Cincinnati Children's | Innovation Ventures

Neurology

Using Dantrolene to Treat Neuronopathic Gaucher Disease

Brief Description of Technology

Dantrolene is an antagonist of ryanodine receptors (Ryrs) and blocks Ryr-mediated endoplasmic reticulum calcium release. It is an FDA-approved drug.

TECHNOLOGY ID

2016-0505

BUSINESS OPPORTUNITY

Exclusive License or Sponsored Research

TECHNOLOGY TYPE

Small Molecule

PATENT INFORMATION

US Non-Provisional Filing

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Technology Overview

Gaucher disease (GD) is a lysosomal storage disorder caused by mutations in GBA1 that encodes lysosomal acid β-glucosidase (GCase) that has glucosylceramide (GC) and glucosylsphingosine (GS) as substrates. Accumulated substrates due to defective GCase cause pathology in the central nervous system of GD. Treatments for Type 1 patients, or those without CNS disruption, are ineffective against CNS rescue or lack the ability to cross the blood brain barrier. Cincinnati Children's researchers have found that mice treated with dantrolene starting at postnatal day 5 delayed neurological pathology and prolonged survival; partially normalized Ryr expression and its potential regulators, CAMK IV and calmodulin; and increased residual mutant GCase activity in their brains. Compared to untreated mice, dantrolene treatment significantly improved gait, reduced LC3-II levels (a marker of autophagy), and improved mitochondrial ATP production and reduced CD68 (a biomarker of inflammation in the brain). Data suggests that modulating Ryrs has neuroprotective effects in nGD through mechanisms that protect the mitochondria, autophagy, Ryr expression, enhance GCase activity, and mitigate inflammation and neurodegeneration. Calcium signaling stabilization (e.g. with dantrolene) could be a disease modifying treatment for nGD.

Applications

Treatment for neurological manifestations of GD (Type 3)

Advantages

- There are no approved therapies to treat Type 3 GD
- Increase life expectancy for Type 3 GD patients

Market Overview

Gaucher disease is a rare disease with a frequency of ~1/60,000 live births. GD Type 3 represents about 5% of all patients with GD.

Investigator Overview

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