Program/Abstract # 421
Evolutionary conservation of the role of Sox6 in terminal differentiation of skeletal muscle
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Recent findings in mice and zebrafish (Hagiwara et al. Dev Dyn 236: 2062–; von Hofsten et al. EMBO Rep 9: 683–) suggest that the role of Sox6 in skeletal muscle development is conserved in vertebrates. In mice, it has been shown that Sox6 null skeletal muscle sustains expression of slow fiber specific genes in the fetal and early postnatal stages. Based on this observation, we have proposed that Sox6 functions as a suppressor of slow fiber specific genes in developing muscle. In zebrafish, Sox6 has also been shown to function as a suppressor of slow fiber specific genes. These results suggest, although body patterns and temporal emergence of slow and fast fibers differ, the role of Sox6 in muscle development is evolutionarily conserved. Here, we report our recent data concerning the role of Sox6 in vertebrate skeletal muscle development. First, using Sox6 conditional knockout mice, we show that the slow fiber phenotype is maintained, and even more exaggerated, in adult Sox6 null skeletal muscle. Second, to examine the conserved nature of Sox6 function, the role of Sox6 in Xenopus muscle is being investigated. We report, in Xenopus: 1) Sox6 mRNA expression in embryonic muscle corresponds to the developing fast fibers, and 2) Sox6 overexpression by the Sox6 transgene has a negative effect on myoblast fusion. These new findings indicate that: A) Sox6 likely determines the fiber type specific gene expression pattern at the very beginning of the muscle fiber type differentiation, B) Sox6 may also play a role in myoblast fusion, and C) Sox6 function as a suppressor of slow fiber specific genes is conserved in vertebrate skeletal muscle development.

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Program/Abstract # 422
Lrp4 and the mammalian neuromuscular junction
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Regional specialization of the pre- and postsynaptic membrane is a common feature of all synapses. At vertebrate neuromuscular synapses, neural Agrin binds to Lrp4 in muscle, which in turn activates MuSK, a receptor tyrosine kinase. Activation of MuSK leads to pre- and postsynaptic differentiation. By mutating the intracellular domain of Lrp4, I demonstrate that the extracellular domain of Lrp4 is sufficient to mediate postsynaptic differentiation in cultured myotubes. To address the function of Lrp4 in synaptogenesis in vivo, I have generated mice carrying transgenes that confer muscle-specific expression of wild-type and mutant forms of Lrp4. I am currently crossing these transgenes into / Lrp4−/− mutant mice to assess the contribution of muscle-derived Lrp4 in synapse formation and the role of the intracellular domain of Lrp4 in presynaptic differentiation in vivo.

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Program/Abstract # 423
Evidence for a rudimentary colon in the elasmobranch, Leucoraja erinacea
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The emergence of aquatic animals onto land 370 mya required development of a water-absorbing colon in the digestive tract to prevent desiccation. The elasmobranch, Leucoraja erinacea provides a system in which to investigate how morphological changes occur in the vertebrate digestive tract during evolution. The cartilaginous fish are nearly isotonic with their ocean environment and thus do not actively drink seawater to maintain osmotic consistency. Despite this, we have histological, immunohistochemical and physiological evidence that a region of the spiral intestine in marine elasmobranchs can absorb water. High concentrations of acid mucins and the water specific channel protein AQ4 are expressed in the distal-most region of the skate spiral intestine. In addition, we found water absorption in the spiral intestine occurs at higher rates than the stomach in L. erinacea. Water absorption is unaffected by increases in lumen pressure, suggesting that water transport across the membrane is not due to changes in osmotic pressure, but is the result of facilitated diffusion likely through aquaporins. Furthermore, Hoxa13 and Hoxd13 are expressed in the developing skate gut, suggesting conserved roles for Hox genes in patterning the early colon. Evidence of a colon in L. erinacea is surprising, since the formation of a colon was considered to be an adaptation to the evolution of terrestrial life and not a marine novelty. Our finding that the L. erinacea spiral intestine absorbs water is a novel function for the intestine of cartilaginous fish and suggests several models for colon development in the vertebrate lineage.

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Program/Abstract # 424
Evolution of pancreatic endo- and exocrine cells in deuterostomes
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The pancreas is a vertebrate endocrine/digestive organ that develops from foregut endoderm and plays an important role in metabolic regulation. Within the pancreas are the hormone-secreting islet cells (endocrine) and digestive enzyme-secreting acinar (exocrine) cells. The transcription factors Pdx1 and Ptf1a are necessary for endo- and exocrine tissue development in vertebrates. Together they are sufficient to induce ectopic pancreatic tissue in naïve vertebrate gut endoderm, suggesting they play a key role in the initial activation of the pancreatic developmental plan. Invertebrate deuterostomes and some fish lack more specialized gut organs, such as the pancreas. In these organisms, pancreatic function is instead accomplished by endo- and exocrine cells scattered throughout the lining of the gut. How did this change in the organization of pancreatic cells, from dispersed to localized to a single gland, occur during deuterostome evolution? To address this we are currently studying the expression and function of Pdx1, Ptf1a, and insulin in the hemichordate marine acorn worm, Saccoglossus kowalevskii. These basal deuterostomes show a remarkable similarity in early body plan organization to vertebrates but lack a pancreas, making Saccoglossus an attractive model for studying the evolution of deuterostome pancreatic development. Our results indicate that Pdx1 and Ptf1a are fairly well conserved within the Saccoglossus genome and along with insulin, are expressed in the gut during development. Co-expression studies