Washington University in St. Louis
Office of Technology Management

NOVEL BILE ACIDS AS BIOMARKERS FOR NIEMANN-PICK TYPE C DISEASE

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Technology Description

Researchers at Washington University have developed and validated a set of bile acid biomarkers to screen, diagnose, and monitor the progression of Niemann-Pick disease type C (NPC), a genetic lysosomal storage disorder resulting from a defect in lipid transport. Previous efforts by the Washington University researchers led to discovery of oxysterol biomarkers and development of a clinical assay based on this technology. This assay has been widely adopted and has resulted in improved diagnosis of NPC, but there are limitations to the assay for oxysterol biomarkers. These newer bile acid biomarkers have been shown to be more sensitive and specific for detection of NPC, are suitable for monitoring response to treatment, and are the only biomarker demonstrated to be sufficiently robust for newborn screening.

Niemann-Pick disease is a lethal neurovisceral lysosomal storage disorder caused by genetic mutations that disrupt the metabolism and trafficking of sphingolipids. The type C form is the most common and results from mutations in NPC1 or NPC2 genes, producing a defect in lysosomal cholesterol transport. Existing diagnostic tests are invasive (requiring skin biopsies), slow, or lack sensitivity.

Stage of Research

The inventors have identified several novel bile acids that are effective biomarkers for NPC. They have developed an FDA-compliant clinical grade assay for quantifying these biomarkers using liquid chromatography-tandem mass spectrometry (LC-MS/MS) and compared this method to existing diagnostics.

Publications

- Jiang X and Ory, DS. (2016). Towards a new diagnostic standard for Niemann-Pick C. *EBioMedicine,* 4:18-9.
- Jiang X, Sidu R, Mydock L, Hsu F-F, … and Ory DS. (2016). Development of a Bile Acid-Based Newborn Screen for Niemann-Pick C Disease. *Sci Trans Med,* 8(337):337ra63.
- Jiang X, Sidhu R, Orsini JJ, Farhat NY, Porter FD, Berry-Kravis E, Schaffer JE, and Ory DS. (2019). Diagnosis of Niemann-Pick C1 by Measurement of Bile Acid Biomarkers in Archived Newborn Dried Blood Spots. *Mol Genet Metab*, 126:183-187.
- Sidhu R, Kell P, Dietzen DJ, Farhat NM, … and Jiang X. (2020). Application of a glycinated bile acid biomarker for diagnosis and assessment of response to treatment in Niemann-Pick disease type C1. *Mol Genet Metab*., in press.

Applications

- Diagnosis and monitoring of Niemann-Pick disease type C

Key Advantages

- Increased sensitivity and specificity
- Suitable for newborn screening
- Decreased processing time: 24 hours vs. 48 hours for oxysterols, 14 days for genetic testing, 3 months for filipin staining
- Non-invasive: does not require skin biopsy, can be performed using blood sample

Patents: US20170285015

Related Web Links: Jiang Profile, Ory Lab