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Melatonin: A mitochondrial resident with a diverse skill set

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Abstract

Melatonin is an ancient molecule that originated in bacteria. When these prokaryotes were phagocytized by early eukaryotes, they eventually developed into mitochondria and chloroplasts. These new organelles retained the melatonin synthetic capacity of their forerunners such that all present-day animal and plant cells may produce melatonin in their mitochondria and chloroplasts. Melatonin concentrations are higher in mitochondria than in other subcellular compartments. Isolated mouse oocyte mitochondria form melatonin when they are incubated with serotonin, a necessary precursor. Oocyte mitochondria subsequently give rise to these organelles in all adult vertebrate cells where they continue to synthesize melatonin. The enzymes that convert serotonin to melatonin, i.e., arylalkylamine-N-acetyltransferase (AANAT) and acetylserotonin-O-methyltransferase, have been identified in brain mitochondria which, when incubated with serotonin, also form melatonin. Melatonin is a potent antioxidant and anti-cancer agent and is optimally positioned in mitochondria to aid in the maintenance of oxidative homeostasis and to reduce cancer cell transformation. Melatonin stimulates the transfer of mitochondria from healthy cells to damaged cells via tunneling nanotubes. Melatonin also regulates the major NAD^+-dependent deacetylase, sirtuin 3, in the mitochondria. Disruptions of mitochondrial melatonin synthesis may contribute to a number of mitochondria-related diseases, as discussed in this review.

Keywords: Acetyl coenzyme a; Pyruvate metabolism; SIRT3; Tunneling nanotubes; cancer; sepsis.

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