Damaged protein could be key to premature ageing

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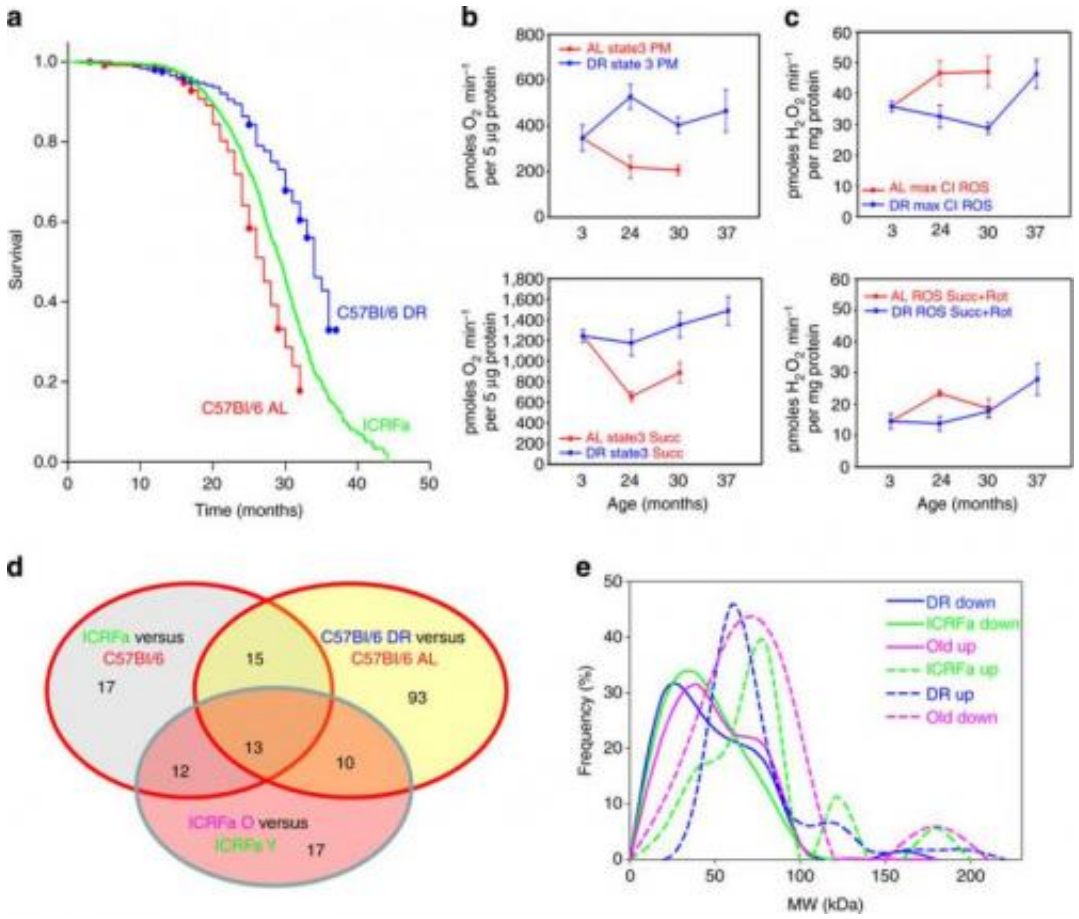

Longevity and liver mitochondrial function in male long-living mice. Credit: *Nature Communications*, doi:10.1038/ncomms4837

(Medical Xpress)—Scientists have found that the condition of key proteins in the mitochondria -the batteries of cells- could be used to

predict, and eventually treat premature ageing. And restricting diet could be one way of making this happen.
The researchers from Newcastle University used interventions, like calorie restriction, a system whereby the cells are deprived of nutrients and which in previous studies has been shown to cause mice to live longer than normal.

These interventions also resulted in more efficient assembly of important mitochondrial proteins into complexes. In a complex state, proteins work together more effectively, while on their own they generate toxic free radicals, which in turn cause cells to age more rapidly. If a similar mechanism is found in people it could lead to treatments, such as new drugs to improve protein assembly. In a paper published today in the journal *Nature Communications* the team describe their findings.

Ageing process

Thomas von Zglinicki, Professor of Cellular Gerontology at the Institute for Ageing and Health, Newcastle University, said: "Free radicals have long been linked with the ageing process. Mitochondria generate the energy required to keep our bodies going but they also generate free radicals. How exactly they are involved in ageing is still controversial. Our data shows that quite minor differences can explain large variations in healthy lifespan. Essentially what we have found is that the ageing process goes slower than normal in mice that managed to form mitochondrial protein complexes more efficiently, and that we actually could help them to do so."

A complex of 96 proteins is at the heart of the mitochondrial power station. Comparing the protein composition in mitochondria from mice that had more or less propensity to long life, the team found the mitochondria from long-lived animals surprisingly had less of these

proteins and thus seemed less well suited for energy production than the shorter-living mice.

However, further research showed that assembly of the protein complex was the key: If individual components were more scarce, assembly was perfect, but became more sloppy if more material was around. This then led to less efficient energy production and more release of oxygen free radicals, toxic by-products of mitochondrial metabolism.

Calorie restriction could extend lifespan

Dr Satomi Miwa, joint lead researcher on the team and a specialist on mitochondrial function, said: "These data go a long way to explain how calorie restriction can improve mitochondrial function, extend lifespan and reduce or postpone many age-associated diseases."

Professor Thomas von Zglinicki added: "We have shown here that complex assembly efficiency correlates to longevity differences in mice that correspond to one or two decades of healthy life in humans. We have also shown that human cells age faster if we corrupt complex assembly. What we now need to do is to see how we can improve the quality of these protein complexes in humans and whether this would extend healthy life."

More information: Low abundance of the matrix arm of complex I in mitochondria predicts longevity in mice. Satomi Miwa, et al. *Nature Communications* 5, Article number: 3837. DOI: 10.1038/ncomms4837 . Received 24 January 2014 Accepted 09 April 2014 Published 12 May 2014

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