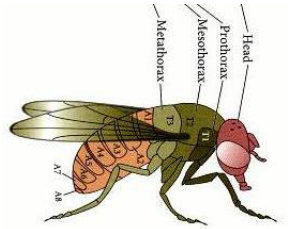
Come si forma il piano corporeo

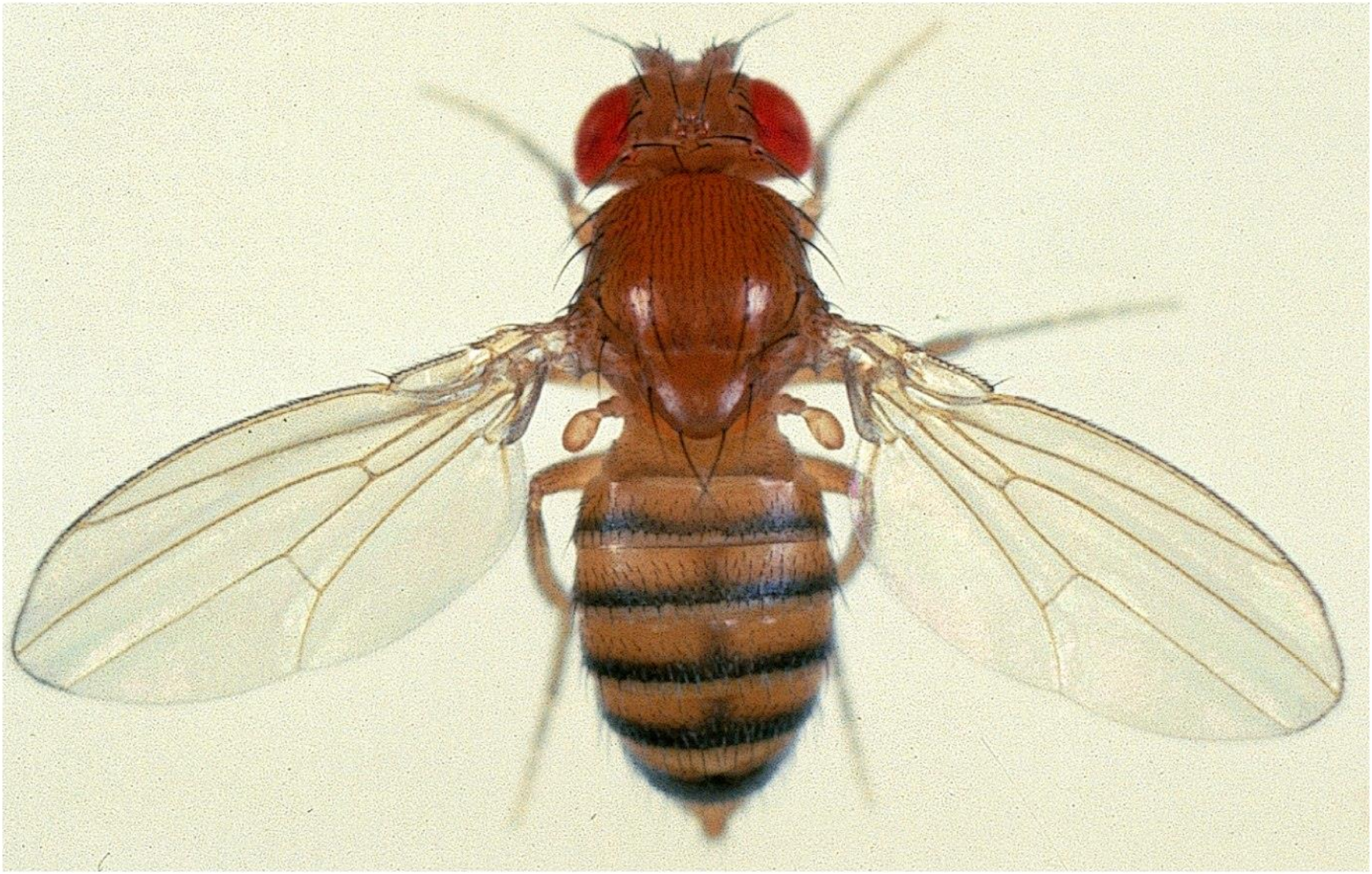
Studi integrati di genetica e di biologia molecolare

Il modello Drosophila



- Ottima conoscenza della genetica
- Facile da allevare, poco costosa, prolifica
- Facile da mutagenizzare
- Cromosomi politenici, facili da studiare
- Circa 14,000 geni, sequenza nota
- Dati accessibili
- Struttura corporea complessa e non trasparente
- Biologia molecolare l’ha riscoperta

Aree organogenetiche o campi



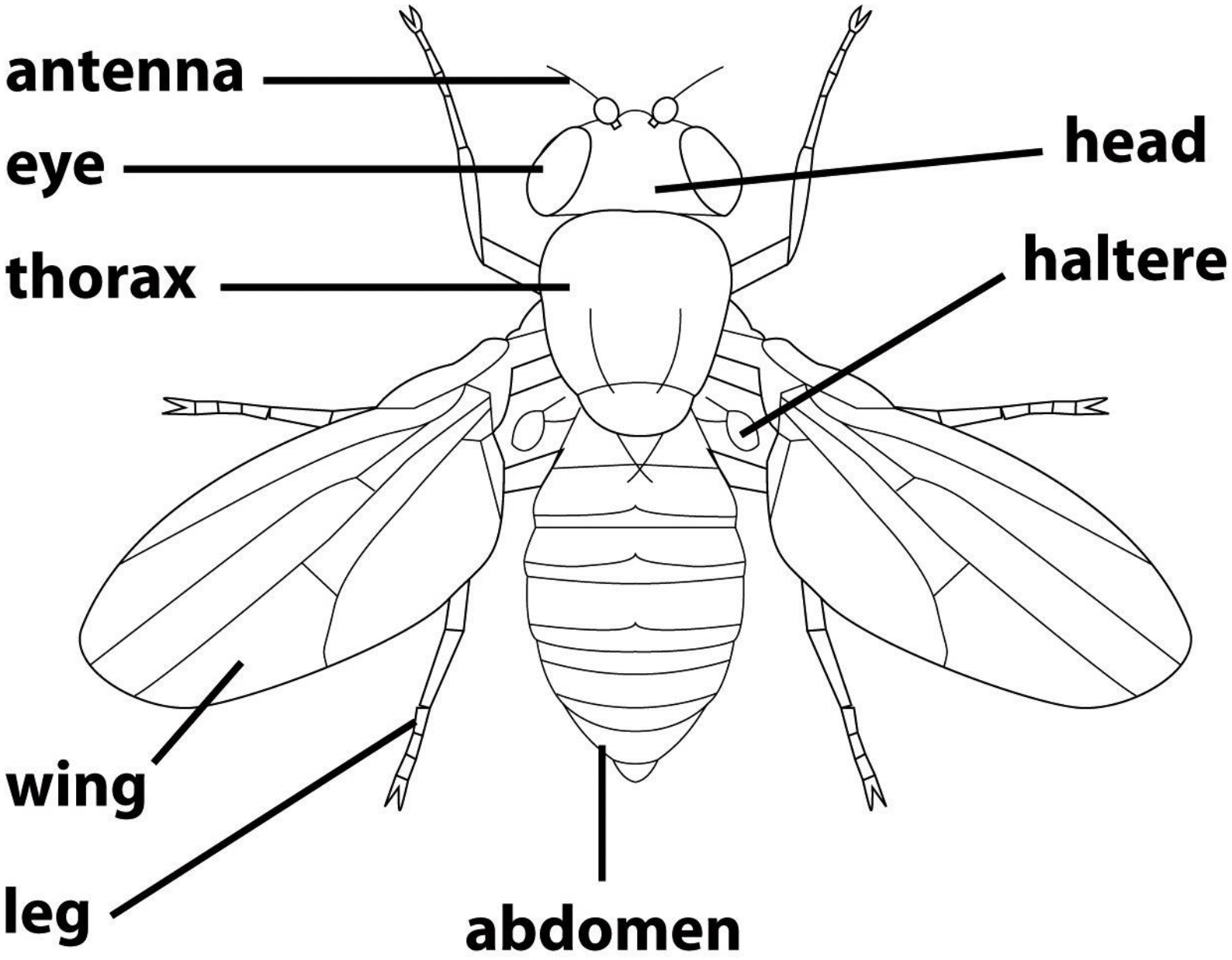


Figure 22-24b *Molecular Biology of the Cell* (© Garland Science 2008)

Ciclo vitale della Drosophila

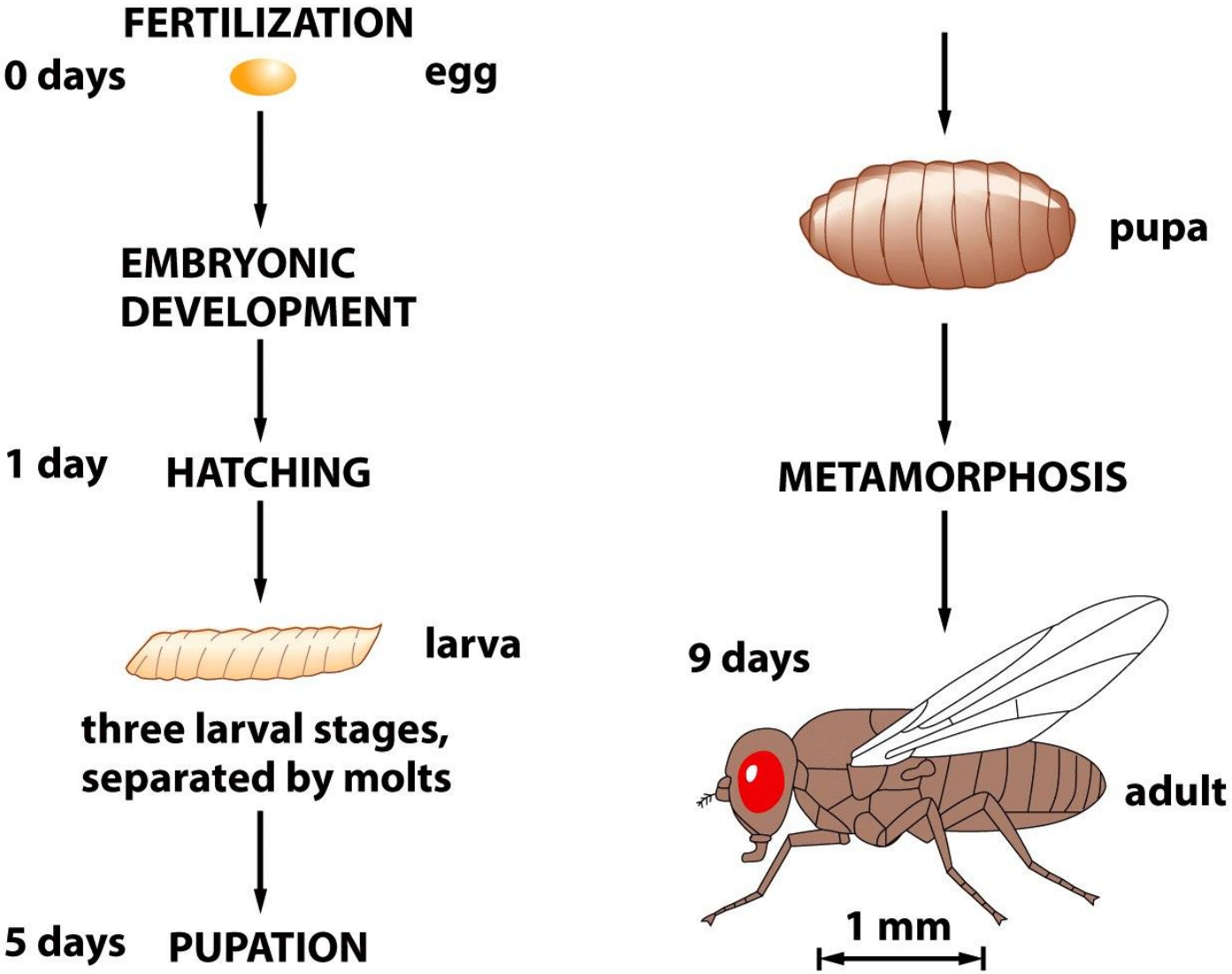


Figure 22-25 *Molecular Biology of the Cell* (© Garland Science 2008)

Segmentazione della Drosophila

Prime fasi dello sviluppo della Drosophila

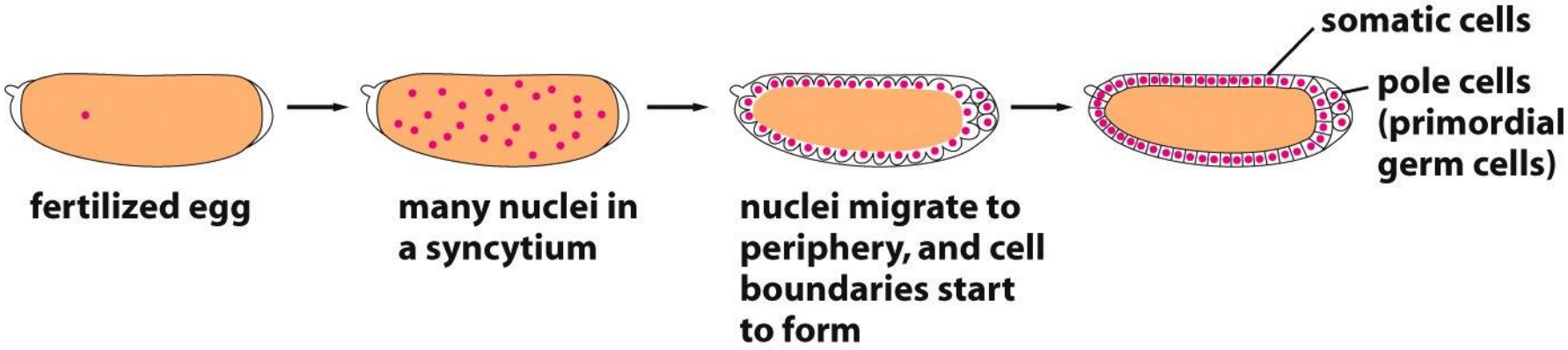
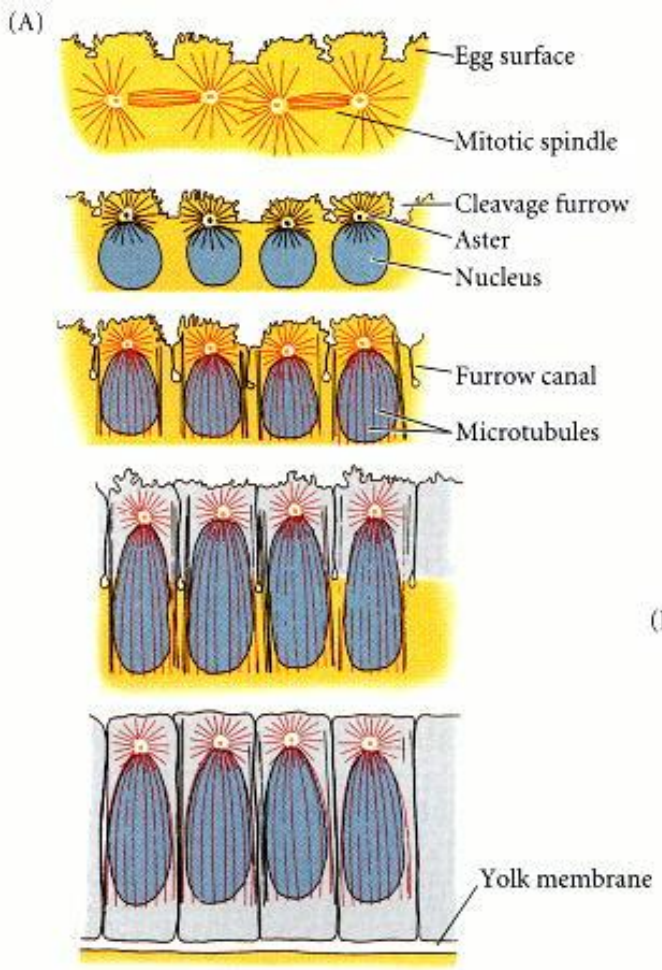
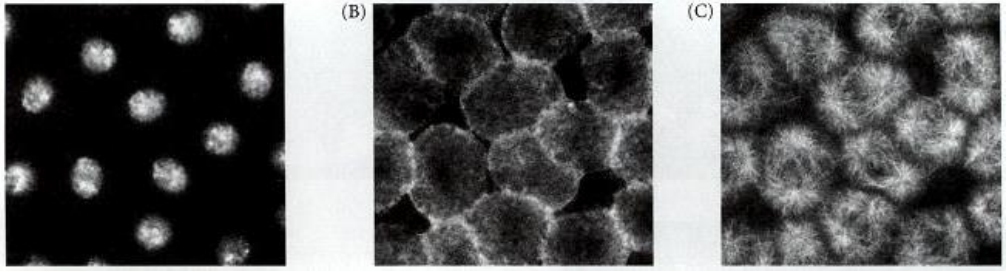


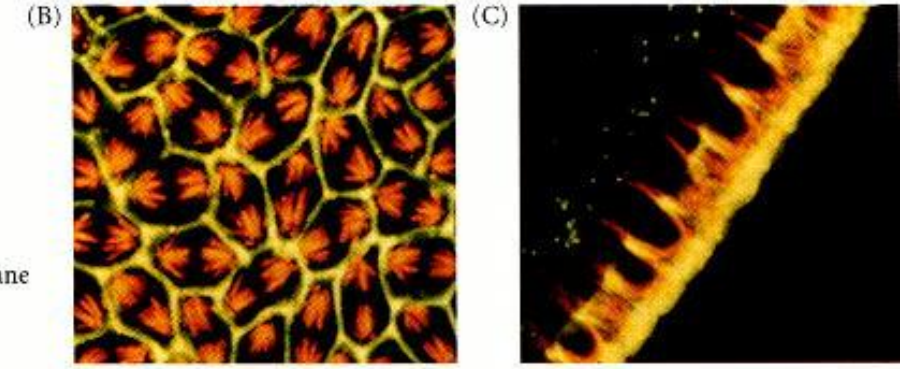
Figure 22-28a *Molecular Biology of the Cell* (© Garland Science 2008)

