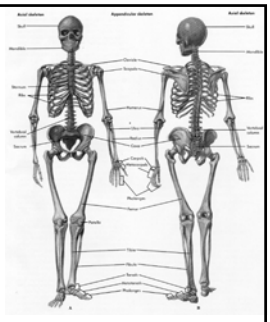
Skeletal Development

Multiple Cellular Origins



1 - **Paraxial Mesoderm**
Somite, Sclerotome
Axial Skeleton (e.g. vertebra)

2 - **Lateral Plate Mesoderm**
Appendicular Skeleton – (e.g. limb)

3 - **Neural Crest**
Head Skeleton

Established as

- 1 - **Hyaline Cartilage** – replaced by **Endochondrial Ossification**
- 2 – **Intramembranous Bone Formation** - direct ossification

Intramembranous Bone

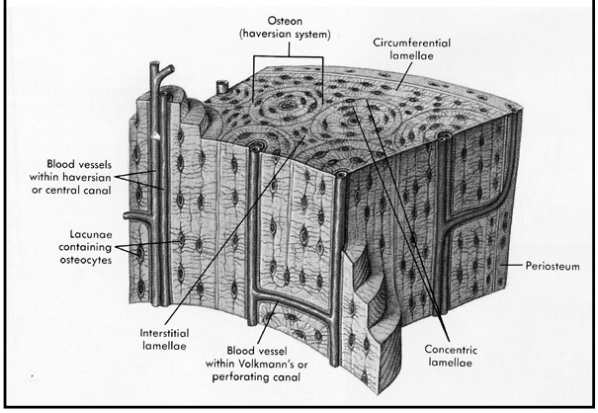
Intramembranous bone = dermal bone (e.g. skull, clavicle)

Mesenchymal condensation, becomes vascularized

Osteoid Tissue (prebone) - cells differentiate into osteoblasts - matrix deposition - Calcium Phosphate

Osteoblast → Osteocytes - trapped in matrix

Bone Spicules organized around blood vessels - concentric layers = Haversian system.

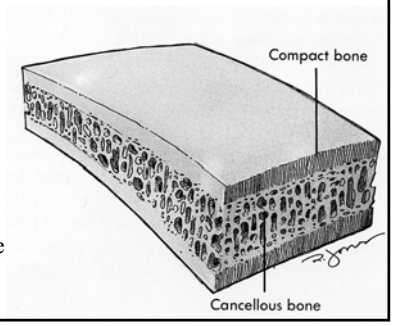


Compact Bone - Osteoblast in periphery lay down layers of compact bone

Spongy bone - beneath bony plates - osteoclasts breaks down bone

Continual bone remodeling via action of osteoblasts and osteoclast

Bone marrow differentiates from mesenchyme in spongy bone



Endochondrial Bone

Endochondral ossification – Hyaline cartilage template of bone forms

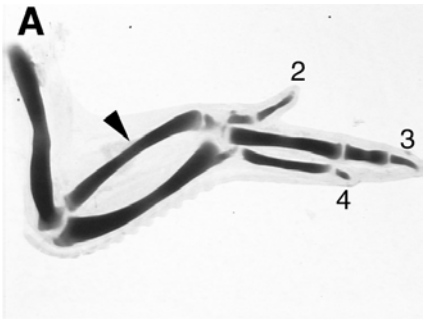
Cartilage - differentiates from mesenchyme cells

Chondroblasts - condenses - become rounded and deposit matrix - collagen fibers or elastic fiber

Three types of cartilage - hyaline (most common), fibrocartilage, elastic cartilage

Perichondrium - outer layer of cells

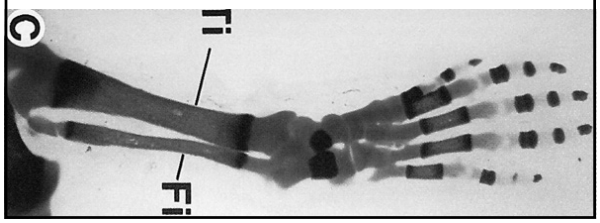
Cartilage template of the limb in the Chick wing



Endochondrial Bone

Primary ossification center - initiation of ossification

Perichondrial cells differentiate into Osteoblasts - deposit matrix as a collar in center of long bone – diaphysis



Endochondrial Bone

Perichondrium becomes Periostium

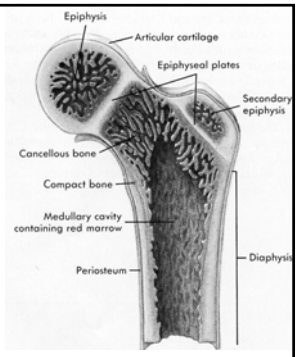
Ossification spreads towards ends of bone

Osteoclasts differentiate and begin to breakdown bone

Chondrocytes die off – center is invaded by vascular system – the bone marrow.

