CDB SEMINAR

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13:30~14:30 A7F Conference Room

A molecular mechanism for balancing self-renewal with differentiation in *Drosophila* neural stem cells

Summary

Multicellular organisms consist of a variety of cell types. Asymmetric cell division is a widespread mechanism for the generation of diverse cell types during development. It has been shown that stem cells use asymmetric cell division to balance their self-renewal with the production of differentiating progeny. Imbalances in the self-renewal and differentiation of stem cells as a result of defects in asymmetric cell division may lead to stem cell-derived tumors. A major question in developmental biology is: how is the stem cell pool maintained through self-renewal while allowing the production of differentiated progeny? Stem cells in the *Drosophila* nervous system, neuroblasts, are thought to self-renew by segregating cell fate determinants into the differentiating daughter cell during mitosis and/or by expressing positive 'stem cell' factors in the self-renewing neuroblast.

In this seminar, I would like to talk about the molecular mechanism whereby the cell fate determinant Numb is localized asymmetrically only in mitosis. We recently showed that a phosphorylation cascade triggered by the activation of the mitotic kinase Aurora-A is responsible for the asymmetric segregation of Numb. These results demonstrated how cell polarity can be coupled to cell-cycle progression in self-renewing neuroblasts.

A large body of previous data suggests that the organization of chromatin by epigenetic mechanisms is essential for establishing and maintaining cellular identity in development. We screened *Drosophila* genes involved in epigenetic regulation for genetic interactions with cell fate determinants using transgenic RNAi. Further characterization of the positive hits revealed that cellular growth of the neuroblast is critical for maintaining its self-renewal. A signaling network for balancing the self-renewal and differentiation of stem cells will be discussed.

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