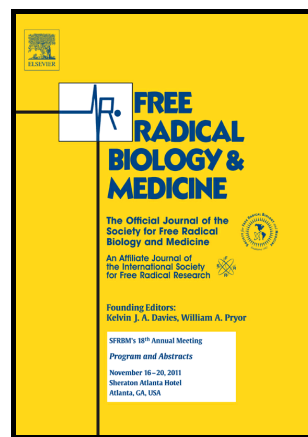


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An mtDNA mutation accelerates liver aging by interfering with the ROS response and mitochondrial life cycle

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Abstract

Mitochondrial dysfunction affects liver metabolism, but it remains unclear whether this interferes with normal liver aging. We investigated several mitochondrial pathways in hepatocytes and liver tissue from a conplastic mouse strain compared with the control C57BL/6NTac strain over 18 months of life. The C57BL/6NTac-mtNODLtJ mice differed from C57BL/6NTac mice by a point mutation in mitochondrial-encoded subunit 3 of cytochrome c oxidase. Young C57BL/6NTac-mtNODLtJ mice showed reduced mitochondrial metabolism but similar reactive oxygen species (ROS) production to C57BL/6NTac mice. Whereas ROS increased almost equally up to 9 months in both strains, different mitochondrial adaptation strategies resulted in decreasing ROS in advanced age in C57BL/6NTac mice, but persistent ROS production in C57BL/6NTac-mtNODLtJ mice. Only the conplastic strain developed elongated mitochondrial networks with artificial loop structures, depressed autophagy, high mitochondrial respiration and up-regulated antioxidative response. Our results indicate that mtDNA mutations accelerate liver ballooning degeneration and carry a serious risk of premature organ aging.

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