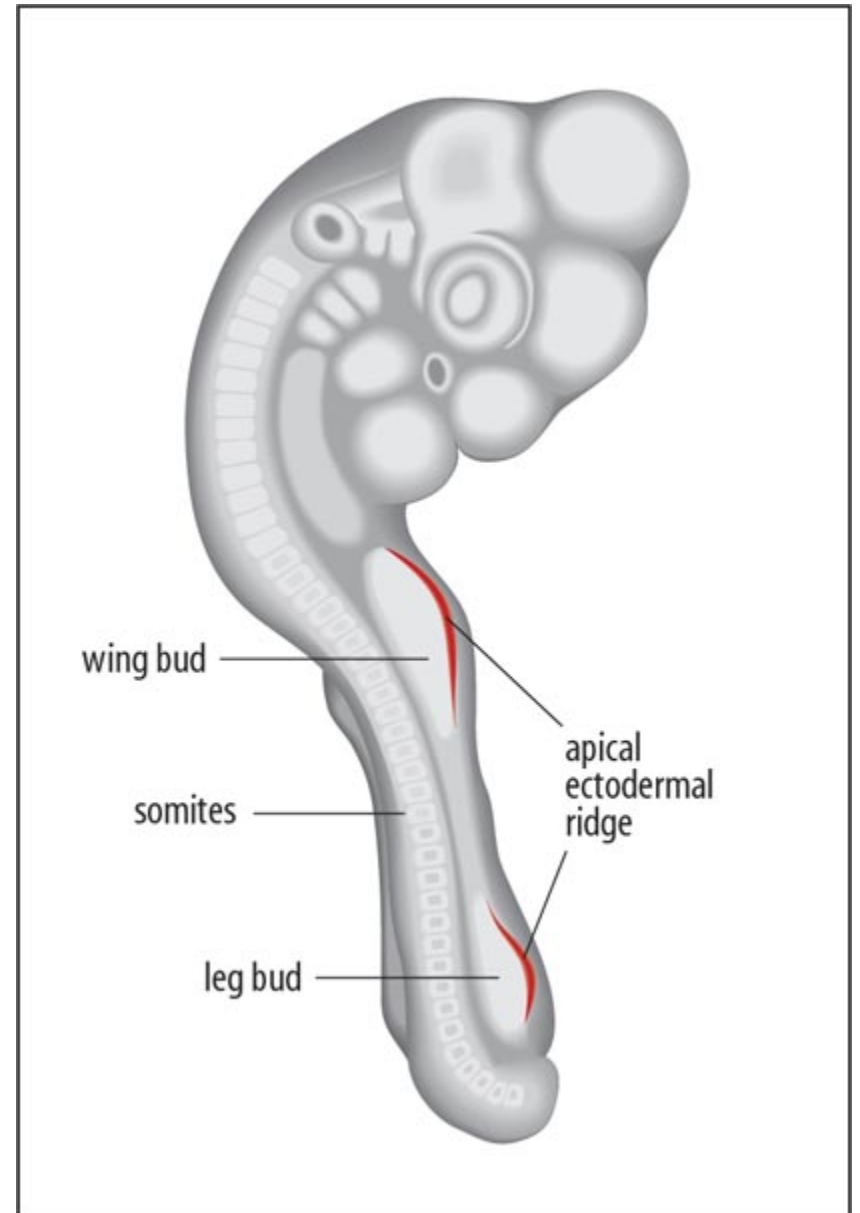
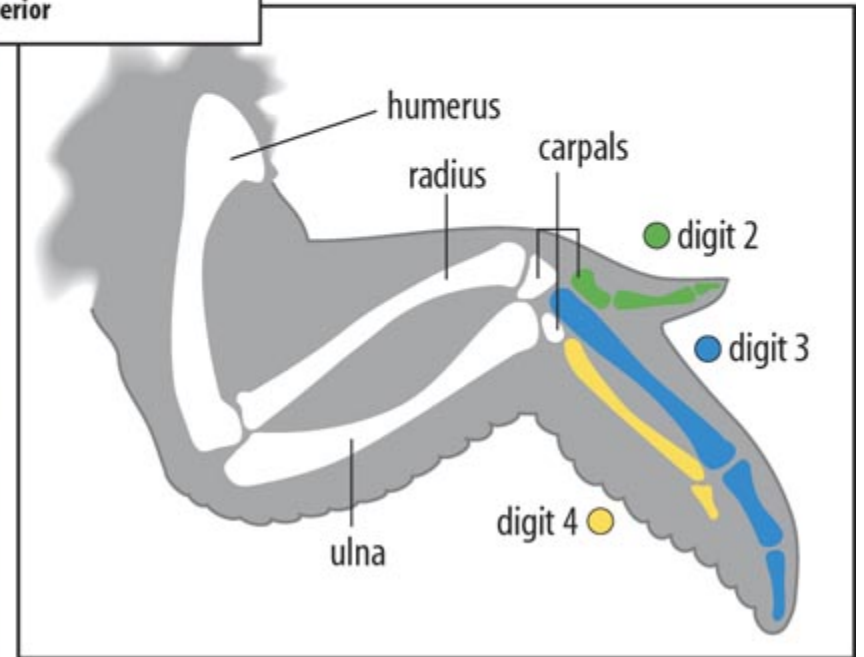
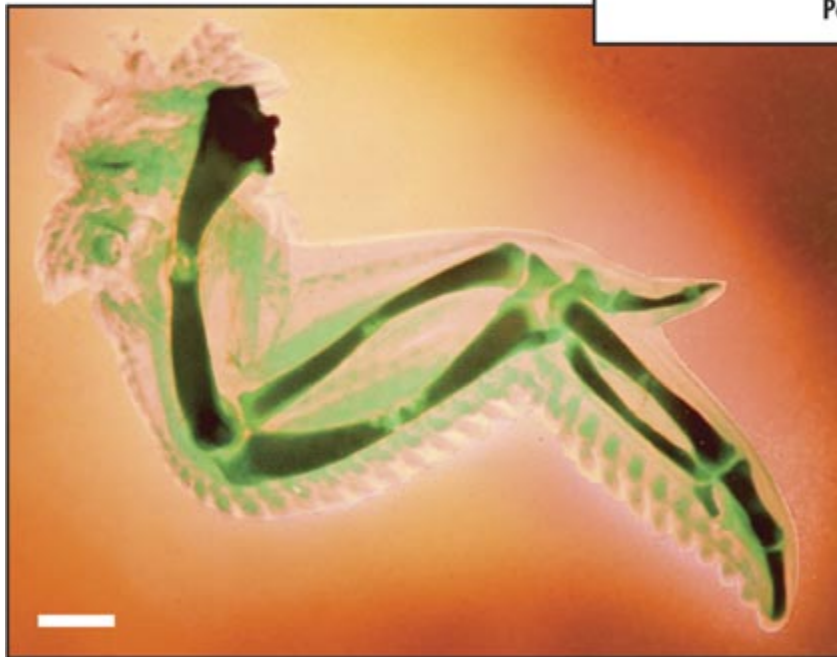
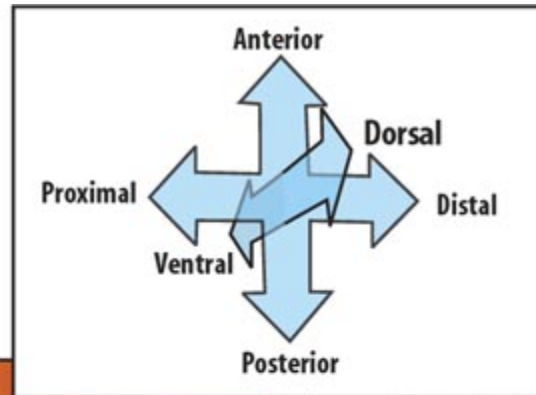
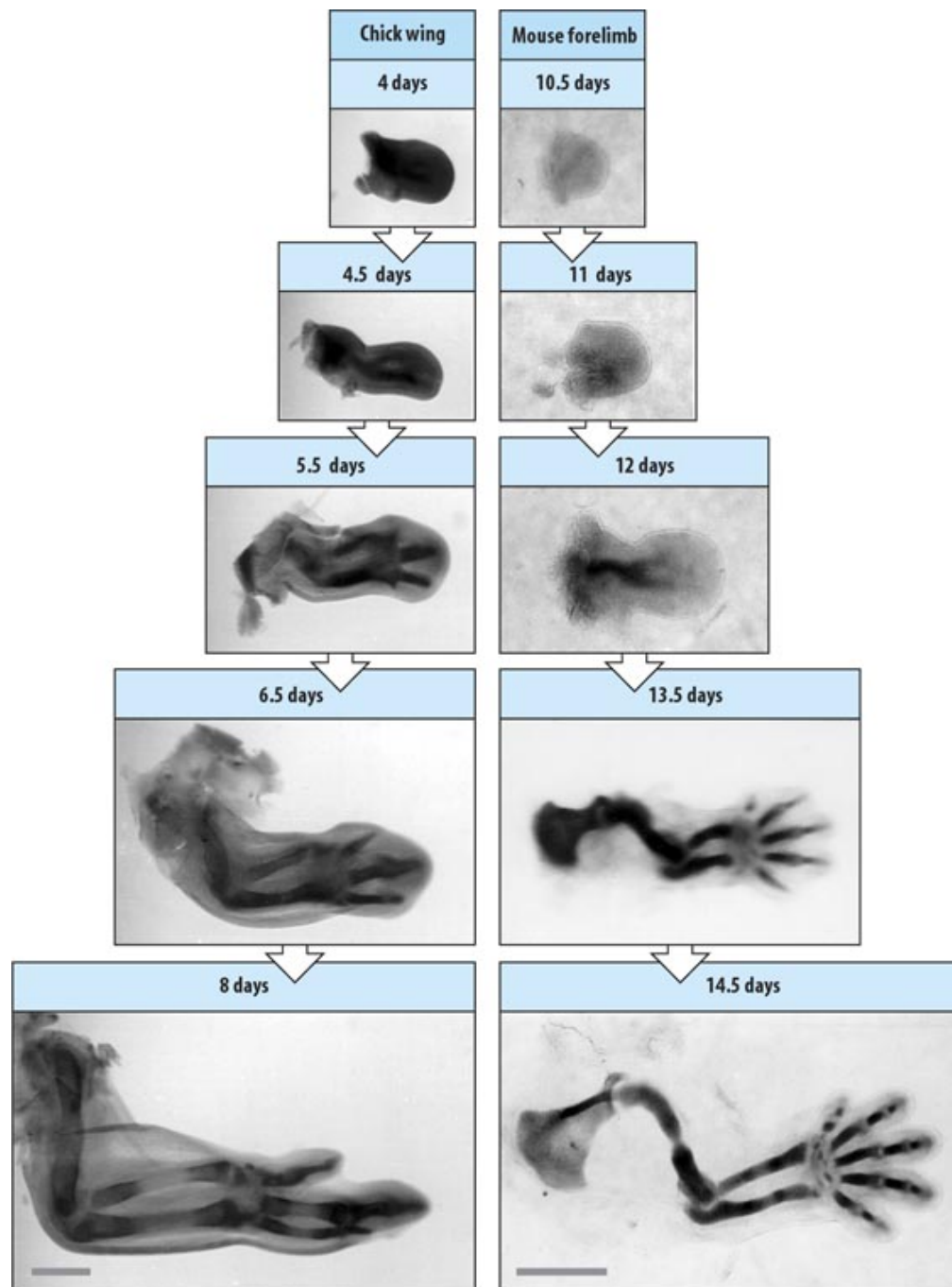


