bodies after discussions with the Helmholtz centres and the Helmholtz Senate and Assembly of Members. Within this framework, the scientists of the Helmholtz centres determine the themes of their research through strategic programmes in the six research areas across centres.

(Source: “Strategy of the Helmholtz Association,” Berlin 2009 - updated 2012)

www.helmholtz.de

Helmholtz Centres

- Alfred Wegener Institute for Polar und Marine Research
- Deutsches Elektronen-Synchrotron DESY
- German Cancer Research Center
- Deutsches Zentrum für Luft- und Raumfahrt
- Deutsches Zentrum für Neurodegenerative Erkrankungen
- Forschungszentrum Jülich
- GEOMAR | Helmholtz Centre for Ocean Research Kiel
- GSI Helmholtz Centre for Heavy Ion Research
- Helmholtz Centre Potsdam GFZ, German Research Centre for Geosciences
- Helmholtz Centre for Environmental Research – UFZ
- Helmholtz Centre for Infection Research
- Helmholtz-Zentrum Berlin für Materialien und Energie
- Helmholtz-Zentrum Dresden-Rossendorf (HZDR)
- Helmholtz-Zentrum Geesthacht Centre for Materials and Coastal Research
- Helmholtz Zentrum München, German Research Center for Environmental Health
- Karlsruhe Institute of Technology
- Max Delbrueck Center for Molecular Medicine (MDC) Berlin-Buch
- Max Planck Institute for Plasma Physics (associated member)

This paper presents a consensus of the views
of the Helmholtz Association and its centres.

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