<Further Development 17_01>

Learn How These Four Pioneer Transcription Factors Differentiate Neural Crest Cell Fates

When Foxd3, Snail, Sox9, and Sox10 are experimentally expressed in the lateral neural tube, the lateral neuroepithelial cells become neural crest-like, undergo epithelial-to-mesenchymal transition (EMT) and delaminate from the neuroepithelium:

- Sox9 and Snail together are sufficient to induce EMT in neuroepithelial cells. Sox9 is also required for the survival of trunk neural crest cells after delamination (in the absence of Sox9, neural crest cells undergo apoptosis as soon as they delaminate).
- Foxd3 may play many roles. It is needed for the expression of the cell surface proteins that are required for cell migration, and it also appears to be critical for the specification of ectodermal cells as neural crest. Inhibiting expression of the *Foxd3* gene inhibits neural crest differentiation. Conversely, when *Foxd3* is expressed ectopically by electroporating the active gene into neural plate cells, those neural plate cells express proteins characteristic of the neural crest (Nieto et al. 1994; Taneyhill et al. 2007; Teng et al. 2008).
- The *Sox10* gene appears to be one of the most critical regulators of neural crest specification. It is crucial not only for the delamination of neural crest cells from the neural tube, but also for the differentiation of the numerous neural crest lineages (Kelsh 2006; Betancur et al. 2010). Sox10 protein binds to the enhancers of numerous target genes that encode the neural crest effectors; these include the genes for some small G proteins, such as Rho GTPases, that allow cells to change shape and migrate; cell surface receptors, such as receptor tyrosine kinases and endothelin receptor (e.g., ENDRB2), that allow the neural crest cells to respond to patterning and chemotactic proteins in their environments; and transcription factors, such as MITF in the melanocyte lineage that forms pigment cells (see Figure 15.6**;** Simões-Costa and Bronner 2015).

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