Vertebrate Limb Development

Limb Buds - Day 3





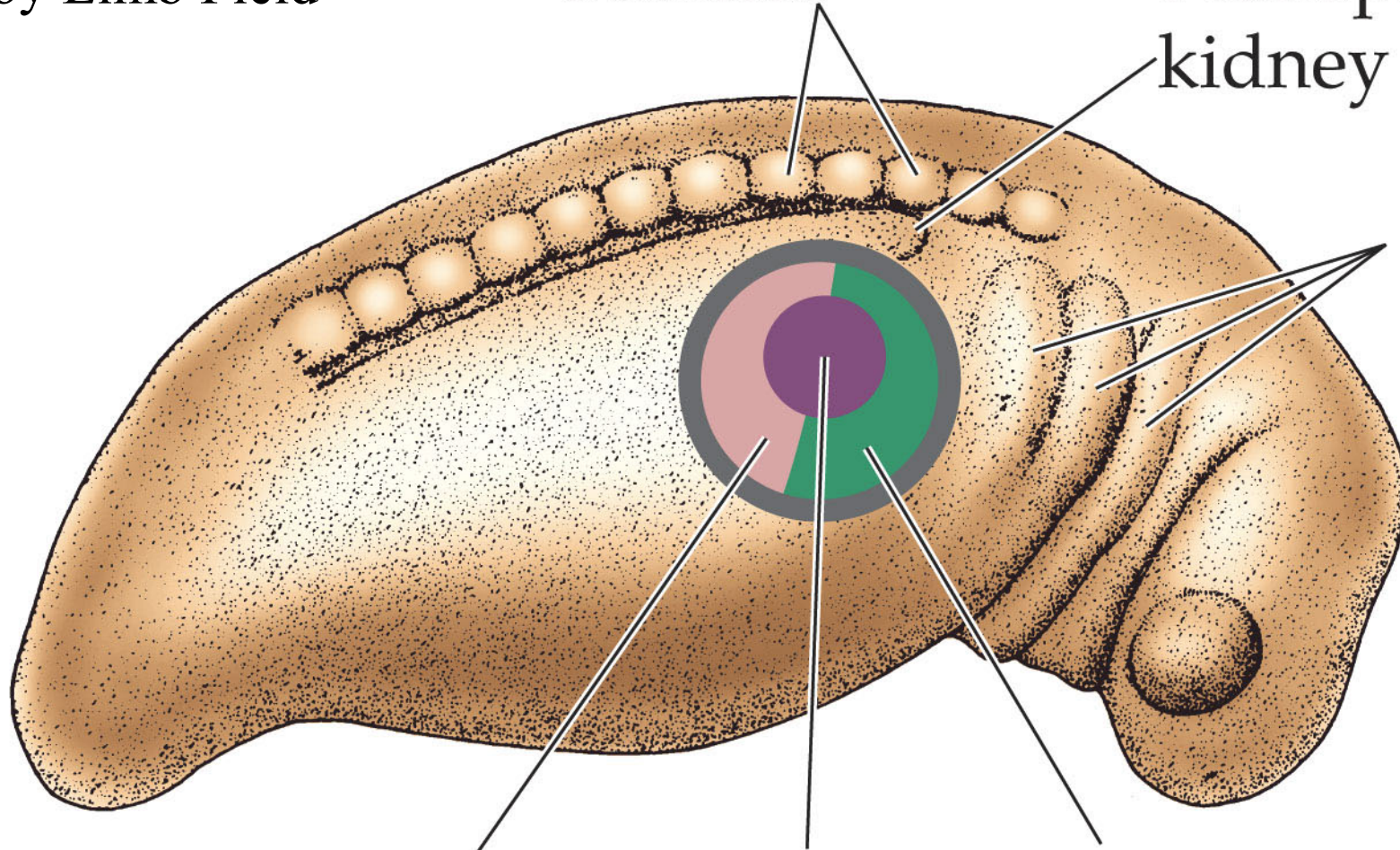


Limb Disc surrounded
by Limb Field

Somites

Pronephric
kidney

Gills



Peribrachial
flank tissue

Free
limb

Shoulder
girdle

Limb Field

- Forms limb bud
- Only part of limb field required
 - All parts of the limb field have the capacity to produce a limb
 - Transplant experiments

