CDB SEMINAR

Daniel St Johnston

The Gurdon Institute & the Department of Genetics, University of Cambridge

Friday, December 7, 2007

16:00~17:30 C1F CDB Auditorium

Alternative pathways to polarize the anterior-posterior axis and epithelia in *Drosophila*

Summary

The anterior-posterior axis in *Drosophila* is defined at stage 9 of oogenesis through the localisation of *bicoid* and *oskar* mRNAs to opposite ends of the oocyte. This depends on the correct polarisation of the oocyte's microtubule cytoskeleton, which is controlled in turn by the establishment of complementary cortical domains of PAR proteins. The Bazooka (PAR-3) complex marks the anterior and lateral cortex where microtubule minus ends are nucleated or anchored, whereas PAR-1 defines a posterior cortical domain where microtubule plus ends become enriched. Complementary PAR domains play a similar role in the apical-basal polarity of epithelial cells, with PAR-1 localising to the lateral cortex to control microtubule stability. The activity of PAR-1 is regulated by phosphorylation by LKB1 (PAR-4), and *lkb1* mutants give the same phenotype as *par-1* mutants in both axis formation and epithelial polarity.

Human LKB1 is mutated in both familial and spontaneous tumours, and acts as a master kinase that activates both PAR-1 and the main cellular energy sensor, AMPK, which inhibits growth under conditions of energetic stress. This has led to the hypothesis that LKB1 acts as a tumour suppressor because it is required to maintain cell polarity and growth control through PAR-1 and AMPK respectively. However, we have recently shown that mutations in the single *Drosophila* AMPK catalytic subunit disrupt both growth control and cell polarity under conditions of energetic stress. LKB1 is required *in vivo* for AMPK activation in *Drosophila* and *lkb1* mutations cause similar phenotypes to *ampk*α mutations in starved flies. Furthermore, starved *lkb1* mutants are rescued by a phosphomimetic version of AMPKα. Thus, LKB1 signals through AMPK to coordinate the regulation of cell polarity and proliferation with cellular energy status, and this might underlie the tumour suppressor function of LKB1. This prompted us to investigate whether there are other links between the pathways that control cell growth and cell polarity, and I will report on our recent identification of several other proteins that are specifically required for cell polarity under conditions of energetic stress, including the TOR pathway. Our results reveal the existence of two alternative pathways to generate cell polarity that operate under different nutrient conditions.

Host:
Akira Nakamura
Germline Development, CDB
akiran@cdb.riken.jp
Tel:078-306-0103 (ext:1442)