

Segmentation

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What are segments?

Repeated units of anatomical but not necessarily biochemical identity.

Segments develop from unsegmented tissue and acquire strict borders.

A “no mixing rule” contributes to segment identity.

In vertebrates segments are most prominent in the paraxial mesodermal and are called somites.

Topics

1. Segmentation of trunk mesoderm: the derivatives of paraxial mesoderm = the somites.

A. Cells of origin of somites.

B. Follow anatomical changes and molecular underlying.

C. Imposition of segmentation on trunk PNS.

D. Concept of homeotic transformations and hox (homeobox) genes.

2. Segmentation CNS –the rhombomeres of the hindbrain.

Compaction: establishment of inner and outer lineages

I. PATTERNS OF DEVELOPMENT

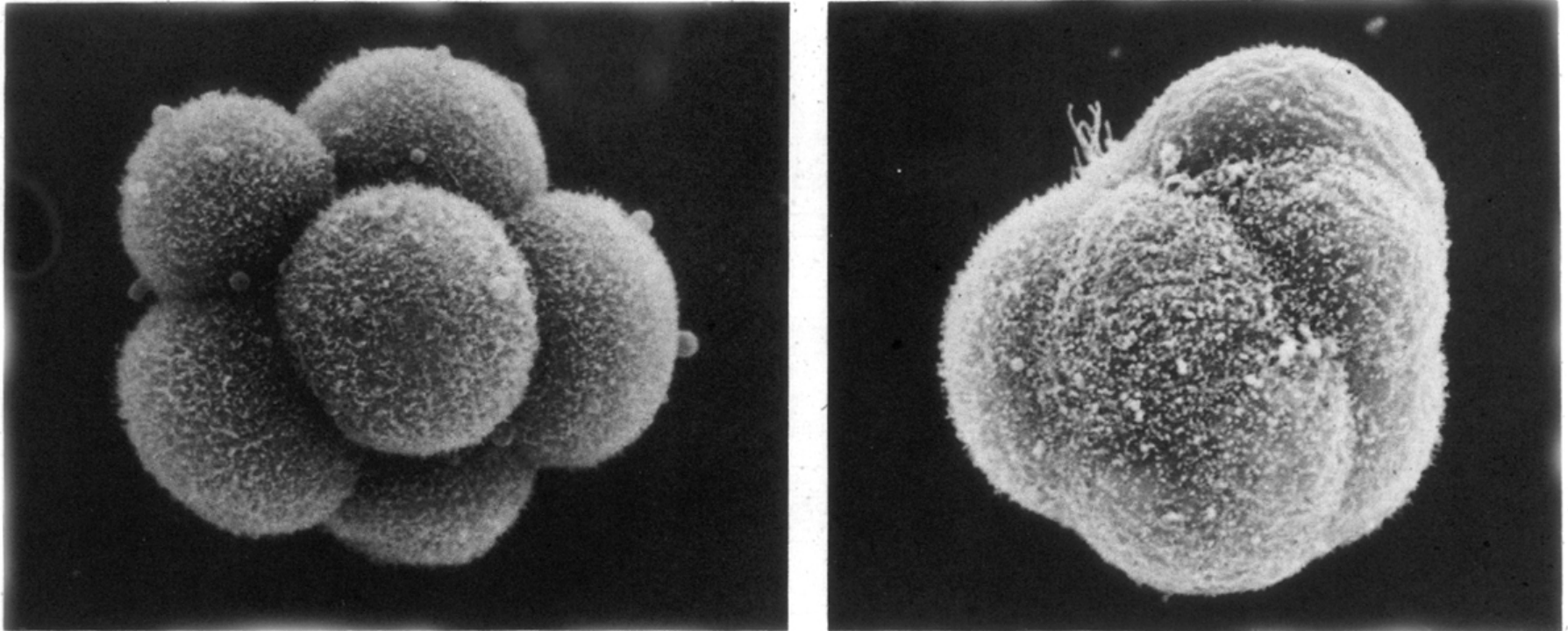
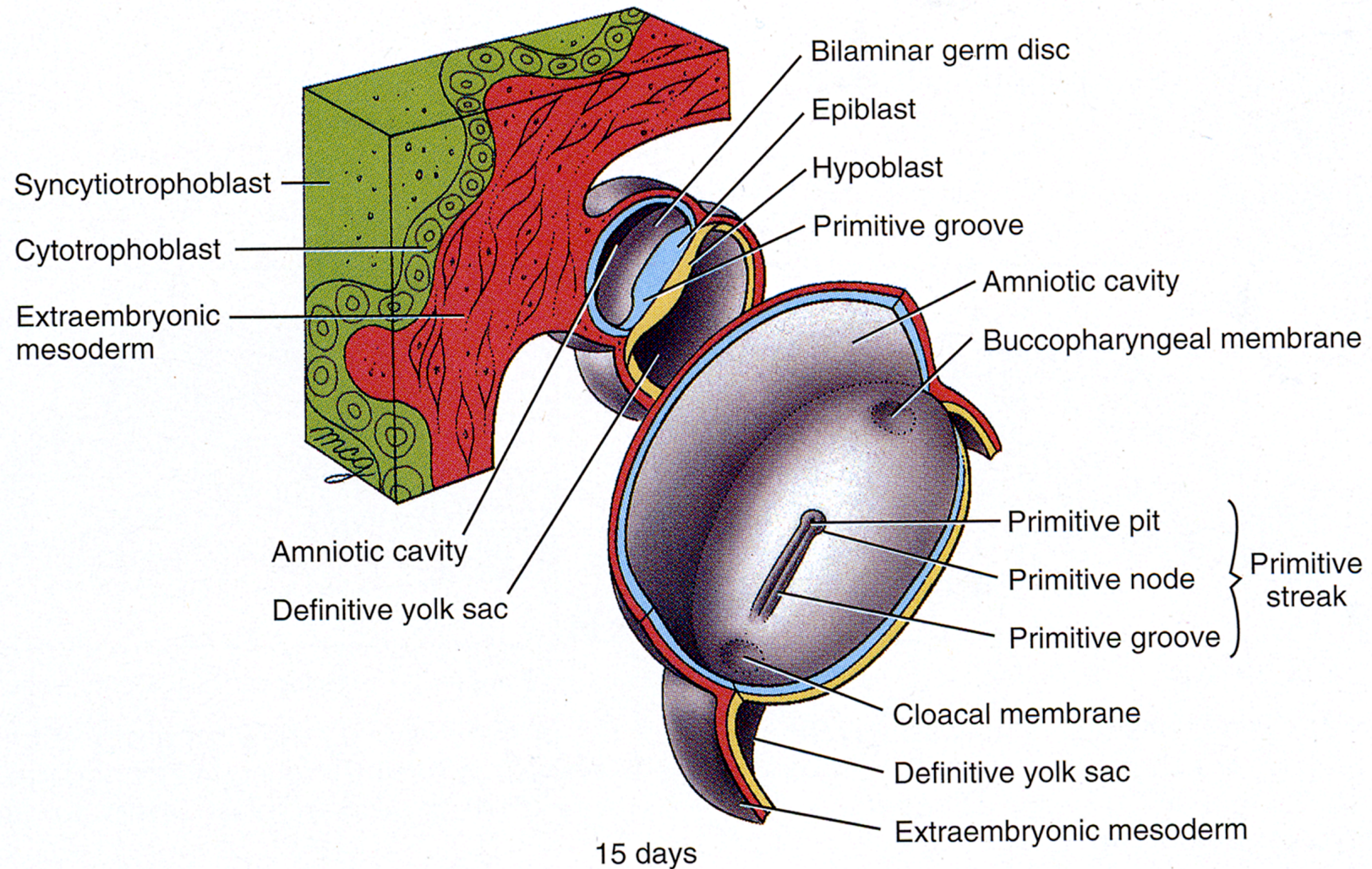


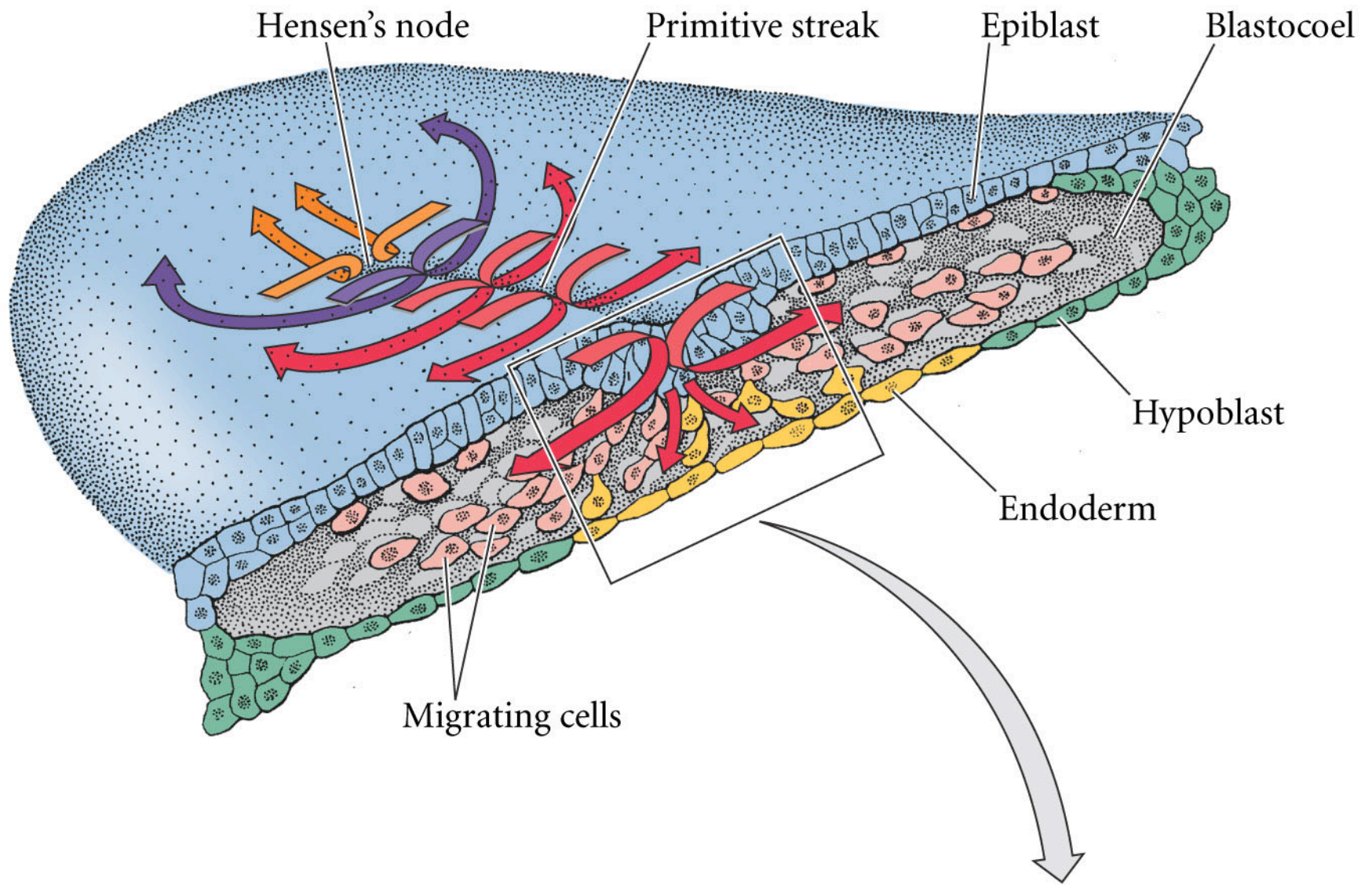
FIGURE 21

Scanning electron micrograph of uncompact (left) and compact (right) 8-cell mouse embryo. (Photographs courtesy of C. Ziomek.)