Nematode induced limb duplication in frogs

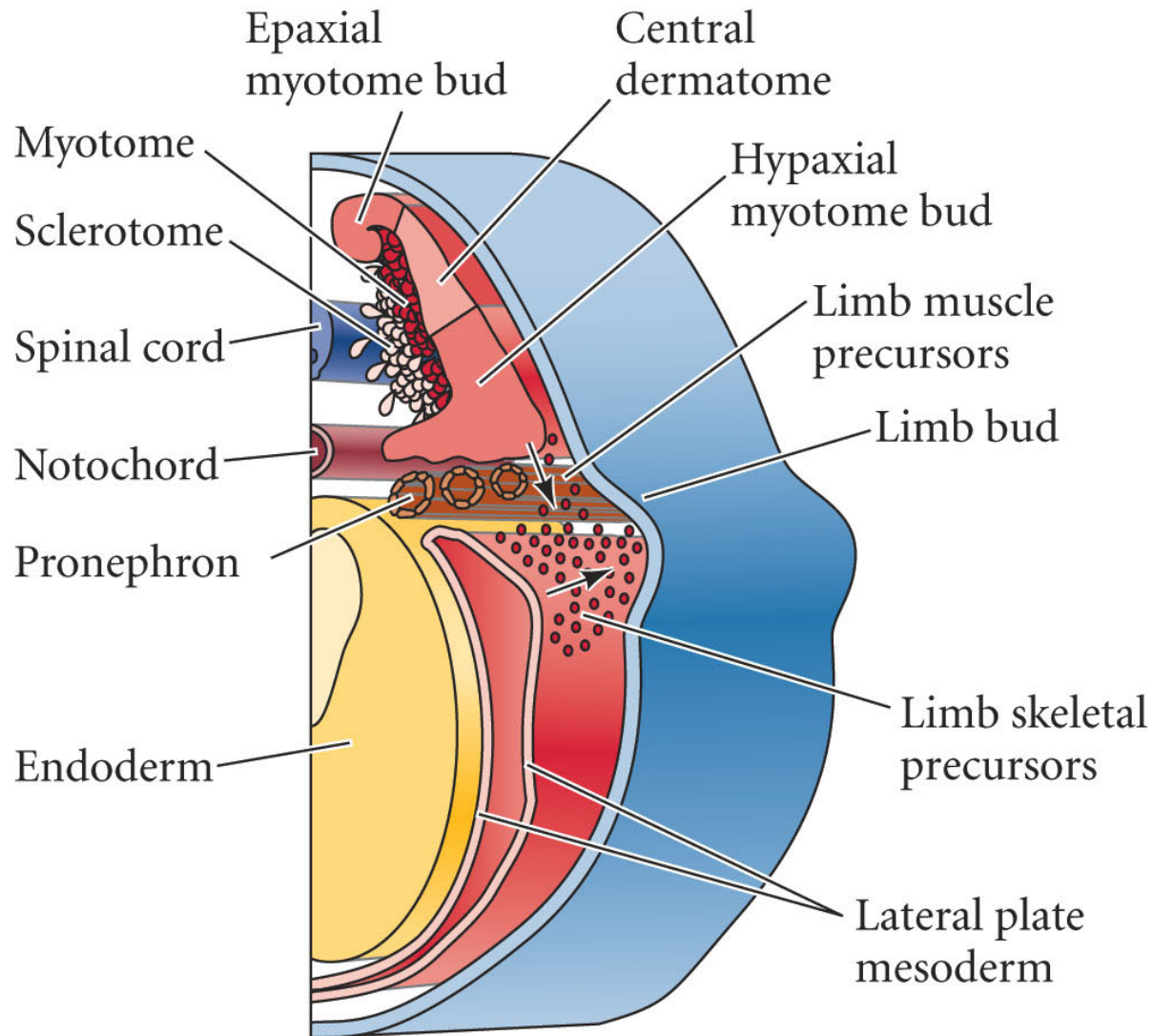


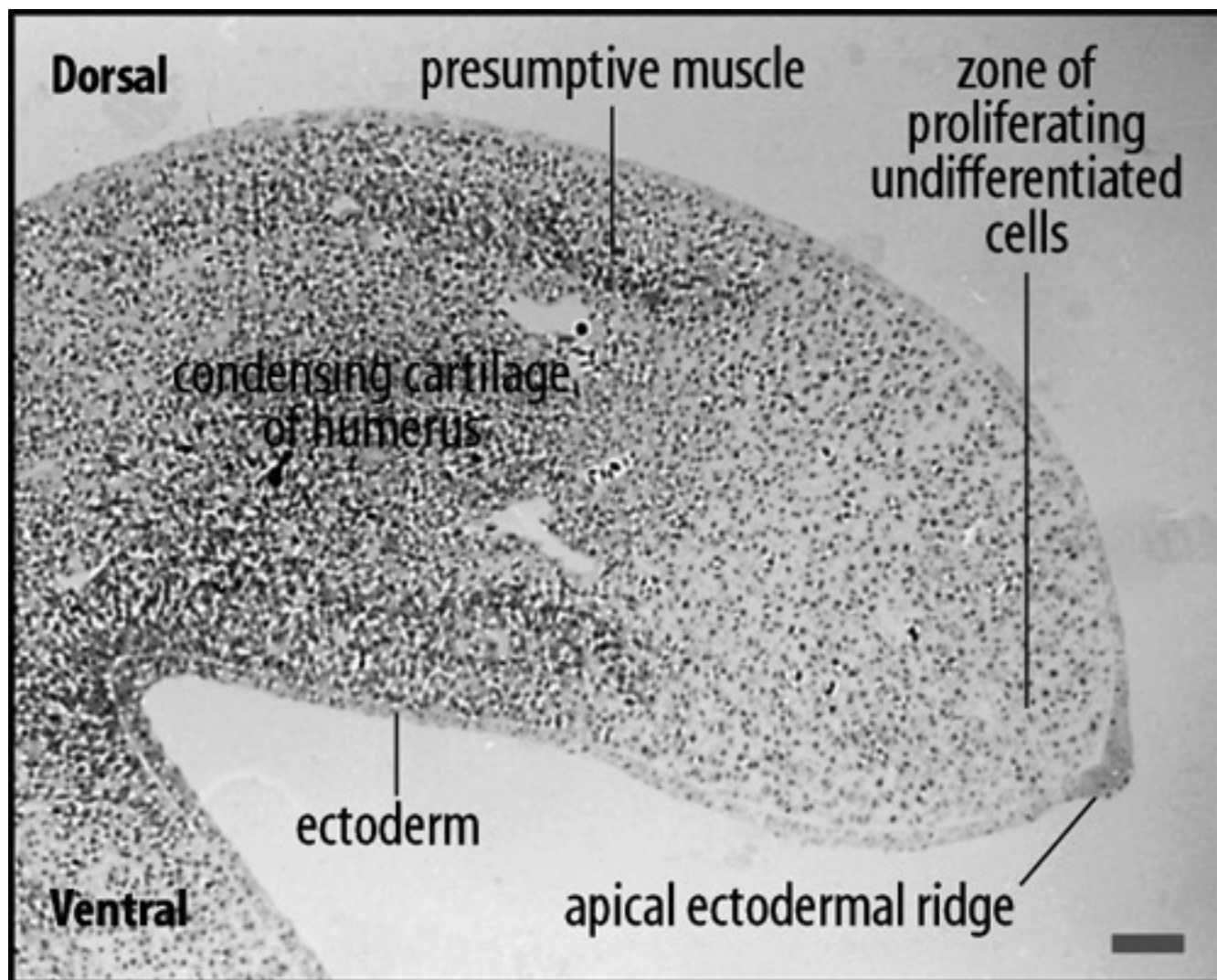
Limb Bud Formation

- Mesenchyme cells from the lateral plate mesoderm proliferates and migrates toward limb bud location to form the skeleton
- Myotome cells follow to form the musculature

Limb Bud

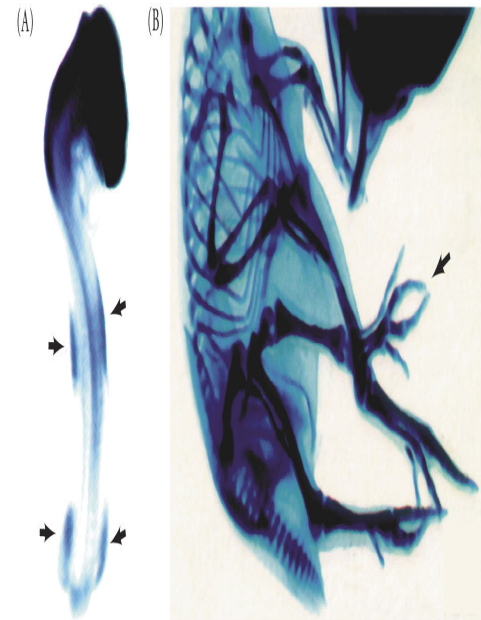
(A)



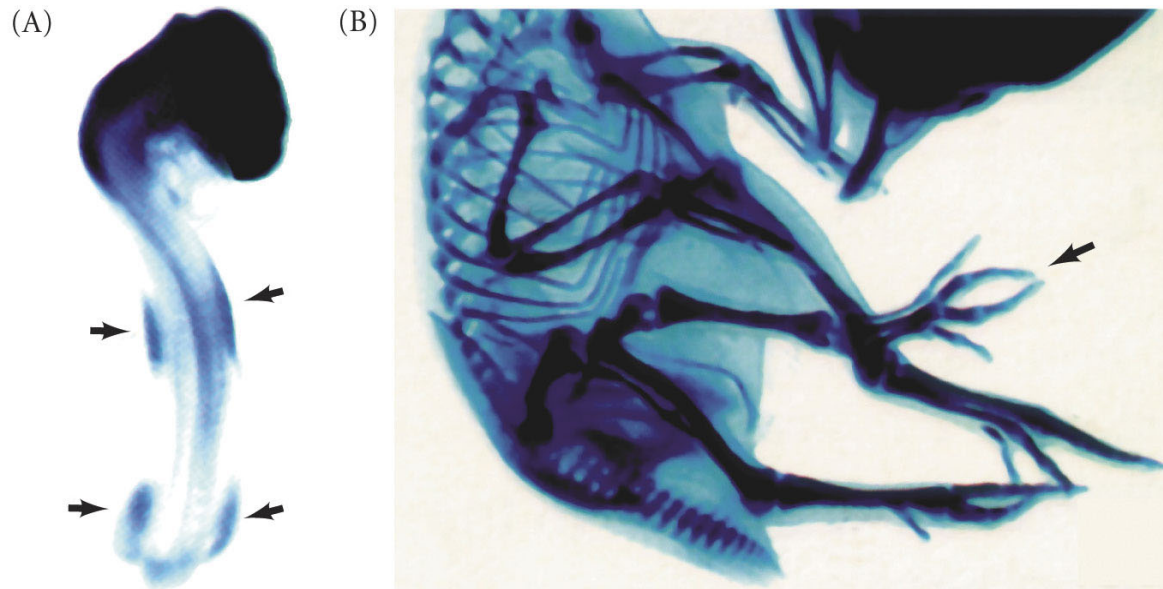


Mesenchyme induction

- Lateral plate mesoderm cells that migrate start expressing Fgf10 (arrows)
 - Paracrine factor
 - Activates limb forming genes in ectoderm and mesoderm



Ectopic limb – cells expressing Fgf10 transplanted into embryo

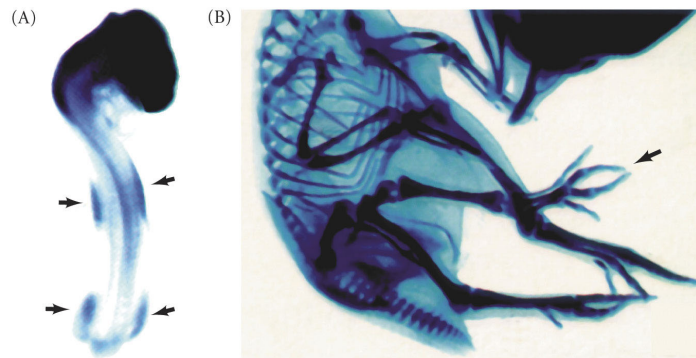


How does the limb bud know where to form?

