Mitochondrial mutations and disease

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Mitochondria are cellular organelles with their own DNA. Their role in power generation makes them susceptible to oxidative damage, including the formation of DNA-damaging chemical complexes called adducts.

While one such adduct, M1dG, is normally excised by cells from the genomic DNA, mitochondria apparently lack this repair mechanism. This month in the journal *Nucleic Acids Research*, Lawrence Marnett, Ph.D., and colleagues report that levels of M1dG are much higher in mitochondrial DNA than in genomic DNA.

They also found that M1dG levels in mitochondrial DNA from pulmonary microvascular endothelial cells were two-fold higher in mice with a mutation in the bone morphogenetic protein receptor 2 (BMPR2) gene compared to wild-type mice. Pulmonary arterial hypertension has been associated with BMPR2 mutations.

These findings strongly suggest that increased oxidative stress leads to a direct increase in M1dG levels in mitochondrial DNA, and provide the first clear evidence linking this increase to a disease state. M1dG thus may be a biomarker of mitochondrial dysfunction in disease.

More information: Orrette R Wauchope et al. Oxidative stress increases M1dG, a major peroxidation-derived DNA adduct, in mitochondrial DNA, *Nucleic Acids Research* (2018). DOI: 10.1093/nar/gky089