

Classifying cell type-, cognition- and neuropathology-associated mRNA changes in Alzheimer's disease

Soreq, H. and Barbash, S.

Dept. of Biological Chemistry, The Hebrew University of Jerusalem, Jerusalem, Israel.

Classifying cell type-, cognition- and neuropathology-associated mRNA changes in Alzheimer's disease (AD) is a major research challenge. We employ multiple 3'-selective cDNA amplifications to generate novel in-depth RNA sequencing datasets identifying alternatively polyadenylated (APA) transcripts in temporal gyrus tissues from AD patients compared to apparently healthy and histopathology-affected donors with or without known cognitive impairments. The human samples in the study were attained from the Netherland Brain Bank (NBB). APA-based classification differentiated advanced AD patients from both non-demented cohorts more successfully than total transcript-based classifications. Advanced statistics, microfluidics RT-PCR and protein measurements further enabled cell-type classification of such changes. Intriguingly, APA changes in ATP synthesis and mitochondria of non-demented donors with histopathology indicate metabolically facilitated delay in AD dementia whereas both histopathology-affected groups showed APA changes in RNA metabolism-related neuronal genes. Furthermore, several drug-targeted genes of other brain, vascular and autoimmune disorders showed AD neuropathology-specific APA differences. These findings will soon be submitted for publication with acknowledgment to the NBB.