of various molecules and signaling pathways in mouse mesendoderm formation and axial elongation morphogenesis.

doi:10.1016/j.ydbio.2010.05.207

Program/Abstract # 167
BMP signaling through ACVR1 is crucial for establishment of the left–right asymmetry via proper formation of node cilia in the mouse
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Bone morphogenetic proteins (BMPs) have multiple functions including their role in the establishment of left–right patterning in vertebrate development. Recently, we discovered that BMP type 1 receptor Acvr1 in the epiblast is required for proper left–right patterning. To address further how Acvr1 is involved in the process, we utilized a conditional gene inactivation strategy to rescue the gastrulation defects of the Acvr1 null mutation. Mosaic inactivation of Acvr1 mutants in the epiblast by using Mox2-Cre (Acvr1:Mox2-Cre) resulted in abnormal heart looping and bilateral expression of left side markers in the lateral plate mesoderm. The mutant embryos displayed an abnormal cilia development that resulted in a defect of a cilia-driven leftward fluid. Complete inactivation of Acvr1 in the epiblast by using Sox2-Cre resulted in complete lack of cilia in the node. Expressions of intraflagellar transport genes, which are important for node cilia formation, were downregulated. Interestingly, Acvr1:Mox2-Cre embryos displayed abnormal cilia development in a ventral part of the neural tube. Mouse embryonic fibroblasts deficient in Acvr1 fail to form the primary cilium, when stimulated by serum starvation. These suggest that ACVR1 is essential for proper development of primary cilia by regulating cell cycle progression to establish a left–right asymmetry at the node.

doi:10.1016/j.ydbio.2010.05.208

Program/Abstract # 168
Functional analysis of the mouse Nodal antagonist, Cerl2, during left–right axis formation
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Although recently our understanding of how the LR asymmetry is generated in vertebrate embryos has seen rapid progress, many important questions remain to be explained. In mouse embryos, the leftward flow of the extra-embryonic fluid in the node cavity, called nodal flow, seems to be the symmetry-breaking event. However, it is not yet know how this flow functions or how the asymmetric signal(s) generated in the node is/are transferred to the lateral plate mesoderm. The mouse gene cerberus-like2 (cerl2) encodes a 20-kDa protein with a predicted signal peptide sequence and a cysteine-rich domain (CRD) containing nine cysteines characteristic of the Cerberus/DAN family. Whole-mount in situ hybridization studies showed that cerl2 transcripts could be first detected in a horseshoe-shaped expression pattern in the perinodal region of the mouse embryo (E7.0), resembling Nodal expression at this stage. At stage E7.5, expression of cerl2 begins to decrease in intensity on the left side, and by early somitogenesis (E8.5), it can be strongly detected in the right side of the node, assuming a complementary expression pattern to that observed in Nodal. Furthermore, it was shown that Cerl2 activity is upstream of the Nodal receptor inhibiting Nodal and its downstream targets. A physical interaction between these two proteins exists, which suggests that Cerl2 is a secreted Nodal antagonist. Here, to elucidate the role of Cerl2 protein in the early events of symmetry breaking the functional activity of this Nodal antagonist will be discussed.

doi:10.1016/j.ydbio.2010.05.209

Program/Abstract # 170
Left–right determination requires endoderm function in mice
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The asymmetric placement and morphogenesis of visceral organs along the left–right (LR) axis is crucial for proper embryonic development. The development of LR asymmetry requires symmetry breaking at the node and the left–side specific expression of the TGFβ ligand, Nodal in the lateral plate mesoderm (LPM) as a left-side determinant at E8.5. Our previous work has shown that Nodal expression in the node is required for the expression of Nodal in the left LPM, although the mechanism by which the asymmetric signal generated at the node is transferred to the LPM is still unknown. To test the significance of definitive endoderm in LR asymmetry, we have investigated the role of Sox17, a HMG-box transcription factor required for endoderm differentiation in mice. The Sox17 expression pattern suggests that endoderm may be involved in node formation and LR signal transfer. Analysis of Sox17 mutant embryos showed abnormal node morphogenesis and absence of Nodal expression in the LPM, suggesting that endoderm differentiation is required for LR asymmetry. The reduced node size and altered protein localization in