CDB SEMINAR

Yuu Kimata

Cancer Research UK Career Development Fellow, Department of Genetics, University of Cambridge, UK

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15:00~16:00 A7F Seminar Room

Coupling cell cycle to cell fate: Cell-cycle regulation of Wnt signalling by the APC/C-Nek2 axis

Summary

Tight coordination between cell proliferation and differentiation is vital for the formation and homeostasis of tissues and organs in multicellular organisms. Disruption of this coordination underlies various pathological conditions including tumorigenesis, tissue degeneration and ageing. Despite its significance, the mechanisms that couple the cell cycle to differentiation remain poorly understood. It has been generally acknowledged that developmental signalling plays a primary role in such coordination by dictating the expression of cell cycle genes in conjunction with fate specification. However, it is becoming more evident that cell cycle regulators, in reverse, modulate the activity of developmental signalling, pointing to intensive molecular crosstalk between cell cycle machineries and developmental signalling pathways.

We have been exploring the role of cell cycle regulators in such crosstalk in a model organism, *Drosophila* melanogaster. Through an *in vivo* RNAi screen in the *Drosophila* eye, we have recently uncovered a novel non-mitotic role for a master cell cycle regulator, the Anaphase Promoting Complex/Cyclosome (APC/C). We have demonstrated that the APC/C attenuates the activity of the canonical Wnt signalling pathway through cell cycle-dependent degradation of a positive Wnt regulator, Nek2. Thus, the APC/C couples the initiation of retinal differentiation to synchronous G1 arrest during the eye development. We have also provided evidence that Decapentaplegic/BMP signalling regulates this APC/C function via a post-translational mechanism.

Cumulative evidence suggests a strong link between Wnt signalling and mitosis. Nek2 is an evolutionarily conserved mitotic kinase known to regulate the centrosome. I will discuss a potential centrosome-mediated cell-cycle control of Wnt signalling and its implications.

Host:
Shigeo Hayashi
Morphogenetic Signaling, CDB
shayashi@cdb.riken.jp
Tel:078-306-3185 (ext:1523)