CDB SEMINAR

Speaker: **Chris Q. Doe**

< Institutes of Neuroscience and Molecular Biology,
HHMI, University of Oregon>

Title: **"Asymmetric cell division and neuroblast self-renewal in Drosophila"**

Date: Friday, November 18
Time: 16:00～17:30
Place: 1F Auditorium of Building C

Since his graduate study at Goodman lab, Dr. Doe has been pursuing the problem of how neuronal identity is determined during *Drosophila* neurogenesis, and has led this research field by his work that also influences other areas of study, as you might know his recent discovery of an invariant temporal pattern of gene expression in neuroblasts. At this seminar, he will present you a new view for a fundamental problem;
－ What promotes the self-renewal of progenitors?

Summary:

An important question in stem cell and cancer biology is how a cell chooses to proliferate or differentiate. *Drosophila* larval brain neuroblasts divide asymmetrically to undergo self-renewal with every cell division. During neuroblast mitosis, the larger daughter cell inherits the evolutionarily-conserved cell polarity proteins aPKC, Bazooka, Par6, Pins, and Galphai and remains a neuroblast; the smaller daughter cell inherits Miranda, Prospero, Numb, and Staufen proteins and commits to neuronal or glial differentiation. We tested whether cell polarity genes, known to regulate neuroblast asymmetric cell division, also regulate neuroblast self-renewal. Clonal analysis showed that *pins* mutant neuroblasts rapidly fail to self-renew, while *lgl* mutant neuroblasts generate multiple neuroblasts. Remarkably, *lgl pins* double mutant neuroblasts all divide symmetrically to self-renew, filling the brain with neuroblasts at the expense of neurons. The *lgl pins* neuroblasts showed ectopic cortical aPKC localization, and reduced aPKC levels suppressed the *lgl* ectopic neuroblast phenotype, suggesting that aPKC promoted neuroblast self-renewal. In support of this hypothesis, neuroblast-specific overexpression of membrane-targeted aPKC, but not a kinase-dead version, induced ectopic neuroblast self-renewal. Thus, cortical aPKC kinase activity is a potent inducer of neuroblast self-renewal. Genetic screens and mass spectrometry are being used to identify aPKC target genes, and we have identified at least one complementation group that acts downstream of aPKC to promote self-renewal.

Host : Fumio Matsuzaki <Cell Asymmetry, CDB>
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