Integrative Proteomics for Biomarker Discovery in AD

Nick Seyfried

Associate Professor Departments Biochemistry and Neurology Director, Emory Integrated Proteomics Core Goizueta Alzheimer's Disease Research Center Emory School of Medicine







Integrated Analysis of the Human Brain and CSF Proteome in AD

Goal: Identify CSF biomarkers linked to biological and pathological phenotypes in the AD brain proteome









Network based approaches



WGCNA



Comprehensive Quantification of the Human Brain Proteome in AD and ADRDs



Enhancing the Depth and Throughput of the AD Proteome with Multiplex Tandem Mass Tags (TMT)



TMT Protein Co-expression Network Analysis

- Modules associated with clinical and pathological phenotypes. (Seyfried et. al., 2017 Cell Systems, Umoh et. al., EMBO Mol Med. 2018, Wingo et. al., Nat Commun. 2019)
- Modules are associated with specific biological ontologies, cell-type and genetic risk. (Dai & Johnson et. al., Front Mol Neurosci. 2018, Seyfried et. al., 2017 Cell Systems)
- The TMT brain networks identify ~3-fold more modules compared to LFQ-MS networks (Johnson et. al., Mol Neurodegener. 2018)

Moving From Brain to Cerebrospinal Fluid (CSF) for AD Biomarker Discovery





Comprehensive Quantification of the CSF Proteome by TMT



Integrated Analysis of the Brain and CSF Proteome in AD



CSF Biomarker Panels that Reflect Diverse Biological and Pathological Phenotypes in AD Brain



Validation of AD Biomarkers in CSF by Targeted MS



*** p-value < 0.01

Zhou M et. al., J Proteome Res. 2019 Apr 29.

Brain-based Protein Biomarkers in Alzheimer's Disease CSF



Acknowledgements



Allan Levey **Eric Dammer** Jim Lah **Duc Duong** Marla Gearing Lingyan Ping Lenora Higginbotham Ranjita Betarbet Thomas Wingo Measho Abreha Erik Johnson **Maotian Zhou** Luming Yin **AMP-AD Collaborations COLUMBIA UNIVERSITY** MEDICAL CENTER

HARVARD MEDICAL S

MEDICAL SCHOOL

UNIVERSITY of **FLORIDA**











UNIVERSITY





David Geffen School of Medicine

for tomorrow's cures

Biogen abbvie



Funding:





National Institute on Aging

U01AG046161 **RF1AG057471** P50AG025688 R01AG057330 **RF1AG057470** R01AG053960