Organogenesis Encompasses:

- The Emergence of the Ectoderm
- Neural Crest Cells and Axonal Specificity
- Paraxial and Intermediate Mesoderm
- Lateral Plate Mesoderm
- Endoderm

Student Learning Objectives

1. You should understand that the mesoderm forms all of the organs between the ectodermal wall and the endodermal tissues.

2. You should understand that the paraxial mesoderm forms structures at the back of the embryo surrounding the spinal cord, including the somites and their derivative cartilage, bone, muscle and dermis.

3. You should understand that the intermediate mesoderm forms the structures of the urogenital tract, including the kidneys, gonads, ductwork and the adrenal cortex.

4. You should understand that the mesoderm helps both the ectoderm and the endoderm form their own tissues.
The mesoderm forms during gastrulation and neurulation, same as ectoderm.

Major lineages of the mesoderm

Paraxial mesoderm is made up of head mesoderm and somites
Somitogenesis

1. Establishment of periodicity
2. Fissure formation (separation)
3. Epithelialization
4. Specification
5. Differentiation

Somitogenesis: Periodicity

Periodic formation of somites is inherent to the cells of the mesoderm

Every 90 minutes in chick (less exact in mice)
Total of 50 in chick
  65 in mice
  500 in snakes
Notch and Wnt signals oscillate like a clock
FGF signals sweep rostral-to-caudal in wave

Delta-Notch are expressed at presumptive boundaries

Delta-Notch dictates WHERE a somite will form
Notch controls the wavelike expression of *hairy1*

Where Notch is expressed Hairy-1 stays on long-term

The posterior edge is the edge that signals separation

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Fissure Formation: Separation from unsegmented mesoderm

The FGF wavefront sets up an oscillation in Wnt and Notch signaling as it passes

Notch expression gives final position of Hairy-1

Hairy-1 causes Ephrin expression which repels neighbors (remember how Ephrin repelled motor axons here also)

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Epithelialization of somites

That same posterior edge starts mesenchymal to epithelial transition

- N-cadherin
- rho family
- actin change
Specification of paraxial mesoderm

occurs early due to Hox expression....

transplants form what they would have in original position

Determination and differentiation in somites

• All of the cells of the somite are competent to form all of the derivative cell types – cartilage, bone, muscle, tendons, dermis, vascular cells, meninges

• Their fate depends on their position near the neural tube, notochord, epidermis and intermediate mesoderm

Determination and differentiation in somites

First step is notochord induction of sclerotome

Epithelial to mesenchymal transition causes them to migrate to form vertebral cartilage, leaves dermamyotome epithelium
Determination and differentiation in somites

The second step is the segregation of dermamyotome

- Primaxial myotome forms back and intercostal muscles
- Abaxial myotome forms abdominal muscle, tongue, limbs
- Central myotome proliferates madly and makes most cells

Dermatome forms back dermis, brown fat

Central and bilateral myotome surrounds dermatome

Figure 11.12  Primaxial and abaxial domains of vertebrate mesoderm (Part 2)
Mechanisms of Tissue Formation from Somites

- Myogenesis: Muscle Formation
- Osteogenesis: Bone Formation
- Vascular Replacement in the Dorsal Aorta
- The Syndetome: Tendon Formation

Myogenesis: Muscle Formation

- The paraxial, abaxial and central somite
- Cells in the center give rise to satellite cells
  - maybe stem cells, maybe committed progenitors
  - remain viable for the life of the organism
  - exit cell cycle upon injury and differentiate to muscle
- Classic skeletal muscle differentiation
  - paracrine signals induce MyoD, Myf-5
  - TFs for muscle genes and for themselves!

Adult muscle cells (myotubes) are large and multinucleated
In culture it doesn’t matter what species you place together they will fuse.

- Four different sources of bone:
  - Somites form the axial skeleton
  - Lateral plate mesoderm form the limb skeleton
  - Cranial neural crest forms the bones of face and head
  - Mesodermal mesenchyme in patella, periosteum

- Two different processes:
  - Endochondrial ossification in the first two
  - Intramembraneous ossification in the second two
Osteogenesis: Bone Formation

Endochondrial literally means “within cartilage”

- vertebrae
- ribs
- pelvis
- limbs

**Bone Model**

- Hypertrophic chondrocytes leave cell cycle, enlarge, calcify their ECM and then apoptosis

The calcified ECM plus Ihh cause bone cells (osteoblasts) to differentiate from somite progenitors.

- The step-wise progression continues out away from the center - “growth plates”
- Bone growth ceases when the secondary center finishes up

(A) No calcium (B) Normal bone formation
Endochondral Ossification of Vertebrae

1. Sclerotome mesenchyme are attracted by notochord and neural tube secretions

2. As motor axons extend toward muscles they go through sclerotome and split them rostral-to-caudal

The caudal end of one then recombines with the rostral end of the next to form the bone model and then bone

Vascular Replacement in the Dorsal Aorta

Blood vessels are a single layer of endothelium surrounded by multiple layers of smooth muscle

The dorsal (or descending) aorta forms a primary model by vasculogenesis and then both the endothelium and smooth muscle are replaced by somite. (the same thing happens to the ascending aorta by neural crest cells!)

The Syndetome: Tendon Formation

Tendon joins bone to muscle. The last row of sclerotome is induced by the overlying myotome to differentiate into those connectors.
Formation of the Kidneys from Intermediate Mesoderm

- The adult kidney is very complex
  - A single nephron has 10,000 cells, 12 cell types
  - Each is positioned exactly for its job relative to others
- The embryo increasingly needs to filter blood
  - IM mesoderm 1st forms organizer, the pronephric duct
  - This tissue then induces three stages of kidney
  - The first two are transitory, the third persists

General scheme of development in the vertebrate kidney

Metanephros formed by reciprocal induction with Wolffian Duct
...the Wolffian Duct matures into the collecting duct