MBG FOCUS TALK

hosted by Tinna Stevnsner

Monday 5 January 2015 at 13:15-14:00

Science Park, Conference room 3130-303

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Neurodegeneration in accelerated aging

Accelerated aging disorders represent a phenotypically diverse group of diseases associated with defects in DNA maintenance. In a subset of these disorders, Cockayne syndrome, Xeroderma Pigmentosum A and Ataxia-telangiectasia, neurodegeneration is prominent. What drives this particular phenotype is unknown but may involve a novel nuclear-mitochondrial cross talk. We have found mitochondrial dysfunction in these diseases caused by hyperactivation of the DNA damage responsive enzyme PARP1 leading to loss of NAD+, acetyl-CoA and attenuation of SIRT1 activity. The accelerated aging can be rescued with supplementation of NAD+ precursors or through PARP inhibition. Interestingly, high fat diet feeding rescues the accelerated aging of Cockayne syndrome mice through ketone-mediated activation of SIRT1. Ketones increase acetyl-CoA levels and ketones as well as PARP inhibitors non-additively extend the lifespan of short-lived Cockayne syndrome worms. Ketones and NAD+ thereby converge on the same longevity pathway, a finding that may be important for normal human aging.

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