Furthermore, we show that both the single known Aplnr ligand, Apelin, and the canonical Gα/i/o proteins that signal downstream of Aplnr are dispensable for Aplnr function. This work suggests a novel mechanism for Aplnr signaling in the establishment of a niche required for the proper migration/development of myocardial progenitor cells. Current work is focused on determining the alternate fate or location of cells destined for the heart-forming region in the absence of Aplnr signaling and when migration of these cells goes awry. The non-autonomous cue mediated by Aplnr signaling is also being investigated.

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Program/Abstract # 280
Cardiac BAF complex promotes heart progenitor differentiation and migration in the zebrafish embryo
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Congenital heart defects and adult-onset heart disease are among the most critical health problems in developed countries. A greater understanding of cardiac progenitor biology will ultimately be essential for regenerative and early-intervention therapeutic applications. At the onset of cardiomyocyte differentiation, a cardiac progenitor-specific gene expression module must somehow be initiated. This initial event must depend on appropriate epigenetic regulation activities, including chromatin-remodeling, which can modify DNA-histone interactions, thereby changing the availability of transcription factor binding sites. In eukaryotes, the BAF (Brg1 associated factor) complexes are large multi-subunit 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 is sufficient to promote differentiation of mesodermal cells to cardiomyocytes in murine embryos. To uncover the endogenous role of this cardiac BAF (cBAF) complex in cardiac progenitors, we have used the zebrafish model. We first transplanted cells overexpressing gata5/baf60c to a wildtype host and found these cells could spontaneously migrate to the heart-forming region and contribute to myocardium, endocardium and smooth muscle at outflow tract. Remarkably, this occurred independent of the location 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 dispensable for cBAF complex-driven cardiac progenitor migration and differentiation. Global overexpression of these three genes elevated the expression of heart-specific genes, resulting in an enlarged heart. In a fish embryonic cell culture/induction system the overexpression of cBAF also promoted differentiation of contractile cardiomyocyte. 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 downregulation of myocardial gene expression, with the morphants displaying severe heart defects. The ultimate fate of cBAF cells can be modulated, as shown by Fgf signaling inhibition leading to decreased myocardial, but not endocardial, differentiation of cBAF cells. Therefore, cBAF (Gata5/Smarc3b) can promote formation of cells that home to the heart-forming region regardless of inhibitory signals in the embryo. As these cells can form all the lineages of the developing heart, these results show that cBAF can drive, in vivo, a CPC-like state.

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Program/Abstract # 281
Investigating an interchangeable potential between heart and gut mesothelial development
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The mesothelium is an epithelial sheet that covers organs in the coelomic cavity and is involved in development of the vascular system. In the developing heart, the proepicardial organ (PE), migrates to and over the heart to form the epicardium, and undergoes epithelial–mesenchymal transition (EMT) to give rise to the cells of the coronary blood vessels. The gut mesothelium (GM) serves as a major source of vascular smooth muscle cells for the gut tube in development. The role of mesothelial cells in both the heart and gut in the formation of blood vessels suggest that there may be similarities, possibly an interchangeable potential, in mesothelial development that exists among coelomic organs. To test the interchangeable potential of mesothelial cells, we used the chick-quail chimera system to transplant quail PEs into the peritoneal cavity of a chick embryo and quail GM cells into chick pericardial cavities. Our initial findings have revealed that both cell types have the potential to migrate into organs in the coelomic cavities, but PE cells do not incorporate into the endogenous GM, while GM cells will incorporate into the endogenous epicardium. However, in both systems, transplanted PE and GM cells become positive for smooth muscle. Taken together, our current data suggest that although the epicardium and GM appear similar in structure in the embryo and adult, and can potentially give rise to smooth muscle actin positive cells, we observe fundamental differences in how the mesothelium develops in the heart and gut.

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Program/Abstract # 282
The role of β-catenin and Eomesodermin in the establishment of progenitor and stem cell lineages during intestinal endodermal development
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Many disorders are a direct result of the impaired development of the primitive gut tube, which is derived from the endodermal germ layer. Although the canonical Wnt pathway is central for many developmental processes, few studies have examined Wnt and its key player, β-catenin, in early endoderm specification. Similarly, Eomesodermin has only recently been implicated in definitive endoderm development. In addition, many of the genes that, in articulation with Eomesodermin, orchestrate trophectoderm lineage establishment in the early embryo, including Nodal, Cdx2, Fgf4 and Ascl2, will later prove decisive in initiating posterior endodermal fates and intestinal identity. In order to determine the role of β-catenin and Eomesodermin in the regional specification of gut endoderm progenitors, we designed a novel approach combining Cre-mediated mutagenesis and