Hox genes play a critical role in the patterning of the axial skeleton. This has been clearly demonstrated in mice mutant for the entire *Hox10* or *Hox11* paralogous group. *Hox10* triple mutants demonstrate an anterior homeotic transformation of all lumbar vertebrae toward a thoracic fate with rib processes protruding from each vertebral segment through the lumbar and sacral regions. *Hox11* triple mutants display normal development of the thoracic and lumbar region; however, no sacral vertebrae are formed. The vertebral elements in the sacral region are transformed to a lumbar fate. Although genetic analyses have provided important insight regarding *Hox* gene patterning of the axial skeleton, the molecular mechanisms involved in this process are not understood. In order to elucidate the genes and pathways that are regulated by Hox in axial patterning, I have performed microarray analysis on isolated sclerotomal cells, the precursors of vertebrae, from wild type and *Hox11* triple paralogous mutants at several developmental stages to identify genes that are differentially expressed in these animals. This analysis has uncovered differential expression of several genes, including several BMP pathway members. *In situ* hybridization analyses have shown that *Bmp2* expression is significantly reduced in the developing sacral region of *Hox11* mutants. Together, our data suggest that regional *Hox* expression might control localized expression of *Bmps* during morphogenesis of the axial skeleton.

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Program/Abstract # 467
Hox genes control the timing of somite precursor cells ingression during gastrulation in the chicken embryo
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A striking characteristic feature of the spine is the subdivision of groups of vertebrae into anatomical domains such as the cervical, thoracic, lumbar, sacral and caudal regions. This axial regionalization is controlled by a set of transcription factors called Hox genes. These genes are arranged along chromosomal domains, which are linearly deployed during embryonic development – a property termed colinearity. This striking genomic organization is translated into the colinear Hox expression domains during gastrulation. Recently, it has been shown that the genes from the *Hoxb* cluster are activated in the somite precursors of the epiblast in a temporal sequence that reflects their colinear arrangement and subsequently controls the progressive ingression of somite precursors into the nascent paraxial mesoderm (Iimura et al., 2006). Because the *Hoxa*, *c* and *d* clusters are expressed also in the epiblast during gastrulation, we explored the hypothesis of a conserved role of Hox paralogs during this process by overexpressing various Hox genes from the four clusters using the successive electroporation technique in the chicken embryo. We show that all of the paralogs we tested control the timing of epiblast cells ingression into the primitive streak in a colinear fashion. In parallel, we are currently using a microarray-based approach to identify the Hox target genes responsible for the progressive ingression of the somite precursors.

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Program/Abstract # 468
Role of Hox11 genes in anteroposterior patterning of nephrogenic mesenchyme
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Hox genes are critically important for anteroposterior (AP) patterning in a wide variety of organisms. Specific spatial and temporal expression of *Hox* genes along the AP body axis is necessary for proper embryonic development. In the mammalian kidney, it has been shown that *Hox11* paralogous genes are essential for ureteric bud induction, one of the first steps in kidney organogenesis. Further work has demonstrated that Hox11 proteins directly regulate *Six2* and *Gdnf* to control these early processes. Embryos in which five of the possible six alleles are mutated do not exhibit loss of induction, but demonstrate severe AP patterning defects in the nephrogenic mesenchyme. In five allele mutants, the mesonephros persists at later developmental stages and the mesonephric mesenchyme does not separate from the metanephric mesenchyme. These animals die perinatally due to hydronephrosis at the ureteric pelvic junction. Here, we begin to analyze the structural and molecular phenotype of the nephrogenic mesenchyme in these mutants. We believe that these studies will lead to an understanding of how *Hox* genes pattern the nephrogenic mesenchyme along the AP axis.

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Program/Abstract # 469
Functional relevance of Hox-specified positional identities in adult vasculature
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Hoxa3 and *Hoxc11* are expressed in vascular smooth muscle cells (VSMCs) and endothelial cells (ECs) in regionally restricted patterns that closely resemble their respective embryonic expression domains (Pruett et al., 2008). To investigate whether this regionalized expression plays a role in determining the physiological diversification of vessel segments we explored the functional relevance of *Hoxc11* in VSMCs both in vitro and in vivo. Primary cultures of VSMCs established from explanted hindlimb vessel segments of *Hoxc11* reporter mice revealed persistent reporter transgene expression in distinct VSMC subpopulations facilitating phenotypic characterization of *Hoxc11*-positive versus -negative VSMCs. In vitro wound healing and serum-response assays provide evidence that *Hoxc11* expression promotes differentiation towards a contractile SMC phenotype. These results were supported by subsequent functional assays involving *Hoxc11*-transfected mouse vascular cells (MOVAS). These in vitro functional data suggest an important role for *Hoxc11* in the regulation of the phenotypic properties of VSMCs.To study the functional relevance of *Hoxc11* expression in vivo we adopted an innovative murine, doxycycline (Dox)-inducible transgene system, which results in the systemic over-expression of *Hoxc11* in VSMCs using VSMC-specific control elements of the Transgelin (SM22-alphaA) promoter. Together these in vitro and in vitro analyses demonstrate a significant role for Hox code-specified positional identities in the vascular network.

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Program/Abstract # 470
Identification and characterization of Six1 enhancers
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Six1, one of the members of Six homeobox family genes, is expressed in sensory organs and ganglia such as olfactory epithelium,