EDITORIAL

Oxygen in Biochemistry – Breathtaking Research

The availability of molecular oxygen (O_2) in the environment has had a fundamental impact on the biochemistry of life. We all know how important oxygen is – try reading this editorial without breathing! However, the ability of oxygen to provide a terminal electron acceptor for the efficient production of energy is somewhat counteracted by the propensity of oxygen to generate toxic, reactive products. Thus the homeostasis of both oxygen and its reactive products is essential for metazoan life, and disruption to this fine balance plays a role in essentially all major diseases.

Oxygen and oxidative stress remains a topic of great interest in biochemical research, and extends well beyond oxidative phosphorylation. This Showcase on Research comprises four articles from accomplished Australian researchers covering the diverse field of oxygen biochemistry.

Oxygen homeostasis is intimately linked to the detection of both environmental and cellular oxygen levels, specifically hypoxia when cellular demand exceeds supply. The cellular response to hypoxia is characterised by the coordinated regulation of target genes to mediate oxygen consumption, oxygen delivery, cell metabolism, survival and differentiation. In the first article, Jonathan Gleadle covers transcriptional responses to hypoxia mediated by the hypoxia-inducible transcription factors (HIFs), with the essential 2-oxoglutarate-dependent dioxygenases acting as cellular oxygen sensors. This field is of considerable interest due to its direct relevance to cancer and ischaemic disease, and its role in development. The recent discovery of dioxygenases as cellular oxygen sensors provides novel insight into the regulation of oxygen homeostasis and attractive new therapeutic targets, and other enzymes in this family are also generating interest.

The uncontrolled generation of reactive oxygen species or oxidants (oxidative stress) causes considerable damage to cells, and their production is carefully balanced by protective systems within a cell. More recently, reactive oxidants have also been shown to mediate cell signalling in normal, healthy tissue. Michael Davies introduces the different types of biological oxidants and their reactive properties, briefly covers the types of protective systems used, and provides a detailed discussion on protein damage by oxidants. Whilst proteins are not the only target of oxidative stress, it is obvious that they are crucial in terms of disruption to normal cellular function.

The existence of reactive oxidants was postulated over a century ago, but characterisation was delayed due to the inability to efficiently detect them. Understanding cellular redox homeostasis remains difficult, particularly in the context of a cell where it is influenced by numerous factors including oxygen concentration and pH. Anita Ayer and Ian Dawes describe the use of specific fluorescent probes to determine redox states within subcellular organelles of living yeast, plant and mammalian cells. The changes in redox state in response to oxidative stress can be followed over time, and demonstrate clear differences between different organelles. This and similar techniques are invaluable in understanding the cellular responses to oxidative stress *in vivo*.

Oxidative stress in neurons can lead to cell death, as occurs in a number of neurological diseases. In the last article, Gavin Higgins, Philip Beart and Phillip Nagley cover the diverse mechanisms by which reactive oxidants can induce neuronal cell death, including programmed (apoptosis, necrosis and autophagy) and unprogrammed cell death. This is also an exciting area of oxygen research, with the complexity and regulation of the different mechanisms of neural cell fate poorly understood, but with considerable potential to produce novel therapeutic approaches to reduce neurological damage.

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Cover Illustration

Cellular responses to oxidative stress leading to the various types of programmed cell death in neurones. Reprinted from *Journal of Alzheimer's Disease*, volume 20 (Supplement 2), G.C. Higgins, P.M. Beart, Y.S. Shin, M.J. Chen, N.S. Cheung and P. Nagley, Oxidative stress: emerging themes and variations in neuronal injury, pages S453–S473, Copyright 2011, with permission from IOS Press.

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Guest Editor: Dan Peet

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In August, the Showcase on Research will be on **Venoms and Toxins** - *Guest Editor: Norelle Davy*

Australian Biochemist - **Editor** Rebecca Lew, **Editorial Officer** Liana Friedman