Executive summary of the workshop
"A roadmap for the future of ageing research in Europe"
Brussels, 11-12 July 2007

This workshop was co-organized by the Directorate General Research of the European Commission and by the European Coordination Action Link-Age (LSHM-2005-513866).

Participants:

Patrick Kolar	European Commission, head of unit F4 "Genomics and Systems Biology"
Beatrice Lucaroni	European Commission, project officer "Human development and ageing"
Kevin McCarthy	European Commission, project officer "Medical and Public Health R&D"

experts

Alexander Bürkle	University of Konstanz
Gillian Butler-Browne	Faculté de Médecine Pierre et Marie Curie, Paris
Bertrand Friguet	University of Paris 7
Jan Hoeijmakers	Erasmus University, Rotterdam
Pascal Kahlem	EMBL-EBI
Graham Pawelec	University of Tübingen
Jonathan Powell	Unilever
Peter Roepstorff	University of Southern Denmark

coordinators

Gérard Chaouat	Unité 782 Inserm, Toulouse, coordinator of EMBIC
Brian Clark	University of Aarhus, coordinator of Proteomage
Barbara Demeneix	UMR CNRS 5166, Paris, coordinator of Crescendo
Claudio Franceschi	University of Bologna, coordinator of Geha
Stathis Gonos	University of Athens, deputy coordinator of Proteomage
Pidder Jansen-Dürr	Institute for biomedical ageing research, Vienna, deputy coordinator of Proteomage
Tom Kirkwood	University of Newcastle, coordinator of Age-Action
Heinz Osiewacz	University of Frankfurt, coordinator of MiMage
Oliver Schildgen	University of Bonn, coordinator of RESP-viruses
Pascal Sommer	UMR CNRS 5086, Lyon, coordinator of Elast-Age
Olivier Toussaint	University of Namur, coordinator of Link-Age
Rudi Westendorp	Leiden University Medical Center, coordinator of Lifespan
Julia Szekeres Bartho	Pecs University Medical School, vice-coordinator of EMBIC

Béatrice Rayet	University of Namur, deputy coordinator of Link-Age
Florence Chainiaux	University of Namur, notes taker

Related websites

ERA-AGE, the European Research Area Network.	*http://era-age.group.shef.ac.uk*
AAL, Ambient Assisted living.	*http://www.aal169.org*
ERC, the European Research Council.	*http://erc.europa.eu/index.cfm*
CORDIS, 7th Research Framework Programme	*http://cordis.europa.eu/fp7/home_en.html*
LINK-AGE	*http://www.link-age.eu*
AGEACTION	*http://ageaction.ncl.ac.uk*
EMBIC	*http://www.embic.org*
LIFESPAN	*http://www.lifespannetwork.nl*
CRESCENDO	*http://www.crescendoip.org*
GEHA	*http://www.geha.unibo.it*
RESPVIRUSES	*http://www.medical-surveillance.com/index.html*
MIMAGE	*http://www.mimage.uni-frankfurt.de*
ELASTAGE	*http://www.elastage.org*
PROTEOMAGE	*http://www.proteomage.eu*
CELLS INTO ORGANS	*http://www.cellsintoorgans.net*
ANABONOS	*http://www.abdn.ac.uk/anabonos*
OSTEOGENE	*http://folk.uio.no/sreppe/index.html/OSTEOGENE.html*

This workshop entitled “A roadmap for the future of ageing in Europe” brought together coordinators of the “Human ageing and development” projects funded under the 6th Framework Programme (FP6) and selected experts of the domain. The aims of the workshop were to determine what should be the priority themes in ageing research to be developed in the next ten to fifteen years and to identify research needs that participants wish to be considered by the Commission in future FP7 calls for proposals. During the workshop, the most recent advances and scientific contributions made to the area of ageing as well as some related research in development (embryo implantation) were reviewed. The impact provided by the –omics studies, the relations between clinical and basic research, the ageing policies in Europe, the involvement of and communication with the stakeholders, the translational research and the involvement of industry were assessed and discussed.

