A Comprehensive LC-MS Metabolomics Approach Reveals a Novel Panel of Markers in an APOE4 Mouse Model of Alzheimer's Disease

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Alzheimer’s is a terrible neurodegenerative disease affecting millions of individuals around the world. However, all FDA approved drugs for the illness offer only symptomatic treatment and have limited effectiveness in slowing the progression of the disease. APOE4 is the strongest genetic risk factor for Alzheimer's disease. Having one copy of the allele increases likelihood for Alzheimer's by three-fold while individuals with two copies are 15-times more likely to have the disease. This study aims to gain insight on the molecular impact of APOE4 over time using a liquid chromatography-mass spectrometry(LC-MS) untargeted metabolomic approach. Analysis of 63 cerebellum tissue samples from targeted replacement E3 and E4 mice at ages 6, 12, 18, and 21 months was conducted and results have identified 64 dysregulated features at 6 months, including 10 downregulations and 54 upregulations. Tracing these markers throughout the mouse lifespan has revealed these markers to also be upregulated at 18 months, indicating that molecular dysregulations perpetuate over time. Comparing metabolic profiles between sex reveals females at 12 months to have the most drastic change, showing how APOE4 can adversely affect already susceptible populations of Alzheimer’s. This project uses an emerging technique to gain further insight into the mechanism by which E4 increases susceptibility for Alzheimer’s disease in hopes of furthering therapeutic development for carriers.