CDB SEMINAR

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Tuesday, May 30

16:00~17:00 C1F CDB Auditorium

Heterotrimeric G Protein Signalling and Asymmetric Cell Division in *Drosophila*

Summary

Asymmetric division of *Drosophila* neuroblasts (NBs) and the *C.elegans* zygote utilises polarity cues provided by the Par proteins as well as heterotrimeric G-protein-signalling activated via a receptor independent mechanism mediated by GoLoco/GPR motif proteins with Guanine Nucleotide Dissociation Inhibitor (GDI) activity as well as a cytosolic Guanine Nucleotide Exchange Factor (GEF). Locomotion defects (Loco) interacts and colocalizes with Gαi and, through its GoLoco motif, acts as a guanine nucleotide dissociation inhibitor (GDI) for Gαi. Simultaneous removal of the two GoLoco motif proteins, Loco and Pins, results in defects that are essentially indistinguishable from those observed in *G13F* or *Gγ1* mutants, suggesting that Loco and Pins act synergistically to release free G in neuroblasts. Furthermore, the RGS domain of Loco can also accelerate the GTPase activity of Gi to regulate the equilibrium between the GDP- and the GTP-bound forms of Gi. Thus, Loco can potentially regulate heterotrimeric G-protein signaling via two distinct modes of action during *Drosophila* neuroblast asymmetric divisions. Another key component of this non-canonical G-protein activation mechanism is a non-receptor GEF for Gαi, RIC-8, which has recently been characterised in *C.elegans* and mammals. We show here that DmRIC-8, the *Drosophila* RIC-8 homologue, is required for asymmetric division of both NBs and pI cells. *DmRIC-8* is necessary for membrane targeting of Gαi, Pins and Gβ13F, presumably by regulating multiple Gα subunit(s). DmRIC-8 forms an in vivo complex with Gαi and interacts preferentially with GDP-Gαi, consistent with DmRIC-8 acting as a GEF for Gαi. Comparisons of the phenotypes of *Gαi*, *DmRIC-8*, *Gβ13F* single and *DmRIC-8;Gβ13F* double loss-of-function mutants suggest that in NBs DmRIC-8 positively regulates Gαi activity on the cortex whereas Gβγ acts to restrict Gαi (and GoLoco proteins) to the apical cortex where Gαi (and Pins) can mediate asymmetric spindle geometry.

Speaker profile

Dr. Yu is a rising star in the field of *Drosophila* cell biology. His thesis work at Bill Chia's lab in IMCB, Singapore began with the discovery of a key molecule regulating asymmetric division of neural precursor cells, known as "Partner of Inscuteable (Pins)". He has subsequently made outstanding achievements in examining the roles of the receptor-independent G-protein signaling involving Pins. He is temporarily staying at the Yuh-Nung Jan's lab for a year as a visiting scientist.

Host:
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