Formazione del blastoderma cellulare della Drosophila





nuclei actina microtubuli



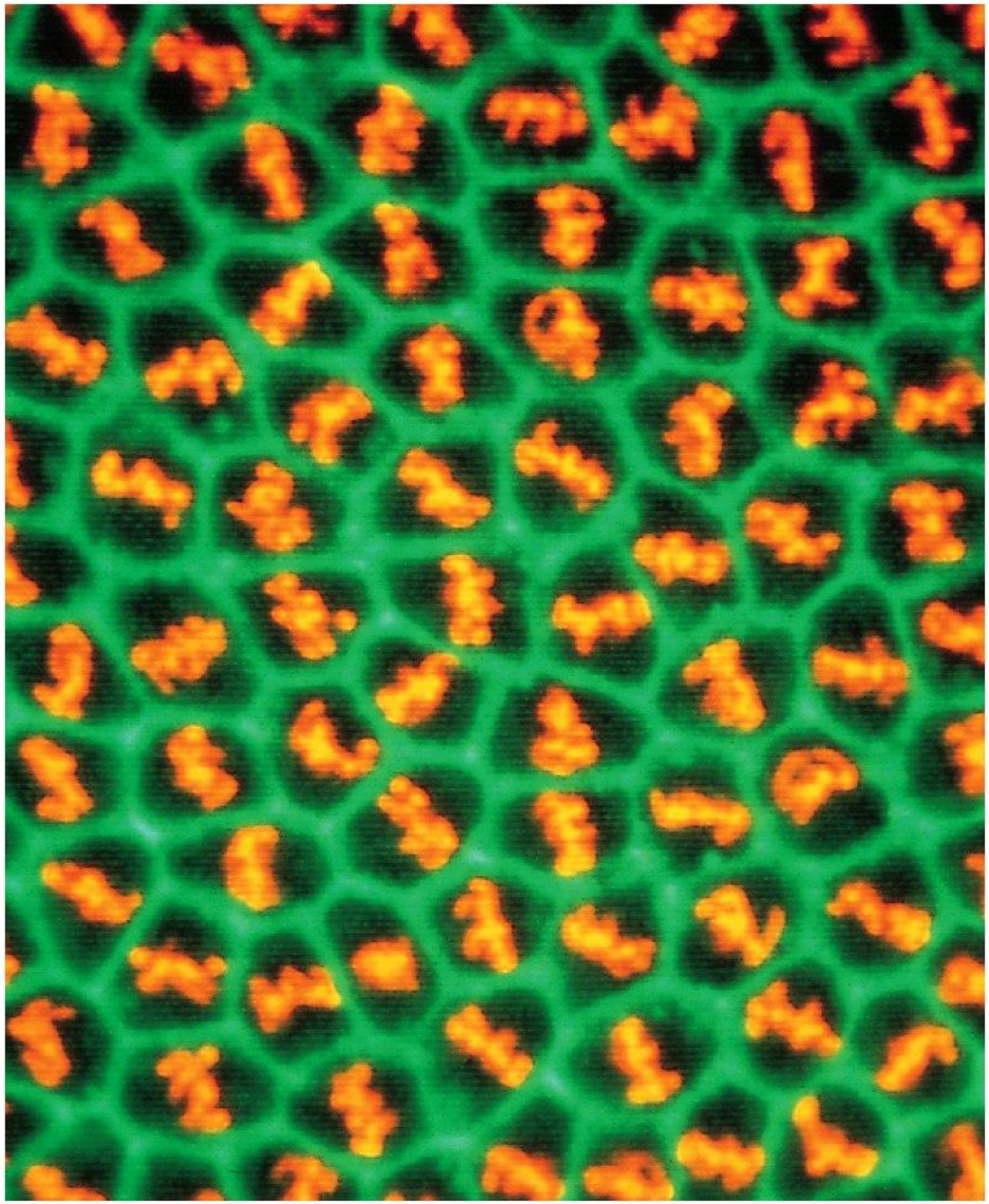
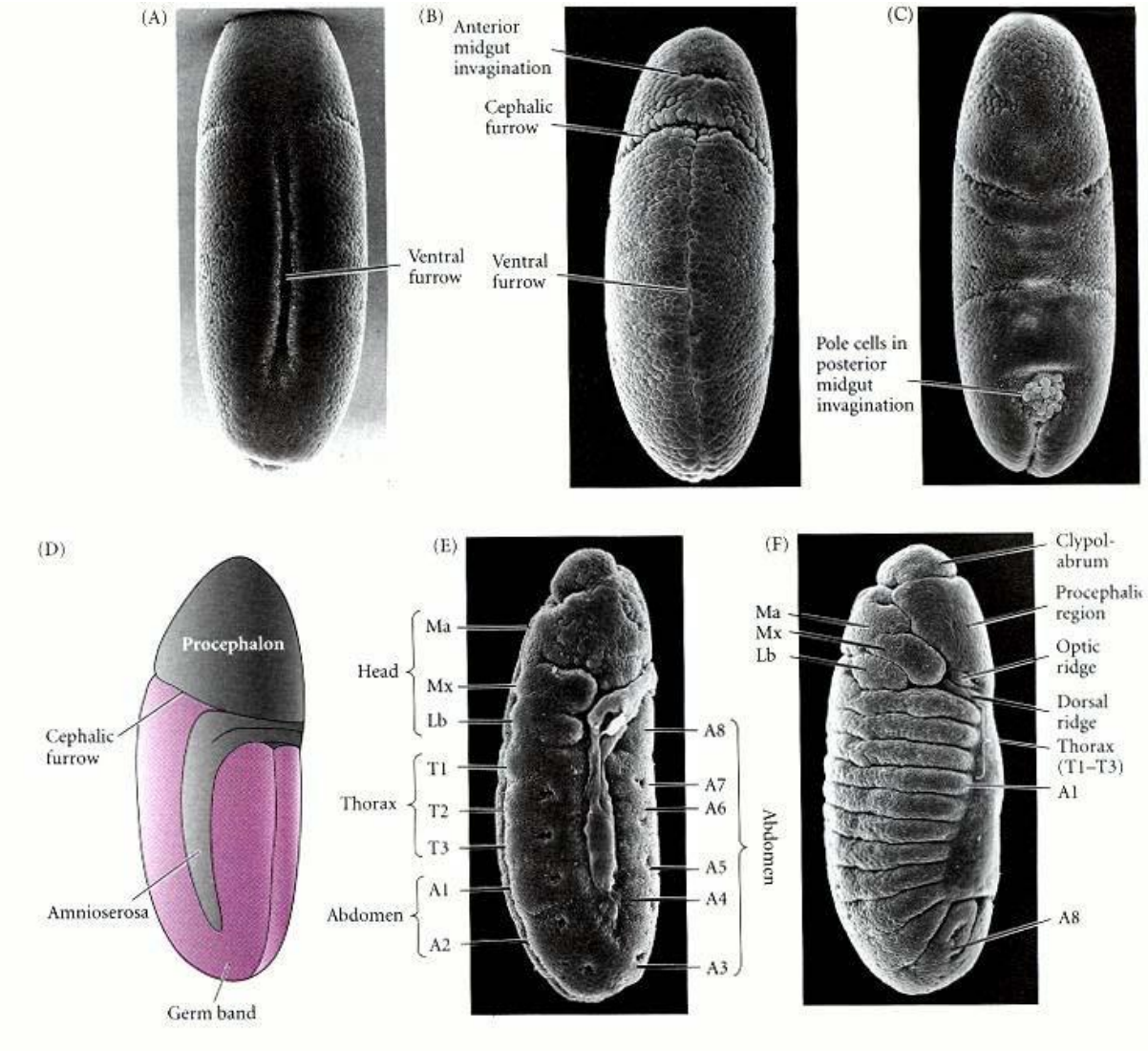


Figure 22-28b *Molecular Biology of the Cell* (© Garland Science 2008)

La gastrulazione nella Drosophila



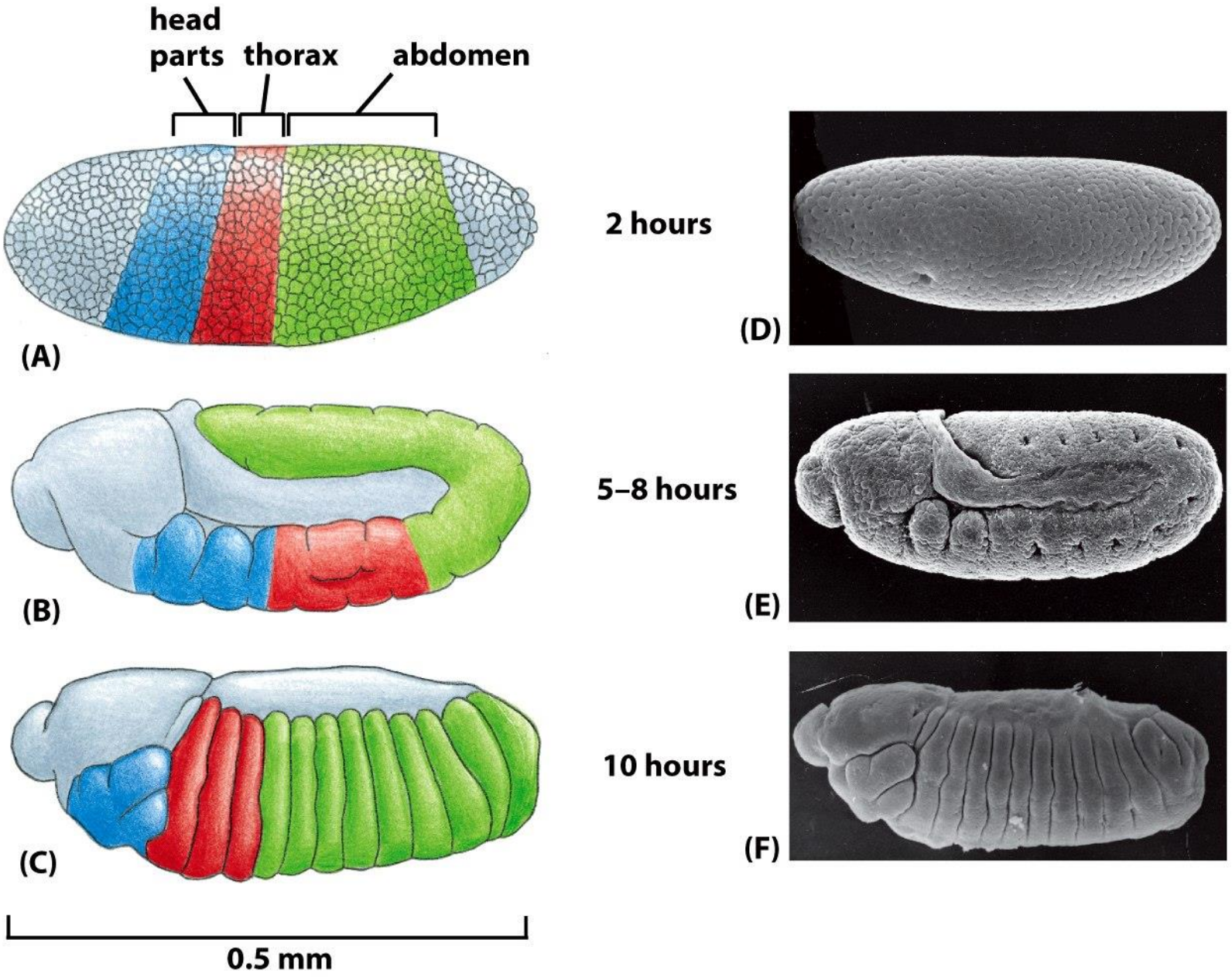
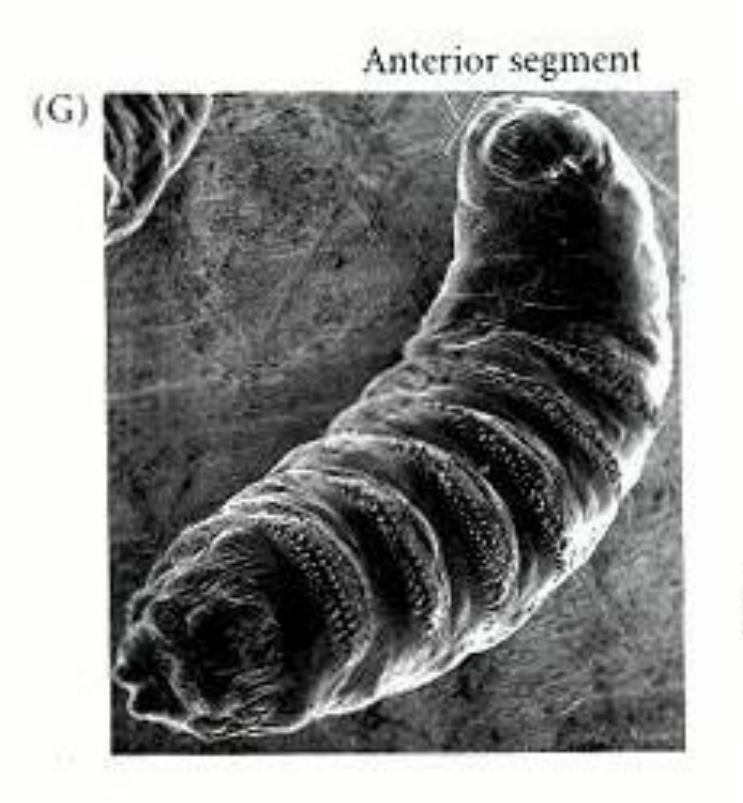
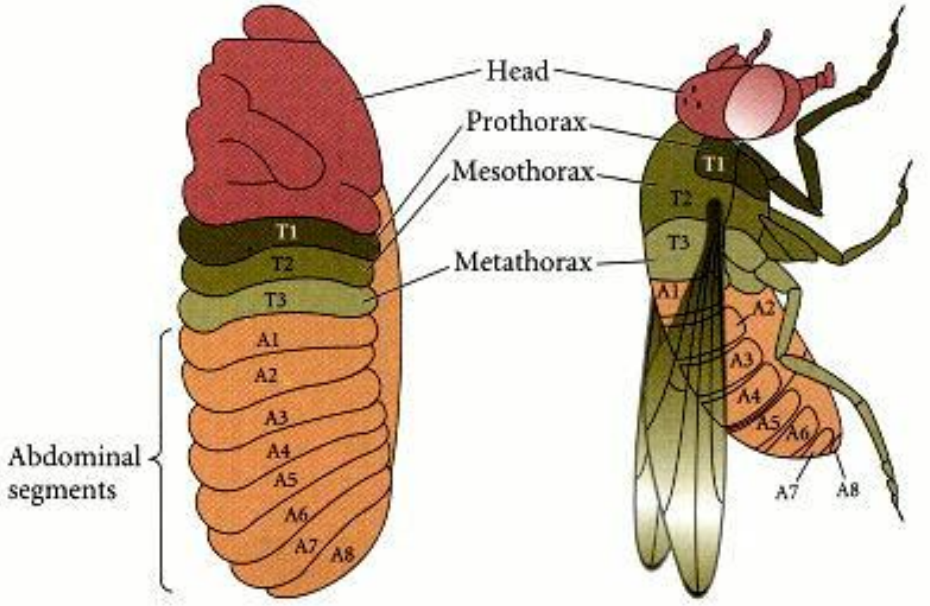


Figure 22-26 *Molecular Biology of the Cell* (© Garland Science 2008)

Larva e animale adulto





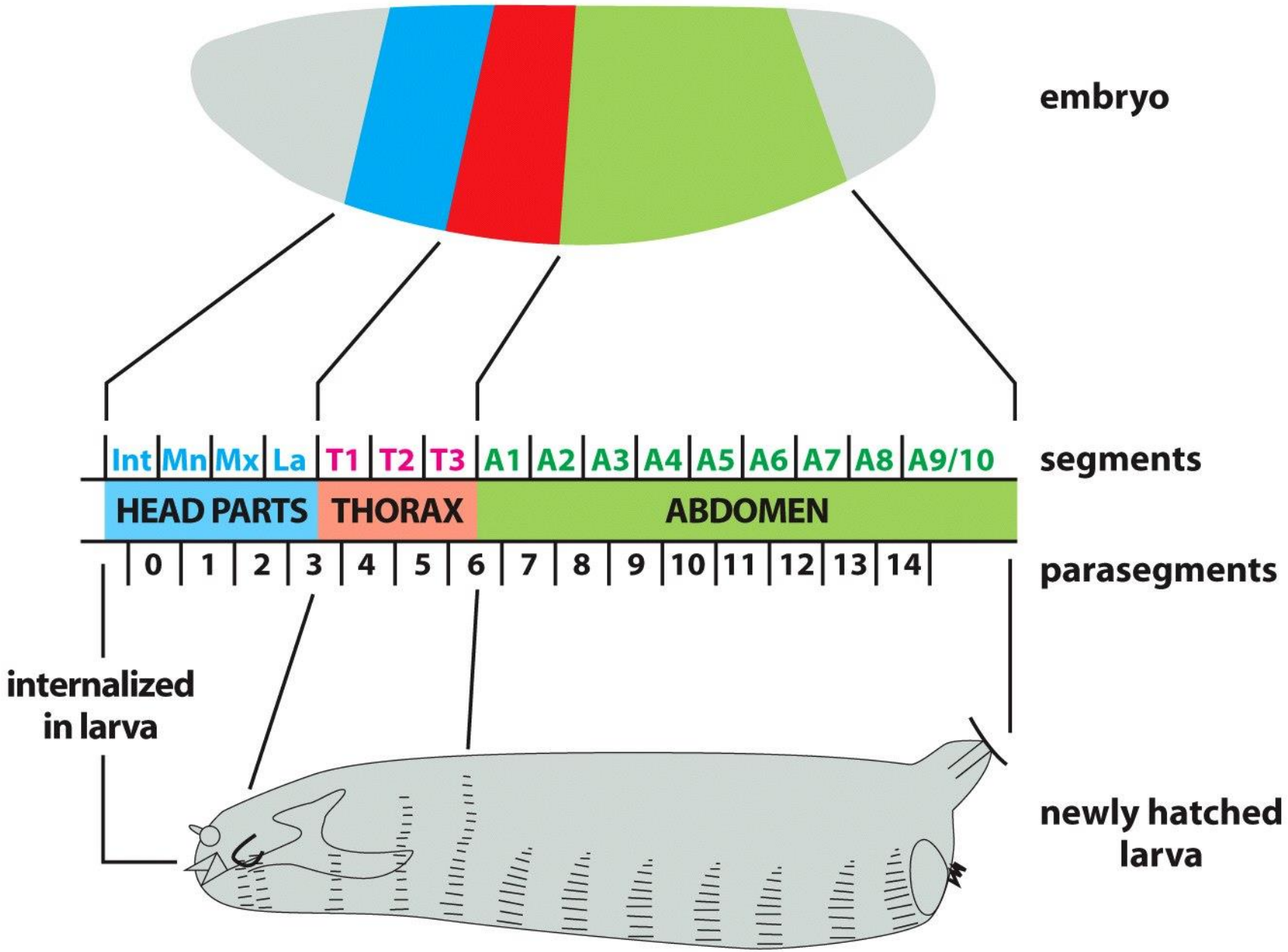


Figure 22-27 *Molecular Biology of the Cell* (© Garland Science 2008)

Mappa presuntiva dello sviluppo dell'embrione di Drosophila

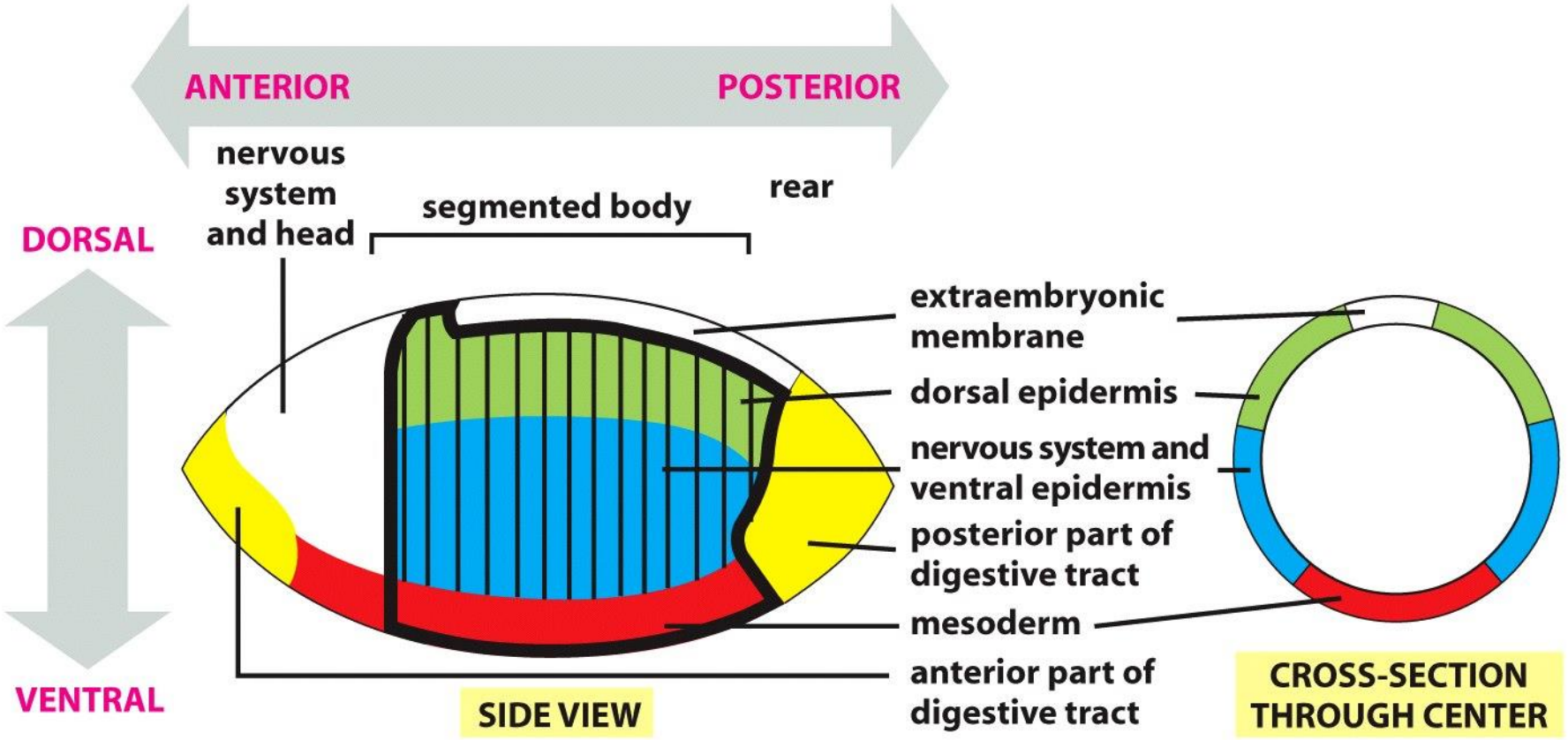


Figure 22-29 *Molecular Biology of the Cell* (© Garland Science 2008)

