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TEMASEK LIFESCIENCES LABORATORY

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7 Jul 2023 (Fri), 11am

Seminar Rm 05-41 (Level 5)

Hosted by: Dr YU Fengwei

Expression and functional profiling of sphingolipid enzyme network in the Drosophila nervous system

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Prof. Chih-Chiang Chan, a Professor at National Taiwan University, earned his PhD and conducted post-doctoral training at the University of Texas-Southwestern Medical Center. His research focuses on neuronal cell biology using Drosophila as a test organism, with a focus on sphingolipid-modifying enzymes. Additionally, he models and studies novel variants associated with neurodegenerative disorders using fly genetics.

Sphingolipids are a diverse group of lipids serving as both structural components and signaling molecules. Their synthesis and degradation are regulated by a set of sphingolipid-metabolizing enzymes, mutations of which lead to various types of neurological disorders. To systemically reveal how sphingolipid homeostasis is maintained, we have generated a complete set of reporter flies to visualize the entire network of sphingolipid metabolizing enzymes. The reporter flies were CRISPR-engineered to knock-in HA-T2A-Gal4 cassette at the c terminus of the coding region in the endogenous locus, allowing for expression profiling at both the transcription and translation levels. Using this toolset, we constitute a 4D map of the enzymatic network, showing the spatiotemporal patterns of the expressing cells and functioning cells of each enzyme in the larval and adult CNS, as well as the leg as a peripheral tissue, in the contexts of normal aging, metabolic challenge, and neurodegenerative diseases. Our preliminary results identify distinct cell types for ceramide synthesis and degradation and highlight the glial role in degrading complex sphingolipids. Our data also suggest an expansion of several key metabolizing proteins from its specific glia types to subsets of neurons, underscoring the importance of neuro-glia communication. We argue that there is not an omnipotent cell in the brain that does everything to cell-autonomously regulate sphingolipid homeostasis. Furthermore, our screen also reveals candidate genes of regulators of neurodegenerative disease, and I will discuss the possible mechanisms of individual genes in the presentation.

Recent Publications:

1. Hung YC, Huang KL, Chen PL, Li JL, Lu SHA, Chang JC, Lin HY, Lo WC, Huang SY, Lee TT, Lin TY, Imai Y, Hattori N, Liu CS, Tsai SY, **Chen CH,** Lin CH, Chan CC: UQCRC1 engages cytochrome c for neuronal apoptotic cell death. Cell Reports (2021) 36(12):109729
2. Tzou FY, Su TY, Lin WS, Kuo HC, Yu YL, Yeh YH, Liu CC, Kuo CH, Huang SY, **Chan CC**: Dihydroceramide desaturase regulates the compartmentalization of Rac1 for neuronal oxidative stress. Cell Reports (2021) 35(2):108972
3. Lien WY, Chen YT, Li YJ, Wu JK, Huang KL, Lin JR, Lin SC, Hou CC, Wang HD, Wu CL, Huang SY, **Chan CC**: Lifespan regulation in α/β posterior neurons of the fly mushroom bodies by Rab27. Aging Cell (2020) 19(8):e13179