TEM study of Alzheimer’s disease lesion proteins

Wang-Xia Wang, PhD

Sanders-Brown Center on Aging, Department of Pathology & Laboratory Medicine
University of Kentucky
Lexington, Kentucky, USA

In collaboration with Mr. Doug Price and Dr. Peter Nelson

Supported by EM Voucher Program, and the UK-ADRC Developmental Project grant (P30 AG072946)
Introduce research question and why EM was needed to answer

Alzheimer’s disease (AD) is ranked as the seventh leading cause of death in the United States and is the most common cause of dementia among older adults.

The impact of AD to public health is going to get worse as the population ages: AD is predicted to affect almost 15 million Americans by 2050.

The hallmark neuropathological lesions of AD are amyloid-beta (Aβ) plaques and hyperphosphorylated tau tangles. Other proteins, including Apolipoprotein E (ApoE), are also known to be aberrantly aggregated.

Not much study has been done on the ultrastructure, subcellular localization, and development of these aggregates in human brain.

Our goal is to study the ultrastructural feature of these aggregates focusing on detecting early stage of aggregates and protein interactions.

Amyloid-beta plaques, tau tangles, and ApoE
Immunogold-labelling Transmission Electron Microscopy (TEM)

Immunogold EM is a powerful technique that combines the ability of an antibody-labeling and ultrastructural resolution of EM, providing detailed information on the subcellular localization of a labeled protein.

Ultra-small (0.8 nm) gold labeling in conjugation with silver enhancement

The ultra-small gold particles allow for better tissue penetration, and the silver enhancement makes them visible under EM.

Immunogold EM can be done pre-tissue fixation or post-tissue fixation.
Plaques in human brain-immunofluorescence-light microscope
A plaque imaged by TEM
Neurofilaments

Laminated body

Amyloid plaque core

Degenerated neurites
ApoE proteins are often co-aggregated with plaques.
Immunohistochemistry of tau tangles (anti-PHF1)
Tau tangles in a neuron

Nucleus
ApoE protein were seen to co-localize with tau tangles.
Major challenges:

Antibody/gold particle penetration – maintaining ultrastructure of tissue

Specificity of antibody/gold labeling

Thank you!