Compartimentalizzazione del corpo

Graduale nel tempo:

- Geni della polarità o degli assi corporei
  ant-post e dorso-ventr
- Geni della segmentazione
  geni gap
  geni di coppia (pair-rule)
  geni di compartimentazione del segmento
  (segment polarity)
- Geni dell'identità del segmento corporeo
  geni omeotici

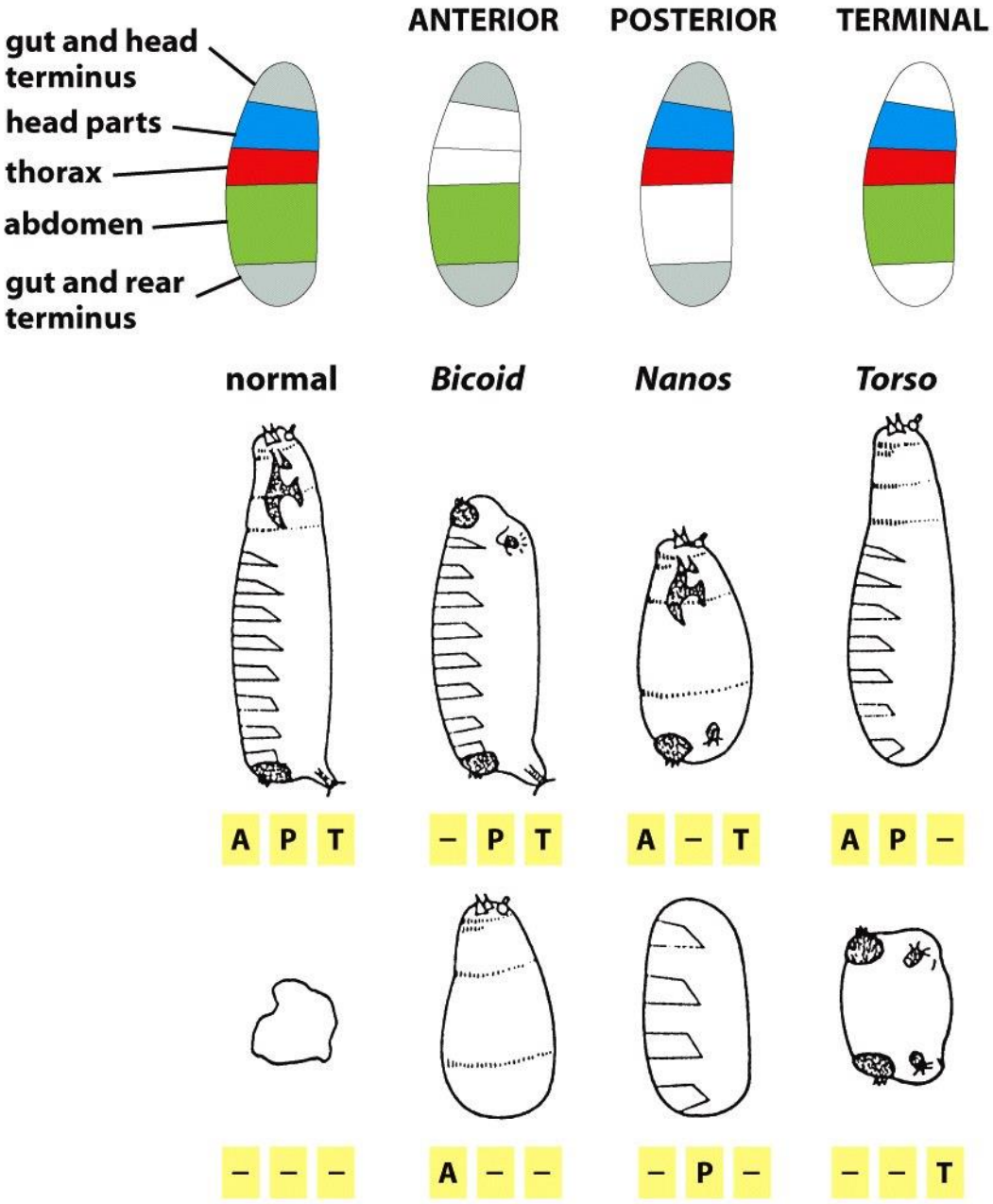


Figure 22-30 *Molecular Biology of the Cell* (© Garland Science 2008)

L’oocito della Drosophila è polarizzato

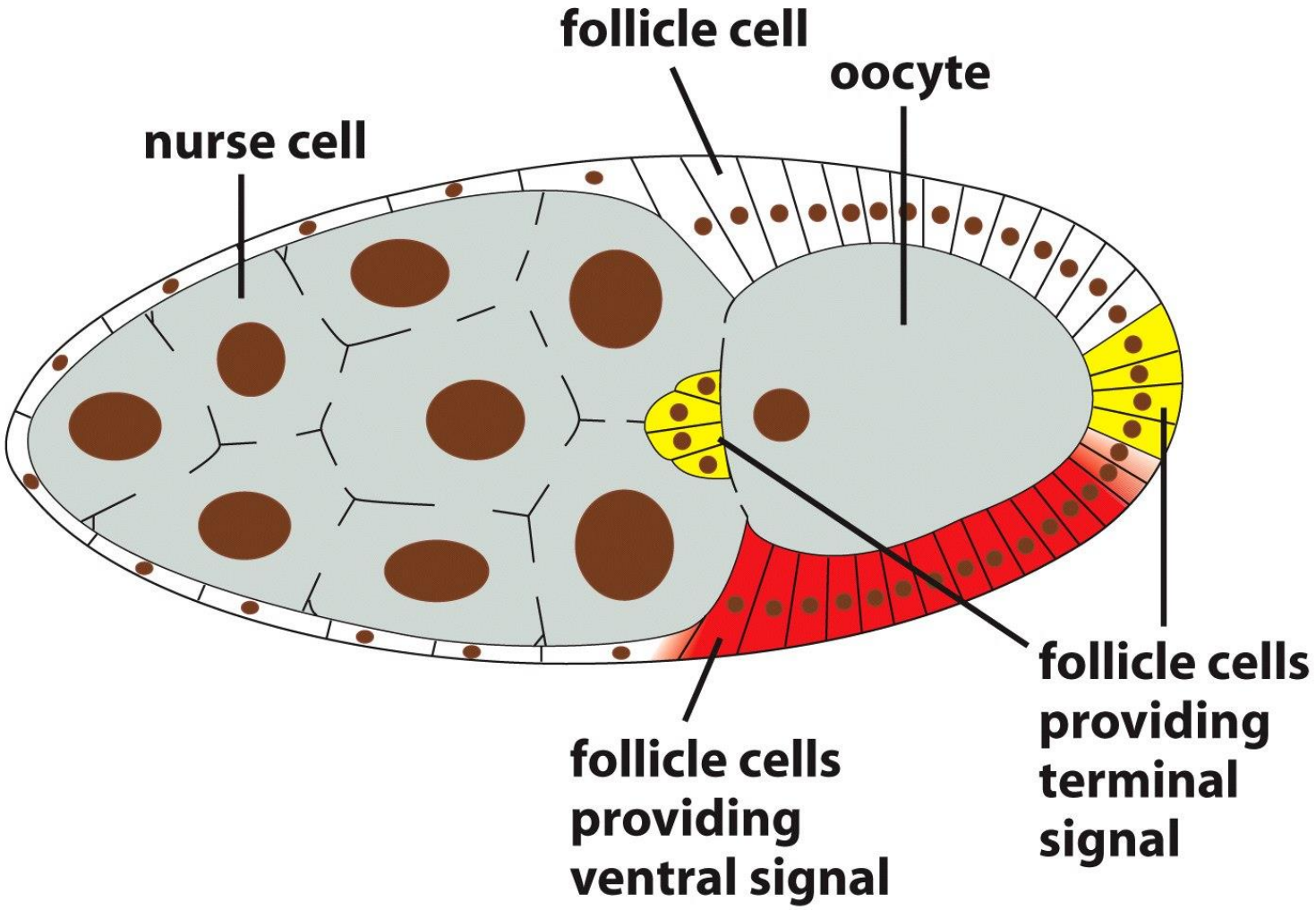


Figure 22-31 *Molecular Biology of the Cell* (© Garland Science 2008)

Compartimentalizzazione del corpo

Graduale nel tempo:

- Geni della polarità o degli assi corporei
  ant-post e dorso-ventr
- Geni della segmentazione
  geni gap
  geni di coppia (pair-rule)
  geni di compartimentazione del segmento
  (segment polarity)
- Geni dell'identità del segmento corporeo
  geni omeotici

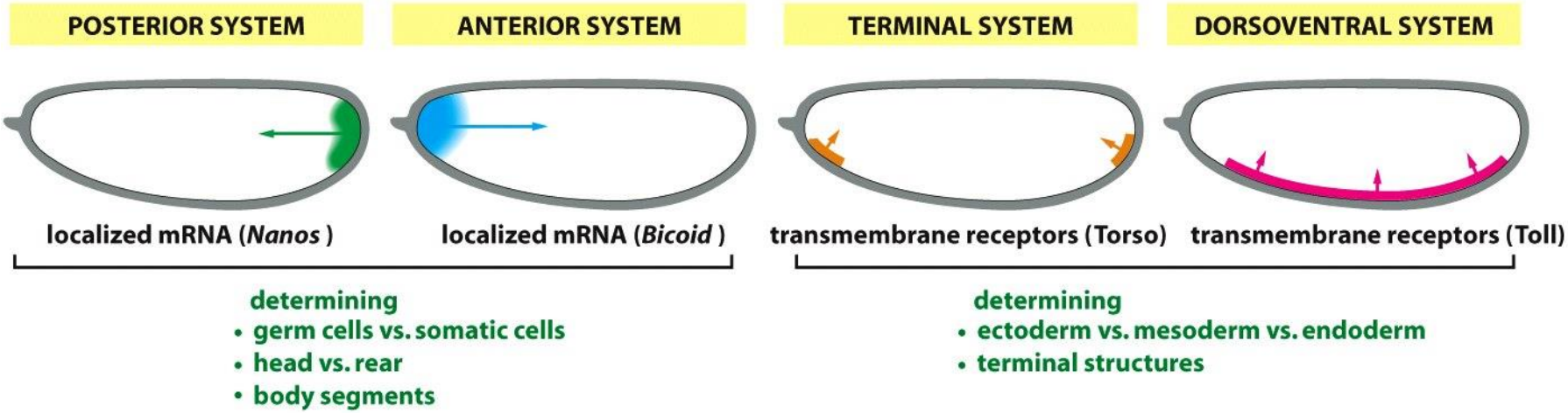
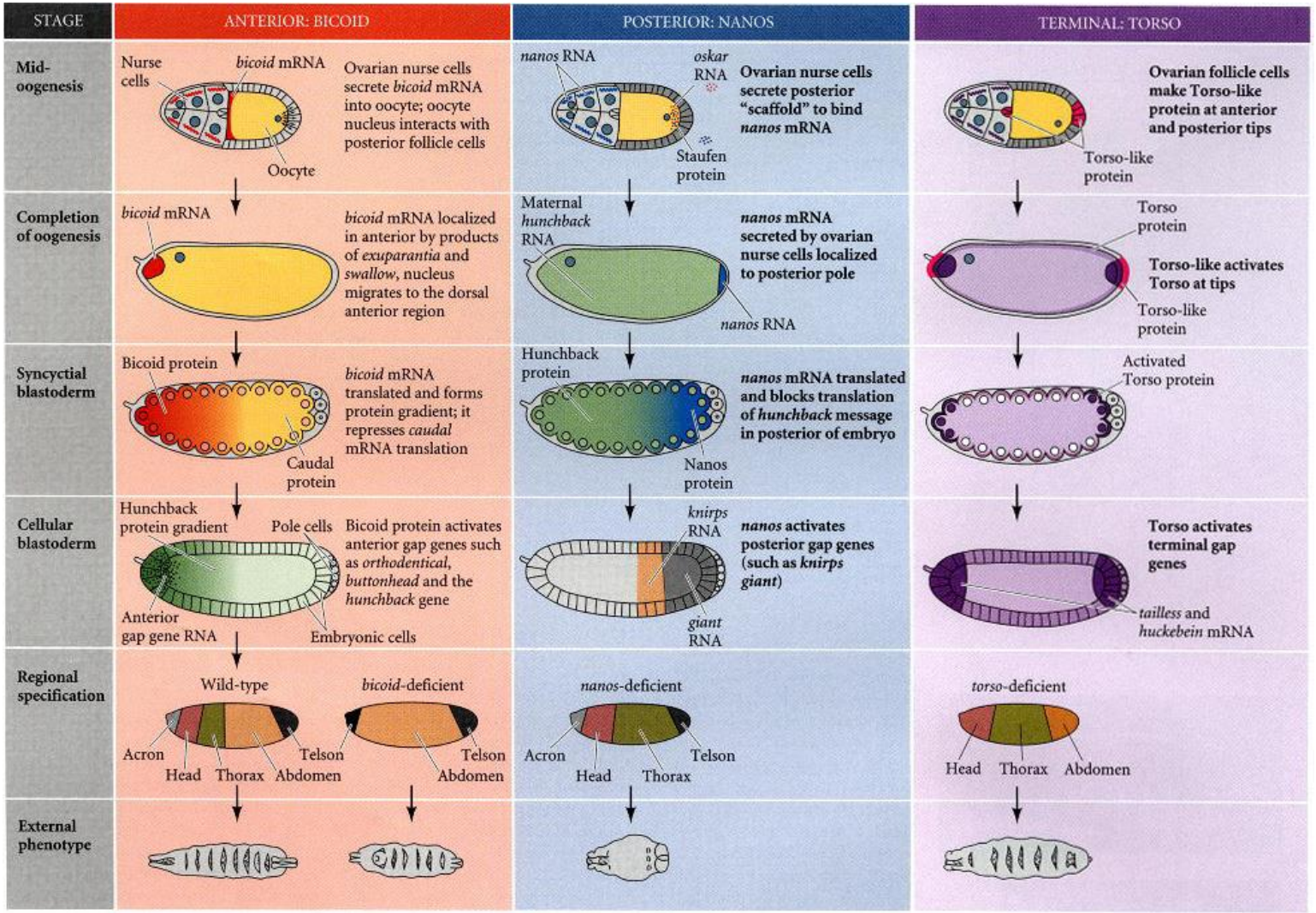


Figure 22-32 *Molecular Biology of the Cell* (© Garland Science 2008)