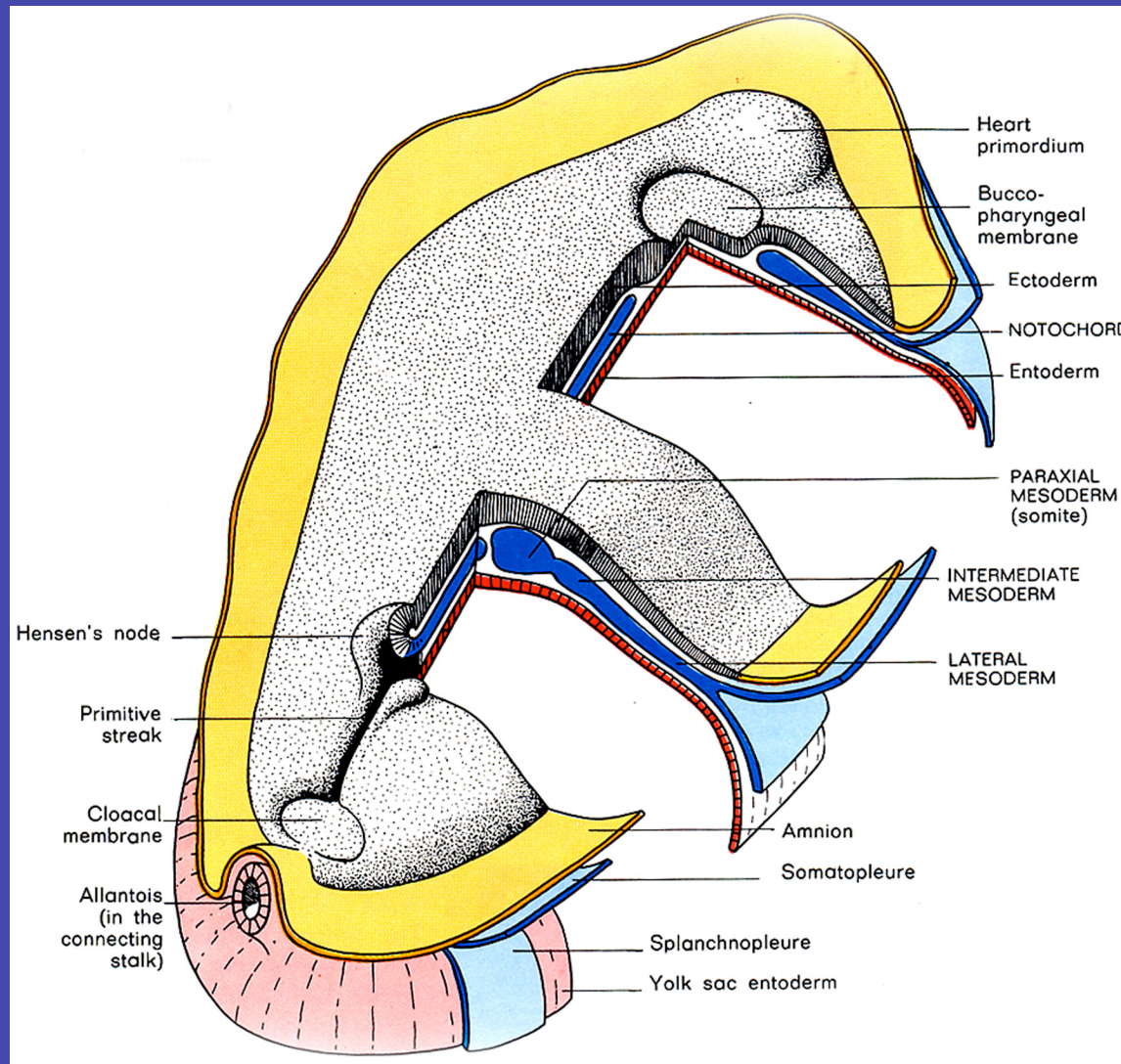
their behavior. They suddenly huddle together, maximizing their contact with the other blastomeres and forming a compact ball of cells (Figure 21). This tightly packed arrangement is stabilized by tight junctions that form between the outside cells of the ball, sealing off the

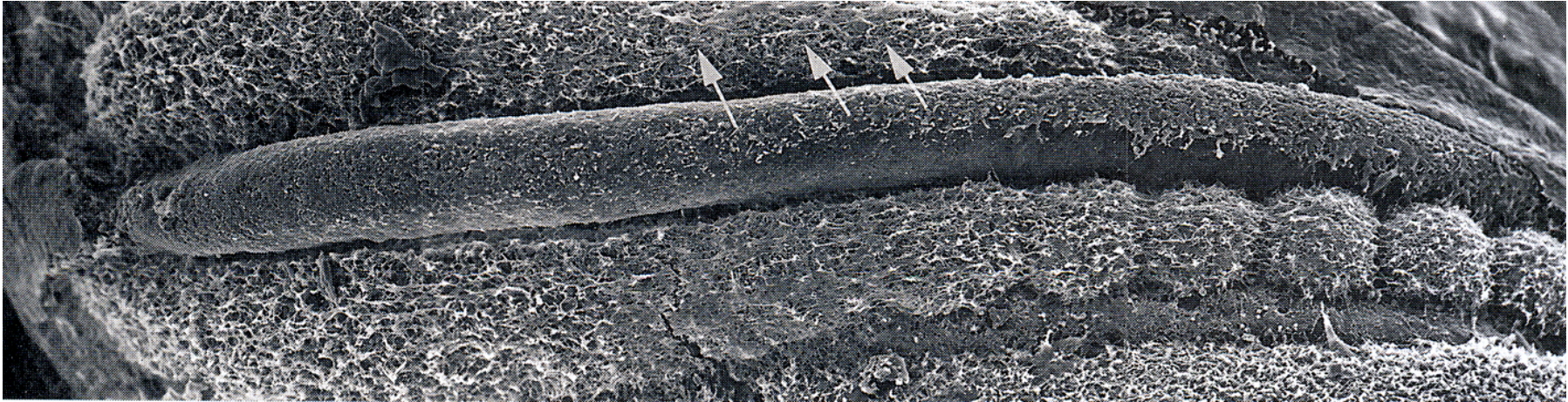


First sign of gastrulation
is the formation at midline of primitive streak.
Formation of streak defines cranial and caudal axes.

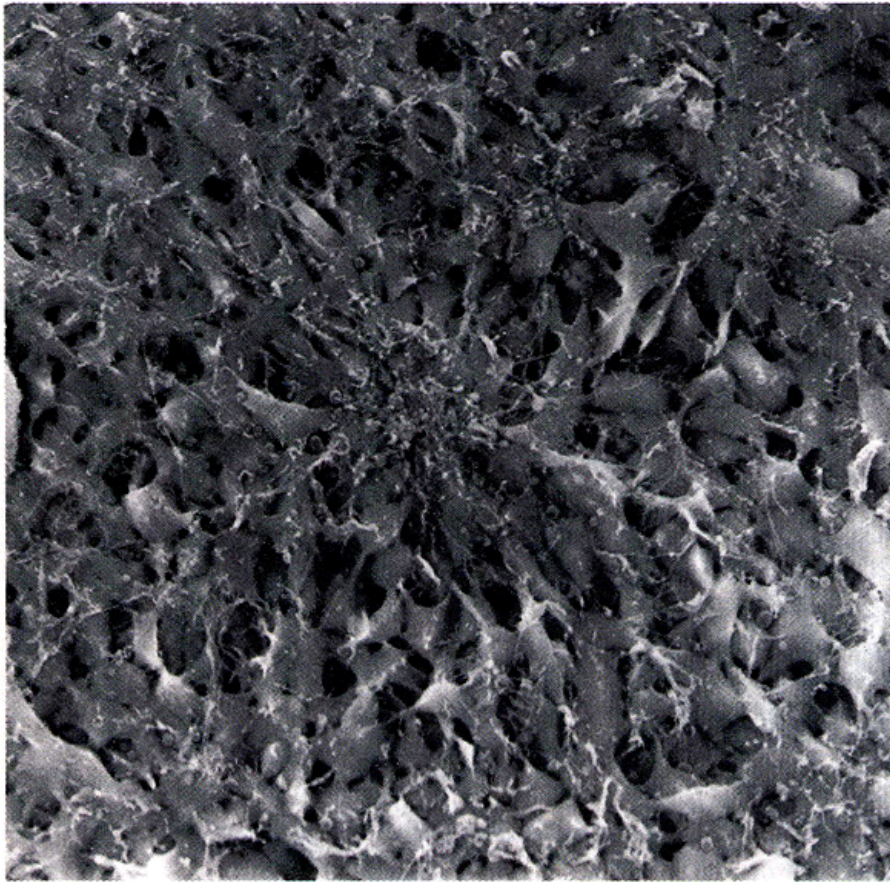


At the end of gastrulation the 3 primary germ layers are present. The 3 axes of the embryo are established. The embryo still touches extra-embryonic tissue on all edges.

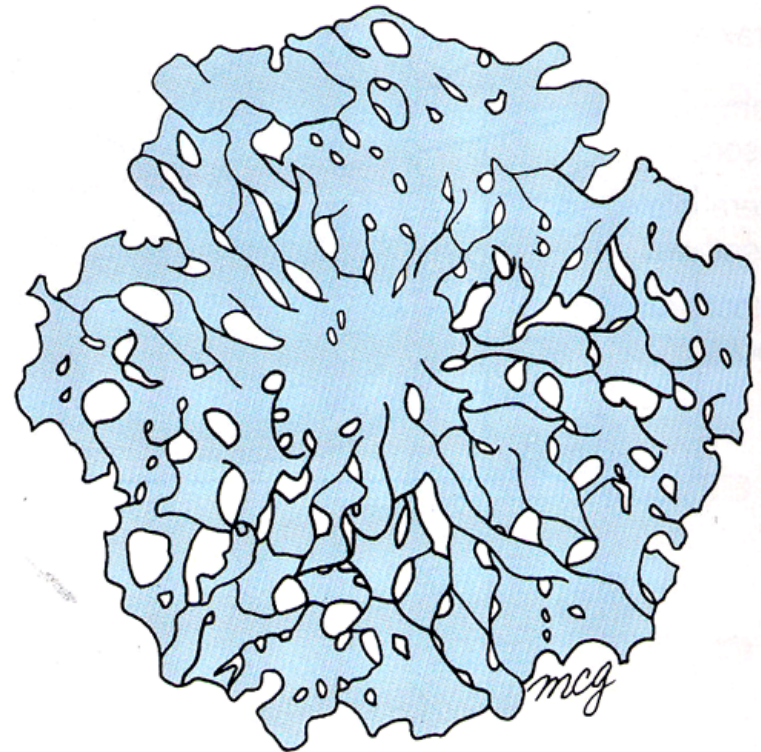




Scanning EM and diagram of a somitomere: organized whorl of cells that **prefigure** the somites.