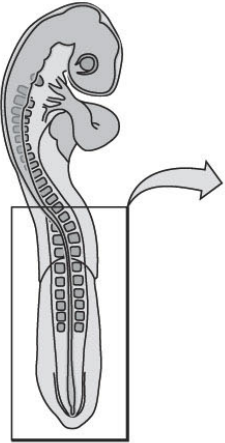
- Hox gene expression

How is limb type determined?

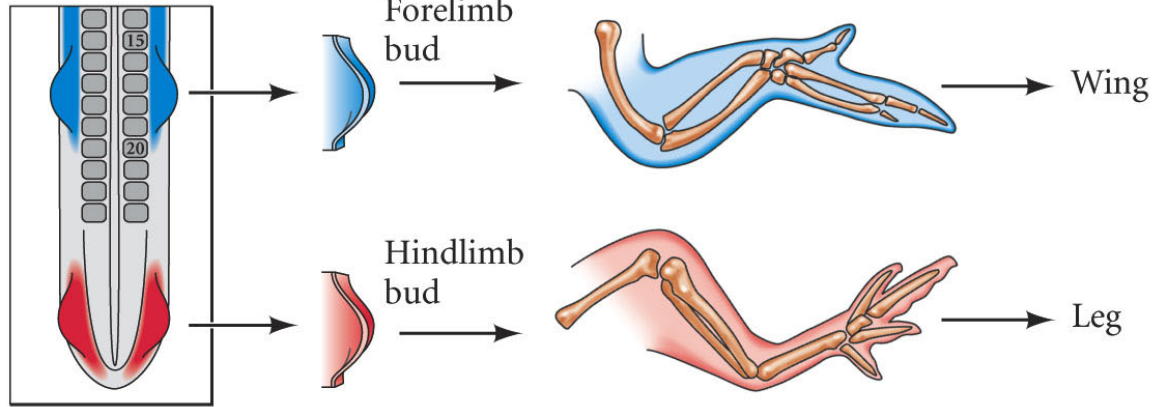
- Tbx4 expressed in hindlimbs (somite 25)
- Tbx5 expressed in forelimbs (somite 17)



Stage 14/15
(early day 3)

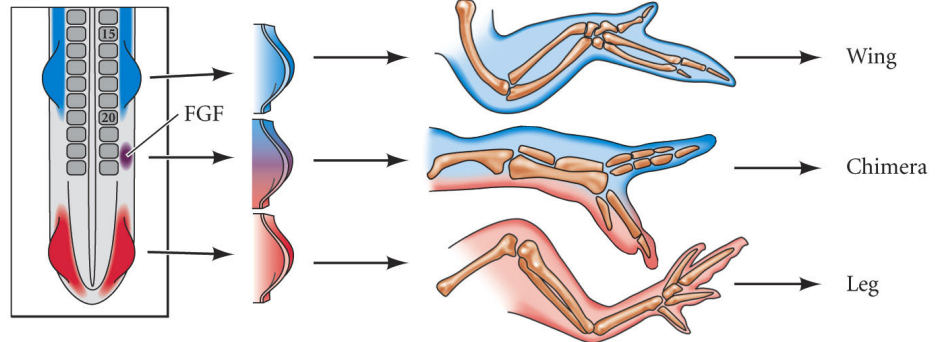


(A) Normal



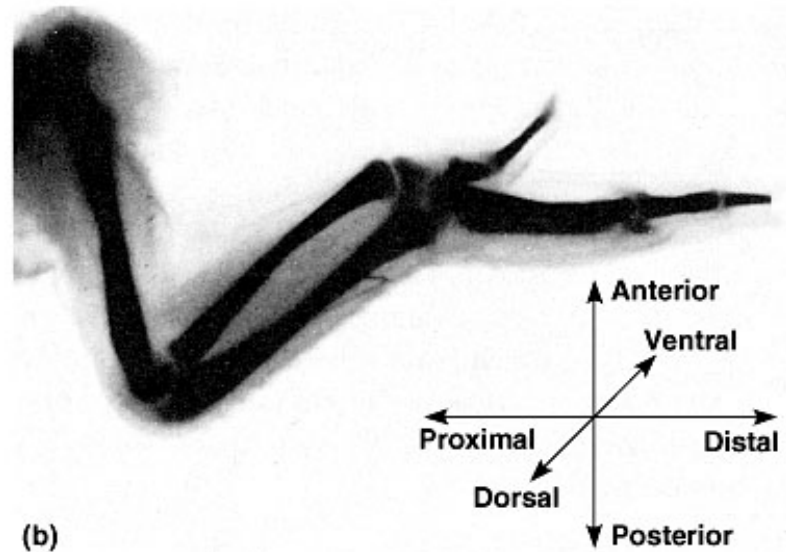
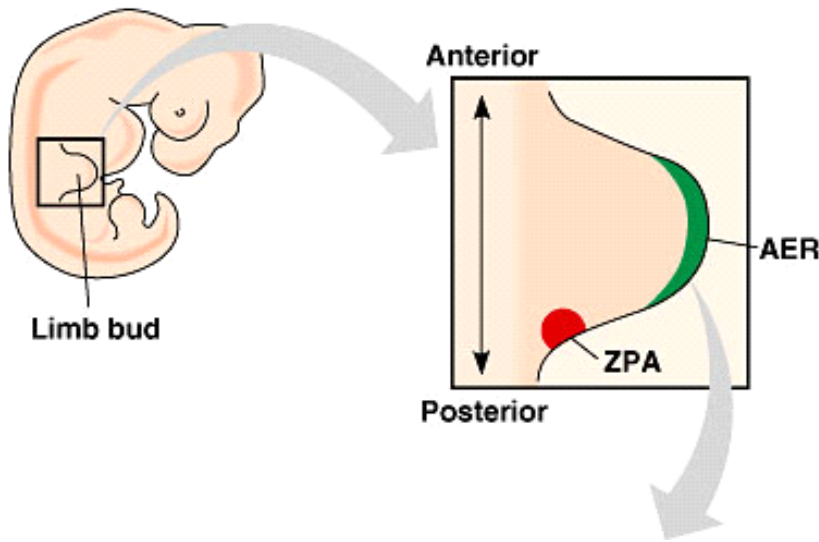
■ Tbx5
■ Tbx4

(B) FGF induced

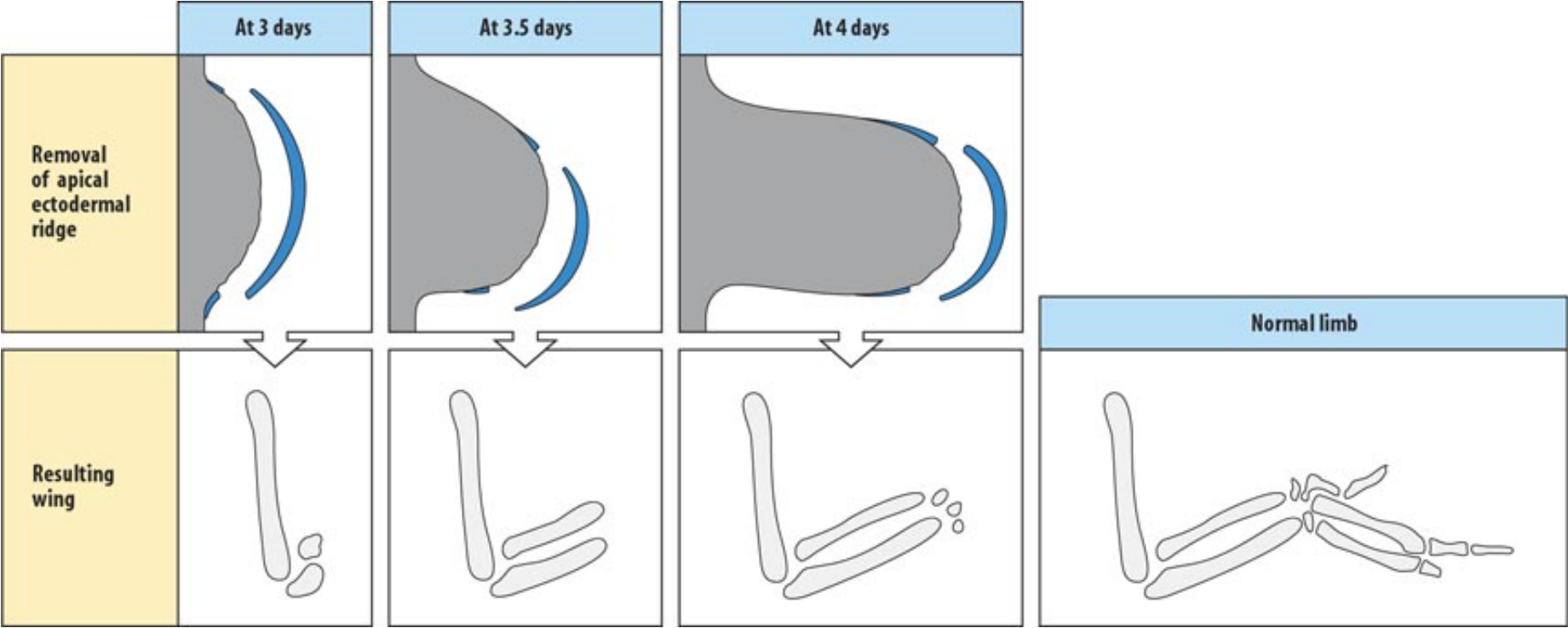


■ Tbx5
■ Tbx4

- Pattern Formation in the Vertebrate Limb.
 - Induction plays a major role in **pattern formation**.
 - **Positional information**, supplied by molecular cues, tells a cell where it is relative to the animal's body axes.



