CDB SEMINAR

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Friday, June 5, 2009

16:00~17:00 A7F Seminar Room

Post-translational regulation in the *Drosophila* germ line

Summary

In *Drosophila*, molecular asymmetries guiding embryonic development are established maternally. I will review earlier published work indicating that Vasa is a positive regulator of translation of target mRNAs that operates through a direct interaction with the general translation factor eIF5B. Vas is expressed in all ovarian germ line cells, and aspects of the *vas*-null phenotype suggest a function in regulating the balance between germ line stem cells (GSCs) and their fate-restricted descendants. Using a biochemical approach to recover Vas-associated mRNAs, we obtained *mei-P26*, whose product represses microRNA activity and promotes GSC differentiation. I will show that *vas* and *mei-P26* mutants interact, and that *mei-P26* translation is substantially reduced in *vas* mutant cells. In gel-shift assays, Vas protein binds specifically to a U-rich motif in the *mei-P26* 3'-untranslated region (3' UTR). The ability of Vas to activate *mei-P26* expression in vivo was abrogated by a mutation that greatly reduces its interaction with eIF5B. We also found that Vas-dependent regulation of expression of *GFP-mei-P26* transgenes required the inclusion of the U-rich 3' UTR domain. Taken together, our data support the conclusion that Vas promotes germ cell differentiation by directly activating *mei-P26* translation in early-stage committed cells. Vas accumulates to high levels in the posterior pole plasm, and is protected from degradation there by the deubiquitinating enzyme Fat facets. We have further explored the contribution of ubiquitin-dependent pathways to Vas deployment. We found that Gustavus and Fsn, two ubiquitin Cullin-RING E3 ligase specificity receptors, bind to the same motif on Vas. Overexpression of either receptor protein reduced ovarian Vas levels, and germ cell number in progeny embryos. Decreased *gustavus* function also reduced germ cell number, suggesting that Gustavus promotes Vas stability and/or function in the pole plasm. In contrast, endogenous Fsn destabilizes Vas. We conclude that Gustavus and Fsn act antagonistically in the pole plasm, and function to fine-tune Vasa level and activity.

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