Tohoku-NYCU Online Seminar for Neuroscience

Organized by :
Tohoku University, Graduate School of Medicine,
National Yang Ming Chiao Tung University, College of Medicine
Endorsed by :
Tohoku University [Neuro Global International Joint Graduate program,
Tohoku University Brain Science Center

Date

Wednesday, December 3, 2025, 16:00 – 17:35 TST
17:00 – 18:35 JST

1st Speaker

Irene Han-Juo Cheng (鄭菡若), PhD.

Associate Professor, The Institute of Brain Science of National Yang Ming Chiao Tung University

Title

Targeting Aberrant STEP and FGFR1 Signaling Pathways to A Cognitive and Nociceptive Deficits in Alzheimer's Disease

2nd Speaker

Zhiqian Yu (俞 志前), DDS, PhD

Lecturer, Department of Psychiatry, Graduate School of Medicine, Tohoku University

Title

Sex-Specific Association Between Maternal Perinatal Depression and Autistic-Related Traits in Early Childhood

Registration

Please send a message to NGP Office (neuroglobal@grp.tohoku.ac.jp)

Program

16:00 TST (17:00 JST) Opening Remarks (10mim)
16:10 (17:10) Lecture by **Irene Han-Juo Cheng (鄭菡若), PhD** (35min)
16:45 (17:45) Q&A (5min)
16:50 (17:50) Lecture by **Zhiqian Yu (俞 志前), DDS, PhD** (35min)
17:25 (18:25) Q &A (5min)
17:30 (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. Ken-Ichiro TSUTSUI
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Speaker：Irene Han-Juo Cheng (鄭菡若), PhD.

Title: Targeting Aberrant STEP and FGFR1 Signaling Pathways to Alleviate Cognitive and Nociceptive Deficits in Alzheimer's Disease

Abstract:.

Alzheimer's disease (AD), the leading cause of dementia, is characterized by amyloid plaques and neurofibrillary tangles that lead to neuronal damage and trigger neuroinflammatory responses in glial cells. While cognitive decline is the hallmark symptom, a substantial proportion of AD patients also exhibit significant changes in pain sensitivity (nociception). The complex signaling mechanisms underlying this diverse range of symptoms remain unclear. This presentation will discuss our investigation into two distinct signaling pathways—STEP and FGFR1—as novel therapeutic targets for AD.

First, we explored the mechanism of nociception deficits, hypothesizing their link to the aberrant activation of striatal-enriched protein tyrosine phosphatase (STEP) signaling. We found that APP transgenic mice exhibited lower sensitivity to mechanical and thermal stimulation, which correlated with elevated STEP activity and decreased phosphorylation of nociception-related proteins in the hippocampus. Critically, pharmacological inhibition of STEP using TC-2153 successfully reversed both these nociceptive deficits and associated cognitive impairments, rescuing protein phosphorylation and indicating STEP's key role in this sensory alteration.

Second, we investigated the fibroblast growth factor receptor 1 (FGFR1) pathway, known to support neuronal function and modulate neuroinflammation. We found that administration of FGFR1 agonists (FGF1 and FGL) to an AD mouse model reversed spatial memory impairment, enhanced neurogenesis, suppressed reactive astrogliosis, and restricted dystrophic neurites. Furthermore, FGF1 treatment significantly reduced senile plaque deposition and improved the phagocytic ability of microglia in an FGFR1-dependent manner.Together, our findings identify both STEP and FGFR1 as critical and distinct signaling pathways whose dysregulation contributes to AD pathology. Targeting these pathways—by inhibiting STEP or activating FGFR1—alleviates a wide range of pathological, cognitive, and sensory impairments in AD mouse models, suggesting they represent promising, multi-faceted therapeutic strategies to improve the quality of life for patients with AD.

Reference:

1. Lee ZF, Huang TH, Chen SP, Cheng IH. Altered nociception in Alzheimer disease is associated with striatal-enriched protein tyrosine phosphatase signaling. **Pain.** 2021 Jun 1;162(6):1669-1680.
2. FGFR1 agonists alleviate pathology and cognitive impairment in an Alzheimer‘s disease mouse model. Hung WC, Sun WC, Su TC, Lee YJ, Cheng IH. **Exp Neurol**. 2025 Oct;392:115357.