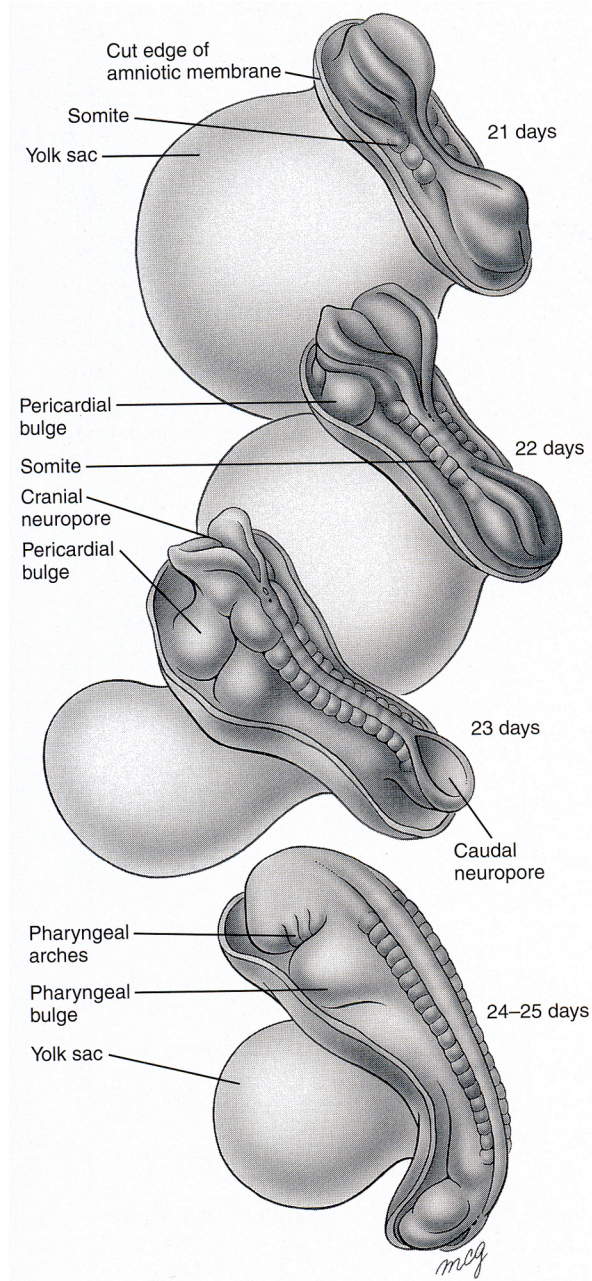
A



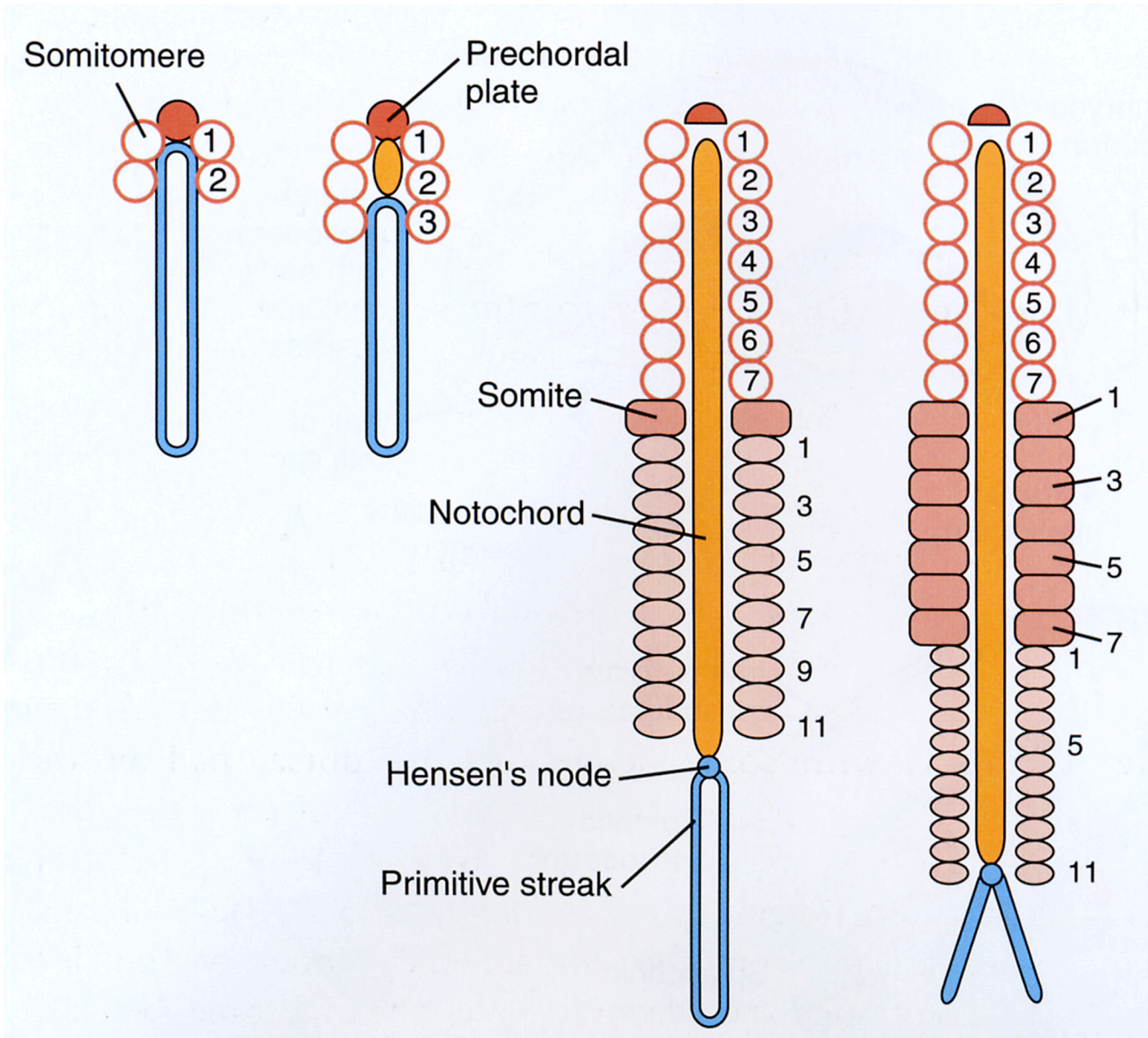
B

Sequential addition of somites from day 21- day 25 post-conception

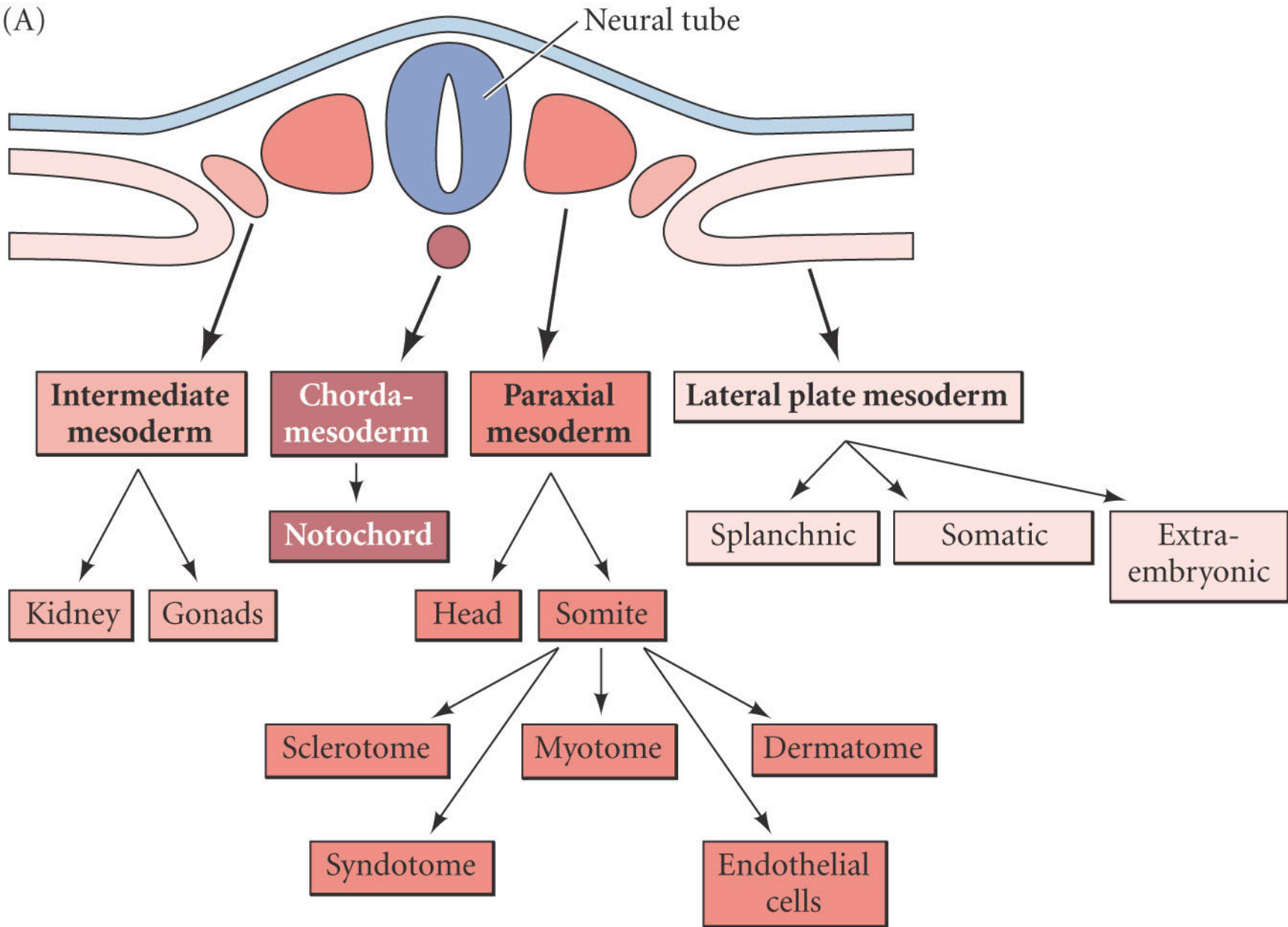
Humans are estimated to have 42-44 pairs



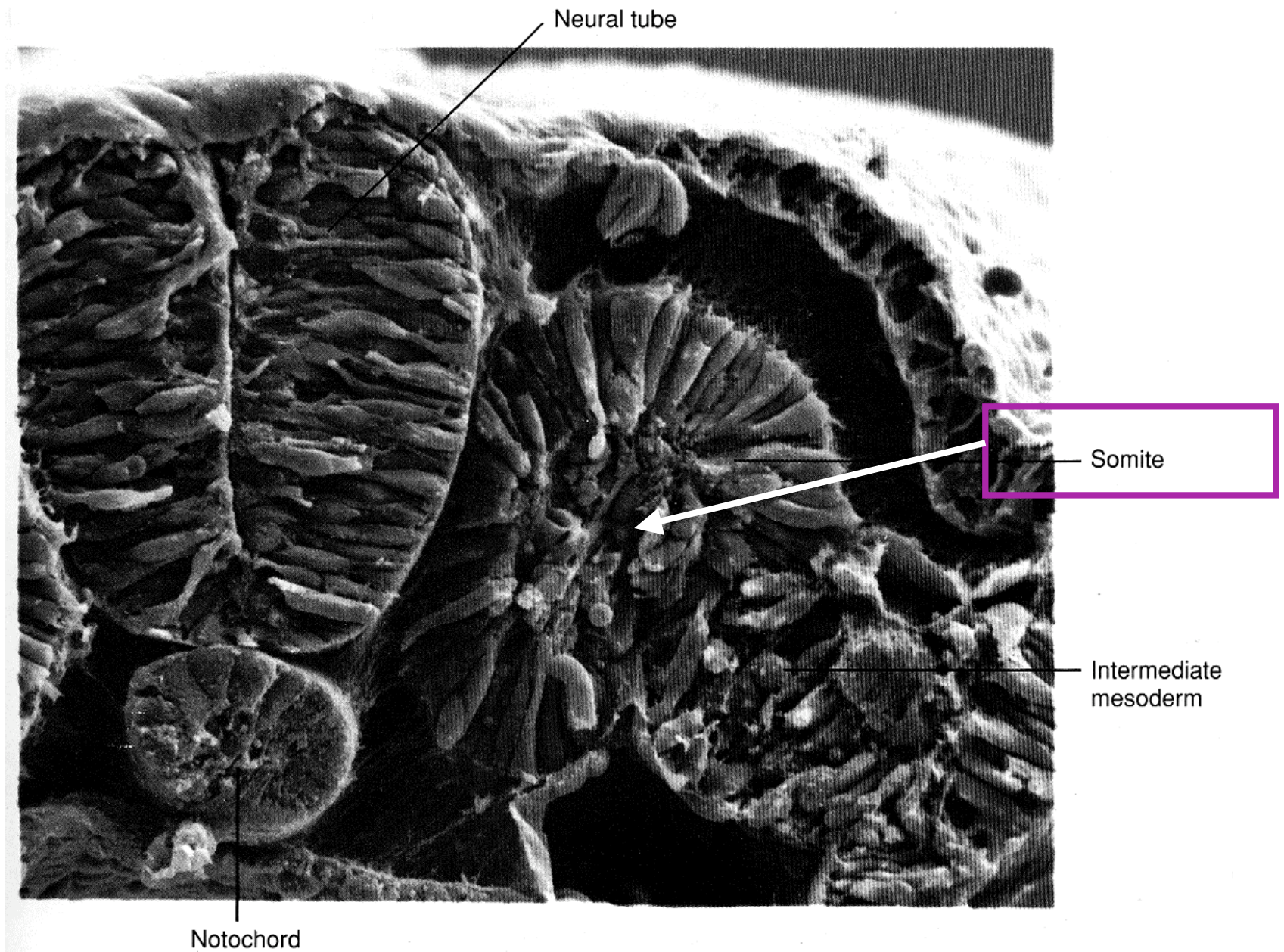
Sequential appearance of somitomeres and somites



(A)



Scanning EM of the epithelial somite.



