The Muscular System

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💪 Development of the Muscular System

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:
    - Border between primaxial vs abaxial muscle precursors
    - Border between dermis of back (somite) vs dermis of body wall (lateral plate)
    - 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 (High-

Yield Points)

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.