NYCU-Tohoku Online Seminar for Neuroscience

Organized by :
National Yang Ming Chiao Tung University, College of Medicine,
Tohoku University, Graduate School of Medicine

國立陽明交通大學
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Endorsed by :
Tohoku University [Neuro Global International Joint Graduate program,
Tohoku University Brain Science Center

TOHOKU UNIVERSITY

Date

Wednesday, August 6, 2025, 17:00 – 18:35 JST
(16:00 – 17:35 TST)

1st Speaker

Naoki Suzuki (鈴木直輝), MD, PhD

Associate Professor, Department of Graduate School of Medicine, Tohoku University

Title

Elucidating ALS molecular pathology

2nd Speaker

Hong-Ru Chen (陳虹如), Ph.D.

Assistant Professor, Department of Life Sciences and the Institute of Genome Sciences, National Yang Ming Chiao Tung University

Title

Monocyte-Derived Macrophage Mediated Transmission of Tauopathy

Registration form

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

Program

17:00 JST Opening Remarks (10mim)
17:10 Lecture by **Naoki Suzuki (鈴木直輝), MD, PhD** (35min)
17:45 Q&A (5min)
17:50 Lecture by **Hong-Ru Chen (陳虹如), Ph.D.** (35min)
18:25 Q &A (5min)
18:30 Closing Remarks (5min)

【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】【[Advanced] brain science seminar series Ex】1 point
【医学系研究科・医学履修課程】国際交流セミナー【Medical Science Doctoral Course】 International Interchange Seminar 1 attendance
【生命科学研究科・イノベーションセミナー（留学生のみ）、単位認定セミナー】【Innovation seminar, Credit-granted seminar】2 points

Contact: Prof. Hsueh-Te (Max) Lee（李學德）
[incubator.lee@nycu.edu.tw]

Speaker：**Naoki Suzuki （鈴木直輝), MD, PhD**

Title：**Elucidating ALS molecular pathology**

Abstract: Amyotrophic Lateral Sclerosis (ALS) is an intractable disease characterized by progressive muscle weakness and atrophy due to selective degeneration of motor neurons, ultimately leading to respiratory failure and death. Developing effective treatments remains an urgent challenge. In recent years, compelling evidence has accumulated supporting the "dying-back" hypothesis, which suggests that structural and functional abnormalities at the neuromuscular junction (NMJ) precede clinical symptom onset and pathological loss of motor neuron cell bodies. Focusing on these axonal pathologies, we have elucidated aspects of the molecular mechanisms using experimental systems combining iPSC genome editing technology with microfluidic devices. Furthermore, through proteomics of the distal axonal neuromuscular junctions using mouse models and the iSDAC method for efficient recovery of trace proteins, we identified molecules crucial for synaptic maintenance. Additionally, protein aggregate deposition is observed in the axons of ALS patients. We have clarified the mechanisms of toxicity expression of these abnormal proteins using structural biology approaches such as NMR analysis. By integrating insights gained from these approaches, we present a comprehensive understanding of ALS pathology and prospects for developing novel therapeutic strategies.

Reference:

1. Akiyama T, Suzuki N,.. Okano H, Aoki M. Aberrant axon branching via Fos-B dysregulation in FUS-ALS motor neurons. ***EBioMedicine*** 45:362-378. (2019)
2. Yee KKL, Kumamoto J, Inomata D, Suzuki N, Harada R, Yumoto N. Harnessing synaptic vesicle release and recycling with antibody shuttle for targeted delivery of therapeutics to neurons. ***Mol Ther Methods Clin Dev*** 33:101476. (2025)
3. Iguchi N, Isozumi N, Hattori Y,.. Suzuki N,.. Mori E. Zinc finger domains bind low-complexity domain polymers. ***bioRxiv*** (preprint)

Profile: Field of interest: Neurodegenerative Disease/Neuro-Rehabilitation

- Analysis of ALS pathology models using iPSC-derived motor neurons
- Elucidation of dying-back pathology in ALS mouse models
- Interaction network analysis of ALS-associated proteins

Dr. Naoki Suzuki is an Associate Professor at the Tohoku University Graduate School of Medicine. After graduating from Tohoku University School of Medicine in 2001, he earned his Ph.D. in Medicine from Tohoku University in 2007. In 2004, he conducted research on the molecular mechanisms of muscle atrophy at the National Institute of Neuroscience, National Center of Neurology and Psychiatry. From 2007, he was involved in ALS research at the Department of Neurology, Tohoku University Hospital. Between 2011 and 2014, he served as a postdoctoral fellow at the Eggan Lab, Harvard Stem Cell Institute, where he focused on elucidating the pathogenesis of ALS using human stem cells and mouse models. After returning to Japan, he advanced his ALS research utilizing iPSC technology, mouse models, and human autopsy specimens, incorporating microfluidic devices and omics analysis approaches. During this period, he also contributed to the development of the world's first ultra-orphan drug for distal myopathy. Since April 2024, he has expanded his field to include rehabilitation medicine, pursuing clinical practice and research under the motto "Empowering Lives, Embracing Challenges: Overcoming Rare Diseases and Disabilities."