Fate of somites

vertebral column

skeletal/segmental muscles of trunk

skeletal muscle of limb.

Somite undergoes epithelial to mesenchymal transformation (down regulate adhesion factors).

Somite has territories.

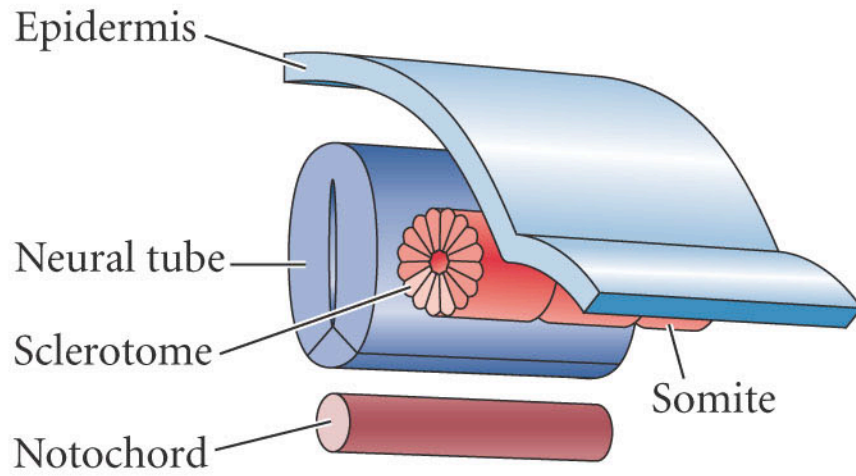
Medial = sclerotome = vertebrae

Lateral = dermamyotome

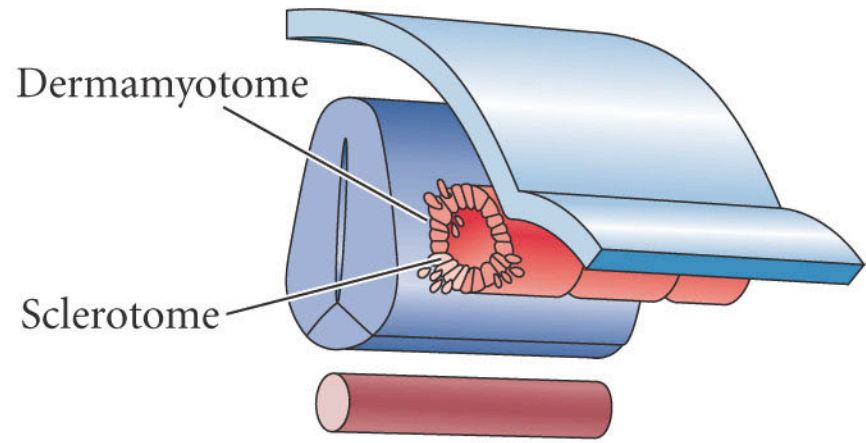
- dermatome = dermis derived from most lateral aspect.

- myotome = epimere and hypomere = segmented muscles and muscles of the limb.

