CDB SEMINAR

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13:00~14:00　A7F Conference Room

C. elegans: A simple approach to understand stem cells

Summary

The nematode *C. elegans* has proven to be a premier model for discovery of fundamental regulatory mechanisms that are used broadly throughout the animal kingdom, including humans. Well known examples include regulators of cell death and RNAi. Stem cell controls are no exception. Stem cells have the magical ability to produce more of themselves and to also differentiate into specialized cells (e.g. muscle or nerve cells). To unravel molecular mechanisms of stem cell regulation, I have focused on three fundamental aspects in stem cell biology using *C. elegans* as a model organism: stem cell control, cell fate specification, and dedifferentiation. In *C. elegans*, Notch signaling and PUF (Pumilio and FBF) RNA-binding proteins control germline stem cells (GSCs). We found that Notch signaling promotes the transcriptional activation of two MAPK regulators. One such regulator is FBF-2, a PUF RNA-binding protein that represses MAPK mRNA; the other is LIP-1, a homolog of MKP/DSP dual specificity phosphatases that inhibit MAPK activity. When both regulators are removed, germ cell death increases dramatically compared to removal of either control alone. In addition to germ cell death, we also found that MAPK activity is required to promote differentiation into sperm and de-differentiation into cancer stem cells under certain mutant background. Furthermore, we tested whether PUF regulation of MAPK (Erk2 and p38α) mRNAs is conserved in human embryonic stem cells since the PUF proteins and MAPK signaling are highly conserved in all eukaryotes. The Pum2 protein binds specifically to 3'UTR of both Erk2 and p38α mRNAs *in vitro*, and represses their expression *in vivo*.

Our analysis of the regulatory network controlling *C. elegans* GSCs is therefore likely to have important parallels for stem cell controls broadly in the animal kingdom.

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