Decoding Morphogen Signaling in the Developing Organ of Corti


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The mature sensory epithelium of the inner ear, the organ of Corti (OC), demonstrates exquisitely resolved patterning crucial for its function as the transducer of auditory signals from vibrations to electrochemical signals. The radial pattern—consisting of 13 to 15 adjacent cells, each with a unique functional purpose—repeats approximately 3500 times along the organ length with low variation. This pattern emerges from progenitors exposed to spatiotemporal morphogenic signals. An incompletely resolved network involving Bmp, Wnt, Notch, Fgf, RA, and Shh pathways is active during the earliest cochlear developmental stages. As a first step towards a quantitative understanding of this system, we explore the properties of the Bmp4 pathway at E12.5 by characterizing its contribution to positional information (in an information theoretic sense) and exploring mechanisms by which its activity profile may arise through simulation.

Preliminary results show a tightly distributed P-Smad signal (the Bmp secondary messenger). P-Smad takes the form optimized for information content of a linear profile over a domain spanning the future OC, mimicking the classically described profile of an ideal source-sink system. Reaction-diffusion simulations using Bmp4 transcript measurements suggest underexplored contributions from variable receptor densities and/or extracellular ligand modulators, which are implicated in many other developmental systems. However ideal, Bmp4 alone is insufficient to comprehensively specify position along the axis, corroborating partial patterning achieved within in vitro organ explants inhibited for Bmp signaling. Integrating this information with Jag1 and Wnt ligands will increase the accessible information and inform hypotheses of information transference in the developing cochlea.