WashU

Office of Technology Management

DISEASE-MODIFYING ASO THERAPY FOR MITCHELL SYNDROME AND OBESITY

Bucelli, Robert, Hubler, Zita, Miller, Timothy, Schoch, Kathleen

Richards, Jennifer

T-021317

Published date: 6/2/2026

Value Proposition*: First-in-class antisense oligonucleotide (ASO) therapy selectively lowering ACOX1 to enable disease-modifying treatment of Mitchell Syndrome and unlocking a metabolic shift facilitating weight loss.*

Technology Description: Mitchell Syndrome is an ultra-rare, progressive neurodegenerative disorder resulting from a gain-of-function mutation in acyl-CoA oxidase 1 (ACOX1). To directly address the root cause, Tim Miller, MD, PhD, neurodegeneration clinical expert and experienced ASO inventor, and his team developed novel ACOX1-lowering ASOs to reduce ACOX1 mRNA and protein levels and combat its devastating effects. These ACOX1-lowering ASOs represent a first-in-class composition of matter for human therapeutic use, directly targeting the disease cause in ACOX1-associated disorders characterized by glial cell and axonal degeneration.

A fellow WashU researcher from the Division of Endocrinology, Metabolism and Lipid Research, Irfan Lohdi, previously demonstrated that inhibiting ACOX1 protects against high-fat diet-induced obesity, inflammation, and insulin resistance. So, the teams partnered to evaluate the effect of the lead ACOX1-lowering ASO on human liver cells. The experiments demonstrated decreases in mRNA and protein levels and increases in key metabolites (THA and HHA) involved in fat browning.

Stage of Research: in vitro data for both Mitchell syndrome and weight loss

Applications/Uses:

· Mitchell syndrome (neurodegeneration),

· Obesity/weight loss, and

· Possible therapeutic impact for some cancers

Key Advantages:

· Novel disease-modifying ASO therapy

· Induces fat cell remodeling, which may protect against high-fat diet-induced obesity, inflammation, and insulin resistance

Patent: International patent application pending, PCT/US2026/010845

Lead inventor: Tim Miller, Profile and Lab