



CDB SEMINAR

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Thursday, July 5, 2012

16:00~17:00 A7F Seminar Room

Investigation of the physical and functional links between the APC/C and the centrosome in *Drosophila*

Summary

The multisubunit ubiquitin ligase complex, the Anaphase-Promoting Complex or Cyclosome (APC/C), mediates ubiquitin-dependent destruction of key molecules to control cell cycle progression. Successful passage of the genome through cell division is therefore reliant upon tight spatial and temporal control of APC/C activity.

In various metazoan tissues APC/C subunits and cofactors localise at the centrosome, which is the major microtubule organising centre that drives chromosome segregation and cell motility by organizing microtubules. Deregulation of the centrosome is a recurrent theme in chromosome instability and over-proliferation of stem cells, which lead to tumorigenesis, thus the precise control of the centrosome integrity and functions is essential for tumour suppression. In recent years it has become evident that the APC/C plays important roles in the regulation of the centrosome by targeting major centrosome regulators such as HsSas-6, Plk1 and Aurora A. However, the significance of their destruction for faithful genome inheritance, stem cell homeostasis and tumourigenesis remain to be elucidated.

To define the roles of the APC/C at the centrosome, we have started biochemical and proteomic screenings to identify centrosomal APC/C substrates and interactors in the multicellular model system, *Drosophila melanogaster*. We have been screening for APC/C substrates in reconstituted APC/C-dependent destruction and ubiquitination. We have been building the APC/C-centrosome interactome utilizing protein A tag affinity purification followed by mass spectrometry. We have identified the evolutionarily conserved centrosomal protein, Spd-2/Cep192, in both screenings. Spd2 directly interacts with the APC/C coactivator, Fzr/CDH1, in a KEN-box dependent manner and is required for centrosomal localization of Fzr in cultured cells. Our biochemical data suggests that Spd-2 may be a pseudosubstrate inhibitor of the APC/C. I discuss the potential role for the Fzr-Spd2 interaction in asymmetric cell division of neural stem cells.

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