Homeobox-containing (*Hox*) genes play a role in specifying the identity of regions of the limb, as well as the body as a whole.

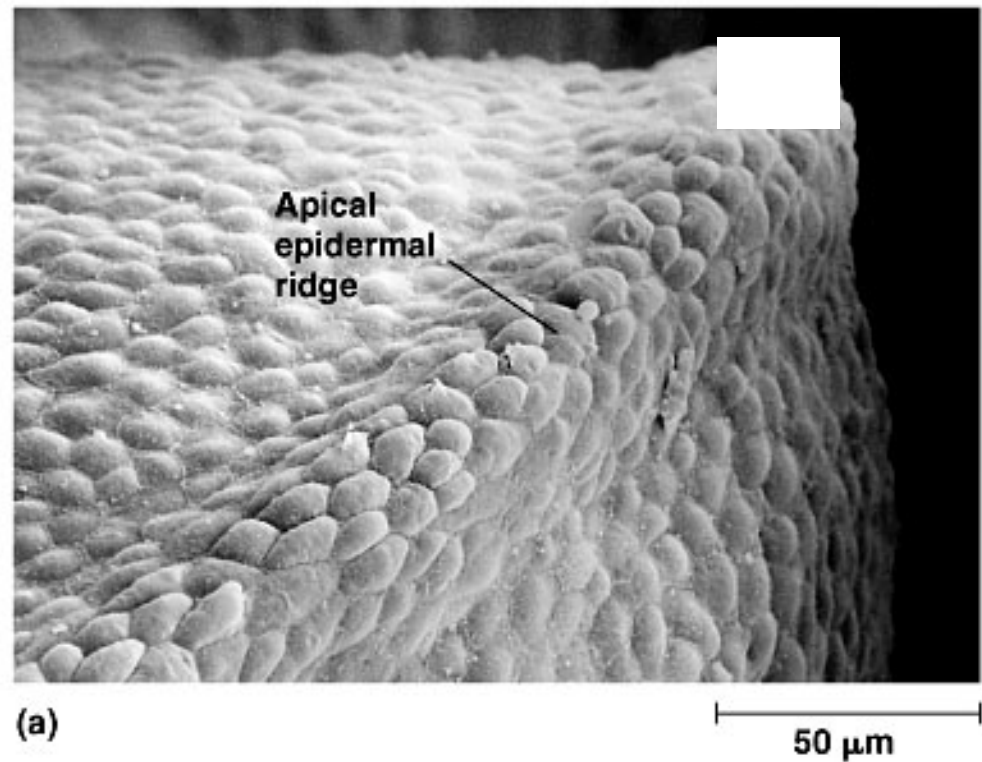


Mutual Induction

Limb Bud stage

Somatic mesoderm → Ectoderm to become AER

AER → mesoderm proximal to distal growth

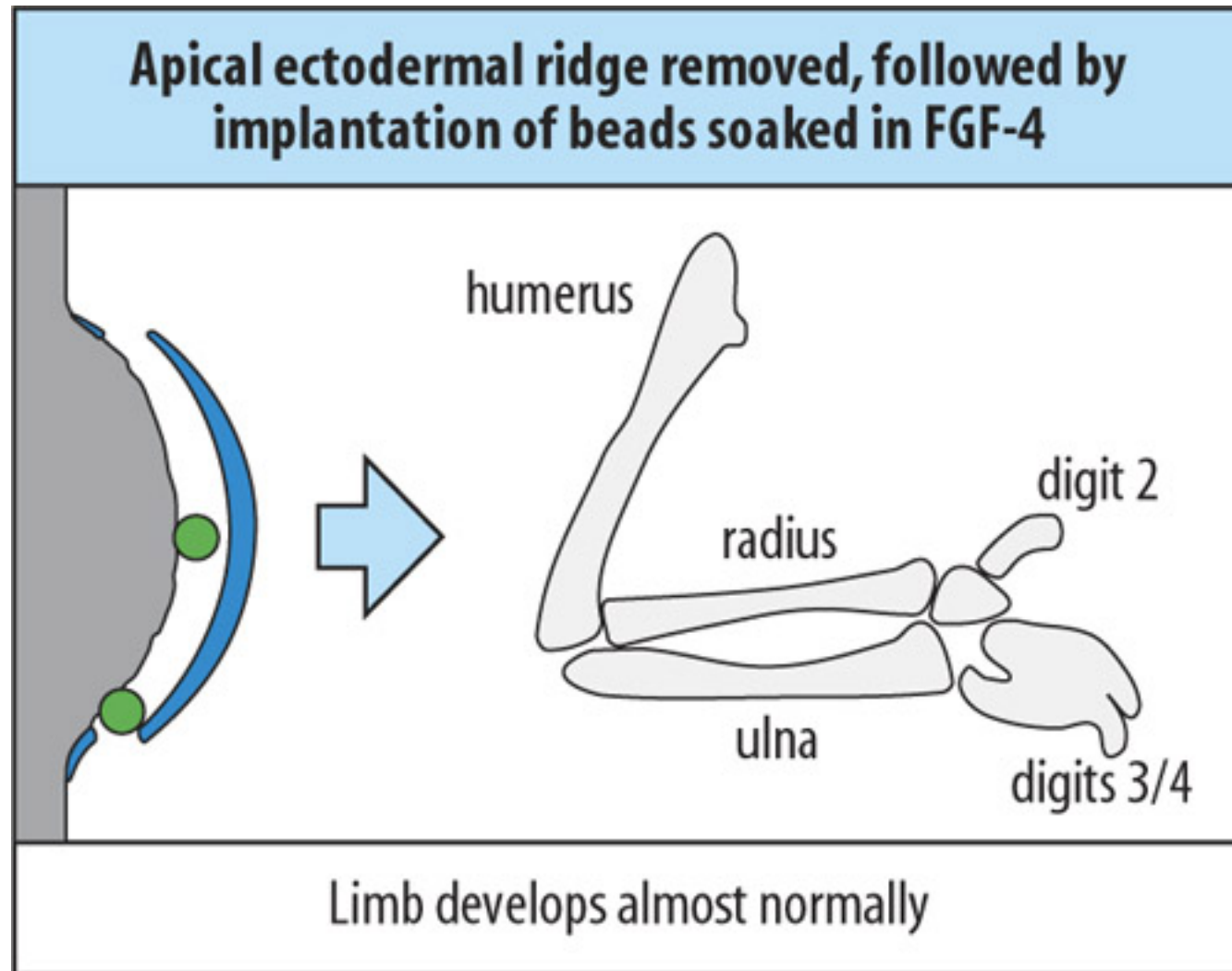


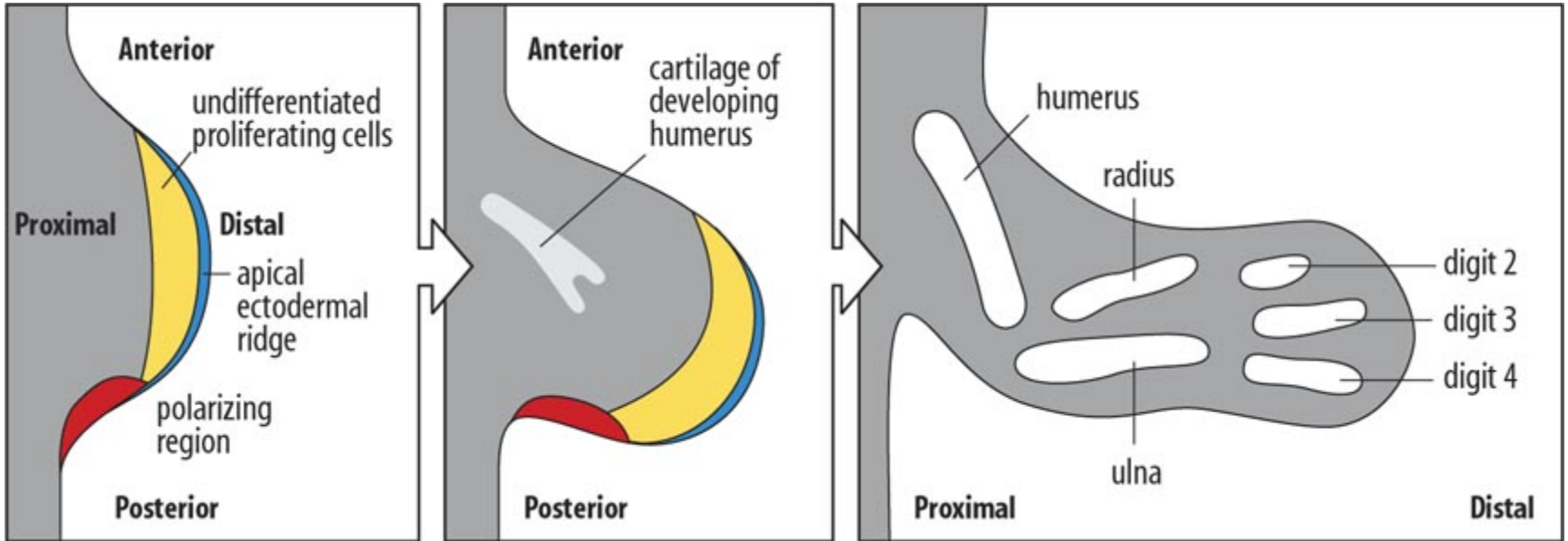
- **Apical ectodermal ridge (AER).**
- Secretes fibroblast growth factor (FGF) proteins.
 - Required for limb growth and patterning along the proximal-distal axis.

