

Oxidative Stress & Ageing

Electron Paramagnetic Resonance

Detecting Radicals

Protecting Cells

Understanding Ageing

Chemical Biology and EPR Spectroscopy

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The Project

Ageing at a cellular level is largely the result of damage caused by radicals, particularly by oxygen-centred radicals known as reactive oxygen species (ROS).¹ ROS not only cause pathologies associated with ageing such as arteriosclerosis, neoplasia, and cataracts, but also mediate the deleterious effects of other major diseases that particularly affect older people, e.g. stroke, neurodegeneration, diabetes and autoimmune diseases. 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, and of ameliorating the diseases of old age.² EPR (electron paramagnetic resonance) is the only spectroscopic technique that detects radicals unambiguously; other techniques such as fluorescence provide only indirect evidence of their presence. This project deals with the combination of EPR spectroscopy and new probes to detect different ROS unambiguously at the sites where they cause damage.

General Aims

To investigate the relationship between oxidative stress and cellular ageing by:

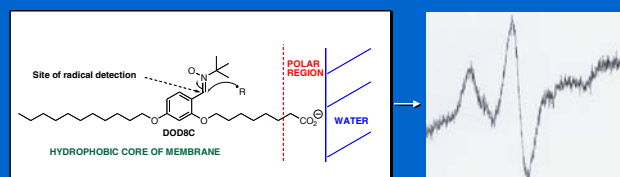
- Developing new probes for detecting radicals in different environments, organelles and tissues.
- Ameliorating the process of oxidative stress using targeted antioxidants so that the genes and proteins associated with the antioxidant defence and cellular senescence may be better understood.
- Ameliorating oxidative stress and observing what phenotypic changes associated with ageing are affected.

Methodology and Resource

We will use two key methodologies:

- Chemical Synthesis of Antioxidant Probes designed to interact with radicals (funding from Wellcome Trust, EPSRC and University of Glasgow).
- EPR Spectroscopy to determine whether and where ROS are intercepted by our probes (funding from SPARC).

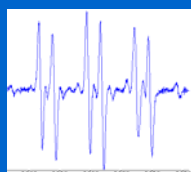
And we will work with our collaborators (Dr Paul Shiels, University of Glasgow, Prof. Ian Megson, UHI Inverness) to see how our compounds protect cells and organs, reduce radical damage and ameliorate conditions associated with oxidative stress.



Probe reacting with radical in membrane and resulting EPR spectrum³

References

- [1] Schriener, S. E. *et al. Science* **2005**, 308, 1909-1911.
- [2] Rovner, S. L. *C&EN* **2004**, 82(34), 30-37.
- [3] Hay, A.; Burkitt, M. J.; Jones, C. M.; Hartley, R. C. *Arch. Biochem. Biophys.*, **2005**, 435, 336-346.

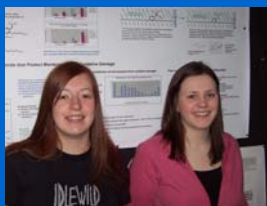


EPR Spectrometer and spectrum of tumbling radical



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