Origins of neural crest cells and cranial placodes at the edge of the neural plate

- Placode precursors
  - (six1, six4, eya)
- Neural ridge
- Neural plate
- Neural crest precursors
  - (foxD3, slug, dll, pax3)
- FGF
- No Bmp and no Wnt
  - (due to Bmp antagonists and Wnt antagonists from head organizer and anterior neural plate)
- FGF + Bmp + Wnt

Xenopus embryo, neurula stage, dorsal view
Table 13.1.  Some derivatives of the neural crest

<table>
<thead>
<tr>
<th>Derivative</th>
<th>Cell type or structure derived</th>
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<tbody>
<tr>
<td>Peripheral nervous system (PNS)</td>
<td>Neurons, including sensory ganglia, sympathetic and parasympathetic ganglia, and plexuses</td>
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<tr>
<td></td>
<td>Neuroglial cells Schwann cells</td>
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<tr>
<td></td>
<td>Neuroglial cells</td>
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<tr>
<td></td>
<td>Schwann cells</td>
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<tr>
<td>Endocrine and paraendocrine derivatives</td>
<td>Adrenal medulla</td>
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<tr>
<td></td>
<td>Calcitonin-secreting cells</td>
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<td></td>
<td>Carotid body type I cells</td>
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<tr>
<td>Pigment cells</td>
<td>Epidermal pigment cells</td>
</tr>
<tr>
<td>Facial cartilage and bone</td>
<td>Facial and anterior ventral skull cartilage and bones</td>
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<tr>
<td>Connective tissue</td>
<td>Corneal endothelium and stroma</td>
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<td></td>
<td>Tooth papillae</td>
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<td></td>
<td>Dermis, smooth muscle, and adipose tissue of skin of head and neck</td>
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<tr>
<td></td>
<td>Connective tissue of salivary, lachrymal, thymus, thyroid, and pituitary glands</td>
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<tr>
<td></td>
<td>Connective tissue and smooth muscle in arteries of aortic arch origin</td>
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</tbody>
</table>

*Source: After Jacobson 1991, based on multiple sources.*
Trunk neural crest migration pathways

Path 1 cells travel ventrally through the anterior sclerotome.

Path 2 cells take a dorsolateral route between the epidermis and the dermamytome.
Neural crest migrates over and through the anterior sclerotome (of the somite), but not the posterior, due to repulsion from the posterior sclerotome.

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Lineage tracing shows that neural crest cells are not committed to specific fates as they emigrate from the neural tube.

(A) Case 1 injection
Fluorescent dextran
Neural crest

(B) Case 2 injection
Melanocytes
Dorsal root ganglia
Ventral root Schwann cells
Sympathetic ganglia
Adrenal medulla

Case 1 results
Case 2 results
Aorta
Neural crest migration pathways and derivatives

11-4. Major neural crest migratory pathways and derivatives in the trunk. **Left**, Pathways in the embryo. The dorsolateral pathway is indicated by the green arrow, the ventral (sympathoadrenal) is indicated by the red arrow, and the ventrolateral pathways is indicated by the purple arrow. Derivatives of the trunk neural crest.
Trunk neural crest cells:
Sensory neurons of dorsal root ganglia,
Sympathetic neurons and ganglia

- NT3-responsive neurons
- Afferent to low-threshold mechanoreceptors
- Temperature and pain receptors
Melanocytes from neural crest cells

(A) Epidermal ectoderm
(B) Condensed mesoderm
(C) Developing hair canal
(D) Tip of hair
(E) Dermal papilla

(A) Hair follicle

- Hair shaft
- Sebaceous gland
- Outer root sheath
- Inner root sheath
- Bulge
- Melanocyte stem cell
- Bulb
- Melanocytes

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cells that migrate past the BMP producing aorta, are induced to become neurons (of the sympathetic ganglia)
The midbrain-hindbrain boundary acts as an “isthmic organizer”

The Hox code of rhombomeres r1-r8

Figure 1 | Boundaries and local signalling centres in the developing vertebrate neural tube. Lateral view of embryonic avian brain. a | Hamburger-Hamilton stage 13 (HH 13), anterior

Figure 2 | Hindbrain segmentation. Schematic representation of a vertebrate (chick)
Similarly exit from even-numbered rhombomeres, where neuronal differentiation is similarly delayed in odd-numbered rhombomeres (Bally-Cuif et al., 1998; Higashijima et al., 2000) and where cranial neural crest similarly migrates from even-numbered rhombomeres (Schilling and Kimmel, 1994). A two-segment periodicity in cell adhesive properties has also been observed, and recent work in the zebrafish has uncovered a molecular basis for these adhesive differences (see below; reviewed in Klein, 1999).

Each rhombomere is unique. Differences in the size, number, and projections of the reticulospinal neurons in each segment illustrate another principle of hindbrain organization, which is that, overlying the basic reiterated pattern, are clear segment-specific differences. For example, the prominent Mauthner neuron in rhombomere 4 has a much larger cell body and axon than do its segmental homologs in other rhombomeres (Fig. 3A). This picture of a basic segmental plan overlain by segment-specific differences is reminiscent of the body plan of the fly, where homeotic selector genes, the Hox genes, specify differences between initially similar segments. As we will discuss further below, the vertebrate homologs of the fly Hox genes are expressed in rhombomere-restricted domains, and work in several vertebrate systems has demonstrated that, although the segmenting mechanisms appear to be different in flies and vertebrates, the Hox genes play conserved roles in specifying segment identities.

PATTERNING THE ANTERIOR–POSTERIOR AXIS OF THE ZEBRAFISH CENTRAL NERVOUS SYSTEM

Long before the hindbrain becomes segmented and hindbrain neuroanatomy is elaborated, the presumptive neurectoderm is broadly patterned along its anterior-posterior axis into forebrain, midbrain, hindbrain, and spinal cord. Indeed, as early as the beginning of gastrulation, largely nonoverlapping regions of the presumptive neurectoderm are fated to give rise to distinct anterior-posterior identities (Fig. 4A; Kimmel et al., 1990; Woo and Fraser, 1995). The early gastrula resembles a cap pulled halfway over a round head (the yolk), with a thickened edge—the margin or germ ring—where the first mesendodermal precursors have begun involuting. The dorsal side of the embryo is marked by the embryonic shield, a thickening that is the equivalent of the organizer of the Xenopus embryo and the node of amniote embryos, which gives rise to midline, or axial, mesendoderm (including notochord and prechordal plate). The cells in the lateral and ventral germ ring are fated to become nonaxial mesoderm (including somites and blood) and endoderm. Cells further from the margin (closer to the animal pole) give rise to ectoderm, with the neurectoderm mapping to

Rhombomeres: repeating morphological and organizational units of the hindbrain (here in the zebrafish) from Moens and Prince, 2002
fig. 7 of Moens and Prince, 2002
Compartment (intrinsic segmentation) in the hindbrain
Lumsden A. 2004

Rhombomeres (in the chick) are visible as local “bumps” of increased proliferation, and as units of axonal projection.
Rhombomeres become lineage restriction units, at about the ten somite stage (stage X)
Cranial neural crest, rhombomeres, and branchial arches
Cranial placodes and their derivatives, from Streit, 2008
The lens placode and lens development

an example of reciprocal interaction between optic cup and epithelium