Seminar/Talk

Coordinate Regulation of Development by a Shared RNA Element

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Host: Carl-Philipp Heisenberg

During development gene expression is controlled by regulatory mechanisms that act at the level of DNA and/or RNA. We find that a 3' un-translated region (3'UTR) RNA element that we previously identified in zebrafish nodal-related1/squint (sqt), is shared by multiple components of the Nodal signaling pathway: ligand, receptor, inhibitor and transcriptional effector. RNA localization assays in early zebrafish embryos using fluorescent reporters show that the 3'UTR RNA elements in lefty 1 and lefty2 inhibitor RNAs, acvr2 receptor RNA and to a lesser extent, smad2 effector RNA, behave similarly to sqt/nodal ligand RNA. The RNA-binding protein (RBP) and translational repressor, Y-box binding protein 1 (Ybx1) binds to the 3'UTR element and translation pre-initiation complex proteins to prevent translation. Whereas ybx1 mutant embryos show premature Nodal/Sqt translation and gain-of-Nodal signaling, compound ybx1;sqt mutants manifest premature and elevated Lefty protein expression and loss-of-Nodal signaling. These findings demonstrate translational co-regulation of multiple components of a developmental pathway by a shared RNA element/RBP "regulon". This module regulates NODAL RNA in human cells as well, suggesting broader conservation.
To understand the basis of Ybx1 RBP/RNA element recognition, we performed computational analysis of the zebrafish transcriptome. We identified >800 candidate RNAs harboring the 3'UTR element, of which many encode components of signaling pathways (e.g., midkine, FGF) or factors that function in the same biological process (e.g., metabolism, germ-line development). To determine the role of the putative elements, we are establishing high-throughput assays for localization and translation in zebrafish embryos. Our findings suggest that the RNA regulatory module that we first identified in nodal RNA might be used for co-regulation of multiple signaling pathways and sets of functionally connected genes during development.

Thursday, February 23, 2017 04:45pm - 05:30pm
Experimental Biology Room (I04.2OG - LAB)

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