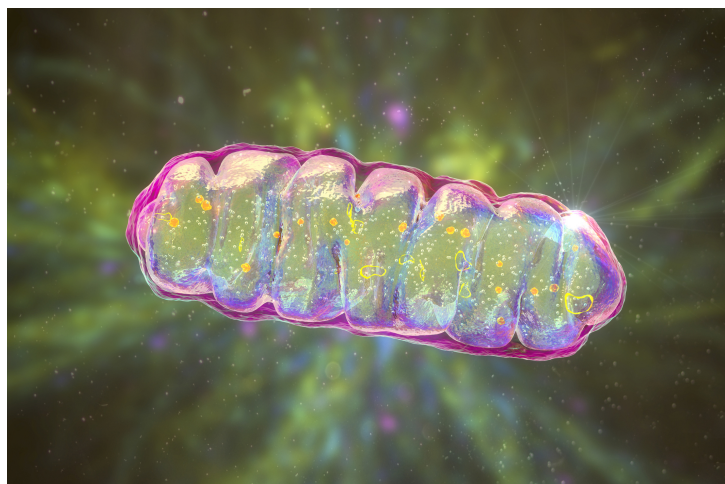


Mitochondrial Targeting Compounds for the Treatment of Associated Diseases

TECHNOLOGY NUMBER: 2020-134



OVERVIEW

A novel class of compounds that disrupt oxidative phosphorylation within mitochondria

- Selective inhibition of complex I of the mitochondrial electron transport chain
- Provides a method to treat cancer and multiple other mitochondrial disorders

BACKGROUND

Oxidative phosphorylation (OXPHOS) is an important process that occurs within the mitochondria of cells. This cascade consists of over 90 proteins which work together to link the tricarboxylic acid (TCA) cycle to the production of adenosine triphosphate (ATP). Tumor cells rely on this process similarly to normal cells do for bioenergetics and biomass production. Inhibitors of OXPHOS currently exist and are used in the treatment of cancer as well as other mitochondrial functional disorders including inflammatory diseases, autoimmune disease, cardiovascular disease, diabetes, and neurodegenerative disease. However, current therapeutics often fall short of effectively treating these ailments, so a need exists for improved methods to inhibit OXPHOS.

INNOVATION

Researchers have created a technology that permits the preparation and use of several mitochondrial compounds which inhibit OXPHOS. These agents cause selective inhibition of complex I of the mitochondrial electron transport chain, which is one of the key protein

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complexes involved in the process of oxidative phosphorylation within mitochondria. Complex I, also known as NADH:ubiquinone oxidoreductase, is responsible for the transfer of electrons from NADH to ubiquinone (coenzyme Q) in the electron transport chain. These targets represent a new class of compounds which can be used for the treatment of several cancers or disorders of mitochondrial function including brain cancer, pancreatic cancer, ovarian cancer, renal cancer, breast cancer, lung cancer, leukemia, and lymphoma among others. These compounds can be used in combination with existing therapeutics or on their own to treat cancer and other mitochondrial disorders.