FGF-4 Injection



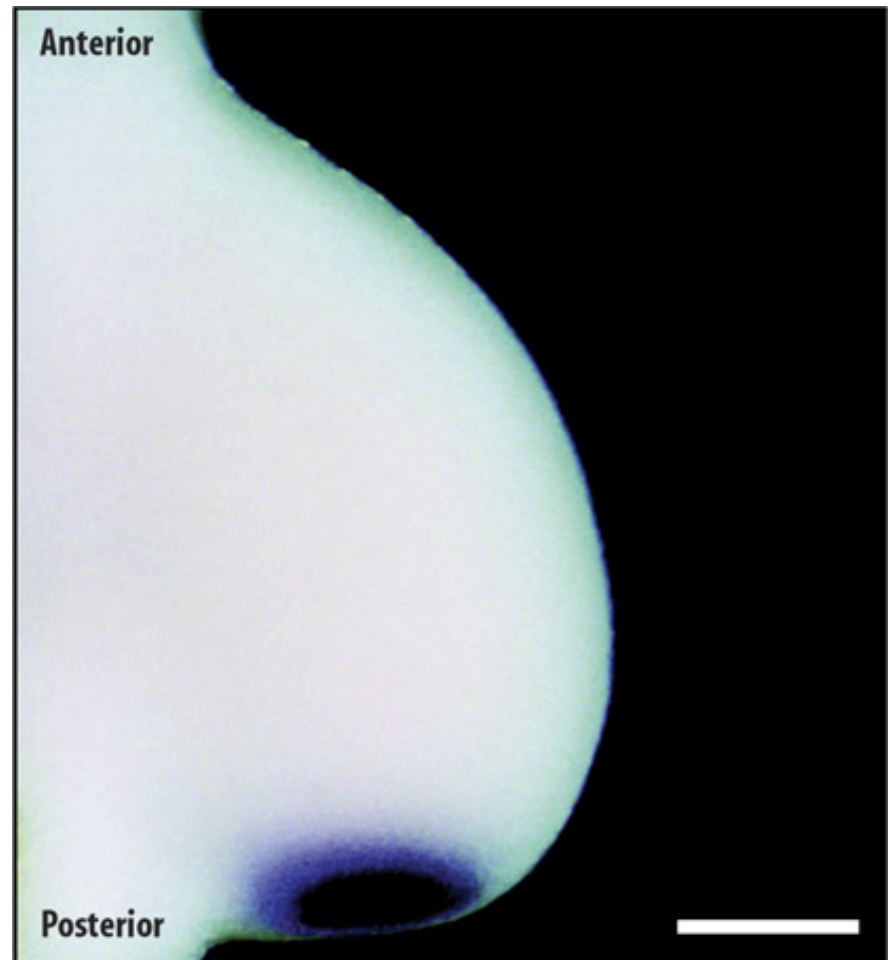
FGF-4 Can Replace AER Function

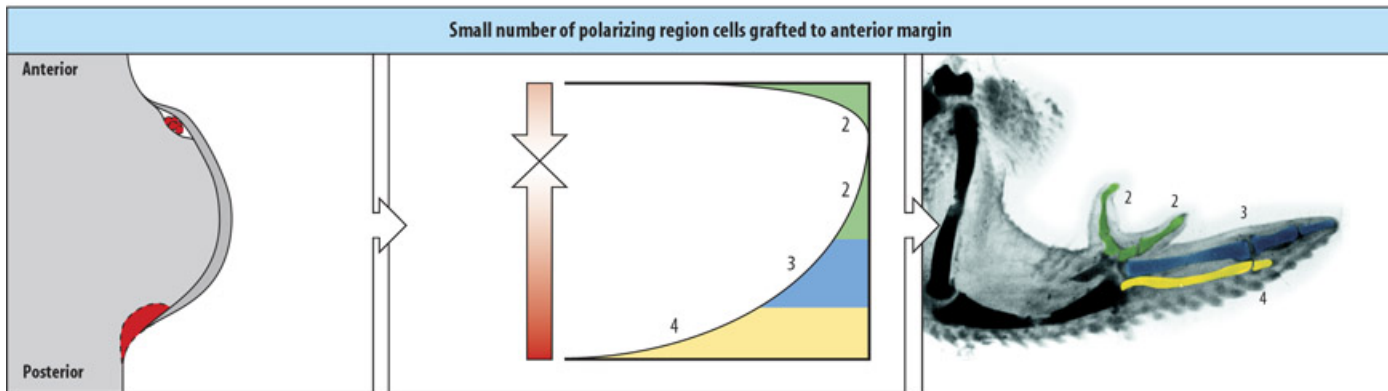
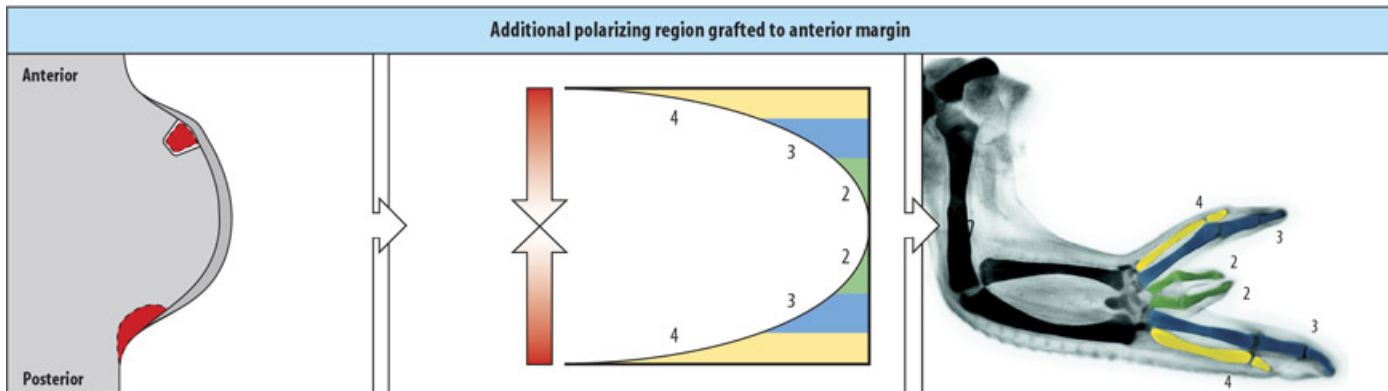
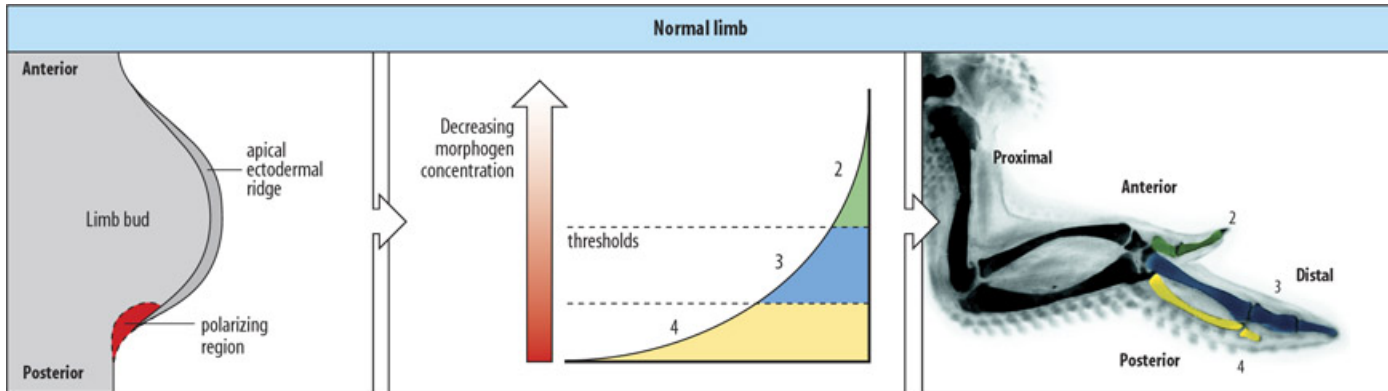