Cells also invade and differentiate into osteoblasts - forming bone spicules that are remodeled by osteoclasts

Bone Growth

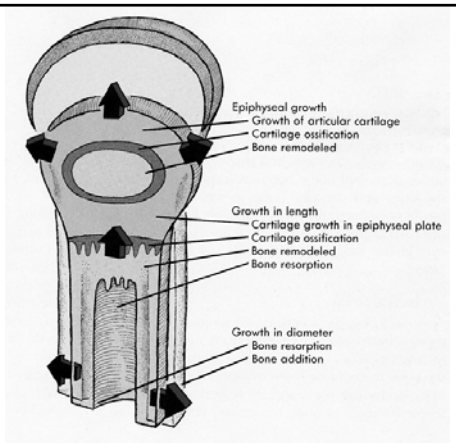


Bone lengthening occurs at diaphyseal-epiphyseal junction - epiphyseal cartilage plate (growth plate)

Epiphysis - chondrogenic

Secondary ossification centers in the epiphysis after birth

After growth termination the epiphyseal cartilage plate is replaced with spongy bone



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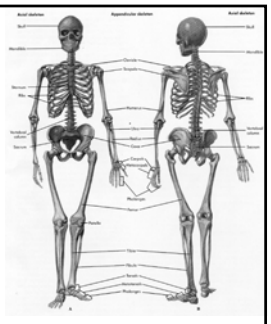

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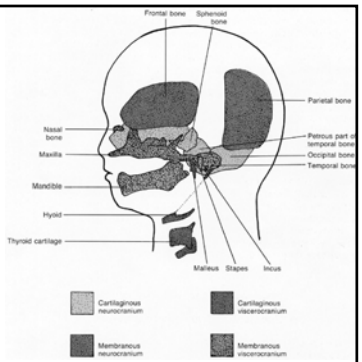
Skull / Head



Neurocranium
skeleton around the brain

Viscerocranium
skeleton of the face

Both consist of two components:
Membranous (Intramembranous ossification)
Cartilaginous (Endochondrial ossification)

Neurocranium

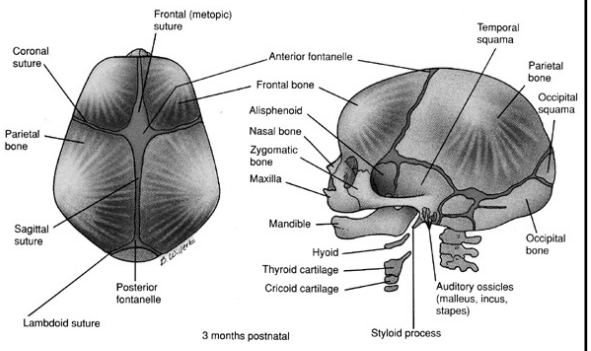
Membranous neurocranium
- cranial vault = calvaria
- flat bones of skull

Sutures - fibrous joints between flat bones

Fontanelles - where several sutures meet

Moldling - bones are soft, sutures are loose – allows for changes during birth

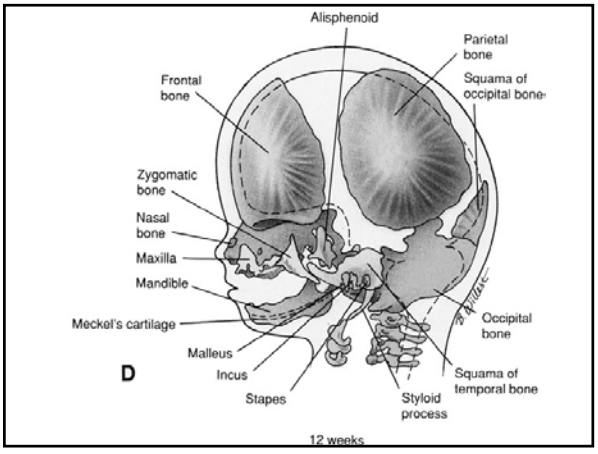
Cartilaginous neurocranium – bones at the base of the skull



