EMBRYOLOGY OF MUSCLE

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OUTLINE

SUMMARY OF ABBREVIATIONS

FGF	Fibroblast Growth Factor
AER	Apical Ectodermal Ridge
ZPA	Zone of Polarizing Activity

LEGENDS

Must know	Lecturer	Book	Presentation	Old Trans
❗	👩‍⚕️	📖	🖥️	📝

LEARNING OBJECTIVES

At the end of the lecture, the student should be able to:

✔ Identify the areas and/or cells of origin of the muscle

✔ Discuss the development of the different types of muscle

EMBRYOLOGY OF MUSCLE

MUSCULAR SYSTEM

- **Mesoderm**
- **Skeletal muscle**
  - Paraxial mesoderm - somites and somitomeres
- **Smooth muscle**
  - Visceral **splanchnic mesoderm -** gut and gut derivatives
  - **Ectoderm -** pupillary, mammary gland, sweat gland muscles
- **Cardiac muscle**
  - Visceral **splanchnic mesoderm -** heart tube

EMBRYOLOGY OF MUSCLE: STRIATED SKELETAL MUSCULATURE

STRIATED SKELETAL MUSCULATURE

- **Head**
  - Seven **somitomeres -** mesenchymal cells derived from paraxial mesoderm
    - Mesenchymal cells = Embryonic connective tissue
- **Axial skeleton, body wall, limbs**
  - **Somites -** occipital region to the tail bud
- **Epithelialization**
  - Somitomeres immediately after segmentation
  - Form a "**ball" of epithelial cells** with a small cavity
- NOTE: Yung Ventral somite wall yung nasisira nagiging sclerotome cells that migrate and differentiate

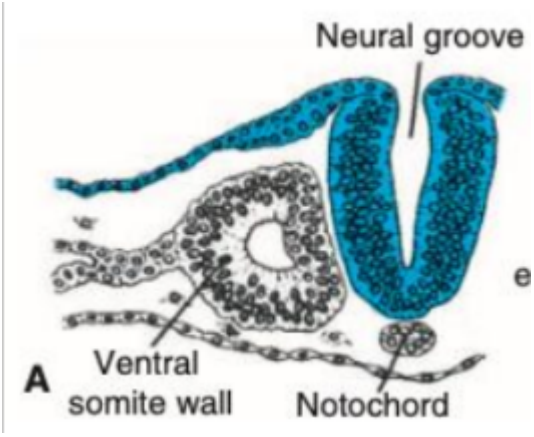

Figure 1. Striated Skeletal Musculature

- **Sclerotome**
  - **Ventral region** of the somite becomes mesenchyme
  - **Bone-forming cells** for vertebrae and ribs
  - **Upper part:** dermatome
  - **Dorsomedial and ventrolateral:** muscle-forming areas