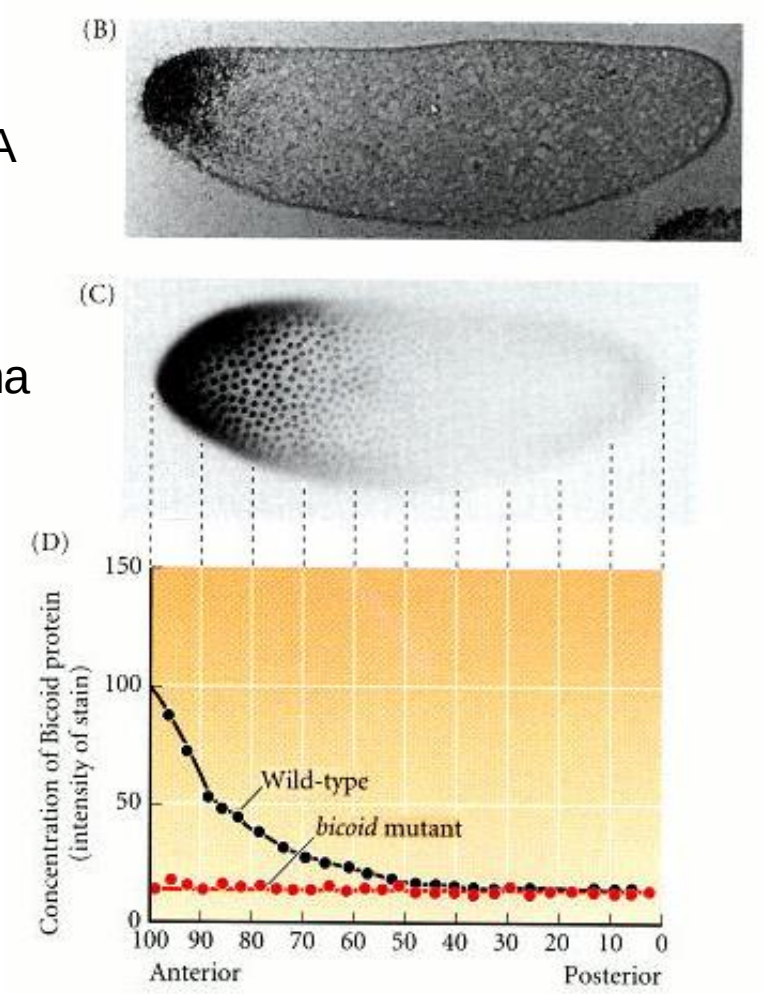
Ruolo dei geni ad effetto materno



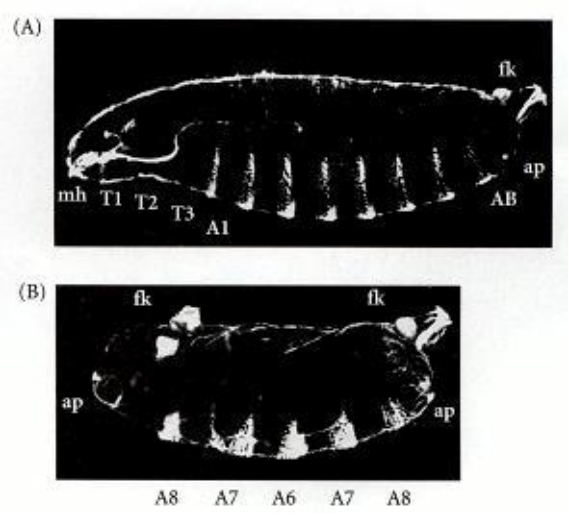
Espressione di bicoid

mRNA

proteina

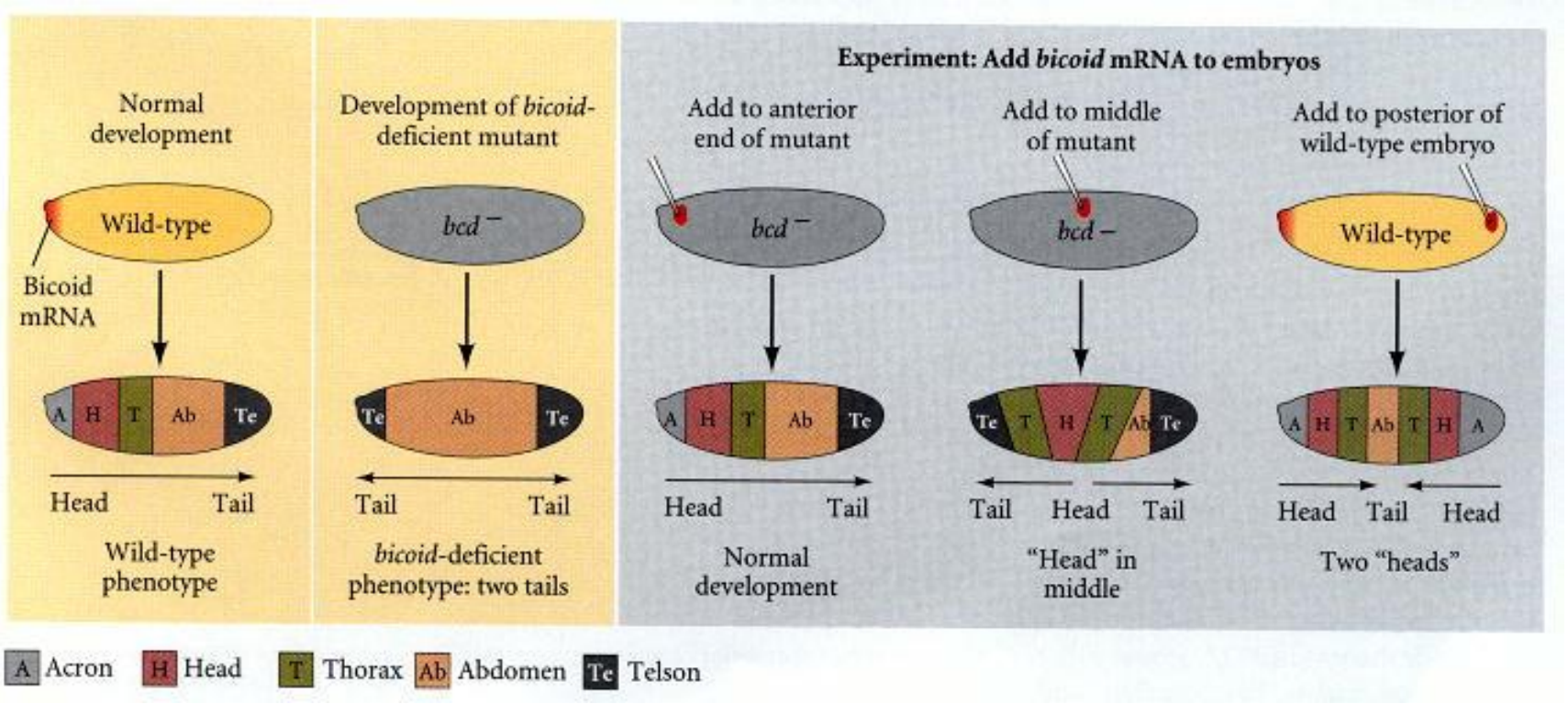


selvatico

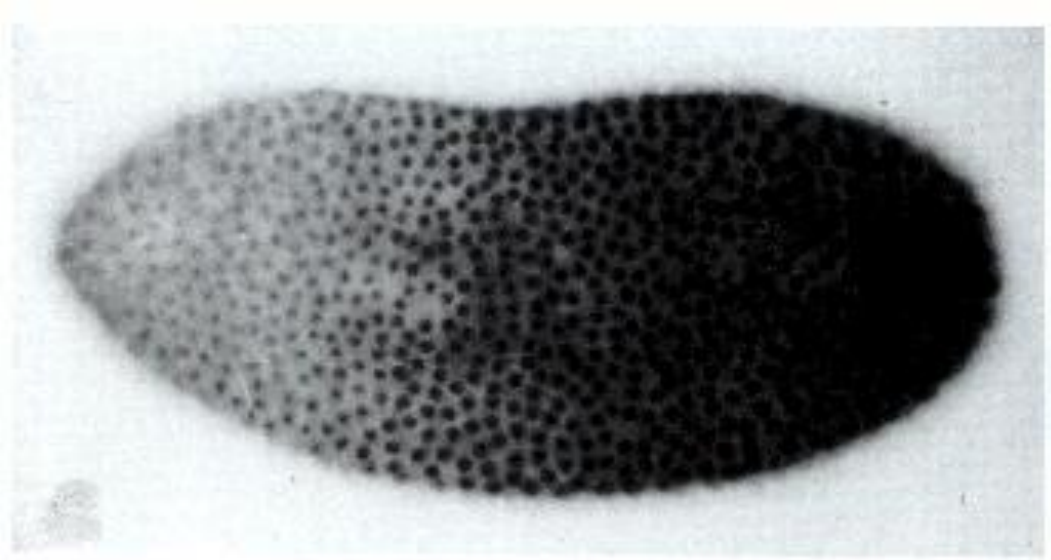


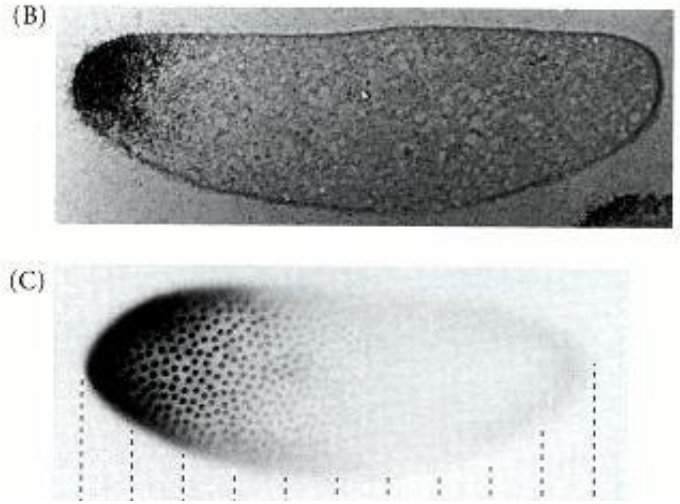
mutante

Bicoid codifica il morfogeno responsabile delle strutture cefaliche



Espressione della proteina Caudal (blastoderma sinciziale)

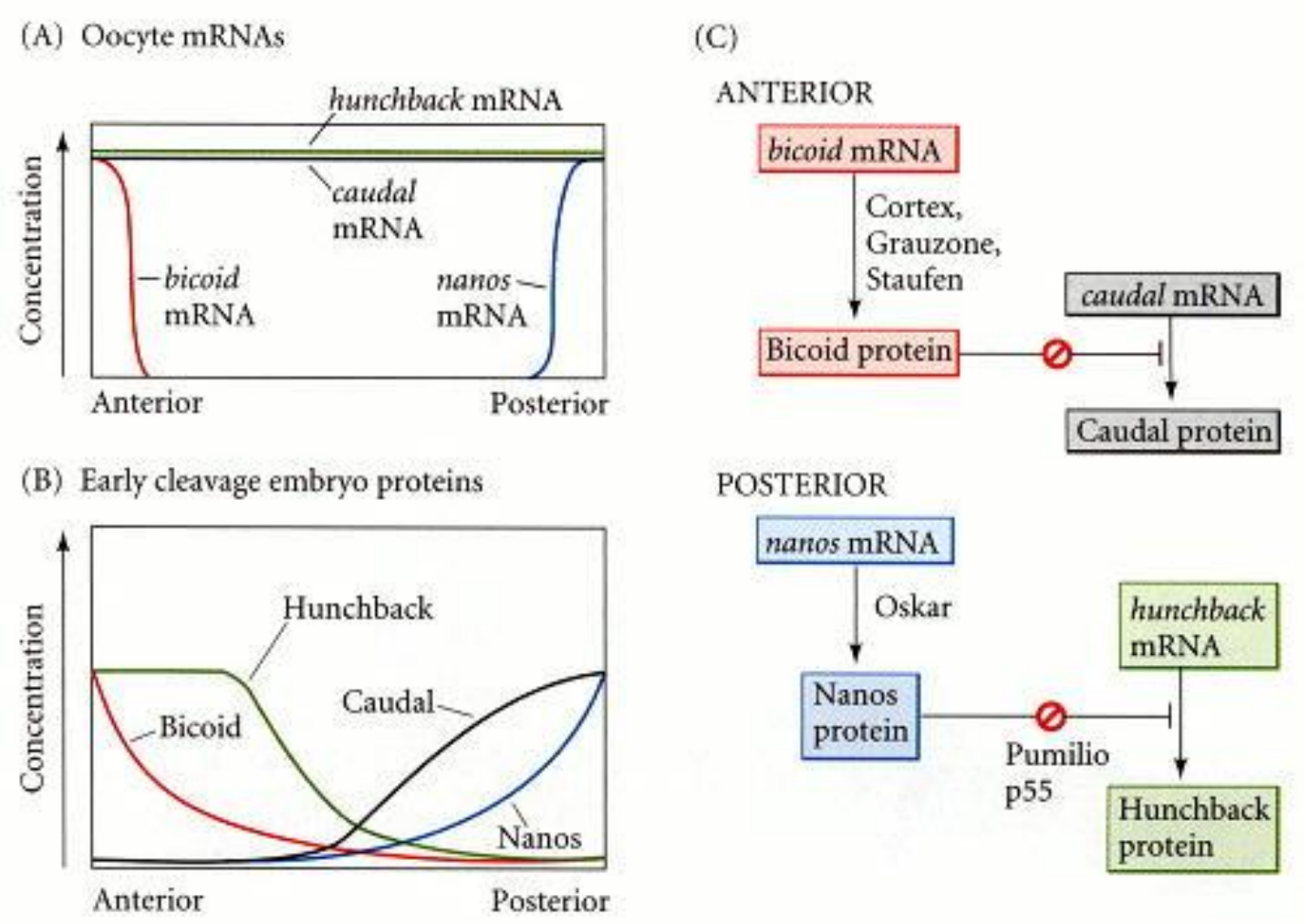




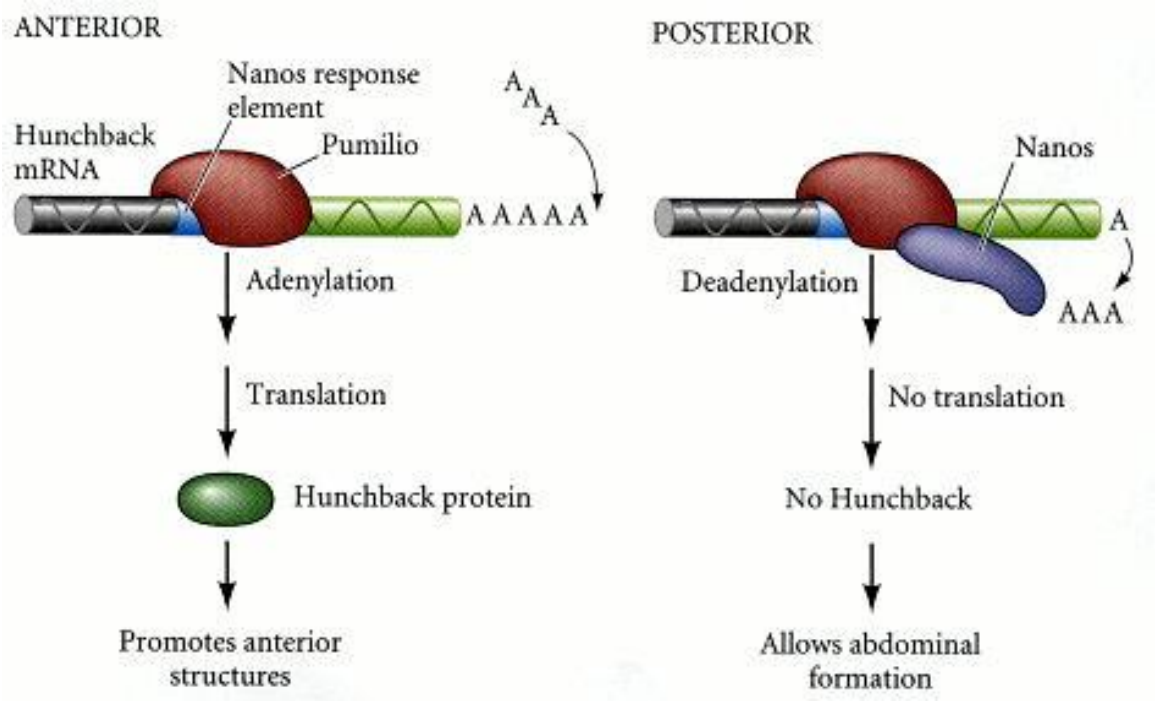
Caudal

Bicoid

Meccanismo molecolare dei geni ad effetto materno (asse ant/post)

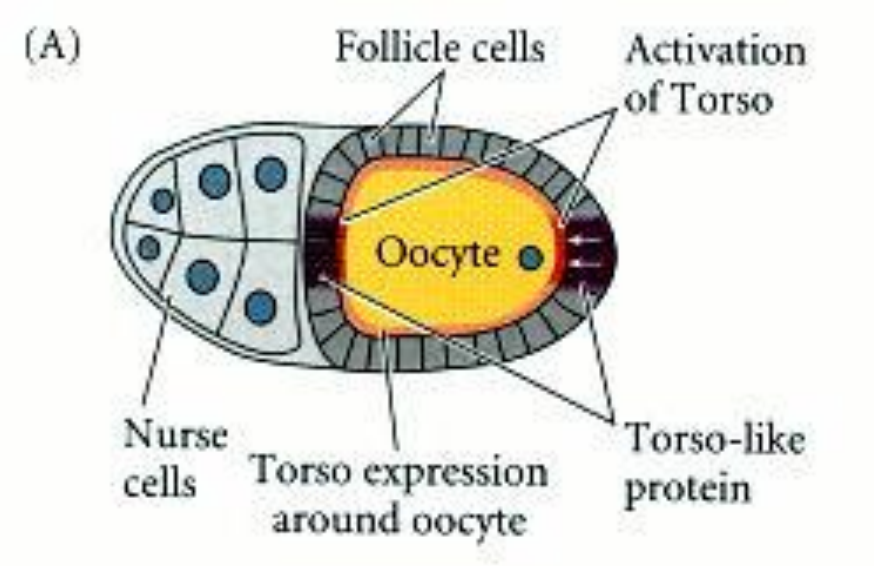


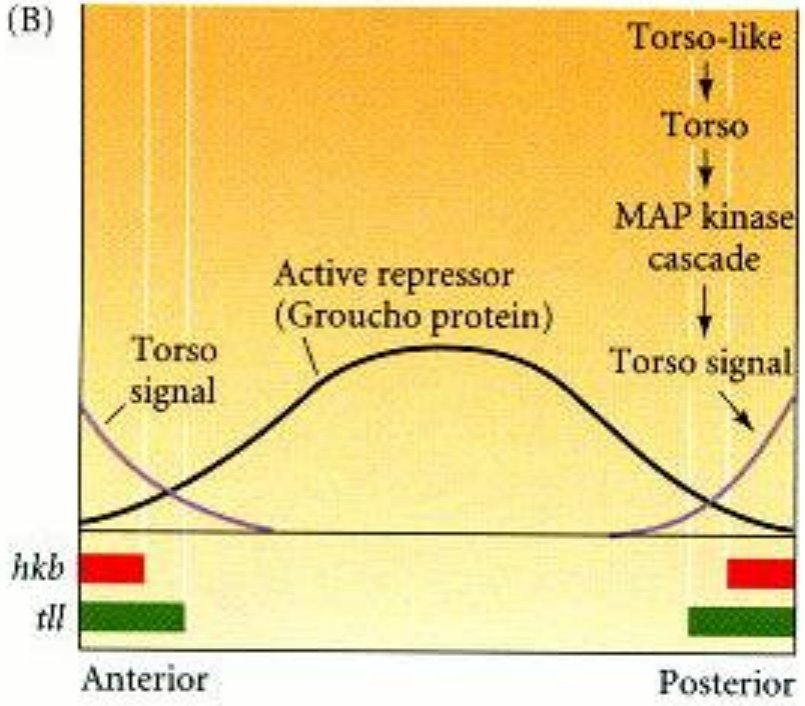
Nanos blocca l'espressione di Hunchback



Nella zona posteriore Nanos induce deadenilazione Pumilio-dipendente di Hunchback

