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, February 19, 2025
17:00 – 18:35 JST (16:00 – 17:35 TST)

1st Speaker

Hsiao-Ying Kuo, Ph.D.

Assistant Professor, Institute of Anatomy and Cell Biology, National Yang Ming Chiao Tung University

Title

Molecular and Cellular Mechanisms of Speech- and Language-Linked FOXP2 in the Rodent Striatum during Vocal Circuit Formation

2nd Speaker

Noriko Osumi, Ph.D., DDS.

Vice President, Tohoku University
Professor, Department of Developmental Neuroscience,
Tohoku University Graduate School of Medicine

Title

Regulation of Neural Stem/Progenitor Cells by Kif23 and Kif2C During Cortical Development

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

Program

17:00 JST (16:00 TST) Opening Remarks (10mim)
17:10 (16:10) Lecture by **Hsiao-Ying Kuo, Ph.D,** (35min)
17:45 (16:45) Q&A (5min)
17:50 (16:50) Lecture by **Noriko Osumi, Ph.D.,DDS.** (35min)
18:25 (17:25) Q &A (5min)
18:30 (17:30) 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 2 attendances
【生命科学研究科・単位認定セミナー】【Credit-granted seminar】2 points

Contact: Prof. Ken-Ichiro TSUTSUI
[tsutsui@tohoku.ac.jp]

Speaker：**Hsiao-Ying Kuo, Ph.D.**

Title: Molecular and Cellular Mechanisms of Speech- and Language-Linked FOXP2 in the Rodent Striatum during Vocal Circuit Formation

Abstract:
Exquisite speech and language skills are not only unique and essential abilities for emotional expression and social communication in human beings, but also indispensable media for broadcasting and passing down human culture over time. Impairments in vocal communication are found in several neuropsychiatric disorders, including autism spectrum disorder and dysphasia. The underlying mechanisms of how the human brain develops and establishes abilities of vocal communication are not yet clear, which impedes the understanding and treatments of patients manifesting vocal impairments. We are interested in how the vocal circuits develop and wire, and how they regulate vocal functions during social communication or under pathological conditions. The discovery of a mutation in the transcription factor *FOXP2* in KE family members with speech disturbances has been a landmark example of the genetic control of vocal communication in humans. Cellular mechanisms underlying this control have remained unclear. Using *FOXP2* mutant mouse models, we demonstrated that the KE family $FOXP2^{R553H}$ mutation directly disables intracellular dynein-dynactin 'protein motors' in the striatum by elevating a disruptive high level of dynactin1. This abnormal elevation of dynactin 1 impairs TrkB endosome trafficking, microtubule dynamics, dendritic outgrowth, and electrophysiological activity in striatal neurons, leading to vocalization deficits. Notably, knocking down dynactin1 in mice carrying $FOXP2^{R553H}$ mutations rescued these cellular abnormalities and improved vocalization. Our findings indicate that FOXP2 regulates vocal circuit formation by maintaining protein motor homeostasis in striatal neurons, and its disruption could contribute to the pathophysiology of speech disorders associated with *FOXP2* mutations or deletions.

Reference:

Hsiao-Ying Kuo, Shih-Yun Chen, Rui-Chi Huang, Hiroshi Takahashi, Yen-Hui Lee, Hao-Yu Pang, Cheng-Hsi Wu, Ann M. Graybiel and Fu-Chin Liu: Speech- and language-linked FOXP2 mutation targets protein motors in striatal neurons. ***Brain***, 146(8):3542-3557, 2023.

Profile:

Field of interest: Developmental Neuroscience

- Postnatal Development of the Basal Ganglia Circuit
- Vocal Circuit
- Rodent Models of Neurodevelopmental Disorders

Dr. Hsiao-Ying Kuo is an assistant professor at the Institute of Anatomy and Cell Biology of the National Yang Ming Chiao Tung University in Taiwan, where she has served since 2021. After completing her Ph.D. at the Institute of Neuroscience of National Yang-Ming University, she received the prestigious Five-Year Grant for Young Scientists from the Ministry of Science and Technology of Taiwan to establish her research program.

She is interested in investigating the wiring of basal ganglia circuits during postnatal development, with a particular focus on the vocal circuit and its potential contributions to the pathophysiology of neurodevelopmental disorders, using transgenic mice, viral labeling systems, and cutting-edge microscopy technologies

Speaker：**Noriko Osumi, Ph.D, DDS.**

Title：Regulation of Neural Stem/Progenitor Cells by Kif23 and Kif2C During Cortical Development

Abstract:
The development of the mammalian cerebral cortex is a highly intricate process requiring precise coordination of neural stem/progenitor cell (NSPC) division and differentiation. These processes are essential for generating the correct number of neurons and ensuring their proper positioning—both prerequisites for higher brain function. While kinesin (Kif) family proteins are well-studied in neurons, their roles in NSPCs during embryonic brain development remain largely unexplored. In our laboratory, we focused on two Kif proteins, Kif23 (N-Kif) and Kif2C (M-Kif), which are highly enriched in NSPCs and exhibit dynamic localization changes during the cell cycle. Using *in utero* electroporation to knock down (KD) these genes in mice, we demonstrated that Kif23 is essential for regulating mitotic spindle orientation, cytokinesis, and NSPC maintenance via the γ-H2AX, p53, and p21 pathways. Meanwhile, Kif2C plays a crucial role not only in NSPC pool maintenance but also in NSPC-dependent neuronal migration. The phenotype of *Kif2C* KD resembles a human congenital brain anomaly, polymicrogyria. Furthermore, we successfully rescued *Kif23*-KD phenotypes by co-expressing human *KIF23*, but not a microcephaly-associated mutant variant. In summary, our findings reveal novel roles for motor proteins, Kif23 and Kif2C, in cortical development, providing new insights into the molecular mechanisms underlying congenital brain anomalies such as microcephaly.

Reference:
Sharmin Naher, Takako Kikkawa, Kenji Iemura, Satoshi Miyashita, Mikio Hoshino, Kozo Tanaka, Shinsuke Niwa, Jin-Wu Tsai, Noriko Osumi: Kinesin family member Kif23 regulates cytokinetic division and maintains neural stem/progenitor cell pool in the developing neocortex. ***EMBO J***, 44(2):331-355, 2024

Profile:
Field of interest: Developmental Neuroscience
- Molecular mechanisms of brain development
- Rodent models of neurodevelopmental disorders
- Paternal effect on offspring neurodevelopment

Dr. Noriko Osumi is Vice President of Tohoku University, Director of the Tohoku University Library, and a Professor at the Graduate School of Medicine. She earned her PhD from Tokyo Medical and Dental University and established her neuroscience lab at Tohoku University in 1998, where she conducts her research in molecular mechanisms of brain development and neurodevelopmental disorders. Dr. Osumi has also played a pivotal role in advancing open-access initiatives and diversity efforts at the university. A recognized leader in science communication, she received the MEXT "Commendation for Science and Technology" in 2022.

KIF23 ensures appropriate brain development by controlling proliferation and differentiation of neural progenitors. Taken from a cover of *EMBO J*, in which her recent article is published. (Sharmin et al., *EMBO J*, 2024)