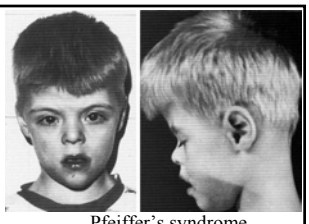
Viscerocranium

Cartilaginous viscerocranium
- middle ear bones - incus, malleus, stapes
- reichert's cartilage
- hyoid bone

Membranous viscerocranium
- Jaw Bones – maxilla, zygomatic, squamous temporal bones, mandible



Apert syndrome



Pfeiffer's syndrome

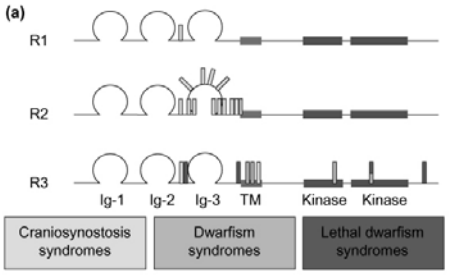
Crouzon's syndrome

Craniosynostosis

Premature closure of sutures

Abnormal skull shape

Multiple causes:
- FGF signaling
- Msx gene function



FGF Receptor (FGFR) mutations cause craniosynostosis

Autosomal dominant – abnormal dimer function

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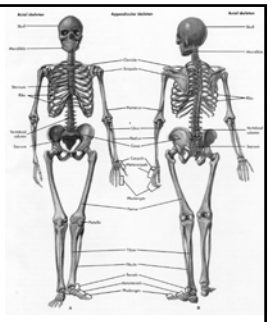

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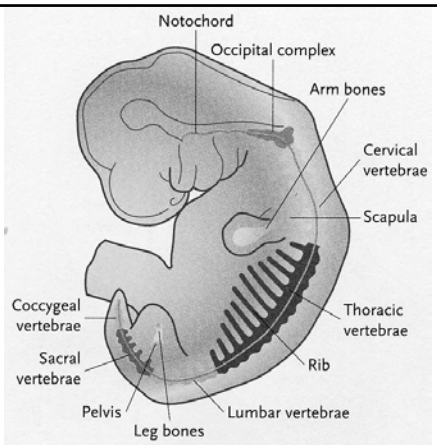
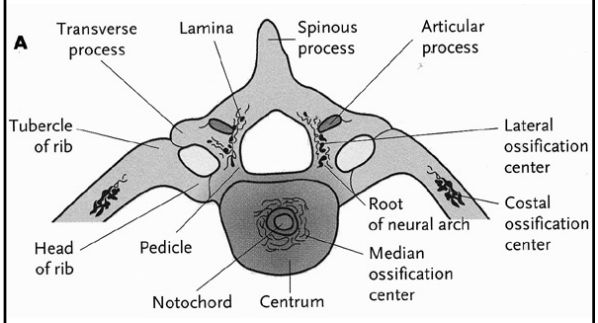
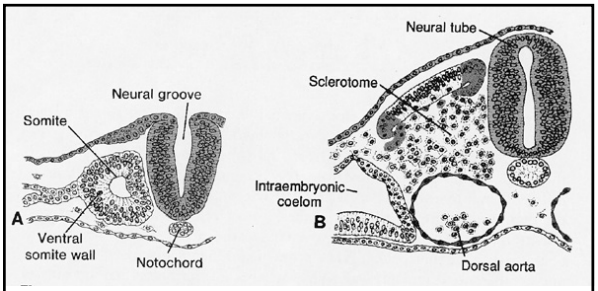


Vertebral Column



Three parts to each vertebra - body, vertebral arch, ribs



Sclerotome cells form a mesenchyme that chondrofies around the notochord to form the centrum

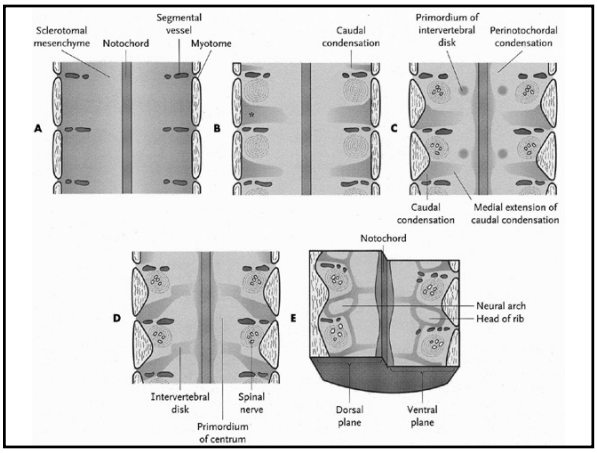
Development of Vertebra

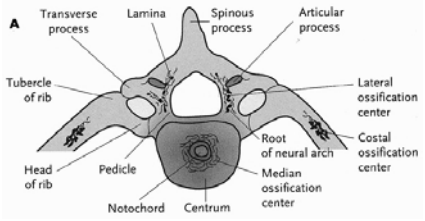
Sclerotome - cells surround notochord on both sides
- cranial - loosely arranged cells
- caudally - densely packed cells