Torso nella formazione delle estremità non segmentate





Torso-like segnala alle due estremità

L’oocito della Drosophila è polarizzato

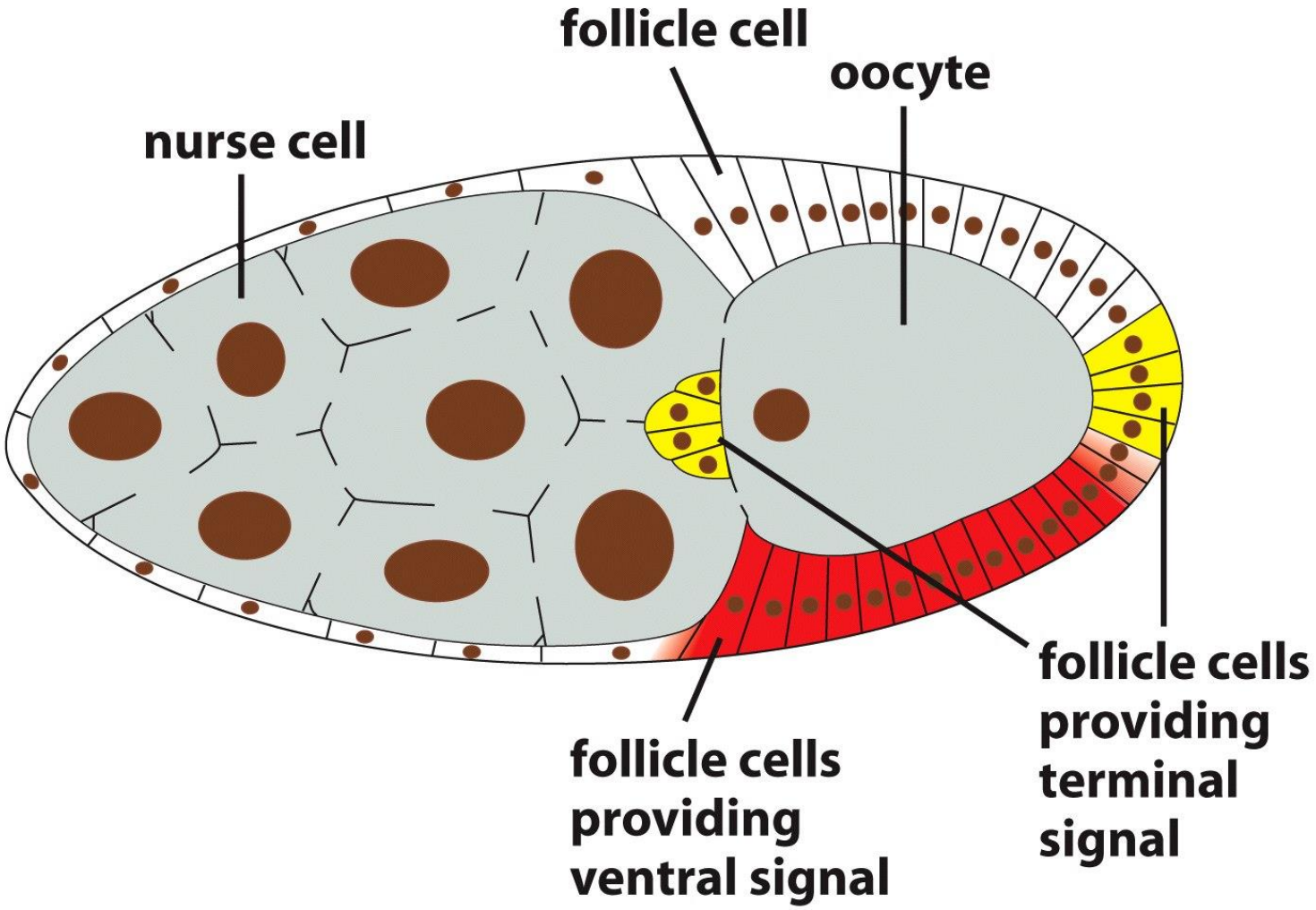
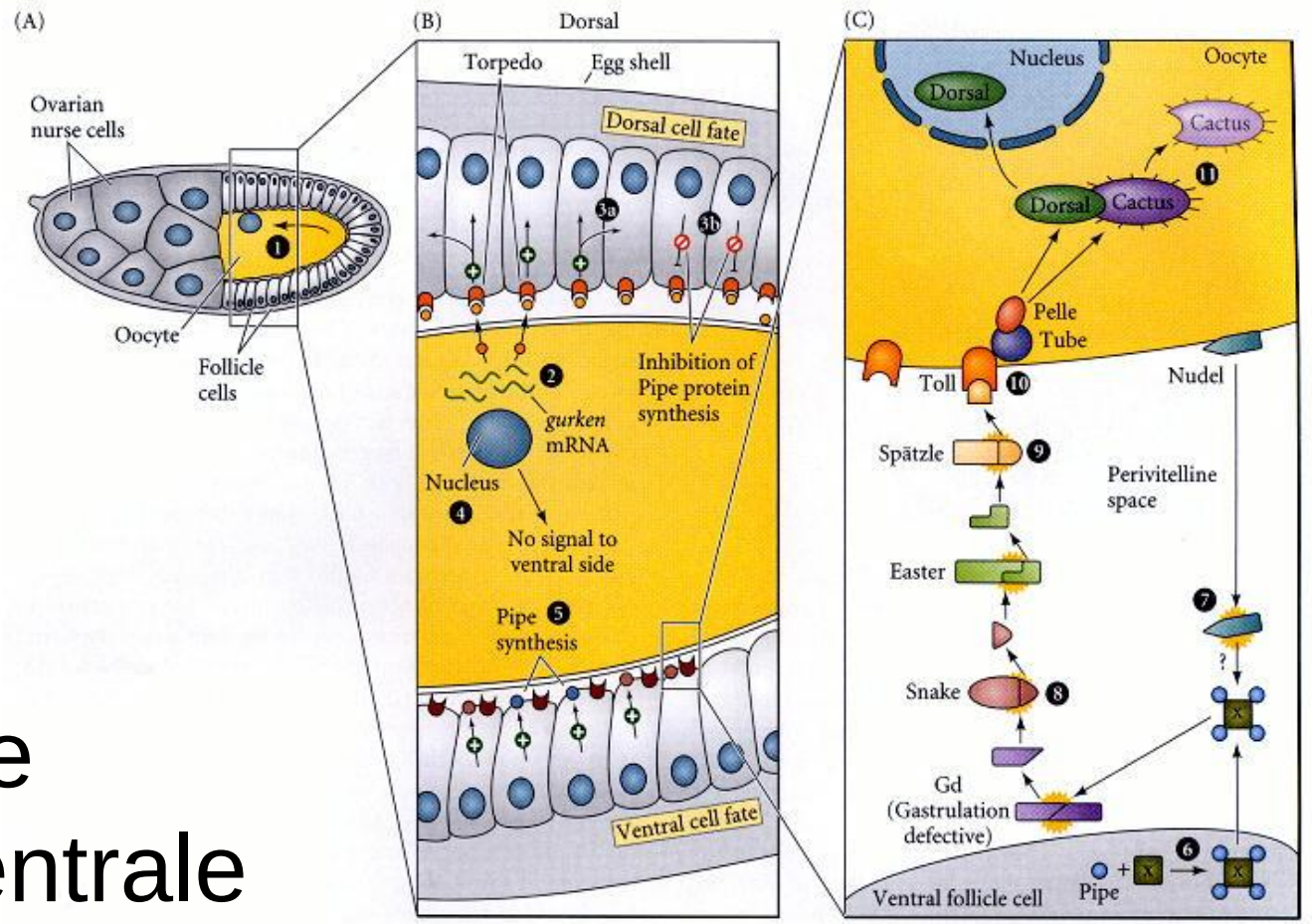


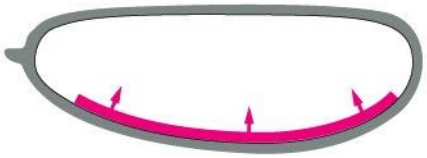
Figure 22-31 *Molecular Biology of the Cell* (© Garland Science 2008)

Asse dorso-ventrale



1. Oocyte nucleus travels to anterior dorsal side of oocyte. It synthesizes *gurken* mRNA which remains between the nucleus and the follicle cells.
2. *gurken* messages are translated. The Gurken protein is received by Torpedo proteins during mid-oogenesis.
3a. Torpedo signal causes follicle cells to differentiate to a dorsal morphology.
3b. Synthesis of Pipe protein is inhibited in dorsal follicle cells.
4. Gurken protein does not diffuse to ventral side.
5. Ventral follicle cells synthesize Pipe proteins.
6. In ventral follicle cells, Pipe completes the modification of unknown factor (x).
7. Nudel and factor (x) interact to split the Gastrulation-deficient (Gd) protein.
8. The activated Gd protein splits the Snake protein, and the activated Snake protein cleaves the Easter protein.
9. The activated Easter protein splits Spätzle; activated Spätzle binds to Toll receptor protein.
10. Toll activation activates Tube and Pelle, which phosphorylate the Cactus protein. Cactus is degraded, releasing it from Dorsal.
11. Dorsal protein enters the nucleus and ventralizes the cell.

DORSOVENTRAL SYSTEM



) **transmembrane receptors (Toll)**

Morfogeni per stabilire l'asse dorso-ventrale

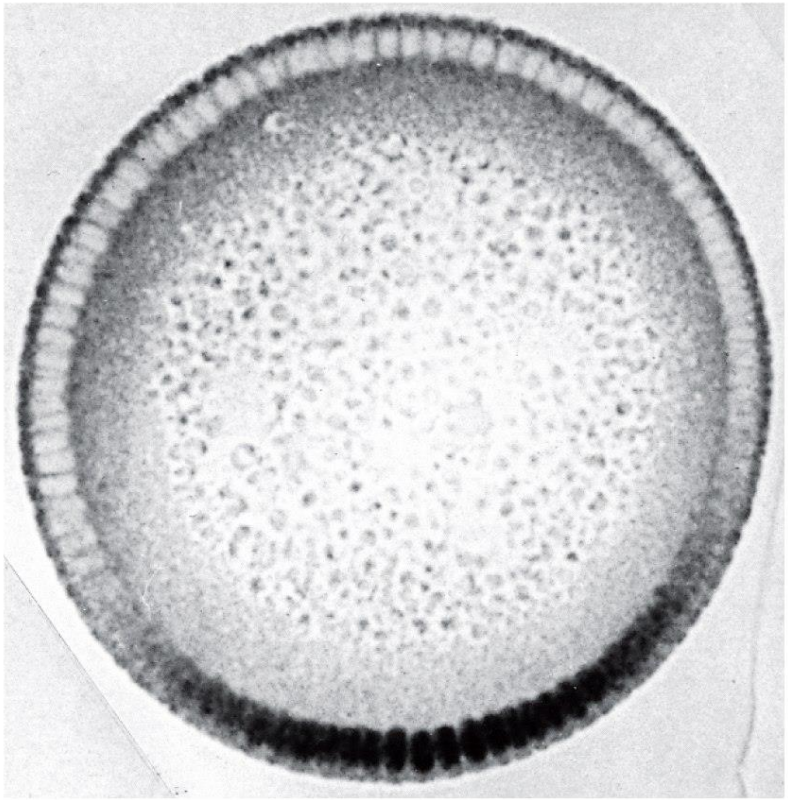


Figure 22-33 *Molecular Biology of the Cell* (© Garland Science 2008)

Meccanismo dell'induzione per stabilire l'asse dorso-ventrale

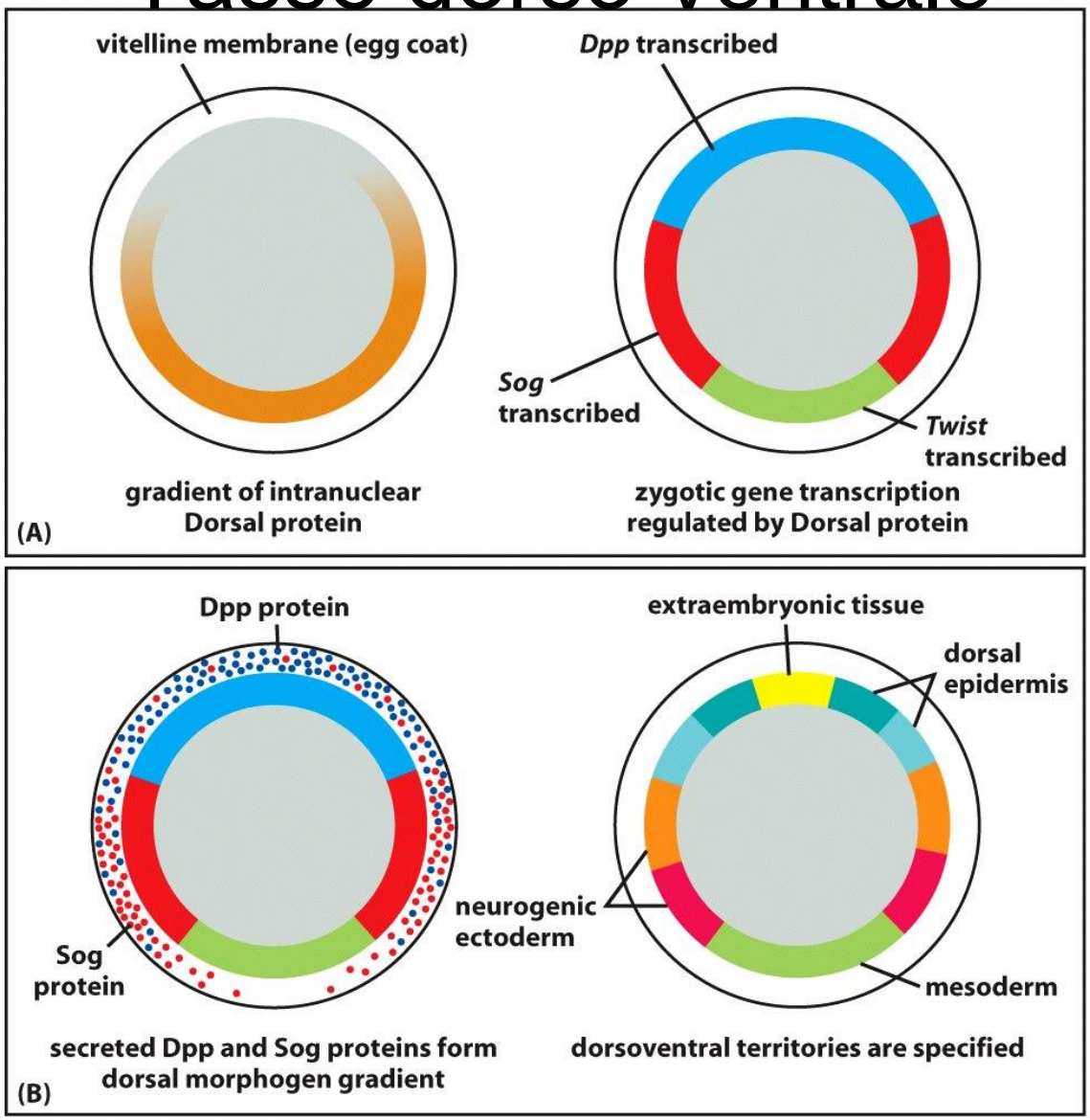


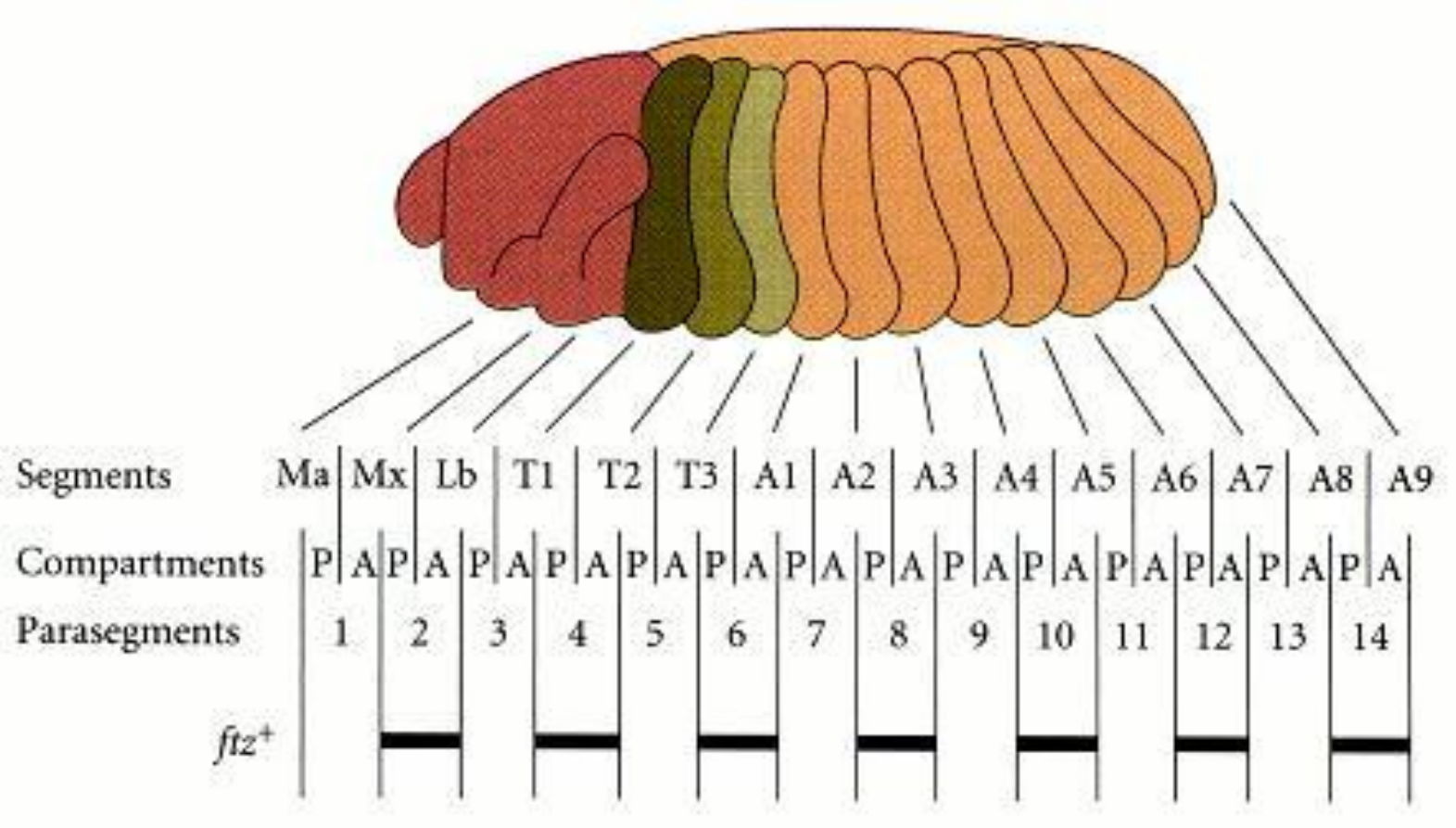
Figure 22-34 *Molecular Biology of the Cell* (© Garland Science 2008)

La gastrulazione nella Drosophila

Colorazione per Twist

Figure 22-35 *Molecular Biology of the Cell* (© Garland Science 2008)

Segmentazione della larva



Compartimentalizzazione del corpo

Graduale nel tempo:

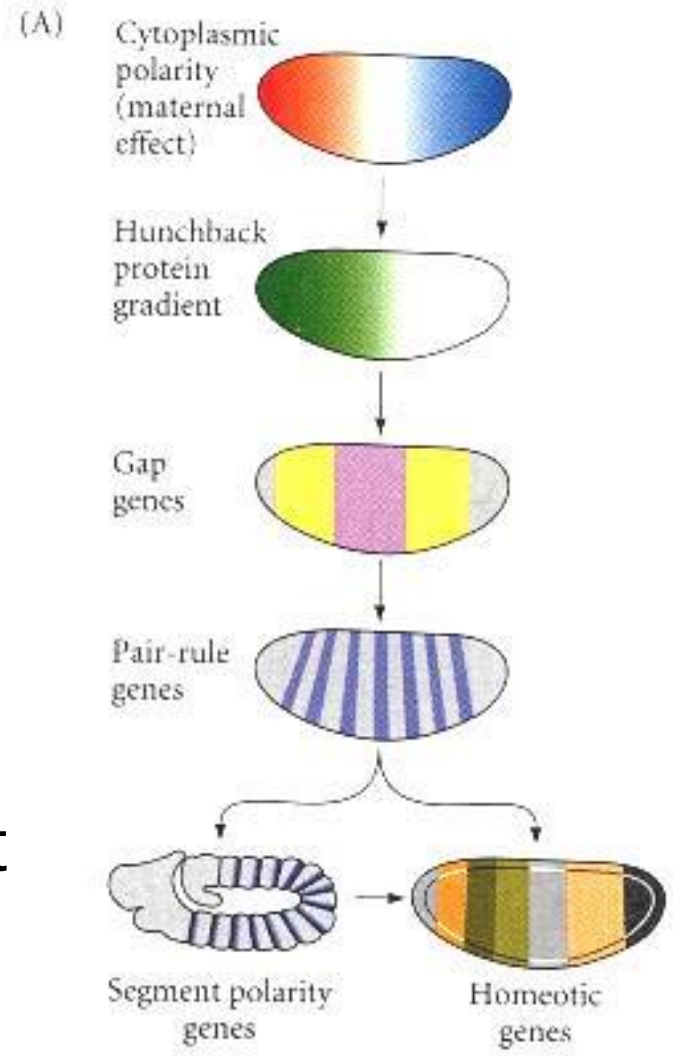
- Geni della polarità o degli assi corporei
  ant-post e dorso-ventr
- Geni della segmentazione
  geni gap (6)
  geni di coppia (pair-rule) (8)
  geni di compartimentazione del segmento
  (segment polarity) (10)
- Geni dell'identità del segmento corporeo
  geni omeotici

