Title: Cross-Transcriptomic Insights into Synaptic and Mitochondrial Dysregulation in Alzheimer's Disease.

Presenting author name

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Abstract:

Alzheimer's disease (AD) is a common neurodegenerative disorder characterized by progressive cognitive decline, including memory loss and impaired learning, with early vulnerability in the hippocampus (HC) and entorhinal cortex (EC). These regions are critical for memory and learning processes. To better understand underlying molecular mechanisms, we performed a cross-transcriptomic analysis using microarray datasets from AD and age-matched non-AD controls, focusing on the HC and EC. Our analysis revealed 564 significantly differentially expressed genes in the HC and 479 in the EC, with 151 genes dysregulated in both regions. These shared genes are involved in processes such as synaptic vesicle clustering, synaptic vesicle exocytosis and endocytosis, mitochondrial ATP synthesis, hydrogen ion transmembrane transport, and structural cytoskeleton function. This finding suggests that disruptions in synaptic dynamics, cytoskeleton integrity, and mitochondrial functions are linked to cognitive decline in AD. Further gene ontology (GO) analysis specific to the HC indicated enrichment in pathways related to aerobic respiration, synaptic vesicle cycling, and oxidative phosphorylation, highlighting the critical role of mitochondrial function in this region. Subregion analysis within the HC, particularly the CA1, identified gene expression changes associated with mitochondrial membrane activities, including those integral to bioenergetics, electron transport, and microtubule-based processes. While in the EC, enriched pathways related to synaptic vesicle dynamics, neurotransmitter release, postsynaptic membrane potential regulation, and GABAergic and glutamatergic synaptic transmission were observed, which are essential for maintaining synaptic stability and effective neurotransmission. In addition, protein-protein interaction analysis further revealed that central hub proteins, predominantly localized within mitochondria, are implicated in regulating oxidative stress and ATP synthesis, with extensive interactions noted between mitochondrial proteins and those associated with the vesicular membrane and neuronal cytoskeleton. This network suggests a central role of mitochondria in maintaining synaptic and structural stability in AD-affected regions. Together, our findings highlight a strong link between AD symptoms and mitochondrial dysfunction, synaptic vesicle dysregulation, and cytoskeletal disorganization in the HC and EC, underscoring these dysregulated pathways as potential therapeutic targets to address cognitive decline and memory impairment in early stages of AD.

Biography:

Dr. Poommaree Namchaiw is a lecturer in the Biological Engineering Program at King Mongkut's University of Technology Thonburi, Thailand. She completed her Ph.D. in Integrative Pathobiology at the University of California, Davis, where she also held a postdoctoral fellowship at the Center for Neuroscience. Her research expertise centers on molecular and cellular neurobiology, focusing on three-dimensional neural cell cultures and exploring herbal medicines for neuroprotective effects against amyloid beta toxicity. Dr. Namchaiw's work is supported by several research grants, and her recent publications highlight her contributions to neurodegenerative disease studies, including Alzheimer's. She is also experienced in teaching various biological engineering courses and has technical expertise in advanced cell culture, RNA sequencing, and neurogenesis research.