NEURO GLOBAL Seminar

Date & Time

Tuesday, September 16, 2025
16:00~17:30 (Including Q&A)

Speaker

Yoshiteru KAGAWA, Ph.D.

Senior Research Fellow,

Florey Department of Neuroscience and Mental Health,

University of Melbourne, Australia

Title Regulation of Aβ and Tau Pathology by ApoE Isoforms in a Lipidation-Dependent Manner

Venue

Main Conference Room, 2 F Seiryo Hall, Seiryo Campus, Tohoku University

（東北大学 医学系研究科　星陵キャンパス・星陵会館2階　大会議室）

【MAP】https://www.tohoku.ac.jp/map/en/?f=SR_B10

Format Onsite ONLY

Registration Please contact NGP Office (neuroglobal@grp.tohoku.ac.jp)

Related Website https://florey.edu.au/researcher/yoshiteru-kagawa/

●**Neuro Globalプログラム生 (Neuro Global Program Students)**
【脳科学セミナーシリーズEx】 【先進脳科学セミナーシリーズEx】 1 point
●医学系研究科(Graduate School of Medicine)
【医学履修課程】国際交流セミナー (アドバンスド講義科目)」 出席1回分
【Medical Science Doctoral Course】 International Interchange Seminar (Advanced Lecture course) 1 attendance
●生命科学研究科(Graduate School of Life Sciences)
【単位認定セミナー】 【イノベーションセミナー（留学生対象）】 2ポイント
【Credit-granted seminar】 【Innovation seminar (For international students)】 2 points

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Seminar

Title

Regulation of Aβ and Tau Pathology by ApoE Isoforms in a Lipidation-Dependent Manner

Abstract

Lipids play fundamental roles in maintaining brain function, serving not only as structural components of membranes but also as regulators of signaling, energy metabolism, and intercellular communication. Disruption of lipid homeostasis has been increasingly recognized as a key contributor to neurodegenerative disorders, particularly Alzheimer's disease (AD). Among lipid-associated proteins, apolipoprotein E (ApoE) is central to cholesterol and phospholipid transport in the brain. Human APOE exists in three major isoforms (E2, E3, and E4), with ApoE4 conferring the strongest genetic risk for late-onset AD, while ApoE2 is considered protective. Mechanistically, the Aβ–Tau hypothesis of AD posits that Aβ accumulation initiates a cascade leading to downstream tau pathology, ultimately driving neurodegeneration. ApoE isoforms differentially influence each step of this process, regulating Aβ aggregation and clearance, tau phosphorylation, synaptic integrity, and neuroinflammation. ApoE's influence on these cascades is thought to be modulated by its lipidation state, which is regulated by astrocytes and may determine whether ApoE acts in a protective or pathogenic manner. However, many previous studies have relied on recombinant ApoE proteins, which lack physiological lipidation, making it difficult to fully capture isoform-specific functions in disease-relevant contexts.

After relocating to the University of Melbourne in 2023, I established a cell-based biological system to dissect ApoE isoform-specific functions under controlled conditions. Because lipidation is thought to critically shape ApoE's stability, receptor interactions, and lipid transport capacity, my approach incorporates culture conditions that mimic differential lipidation states. Using a doxycycline-inducible ApoE expression system in U251 astrocytoma cells, I can generate conditioned media enriched with ApoE2, E3, E4, or the rare E3-Christchurch variant under variable serum conditions. To investigate downstream effects in neurons, I combined this platform with a tau visualization system, enabling dynamic assessment of tau phosphorylation and aggregation in response to ApoE-conditioned media and Aβ exposure. Together, these experimental frameworks provide a foundation to clarify how ApoE isoforms and their lipidation status orchestrate pathological processes in Alzheimer's disease, and to identify molecular pathways that may be targeted for therapeutic intervention.

In this seminar, I would also like to introduce the novelty of these approaches, which allow the study of physiologically relevant, lipidated ApoE in a controlled cellular context.

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