Role for CISD2 gene in human disease and lifespan control

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In the May 15th issue of *G&D*, Dr. Ting-Fen Tsai (The National Yang-Ming University, Taiwan) and colleagues present a new animal model of human Wolfram Syndrome, and effectively link CISD2 gene function, mitochondrial integrity and aging in mammals.

Wolfram Syndrome (WFS) is a rare, inherited neurodegenerative disorder. It is clinically heterogeneous, but it is primarily characterized by juvenile-onset diabetes mellitus, optic atrophy and premature death. Two different categories of WFS (WFS1 and 2) are recognized, each with its own subset of variable symptoms, and resulting from mutations in the WFS1 and CISD2 genes, respectively.

The CISD2 gene is located on the long arm of human chromosome number 4, which has been previously implicated in the regulation of human longevity through a comparative genome analysis of centenarian siblings. Dr. Tsai's group sought to uncover the physiological function of CISD2.

The researchers engineered CISD2-deficient knock-out mice and, by 8 weeks old, observed an obvious premature-aging phenotype. The prematurely-aging CISD2-mutant mice displayed decreased body weight, shortened lifespan, and lower subcutaneous fat deposition, as well as clinical symptoms of WFS2 patients, including early-onset degeneration of optic, muscular and nervous tissues, and glucose sensitivity. Further study revealed that the Cisd2 protein is localized to the mitochondria, where it is required for proper mitochondrial structure

and function.

This work establishes WFS2 as a mitochondrial-mediated disorder, whereby dysfunction in these cellular energy factories underlies muscle and neural cell degeneration, and accelerated ageing. Future work will examine the utility of this CISD2 mouse model to understand WFS2 pathogenesis, as well as explore the potential lifespan-extending effects of increased Cisd2 expression.

Source: Cold Spring Harbor Laboratory (news : web)