The development of the face depends on the regionalization of neural crest precursors into distinct dorsal and ventral domains. Previous research has shown that Endothelin 1 (Edn1) is required for patterning the ventral face, in part by regulating *Dlx* expression; however, little is known about the factors required for development of the dorsal face. We have recently identified a mutation in the zebrafish gene *jag1b* that results in dorsal-specific defects. In *jag1b* mutants, we observe an expansion of *Dlx* genes into the dorsal domain. Jagged is one class of ligands for Notch receptors. Here we show that overactivation of the Notch pathway results in loss of ventral genes and corresponding defects in the ventral facial skeleton, further supporting a role of Jagged-Notch signaling in promoting dorsal facial identity. In addition, we find an autoregulatory loop of *jag1b* and *notch2* expression that propagates in a dorsal to ventral wave of Notch activity during facial development. Based on these results, we propose a model in which dorsal–ventral facial identities are specified by dynamic interactions between a wave of Notch signaling arising dorsally and a gradient of Edn1 signaling arising ventrally. In our model, expression of *jag1b* localizes Notch activity to dorsal skeletal precursors. How then is *jag1b* expression established dorsally? Here we show that the endoderm is required for *jag1b* expression. Moreover, as the endoderm expresses *Fgfs*, we next investigated the role of Fgf signaling in patterning. Using a transgenic to block Fgf signaling at patterning stages, we observe a transformation of dorsal structures to a ventral identity, a defect similar to that observed in *jag1b* mutants.

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Program/Abstract # 491
Hand2 loss leads to aglossia from failure to repress Dlx5/6
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Lower jaw development is a complex process orchestrated by signaling cascades that are regulated temporospatially and are constantly refined through permissive and inhibitory signals. We have previously shown that endothelin-A receptor (Ednra) signaling is crucial for establishing the identity of cranial neural crest cells (NCCs) in the mandibular pharyngeal arch through a mechanism that involves Dlx5 and Dlx6. Dlx5/6 in turn induce expression of the gene encoding the basic helix–loop–helix transcription factor Hand2. While this pathway places Hand2 at the center of a complex signaling cascade, little is known about the function of Hand2 in mammalian facial development because *Hand2*$^{-/-}$ embryos die by embryonic day (E) 10.5 from vascular failure. To circumvent this lethality, we created a conditional targeted *Hand2* mouse line using a Cre-*lox*P approach. Using the *Wnt1-Cre* mouse line, we selectively deleted *Hand2* within all NCCs. We find that *Hand2* conditional knockout mice exhibit facial defects that include mandibular hypoplasia and absence of the tongue (aglossia). The aglossia is preceded by aberrant maintenance of *Dlx5* expression in the disto-oral mandibular arch mesenchyme. In vitro studies show that Hand2 represses the Dlx5/6 pharyngeal arch-specific enhancer. Together, these data suggest that Hand2 normally ensures normal tongue development by repressing *Dlx5/6* expression within the disto-oral mandibular arch. In the absence of Hand2, *Dlx5/6* expression is maintained and ectopically activates an osteogenic program at the expense of a tongue development program.

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Program/Abstract # 492
prdm1 is required for zebrafish craniofacial development
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Defects in neural crest cell (ncc) differentiation result in many human congenital birth defects. A better understanding of cell fate determination, migration, and differentiation of nccs during formation of the craniofacial skeleton is an important step towards developing approaches to prevent and repair human ncc-associated birth defects. We focused on the role of the transcription factor *prdm1* in the differentiation of nccs into the craniofacial skeleton. It does not appear that *prdm1* is required for ncc migration but beginning at 16 hpf and continuing through 56 hpf, it is expressed in the correct temporal and spatial pattern to be involved in the differentiation of craniofacial structures. During early craniofacial development, *prdm1* is expressed in the pharyngeal arch region and later appears to be expressed in an endodermal pouch, the otic vesicle, and pharyngeal teeth. A loss of *prdm1* results in defects in posterior pharyngeal arches including a loss of cartilage and dermal bone. A reduction in Fgf and retinoic acid signaling alters *prdm1* expression suggesting that *prdm1* is operating via these signaling pathways to pattern the posterior craniofacial skeleton. Finally, loss of *prdm1* results in a reduction in proliferating cells suggesting that the cartilage defects may be due to a reduction in the number of nccs. Future experiments will further determine the interactions between *prdm1* and other known craniofacial genes as well as the function and tissue specific requirement for *prdm1* during craniofacial development.

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Program/Abstract # 493
RA-Noggin beads induce TBX22, a frontonasal mass-specific gene in the maxillary prominence, however over-expression causes clefting rather than a transformation in identity
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Previous data from our lab has shown that RA and Noggin, when applied to the early avian face, can transform the maxillary prominence to a frontonasal mass. Here we use Affymetrix microarrays to determine the transcriptional consequences, 16 h after implantation of RA-Noggin beads. We also compared expression to stage-matched normal stage 17 embryos to determine whether frontonasal mass-specific genes were induced. Chip-wide analysis revealed that the RA-noggin samples clustered together but were distinct from either the frontonasal mass or maxillary prominence. RA-noggin induced several genes that are highly expressed in the normal frontonasal mass including *TBX22, SOX8*, *ALX1*, and *OSF2*. Validation with QPCR and wholemount in situ hybridization confirmed that *TBX22* was ectopically expressed in the RA-Noggin treated maxillary prominence and that Noggin induced expression to a greater extent than RA. We then tested the effects of ectopic expression of *TBX22* using retroviruses and found that instead of inducing frontonasal mass characters such as ectopic egg teeth or cartilages, facial clefting