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Inventors

Sidney Hecht**Xiaoqing Cai****Omar Khmour**

Contact

Jovan Heusser

jovan.heusser@skysonginnovations.com

Multifunctional Radical Quenchers and Simplified Synthesis Routes

Mitochondrial diseases are a group of disorders associated with dysfunctional mitochondria, often caused by genetic mutations to mitochondrial DNA. Mitochondrial defects are damaging, particularly to tissues with high energy demands such as neural and muscle tissues. Energetic defects have been implicated in forms of movement disorders, cardiomyopathy, myopathy, blindness and deafness. Membrane-penetrating antioxidants are often prescribed but treatment options are limited. There have been extensive efforts to find alternative, synthetic antioxidants with superior activities and simplified synthesis routes.

Researchers at the Biodesign Institute of Arizona State University have developed methods for designing and optimizing antioxidant analogs which may be useful for the treatment of mitochondrial diseases. Additionally they have identified promising coenzyme Q10 analogs as well as several novel lipophilic analogs with facile approaches to their synthesis.

The coenzyme Q10 analogs act as radical quenchers while augmenting ATP production. The lipophilic analogs suppress ROS levels in cultured cells, and quench the peroxidation of mitochondrial membranes. Moreover, the lipophilic compounds function catalytically, thus increasing their potency of action.

These inventions promise to help researchers more efficiently identify therapies for mitochondrial diseases as well as offers several candidates that have shown very promising therapeutic effects.

Potential Applications

- Platform for identifying and optimizing novel antioxidant analogs
- Therapeutic candidates for Mitochondrial Diseases such as:
 - Friedreich's ataxia
 - Leber's Hereditary Optic Neuropathy
 - Kearns-Sayre Syndrome
 - MELAS (Mitochondrial Encephalomyopathy with Lactic Acidosis and Stroke-like Episodes)

Benefits and Advantages

- Coenzyme Q10 Analogs:
 - Quenching of reactive oxygen species (ROS) and carbon-centered lipid radicals
 - Augmentation of ATP production
- Antioxidant Lipophilic Analogs:
 - Multifunctional radical quenchers

- Simplified synthesis routes - five or fewer steps
- More effective suppression of autoxidation of methyl linoleate over α -tocopherol
- Catalytic functionality to improve potency of action
- Augmentation of ATP production

For more information about the inventor(s) and their research, please see [Dr. Hecht's departmental webpage](#)