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Small Molecule Modulators Of Mitochondrial Protein Import

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SUMMARY

UCLA researchers in the Department of Chemistry & Biochemistry have discovered a set of small molecules that modulate the protein translocation across the mitochondrial membranes, which in turn controls the assembly and function of the mitochondria.

BACKGROUND

Mitochondria are rod-shaped organelles that play an essential role in the generation of metabolic energy derived from the breakdown of carbohydrates and fatty acids in eukaryotic cells. Although mitochondria contain their own DNA, which encodes tRNAs, rRNAs and some mitochondrial proteins, most mitochondrial proteins, as well as the assembly of mitochondria depend on proteins encoded by the nuclear genome, which are translated on free cytosolic ribosomes and imported into the mitochondria by specific targeting signals. Mitochondria have a double membrane system, consisting of an outer membrane and a highly convoluted inner membrane. A complex translocation system, including the TOM (translocons of the outer membrane) complex, and the TIM23 (translocons of the inner membrane) and TIM22 complexes, which differ in their substrate specificity are required for the import of proteins from cytosol into the proper location within mitochondria in order to achieve their fully functional state. Defects in the TIM22 import pathway lead to inherited deafness-dystonia syndrome, in which patients have deafness, blindness and dystonia. Disease modeling via modulating mitochondrial biogenesis using genetic manipulation or non-specific drug treatment is limited as many times these approaches also block cellular respiration. Currently, there is no available drug that specifically targets the protein translocation/import pathway with respect to mitochondria assembly.

INNOVATION

Researchers at UCLA have discovered a set of small molecules that modulate the protein translocation across the mitochondrial membranes. These molecules have specific effects on the steps involved in the formation and function of mitochondria, and can be used for bioscience researches and putative chemotherapeutic agents to treat/model certain human diseases.

APPLICATIONS

- ▶ Research tool to modulate the biogenesis of mitochondria, model human diseases by targeting specifically mitochondrial protein translocation/import
- ▶ Potentially chemotherapeutic agents to treat certain human diseases

ADVANTAGES

Specific to mitochondrial protein translocation/import pathway without affecting cellular respiration

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	10,718,513	09/01/2020	2009-221

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OTHER INFORMATION

KEYWORDS

Mitochondrial protein import, mitochondria, protein translocation, protein import, mitochondria assembly, mitochondrial biogenesis, translocons of the outer membrane, TOM, translocons of the inner membrane, TIM22, TIM23

CATEGORIZED AS

- ▶ **Medical**
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- ▶ **Research Tools**
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