Innovations
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Diagnostic Markers for Pyridoxine Dependent Epilepsy

Category
Diagnostics – Biomarker for Disease Detection

Problem
Unstable PDE biomarkers result in delayed diagnosis and reduction in therapy effectiveness

Technology Overview
Quantitation method for novel and stable PDE biomarker

IP Status
- Available for Exclusive and Non-exclusive Licensing

Value Proposition
- Biomarker which can be directly detected from fluid samples
- Ease of integration into existing newborn screening protocols

Market Attractions
- Rare disease but likely being underreported. An effective diagnostic could help elucidate the epidemiology and create a market

Patent Information
- Published patent application - WO/2019/161383

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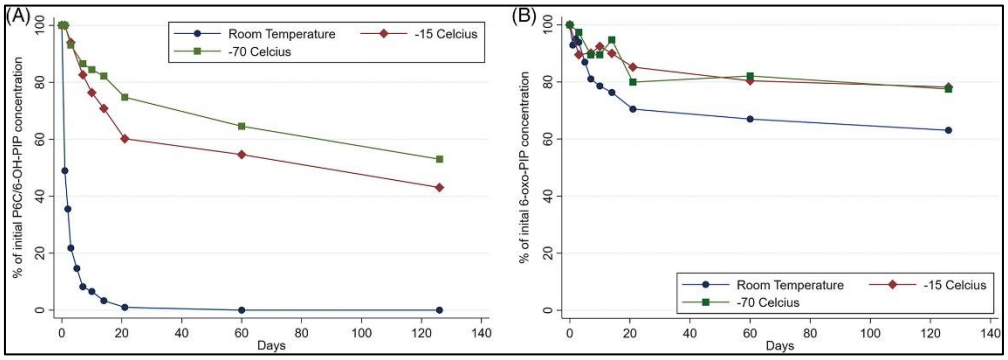
Problem: Pyridoxine dependent epilepsy (PDE) is a rare genetic disorder characterized by intractable seizures in the prenatal and neonatal period. Although current treatments provide adequate seizure control, approximately 75% of individuals with PDE develop significant intellectual disability and developmental delay. The root cause of PDE is a mutation in the ALDH7A1 gene, which results in α-AASA dehydrogenase deficiency and the accumulation of α-AASA and Δ^1-piperideine-6-carboxylate (Δ^1-P6C) in the blood. Lysine restriction therapies aimed at reducing accumulation of these compounds are effective but must be initiated within the first year of life for optimal prognoses. In order to diagnose PDE, Δ^1-P6C is first detected and quantified from blood, plasma, or urine samples. Research groups and diagnostic laboratories then must derivatize the compounds and perform tandem liquid chromatography mass spectrometry due to room temperature instability of the original biomarkers. This derivatization scheme is quite slow and costly, often delaying clinical diagnosis and contributing to the overall morbidity of PDE. Therefore, there is a need for a faster, more accurate and less expensive diagnostic method for PDE.

Solution: Researchers at the University of Colorado, led by Curtis Coughlin, have identified a novel biomarker and quantitation method for the diagnosis of PDE. The team has shown a mixture of Δ^1-P6C and its derivatives are detectable in blood, plasma, urine, and cerebral spinal fluid of PDE patients. Additionally, they have found that one of these derivatives in particular, 6-oxoPIP, is remarkably stable at room temperature (see figure) and can be directly detected and quantified using liquid chromatography mass spectrometry to diagnose PDE. Current newborn screening protocols depend on the samples being collected, dried, and shipped at room temperature and utilize liquid chromatography. Given the urgency with which PDE must be diagnosed and the benefit of early treatment, quantitation of the stable marker provides an essential route to administering effective PDE therapeutics.



A 4-month stability study was performed of Δ^1-P6C/P6CH (A) mixture and the 6-oxo-PIP (B). At room temperature, the Δ^1-P6C/P6CH mixture had completely degraded after 20 days while the 6-oxo-PIP compound was stable over the entirety of the 4-month period.

Additional Documents:

Wempe, MF, Kumar, A, Kumar, V, et al. Identification of a novel biomarker for pyridoxine-dependent epilepsy: Implications for newborn screening. J Inherit Metab Dis. 2019; 42: 565– 574. https://doi.org/10.1002/jimd.12059