The Emergence of the Ectoderm: Central Nervous System and Epidermis

November 27, 2007
Ectoderm - Overview

Ectodermal derivatives

Neurulation
   Neural plate
   Neural tube
   Neurulation

Neural tube specification and differentiation

Spinal cord development

Brain development

Eye development

Ectodermal structures: e.g. hair development
Germ Layer Derivatives

Gastrulation produces three germ layers in proper relation to one another.

What do the germ layers produce?
**Ectodermal Derivatives**

**Surface ectoderm; e.g.**
- epidermis
- hair, etc.
- mouth epithelium
  - tooth enamel, etc.
- lens, cornea

**Neural crest; e.g.**
- peripheral nervous system
  - neurons
  - glia
- melanocytes
- facial cartilage

**Neural tube; e.g.**
- brain
- spinal cord
- retina
Neural Plate, Neural Tube Formation

Neural plate formation:
- **neurectoderm** induced by pharyngeal endoderm and dorsal mesoderm

Neural plate
Neural fold
Notochord
Archenteron
Endoderm
Mesoderm
Epidermis

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Neural fold
Notochord
Archenteron
Neural plate
Endoderm
Mesoderm
Epidermis
Blastopore
Remnant of blastocoel

Neural plate

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Chick Neurulation

**Neurulation** – neural tube formation
- anterior – brain
- posterior – spinal cord

Note - the anterior region undergoes neurulation while the posterior region is still undergoing gastrulation

**Anterior** – **primary neurulation**

**Posterior** – **secondary neurulation**
Neurulation: Neural Plate Formation

Chick

- Neural plate
- Notochord
- Primitive streak
- Pharynx
- Neural folds

Midline ectodermal cells become columnar - induced by dorsal mesoderm and pharyngeal endoderm
Mechanism of Primary Neurulation

**medial hinge point** cells (MHP)
- induced by notochord
- anchored to notochord
- decrease in height, form wedge shape
  (cytoskeletal changes)
Primary Neurulation

- surface ectoderm (epidermis) pushes folds together

Dorsolateral hinge points (DLHP)
- anchored to surface ectoderm
- decrease height, become wedge-shaped
Neural tube pivots around hinge points

Neural crest cells – migrate individually
Secondary Neurulation

Chick – posterior regions

(A) Surface ectoderm
Condensing mesenchymal cells

(B) Medullary cord
Transitional region

(C) Neural tube

(D) Notochord

cavitation within cord
Neurulation – Neural Tube Closure

Neural tube closure is not simultaneous or continuous throughout the tube:

- in mammals, there are 3 closure initiation sites, and
- two open ends: **anterior neuropore** and **posterior neuropore**

Failure to close any portion of the neural tube can result in severe medical consequences
Neural Tube Defects (NTDs)

Neural tube defects: ~ 1:1000 U.S. live births; worldwide may be double

Failure of posterior neuropore closure - **spina bifida**

failure of anterior neuropore closure - **anencephaly**
Neural Tube Defects (NTDs)

NT closure is dependent on cell adhesion; governed by surface molecules
- NT cells must adhere to each other; move as a tissue; separate from neural crest and epidermis
- requires *Pax6*, *Sonic hedgehog*, *openbrain* expression
- recent evidence in zebrafish implicate *Nodal* in very early stage

NT closure failure has multiple causes; both genetic and environmental factors have been implicated

Dietary folate (*folic acid*; *vitamin B_{12}*/*B_{12}*/*vitamin B_{12}*) can prevent many NTDs (mechanism not completely understood)
- folate receptors appear on the dorsal-most regions of the neural tube

Epidemiological data suggests that environmental toxins may also contribute.
Neural Tube Specification

(A) BMP4, 7 in ectoderm

(B) BMP4 in roof plate

(C) TGF-β family:
- BMP4, BMP7
- BMP5, Dorsalin, Activin

(D) Shh in notochord

BMP7, Dorsalin, Activin

Gradient of TGF-β family

Shh

Gradient of Shh

Roof plate
- D1 interneurons
- D2 interneurons
- V0 interneurons
- V1 interneurons
- V2 interneurons
- Motor interneurons
- V3 neurons
- Floor plate
Differentiation of the Neural Tube

In mammals the neural tube starts off as a straight tube of constant thickness and ends up as a convoluted organ of enormous complexity. How does this happen?

Differentiation occurs simultaneously on three different levels:

1. **Gross anatomical level**: the neural tube and its lumen (central canal) bulge and constrict to form the chambers of the brain and spinal cord.