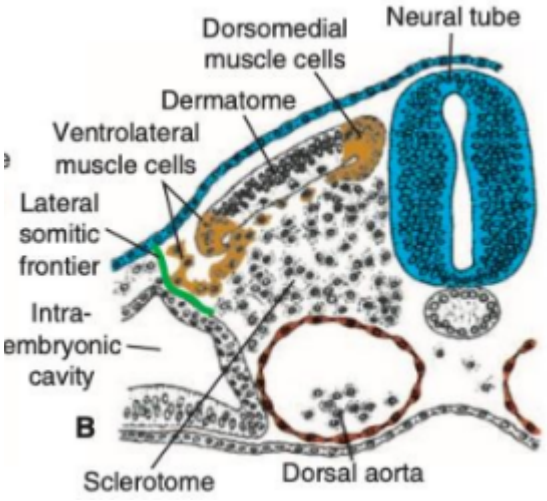

Figure 2. Sclerotome

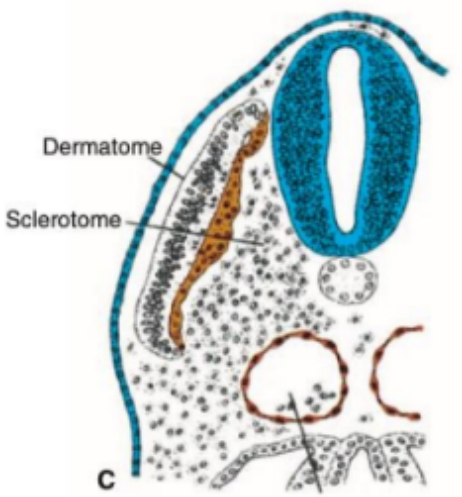

Figure 3. Sclerotome and Dermatome

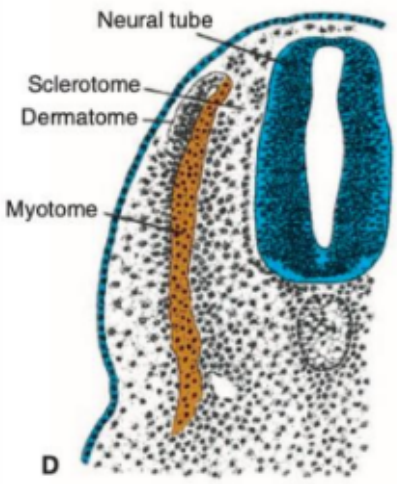

Figure 4. Myotome and Neural tube

- **Dermomyotome**
  - Cells from VLL and DML lips migrate and proliferate
  - 👩‍⚕️ *Parang pinagcombine mo sila na dermatome na nilagyan mo na ng muscle-forming cells. Because eventually, magkakamuscle. So you call it your DERMO-MYO-tome*

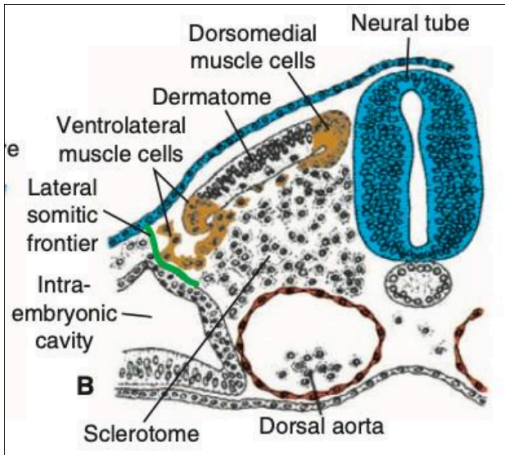

Figure 5. Dermomyotome

- Progenitor muscle cells ventral to the dermatome
  👩‍⚕️ *kasi magfoform na siya ng muscle. Maraming magmimigrate sa VLL at DLL…Iba din yung shape.*

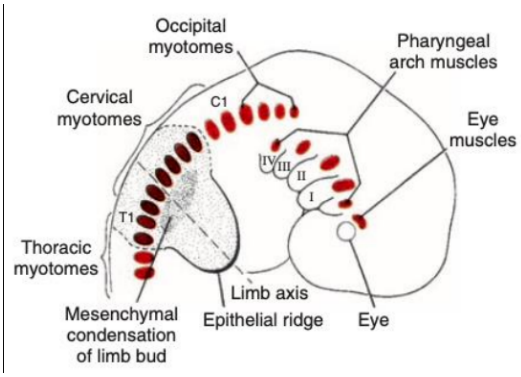

Figure 6. Myotomes

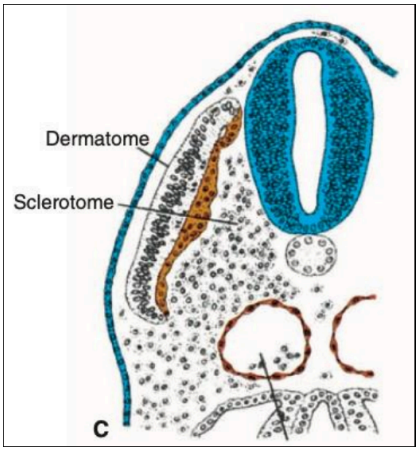

Figure 7. Dermatome and Sclerotome

- Cells of VLL migrate into the parietal layer of the **Lateral Plate Mesoderm**
  👩‍⚕️ *Diba may mga cells na nagstay dito sa ventral()dermatome. Meron din nagcross ng border:*
  - **Infrahyoid**
  - **Abdominal wall:**
    - rectus abdominis
    - internal and external oblique
    - transversus abdominis
  - **Limb muscles**
    👩‍⚕️ *Ibig sabihin, ito po yung mga muscles na nagcross papunta sa Lateral Plate Mesoderm*

