Concurrent Session 1: Organogenesis

Program/Abstract # 2
Liver specification and morphogenesis in zebrafish
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The vertebrate liver arises in close proximity to the pancreas and lung from the multipotent foregut endoderm. We use zebrafish as a model to elucidate the mechanisms of liver specification and subsequent organ bud morphogenesis. Analyses of amniotes uncovered spatially restricted expression of numerous Wnt pathway components along the digestive tract, suggesting ‘code-like’ functions in patterning and differentiation. We show that two Wnt ligands, Wnt2bb and Wnt2t, are pivotal for patterning the foregut endoderm. Both factors are required for sequentially regulating liver specification and proliferation. Intriguingly, their loss causes liver and swim bladder agenesis, indicating that their combined specific activities are essential for their respective specification. Excess wnt2bb or wnt2 induces a striking expansion of liver tissue at the expense of pancreatic and anterior intestinal tissues. Thus, reveals a broad endogenous competence of the intestinal endoderm to respond to restricted hepatogenic signals, mediating the delicate balance between different organ progenitor populations. Thus, tightly regulated spatiotemporal expression of wnt2bb and wnt2 is central to coordinating early liver, pancreas and swim bladder formation from a multipotent digestive endoderm. In addition, we will discuss our ongoing efforts investigating the cellular and molecular mechanisms directing liver morphogenesis.

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Program/Abstract # 3
Cardiac BAF complex promotes cardiac progenitors in the zebrafish embryo
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Little is known about the earliest events that regulate the behaviour of cardiac progenitor cells fated to form the heart. BAF (Brg/Brm associated factor) complexes are large protein assemblies with chromatin-remodeling activities. These complexes can engage in a number of cell-specific events via differential use of variant subunits. Expression of baf60c, a cardiac specific subunit of the BAF complex, with gata4 and tbx5 has been shown to promote ectopic differentiation of cardiomyocytes in murine embryos. We have used the zebrafish embryo to further examine this cardiac BAF (cBAF) complex. Transplanted cells overexpressing these three factors migrated to the heart-forming region and contribute to myocardium and endocardium of host embryos at a high frequency. Remarkably, this occurred independent of the location that the cells were placed in the host. Further transplantation experiments using hosts with defects in various germ layers indicate that signal(s) emitted from the endoderm is essential for cBAF complex-driven migration and cardiac differentiation. To determine the endogenous function of cBAF, baf60c together with gata5 and tbx5 were knocked down in the zebrafish embryo through morpholino injection. This led to massive down-regulation of myocardial gene expression, with the morphants displaying severe heart defects. In summary, we have recapitulated many of the hallmarks of the earliest cardiac progenitor in vivo. Future studies will be directed at characterizing the mechanisms that govern the activity of the cBAF complex and the behaviors of cBAF-induced cardiac progenitors.

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Program/Abstract # 4
Linking global tissue asymmetry to cell polarity on the plane
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Cells sense the global axes of the tissue to which they belong and manifest polarity for specialized functions. One such example is planar cell polarity (PCP), which is seen in many animals and tissues such as the Drosophila wing, where epidermal cells somehow sense the cue along the proximal-distal (P-D) axis and localize an assembly of actin filaments at the distal cell vertex. The pertinent molecular players have been classified into at least the 2 following categories: the first group includes atypical cadherins Dachsous and Fat that are thought to contribute to the tissue patterning information across the axis. Second, members of the “core group,” including Frizzled (Fz) and flamingo, assemble into asymmetric complexes that straddle the proximodistal junctions between adjacent cells; and they specify the intracellular location of the wing hair formation. Unsolved questions include how the above 2 categories of regulators are functionally related to each other and why Fz is relocalized at distal cell borders in the first place. We previously proposed that cellular mechanisms underlying this relocalization include polarized transport of Fz-containing vesicles along P–D-oriented non-centrosomal microtubules (MTs). We have been analyzing dynamics of the MTs and movements of the vesicles to elucidate 2 questions: first, how do the MTs become aligned along the P–D axis? Second, why are the vesicles transported distally? Our quantitative in vivo imaging has shown that Dachsous and Fat control alignment and asymmetry of the MT growth, and it has also revealed statistical properties of the vesicle movements, which will give us insight into the asymmetric relocalization of the core group.

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