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Zoom Registration

Regulation of the mitochondrial transcriptome in health and disease

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Abstract

Mitochondria produce more than 90% of the energy required by our bodies and thereby have a fundamental role in cell and energy metabolism. Mitochondria are composed of proteins encoded by both the nuclear and mitochondrial genomes and the coordinated expression of both genomes is essential for energy production. Impaired energy production leads to mitochondrial dysfunction that causes or contributes significantly to a variety of diseases including metabolic disorders and cardiovascular diseases. Mitochondrial dysfunction is caused by mutations in nuclear or mitochondrial genes that encode proteins or regulatory RNAs essential for mitochondrial biogenesis. How uncoordinated gene expression causes mitochondrial dysfunction and compromised energy production in heart and metabolic diseases is poorly understood, making it difficult to develop effective treatments. To unravel how mitochondrial function fails and to identify therapeutic targets it is necessary (i) to understand how gene expression is regulated between mitochondria and the nucleus and (ii) how this regulation is disrupted in disease. We have created new and unique models of metabolic and cardiovascular diseases caused by mutations or loss of nuclear encoded RNA-binding proteins (RBPs) that regulate mitochondrial RNA metabolism and protein synthesis. These new models have identified that energy dysfunction can differentially affect specific organs such as the heart or liver, or multiple organs leading to heart failure or metabolic diseases that can be devastating, such as mitochondrial diseases, or may be as common as insulin resistance and obesity. I will discuss the mechanisms behind these diverse pathologies caused by impaired gene expression and energy dysfunction in heart and metabolic disease.

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