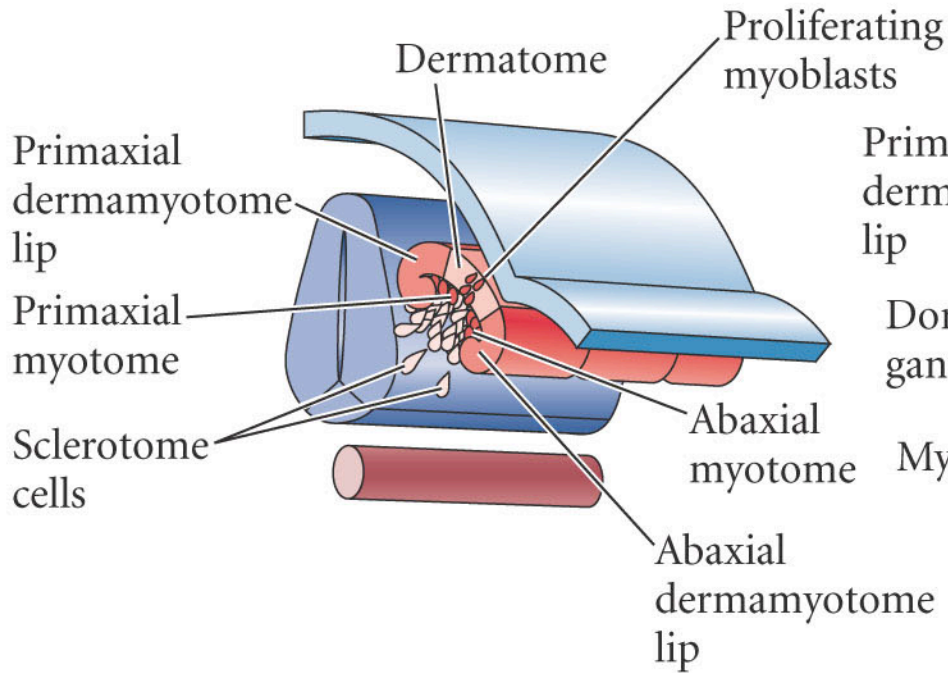
(A) 2-day embryo



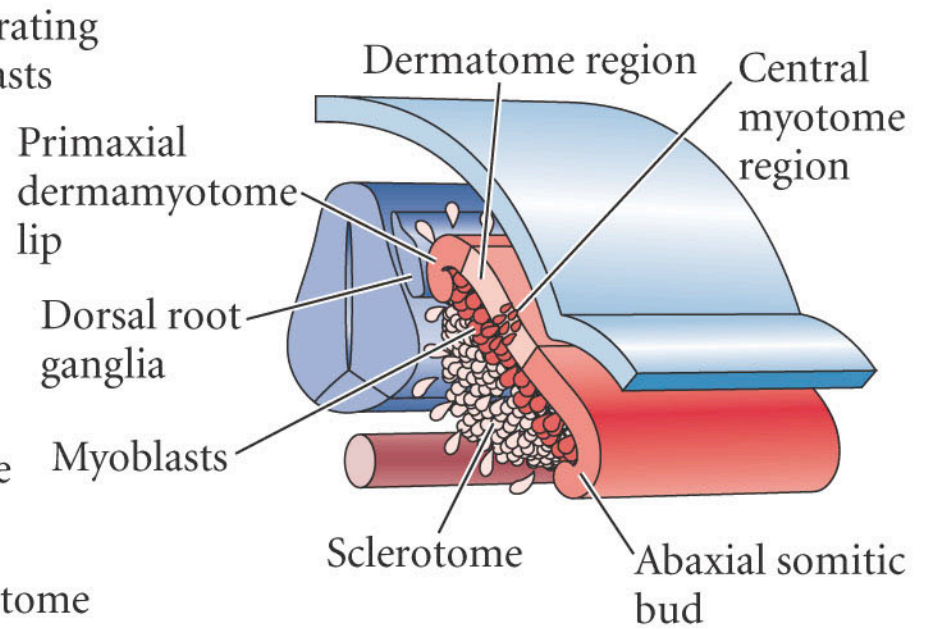
(B) 3-day embryo



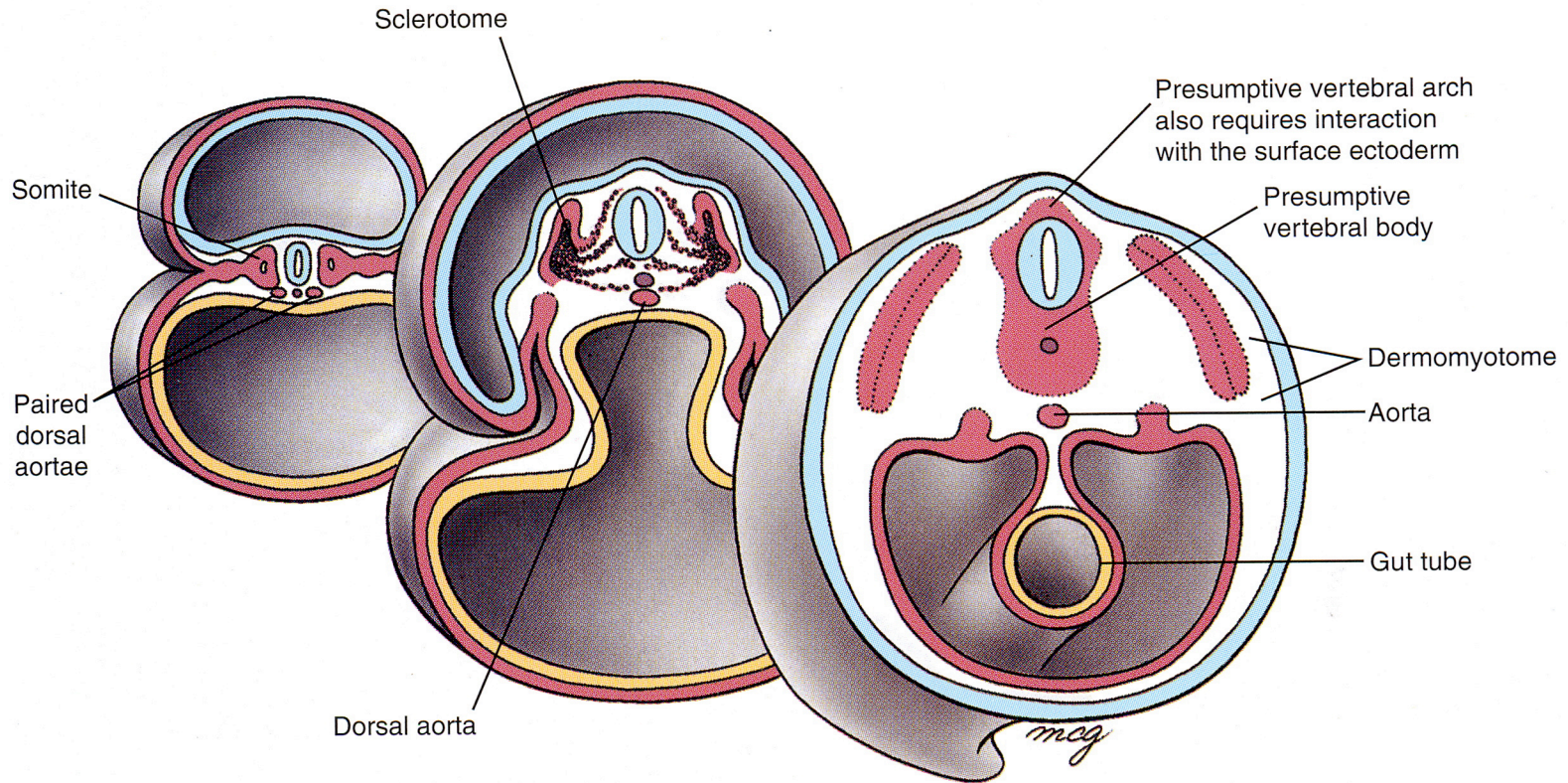
(C) 4-day embryo



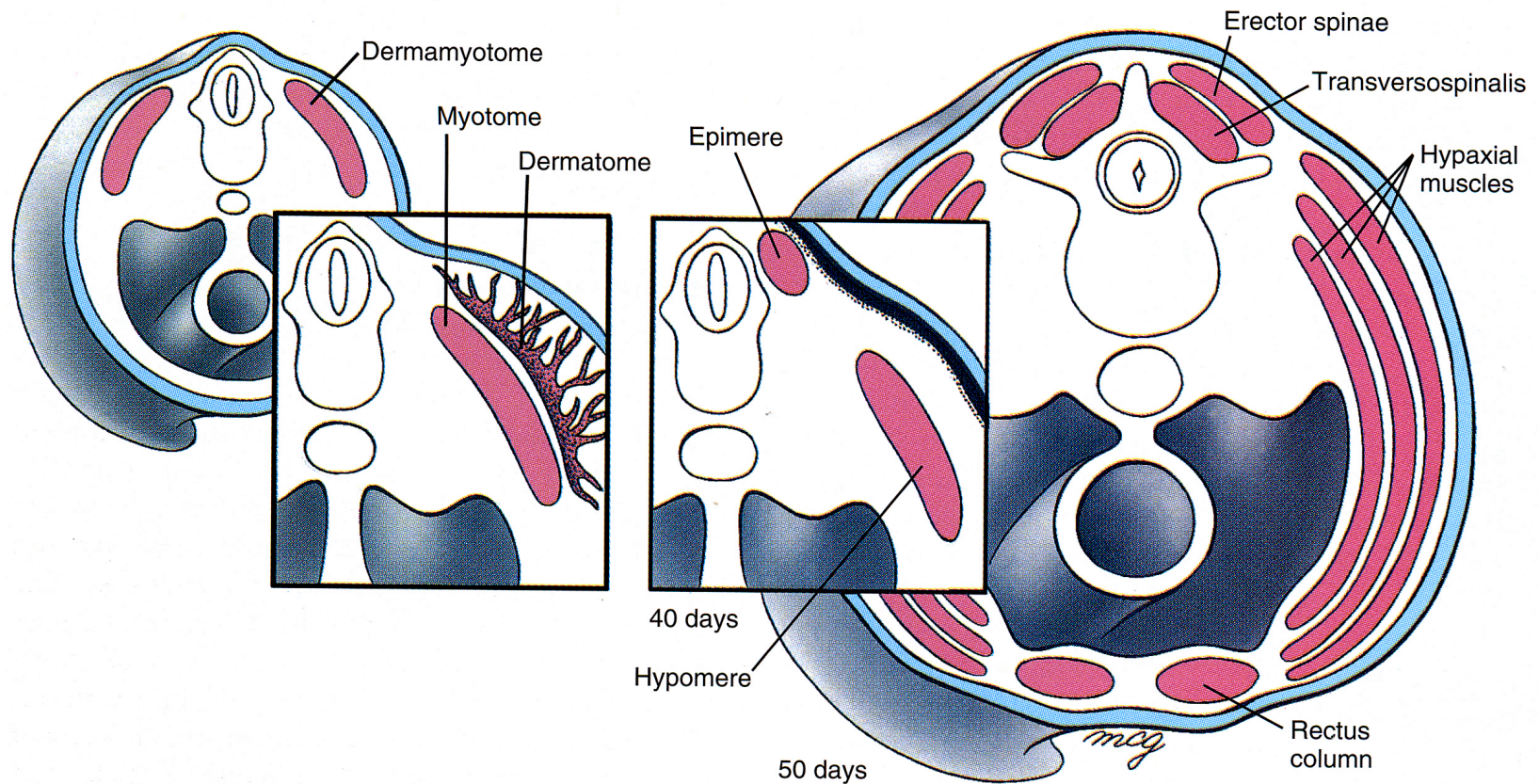
(D) Late 4-day embryo



Fate of the sclerotome.



Migration of dermamyotome cells. All skeletal muscle arises from the myotome.



(A)

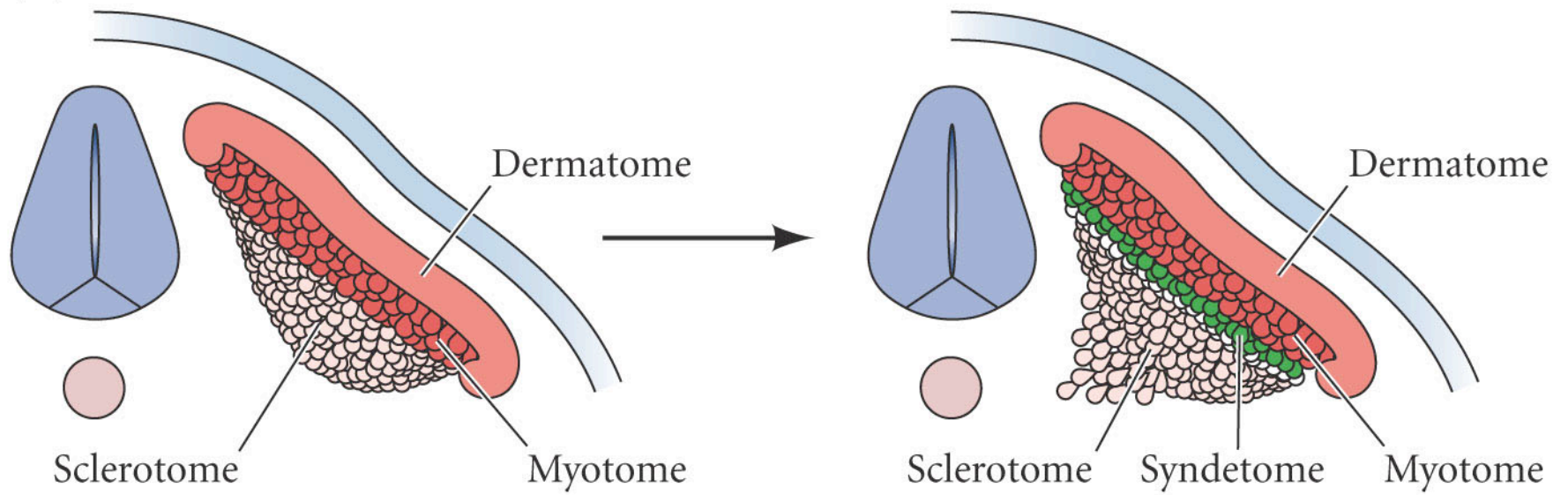
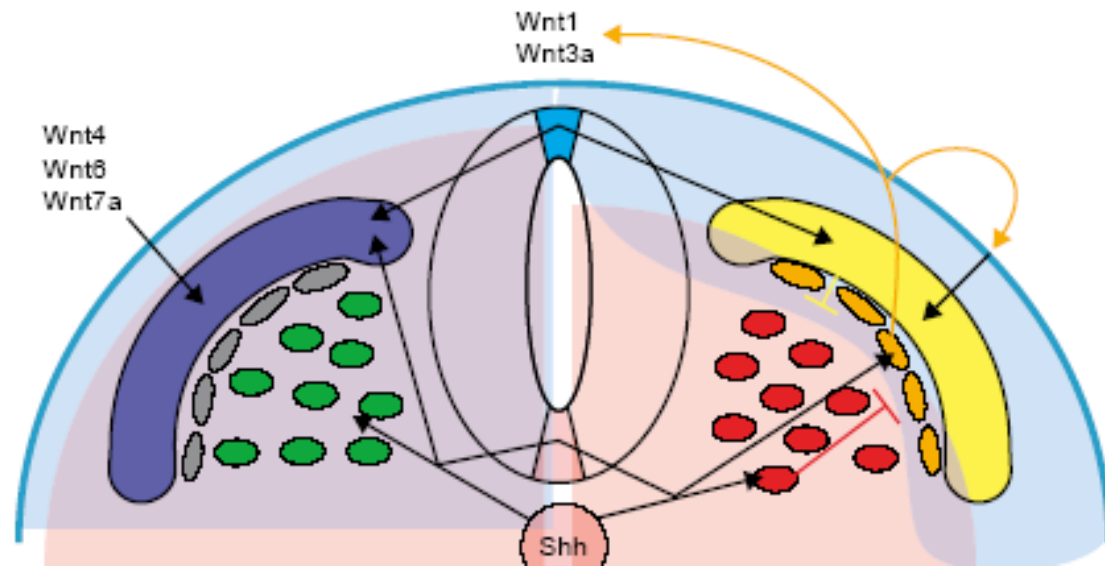


TABLE 6-1 *Subdivisions of the Epithelial Somite*

Dorsal		
DERMATOME		DERMATOME
Dermis		Dermis
Myotome		Myotome
Intrinsic back muscles (epaxial)		Limb muscles
		Muscles of ventrolateral body wall
MEDIAL	SOMITOCOEL CELLS	LATERAL
	Intervertebral joint surfaces	
SCLEROTOME		SCLEROTOME
Vertebral body		Vertebral arch
Intervertebral disk		Pedicle of vertebra
Proximal part of rib		Distal part of rib
Connective tissue		Connective tissue around dorsal root ganglion
Ventral		

- Dermomyotome
- Myotome
- Sclerotome
- Dorsalizing Wnt signals
- Ventralizing Shh signals
- Overlap of dorsalizing and ventralizing signals
- Sfrp2
- Gas1
- QSulf1



Interdependence of tissues in somite formation.

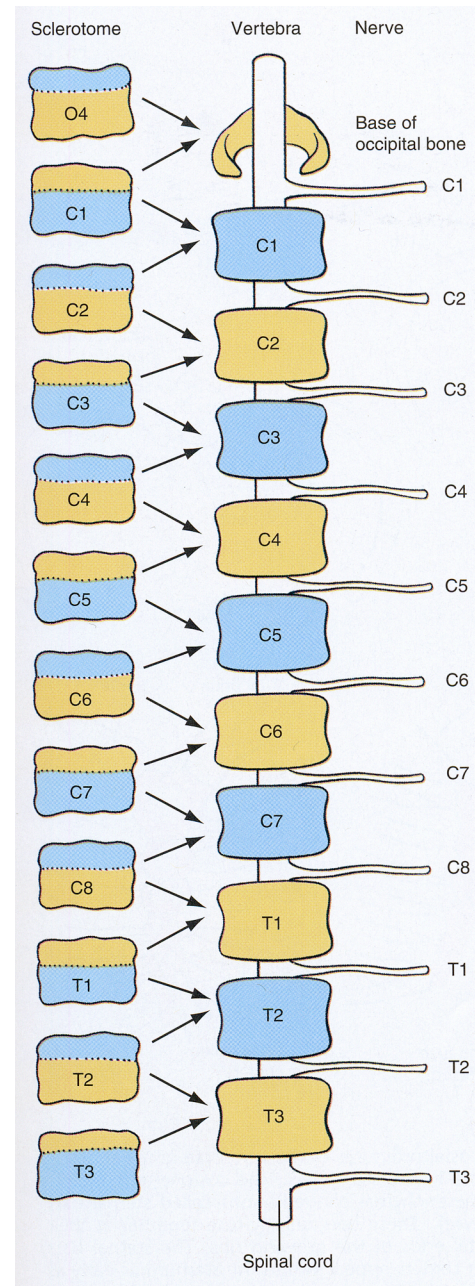
1. **Pre**-somitic mesoderm will form somites in a **cell autonomous fashion**. **However they do not progress normally without their tissue neighbors.**

