Recommended 9.6 New Finding

# Mechanics-guided embryonic patterning of neuroectoderm tissue from human pluripotent stem cells.

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Classified as
New Finding

A highly conserved developmental event crucial for nervous system formation, neural induction, leads to differentiation of the ectoderm into a patterned tissue, containing the neuroectoderm (neural plate, or NP) and the epidermal ectoderm, separated by the neural plate border (NPB). The exposure of the embryo to diffusible signals, such as bone morphogenetic proteins (BMPs) or WNT, is critical for neural patterning. However, neural induction, like any tissue-scale morphogenetic event, occurs within the milieu of biophysical determinants, including changes in shape, number, position and force of cells. Yet it remains undetermined how these tissue-scale morphogenetic changes work in concert with signaling events mediated by diffusible signals for proper cell fate patterning during neural induction. This paper by Xufeng Xue *et al.* demonstrates that cell shape and cytoskeletal contractile forces instruct neuroepithelial/neural plate border patterning via BMP-SMAD signaling and that ectopic mechanical activation and exogenous BMP signaling modulation can perturb NPB patterning.

Using a micropatterned human pluripotent stem (hPS)-cell-based neuroectoderm model, the authors found that when plated as circular colonies, these cells self-organize and autonomously pattern neuroectoderm tissues in the presence of neural induction medium. In this configuration, cells in the colony central region differentiate into NP fate, whereas the peripheral cells commit to NPB. Interestingly, they found that cells in the periphery are positive for pSMAD1/5, whereas the colony centers remain negative. Furthermore, the authors show that mechanical stretching of the cells in the colony center leads to a reversion of the phenotype, triggering SMAD1/5 phosphorylation. In addition, through single-cell micropatterning, they found that cell spreading area positively correlates with SMAD1/5 phosphorylation. Interestingly, these assays were performed in the presence of dual SMAD inhibition in the neural induction medium, suggesting that the biophysical cues these cells are exposed to are capable of overriding the effects of exogenous BMP inhibition on SMAD1/5 signaling.

The authors propose an interesting model through which higher cell contractility and/or larger cell shape triggers SMAD1/5 phosphorylation, ultimately determining cells to commit to NPB phenotype. On the contrary, low contractility and/or smaller cell shape leads to neuroepithelial cell differentiation. Taken together, these findings reveal a critical role for biophysical cues in neuroectoderm formation during embryogenesis.

**Disclosures**
None declared

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