

Cell Differentiation in the Ventral Pathway

The neural crest cells entering the somites differentiate to become two major types of neurons, depending on their location. Those cells that differentiate within the sclerotome give rise to the dorsal root ganglia. These neural crest cells contain the sensory neurons that relay information regarding touch, pain, and temperature back to the CNS.ⁱ As they begin to migrate ventrally, it is likely that the neural crest cells produce progeny that express different receptors. Migrating cells that have receptors for neurotrophin and Wnt respond to those proteins (which are produced by the dorsal neural tube) and differentiate close to the neural tube into the glia and neurons of the dorsal root ganglia (Weston 1963). Within the dorsal root ganglia, those cells having more Notch become the glia, while those cells having more Delta (the Notch ligand) become the neurons (Wakamatsu et al. 2000; Harris and Erickson 2007).

Neural crest cells that lack receptors for Wnt and neurotrophin continue migrating. They migrate through the anterior portion of the sclerotome and continue ventrally until they reach the dorsal aorta (but stop before they enter the gut) and become the sympathetic ganglia (Vogel and Weston 1990). At the trunk level, they contribute to the epinephrine-secreting sympathetic (adrenergic, “flight or fight”) neurons of the autonomic nervous system, as well as to the adrenal medulla (Figure 1A). At the cardiac and vagal axial levels, they become acetylcholine-secreting parasympathetic (cholinergic, “rest and digest”) neurons, including the enteric neurons of the gut (Figure 1B). These cell lineages may each arise from a multipotent neural crest progenitor cell, and the restriction of fate into these three lineages may come relatively late (Sieber-Blum 1989).

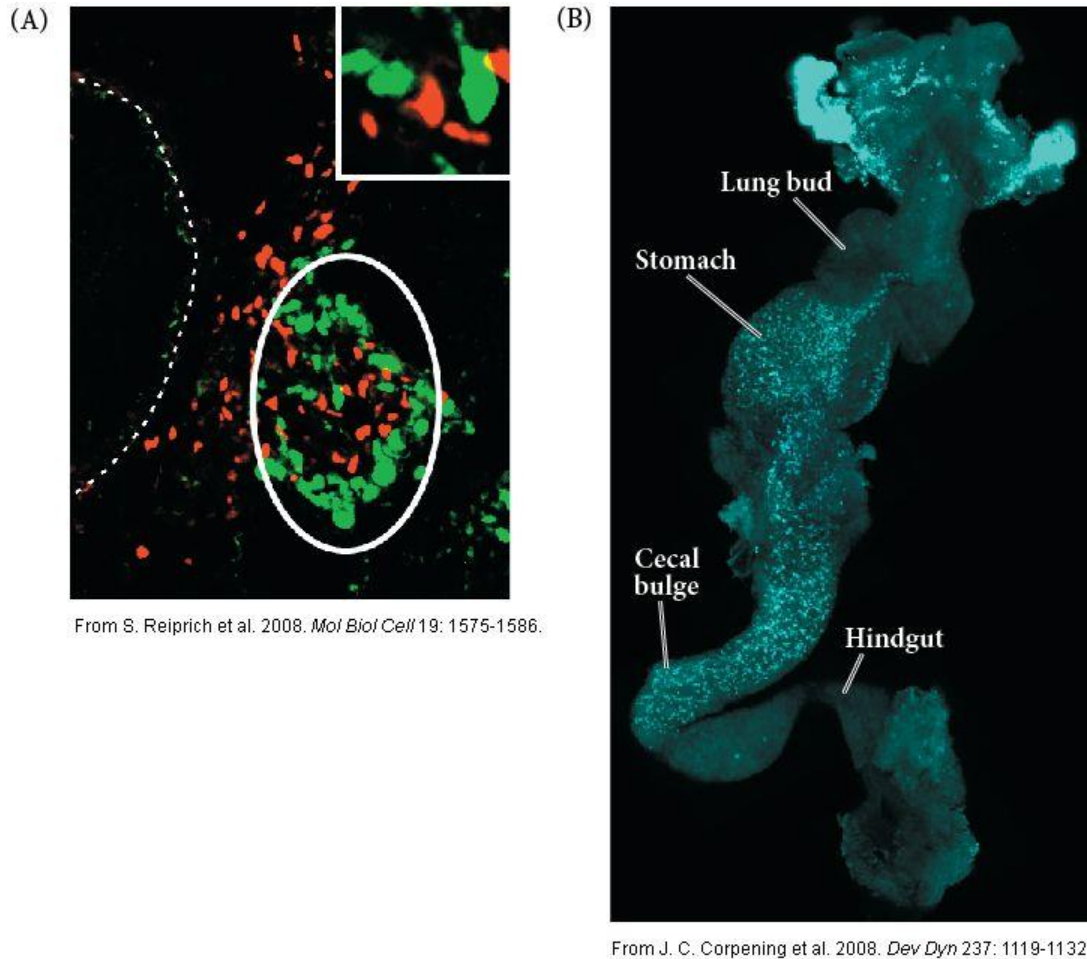


Figure 1 Entry of neural crest cells into the gut and adrenal gland. (A) Migrating neural crest cells (stained red for the Sox8 transcription factor) migrating toward the adrenal cortical cells (stained green for SF1). The limits of the adrenal gland are circled; the dorsal aorta boundary is shown by a dotted line. (B) Neural crest cells form the enteric (gut) ganglia necessary for peristalsis. Confocal image (200 $\times$ magnification) of an 11.5-day mouse gut showing the migration of neural crest cells (stained for Phox2b) through the foregut and into the cecal bulge of the intestine.

BMPs from the aorta appear to convert neural crest cells into the sympathetic and adrenal lineages, whereas glucocorticoids from the adrenal cortex block neuron formation, directing the neural crest cells near them to become adrenomedullary cells (Unsicker et al. 1978; Doupe et al. 1985; Anderson and Axel 1986; Vogel and Weston 1990). The cells destined to become the epinephrine-secreting cells of the adrenal medulla retain their responsiveness to BMP and migrate toward the BMP4-secreting adrenal cortical cells. The remaining cells become the sympathetic ganglia surrounding the aorta (Saito et al. 2012). There is further good evidence that although some neural crest cells are committed soon after their formation, the differentiation of the ventrally migrating neural crest cells depends on the pathway they follow and their final location. When chick vagal and thoracic neural crests are reciprocally transplanted, the former thoracic crest produces the cholinergic neurons of the parasympathetic ganglia, and the former vagal crest forms adrenergic neurons in the sympathetic ganglia (Le Douarin et al. 1975). In addition, Kahn and colleagues (1980) found that premigratory neural crest cells from both the thoracic and the vagal regions contain enzymes for synthesizing both acetylcholine and norepinephrine.

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ⁱ These sensory neurons are *afferent neurons* because they carry information from sensory cells to the central nervous system (i.e., the brain and spinal cord). *Efferent neurons* carry information away from the CNS; these are the motor neurons generated in the ventral region of the neural tube (as discussed in Chapters 13 and 14).