Profile:

Dr Irene Han Juo Cheng is an Associate Professor at the Institute of Brain Science, National Yang Ming Chiao Tung University. She earned her Bachelor’s degree at National Taiwan University, and PhD degree from Department of Molecular Biology and Genetics, Cornell University.
She conducted postdoctoral research on the molecular mechanisms of Alzheimer’s disease at the Gladstone Institute, University of California, San Francisco.
The research focus in the Cheng laboratory is Alzheimer’s disease. We use transgenic mouse, cell culture, and biochemical approaches to dissect the disease mechanism and explore the novel therapeutic approaches.

Speaker ：Zhiqian Yu (俞 志前), DDS, PhD

Title : Sex-Specific Association Between Maternal Perinatal Depression and Autistic-Related Traits in Early Childhood

Abstract:
Perinatal depression in mothers has been linked to altered oxytocin (OXT) signaling and a heightened likelihood of autism spectrum disorder (ASD) traits in offspring. To clarify sex-dependent effects, we analyzed data from 23,218 Japanese mother–child pairs to assess the relationship between maternal depressive symptoms and autistic-related traits (ART) in toddlers, and further investigated underlying mechanisms in a stress-induced mouse model. Maternal psychological distress was evaluated using the Kessler Psychological Distress Scale (K6) and the Edinburgh Postnatal Depression Scale (EPDS), while child ART were measured with the Tokyo Autistic Behavior Scale (TABS). Elevated maternal K6 or EPDS scores during pregnancy or postpartum were significantly correlated with higher TABS scores in toddlers. Offspring of mothers meeting MPD criteria (K6 or EPDS ≥ 9) had a higher incidence of ART (TABS ≥ 15), with the strongest association observed in female toddlers exposed to maternal depression both prenatally and postnatally. In this subgroup, maternal mid-gestation K6 scores were inversely related to infant birth weight and positively associated with ART and impaired maternal bonding. Complementary mouse experiments showed that chronically stressed dams exhibited depressive-like behaviors, and their female offspring demonstrated excessive self-grooming, reduced social interaction, and decreased OXTR mRNA expression in the prefrontal cortex. Collectively, these results indicate that maternal perinatal depression contributes to increased autistic-related traits in offspring through sex-specific pathways involving OXT signaling dysregulation.

Reference:
1. CT Ono, Zhiqian Yu, et al., Association between low levels of anti-inflammatory cytokines during pregnancy and postpartum depression. ***Psychiatry Clin Neurosci.*** Aug;77(8):434-441. (2023)
2. Zhiqian Yu, et al., Plasma metabolic disturbances during pregnancy and postpartum in women with depression. ***iScience***. Nov 24;25(12):105666. (2022)

Profile:
Field of Interest: Neuroimmunology
- Mechanisms of fear memory
- Molecular risk factors of microglia in stress-induced immune responses
- Maternal depressive symptoms and autistic-like behaviors in offspring

Dr. Yu is a Lecturer in the Department of Psychiatry, Graduate School of Medicine, Tohoku University. He earned his Ph.D. in Dentistry from Tohoku University in 2006 and has since focused on elucidating the neuroimmune and molecular mechanisms underlying psychiatric disorders. His research spans mood stabilizer pharmacodynamics, glial function, and stress-related neuropsychiatric conditions such as depression, postpartum depression, PTSD, and schizophrenia. Dr. Yu's work integrates molecular biology, genomics, and behavioral neuroscience, combining analyses of human postmortem tissues, cohort data, and animal models. He has contributed to identifying peripheral cytokine, metabolic, and SNP profiles associated with pregnancy and postpartum depressive symptoms through large-scale genomic studies, aiming to uncover stress susceptibility biomarkers linked to autism risk in offspring. His interdisciplinary efforts seek to bridge molecular neuroscience and mental health resilience, advancing biomarker discovery and therapeutic development for stress-related psychiatric disorders.