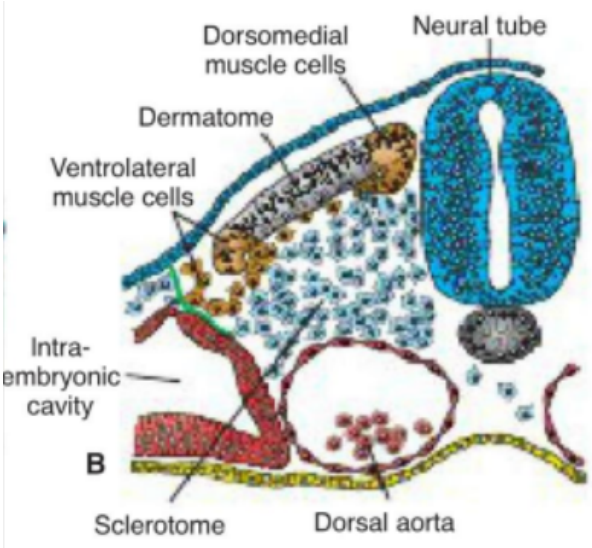

Figure 8. Lateral Plate Mesoderm

- **Remaining Cells**
  - Shoulder girdle
  - Intercostal muscles

TABLE 11.1 *Origins of Muscles from Abaxial and Primaxial Precursors*

	Primaxial	Abaxial
Cervical region	Scalenes	Infrahyoid
	Geniohyoid	
	Prevertebral	
Thoracoabdominal region	Intercostals	Pectoralis major and minor
		External oblique
		Internal oblique
		Transversus abdominus
		Sternalis
		Rectus abdominus
		Pelvic diaphragm
Upper limb	Rhomboids	Distal limb muscles
	Levator scapulae	
	Latissimus dorsi	
Lower limb[a]		All lower limb muscles

[a]The precise origin of muscles in the pelvic region and lower limb has not been determined, but most if not all are abaxial in origin.

Figure 9. Origins of Muscles from Abaxial and Primaxial Precursors

LATERAL SOMITIC FRONTIER

- **Border** between each somite and the parietal layer of lateral plate mesoderm
- Separates mesodermal domains in the embryo

PRIMAXIAL DOMAIN

- **Neural tube**
- Only **somite-derived** (paraxial mesoderm) cells
- **Precursors:** VLL cells and all DML cells that do not cross/ migrate the frontier
  - VLL: VENTRO LATERAL
  - DML: DORSOMEDIAL

ABAXIAL DOMAIN

- Parietal layer of **lateral plate mesoderm with somite cells**
- **Precursors:** VLL edge cells that cross the frontier and enter the lateral plate

- Each myotome receives its **INNERVATION** from spinal nerves derived from the **SAME SEGMENT** as the muscle cells
- **LATERAL SOMITIC FRONTIER**
  - **Border** between dermis from dermatomes in the back and from lateral plate mesoderm in the body wall
  - **Border** for rib development - bony vs cartilaginous components

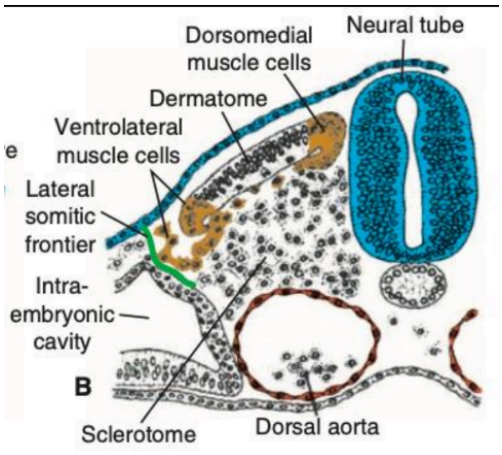

Figure 10. Somitic Frontiers

INNERVATION OF AXIAL SKELETAL MUSCLE

EMBRYOLOGICAL ORIGIN (muscle cell precursors)

- **ABAXIAL**
- **PRIMAXIAL**

👩‍⚕️Newest classification are Abaxial and Primaxial muscle but epaxial and hypaxial are still used as they basically still mean the same

EPAXIAL (above the axis)

- innervated by the **Dorsal Primary Rami**
- such as the back muscles

HYPAXIAL (below the axis)

- Innervated by the **Ventral Primary Rami**
- such as the body wall and limb muscles

SKELETAL MUSCLE AND TENDONS

MYOBLASTS

- forms muscles
- eventually they fuse and form **long, multinucleated muscle fibers**
- **Myofibrils** appear and **cross-striations** appear by the end of the **3rd month**