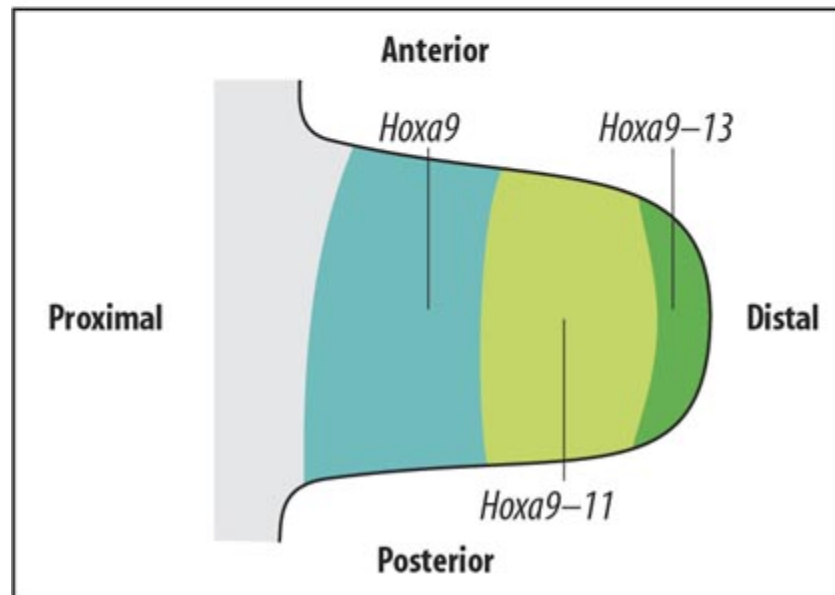
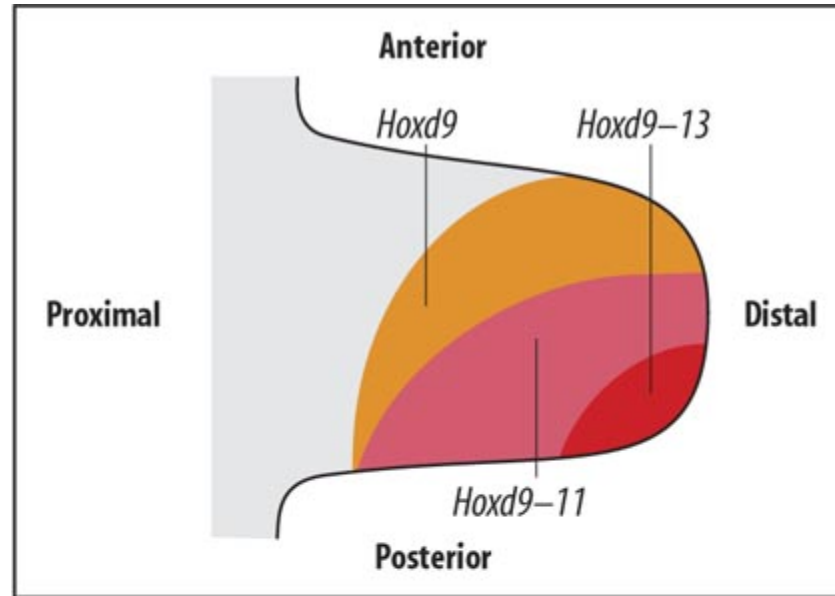


Sonic Hedgehog expression - ZPA

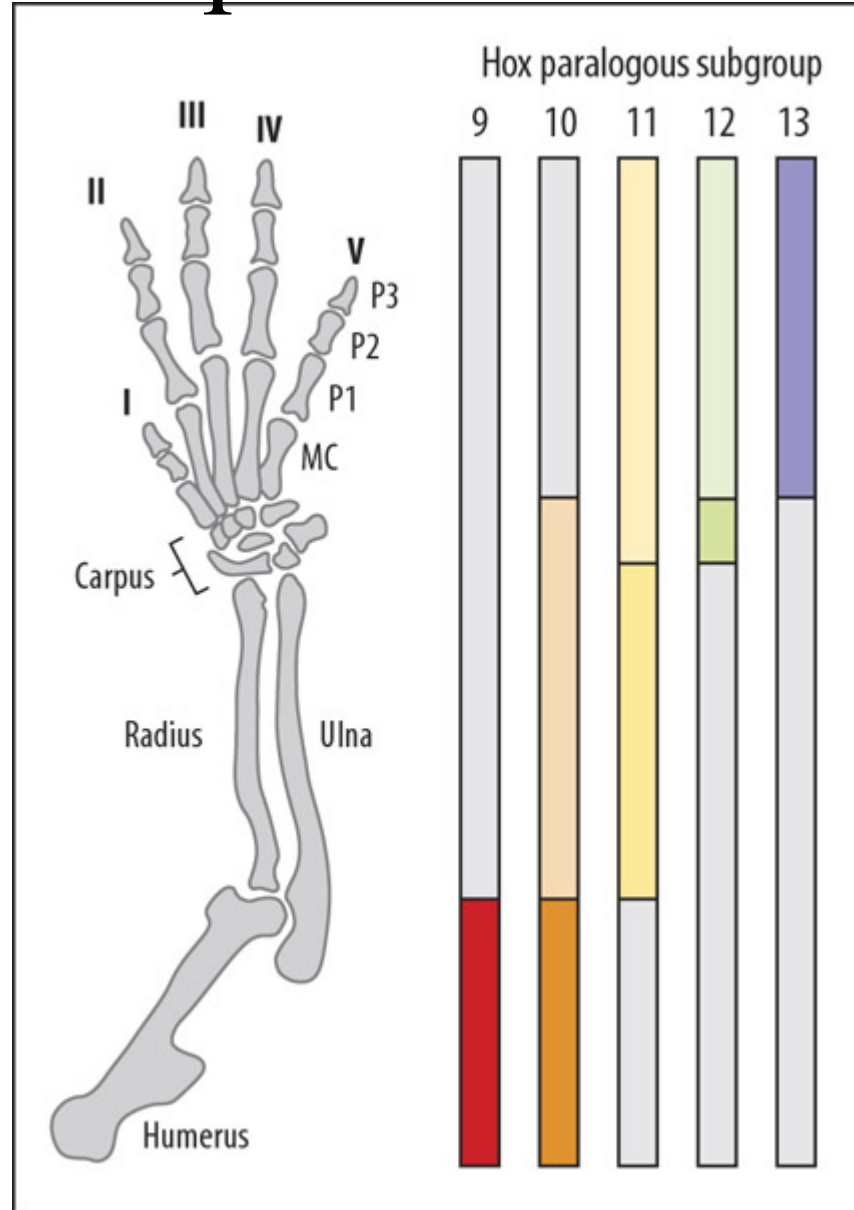
Acts like Spemann
organizer
Determines
developmental axis



