

Integrating research into Development and Ageing

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Summary

Although human ageing has many dimensions it is a biological process that we share with nearly all living organisms. Therefore, we must comprehend the broad principles of the ageing process beyond current preconceptions about the ageing process that it is an ineluctable part of our biology. In line with the continuous increase of our lifespan, ageing may be intrinsically far more malleable than previously thought. The challenging focus of our endeavour is to reveal how conditions in early development influence ageing across a diverse spectrum of species, including humans. Ageing can only be understood by considering the entire human life history. Our life span is determined by genetic, environmental and stochastic factors, and evidence suggests that early-life events determine the individual status at the end of life. Therefore, we aim to bridge research on development with research on ageing, and to integrate these two disciplines that do not have a tradition of close interaction. We will move to and fro between experiments in (in)vertebrate models and observations in humans to test effects detected in one species as candidate longevity mechanism in the other. This approach has only been marginally explored and has never been attempted in one collaborative effort. Some of us have begun to probe this unexplored field of research, but fragmentation in Europe must be avoided. LifeSpan ensures the future framework of ageing research that allows the appropriate questions to be asked, using the most suitable organisms, and taking the appropriate experimental and observational approach. This can only be done effectively when the research groups in Europe have the proper expertise and carry out their research in an integrative manner, in terms of science, organisation, and of a common education programme. All participants excel in science including the expertise and resources necessary for this Network. Crucially then, LifeSpan will provide the essential framework to reach European scientific excellence by "Integrating research into Development and Ageing".

Problem

Why linking research into development and ageing? The answer lies in the notion that ageing is complex and requires an integrated approach that builds together medical science, genetics, and a framework of evolutionary theory. To date, the focus of ageing research has primarily been on which genes, physiological and metabolic processes exert their effects in adult life. However, there is a growing need for research in the field of ageing to include the study of developmental processes within the context of reproduction, longevity, and ageing. The participants in this Network of Excellence (NoE) take this stance not only because there is ample evidence that developmental processes affect adult life but also because evolutionary theory predicts that natural selection has worked to integrate the whole of an organism's life history, which includes development.

To date only little is known about the mechanisms and their functions that underlie such links. Evolutionary conservation of the genetic regulation of ageing among model-organisms opens unique opportunities for understanding human ageing and age-related health problems. LifeSpan will use the power of key (in)vertebrate model-organisms to uncover the mechanisms that are relevant in mankind.

Aim

- **Integration:** LifeSpan will serve as a real and virtual working environment that enables expertise building in the emerging research field "Integrating research into Development and Ageing". LifeSpan should result in an European research community where all participants have mutual and essential cross links. This community as a whole is much more than the sum of its parts.
- **Scientific excellence:** LifeSpan aims to identify the mechanisms that connect the developmental and the adult life phase and how they influence ageing and health at old age. These mechanisms will be described in terms of genetics, epigenetics, development, and physiology. The discovery of these mechanisms and how they interact will be propelled mostly by using experimental manipulations in model organisms. Crucially, these observations will be combined with unique observations in human cohorts to establish the contribution of these mechanisms to variation in human ageing and longevity.
- **Spread results:** Knowledge of the LifeSpan initiative, its results and impact will be made available to professionals and the general public. The professionals include scientists from outside the network and outside Europe, experts working in the healthcare sector, and experts from industry. This is essential for implementing the scientific results in healthcare programmes, and to help develop sustainable solutions.



Expected results

- Identify genetic pathways and mechanisms that link development to ageing and longevity. The effects will be determined in different environments to include descriptions of developmental plasticity and gene by environment interactions.
- Establish for the identified pathways and mechanisms whether they contribute to variation in life span and life histories in human populations.

Potential applications

LifeSpan is aimed at understanding a fundamental process of metazoan life, ageing and its relation with development. The identification of genetic, bio-molecular and physiological pathways that co-ordinate developmental processes and adult longevity and ageing, and the environmental factors that influence their expression, opens the possibility for non-invasive intervention in these pathways by means of a changed life-style, dietary intake, medication, or other. A full understanding of the genetic and environmental factors and of the mechanisms by which they exert their effects will facilitate an individual-tailored healthcare scheme, including both medicinal and non-medicinal treatments.

The exploitation of the results is twofold:

- development of healthcare schemes by the industrial and scientific participants, as well as 'outsourcing' such developments to industry;
- the results can also be exploited by healthcare professionals who can change their advisory and prevention plans by informing their patients and potential future patients how they can change their way of living and child-care to increase the likelihood of healthy ageing.

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