Each vertebra is derived from two sclerotome segments
- Caudal (dense) cells from a cranial sclerotome
- Cranial (loose) cells from the next caudal sclerotome

Intervertebral disc between vertebra

Intervertebral disc forms at the interface between loose and dense cells (center of sclerotome)





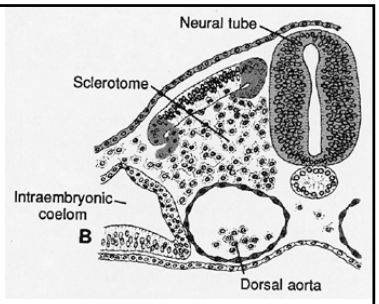
The centrum is the primordium of the body

Notochord degenerates in the center of body

Notochord expands in the intervertebral disc region
forms the nucleus pulposus = gelatinous disc center

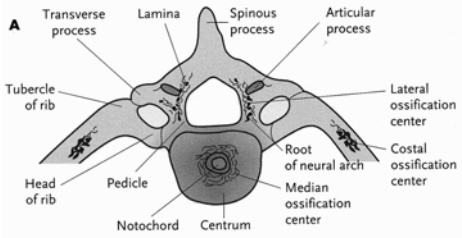
The nucleus pulposus is surrounded by fibrous tissue (concentric) - anulus fibrosus

Development of Vertebra



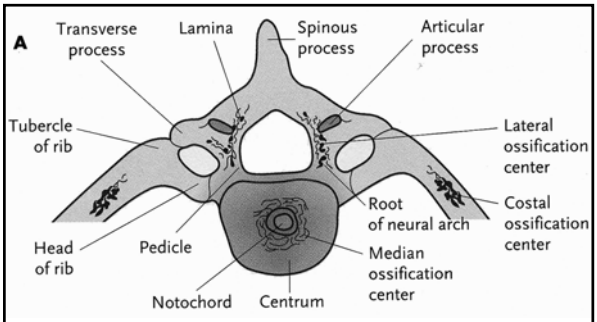
Sclerotome cells surround the neural tube - forms the vertebral arch - fuses ventrally with the centrum

Sclerotome cells in the body wall form the costal processes, the ribs



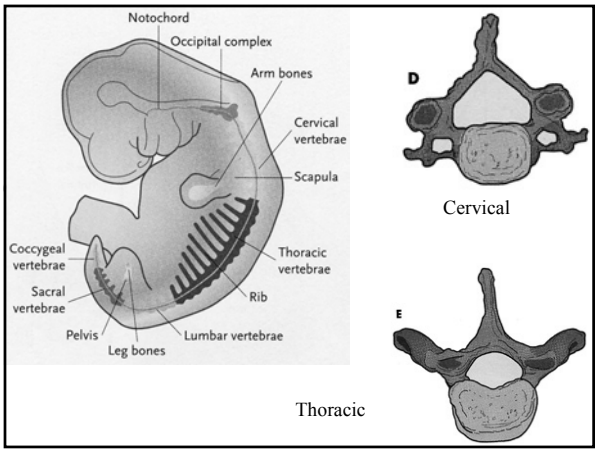
Primary ossification centers
1 - Surrounding the notochord in the centrum
2 - Lateral to the neural tube in the vertebral arch

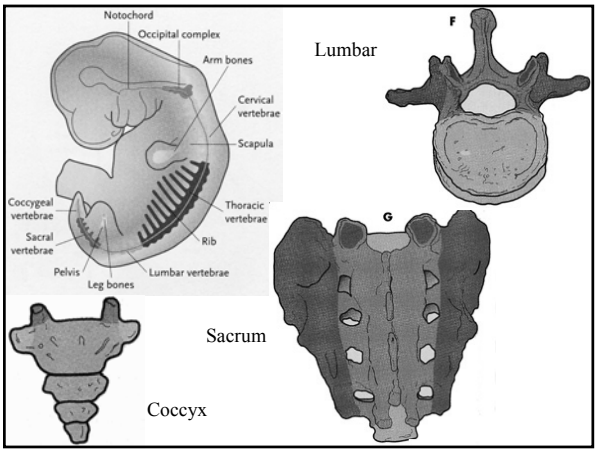
Secondary ossification centers
1 - anular epiphyses - between body and intervertebral disc)
2 - tip of spinous process
3 – tips of transverse processes