Speaker：Hong-Ru Chen (陳虹如), Ph.D.

Title：Monocyte-Derived Macrophage Mediated Transmission of Tauopathy

Abstract: Aberrant tau phosphorylation is a key driver of Alzheimer's disease (AD), contributing to cognitive decline and neurodegeneration. While monocyte infiltration into the hippocampus has been observed in AD patients, their role in disease progression remains unclear. In this study, we investigated the contribution of monocytes to tauopathy using recombinant hyperphosphorylated tau (p-tau) oligomers generated via the PIMAX system and delivered them into the hippocampus of mice. Using *CCR2-CreER;R26R-GFP* transgenic mice, we tracked monocyte infiltration and found that p-tau injection induced a robust immune response, including activation of SYK-coupled C-type lectin receptor signaling, as identified by bulk RNA sequencing. To assess functional consequences, we compared wild-type and CCR2 KO mice. In WT mice, $AT8^{+}$ tau initially localized to the dentate gyrus but progressively spread to the anterior cingulate cortex and contralateral hippocampal fimbria, consistent with tau propagation. This spread was accompanied by anxiety-like behavior and cognitive deficits. In contrast, CCR2 KO mice exhibited reduced tau spread and improved behavioral outcomes. We further demonstrated that pharmacological inhibition of SYK suppressed monocyte-mediated inflammatory responses and alleviated p-tau-induced behavioral deficits. These results suggest that inflamed monocytes promote tau propagation via SYK-CLR signaling, thereby exacerbating disease progression. To further dissect this mechanism, we are employing a monocyte-specific Syk knockdown approach using tamoxifen-inducible *CCR2-CreER* mice. Collectively, our findings highlight a previously underappreciated role for monocytes in mediating tau pathology and identify SYK signaling as a potential therapeutic target in AD.

Reference:

1. Fu, Z., Ganesana, M., Hwang, P., Tan, X., Kinkaid, M., Sun, Y.Y., Bian, E., Weybright, A., Chen, H.R, Francisco J. Quintana, Anne Schaefer, Chia Yi Kuan. Microglia modulate cerebral blood flow and neurovascular coupling through ectonucleotidase CD39. ***Nature communications***, 16:956 (2025)
2. Chen, H. R., Chen, C. W., Kuo, Y. M., Chen, B., Kuan, I., Huang, H., Lee, J., Anthony, N., Kuan, C. Y., Sun, Y. Y. Monocytes promote acute neuroinflammation and become pathological microglia in neonatal hypoxic-ischemic brain injury. ***Theranostics*** thno.64033 (2022)
3. Chen, H. R., Sun, Y. Y., Chen, C. W., Kuan, I., Kuo, Y. M., Smucker, M. R, Kuan, C. Y. Fate-mapping via CCR2CreER mice reveals monocyte-to-microglia transition in development and cerebral ischemia. ***Science Advances***, Aug 26;6(35):eabb2119. (2020)

Profile:

Field of interest: Neuroimmunology
-Monocytes regulate neural physiology and behavior across various neurological conditions

Dr. Hong-Ru Chen is an Assistant Professor in the Department of Life Sciences and the Institute of Genome Sciences at NYCU, Taiwan. She completed her postdoctoral training in Pediatrics at Emory University School of Medicine and later served as a faculty member in Neuroscience at the University of Virginia School of Medicine. She returned to Taiwan in August 2022. Dr. Chen's research focuses on neuroimmunology, particularly how monocyte-derived cells and neurons interact to regulate neural function in neurological conditions such as stroke, neonatal hypoxia ischemia, and neurodegeneration. Her lab combines transgenic mouse models, confocal microscopy, flow cytometry, single-cell transcriptomics, and behavioral analysis to uncover immune mechanisms driving disease. She aims to develop immune-targeted therapies, such as modulating the brain–meningeal immune ecosystem to promote repair and investigates how immune and glial activation contributes to tauopathy progression, including in Alzheimer's disease.