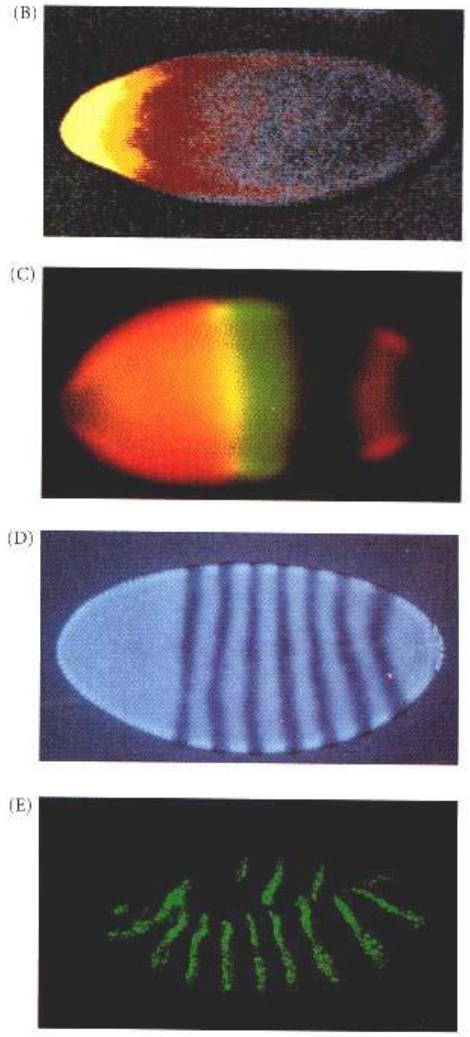
Segmentazione lungo asse ant-post

Gap

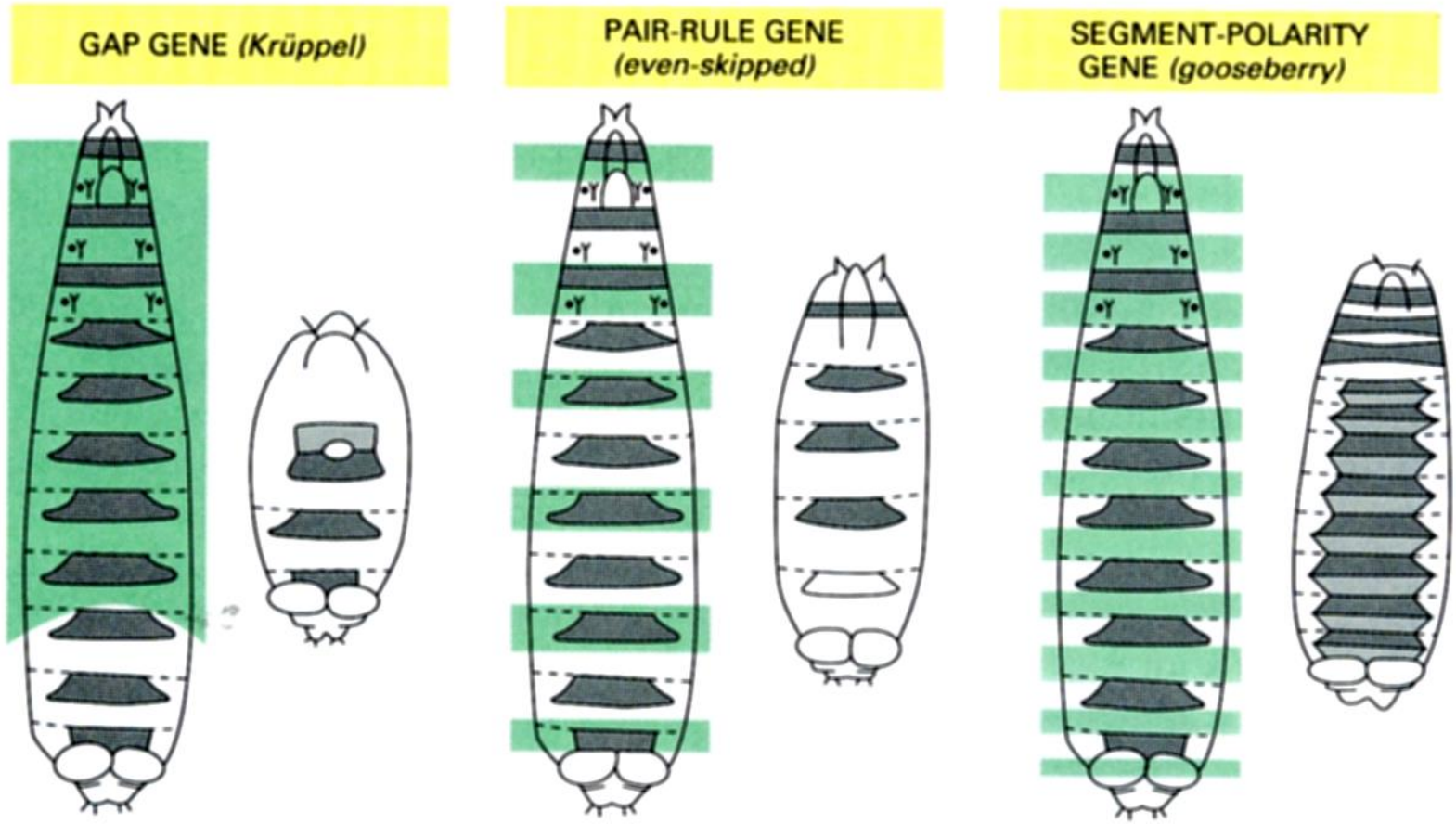
Pair-rule

Segment polarity

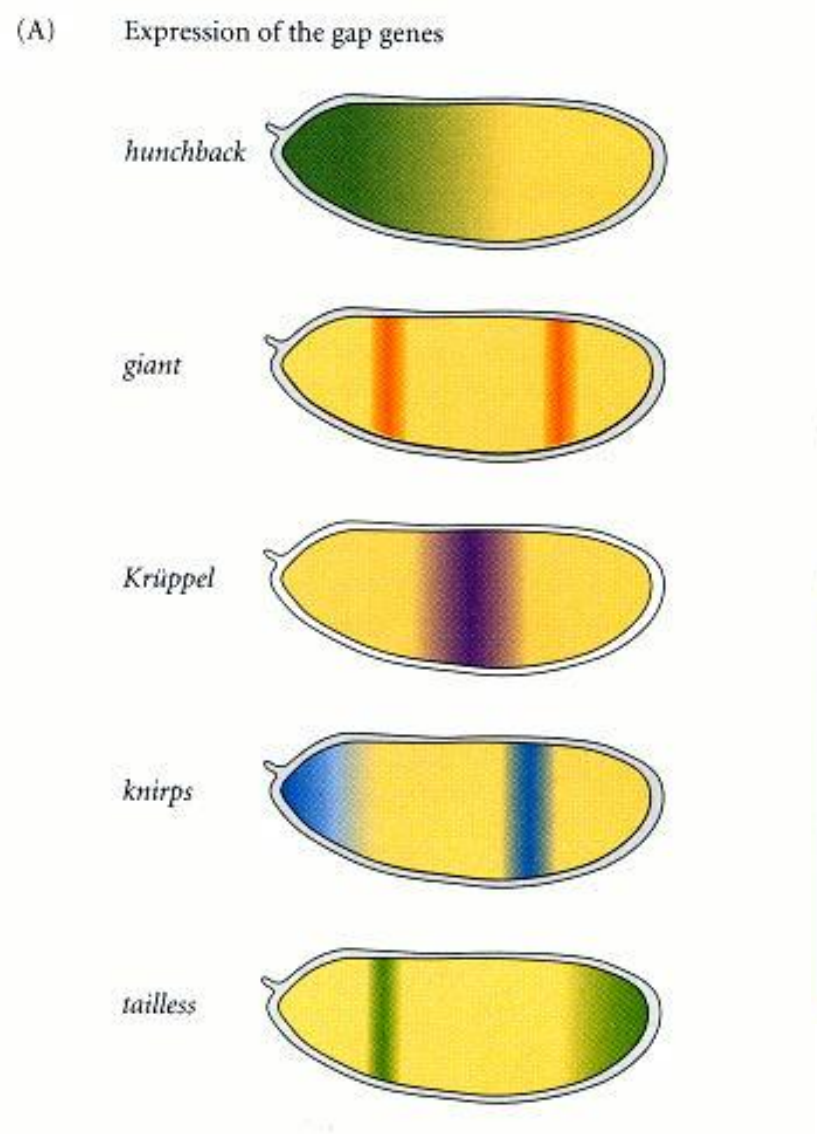


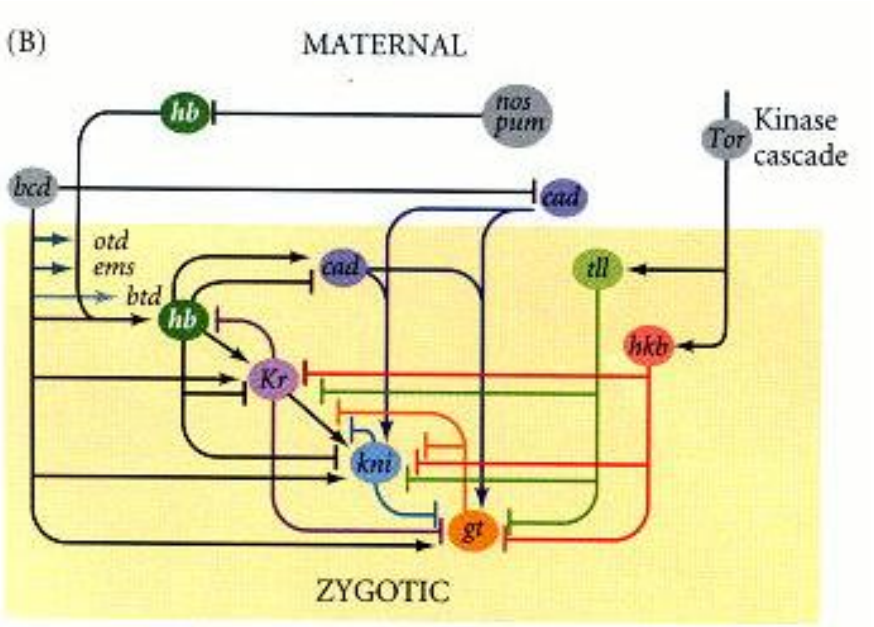


Compartimentalizzazione del corpo



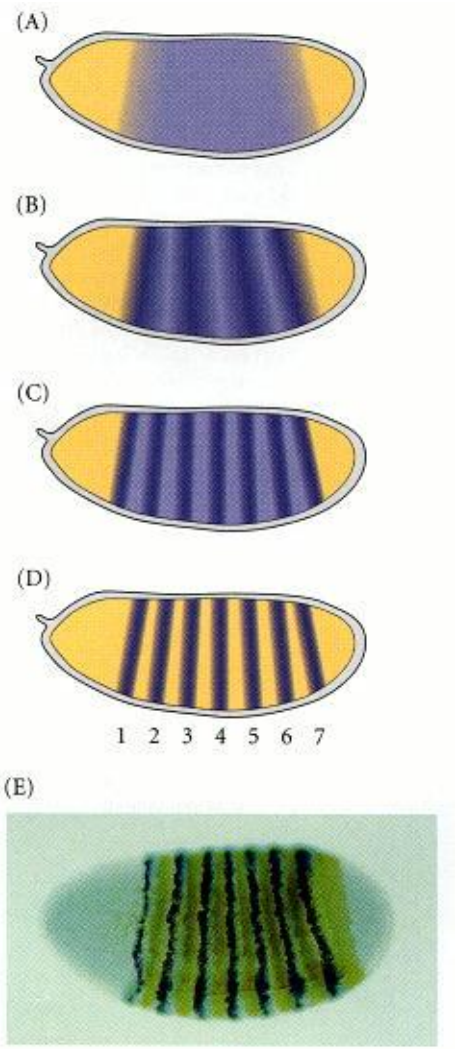
Gradienti di proteine materne controllano l'espressione dei geni gap





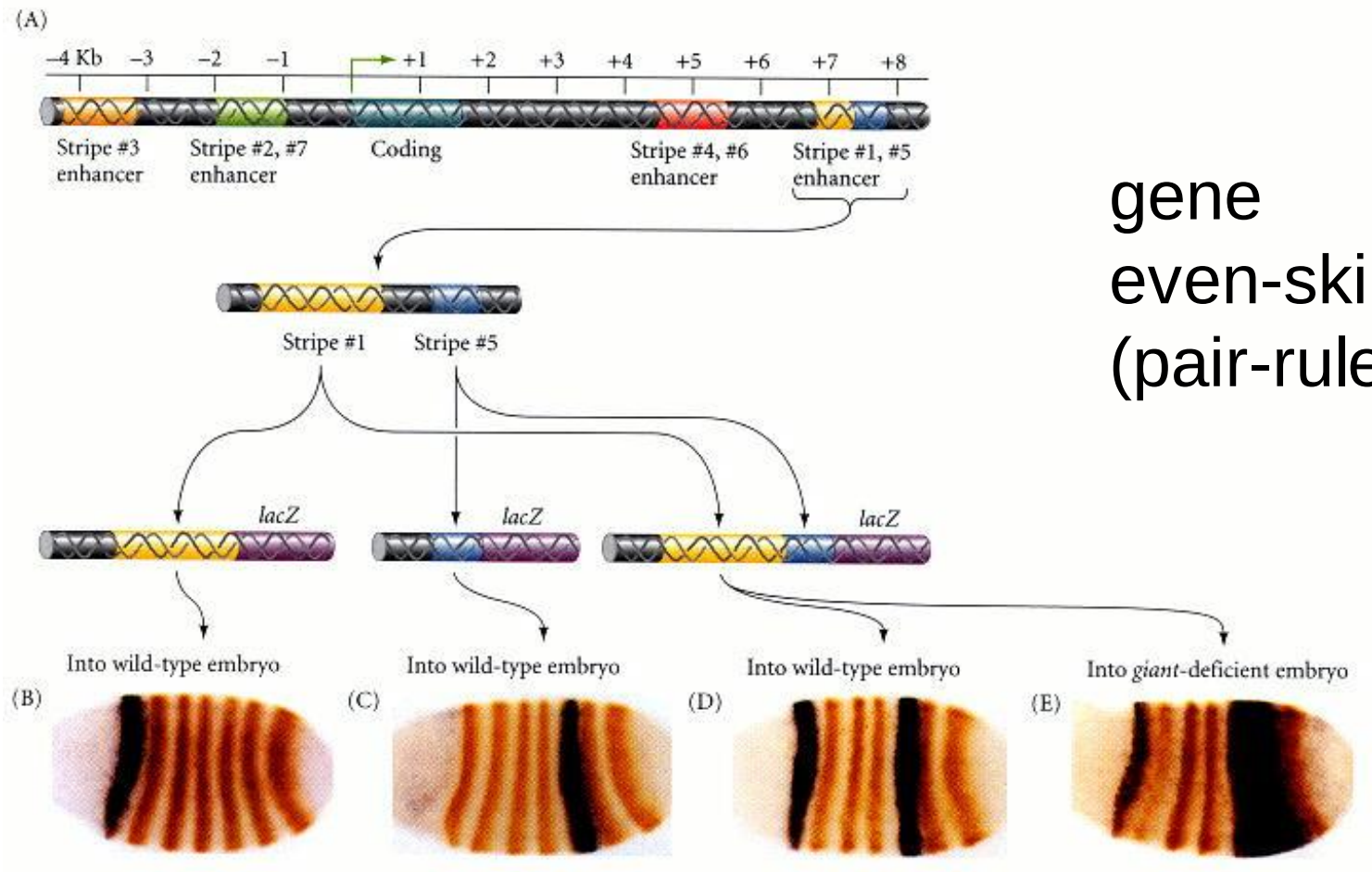
Espressione di fushi-tarazu

(Pair-rule)



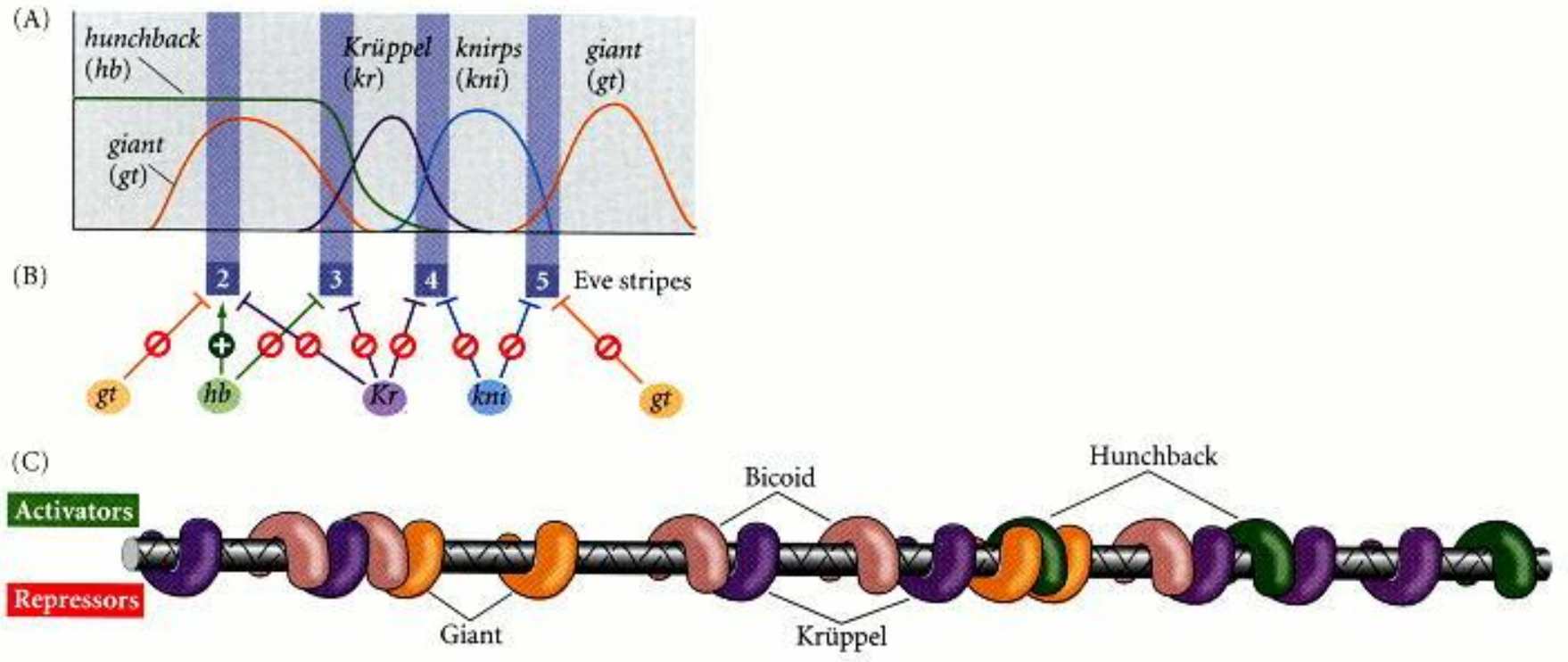
even-skipped (blu)
Fushi-tarazu (bruno)

Organizzazione modulare delle sequenze regolatorie (Promotori/enhancers) di un gene della segmentazione (modello combinatoriale)

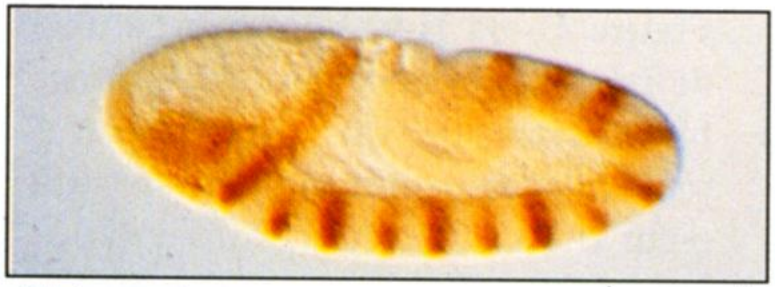


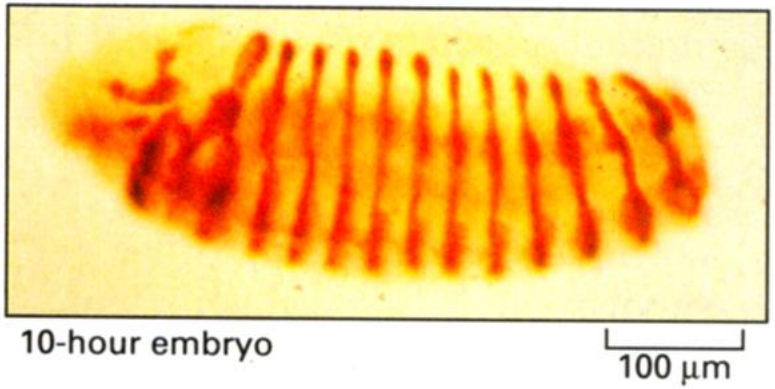
gene
even-skipped
(pair-rule)

