Segmentation

Ann-Judith Silverman
as36@columbia.edu
09 – 24 -07

What are segments?

Repeated units of anatomical but not necessarily biochemical identity.

Segments develop from unsegmented tissue and acquire strict borders.

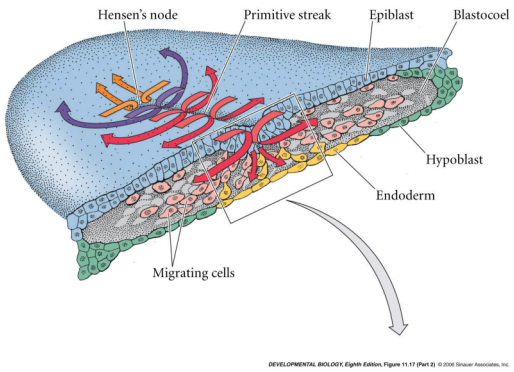
A “no mixing rule” contributes to segment identity.

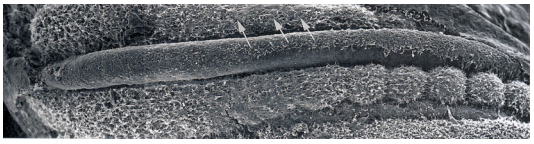
In vertebrates segments are most prominent in the paraxial mesodermal and are called somites.

Topics

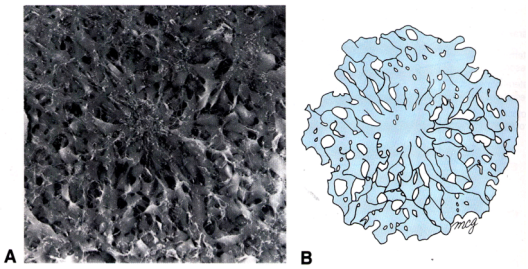
1. Segmentation of trunk mesoderm: the derivatives of paraxial mesoderm = the somites.
   A. Cells of origin of somites.
   B. Follow anatomical changes and molecular underlying.
   C. Imposition of segmentation on trunk PNS.
   D. Concept of homeotic transformations and hox (homeobox) genes.

2. Segmentation CNS –the rhombomeres of the hindbrain.



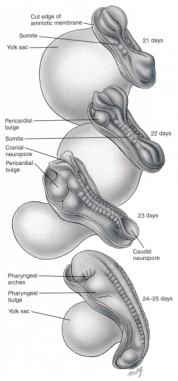


Scanning EM and diagram of a somitomere: organized whorl of cells that **prefigure** the somites.

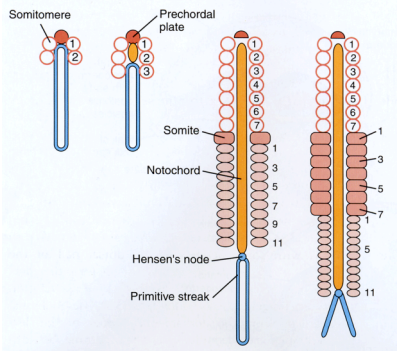


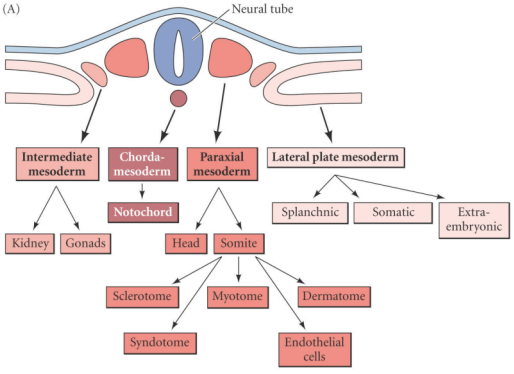
Sequential addition of somites from day 21-day 25 post-conception

Humans are estimated to have 42-44 pairs

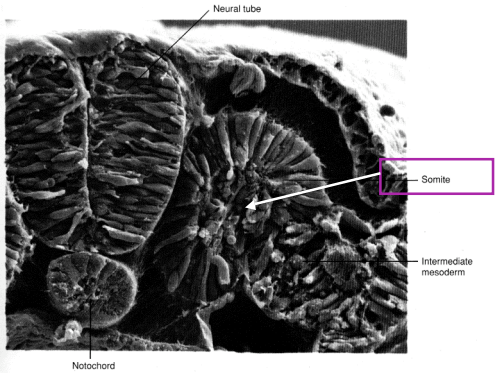


Sequential appearance of somitomeres and somites





Scanning EM of the epithelial somite.

