

# The Muscular System

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## 1. Origin of the Muscular System

Muscle Type	Germ Layer Origin
Skeletal muscle	Paraxial mesoderm (somites & somitomeres)
Smooth muscle	Visceral splanchnic mesoderm around gut + ectoderm (pupil, mammary, sweat glands)
Cardiac muscle	Visceral splanchnic mesoderm surrounding heart tube

## 2. Striated / Skeletal Musculature

### Head Muscles

- Derived from seven somitomeres (paraxial mesoderm).

### Axial, Limb & Body Wall Muscles

- Derived from somites → initially form as somitomeres (occipital → tailbud)
- Somitomeres → form epithelial ball with a central cavity
  - Ventral region → becomes mesenchymal → sclerotome (vertebrae & ribs)
  - Upper region → forms dermatome + 2 muscle forming regions:
    - Dorsomedial (DML)
    - Ventrolateral (VLL)

### Formation of Myotome

- Cells from DML + VLL migrate under dermatome → form dermomyotome
- VLL cells migrate *into lateral plate mesoderm* → form:
  - Infrahyoid muscles

- Abdominal wall muscles (rectus abdominis, internal/external oblique, transversus abdominis)
- Limb muscles
- Remaining myotome cells → back muscles, shoulder girdle muscles, intercostals

### 3. Primaxial vs Abaxial Domains

Domain	Components	Developmental Signal Source
Primaxial	Somite-derived muscle cells that remain near neural tube	Neural tube + notochord
Abaxial	VLL cells that cross the lateral somitic frontier into lateral plate mesoderm	Lateral plate mesoderm

#### Lateral somitic frontier

- Boundary between somite-derived & lateral plate mesoderm-derived components
- Marks:

- o Border between primaxial vs abaxial muscle precursors
- o Border between dermis of back (somite) vs dermis of body wall (lateral plate)
- o Border in rib development:
  - Bony rib → primaxial sclerotome
  - Costal cartilage that attaches to sternum → abaxial sclerotome

#### 4. Innervation

Muscle Type	Innervation
Epaxial muscles (back)	Dorsal primary rami
Hypaxial muscles (body wall & limbs)	Ventral primary rami

⚠ New concept of primaxial vs abaxial is based on origin, not innervation - however, epaxial (back) muscles are still innervated by dorsal rami, hypaxial by ventral rami.

## 5. Differentiation of Skeletal Muscle & Tendons

- Myoblasts (muscle precursors) → fuse → long multinucleated fibers
- Myofibrils form → cross-striations visible by 3rd month
- Tendons formed from sclerotome cells (adjacent to myotome)
- Transcription factor: SCLERAXIS → essential for tendon development



## Molecular Regulation of Muscle Development

### 1. Key Signaling Pathways & Myogenic Regulatory Factors (MRFs)

Signal	Source	Target / Effect
BMP4 + FGFs	Lateral plate mesoderm	Induce VLL cells to express MyoD

WNT proteins	Ectoderm & dorsal neural tube	Work with BMP4 to activate MyoD in VLL cells
SHH (Sonic Hedgehog)	Notochord & floor plate of neural tube	Acts (with WNT) on DML cells → induces MYFS + MyoD

 Important:

- SHH does not act on VLL cells
- MyoD and MYFS are myogenic regulatory factors (MRFs) → transcription factors that activate skeletal muscle differentiation

## 2. Patterning of Muscles - Role of Connective Tissue

Region	Source of Pattern-forming CT
Head	Neural crest cells
Cervical / Occipital	Somitic mesoderm
Body wall & Limbs	Parietal layer of lateral plate mesoderm

💡 Myoblasts migrate into these regions → pattern determined by the connective tissue, not by the myoblasts themselves.

### 3. Head Musculature

- All voluntary muscles in the head = paraxial mesoderm (somitomeres & somites)
- Includes tongue, extraocular muscles, and pharyngeal arch muscles
- Exception → Iris muscles (pupillary muscles) = derived from ectoderm of optic cup
- Patterning directed by neural crest-derived connective tissue

### 4. Limb Musculature

- Appears in 7th week as mesenchymal condensations at limb bud base

- Mesenchyme = from dorsolateral somite cells (migrating into limb bud)
- Patterning → by connective tissue of lateral plate mesoderm (same source that forms limb bones)

## 5. Cardiac Muscle

Feature	Description
Origin	Visceral (splanchnic) mesoderm around heart tube
Myoblasts	Do not fuse (unlike skeletal muscle)
Intercellular junctions	Become intercalated discs
Specialized bundles	Purkinje fibers → conduct electrical impulses

## 6. Smooth Muscle

Site	Origin
Dorsal aorta & large arteries	Lateral plate mesoderm + neural crest cells

Coronary arteries - proximal segments	Neural crest cells
Coronary arteries - distal segments	Proepicardial mesoderm
Gut and gut derivatives	Splanchnic (visceral) layer of lateral plate mesoderm
Pupillary sphincter & dilator muscles, sweat and mammary gland muscles	Ectoderm

## Transcriptional Control of Smooth Muscle Differentiation

- Serum Response Factor (SRF)
  - Master transcription factor for smooth muscle development
  - Activated (upregulated) by growth factor-induced phosphorylation pathways
- Myocardin + MRTFs (myocardin-related transcription factors)
  - Act as coactivators of SRF
  - Drive expression of smooth muscle-specific genes

## Clinical Correlates of Muscle Development

Condition	Description / Key Features
Partial/complete absence of muscle	Common; usually not severe (e.g., palmaris longus, serratus anterior, quadratus femoris)
Poland sequence	Absence of pectoralis minor + partial loss of pectoralis major (sternal head). Often associated with nipple/areola displacement and digital anomalies (e.g. syndactyly, brachydactyly).
Prune belly syndrome	Absence of abdominal musculature → thin abdominal wall. Frequently associated with urinary tract malformations → abdominal distension → atrophy of abdominal muscles.
Muscular dystrophy	Inherited disorders with progressive muscle wasting.
Duchenne muscular dystrophy (DMD)	Most common (1/4,000 male births). X-linked recessive → affects males. No functional dystrophin → severe, early onset (<5 yrs).

Becker muscular dystrophy (BMD)	Milder form, later onset (8-25 yrs). Reduced/abnormal dystrophin.
Dystrophin	Cytoplasmic protein → links cytoskeleton to extracellular matrix via dystrophin-associated complex.

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