Subset of gene expression profiles in human post-mortem brain aging and AD are robust, concordant, and show exaggerated changes in female AD subjects

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Abstracts will be considered for both poster and platform presentations

Other neurodegenerative disorders

Sporadic Alzheimer's disease (AD) is increasing in parallel to the aging population, with the majority (~2/3) of AD cases affecting women. AD is a complex disease characterized by amyloid beta and neurofibrillary tangle pathologies, and risk factors include head injury, high blood pressure, high cholesterol, and inheritance of certain gene variants (e.g., ABCA1, APOEe4, APOEe2, etc.). Despite the vast amount of research, successful therapies that modify the disease have yet to be developed. One reason could be that some unmodifiable risk factors, such as aging and sex, contribute to vulnerability and progression in AD as well, but their molecular roles have not been robustly assessed. We hypothesize that a subset of age-related transcriptional changes precede, and are exaggerated by, AD, and further that female AD sufferers will have exaggerated expression compared to males for this restricted subset of robustly identified genes. To address this, we looked at transcriptional profiles of normal human aging (8 profiles) and AD (9 profiles) to test for a statistically significant agreement for Aging or AD changes across independent samples from different labs. We further tested for a statistically significant relationship between robust aging and AD-related changes. We found 85 genes that were significantly changed with age, worsened in AD, and exaggerated in female vs male subjects These genes also showed very strong directional and magnitude-of-change agreement between normal aging and AD. Taken together, this panel of genes likely contains key candidate molecules for intervention testing and rationale therapeutic development.