SCLEROTOME CELLS

- forms tendons
- Adjacent to **myotomes**
- From the **anterior and posterior borders of somites**
- development is regulated by **SCLERAXIS** transcription factor
  - 👩‍⚕️We will not look much into SCLERAXIS, but do note that the regulation of the development by different transcriptions factors, inhibiting and stimulating proteins are still part of EMBRYOLOGY

PATTERNING OF MUSCLES

- Patterning of muscles is dependent on the connective tissue into which myoblasts migrate.
  - 👩‍⚕️Connective tissue signals the patterning

- Muscles of the head come from **NEURAL CREST CELLS**
- Cervical and occipital come from **SOMITIC MESODERM**
- Body wall and limbs come from **PARIETAL LAYER OF LATERAL PLATE MESODERM**

👩‍⚕️Basically, where they originate from, is also how we determine their patterning.

HEAD MUSCULATURE

- **Paraxial mesoderm -** somitomeres and somites
  - these determine the muscles of:
    - tongue
    - eye (**except** iris since it comes from the optic cup ectoderm)
    - pharyngeal arches
- **Patterning** is directed by connective tissue derived from **neural crest cells**

*Please see appendix for Table 1. Origins of the Craniofacial Muscle

LIMB MUSCULATURE

- **7th week of development**
  - Condensation of mesenchyme near the base of the limb buds.
    - 👩‍⚕️*Lagi munang mag sstart kay mesenchyme kasi ang bones ng limbs ay long bones (endochondral), kailangan muna ng condensation ng mesenchyme to become hyaline cartilage.*

- **Ventrolateral cells** of somites that migrate into the limb bud.
- Initially **segmented** according to somites from which they are derived.

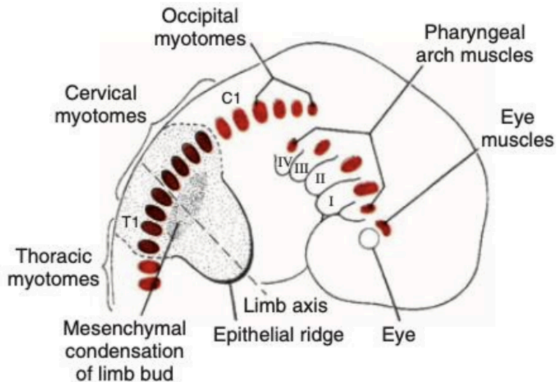

Figure 11. Development of Limbs

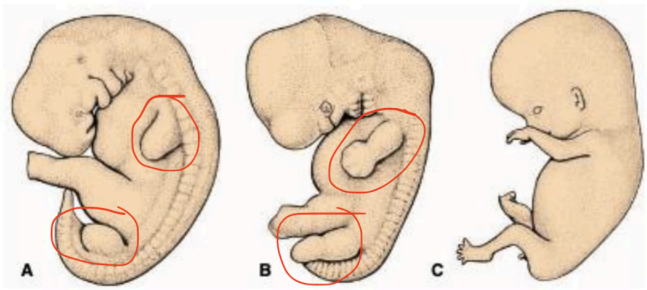

Figure 12. Limb buds (👩‍⚕️*Limb buds that eventually turns into limbs na meron tayo ngayon)*

- 👩‍⚕️*Because of this further development, nagka-karoon na tayo ng components ng muscle ng limbs*

- Splits into **FLEXOR and EXTENSOR**
- Patterning is directed by connective tissue from **parietal layer of lateral plate mesoderm**

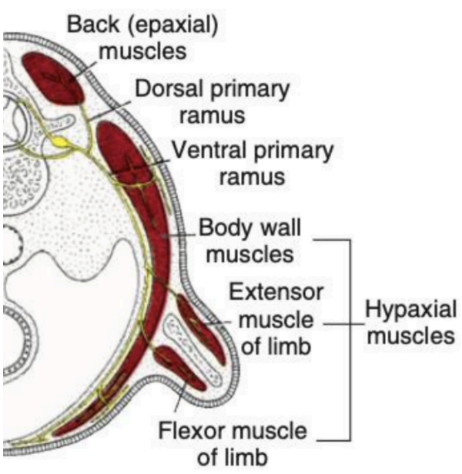

Figure 13. Development of Limb's Muscle Components

- **UPPER LIMB BUDS**
  - Opposite the lower five cervical and upper two thoracic segments
- **LOWER LIMB BUDS**
  - Opposite the lower four lumbar and upper two sacral segments
  - 👩‍⚕️Lower limb buds and upper limb buds technically have the same development and musculature