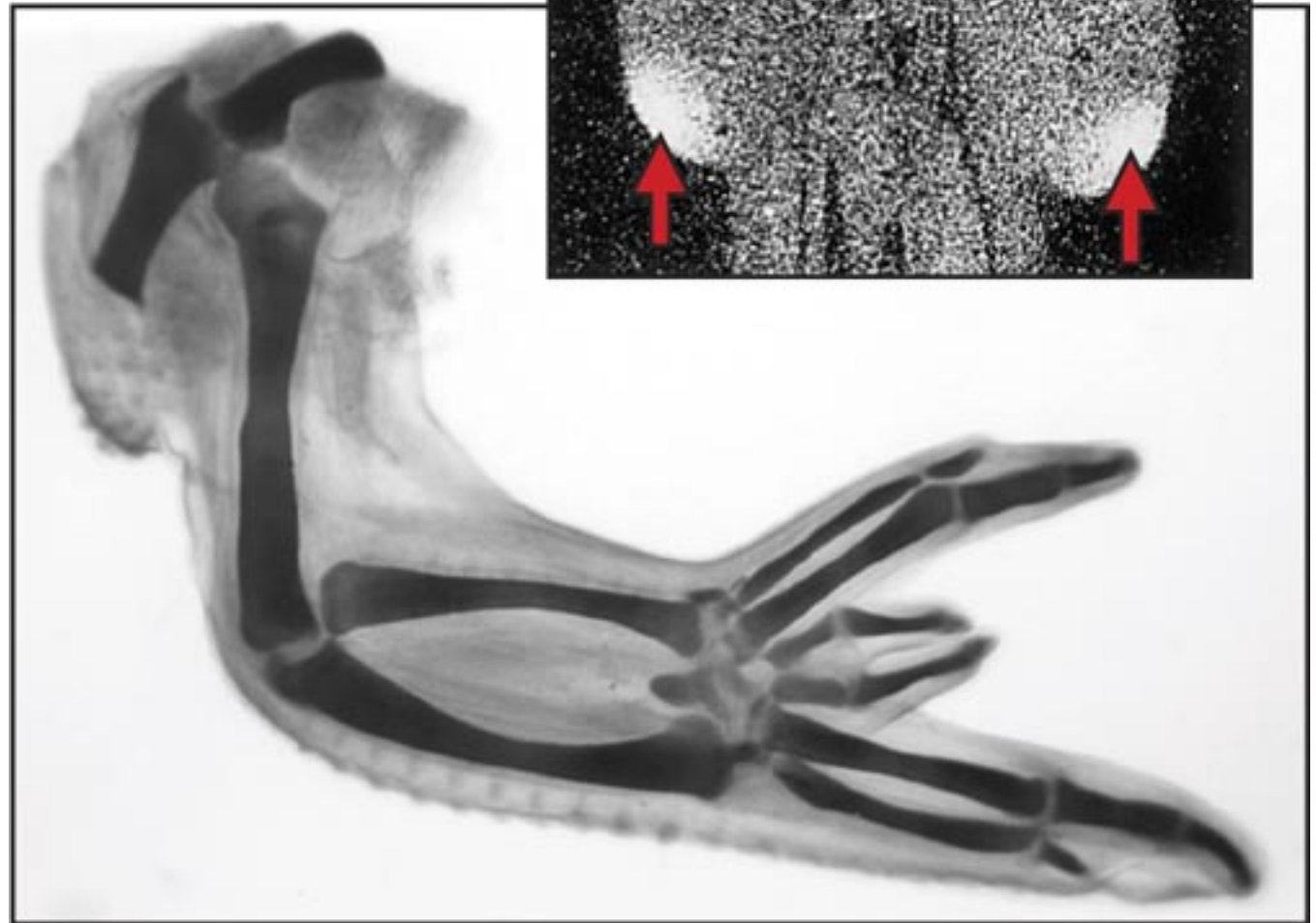




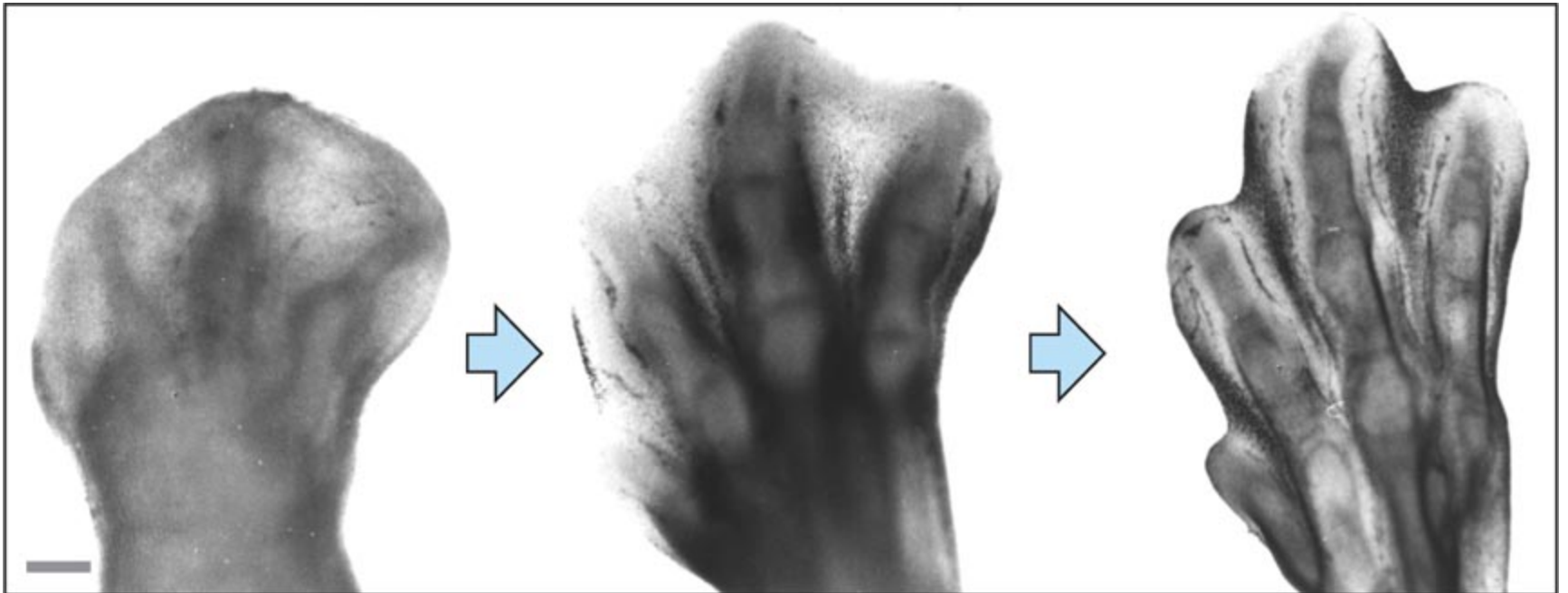
Hox Expression Domains



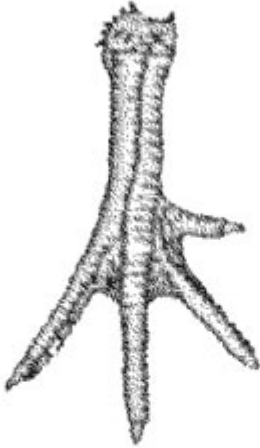
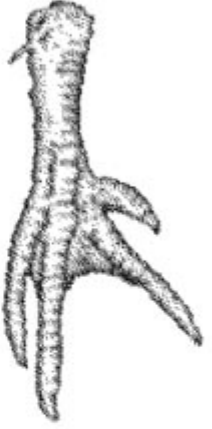
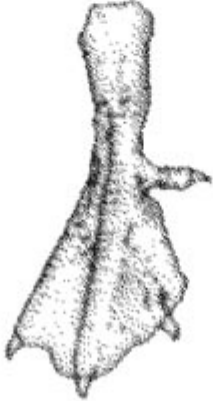
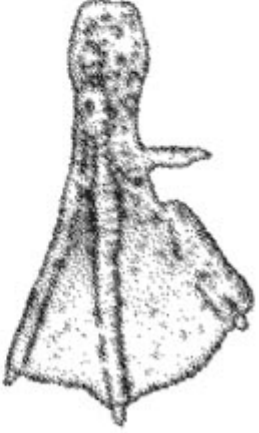
ZPA Transplantation Effects Hoxd Expression



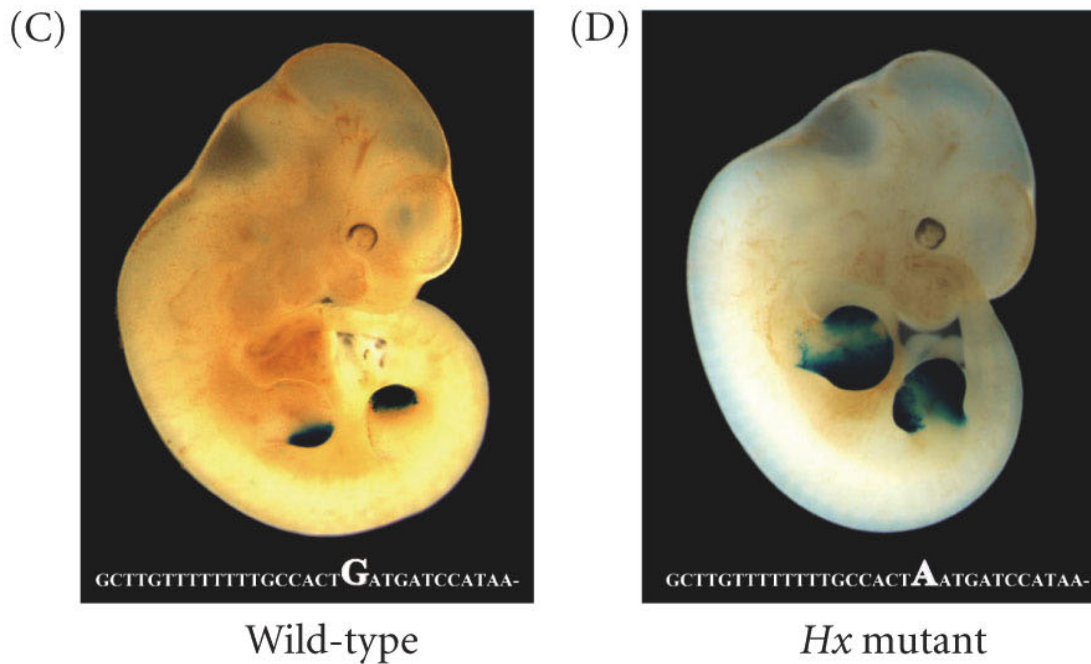
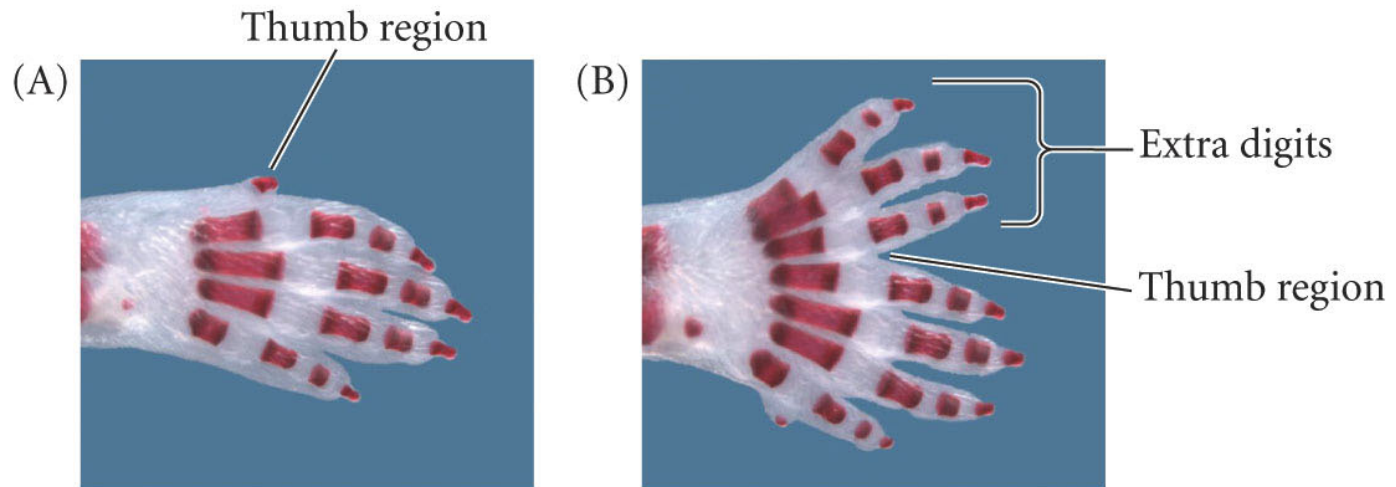
Apoptosis Separates Digits



Apoptotic pattern determined by signals in mesoderm

		Ectoderm	
		Chick	Duck
Mesoderm	Chick		
	Duck		

Sonic Hedgehog Expression



Feed me then leave
me alone