2. Remove neural tube - the vertebrae that develop lack segmentation of the dorsal structures (i.e., the neural arch).

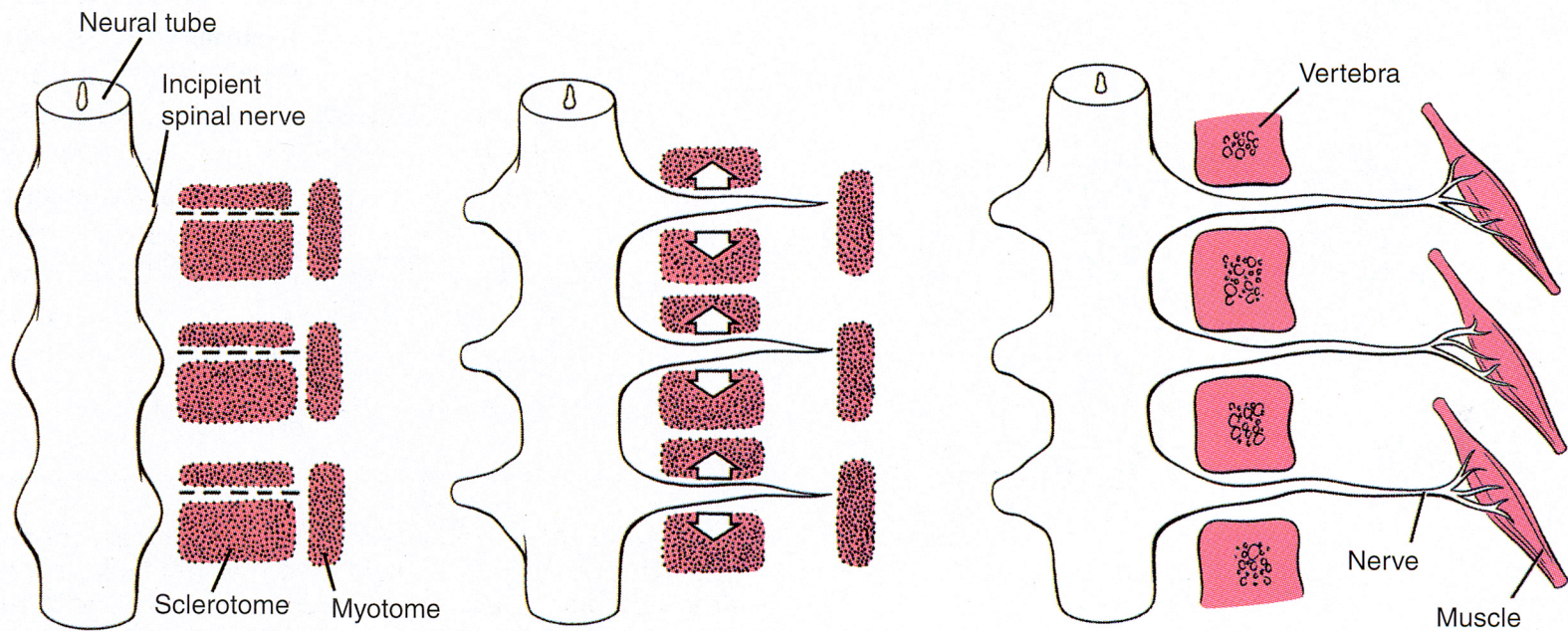
3. Removal of notochord - the ventral half of the vertebrae, the vertebral bodies, lose segmentation and bilaterality so that they fuse ventral to the neural tube.

4. Removal of notochord and floor plate (specialized cells on the midline of the neural tube) and transplantation dorsal to the somite, completely inhibits muscle formation; the myotome differentiates into cartilage.

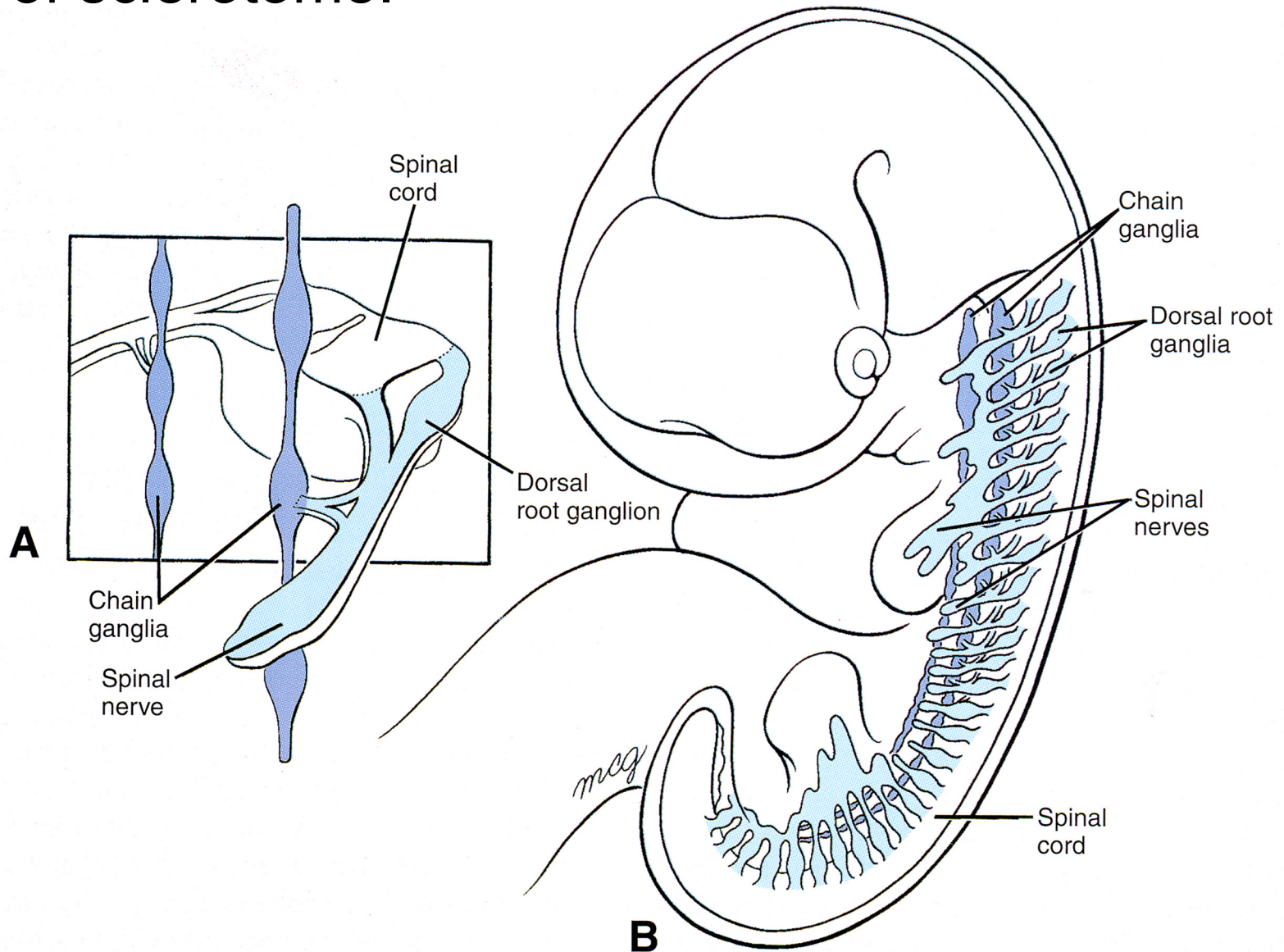
Each vertebra is formed from the caudal portion of one somite and the cranial portion of the next. Note origin of spinal nerve C1.



Each spinal nerve traverses the cranial aspect of the sclerotome as it grows to innervate the myotome. The caudal 1/2 of sclerotome secretes substances inhibitory to axon growth. The segmental nature of the PNS is due to segmentation of somites.



Cells of the neural crest migrate through cranial $\frac{1}{2}$ of sclerotome.



Molecular aspects of somitogenesis.

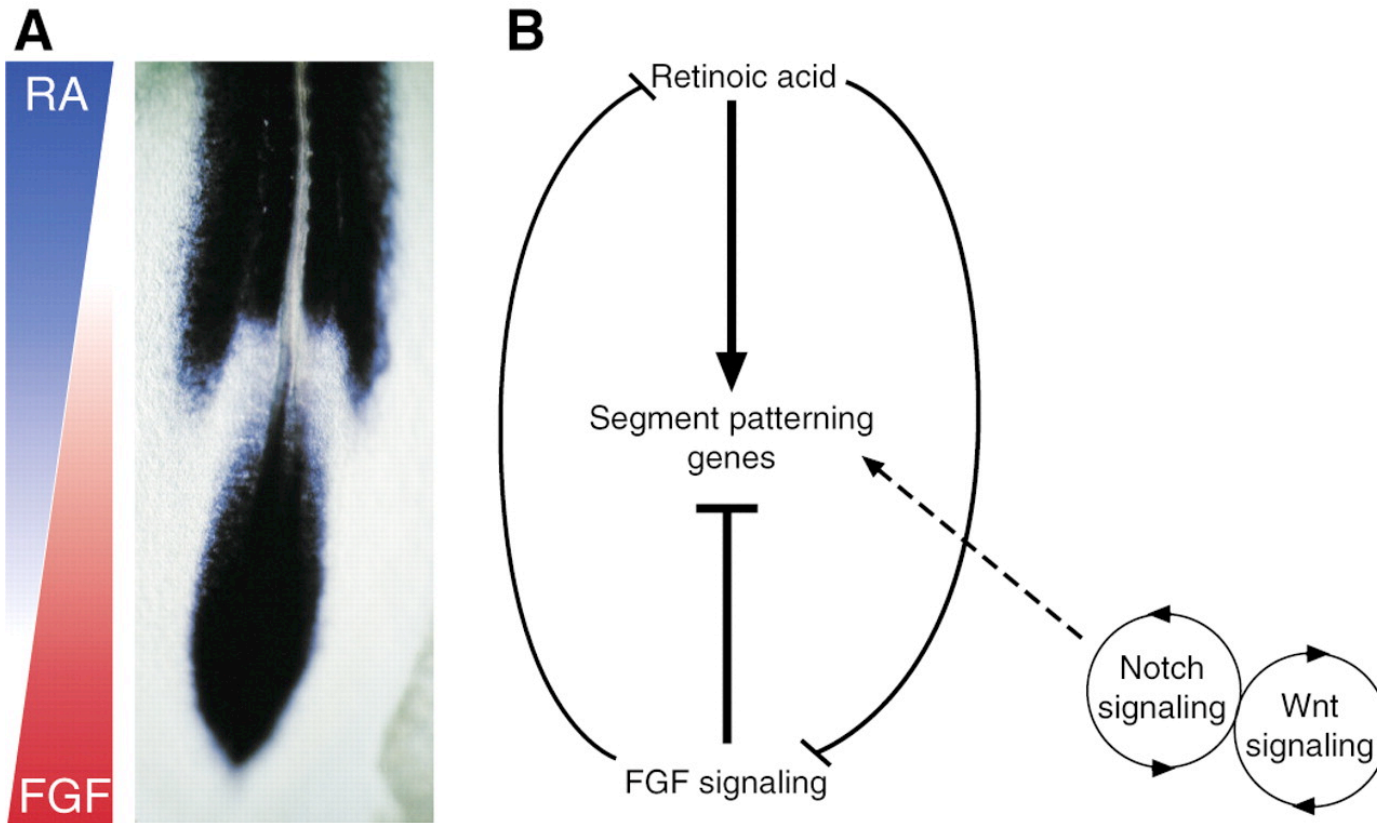
Somitogenesis, the sequential formation of a periodic pattern along the anterior-posterior axis of vertebrate embryos, is one of the most obvious examples of the segmental patterning processes that take place during embryogenesis and also one of the major unresolved events in developmental biology.

