



Strategic Promotion of Ageing Research Capacity

EPR, Oxidative Stress and Ageing

Richard Hartley,
Caroline Quin
Stuart Caldwell &
Alison Hay

*Meeting the challenges of
an ageing society*

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Dr Richard Hartley, Caroline Quin, Dr Stuart Caldwell & Alison Hay
University of Glasgow

The Background

Radicals, such as **reactive oxygen species** (ROS), are highly reactive molecules which are naturally occurring by-products of normal processes within the body. When antioxidant levels are not high enough, or during some diseases, the amount of ROS can increase and may react with DNA, lipids and proteins to cause damage. Oxidative stress is something which can happen if reactive radicals outbalance good anti-oxidants in our bodies.

When studying oxidative stress, it is very important to be able to detect and distinguish between the various chemical contributors to it in order to understand it properly.

Electron paramagnetic resonance (EPR) imaging is a non-invasive method which can be used to create a three-dimensional (3D) map of free radicals within biological tissues. Unlike other techniques, it measures free radicals directly and can detect the chemical composition of the radicals present in order to identify them.

Although many of the radicals found in biological systems are too short-lived for direct detection by EPR, a special technique known as **spin trapping** has been developed to convert the highly reactive radicals into more stable, detectable, radicals.

The Issues

Oxidative stress due to ROS is a major contributor to the process of ageing and to many diseases including neurodegenerative diseases (such as Parkinson's Disease and Alzheimer's Disease) and stroke.

The Aims of the Study

The overall aim of this project was to combine EPR and new **probes** to detect ROS at the sites where they cause damage. The probes are spin traps which allow the components of oxidative stress to be detected and identified by EPR.

The Study

Dual Sensor Probe

Previous studies looking at oxidative stress have used and adapted **single-sensor spin traps** to distinguish between and to stabilise different radicals. This study has successfully used a **double-sensor** system for the first time.

Double sensor probes should help identify the mechanisms of oxidative stress, which is fundamental to a wide range of life-threatening and debilitating conditions associated with ageing and to ageing itself. This understanding will in turn lead to new methods for alleviating or preventing the onset of these conditions.

MitoSPIN

A **spin trap** called **MitoSPIN** was designed to trap radicals in the mitochondria of cells. Mitochondria provide the energy for cells to function and in doing so can be a source of free radicals such as ROS.

When the MitoSPIN spin trap was used with EPR, it enabled the detection and identification of different radicals, and it could also be used with other techniques to detect oxidative stress in the mitochondria.

Discussion and Implications

The aim of this project was to advance understanding into how oxidative stress and ageing are linked. In the future, this information may enable a healthy old age to be achieved through appropriate diets, lifestyle and medicines to alleviate the effects of damage through oxidative stress.

The outcomes from this study have been the development of new probes that should advance this area of ageing research significantly.

MitoSPIN, which was developed as part of this study, may be used to distinguish between different ROS in the future. MitoSPIN should be useful for studying the generation of ROS in mitochondria (the part of the cell responsible for producing energy) and their role in ageing.

Once further investigations have been conducted, samples will be distributed to other research groups who are interested in oxidative stress and cellular ageing. The methods developed in this study will provide an important opportunity for other researchers to further understand the processes associated with oxidative stress and its impact on ageing.

Understanding the biological sources of radicals, their behaviour in different environments, organelles and tissues and the cellular responses to them will be key to understanding the process of ageing itself. Since oxidative stress is associated with the development of neurodegenerative diseases such as Parkinson's and Alzheimer's Disease, understanding how oxidative stress and ageing are linked may help us achieve a healthier old age.

The Research Team



Dr Richard Hartley, Reader
WestCHEM, Department of Chemistry
University of Glasgow,
Glasgow, G12 8QQ
richh@chem.gla.ac.uk



Caroline Quin
Research Student



Dr Stuart Caldwell
Researcher



Alison Hay
Research Student

The Study

The study received financial support from SPARC of £58,533 and ran for 18 months ending in April 2007. Additional support was provided by the University of Glasgow. Further funding came from the Wellcome Trust and EPSRC.

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

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.