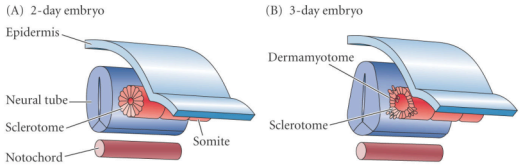


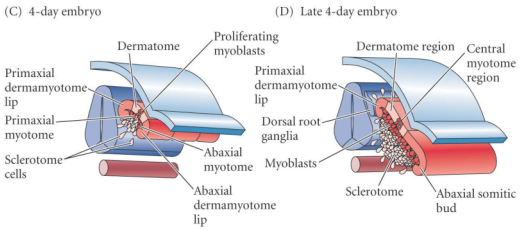
Fate of somites

- vertebral column
- skeletal/segmental muscles of trunk
- skeletal muscle of limb.

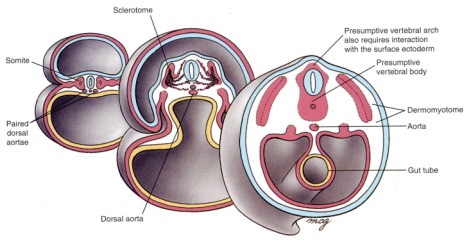
Somite undergoes epithelial to mesenchymal transformation (down regulate adhesion factors).

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.

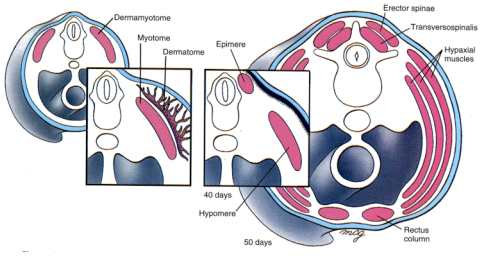




Fate of the sclerotome.



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



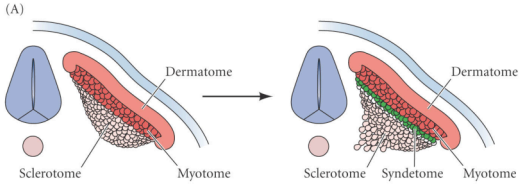
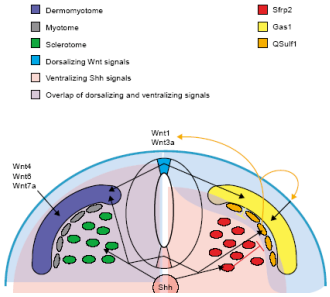


TABLE 6-1 *Subdivisions of the Epithelial Somite*

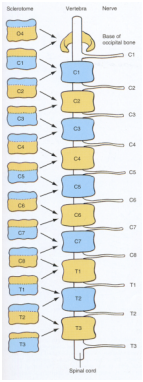
	Dorsal	
	DERMATOME	**DERMATOME**
	Dermis	Dermis
	Myotome	Myotome
	Intrinsic back muscles (epaxial)	Limb muscles
		Muscles of ventrolateral body wall
MEDIAL	**SOMITOCOEL CELLS**	**LATERAL**
	Intervertebral joint surfaces	
	SCLEROTOME	**SCLEROTOME**
	Vertebral body	Vertebral arch
	Intervertebral disk	Pedicle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



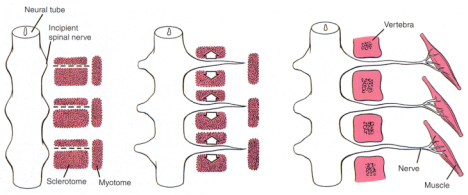
Interdependence of tissues in somite formation.

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.

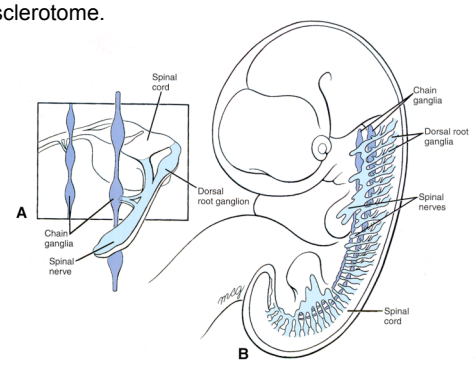
Each vertebrate is formed from the caudal portion of one somite and the cranial portion of the next. Note origin of spinal nerve C1.



Each spinal nerve traverses the cranial aspect of the sclerotome as it grows to innervate the myotome. The segmental nature of the PNS is due to segmentation of somites.



Neural crest migrate through cranial ½ of sclerotome.



Molecular aspects of somitogenesis.

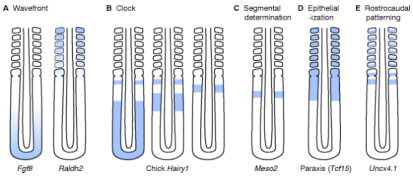
Somitogenesis, the sequential formation of a periodic pattern along the anterior-posterior axis of vertebrate embryos, is one of the most obvious examples of the segmental patterning processes that take place during embryogenesis and also one of the major unresolved events in developmental biology.

