



Strategic Promotion of Ageing Research Capacity

Gene Expression Profiling to Understand Stem Cell Ageing

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*Meeting the challenges of
an ageing society*

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The Background

Ageing is a series of subtle changes in the cells and tissues of our bodies which make us increasingly frail and increase our risks of developing diseases. This frailty is the major problem which faces old people today and which can prevent them from living independently. Understanding the way in which our bodies age, will enable us to develop new ways of tackling some of the diseases associated with ageing such as Alzheimer's Disease, Rheumatoid Arthritis and problems with the immune system.

Stem cells play an important part in the body's ability to renew and repair itself. Most normal cells are committed to being of a certain type with a set lifespan. Stem cells, though, can both renew themselves as well as create new cells of what ever tissue they belong to. These stem cells are therefore essential for the development and maintenance of all tissues in the body because they are able to grow and transform into many different cell types. For example, **haemopoietic stem cells** produce and develop into the cells which make up the blood. In adults, stem cells are important in the general maintenance of healthy tissues and organs, as they are responsible for providing new, healthy cells to replace older ones.

The Issues

The ability of stem cells to grow and transform into different cell types decreases with age. This can mean that tissues and organs within the body are not able to stay as healthy, which can affect function and the development of diseases associated with ageing.

The biological processes which are associated with this stem cell ageing are unknown. Understanding the **genes** within our DNA which are responsible for, and the processes which lead to, stem cell ageing should help in our understanding of ways in which we can extend tissue survival and repair.

The Aims

To identify the genes which are important for stem cell ageing. In particular this research concentrates on the genes involved in haemopoietic stem cell.

The Study

Down's Syndrome is associated with many of the signs of premature ageing, and can be detected from an early phase in development. This provides the opportunity for the study of very early events in ageing before any permanent damage occurs. Therefore this study has used Down's Syndrome as a model for accelerated stem cell ageing.

The DNA of stem cells from patients with and without Down's Syndrome was isolated and analysed using a **Microarray**. A Microarray is a collection of microscopic DNA spots, commonly representing single genes, arrayed on a solid surface. They can be used to show the extent to which specific genes are turned on or off (the expression of the gene or **gene expression**).

Findings

450 genes were found to be expressed differently (i.e. either turned on or off) in the stem cells of volunteers with Down's Syndrome compared to those who did not have the syndrome. This gene expression was found to change with the age of the volunteer. Of these, 393 were genes which had already been identified (i.e. that had a name), and 57 had no associated identifier (i.e. had no name).

293 genes were more highly expressed (i.e. turned on or functional) in the haemopoietic stem cells of the individuals with Down's Syndrome, whereas 192 had a lower expression (i.e. turned off or down). The genes which had a higher or lower expression were found to be mainly involved in processes which are necessary for basic cell survival and repair.

Genes do not always work by themselves; often several genes work together in a network. Of the 15 most significant gene networks identified, 13 were ones which were involved in processes related to renewal and survival. This suggests that the ageing and self renewal process in the haemopoietic stem cells of people affected by Down's Syndrome is altered compared to those not affected by the syndrome.

Discussion and Implications

Understanding stem cell ageing could have a huge impact for older people in the future. This could uncover ways of extending tissue survival and repair, thus preventing or alleviating some of the diseases associated with ageing.

The results suggest that gene expression in haemopoietic stem cells changes during the ageing process. This means that the stem cells in older people may not be able to function as well as in younger people. For example, haemopoietic stem cells are responsible for producing the cells which make up the blood; with age they produce a fewer number of cells which are capable of fighting infections.

The ability to intervene and increase the number of haemopoietic stem cells may have considerable impact on the gradual deterioration of the immune system. This deterioration can be responsible for considerable problems in older people, either by causing disease or by contributing to disease (i.e. a reduced ability to fight infection).

Interestingly, new evidence suggests that accelerated haemopoietic stem cell ageing might be involved in the development of autoimmune diseases such as rheumatoid arthritis. This study contributes to the understanding of the way in which haemopoietic stem cells age, and will inform future work in this area.

Future work could focus on identifying ways in which we might delay or reduce stem cell ageing. This could include gene therapy, or the identification of natural molecules which might affect the expression of genes associated with this ageing process.

The Research Team



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The Study

The study received financial support from SPARC of £28,287 and ran for 10 months ending in July 2007. Additional support was provided by the University of Sheffield.

More information about the study can be found on the SPARC website www.sparc.ac.uk and obtained directly from Dr Bellantuono.

Bibliography and Key References

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SPARC

SPARC is a unique initiative supported by EPSRC and BBSRC to encourage the greater involvement of researchers in the many issues faced by an ageing population and encountered by older people in their daily lives. SPARC is directed, managed and informed by the broader community of researchers, practitioners, policy makers and older people for the ultimate benefit of older people, their carers and those who provide services to older people.

SPARC pursues three main activities:

Workshops to bring together all stakeholders interested in improving the quality of life and independence of older people.

Advocacy of the challenges faced by older people and an ageing population and of the contribution of research to improving quality of life. SPARC is inclusive and warmly welcomes the involvement of everyone with a relevant interest.

Small Awards to newcomers to ageing research, across all areas of design, engineering and biology and at the interfaces relevant to an ageing population and older people. In 2005 and 2006 SPARC received 185 applications for support in response to two invitations for competitive proposals of which 34 were supported.

Executive Summaries

SPARC is supporting its award holders through funding, mentoring, a prestigious dissemination platform, professional editorial assistance, international activities and provision of contacts. Each of the projects has been small, yet the enthusiasm for discovery, and impatience to contribute to better quality of life for older people, has more than compensated for the very limited funding which was provided.

This executive summary is one of a series highlighting the main findings from a SPARC project. It is designed to stand-alone, although taken with summaries of other projects it contributes to a formidable combination of new knowledge and commitment by newcomers to ageing research, with a view to improve the lives of older people. This is a tangible contribution towards ensuring that older people receive full benefit from the best that research, science and technology can offer.