HAND1 Controls Epithelial Morphogenesis and Fate Specification in a Human Pluripotent Stem Cell-Based Amnion Model

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Amniogenesis is triggered in a collection of pluripotent epiblast cells as the human embryo implants. Our previous transcriptomic analyses of stem cell-derived models of amnion implicated a potential role of HAND1, a basic helix-loop-helix transcription factor, in amniogenesis, which showed dynamic expression during amnion fate specification. Strikingly, functional studies reveal a key role for HAND1 in amnion morphogenesis and lineage progression, as loss-of-function mutation of *HAND1* results in impaired epithelial polarization and halted amnion fate specification. Molecularly, we identified *SOX7* as a downstream target of HAND1 activity, and found that *SOX7* is critical for epithelial polarization but not for amnion fate specification. Together, this study reveals a novel requirement of the HAND1-SOX7 axis in maintaining epithelial morphogenesis of developing human amnion.

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