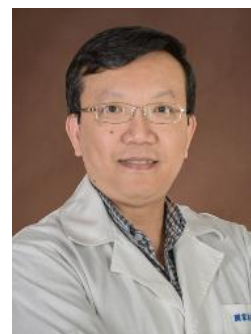

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Education

1995-2000 Ph.D. University of Washington, Seattle, USA

Research and Professional Positions Held in Chronological Sequence

2000-2005 Senior Fellow/Acting Instructor, Division of Neuropathology, Department of Pathology, University of Washington School of Medicine, Seattle, WA, USA.

2005-2011 Assistant Investigator, Division of Mental Health and Addiction Medicine, National Health Research Institutes, Zhunan, Taiwan.

2011-2022 Associate Investigator, Center for Neuropsychiatric Research, National Health Research Institutes, Zhunan, Taiwan.

2022-present Investigator, Center for Neuropsychiatric Research, National Health Research Institutes, Zhunan, Taiwan.

Research Interests

My research focuses on understanding the roles of glial cells in the central nervous system and developing therapeutic strategies for neurodegenerative diseases, particularly Alzheimer's disease (AD). AD is a highly complex and multifactorial disorder involving amyloid pathology, tauopathy, neuroinflammation, vascular dysfunction, and impaired brain homeostasis. Despite extensive research, the precise mechanisms underlying disease initiation and progression remain incompletely understood, limiting the development of effective disease-modifying therapies.

A central theme of my work is the investigation of microglial and astrocytic functions during neurodegeneration. Increasing evidence suggests that glial activation is highly dynamic and context-dependent. Activated glial cells may exert beneficial effects by facilitating amyloid clearance, supporting neuronal survival, and maintaining brain homeostasis. However, chronic or maladaptive glial activation can amplify neuroinflammation, disrupt blood-brain barrier (BBB) integrity, impair synaptic function, and accelerate neurodegeneration. Therefore, understanding how to fine-tune glial activation toward protective rather than detrimental states is critical for developing next-generation AD therapies.

Importantly, AD pathology is believed to begin decades before the onset of clinical symptoms. Early alterations in neuroinflammation, BBB dysfunction, and neuronal stress may occur long before overt cognitive decline becomes detectable. My research aims to identify early pathological

mechanisms and develop therapeutic approaches that enhance brain resilience while interrupting the self-reinforcing cycles of glia-mediated neuroinflammation.

To address these challenges, our laboratory has been developing novel multi-target therapeutic strategies, including combination therapy using small molecules and antibody-based therapies. In particular, we developed NP106, a multifunctional anti-amyloid antibody designed not only to enhance amyloid clearance, but also to modulate glial activation, suppress excessive neuroinflammation, and preserve neurovascular homeostasis. Our studies further integrate spatial transcriptomics, peripheral blood mononuclear cells (PBMC) RNA sequencing, blood-based biomarkers, and animal models to characterize therapeutic responses and to identify biomarkers and molecular pathways associated with brain resilience to neurodegeneration.

Another interest of my research is apolipoprotein E4 (APOE4), the strongest genetic risk factor for late-onset AD. Emerging evidence suggests that APOE4 may not simply promote amyloid accumulation in the pathogenesis of AD or increase the risk of amyloid-related imaging abnormalities (ARIA) during AD immunotherapy, but instead predispose the brain to chronic neurovascular vulnerability and maladaptive immune responses. Interestingly, many APOE4 carriers remain cognitively intact throughout life, indicating that APOE4 alone is insufficient to determine neurodegenerative outcomes and that additional inflammatory, vascular, and environmental stressors are likely required to trigger disease progression. My work seeks to elucidate how APOE4 interacts with glia-mediated neuroinflammation, BBB dysfunction, and PBMC immunity to influence disease susceptibility, therapeutic responsiveness, and cognitive resilience.

Ultimately, my long-term goal is to develop precision medicine strategies for early AD diagnosis through the establishment of a blood-based multidimensional composite prediction index, as well as safer and more efficient disease-modifying therapies with reduced risk of ARIA, by integrating glial biology, APOE4-associated vulnerability, and neurovascular dysfunction into a comprehensive therapeutic framework.

Major Honors and Awards

2025 The 22nd National Innovation Award (Academic Innovation Award)