2. **Tissue level**: cell populations within the neural tube wall rearrange themselves to form different functional regions of the brain and spinal cord.

3. **Cellular level**: neuroepithelial cells differentiate into numerous types of nerve cells (**neurons**) and supportive cells (**glia** or **glial cells**).
Neurons

- impulses received by dendrites
- transmitted through axon to target tissue
- synapses connect to other neurons

- growth cone: sensory & locomotor
- eventually forms a synapse with the axon’s target tissue
Myelination

Schwann cell

Oligodendrocyte

Axon

Node of Ranier

MYELINATION IN CENTRAL NERVOUS SYSTEM

MYELINATION IN PERIPHERAL NERVOUS SYSTEM

Schwann cell

gray matter

white matter
Glial Guidance of Neurons

Glial cells position developing neurons

(A)

Leading process of neuron

Migrating neuron

Process of glial cell

(B)
Spinal Cord Development

Dorsoventral patterns of brain and spinal cord are induced by similar molecular mechanisms; however, organization is different.
**Ventricular Zone Architecture**

**Ventricular zone** - one cell-layer thick
- nuclei occupy different vertical spaces, depending on position in mitotic cycle
- initial divisions are horizontal: daughter cells remain attached to the luminal side
- as neuroepithelial cells differentiate, they divide vertically; one daughter cell migrates

- mitosis occurs on luminal side
Thus, differentiating cells migrate through preceding layers

Different brain/spinal cord regions show different patterns of cell neuronal differentiation and migration

Neural cells divide and migrate
- they will eventually form different layers in the brain and spinal cord
- earliest dividing cells migrate to closest layers
- later dividing cells migrate farther
“Inflation” of the NT caused by osmotic pressure from Na⁺/K⁺-ATPase activity and production of cerebrospinal fluid.
Human Brain Development

25 days

35 days

40 days

50 days

100 days

Five months

Nine months
Brain Neural Differentiation

Cerebral cortex

Cerebellum

Ventricular zone
Intermediate zone
Marginal zone

Neuroblasts

Ventricle

Ventricular zone
Intermediate zone
Granule cell layer
Purkinje cell layer
Marginal zone
External granule cell layer

Cerebral cortex

Ventricle

Ventricular zone
Subventricular zone
Intermediate zone
Cortical plate
Marginal zone
Molecular layer
Vertebrate Brain Development

Brain develops from cranial part of neural tube; spinal cord from posterior

Brain:
- central canal forms fluid-filled spaces - **ventricles**
- brain regions have different structures/functions
  - clusters of neurons called **nuclei**: each works as a functional unit
  - horizontal layers of neurons interact with each other

Further differentiation of gray and white matter
- **neuroblasts** migrate through white matter to form a second layer of neurons at the surface = **neocortex** (gray matter)
- final result - six layers of neuronal cell bodies
  - each layer receives input from different region
- also, horizontal organization into >40 regions
  - e.g. visual cortex, auditory cortex
Neocortex stratifies into 6 layers of neuronal cell bodies.

Adult forms are not completed until mid-childhood.

~ 250,000 neurons added /minute (early post-natal)

~ 30,000 synapses/second/cm² formed during the first few years.
Human Brain Myelination

Vertebrate Eye Induction

(A) 4-mm embryo  (B) 4.5-mm embryo

Placodes – epidermal thickenings:
- olfactory – olfactory epithelium
- otic – inner ear labyrinth
- lens
Vertebrate Eye Induction

(C) 5-mm embryo

(D) 7-mm embryo

Lens vesicle

Retina

Optic cup

Lens

Cornea
Retinal Neurons

(A) Image of retinal layers

(B) Diagram of retinal layers:
- Rods and cones of photoreceptors
- Cell bodies of photoreceptors
- Outer plexiform layer
- Bipolar nerve layer
- Inner plexiform layer
- Ganglion cell layer
- Optic nerve fibers

Light
crystallin-synthesizing

mesenchymal cells condense to form cornea

- fibers elongate
Ectodermal Derivatives

- Epidermis
- Hair
- Nails
- Sebaceous glands
- Olfactory epithelium
- Anterior pituitary
- Mouth epithelium
- Tooth enamel
- Lens, cornea
- Cheek epithelium
Human Epidermis

- Thickened cell membrane
- Keratin
- Keratin granules
- Melanosomes
- Basal lamina
- Melanocyte
- Basal layer
- Spinous layer
- Granular layer
- Transitional cell
- Cornified layer
- Malpighian layer

Germinal layer (stem cells)
Stem cells continually form (or populate) follicles, sebaceous glands, melanocytes, possibly epidermis