Meccanismo di attivazione di even-skipped in segmenti diversi



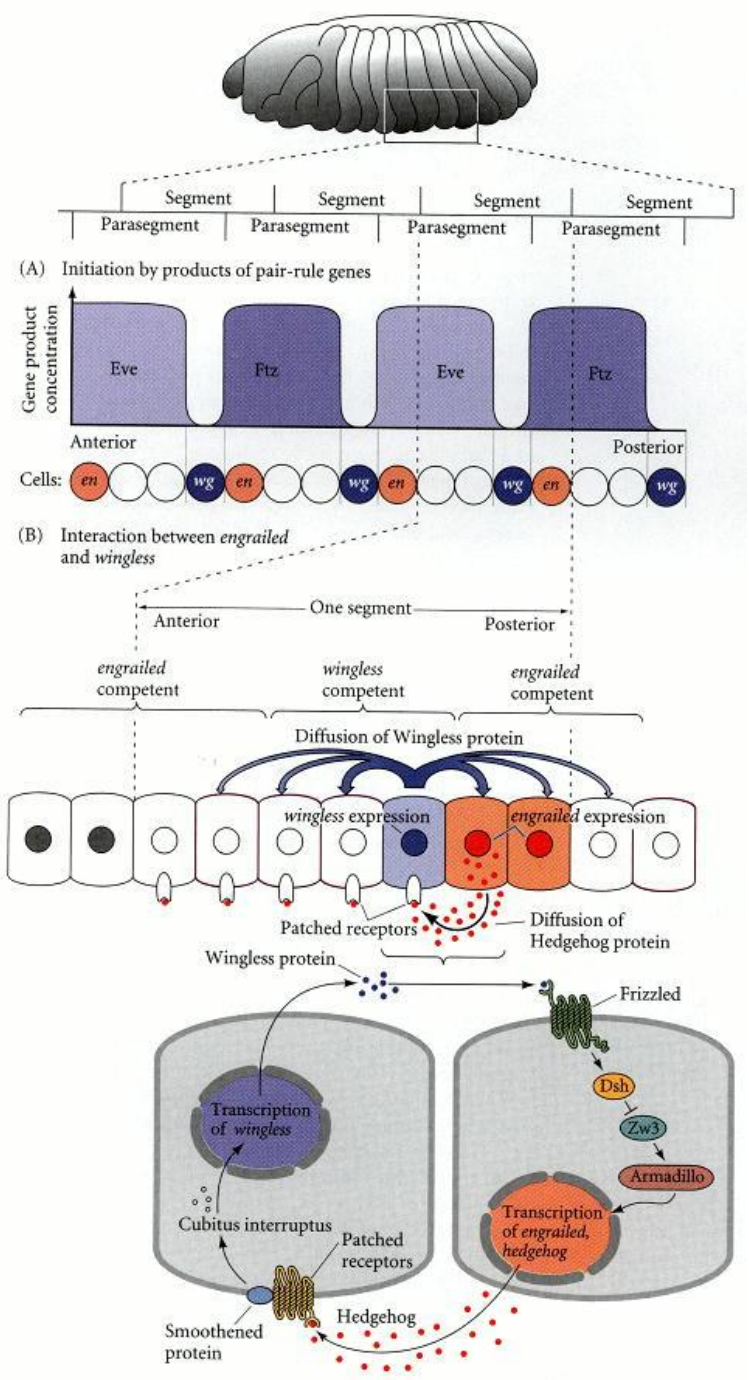
Sviluppo della Drosophila:espressione di un gene della classe segment polarity



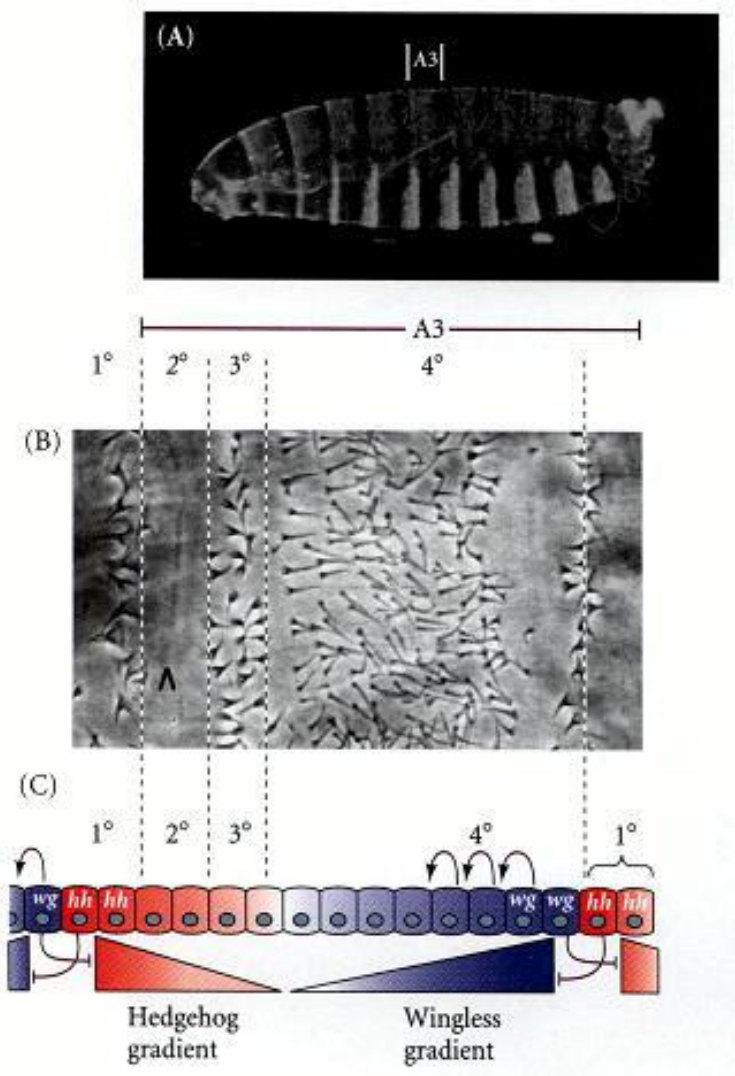


Proteine pair-rule controllano l'espressione dei geni segment-polarity

.....



….. tramite gradienti



- Danno segnali di posizione
- Indotti sequenzialmente secondo un piano gerarchico ben preciso
- Diversa concentrazione
- Cooperano tra di loro (sinergismo o inibizione)

Il piano corporeo dell'insetto è rovesciato rispetto a quello del vertebrato

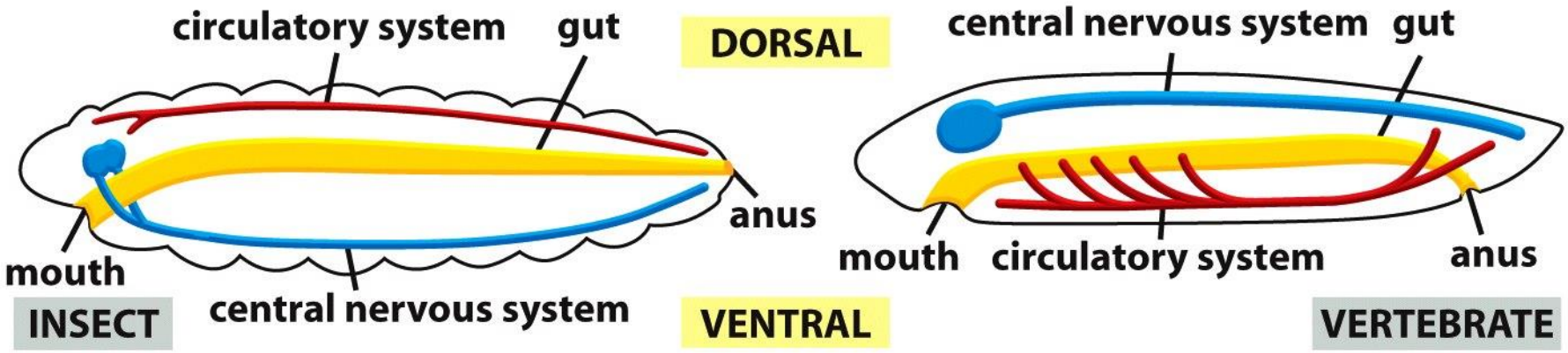


Figure 22-36 *Molecular Biology of the Cell* (© Garland Science 2008)

I dischi imaginali = aggregati di cellule mantenute nelle larve

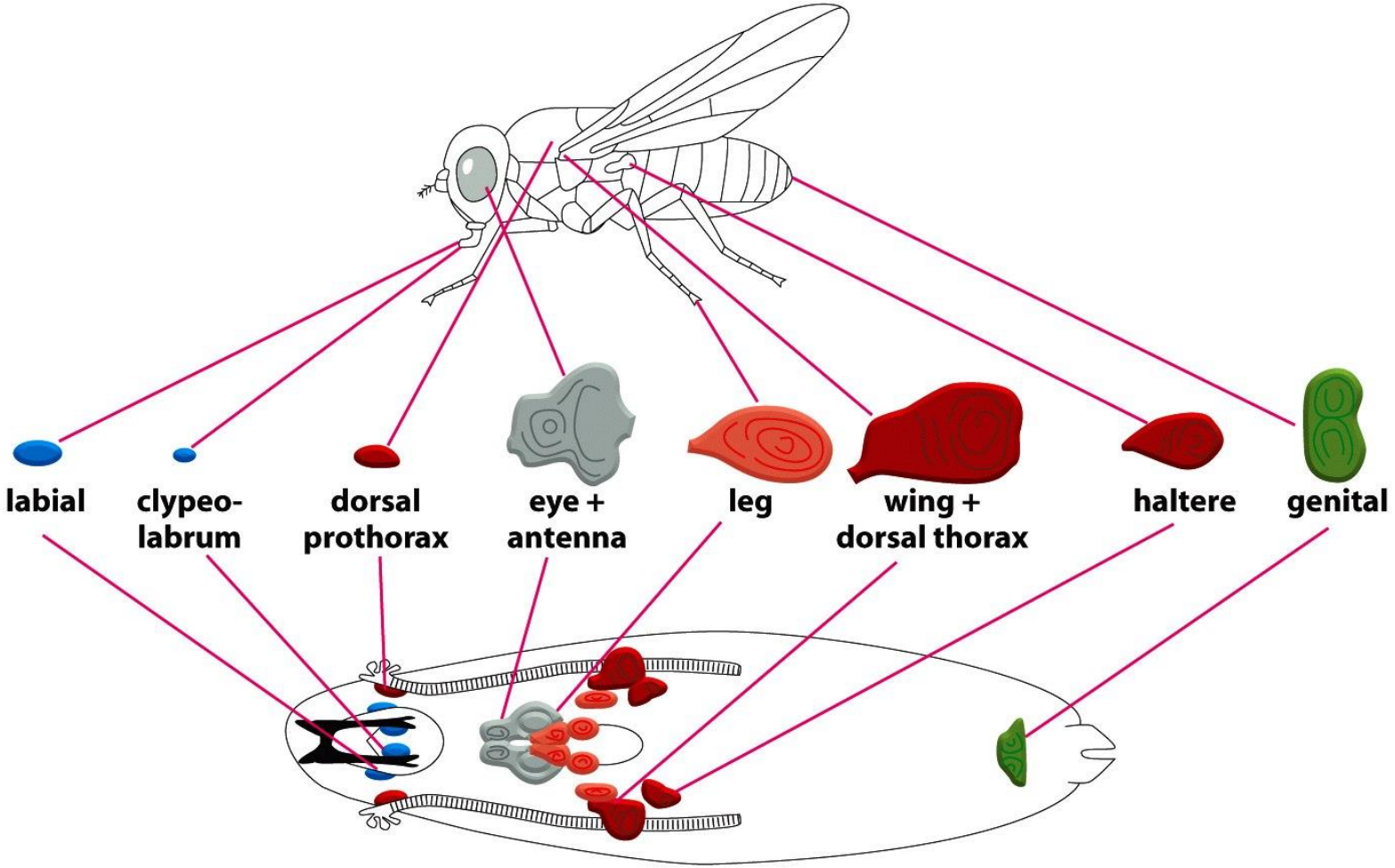


Figure 22-51 *Molecular Biology of the Cell* (© Garland Science 2008)

Compartimentalizzazione del corpo

Graduale nel tempo:

- Geni della polarità o degli assi corporei
  ant-post e dorso-ventr
- Geni della segmentazione
  geni gap
  geni di coppia (pair-rule)
  geni di compartimentazione del segmento
  (segment polarity)
- Geni dell'identità del segmento corporeo
  geni omeotici

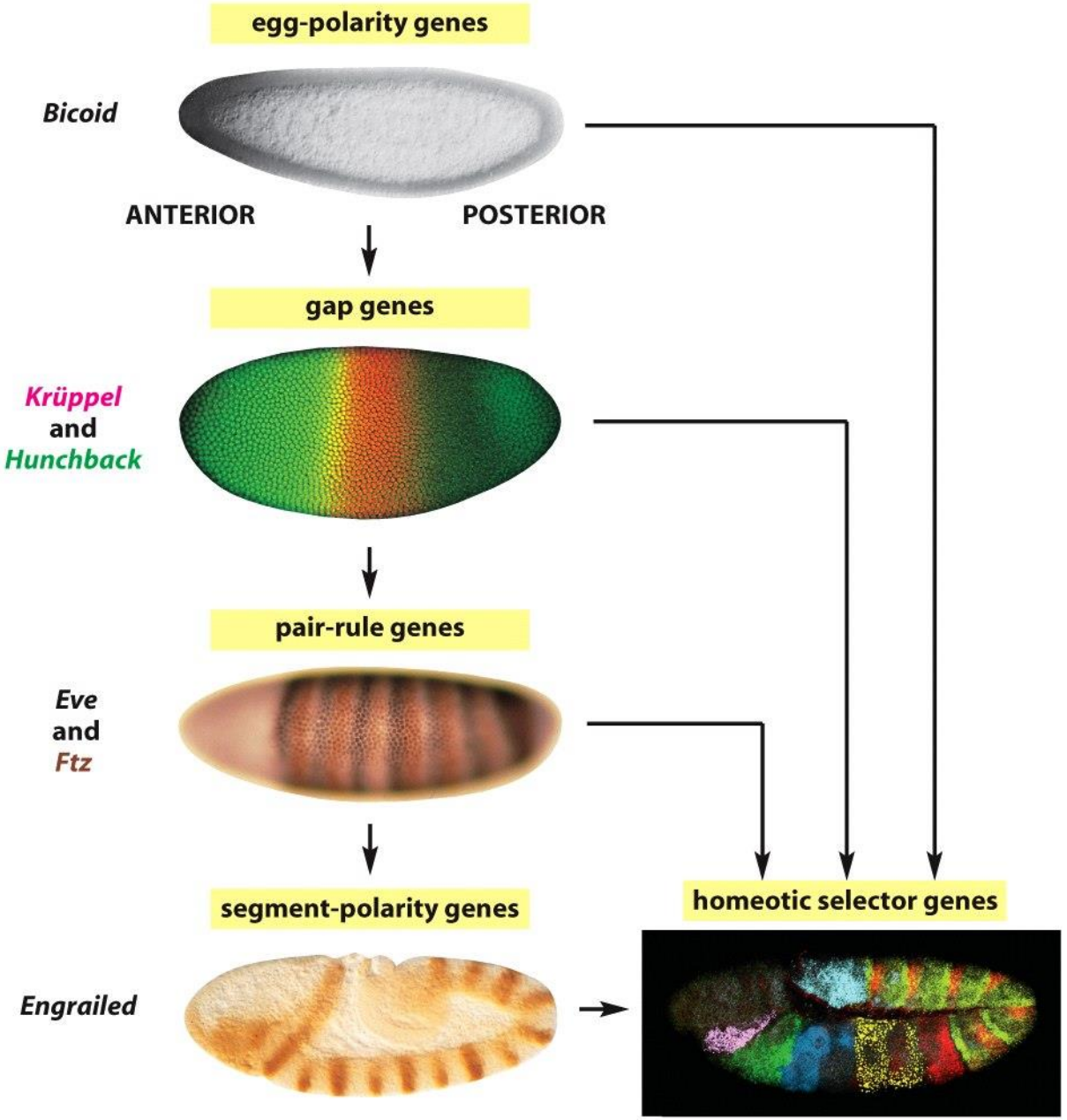
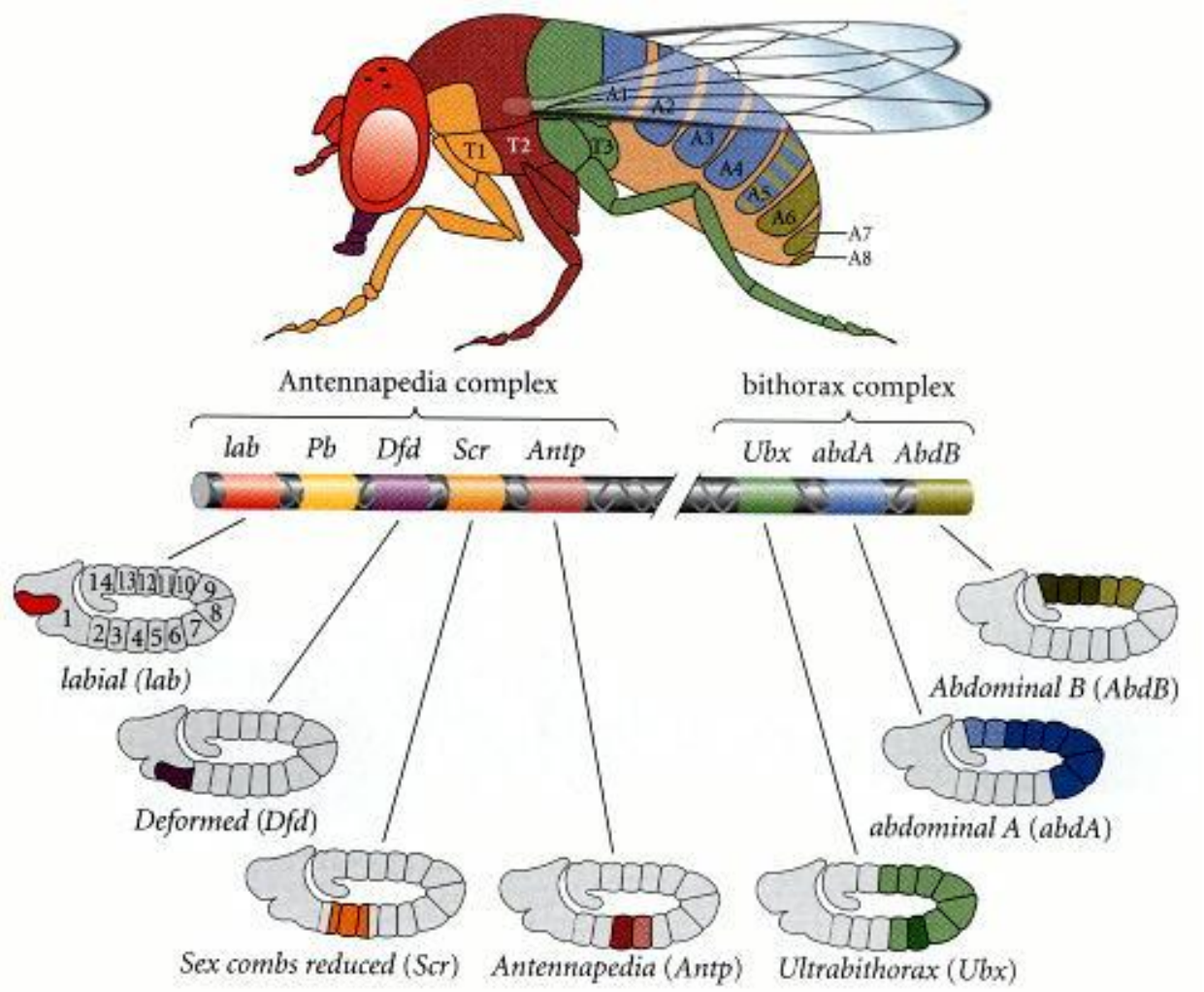
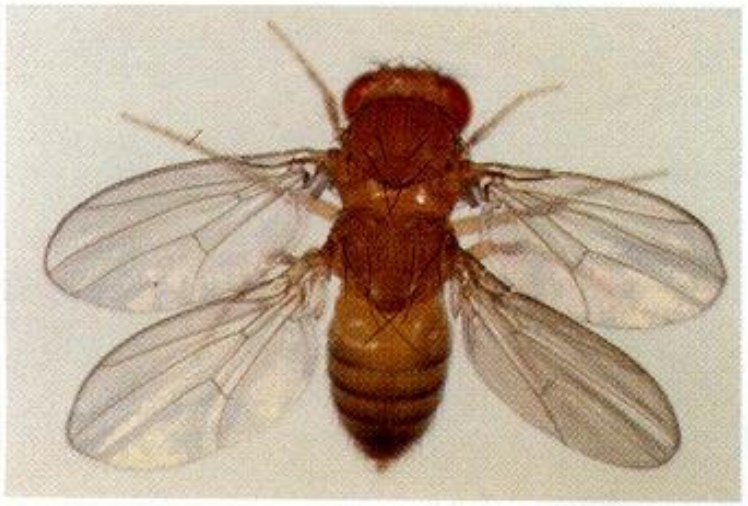