Joints: neurocentral joint - centrum / vertebral arch - allows for growth of the spinal cord until 5 years

Costovertebral synchondrosis - vertebral arch / ribs
synovial joint



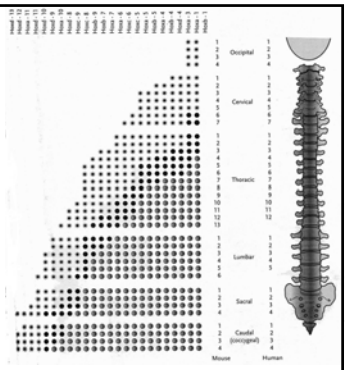


Hox Genes

Regional characteristics of vertebrae are specified by unique combinatorial expression of Hox genes

Homeotic transformations of vertebrae have been described

Retinoic Acid can cause cranial to caudal segment shifts



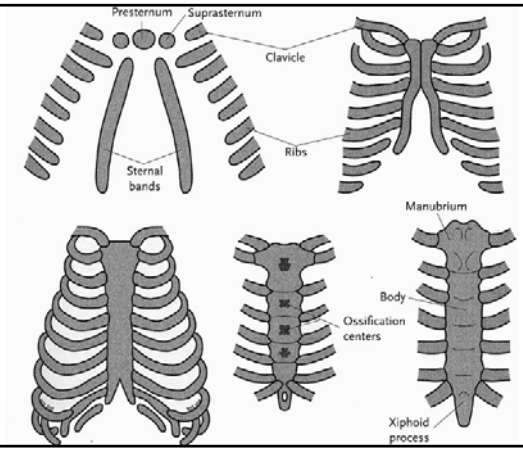
Ribs / Sternum

Sclerotome cells in the body wall form the costal processes that form the ribs

The Sternum forms from a pair of ventral cartilagenous bands that converge at the ventral midline

Converged sternal bands undergo secondary segmentation – similar to joint formation

Sternal segments later fuse



Muscle Development

Muscle types – Skeletal, Cardiac, Smooth

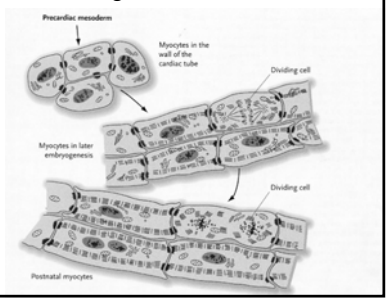
Smooth muscle : Derived from splanchnic mesoderm surrounding gut. Cellular elongation without cell fusion

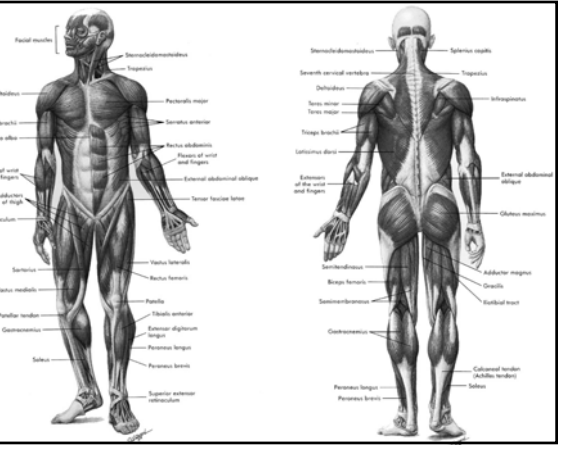
Cardiac muscle

Derived - splanchnic mesoderm

Myoblasts adhere but do not fuse

Form intercalated discs





Skeletal Muscle

Head region skeletal musculature
- Derived from head mesenchyme
- Migration from the cranial somitomeres

Trunk region skeletal musculature
- Myoblasts derived from somites
- Migration - FGF controlled
- Spindle shaped cells - line up and fuse
- Multinucleated syncitium
- Myofibrils with cross-striations - actin-myosin

