Program/Abstract # 301
Fgf4 and Fgf8 are required for maintenance of the primitive streak and somitic clock
Nakisha D. Holder [1], Catherine Wilson [1], Cindy Elder [1], Terry P. Yamaguchi [1], Gregg Duester [2], Mark Lewandoski [1]
[1] *Cancer and Developmental Biology Laboratory, NCI-Frederick, NIH, Frederick, MD, USA*
[2] *Burnham Institute for Medical Research, La Jolla, CA, USA*

Fibroblast growth factor (FGF) activity has been implicated in mesoderm induction and migration, as well as somitogenesis. To study the role of FGF signaling in the emerging mesoderm we inactivated both *Fgf4* and *Fgf8* in the primitive streak (PS), utilizing TCre, a transgene in which Cre is controlled by Brachyurany regulatory elements active in the PS. *Fgf4/8* inactivation results in embryonic lethality due to a severe caudal truncation such that development of all germ layers ceases posterior to the eighth somite due to loss of the PS by E8.5. Prior to PS loss at E8.0, *Fgf4/8* are required to maintain *Brachyura* and *Wnt* gene expression. Preliminary data eliminate changes in apoptosis and proliferation as causes of loss of the PS. TCre/Fgf4/Fgf8 mutant embryos have defects in anterior–posterior patterning of somites as indicated by a shift in the expression of *Mesp2*, which marks the initiation of somitogenesis and a reduction in *Hes7*, an oscillatory gene and part of the somitic clock. Retinoic acid (RA) activity, which is has been postulated to antagonize the caudal–rostral FGF gradient along the anterior–posterior axis of the embryo, is up-regulated in TCre/Fgf4/Fgf8 mutant mice. Our data indicate that *Fgf4* and *Fgf8* play fully redundant roles in maintaining the primitive streak stem cell population, play a role in the maintenance of the clock genes required for somitogenesis and are active in maintaining a balance between FGF and RA signaling.

doi:10.1016/j.ydbio.2007.03.602

Program/Abstract # 302
***Dkk1* and *Wnt3* interaction is critical for head morphogenesis in the mouse**
Patrick P. Tam [1], Samara L. Lewis [1], Poh-Lynn Khoo [1], R. Andrea De Young [1], Heiner Westphal [2]
[1] *Embryology Unit, Children's Medical Research Institute, New South Wales, Australia*
[2] *Laboratory of Mammalian Genes and Development, National Institute of Child Health and Human Development, National Institute of Health, Bethesda, MD 20892, USA*

Dkk1 is essential for head formation and acts by inhibiting canonical Wnt signalling. Loss of *Dkk1* function leads to ectopic WNT signals in anterior germ layer tissues of the gastrulating mouse embryo and head truncation. A study of compound *Dkk1;Wnt3* mutant embryos reveals an interaction between the activity of these two genes is required for embryonic patterning. Compound *Dkk1;Wnt3* heterozygotes display a range of abnormalities in head and trunk morphology, suggesting that an apparently balanced gene dosage of *Wnt3* and *Dkk1* may not achieve a proper level of signalling. However, by reducing the gene dosage of *Wnt3* over the *Dkk1*−/− genotype, the *Dkk1*-null truncated head phenotype can be rescued, showing that head development is sensitive to the level of signalling. The spatial overlap of the expression domains of *Wnt3* and *Dkk1* before and at gastrulation strongly implicates that genetic interaction during early embryogenesis is crucial for head morphogenesis.

doi:10.1016/j.ydbio.2007.03.603

Program/Abstract # 303
Regulation of a novel skeletal muscle signaling center at the occipitocervical somite boundary
Megan Rowton, Douglas Anderson, Bryan Huber, Alan Rawls
School of Life Sciences, Arizona State University, Tempe, AZ, USA

Skeletal muscle groups located in the neck region have evolved along with the and cartilage to control the rotation of the skull, swallowing, respiration and vocalization. Vocalization defects (dysphonia) and swallowing defects (dysphagia) have been implicated in several congenital diseases. Laryngeal, tongue, tracheal, diaphragm and cervical muscles are derived from the occipital and cervical somites. However, little is known about the embryonic events that lead to the development of these muscles. We have used a muscle-specific lacZ transgene to perform a detailed study of myotome formation in this region of the mouse embryo. Our analysis revealed that myogenesis is initiated at the occipitocervical boundary and progresses both rostrally and caudally. Myotome formation as described by the site of myoblast entry into the myotome and the direction of myocyte elongation occurs in a mirror image on either side of the boundary. This indicates that early events in myogenesis are regulated by positional information along the rostrocaudal axis. Members of the Hox 3 gene family are expressed in somites at the occipitocervical boundary. We found that compound Hox 3 mutant neonatal mice exhibit muscle defects in the intrinsic laryngeal muscles, pharyngeal constrictor muscles and deep cervical muscles. Our current observations on the regulation of this novel signaling center will be discussed.

doi:10.1016/j.ydbio.2007.03.604

Program/Abstract # 304
Bone morphogenetic proteins (BMPs) direct formation of a signaling center that regulates facial development
Ralph S. Marcucio, Silvia Foppiano, Diane Hu
Dept. of Orthopaedic Surgery, University of California San Francisco, CA, USA