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Mitochondrial Inhibitors for Treating Aging-Related Metabolic Syndrome

Aging is associated with the decline of mitochondrial function, particularly in related metabolic diseases such as obesity, diabetes, and heart disease. Mitochondrial oxidative stress will lead to its dysregulation, so a pharmacologic intervention targeting mitochondrial cytochrome c oxidase (CCO) is an effective approach to treating metabolic disorders. CCO is the terminal enzyme of the electron transfer chain which leads to ATP synthesis. Moderate inhibition of CCO reduces ATP synthesis and upregulates mitochondrial biogenesis. Resultantly, reactive oxygen species (ROS) production and mitochondrial decay is mitigated. Mouse studies with mild mitochondrial inhibition have demonstrated the improvement of mitochondrial integrity, reduction of visceral fat, and robust glucose homeostasis. Thus, chronic administration of the COO inhibitor slows the onset of, or even reverses, aging-related metabolic syndrome.

Applications

- Pharmacologic treatment for obesity, diabetes, and other metabolic disorders
    - Downregulation of white adipose tissue and upregulation of brown adipose tissue
    - Improvement of glucose levels and insulin sensitivity
    - Reduction of reactive oxygen species (ROS)

Advantages

- Mild inhibition of mitochondrial function improves its health and performance, which can be therapeutically beneficial for patients with aging-related metabolic diseases
    - Novel drug mechanism of action

- Potentially synergistic with existing treatments

Patents

- Published Application: WO2021034548
- Published Application: 20220281902

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