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Concurrent Session 1: Morphogenesis and Organogenesis

Program/Abstract # 1 Beyond guidance: A novel role for Sema-PlxnD1 signaling in vascular development

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Sprouting angiogenesis expands the primitive vasculature of the embryo and its essential for survival and homeostasis. However, the mechanisms that allocate the capacity to form sprouts among endothelial cells to ensure the reproducible anatomy of stereotypical vascular beds remain unknown. Using the zebrafish model system, confocal imaging, RNA in situ hybridization, cell transplantation/ competition experiments and both loss and gain-of-function approaches here we show that Sema-PlxnD1 signaling, previously implicated in sprout guidance, plays precisely this role. Molecularly, Sema-PlxnD1 signaling exerts this effect by modulating the effects of other vascular development pathways.

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Program/Abstract # 2 Specialized ribosomes control Hox mRNA translation and vertebrate tissue patterning

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Control of gene expression in space and time plays an important role in enabling cells to "know" where they are in the developing vertebrate embryo and what to become. Decades of research have demonstrated numerous layers of regulation in gene expression that coordinate this process, although translational control has received less experimental attention. Here we unexpectedly show that a single component of the ribosome establishes the mammalian body plan. Our data reveal that mutations of the Ribosomal Protein L38 (Rpl38) gene in mice lead to tissue specific patterning defects, including pronounced homeotic transformations of the axial skeleton. By optimizing genetic and molecular approaches to study translational regulation within the vertebrate embryo, we uncover an important role for RPL38 in transcript-specific translational control. In Rpl38 mutant embryos, global protein synthesis is unchanged however the translation of a select subset of Homeobox mRNAs is perturbed. Our data reveal that RPL38 facilitates 80S complex formation on these mRNAs as a regulatory component of the ribosome and uncover novel complexity in regulation of Hox gene expression at the level of translational control. We further show that Rpl38 expression is markedly enriched in regions of the embryo, such as somites, where lossof-function phenotypes occur. We extended these findings by performing an expression-profiling screen for the majority of the 79 ribosomal proteins associated with both small and large ribosome subunits. This analysis unexpectedly identified dynamic regulation in the expression of ribosomal proteins, which historically have been considered to be ubiquitously expressed housekeeping genes, within the vertebrate embryo. Collectively, these findings suggest that a "ribosomal protein code" established by distinct expression levels and translational specificity of ribosomal proteins may provide a new level of regulation in gene expression and mammalian development.

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Program/Abstract # 3 Regulation of secretory epithelial morphogenesis and physiological specialization Deborah Andrew

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To understand how secretory organs acquire their final form and function, we focus on a simple well-developed genetic system, the Drosophila salivary gland (SG). The SG is a simple tube that undergoes the same morphogenetic events that occur in organs of more complicated systems, including changes in cell shape, adhesion and movement. The SG is also the largest secretory organ in the embryo, making it ideal for learning how specialized secretory tissues acquire high-level secretory capacity. Our efforts are directed toward learning the molecular basis for the cell shape changes required to transform a field of polarized epithelial cells into a tubular organ, for how the SG expands its secretory machinery to accommodate increases in secretory load, and for how production of SG-specific gene products is coordinated with tissue development. Three transcription factors play major roles in one or more of these processes, the winged helix DNA binding protein Fork head (Fkh), the bZip transcription factor CrebA, and the basic helix-loop-helix DNA binding protein Sage. Fkh is required for the initial events of tube formation and promotes SG survival. Fkh also maintains its own expression and that of CrebA and Sage. CrebA activates expression of proteins that comprise secretory organelles as well as secreted cargo. Sage, together with Fkh, maintains an open, patent salivary gland lumen and sage loss results in massive SG cell death in late embryos. We have identified targets of these transcription factors through