Small Molecule Regulators of Mitochondrial Fusion and Methods of Use

Background:
Mitochondria generate ATP that fuels neuronal growth, activity, repair and regeneration. Mitochondrial dysfunction is implicated in chronic degenerative neurological conditions such as Alzheimer’s, Parkinson’s, and Huntington’s diseases. Mitochondria must traffic within cells, interact with each other, and fuse to exchange genomes and promote mutual repair. Mitochondrial trafficking and fusion require the physiochemical actions of two closely related dynamin family GTPases, mitofusins (Mfn) 1 and 2. The rare autosomal dominant neurodegenerative condition, Charcot Marie Tooth Disease (CMT), which causes motor and sensory neuron loss producing incapacitating muscle atrophy in ~1,000,000 individuals, can be directly caused by loss-of-function mutations of Mfn2. The underlying mechanism that causes this debilitating neuropathy is dominant inhibition of mitofusin-mediated mitochondrial trafficking and fusion. Currently, because there are no pharmacological Mfn agonists or activators, there is no curative treatment for CMT.

Technology Description:
Researchers at Washington University in St. Louis have identified small molecule drug candidates based on Mfn structure:function that activate mitofusins, enhancing mitochondrial trafficking, fusion, and general bioenergetics fitness in CMT neurons. Medicinal chemistry efforts have yielded potent and specific derivatives with improved properties.

Key Advantages:
- Potent modulators of Mfn activity that reverse CMT defects
- Rare disease target with commercialization incentives
- Opportunities to expand to other diseases for which few therapeutic options exist

Patents Pending: yes


Lead Inventor:
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