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Making and breaking symmetry in the zebrafish otic placode

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The vertebrate otic placode—precursor of the inner ear—has the remarkable ability to generate a mirror-image twinned organ under some experimental conditions, as originally described over eighty years ago. Understanding the generation of such duplicated structures can give us fundamental insights into mechanisms of organ patterning, tissue polarity and symmetry-breaking during embryogenesis. We have used both systemic and conditional manipulation of either Fgf or Hedgehog (Hh) signalling to generate double-anterior twinned otic vesicles in the zebrafish embryo. Although the final patterning outcome is similar, we find that the temporal and spatial responses of anterior otic markers to manipulation of each signalling pathway are distinct. Transcriptional responses to mis-expression of *fgf3* are rapid and broad, initially spanning the entire anteroposterior extent of the otic vesicle. Responses to Hh inhibition are slower, and are characterised by the de novo appearance of discrete duplicate domains of gene expression. Unexpectedly, we find that the otic epithelium still mounts a transcriptional response to late mis-expression of *fgf3*, despite a loss of competence to form a complete ear duplication. Expression of *hmx3a* shows an early transcriptional response to disruption of either signalling pathway; our data suggest that *hmx3a* is activated by Fgf signalling and de-repressed by Hh inhibition. These observations make *hmx3a* a good candidate for integrating extrinsic signalling information to give rise to the normal anteroposterior asymmetry in the otic placode. However, we find that mis-expression of *hmx3a* alone is not sufficient to generate complete anterior otic duplications. With a more detailed understanding of the events leading to duplicate mirror-image patterns in the ear, we refine our model for how anterior and posterior identity is normally assigned to the equipotential poles of the zebrafish otic placode.