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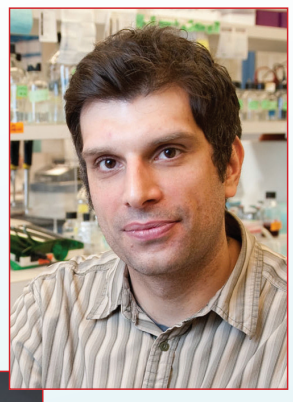

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Cell Metabolism

mTORC1 Controls Mitochondrial Activity and Biogenesis through 4E-BP-Dependent Translational Regulation

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Highlights

mTORC1 regulates synthesis of nucleus-encoded mitochondrial proteins via 4E-BPs
mTORC1 controls mitochondrial activity and biogenesis largely through 4E-BPs
mTORC1 coordinates energy consumption and production via 4E-BPs
An active-site mTOR inhibitor impairs respiration and energy metabolism in mice

Summary

mRNA translation is thought to be the most energy-consuming process in the cell. Translation and energy metabolism are dysregulated in a variety of diseases including cancer, diabetes, and heart disease. However, the mechanisms that coordinate translation and energy metabolism in mammals remain largely unknown. The mechanistic/mammalian target of rapamycin complex 1 (mTORC1) stimulates mRNA translation and other anabolic processes. We demonstrate that mTORC1 controls mitochondrial activity and biogenesis by selectively promoting translation of nucleus-encoded mitochondria-related mRNAs via inhibition of the eukaryotic translation initiation factor 4E (eIF4E)-binding proteins (4E-BPs). Stimulating the translation of nucleus-encoded mitochondria-related mRNAs engenders an increase in ATP production capacity, a required energy source for translation. These findings establish a feed-forward loop that links mRNA translation to oxidative phosphorylation, thereby providing a key mechanism linking aberrant mTOR signaling to conditions of abnormal cellular energy metabolism such as neoplasia and insulin resistance.

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