indicates elevated Wnt signaling in Wise-null tooth germs, and reveals that loss of Wise results in survival and accelerated development of a vestigial tooth bud in the normally toothless diastema region. Gene expression analysis indicate that FGF and Shh signaling is also elevated in Wise mutant tooth buds consistent with the current model that Wnt signaling acts upstream of those pathways to regulate tooth development. In addition, when over-expressed with a Keratin 14-Wise transgene, Wise can disrupts development of ectodermal organs including hair follicles and teeth mimicking other Wnt antagonists. Our results demonstrate that Wise acts as a major regulator of tooth survival, growth and patterning through restricting Wnt activity and its downstream signaling pathways.

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Program/Abstract # 210
Role of WNT11 during avian facial morphogenesis
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Perturbations in normal process of face development cause cleft lip to develop, a condition that affects 1:800 babies each year. Wnts are secreted glycoproteins and there are 19 in mammals. Little is known about the role of Wnts in facial morphogenesis. Here, we investigated the hypothesis that *WNT11* regulates the process of lip fusion. *WNT11* is first localized in the mesenchyme of the maxillary prominence (mxp) close to where the lip will fuse. Later *WNT11* expression is shifted out of the fusion zone and is restricted to the lateral mesenchyme under the eye. *WNT11* is never expressed in the frontonasal mass (fnm) or the middle of the upper beak thus might act as a negative regulator of lip fusion. In the present study, we found that misexpression of *WNT11* in the maxillary prominence/frontonasal mass using an avian retrovirus leads to large gaps in the soft tissues and skeleton. These effects are equivalent to cleft lip in humans. Recently WNT11 polymorphisms have been found in patients with clefts. We also found that WNT11 overexpression down-regulates the expression of *MSX1* whereas upregulates *DKK1* (canonical Wnt antagonist) thus the cleft phenotype caused by WNT11 is due to blocking the activity of canonical WNT signalling. Further we also found that SHH, BMP4 and FGF8 negatively regulate *WNT11* expression whereas RA induces *WNT11*. These results are the first to show the context dependent regulation of *WNT11* and its interaction with the other known signalling pathways involved in normal facial development. Thus, we identified WNT11 as a new gene involved in facial clefting.

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Program/Abstract # 211
Folate's role in the development of the face, jaw, palate and teeth — Does one size fit all?
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Prenatal folate supplementation inhibits the onset of neural tube defects such as cranial facial malformations which are diagnosed in 75% of all congenital birth defects in humans, affecting the head, face and oral cavity. This study examines the effects of folate concentration on cranial facial, palate and tooth development. Timed pregnant ICR mice were treated on the evening of either E11 or E14 with sterile saline, 1 X FA (12 mg/kg folinic acid) or 4 X FA (48 mg/kg folinic acid). On days E12 and E13 they were treated in the morning with either sterile saline or 20 mg/kg Methotrexate (MTX) and 1 X FA or 4 X FA and in the evening either sterile saline or 1 X FA or 4 X FA resulting in 4 experimental groups for each treatment period. Various levels of folate supplementation have led to stage specific differences in jaw and tooth primordia formation. Clefting was only observed in the 1 X FA E14 group of embryos suggesting that the administered folate concentration was insufficient. Alterations in embryonic head and jaw shape were noted for both the E14 and E17 embryos with the most pronounced differences being seen in the 4 X FA groups. The changes seen in either E14 or E17 embryos were not as pronounced among adult mice from these treatment groups suggesting that some type of compensatory mechanism might be at work. This study provides insight into the role of folate concentration and timing during cranial facial embryonic development.

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Program/Abstract # 212
The role of actin dynamics and the PCP pathway in mammalian convergent extension and establishment of leftright asymmetry
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In many model organisms the planar cell polarity (PCP) pathway is required for the morphogenesis of embryonic structures. These changes in cellular architecture are achieved by the pathway's ability to rearrange the actin cytoskeleton within a single cell. In accord with these observations, it has previously been shown that proteins that control actin dynamics may also influence the PCP pathway. An example of this is the protein Cofilin, which severs existing actin filaments and is required for cell motility. When Cofilin is mutated in *Drosophila* there are defects in the PCP pathway, suggesting that the actin cytoskeleton is required for PCP signaling. Mutations in the PCP pathway in mice have been shown to cause a defect in axis elongation and neural tube closure; however, these mutations do not cause as severe a defect as similar mutations in other vertebrate systems. Therefore, to further investigate the role of the PCP pathway in morphogenesis of the mouse embryo we are investigating a genetic interaction between one of the core PCP proteins, Vangl2, and Cofilin, a protein that regulates the actin cytoskeleton. Through this work I have shown that these two genes cooperate in the morphogenesis of the notochordal plate and in the positioning of nodal cilia that are required for the establishment of leftright asymmetry.

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Program/Abstract # 213
Dissecting the role for ciliary genes in intrinsic cell polarity during PCP signaling
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Planar cell polarity (PCP) refers to coordinated orientation of intrinsically polarized cells along the plane of a cell sheet. During PCP signaling, conserved PCP proteins form asymmetric membrane-associated complexes to establish a planar axis for neighboring cells. The mechanism underlying downstream intrinsic cell polarization during PCP signaling, however, is not clear. The mammalian hearing organ represents a distinct form of PCP. It is showcased by the uniform orientation of V-shaped hair bundles, consisting of microvilli-derived stereocilia and a single primary cilium, at the apical surface of sensory hair cells. Previously, we showed that the inactivation of ciliary genes does not affect the formation of asymmetric membrane-associated PCP