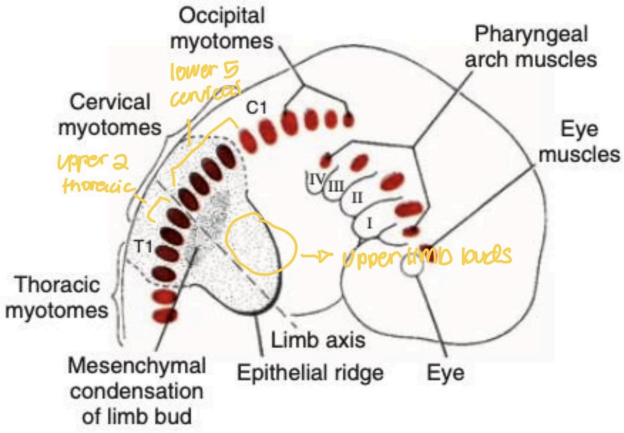

Figure 14. Upper Limb Buds

- **VENTRAL PRIMARY RAMI** penetrate into the mesenchyme
  - Branches unite to form large dorsal and ventral nerves
  - 👩‍⚕️Nagkakaroon ng maraming branches, but those branches eventually unite to form large nerves
  - 👩‍⚕️Ex. From dorsal segmental branches, eventually they will form the radial nerves which will innervate the extensor muscle of the limbs
  - **RADIAL NERVE:** Extensors
    - Dorsal segmental branches
  - **ULNAR AND MEDIAN NERVES:** Flexors
    - Ventral branches

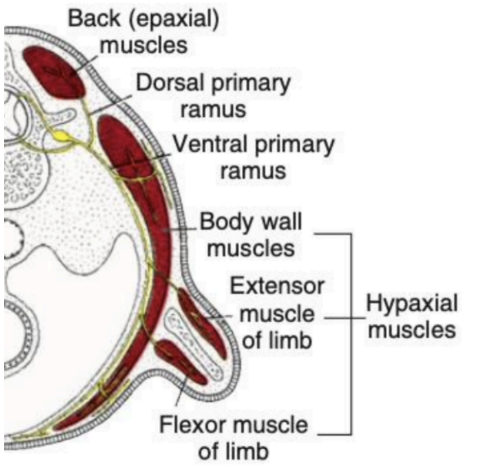

Figure 15. Ventral primary rami

- **COMPLETE DIFFERENTIATION**
  - Crucial: Early contact between the nerve and muscle cells
- **SPINAL NERVES**
  - **Sensory innervation** for the dermatomes
    - 👩‍⚕️Results into different dermatomal patterns
    - 👩‍⚕️When you test different dermatomes, meron kayong marker kung saan mag tetest
    - 👩‍⚕️Not distinct structures or not structures that have distinct boundaries. It overlaps because its embryonic development
  - **Dermatomal pattern** changes with growth and rotation of the extremities

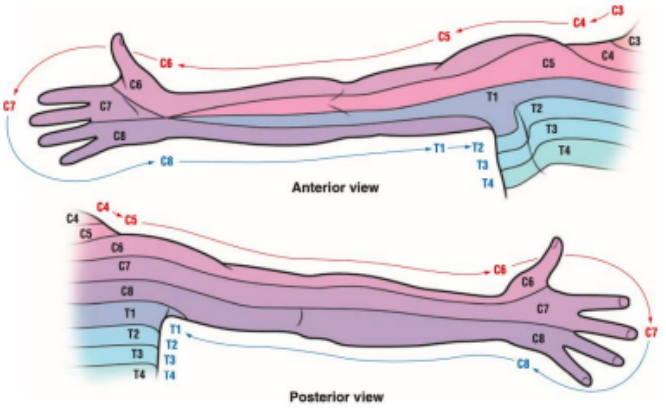

Figure 16. Dermatomal pattern

- Molecular Regulation
  - ❗ HOMEOBOX (HOX) genes – responsible for the proper positioning of the limbs along the craniocaudal axis in the flank regions
  - ❗ HOXB8 – cranial border of the forelimb
    - FORELIMB ONLY
    - Does not go beyond the flank regions area, if it goes beyond, iba yung formation ng limbs mo
  - ❗ FGF4 and FGF8
    - Fibroblast Growth Factor 4 and Fibroblast Growth Factor 8
    - maintains the undifferentiated zone
    - Rapidly proliferating mesenchymal cells adjacent to the ridge
    - Distal growth of the limb
    - When you form the apical ectodermal ridge (AER), there are still undifferentiated mesenchymal cells. Their importance is still linked to the distal growth of the limbs.
      - If you destroy them, it won't grow agad-agad