What governs addition of somites from somitomeres?

There is a molecular oscillator known as the segmentation clock which drives the periodic transcription of cyclic genes in the presomitic mesoderm.

The genes involved include downstream targets of Notch (*aka hairy*) or are regulators of Notch signaling (*aka Lunatic fringe*).

A model for somitogenesis

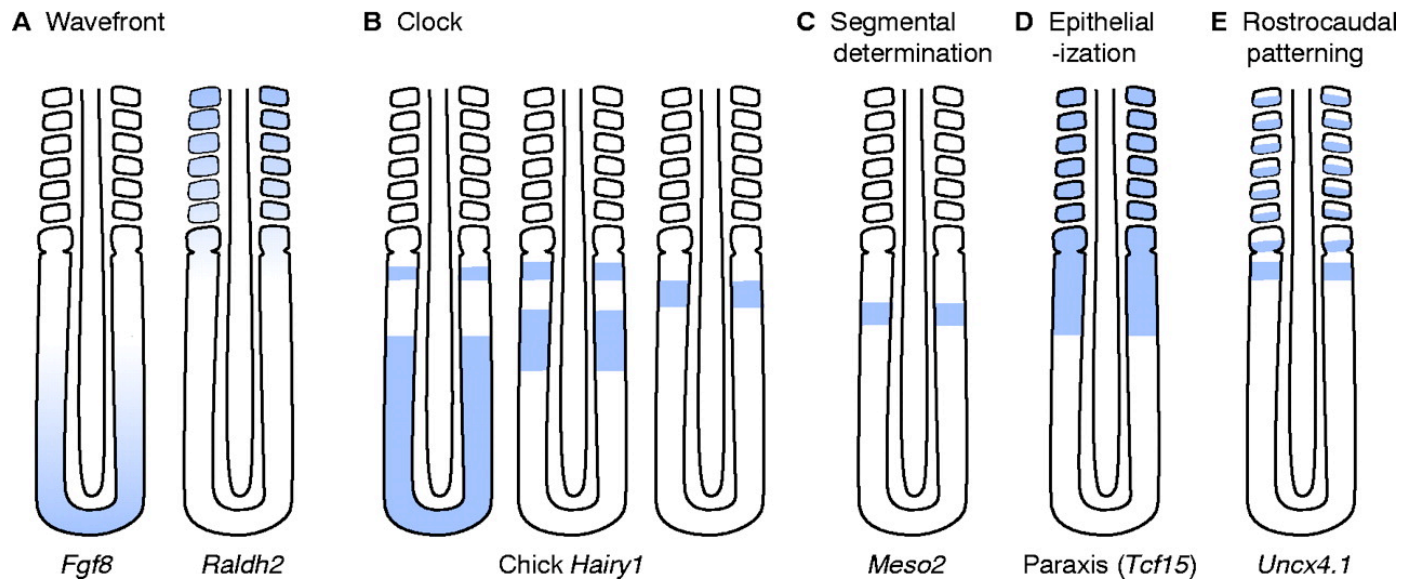


Dubrulle, J. et al. *Development* 2004;131:5783-5793



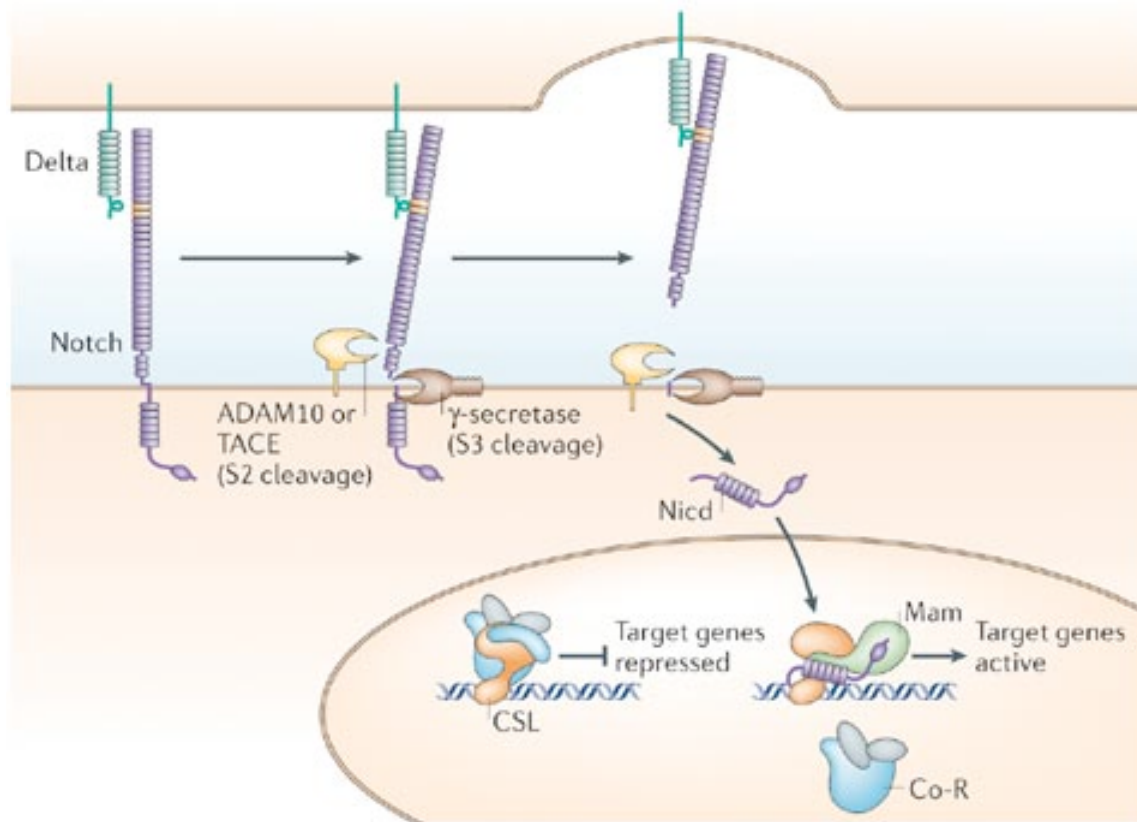
Development

Categories of gene expression patterns that are associated with paraxial mesoderm segmentation and maturation in the chick embryo



Dubrulle, J. et al. *Development* 2004;131:5783-5793





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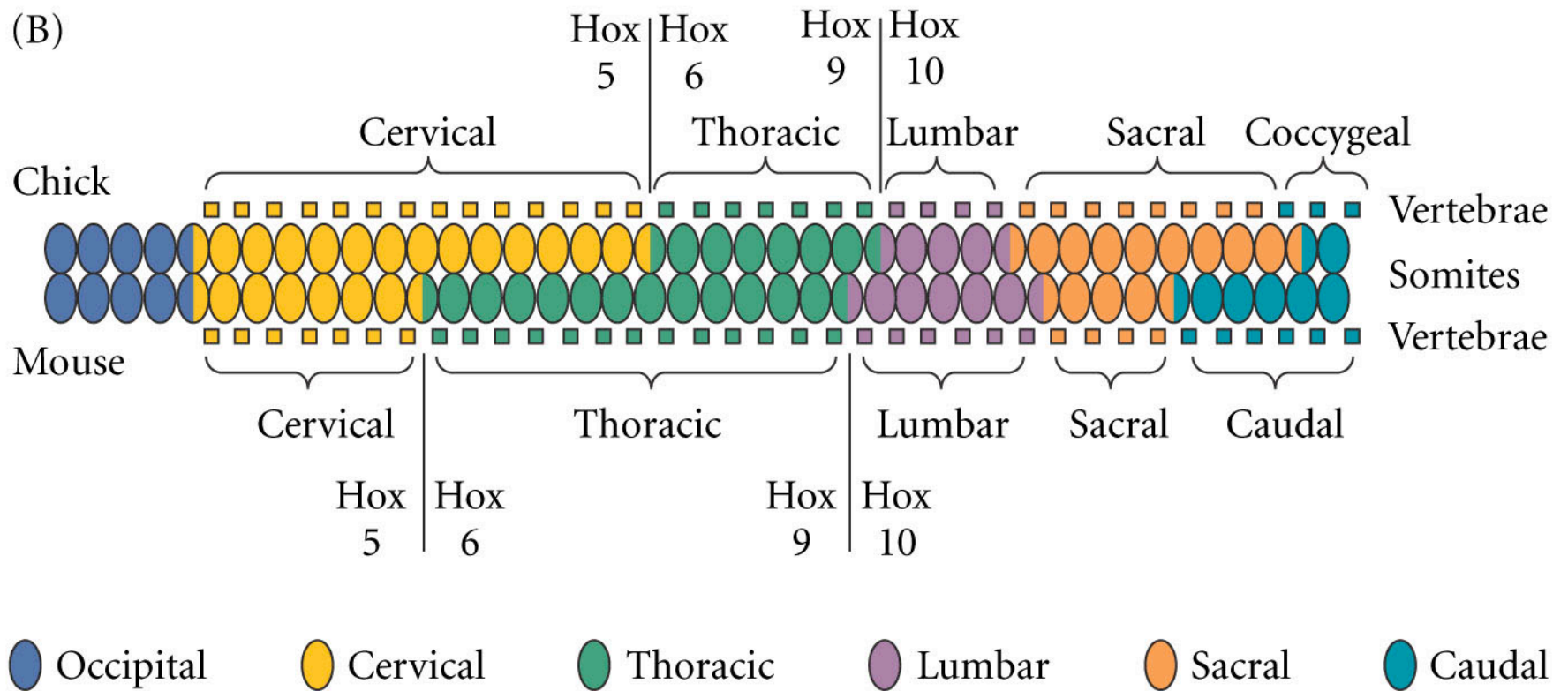
Bray *Nature Reviews Molecular Cell Biology* 7, 678–689 (September 2006) | doi:10.1038/nrm2009