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 to date are downstream targets of Notch (*aka* hairy) or are regulators of Notch signaling (*aka* Lunatic fringe).

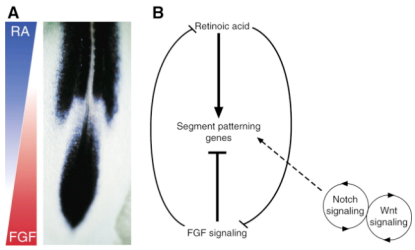
Categories of gene expression patterns that are associated with paraxial mesoderm segmentation and maturation in the chick embryo



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

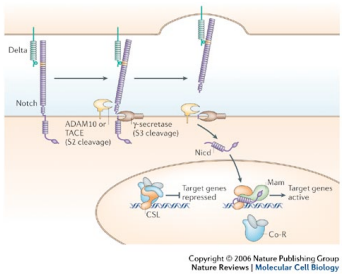
Development

A model for somitogenesis



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

Development



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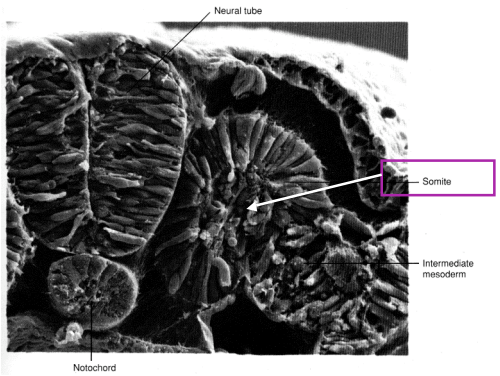
Generation of form and diversity: homeotic transformations

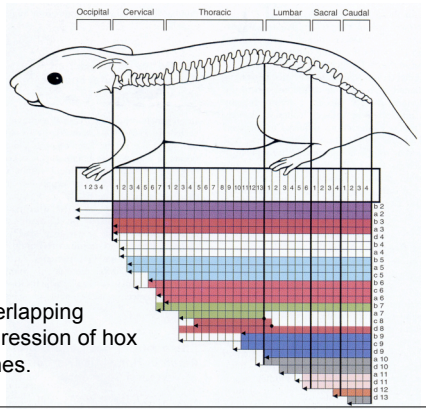
Or: Not all somites are created equal

Generation of diversity.

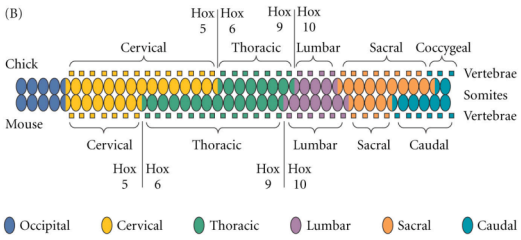
1. Establish a segmental pattern followed by homeotic transformations of each segment.
2. Homeotic transformation is the differentiation of initially identical repeating segments into unique structures; the nature of the homeotic transformation is dependent on the expression pattern of homeotic genes = 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.

Scanning EM of the epithelial somite.



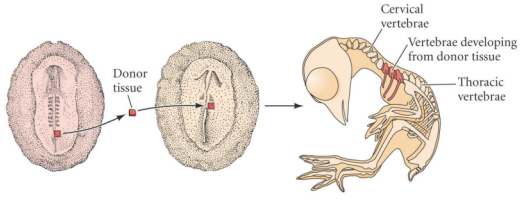


Overlapping expression of hox genes.

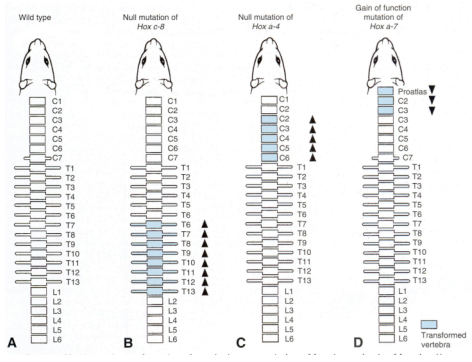


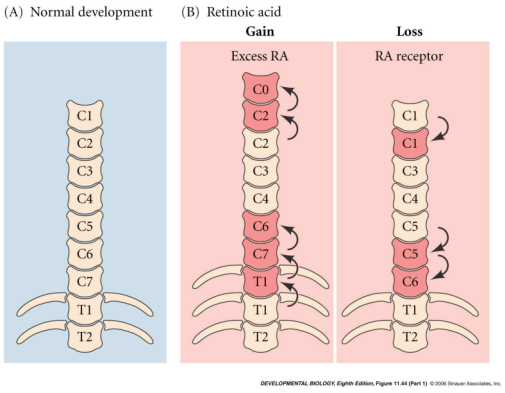
Positional information:
Transplantation of somites

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



Hox mutations alter somite phenotype.





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 or RA.

The end