

Showcase on Research

EDITORIAL

Dangerous but Essential: Genetic Diseases of Reactive Substances

Many biochemical reactions involve the use or generation of potentially toxic agents. These may be reactive intermediates such as free radicals, degradative enzymes such as proteases, or reactive cofactors of enzymes such as metal ions. The cell faces the problem of maintaining these reactive chemicals in a form that does not cause self-destruction. The way in which this is achieved is often by sequestration of the substance into a compartment, or binding to a carrier molecule for delivery to the target molecule in the cell. Yet without these potentially hazardous reactions, life would be impossible.

The articles presented in this Showcase on Research illustrate the consequences of failure of the mechanisms involving these reactive substances in a number of human genetic disorders. The first two articles deal with the genetic disorders of the essential, but redox-reactive metal ions copper and iron. Because of their propensity to generate reactive oxygen species, these two metals have to be carefully sequestered and regulated to avoid toxicity. Greg Anderson in Queensland has been involved in a study of the genetic defects of iron metabolism and including the very common genetic disorder hemochromatosis. In this disease and other iron overload conditions, damage is caused to the liver and central nervous by the accumulated iron. The work from my group with Jim Camakaris has focussed on understanding the mechanisms of copper homeostasis through studies on the copper toxicity condition, Wilson disease, and the copper deficiency disorder, Menkes disease. These are very different diseases due to mutations in very similar proteins that regulate copper efflux from cells. Henrik Dahl and David Thorburn discuss the genetic mitochondrial disorders; the mitochondria also tend to generate reactive oxygen species that can cause mitochondrial damage, and the formation of these can be catalyzed by iron or copper in the mitochondrion. These diseases are particularly interesting because the clinical effects cannot yet be related fully to the biochemical defects.

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Dangerous but Essential: Genetic Diseases of Reactive Substances

Guest Editor: Julian Mercer

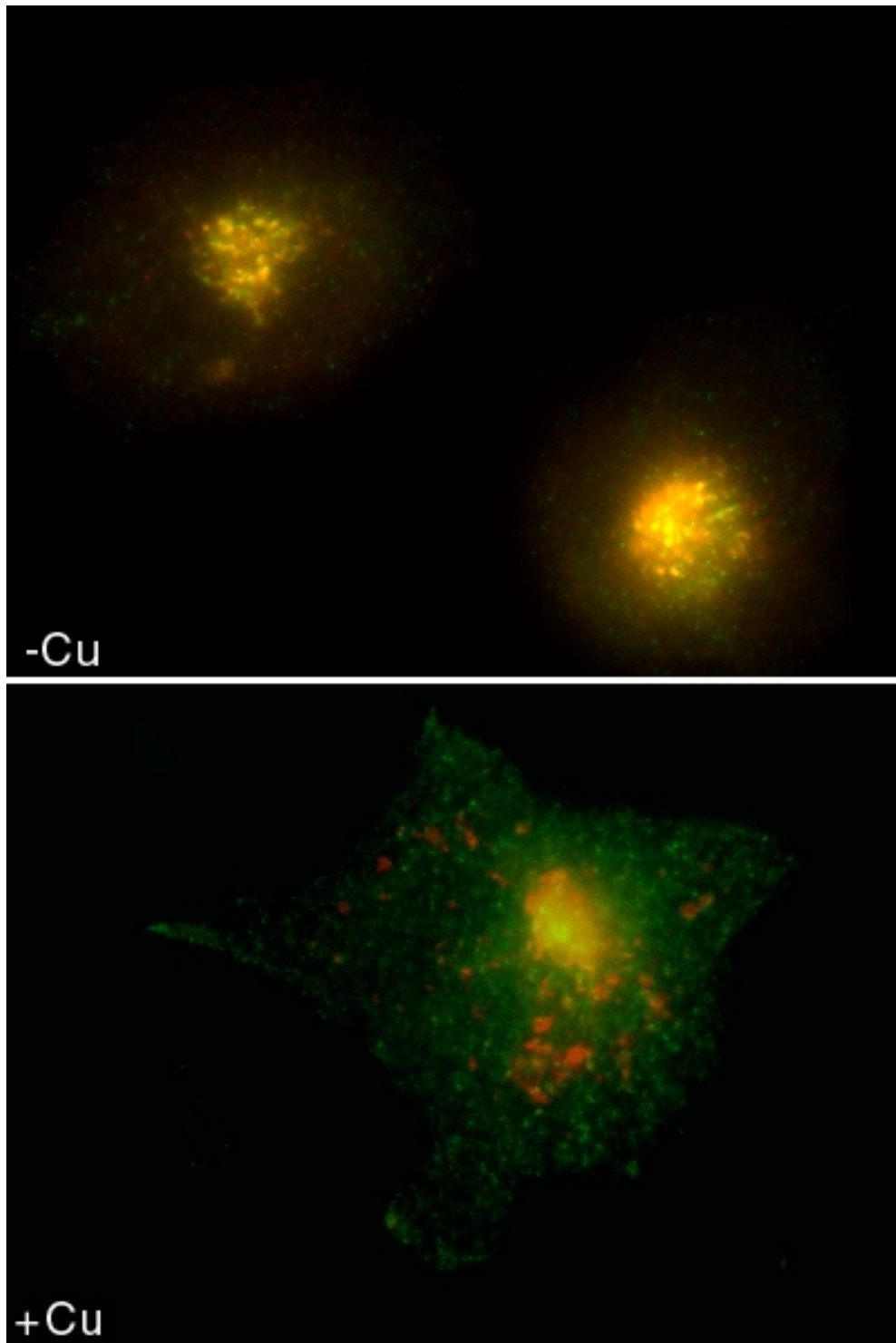
- Inherited Disorders of Iron Metabolism
Gregory J. Anderson
- Genetic Disorders of Copper: Diseases of Toxicity and Deficiency
Julian Mercer and James Camakaris
- Mitochondria: Transducers or Time Bombs?
Hans-Henrik Dahl and David R. Thorburn

Cover Illustration –

Fluorescent images of Chinese hamster ovary cells expressing both the Menkes and Wilson Cu ATPases from cDNA constructs, demonstrating the different effect of copper on the cellular location of the proteins. The Menkes protein is stained green and the Wilson protein red. The top panel (-Cu) shows two cells in low copper media, both proteins are primarily co-localized (shown by the yellow) in the *trans*-Golgi network. When cells are exposed to 200 μ M copper for 2 hours (bottom panel), both proteins traffic to different cellular compartments, associated with their particular modes of copper efflux. [Cells and images kindly provided by Stephen Firth and Natalie Barnes, Centre for Cellular and Molecular Biology, Deakin University.]

In the Next Issue...

In December, Showcase on Research will be on **Biochemistry and Molecular Biology of Plants** – Guest Editor: David Day



Front Cover Image