MedicalXpress

It must be important but what does it do? The strange case of UCP2

August 17 2012

When uncoupling proteins are active, mitochondria produce heat instead of ATP. This may be useful under certain circumstances, such as when an animal is hibernating. But non-hibernating animals also have them. Particularly poorly understood is the uncoupling protein UCP2. Elena Pohl and colleagues at the University of Veterinary Medicine, Vienna, show that the protein occurs mainly in cells of the immune system. The group's highly provocative findings are published in the online journal *PLOS ONE*.

Mitochondria represent the powerhouses of the eukaryotic cell. They are able to use the primary product of the breakdown of sugars to generate a proton gradient across their inner membrane and to exploit this gradient to produce ATP, which drives cellular metabolism. The importance of mitochondria to higher life forms is clear from what happens when their function is blocked: many poisons, such as cyanide, are known to act in this manner.

In this light, the discovery in 1973 of a eukaryotic protein that dissipates the proton gradient without generating ATP was highly unexpected. When this protein, thermogenin, is active, mitochondria produce heat rather than ATP. We now know that thermogenin is merely one member of a family of so-called 'uncoupling proteins' that can use proton gradients to generate heat. The founder member of the family, thermogenin, has been renamed uncoupling protein 1 or UCP1 and is known to be important in helping animals keep warm during hibernation and for babies to maintain their body temperature. The actions of the

other members of the family are less well understood. Particularly enigmatic is UCP2 but important clues to its function have now been provided by Anne Rupprecht and colleagues in the Institute of Physiology at the University of Veterinary Medicine, Vienna. Together with collaboration partners in Germany and Sweden, the researchers carefully examined the distribution of the UCP2 protein in mice. Their results showed clearly that UCP2 was preferentially expressed in cells related to the immune system and not, as generally believed, in neurons.

The implication was that UCP2 might somehow be involved in immune function. This surprising idea was tested by examining the change in UCP2 levels in T cells that were stimulated into action by a specific antigen. Stimulation indeed caused an increase in the amount of UCP2 in the cells. This was paralleled by increases in the concentrations of other proteins known to be produced in response to T-cell activation. When the cells were further stimulated seven and fourteen days later the amount of UCP2 increased although the amounts of the other proteins investigated did not.

It is attractive to speculate that the increase in UCP2 might be involved in signalling T-call stimulation but Pohl is quick to quash the notion. "Anne showed that the increase in UCP2 only starts a few hours after activation of T cells, while other events are seen much sooner. UCP2 thus arrives too late to be involved in stimulating the cells, so the increase must be related to overall metabolic changes in proliferating cells. This fits with our observation that UCP2 is not found in neurons, which no longer proliferate" In other words, although we still cannot be sure of the exact function of this intriguing protein, "at least we now know where to start looking!" And the finding that UCP2 is required by fast proliferating cells may have important consequences for the development of treatments for immune disorders, such as autoimmune and neurodegenerative diseases, and perhaps also for other diseases where cells divide rapidly, such as cancer.

More information: *PLoS ONE* 7(8): e41406.
doi:10.1371/journal.pone.0041406