proliferating cells but only in differentiated pineal photo-receptors with a circadian rhythm of expression, displaying high levels during the dark and very low levels during the light period. We found that Xbsx plays a role in controlling the cell proliferation rate during pineal development. Indeed, overexpression of a glucocorticoid-inducible form of Xbsx induces a reduction of BrdU positive cells while antisense morpholino oligonucleotide injection exerts opposite effects. In agreement with recent findings indicating a circadian control of cell cycle in a variety of organisms, we observed that pineal cell proliferation is characterized by circadian fluctuations in Xenopus embryos. We are currently testing whether Xbsx can control both pineal cell proliferation and its circadian rhythm, thus representing a link between these two essential biological processes.

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Program/Abstract # 373
Mig-2 is required for normal myogenesis in zebrafish
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Integrins are required for normal muscle differentiation, and disruptions in integrin signaling result in human muscle disease. However, the intracellular components that regulate integrin function during myogenesis are poorly understood. Unc-112 is an integrin associated protein required for muscle development in C. elegans. We show here that Mig-2, the vertebrate homologue of Unc-112, plays a critical role in zebrafish myogenesis. Morpholino-mediated knockdown results in a severe myopathy characterized by abnormal body shape, small, disorganized muscle compartments, and alterations in myocyte structure. In common with other myopathy phenotypes seen in zebrafish, morphants displayed defects in swimming and U-shaped somites. Histological analysis further revealed that Mig-2 knockdown altered the proper formation of somatic boundaries, one of the earliest steps in myogenesis. However, Z-bands were present in the muscle of morphants, indicating that Mig-2 does not play a primary role in sarcomerogenesis. Taken together, these results indicate that Mig-2 is a critical regulator of primary myogenesis and is an essential component of integrin dependent functions in muscle.

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Program/Abstract # 374
A screen for recessive mutations affecting mouse limb development
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Despite current knowledge on the genes controlling patterning along the primary axes in the developing limb, there are gaps in our understanding of how a limb is built. For example, it is not known how early anterior–posterior or dorsal–ventral identity is imparted to the limb. Clearly, there is much to learn about the early stages of limb development and the identification of new genes required for limb growth and patterning is needed. To broaden our insight into the genetic mechanisms underlying limb formation and patterning we performed a chemical based mutagenesis screen in the mouse. Our previous studies have shown that forward genetics screens are feasible in the mouse and are an excellent, unbiased method to uncover factors critical for a wide variety of developmental processes. In a screen of ~100 pedigrees we obtained three recessive mutants that affect various aspects of limb development. Two of these, hitchhiker and ker-ouac show preaxial polydactyly and affect anterior–posterior patterning. In contrast, shorthand was identified by defects in proximal–distal outgrowth of the limb. shorthand Mutants show an expansion of Fgf expression during early limb development followed by ruptures in the epithelium similar to alpha3/alpha6 integrin double mutants. The genomic regions linked to these mutants do not contain known limb patterning genes indicating that we have identified novel genes required for limb development. The characterization and cloning of the genes affected in these mutants should provide a better understanding of anterior–posterior patterning and Fgf regulation during limb development.

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Program/Abstract # 375
Transcriptional control of limb initiation and limb-type identity
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We are interested in identifying the signals that control processes from limb bud initiation to final morphogenesis of the individual elements of the limb. Using mouse, chick and zebrafish embryos, we are exploiting gene misexpression and gene deletion approaches to study the function of two members of the T-box family of transcription factors, Tbx5 and Tbx4, and a paired-type homeodomain factor, Pitx1 in limb initiation and specification of limb-type identity. We have carried out gene deletion–gene replacement experiments in which forelimb-restricted Tbx5 was replaced with hindlimb-restricted Tbx4.