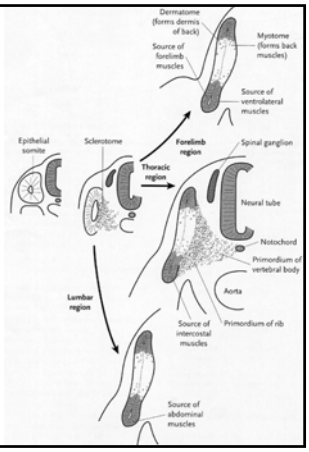
Region-Specific myoblast behavior

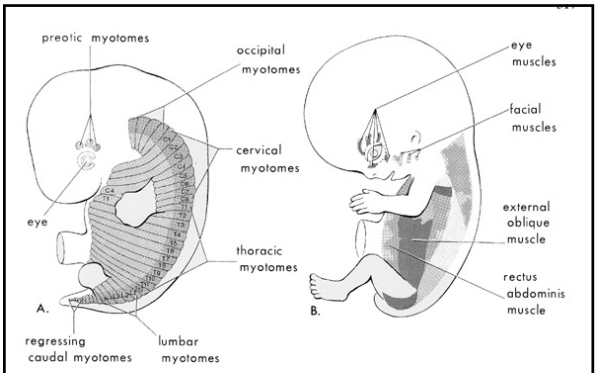
Limb Region – myoblast migration into limb primordia, Differentiation is delayed

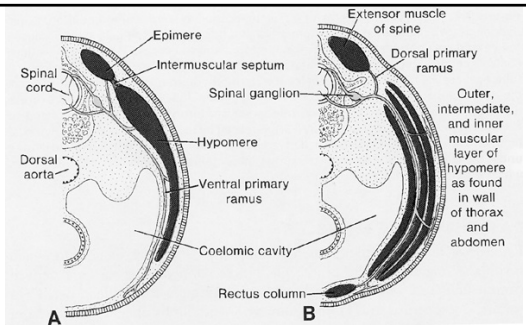
Thoracic Region – myotubes form at the somite – then invade the body wall to form the intercostal muscles

Lumbar Region – myoblast migrate to form the abdominal muscles

Myoblast behavior is controlled by their environment



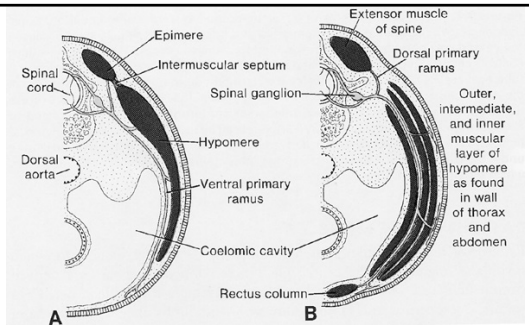




Myotome: two parts

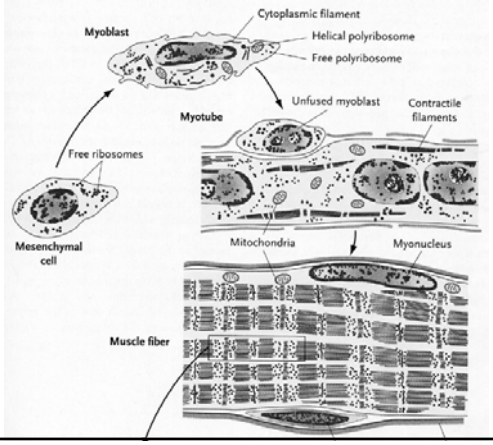
Epimere→Dorsomedial → Extensors of Vertebral column
Hypomere→Ventrolateral → limb/body wall

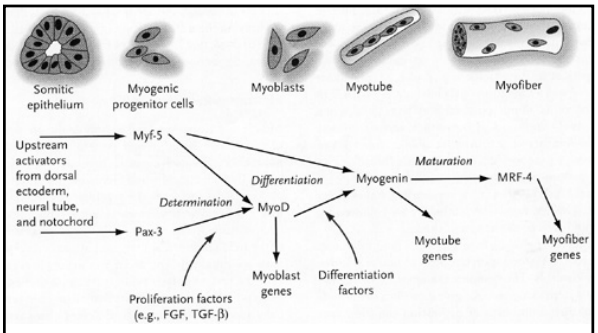
Innervating nerves – Dorsal ramus; Ventral ramus



Thoracic level – 3 myogenic layers – external intercostal, internal intercostal, transversus abdominis muscles

Ribs maintain segmented musculature, elsewhere fusion → large muscle sheets





Determination of myoblast occurs very early
Key regulators – Myf-5, Pax3, MyoD