<Further Development 17_02>

Induced Neural Crest Cells

Demonstration of the regulatory powers associated with the factors in this gene regulatory network and neural crest development have recently been applied to the in vitro reprogramming of human fibroblasts into induced neural crest cells, or iNCCs (Figure 1, parts A and B). Primarily through the modulation of Wnt and dosed induction of Sox10, human fibroblasts are able to be reprogrammed into iNCCs, which as multipotent stem cells can then be coaxed into all the neural crest lineages seen in the developing embryo (Kim et al. 2014). This characteristic continues to lend support to the inherent multipotency of neural crest cells. The ability to generate iNCCs offers the opportunity to study neural crest-related human diseases at the developmental level, such as patients with familial dysautonomia, a congenital and degenerative disease affecting the sensory and autonomic nervous system (Figure 1, parts C and D; Kim et al. 2014; comment by Varum and Sommer 2014).

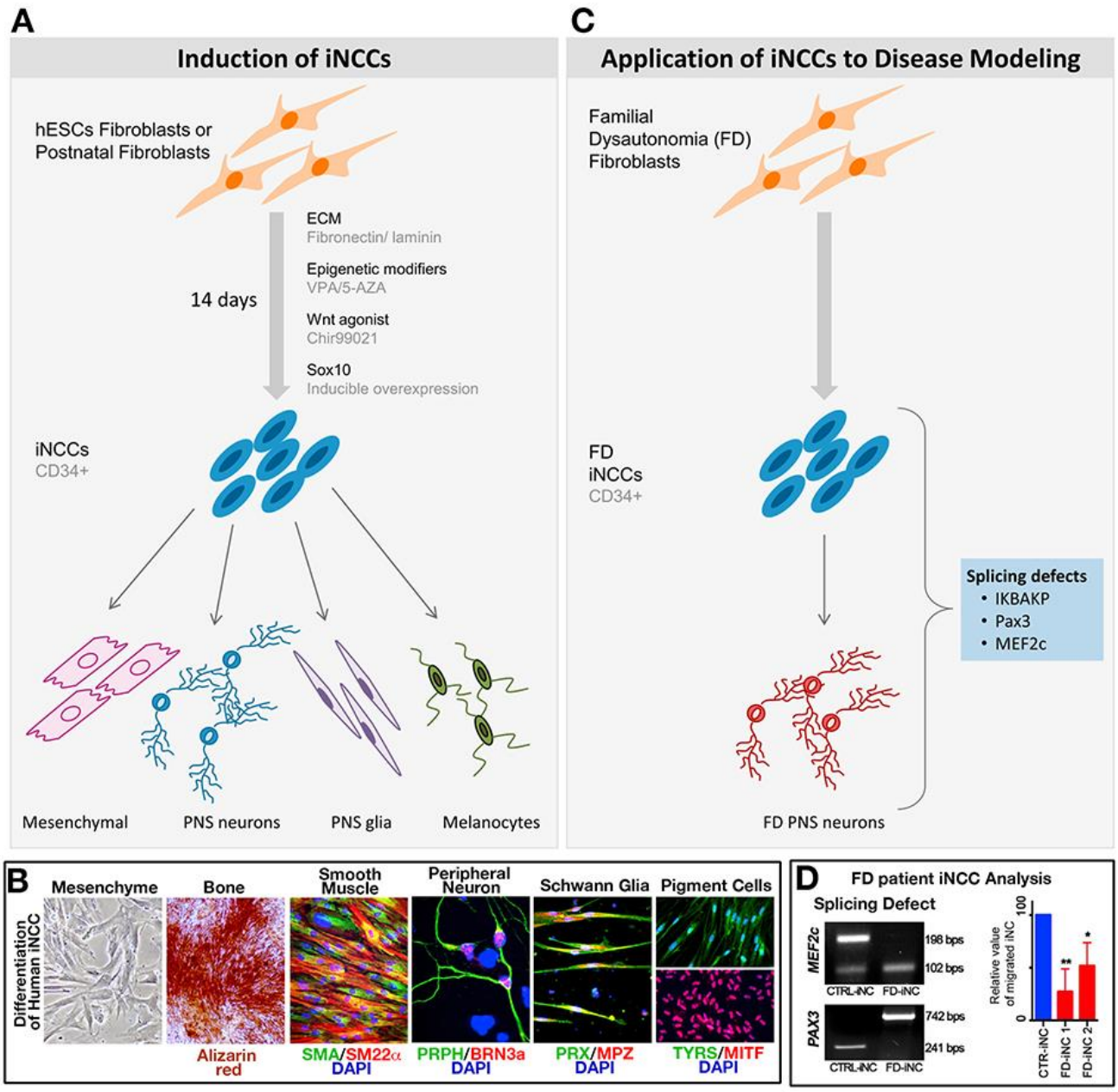

Figure 1 Derivation of human-induced neural crest cells and their use in modeling familial dysautonomia. (A) Illustration of the experimental flow and use of specific factors to generate neural crest cells. Subsequent derivation of specific cell types was possible from these cultures and even from individual iNCC clones. (B) Examples of cell types derived from human iNCCs. (C) A similar experimental approach was done to generate iNCCs from patients with familial dysautonomia (FD), enabling the study of these disease-relevant cells. (D) FD is known to be affiliated with mutations in the *IKBAKP* gene, a transcriptional elongation factor. iNCCs showed this mutation and discovered unique defects in the splicing of *Pax3* and *Mef2c*, two genes important in the development of neural crest cells. FD-iNCCs also showed reductions in their ability to migrate (graph, red bars compared to blue). (Parts A and C from Varum and Sommer 2014; Parts B and D from Kim et al. 2014; adapted by Michael Barresi.)

Literature Cited

Kim, Y. J. and 7 others. 2014. Generation of multipotent induced neural crest by direct reprogramming of human postnatal fibroblasts with a single transcription factor. *Cell Stem Cell* 15: 497–506.
PubMed Link

Varum, S. and L. Sommer. 2014. Reinventing the neural crest: Direct reprogramming makes iNCCs. *Cell Stem Cell* 15: 397–399.
PubMed Link