



# 第 491 回つくば分子生命科学セミナー

TSUKUBA MOLECULAR LIFE SCIENCE SEMINAR

**Title : A genetic platform to study SMPD4-associated microcephaly in *Drosophila***

**Speaker : Dr. Chih-Chiang**

Graduate Institute of Physiology, National Taiwan University  
College of Medicine

**Date : Oct. 31, 2025 (Fri) 13:00-14:00**

**Venue : TARA center Building A, Seminar room**

**Abstract :** Sphingolipids (SPLs) govern diverse cellular processes, and their dysregulation underlies numerous human diseases. Despite extensive biochemical characterizations, understanding the orchestration of the SPL metabolic network within living organisms remains challenging. To systemically investigate SPL metabolism, we established a versatile genetic platform that included CRISPR-engineered reporters of 52 SPL regulators, recapitulating endogenous gene activity and protein distribution. The platform also allows conditional protein degradation for functional assays. Additionally, we developed a biosensor for visualizing sphingomyelin/ceramidephosphoethanolamine (SM/CerPE) dynamics in vivo. Using this platform, we revealed the spatiotemporal heterogeneity of the SPL metabolic network in the brain, even within the same branch of the SPL regulatory pathways. For example, we identified distinct cellular requirements for SMases, particularly the microcephaly-associated CG6962/SMPD4. Furthermore, neurons and glia degrade SM/CerPE at specific organelles with coordinated lipoprotein-mediated intercellular transfer. This platform enables comprehensive investigation of SPL metabolism in vivo, offering new avenues for deciphering its pathophysiological mechanisms.

本セミナーは、医学学位プログラム（博士）「医学セミナー」（担当：専攻各教員）、及び、フロンティア医科学学位プログラム（修士）「医科学セミナーII」（担当：入江賢児）の関連セミナーに相当します。

連絡先：筑波大学生存ダイナミクス研究センター

佐奈喜祐哉（内線7337、[yuya-sanaki@tara.tsukuba.ac.jp](mailto:yuya-sanaki@tara.tsukuba.ac.jp)）

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協会代表：筑波大学医学医療系 久武幸司 TSMM セミナー担当：筑波大学医学医療系 蕨栄治