# MCDB 4650 DEVO

## Patterning the vertebrate skull and the neural crest

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**Learning Objectives:**

- Describe the specification of neural crest cells
- Describe the migration of neural crest cells
- Describe the different neural crest derivatives and their origin
- Design experiments to test gene function in the control of neural crest biology

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*Development 139, 3-14 (2012) doi:10.1242/dev.060095*

Cell fate decisions and axis determination in the early mouse embryo  
Katsuyoshi Takaoka1,2 and Hiroshi Hamada1,2

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Only up to Figure 5, page 8  
(stop before Origin of AP axis and the distal visceral endoderm)
Morphological Innovation

Evolution of Craniofacial Structures

![Images of various species showing craniofacial differences over evolutionary time.](image)

![Diagram showing embryonic and adult craniofacial development.](image)

- Neural Crest-derived
- Paraxial Mesoderm-derived
- Neural Crest- and Paraxial Mesoderm-derived
r = rhombomeres
Hox genes regulate rhombomere patterning

Cell intrinsic or influenced by environment or both?
Neural crest (NC) cells are multipotent embryonic progenitor cells.
Describe the specification of neural crest cells

Learning Objectives

Describe the migration of neural crest cells

Describe the different neural crest derivatives and their origin

Design experiments to test gene function in the regulation of neural crest biology

Describe the specification of neural crest cells

Neural crest cells arise at the border between the neural plate and the non-neural ectoderm

Juxtaposition of these tissues and the signals that they produce induces neural crest-specific transcription factors
How do equipotent cells become different from one another?

**Competence:**
cells have ~equal potential to form one of three distinct cell types
neural, neural crest, or ectoderm

**Key Question:**
How do equipotent cells become different from one another?

Cells have ~ equal potential to be neural, neural crest, or ectoderm (competence)

**Induction** - signal(s) that act to restrict fate
BMP as a Morphogen

Morphogen present in a graded distribution
different levels of signal specify different fates.

Morphogens allow several fates to be instructed by a single
organizer, so that the fates are in the correct spatial relationship
to each other.

How is a graded signal resolved into distinct borders?

Refining the cell fate borders by refining the morphogen signal:
Source (Faucet) and Sink (Drain)
Refining the cell fate borders by refining the morphogen signal: Source (Faucet) and Sink (Drain)

In the scenario below, what molecule(s) would the source and what would be the sink?

A. Source = Notch/Delta; Sink = BMP
B. Source = BMP; Sink = BMP antagonists
C. Source = BMP antagonists; Sink = BMP

Refining the cell fate borders by refining the signal: Source and Sink

How is a graded signal resolved into distinct borders?

Sink = BMP antagonists, Notch/Delta  Source = BMP

Reinforce neural crest fate by combination of inhibition of BMP and positive WNT & FGF

Signals from neighboring tissues = mesoderm
Induction of neural crest-specific transcription factors

How does one functionally test a GRN?
How do equipotent cells become different from one another?

Induction of neural crest-specific transcription factors

How does one functionally test a GRN?

Gain of Function
Loss of Function

How do changes in transcription affect cell behaviors?

Migration
Neural crest cells are highly motile: migrate all over the body, picking up information from their environment as they migrate.

What process is occurring in these yellow-red cells?

a. Epithelial to mesenchymal transition
b. Mesenchymal to epithelial transition

What is needed for EMT and cell migration?
What is involved in Neural Crest Cell migration?

- NC migration begins with an epithelial to mesenchymal transition (EMT)
- Involves vast changes in gene expression: downregulation of E-cadherin and tight junction proteins, loss of apical-basal polarity, and upregulation of key motility genes

Neural crest cells are highly motile: migrate all over the body, picking up information from their environment as they migrate

Premigratory neural crest cells are exposed to BMP and Wnt signaling

Transcription factor Snail-2 activated:
Snail-2 represses N- and E-cadherin, but allows a different cadherin, Cadherin 6B to be upregulated

Cadherin 6B activates RhoA, which allows initiation of delamination (activates actomyosin contractile fibers)

What experiment would you do next?

Outline your hypothesis, the type of experiment and your predicted effect


What might be involved in directed migration?
Collective migration of neural crest cells

-loosely adherent to each other
-but begin to repel each other and stream away from origin

Contact inhibition
Attractive signal
Restricted streams

Trunk neural crest cells migrate only through the anterior region of each sclerotome
### What is directing the migration?

**Differentially expressed molecules within the somite.**

**Molecule?**

**Ephrins: regulate adhesion**
Are only localized to the posterior half of each sclerotome

**How do Ephrins appear to guide the migration of neural crest cells?**
- Provide an inhibitory signal
- Provide an attractive signal

### Early Craniofacial Development

- **Cleft lip/palate**
  - Baby with cleft palate

- **Treacher Collins Syndrome**
  - Week 5-6 Human Development
Treacher Collins Syndrome

Green = apoptosis

Cell intrinsic or influenced by environment or both?