

Lay Summary

A major barrier to delivery of effective treatment for NPC disease has been significant delays in diagnosis (> 5 years) due to the lack of an inexpensive, reliable and easy to use test for diagnosis. We have developed a highly sensitive and specific clinical diagnostic assay for NPC disease based on an oxysterol biomarker. This assay is at various stages of implementation in nearly a dozen laboratories worldwide and is replacing filipin staining of fibroblasts as the diagnostic standard. Our continued biomarker efforts have led to discovery of an even more sensitive bile acid marker that may have significant advantages over the oxysterol marker, including ease of detection and simplification of the diagnostic assay. The latter will help with dissemination of the assay into clinical laboratories and accelerate adoption of this new blood test.

Using the bile acid biomarker, we have developed a newborn screening assay that is highly sensitive and specific. This assay can also detect NPB patients, suggesting that this bile acid marker also has significant potential to facilitate development of a newborn screen for NPB and NPC diseases. A newborn screen would enable for the first time routine initiation of drug therapy in pre-symptomatic NPB and NPC patients, the group that would benefit the most from early medical treatment. Efforts are underway to test the newborn screen in newborn screening facilities.

We further developed a blood-based bile acid assay for diagnosis of NPC disease. Based on results from newborn screening assay, the blood test is expected to permit discrimination between NPC carriers and patients and may be a more optimal test for diagnosis of NPC in the setting of neonatal jaundice.