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Mitochondrial Actions of Thyroid Hormone

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Abstract

The hypermetabolic effects of thyroid hormones (THs), the major endocrine regulators of metabolic rate, are widely recognized. Although, the cellular mechanisms underlying these effects have been extensively investigated, much has yet to be learned about how TH regulates diverse cellular functions. THs have a profound impact on mitochondria, the organelles responsible for the majority of cellular energy production, and several studies have been devoted to understand the respective importance of the nuclear and mitochondrial pathways for organelle activity. During the last decades, several new aspects of both THs (i.e., metabolism, transport, mechanisms of action, and the existence of metabolically active TH derivatives) and mitochondria (i.e., dynamics, respiratory chain organization in supercomplexes, and the discovery of uncoupling proteins other than uncoupling protein 1) have emerged, thus opening new perspectives to the investigation of the complex relationship between thyroid and the mitochondrial compartment. In this review, in the light of an historical background, we attempt to point out the present findings regarding thyroid physiology and the emerging recognition that mitochondrial dynamics as well as the arrangement of the electron transport chain in mitochondrial cristae contribute to the mitochondrial activity. We unravel the genomic and nongenomic mechanisms so far studied as well as the effects of THs on mitochondrial energetics and, principally, uncoupling of oxidative phosphorylation via various mechanisms involving uncoupling proteins. The emergence of new approaches to the question as to what extent and how the action of TH can affect mitochondria is highlighted. © 2016 American Physiological Society. *Compr Physiol* 6:1591-1607, 2016.

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