



## Neural Crest Single Cell Population Produces a Multitude of Cell Types: On-Line Self-Study

All Quoted material and cited references are from Wilson et al, 2004.

### Goals of this Exercise

- To understand aspects of neural crest cell development not covered in lecture
- To overview some current research approaches in developmental biology

“A major issue in development is how an apparently homogeneous population of precursor cells gives rise to a large and diverse array of differentiated progeny. This diversity is particularly evident in the embryonic neural crest (NC), which gives rise to cells of the peripheral nervous system, many mesenchymal cell types in the craniofacial region, and skin melanocytes (Le Douarin and Kalcheim, 1999). NC cells are induced within the developing neural tube (NT), and migrate into the embryo to develop into their differentiated progeny.

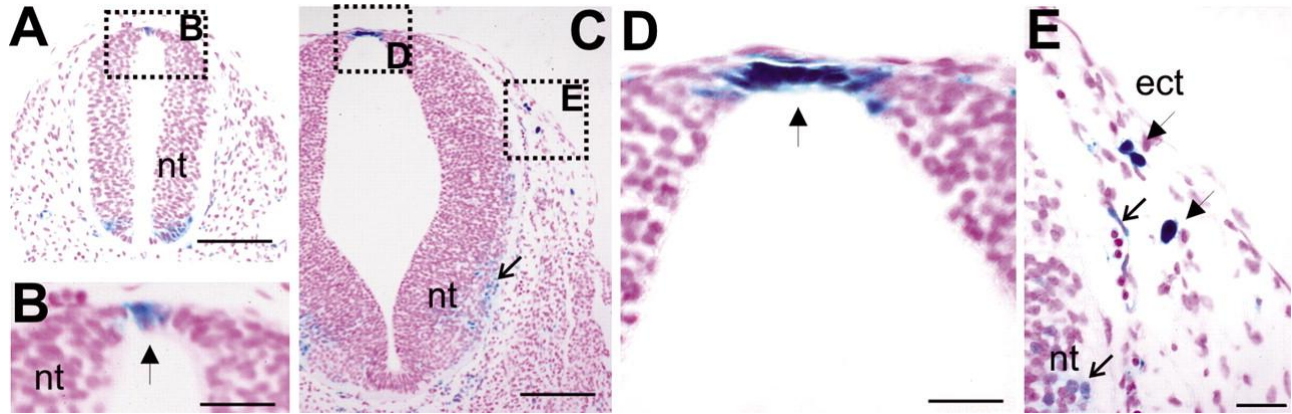
A number of experimental approaches have been used to address the question of when and where cell fate decision is made in the NC. The classic experiments from Le Douarin and co-workers employed grafting of neural primordium between quail and chicken (Le Douarin and Kalcheim, 1999), and tracing the quail NC cells throughout the embryo. Cells derived from any region of the NT could generate most NC derivatives, supporting the idea that fate is decided where the cells migrate. However, certain restrictions in developmental potential applied; for example, trunk NC was unable to give rise to the mesenchymal derivatives of the head.”

“Neural crest (NC) cells arise in the dorsal neural tube (NT) and migrate into the embryo to develop into many different cell types. A major unresolved question is when and how the fate of NC cells is decided. There is widespread evidence for multipotential NC cells, whose fates are decided during or after migration. There is also some evidence that the NC is already divided into subpopulations of discrete precursors within the NT.”

Wilson et al found... “that a subpopulation of cells on the most dorsomedial aspect of the NT express the receptor tyrosine kinase Kit (previously known as c-kit), emigrate exclusively into the developing dermis, and then express definitive markers of the melanocyte lineage. These are thus melanocyte progenitor cells. They are generated predominantly at the midbrainhindbrain junction and cervical trunk, with significant numbers also in lower trunk.”

“These data provide direct in vivo evidence for NC lineage segregation within the mouse neural tube.”

## Neural Crest: Single Population Produces Many Cell Types



**“Fig. 1.** Development of  $\beta$ gal expression in dorsal regions of *WlacZ/+* embryos. (A) Low-power view through the trunk section of an E9.5 embryo. (B) High-power view reveals faint  $\beta$ gal<sup>+</sup> cells (arrow) within the dorsal midline at E9.5. (C) Low-power view through the trunk at the level of the forelimb of an E10.5 embryo. (D) High-power view of the dorsal midline reveals strong  $\beta$ gal<sup>+</sup> cells (filled arrow) on the dorsal midline of the NT. (E) High-power view of the ectoderm reveals strong  $\beta$ gal<sup>+</sup> cells (filled arrows). There are also  $\beta$ gal<sup>+</sup> cells in ventrolateral regions of the NT and surrounding it (open arrows in C and E). ect, ectoderm. Scale bars: 250  $\mu$ m in A,C; 50  $\mu$ m in B,D,E.)”

### **Kit<sup>+</sup> cells arise on the dorsal midline of the NT and emanate out from it**

“In order to look for putative Kit<sup>+</sup> melanocyte precursors within the NT, we used a mutant mouse strain (*WlacZ*) containing the *lacZ* reporter gene inserted into the first exon of the *Kit* gene (Bernex et al., 1996). We visualized the presence of Kit<sup>+</sup> cells in the embryo by histochemical staining for  $\beta$ gal activity in heterozygous mice, which accurately recapitulates Kit expression (Bernex et al., 1996). In trunk regions of heterozygous mice, there were  $\beta$ gal<sup>+</sup> cells within the neuroepithelium on the dorsal midline from as early as E9, and  $\beta$ gal<sup>+</sup> cells were observed in significant numbers by E9.5 ( $n=5$ ; Fig. 1A,B). No  $\beta$ gal<sup>+</sup> cells were present in the ectoderm at this stage (Fig. 1A). By E10.5, there were many strong  $\beta$ gal<sup>+</sup> cells on the dorsal midline of the NT (Fig. 1C,D;  $n=5$ ), and on a dorsolateral path from the NT under the ectoderm (Fig. 1C,E). In addition, there were weak  $\beta$ gal<sup>+</sup> cells surrounding the NT in the mesenchyme, often associated with blood cells (Fig. 1E). There were also weak  $\beta$ gal<sup>+</sup> cells in ventrolateral regions of the NT (Fig. 1C,E), which may be precursors for ventrolateral spinal cord cells.”

These Kit<sup>+</sup> cells were then demonstrated to represent a sub-population of neural crest cells that formed melanocytes.

### **References**

Wilson et al, 2004. Neural crest cell lineage segregation in the mouse neural tube. *Development* 131, 6153-6162.

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