The 1st half-day of the meeting was devoted to the presentation by the coordinators of the purpose; the advances and what should be the continuation of their current FP6 funded projects. The 2nd day was devoted to discussion on themes of research to be developed in the future. The complete report is given in annexe while the major conclusions reached during the workshop are summarized below.

Scientific themes to be developed in the future

- ✓ *The mechanisms of ageing*

Obviously, the understanding of the molecular basis of ageing is a prerequisite to prevention and intervention, early detection, diagnosis and therapy.

There is an urgent need for more powerful **model systems** (preferentially short term models, new or improved models). These models should include cell systems (cellular senescence, reconstructed tissues, etc.) and model organisms (“classical” or not). These models must be relevant and allow translation / extrapolation to the human population. The other way round is also true: when we have a question in humans, we should be able to find the right models to look for an answer.

These models are complementary to studies in **humans**. Nevertheless, some topics as inflammation or genetic variance must be studied directly in humans. Moreover, long-term longitudinal studies on specific human populations (very old, young, centenarians, etc) also need to be performed.

The stochastic **accumulation of damage** is a key to ageing. It is important to determine the extent and biological relevance of molecular damage as well as the efficiency and effectiveness of specific maintenance and repair pathways of cells (stem cells >< differentiated cells), organelles (mitochondria, nucleus, etc.) and molecules (DNA, protein). Models must be created with improved maintenance and repair systems, suppression of the somatropic axis, tissue-specific or reporter animals.

The role of **stem cells** in ageing (*What is the consequence of stem cell dysfunction or loss on tissue homeostasis and tissue ageing? Are there any differences in maintenance and repair functions in germline/stem cells >< differentiated cells?*) as well as the role of ageing in stem cells (*What are the mechanisms? Are they mediated by stem cell niche? Role of Notch signaling?*) must be investigated.

The **epigenetic** question in ageing is gaining more and more importance but has escaped detailed analysis up to now. New techniques are now available. Epigenetic imprinting and its consequences on ageing must be determined (with the use of existing data such as those collected in the GEHA project). The epigenetic imprinting of special human populations (ageing individuals from *in vitro* fertilization, effect of freezing and thawing, reduction of fertility) must also be studied. Epigenetic also includes studies on micro RNAs.

Several themes are developed in projects funded in FP6 and need a continuation in FP7:

- the role of **nuclear receptors** (NR) in ageing: nuclear receptors are vital and follow ageing. It is important to determine whether it is a cause or a consequence. There are many perspectives for research on NR (*mitochondrial-located NR, crosstalk between NR, early effects on development and impact on ageing, etc*.).
- **immunosenescence** and **infectious diseases** (beyond the Influenza virus, as new respiratory viruses and long term Hepatitis B virus) in the elderly need more research effort.
- the role of **mitochondria** in ageing by integrative and translational studies of data obtained in the different EC collaborative projects.
- the **ageing of elastic tissue** and more precisely the connection between the external barrier plasticity and behavioral stress.
- **protein homeodynamics** and its perturbation in ageing.
- researches on **early developments** that have an interface with ageing. The consequences of early deficiency on gamete quality, embryo, as well as inappropriate early uterine function in genetically affecting/imprinting the ageing process, need to be investigated. Also, the cycling uterus and the "ageing placenta" offer both interesting models of self renewing but cyclically ageing organs, on one hand, and a relatively quick ageing process, on the other hand.

Innovative domains to be developed:

- **neuroendocrine/immune disruption** and restoration are innovative domains of important research.
- **systems biology** is currently of major importance and could be an important tool to understand complex physiologic networks.

✓ *The relationships between diseases and intrinsic ageing*

For many important diseases, **ageing is the largest single "risk factor"**. Understanding why aged cells / organs are more vulnerable to pathology will open new paths to prevention and cure. Translation has to be done with models.

Cellular senescence could be used as basis for age-related diseases.

Relationships between humans and models must integrate **(bio)gerontologists and geriatricians**. Indeed, there is an urgent need for reinforcing collaboration and communication between both disciplines. Bridges between both disciplines should be flagged within future calls when appropriate.

Studies should be performed on **Healthspan** and **Lifespan**. The **determinants** (social, economic, environmental, etc.) of health in old age (maintenance mechanisms) must be defined, from humans to models. The implication of **interventions** (drugs, functional food, etc) on ageing should be tested.

