Slime Mould Model of Mitochondrial Disease Earns *Australasian Science* Prize

Prof Paul Fisher of La Trobe University has been awarded the 2007 *Australasian Science* Prize for discovering how an alarm protein that senses energy can cause cellular damage in mitochondrial diseases. Mitochondria are the organelles that produce energy within cells.

Mitochondrial diseases result from a reduced capacity of the mitochondria to generate energy for the cell in the form of adenosine triphosphate (ATP). Mitochondrial defects play a central role in major neurodegenerative diseases like Alzheimer's, Parkinson's and Huntington's.

Over 15 years Fisher has studied the slime mould *Dictyostelium discoideum* as a genetic model for understanding how malfunctioning mitochondria lead to diseases. Fisher's research eventually upturned a long-held belief that these diseases were consequences of an insufficient supply of ATP that led to dysfunction and ultimately death of cells. Instead, a protein called AMPK warns of an impending loss of energy and immediately takes remedial action by stimulating production of more energy and shutting down energy-consuming processes such as the growth and division of cells.

Fisher explained his research group's key findings with "Dicty" in *Australasian Science* (September 2007, pp.22–26): "As in human cells, AMPK in Dicty stimulates the proliferation of mitochondria and the production of energy… However, the ongoing activity of AMPK in mitochondrially diseased Dicty cells permanently impairs growth and development."

Similarities between these cellular processes and the genetic makeup of Dicty and humans led Fisher to believe that the AMPK alarm behaves likewise in humans. "This is a cause for hope," he says. "Although the cell cannot turn off AMPK, maybe it will be possible to find drugs that will inhibit AMPK and provide a way to treat these currently incurable diseases."

Paul Fisher holds a Petri dish containing a culture of *Dictyostelium*. Inset: When faced with starvation, up to a million "Dicty" individuals form a "slug" that migrates to the soil surface, where it forms a fruiting body 1–2 mm tall (shown here).

Since publishing the results in a May 2007 paper in *Molecular Biology of the Cell*, Fisher and postgraduate colleagues have attracted international attention. Prof Jeff Williams of the University of Dundee, Scotland, a leading researcher on the stalk differentiation pathway (a programmed cell death pathway) in Dicty, says this paper is "a major breakthrough that has enormous scientific and medical potential... I cannot overstate the importance and originality of this contribution.

"There are rare occasions in biology when a radically new idea comes along that turns orthodoxy on its head. Such ideas usually open up whole new research avenues that lead, eventually but inexorably, to important medical advances. A strong indication that this work will aid in identifying novel therapeutic regimes comes from the last experiment in their paper."

Prof David Vaux of La Trobe University, who is an expert on cell death, describes Fisher's work as "exciting, basic biology which provides a totally fresh angle towards understanding a lot of diseases. It now needs to be tested for its applicability to humans."

In September at an international conference in Dundee, Fisher's group reported preliminary data on the roles in mitochondrial disease of another protein (NDPK) that interacts with AMPK and may be required for its ability to damage specific aspects of cellular function.

They also reported at another international conference in Rotenburg, Germany, that mitochondrially diseased cells are more susceptible to Legionella infection. This, too, is due to the alarm protein AMPK. Fisher says they are beginning to analyse the mechanisms behind this. Other researchers have reported that patients with mitochondrial disease are more prone to infection.

Peter Pockley

PAST WINNERS OF THE PRIZE

- 2006 A/Prof Alex Hamilton and the Quantum Electronic Devices Group (University of NSW) for developing quantum semiconductor devices that use holes instead of electrons.
- 2005 Alexander Argyros, Dr Martijn van Eijkelenborg and Dr Maryanne Large (University of Sydney) for developing polymer optical fibres that perform competitively with silica fibres.
- 2004 Prof Levon Khachigian (University of NSW) for developing DNA drugs with potential in cancer treatment.
- 2003 Prof Mark Rowe (University of NSW) for determining how sensations are processed and transmitted in the brains of mammals.
- 2002 Dr Mark Hindell (University of Tasmania) for research on the behaviour of southern elephant seals and other marine predators.
- 2001 Prof Mandyam Srinivasan, Dr Shaowu Zhang & Dr Javaan Chahl (Australian National University) for extending knowledge of the behaviour and intelligence of bees to artificial intelligence.
- 2000 Dr Charlie Veron & Dr Mary Stafford-Smith (Australian Institute of Marine Science) for the discovery of 169 species of corals and documenting all known species in *Corals of the World*.