

DEVELOPMENT

Instructions for induction

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Neural crest cells are stem cells that appear along the border of the neural plate early in development, destined to differentiate into a wide variety of cell types throughout the body. Because interactions between neural and non-neural ectoderm and/or mesoderm were thought to be important for neural crest induction, it was previously assumed that induction occurred after neural plate formation (stage 5). Contrary to this, in new work reported in *Nature*, Basch *et al.* show that early neural crest induction occurs at or before gastrulation (stage 3), and requires the transcription

factor PAX7.

To investigate neural crest induction, the authors looked at the expression of known neural crest markers at progressively earlier stages and identified a region of PAX7 expression — first appearing with the definitive primitive streak (stage 4+) — that correlated with the putative neural crest domain. They then looked even earlier, at bilaminar chick embryos undergoing gastrulation (stage 3/4). Using a fluorescent lipophilic probe, they traced the fate of cells in the prospective PAX7 domain, prior to expression of PAX7. Cells from this region were incorporated into dorsal neural folds and, later, into the migrating neural crest cell population.

To determine whether cells within the prospective PAX7 expression domain have the ability to form neural crest cells in the absence of exogenous signals, Basch and colleagues explanted onto collagen gels several segments of a strip of epiblast — the outer layer of a blastula that gives rise to the ectoderm after gastrulation. Medial segments — between the primitive streak and the area opaca/area pellucida border — were able to generate migratory neural crest cells. No neural, node or mesodermal markers were found

in these explants, showing that they were already specified to form neural crest cells, and contradicting the previous belief that interaction between tissue layers is required for neural crest induction.

Antisense oligonucleotides were then used to block the translation of *Pax7* mRNAs to investigate the role of PAX7 *in vivo*. When these were electroporated into the presumptive neural crest domain of stage 4 embryos, there was a marked decrease in PAX7 protein levels and expression of neural crest markers compared with the contralateral side, confirming the necessity of PAX7.

These findings reveal an important role for PAX7 in neural crest formation, which is induced earlier than was previously thought and can occur independently of mesoderm and neural tissues. Preliminary findings in the same laboratory suggest that this mechanism of neural crest induction might be conserved in all amniotes.

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ORIGINAL RESEARCH PAPER Basch, M. L. *et al.* Specification of the neural crest occurs during gastrulation and requires Pax7. *Nature* **441**, 218–222 (2006)