Characterization of Hair Metabolome in 5xFAD Mice and Patients with Alzheimer's Disease Using Mass Spectrometry-Based Metabolomics

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Abstract:

Hair is considered as a novel biospecimen for investigating long-term alterations of endogenous metabolites and for reflecting circulating chemicals in the bloodstream over the past months. Although hair is an emerging biospecimen, characterizing hair metabolome in Alzheimer's disease (AD) remains limited. Here, an analytical approach that integrates both untargeted and targeted metabolomic approaches was employed to discover hair biomarker candidates and identify the key metabolic pathways associated with AD in the 5xFAD mice, a widely used AD mouse model. Furthermore, the discovered biomarker candidates were applied to human subjects. The hair samples collected from 6-month-old 5xFAD mice, a stage marked by widespread accumulation of amyloid plaques in the brain, underwent sample preparation and were subsequently analyzed by high-resolution mass spectrometry. Forty-five biomarker candidates were discovered in the hair of 6-month-old 5xFAD mice compared to wild-type mice. Enrichment analysis was used to reveal arachidonic acid metabolism, sphingolipid metabolism, and alanine, aspartate, and glutamate metabolism, which are related to AD. Among these pathways, the levels of six metabolites in the hair of 2-month-old 5xFAD mice, a stage prior to the onset of amyloid plaque deposition, demonstrated significant differences, suggesting that they might involve in the early stages of AD pathogenesis. When assessing 45 biomarker candidates for differentiating patients with AD from cognitively healthy subjects, a metabolic panel combining L-valine and arachidonic acid achieved a 0.88 area under the curve. This suggests that this panel can be used to distinguish AD patients from controls. Therefore, the findings highlight the potential use of the hair metabolome to identify biomarker candidates associated with AD.

Biography of Presenter about 100 words:

Dr. Pao-Chi Liao completed his Ph.D. in Analytical Chemistry from Michigan State University (MSU) in 1995 before doing postdoctoral research in the Department of Biochemistry at MSU. Dr. Liao joined the faculty at Department of Environmental and Occupational Health, National Cheng-Kung University, Taiwan in 1997, where he was promoted to full professor

in 2006, and named Distinguished Professor in 2011. Dr. Liao's research interests and fields of specialty include analytical chemistry, mass spectrometry, metabolomics/proteomics, biomarker discovery, cancer biomarkers, lung cancer metastasis, and environmental and occupational health.

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