

## **Nuclear to Mitochondrial DNA damage signaling in Neurodegeneration**

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We find that some DNA repair defective diseases with severe neurodegeneration have mitochondrial defects. Our studies involve cell lines, the worm (*c.elegans*), and mouse models and include the conditions Xeroderma pigmentosum group A, Cockayne syndrome and Ataxia telangiectasia. We find a pattern of hyperparylation, deficiency in the NAD+ and Sirtuin signaling and mitochondrial stress. We are pursuing mechanistic studies of this signaling and interventions at different steps to improve mitochondrial health and the neurodegeneration. I will discuss intervention studies in these disease models including a new Alzheimer mouse model with NAD supplementation.