The concept of **frailty** has to be clearly defined, in collaboration with clinicians.

Organizational recommendations

Out from their own experience of European projects management, coordinators of FP6-funded projects made a round table to point some aspects of coordination that could be even more simplified in the future, as a decrease in the delay of payment, a simplification of the administrative charge and a decrease in the number of reports (one report period per year is a heavy work for the coordinators of IP and NoE).

Several recommendations to increase the visibility of ageing in European research have also be discussed:

Both **large and small** (high risk and innovative) projects are required. In

addition, there is a need for one or a few larger projects for **longer periods** for ageing research in order to:

- perform longitudinal human population studies.
- preserve valuable infrastructure/database/organization.

The objective of these projects is to achieve **multidisciplinarity** and to reduce the gap between gerontology, basic research and geriatric practice as mentioned above.

It is important to increase the **critical mass** of researchers: future projects could request the presence of young principal investigator's (PI) team involved in ageing and/or team(s) labeled "new in ageing".

A structure must be created to allow data collection, integration and storage in **databases** as well as an inventory of existing databases. This would allow maximum exploitation of the data collected in the different projects and to extract the most important information in order to define new areas of research. For instance, the ideal continuation for FP6-funded projects such as GEHA, PROTEOMAGE and MIMAGE is to associate the data obtained in databanks. In this example, this could allow the study of: genetics of nuclear DNA and mitochondrial DNA and their cross talk / epigenetics / molecular biology of the identified genes and variants. The accessibility and interlinks should be determined on the basis of minimal criteria for standardisation in different biological and medical disciplines (EMBL-EBI). This must start with a workshop to make an inventory and to choose the best strategy (LINKAGE). The ownership and the accessibility of the data have to be clearly defined. There is also a need for a long-term commitment (creation of a foundation?) to maintain running such structure and allow a long-term access to the databases.

Coordination of all databanks will obviously require **standardisation** at several levels in the projects (format, accessibility issues, quality control of data, IP issues, ownership items, ethical and private). Standardisation should be as important as ethical aspects in the projects. To help define standards is one of the aims of the Link-Age and Lifespan projects. A workshop should be organized in order to define :

- standardisation of the semantics: definition of ageing, healthspan/lifespan.
- standardisation of the protocols, of the different procedures.
- "harmonized strategic guidelines".

Coordinators suggest the creation of a **coordinator's network** (with regular meetings, preferentially in association with existing conferences). Such a "College of coordinators" would be organized on an unofficial basis (although the Commission would be kept informed and invited to participate). Such a network could also be created for the project managers.

The creation of a (virtual) Institute of Ageing, or **'College of Biogerontology'**, is necessary. It is important to have such a structure at the European level. Institutes will bring together people linked by EU actions. This college composed of a board of advisors would give profile and attract excellence. The Link-Age project is a model to be used to reach this objective. Other instruments needed to go further in the creation of this college are the roadmap calls, more and stronger links developed with ERA-AGE as well as progress towards other supra-national programs such as ERA-NET+ and Article 169.

Many research disciplines are technology-driven and depend on **technological innovations**. Essential for success is close crosstalk/intense integration between those involved in development and those in biologically/medically-relevant applications, including training and use of these new technologies. E.g. new '-omics' techniques including those for determining different forms of oxidation of proteins; *in vitro* models / low oxygen facilities / tissue engineering / organotypic cultures; stress reporter mice (knock-in mice).

Industrial involvement and needs are already implemented in each project.

There must be a true integration: e.g. technology transfer, joint projects. There are still specific topics in which industry can play an active role:

- pharmacogenetics and genomics, with specific attention to the elderly population, who are usually ignored in clinical trials. Neglected items are: Co-morbidity, poly-pharmacy, bio-availability, pharmacokinetics/dynamics, compliance.
- nutrition for the elderly, who have different needs.
- specific and sensitive biomarkers should be validated.
- short term models (50 year interventions are not useful).
- clinical/population trials.

The **training of young scientists** is also a vital issue to be addressed at different levels: master's programmes, PhD, medical disciplines. Training and **dissemination** should be components in each of the teams.