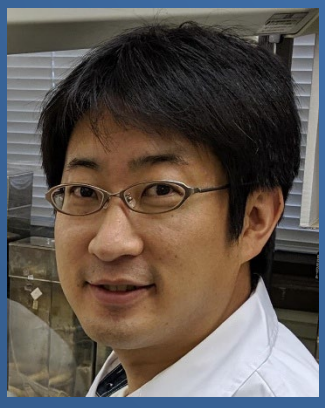
239th WPI-IIIS Seminar
-Mini Symposium-

Chemogenetic activation of G12 signaling illuminates therapeutic potential for G12-coupled GPCRs

Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) are powerful chemogenetic tools that enable selective modulation of specific G protein signaling pathways in vivo. Existing DREADDs for Gs, Gi, and Gq pathways have proven invaluable for dissecting diverse physiological processes ranging from neuronal activity to metabolic regulation. However, G12/13 signaling has remained largely unexplored due to the absence of selective pharmacological tools. To address this gap, we developed G12D, a DREADD that preferentially activates G12 signaling upon clozapine-N-oxide (CNO) administration. By combining G12D with Cre-loxP systems, we generated adipocyte-, hepatocyte-, and POMC neuron-specific models to interrogate tissue-specific G12 functions. Our studies revealed striking context-dependent metabolic outcomes: synergistic enhancement of adipose browning with β-adrenergic signaling, divergent regulation of hepatic lipid versus glucose metabolism, and central control of appetite and energy balance. We are currently developing G13-selective DREADDs to further distinguish G12 from G13 signaling. These chemogenetic approaches establish G12/13-coupled GPCRs as promising therapeutic targets for obesity and metabolic disease.



Dr. Asuka Inoue

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Date: **Thursday, November 6, 2025**

Time: **13:30 – 14:25**

Venue: **1F Auditorium, IIIS Building**

＊On-site participation only

IIIS
INTERNATIONAL INSTITUTE FOR INTEGRATIVE SLEEP MEDICINE

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MOONSHOT RESEARCH & DEVELOPMENT PROGRAM

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