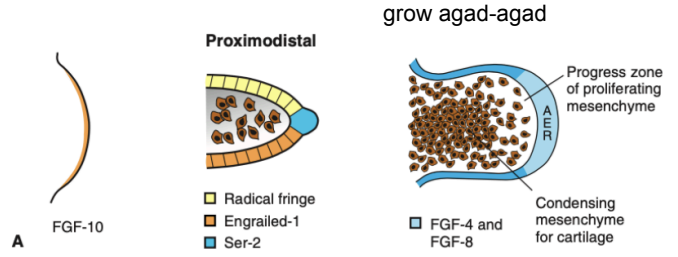

Figure 17. Molecular Regulation of Proximodistal Limb

- Zone of Polarizing Activity – patterning of the anteroposterior axis
  - Cluster of cells at the posterior border of the limb near the body wall
  - ❗ SHH sonic hedgehog
    - Secreted by ZPA
    - Regulating protein transcription factor
  - Significance, if nalipat or mali positioning, may limb pa na tutubo aside from the normal one = ABNORMAL DEVELOPMENT

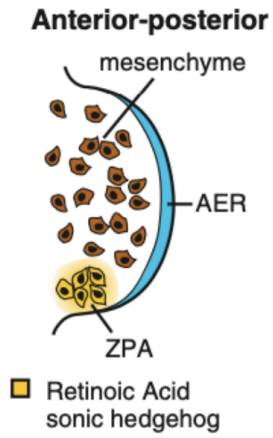

Figure 18. Regulation of Anterior-Posterior Limb Patterning
A specialized group of mesenchymal cells at the posterior margin forms the Zone of Polarizing Activity (ZPA). It is mediated by Retinoic Acid initiation and localized secretion of Sonic hedgehog (Shh). The ZPA establishes a morphogen gradient across the underlying mesenchyme while interacting with the distal Apical Ectodermal Ridge (AER) to direct proper digit identity and spatial organization

EMBRYOLOGY OF MUSCLE: CARDIAC MUSCLE

- Visceral Mesoderm surrounds the endothelial heart tube
- Intercalated Discs
  - Myoblasts that adhered to one another
- NO FUSION of myoblasts
  - If you look under the microscope, iba yung itsura and arrangement of fibers
- Purkinje Fibers: are the conducting system
  - Special bundles with irregularly distributed myofibrils

EMBRYOLOGY OF MUSCLE: SMOOTH MUSCLE

- **Lateral Plate Mesoderm and Neural Crest Cells**
  - Dorsal aorta and large arteries
- **Proepicardial Cells**
  - Coronary arteries
  - Proximal segment from **neural crest cells** (exception).
- **Splanchnic Layer Of Lateral Plate Mesoderm**
  - Gut and gut derivatives
- **Ectoderm**
  - Sphincter and dilator muscles of the pupil
  - Mammary and sweat glands
- **Serum Response Factor**
  - 👩‍🔬 This is attributed to the proper development of smooth muscles to ensure that mesenchymal muscle cells differentiate into smooth muscles.
  - Smooth muscle cell **differentiation.**
  - **Kinase phosphorylation** pathways
    - 👩‍🔬Kinase activates phosphorylation which activates serum response factor.
  - **Myocardin** and **myocardin-related transcription** factors as co-activators

APPENDIX

Table 1. Origins of the Craniofacial Muscles

Mesodermal Origin	Muscles	Innervation
Somitomeres 1 and 2	Superior, medial, ventral recti	Oculomotor (III)
Somitomere 3	Superior oblique	Trochlear (IV)
Somitomere 4	Jaw closing	Trigeminal (V)
Somitomere 5	Lateral rectus	Abducens (VI)
Somitomere 6	Jaw opening, other second arch	Facial (VII)
Somitomere 7	Stylopharyngeus	Glossopharyngeal (IX)
Somites 1 and 2	Intrinsic laryngeals	Vagus (X)
Somites 2-5*	Tongue	Hypoglossal (XII)

**Somites 2 to 5 constitute the occipital group (somite 1 degenerates for the most part)*