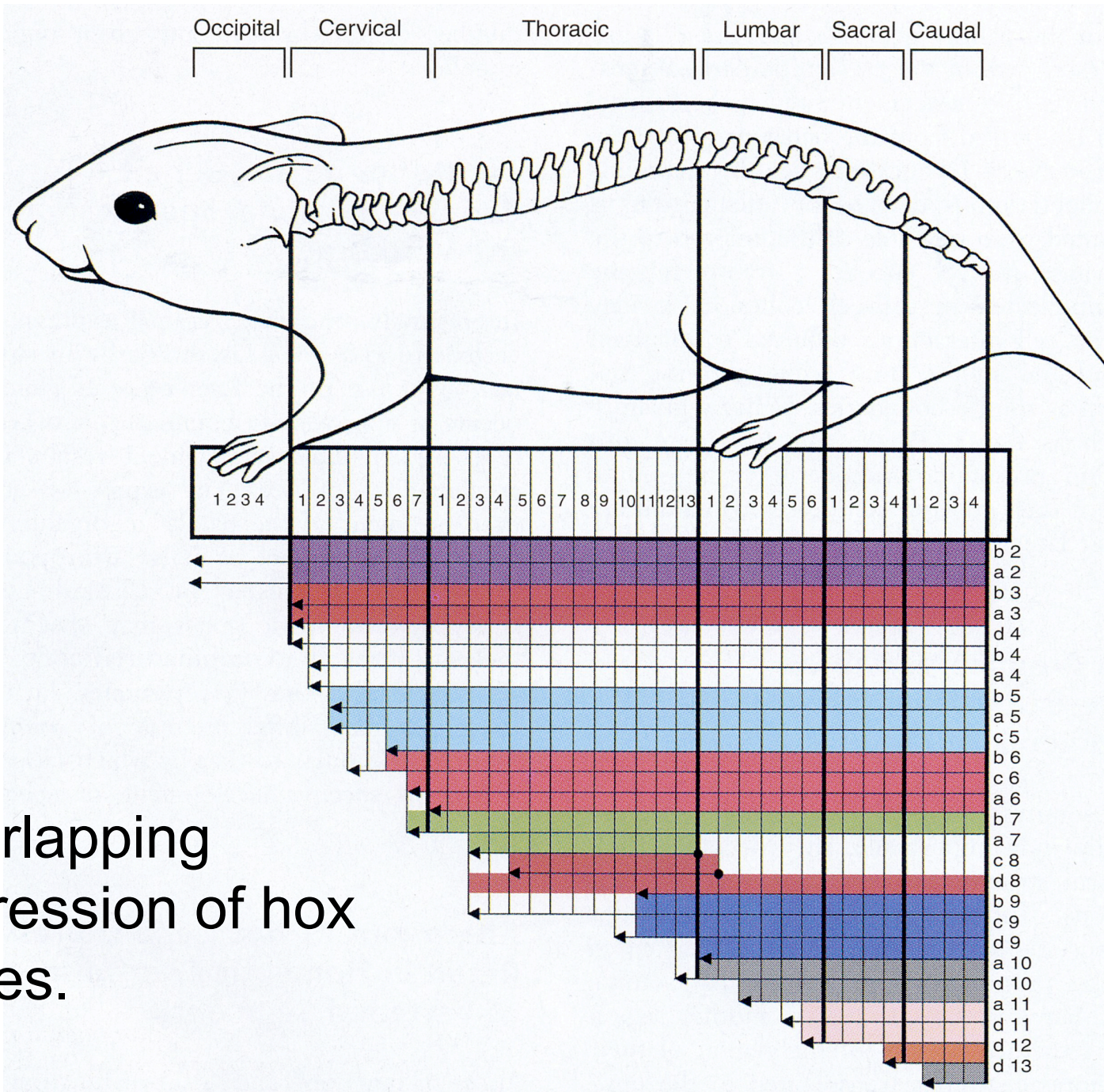
Generation of form and
diversity: homeotic
transformations

Or: Not all somites are created
equal

Generation of diversity.

- 1. Establish a segmental pattern followed by homeotic transformations of each segment.**
- 2. Homeotic transformation is the differentiation of initially identical repeating segments into unique structures; the nature of the homeotic transformation is dependent on the expression pattern of homeotic genes = HOX genes.**
- 3. This strategy is conserved throughout the animal kingdom and vertebrates are recognized as a separate animal phylum because of their most conspicuous segmentation, the vertebral column.**

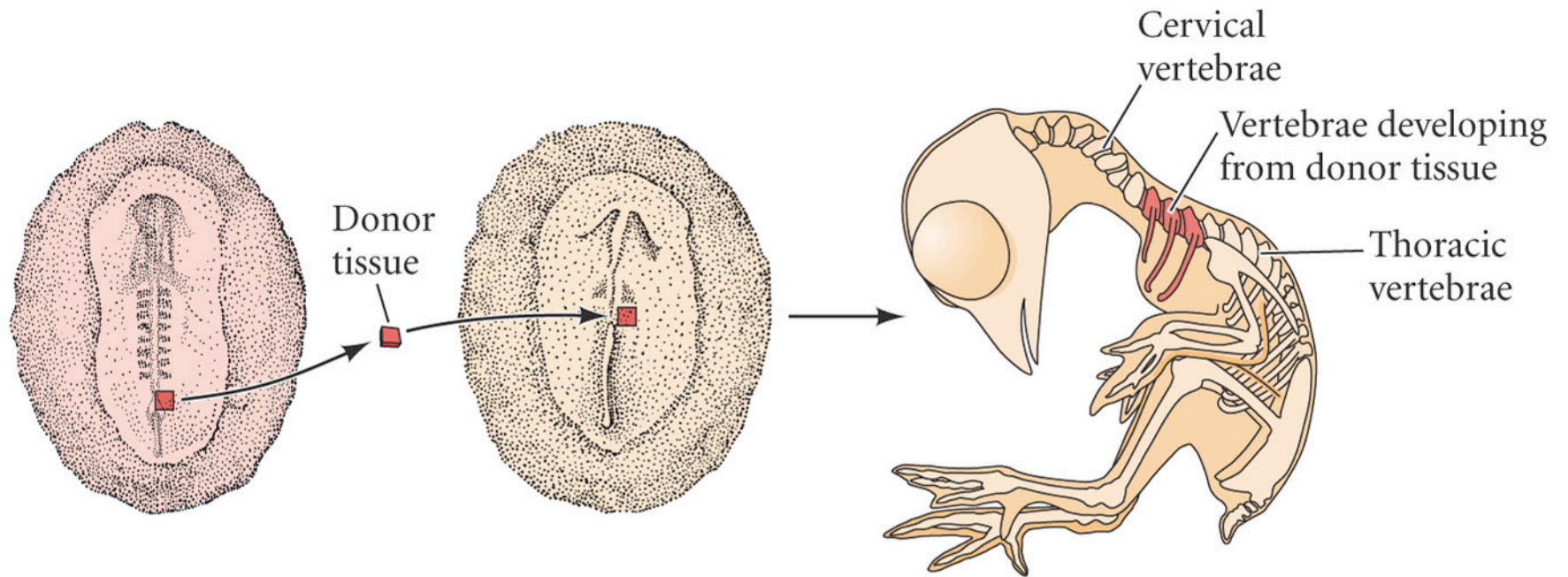




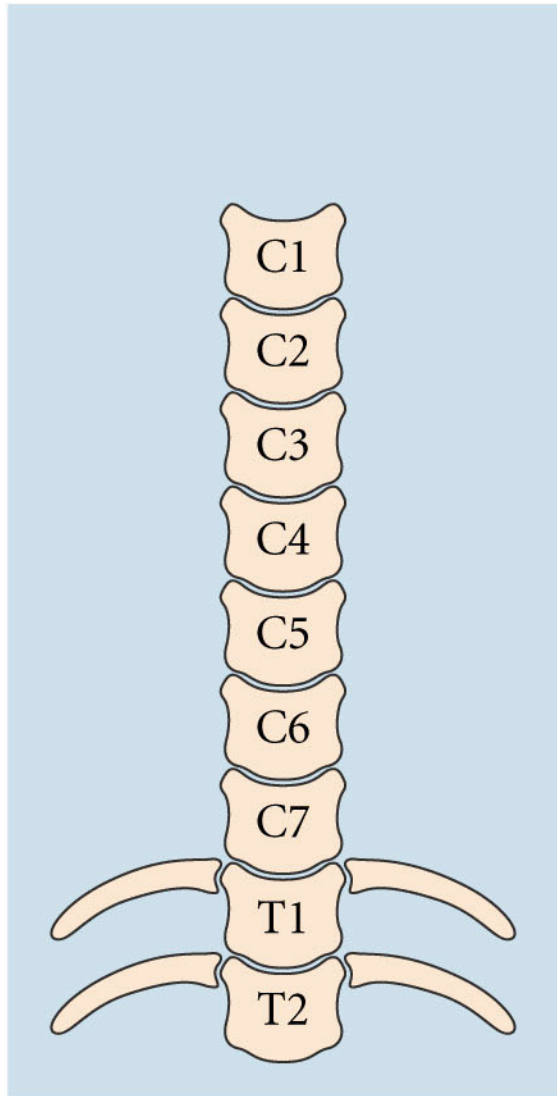
Overlapping
expression of hox
genes.

Positional information: Transplantation of somites

If thoracic somites are moved to the cervical region before they de-epithelialize, the transplant will still give rise to ribs.



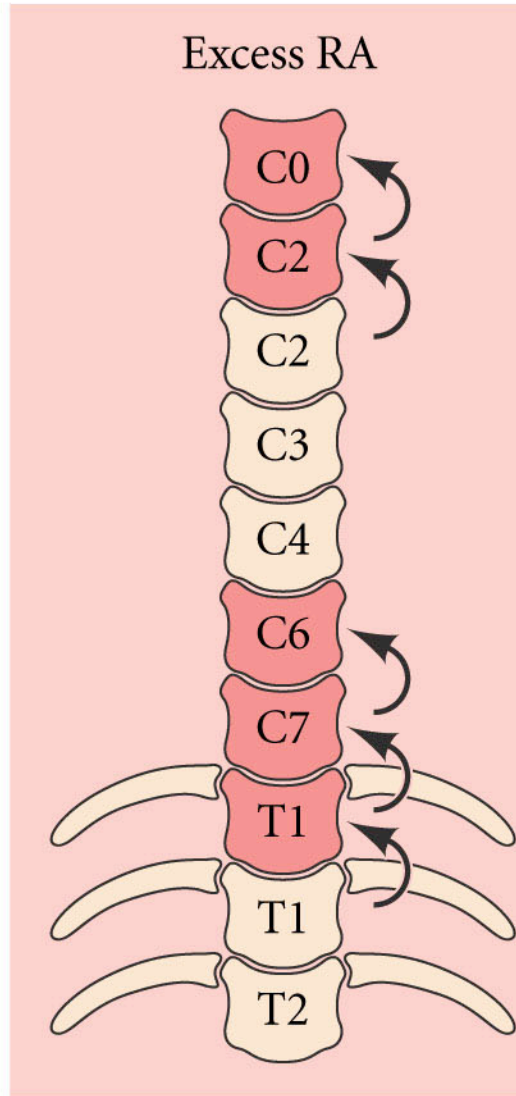
(A) Normal development



(B) Retinoic acid

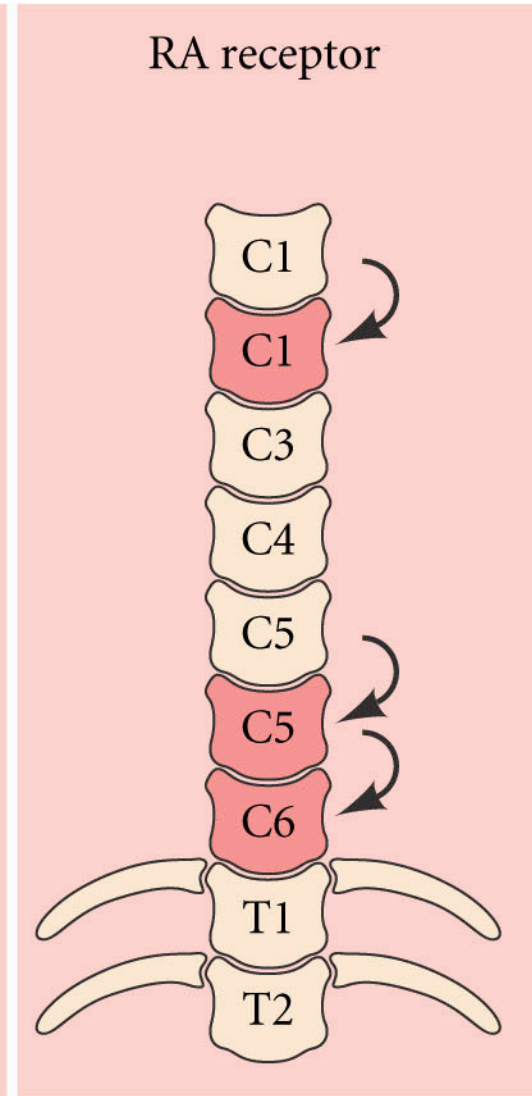
Gain

Excess RA



Loss

RA receptor



Summary:

1. Somites establish body segmentation.
2. Somite has 3 separate compartments.
3. Somites are responsible for the segmentation of the vertebral column, PNS, segmental muscles.
4. Overlapping patterns of HOX gene expression result in somites with individual characteristics.
5. Positional information is present in somites prior to epithelial-mesenchymal transformation perhaps due to gradients of fgf8 and RA.

The end