Figure 22-38 *Molecular Biology of the Cell* (© Garland Science 2008)

I geni selettori omeotici

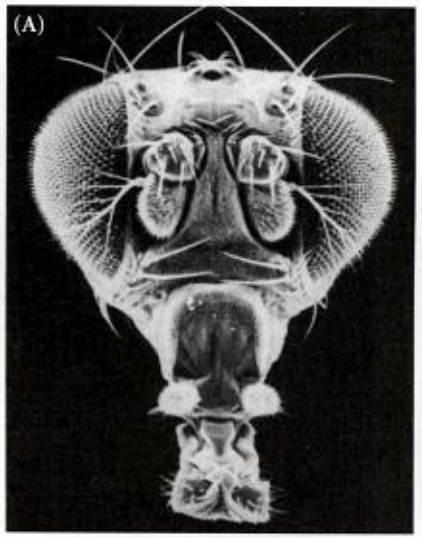


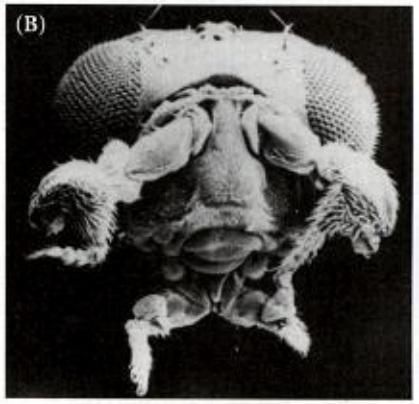
Mutazioni omeotiche



ultrabithorax

antennapedia





Bithorax mutation

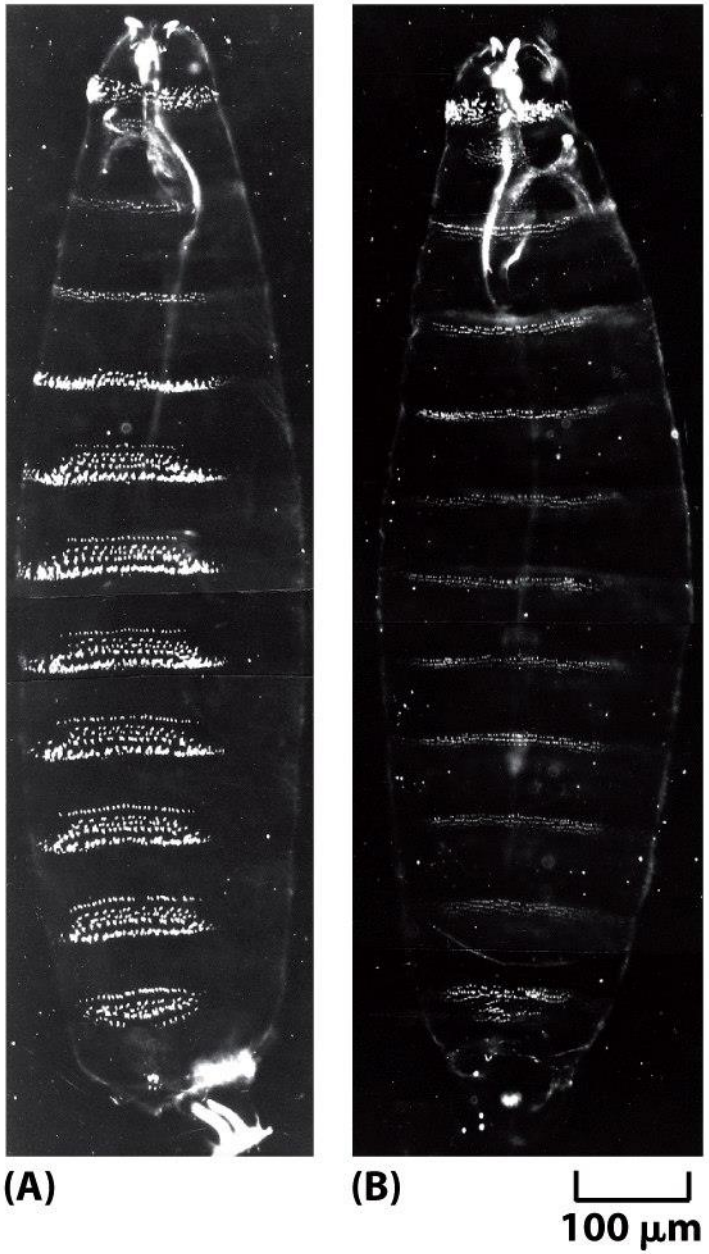


Figure 22-43 *Molecular Biology of the Cell* (© Garland Science 2008)

I geni omeotici sono allineati lungo il cromosoma nello stesso ordine in cui vengono espressi nel corpo

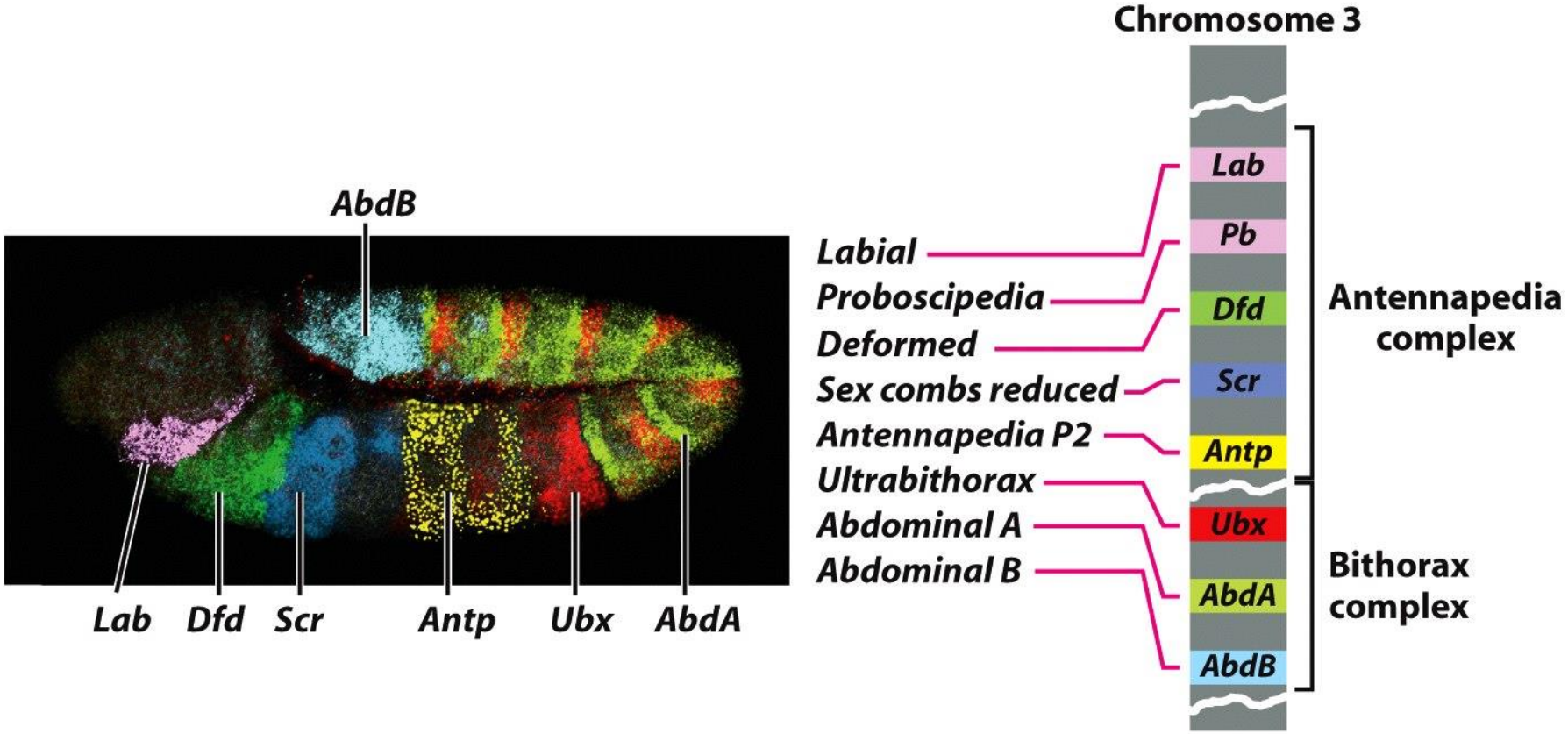
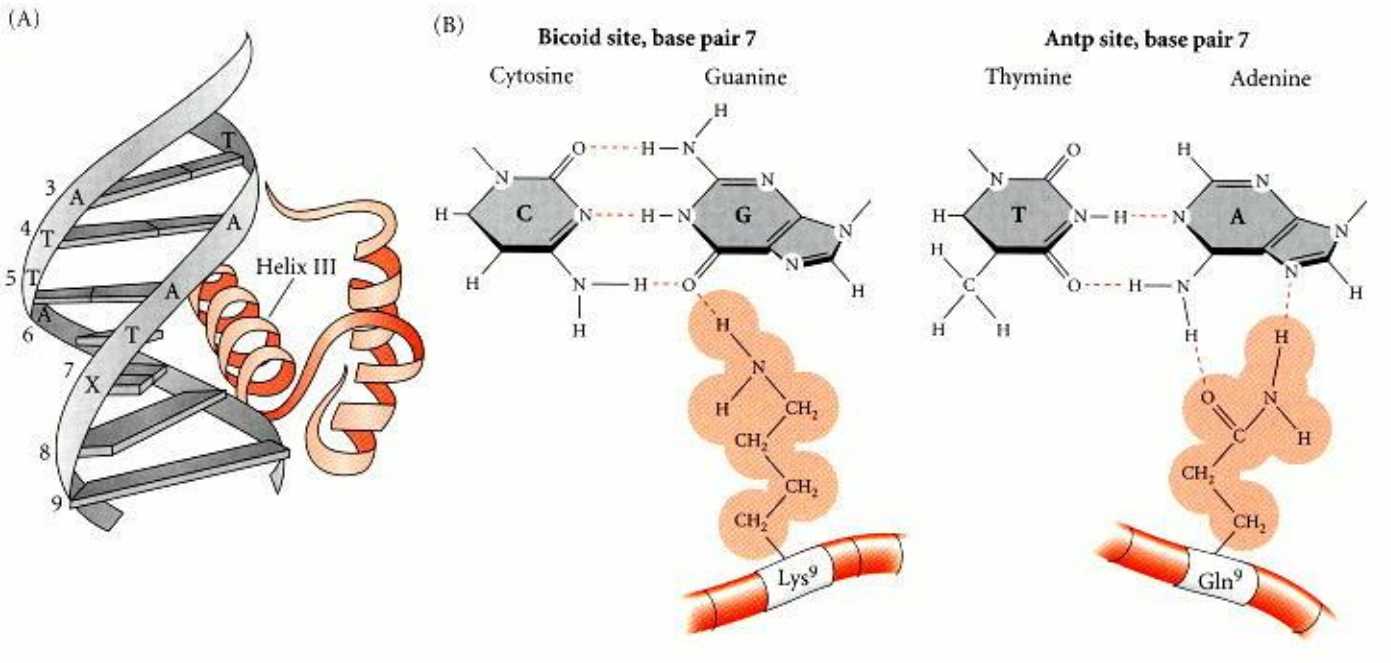


Figure 22-44 *Molecular Biology of the Cell* (© Garland Science 2008)

The homeodomain of the protein



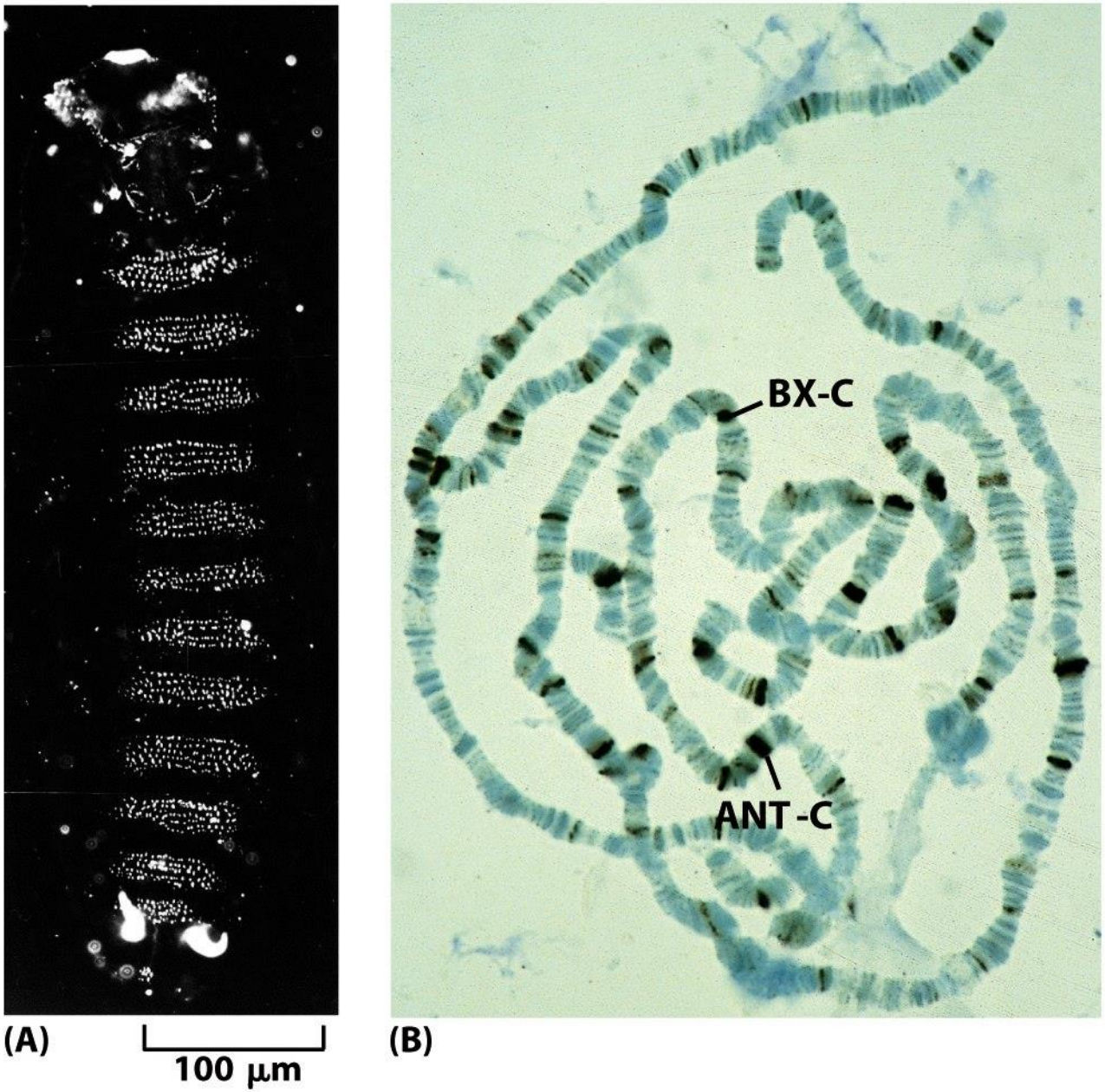
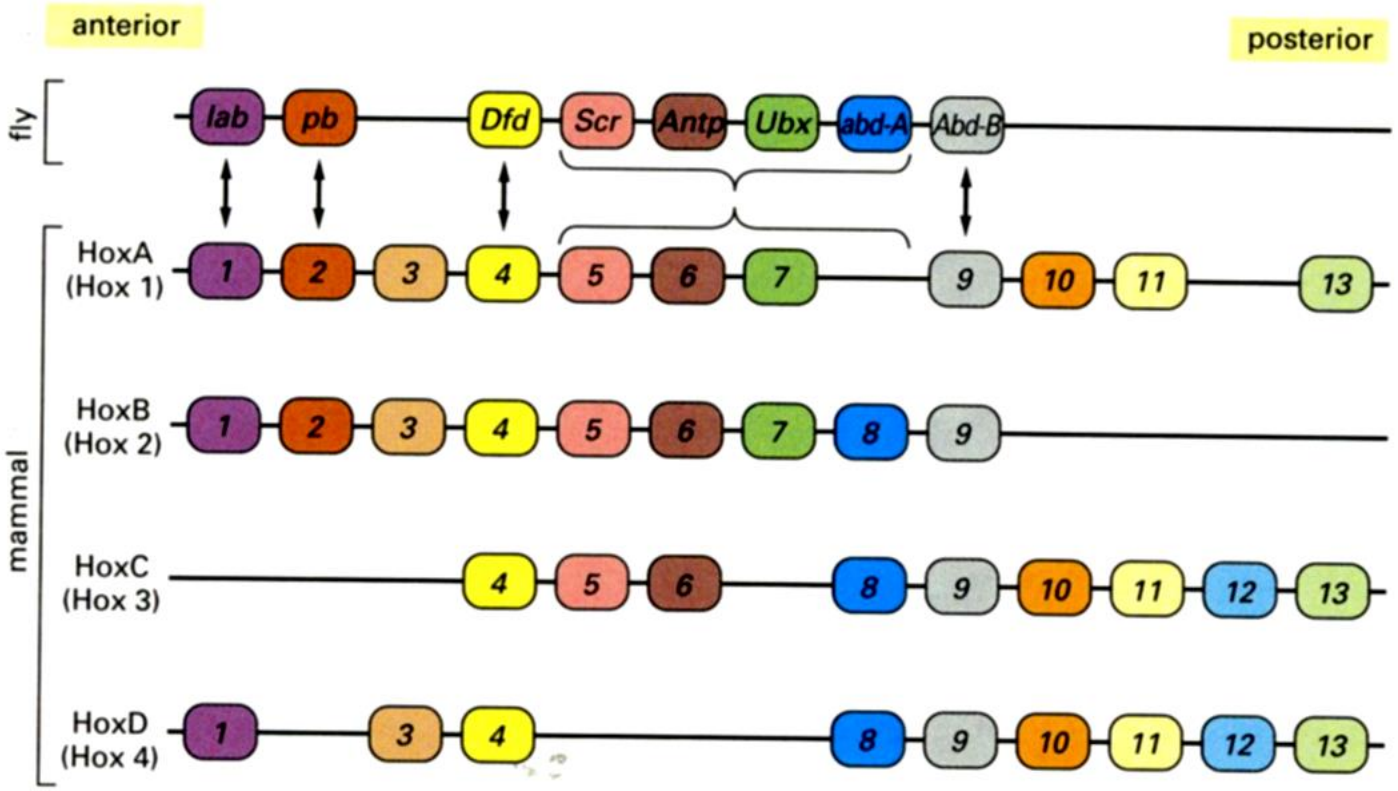


Figure 22-45 *Molecular Biology of the Cell* (© Garland Science 2008)

Geni omeotici nei mammiferi

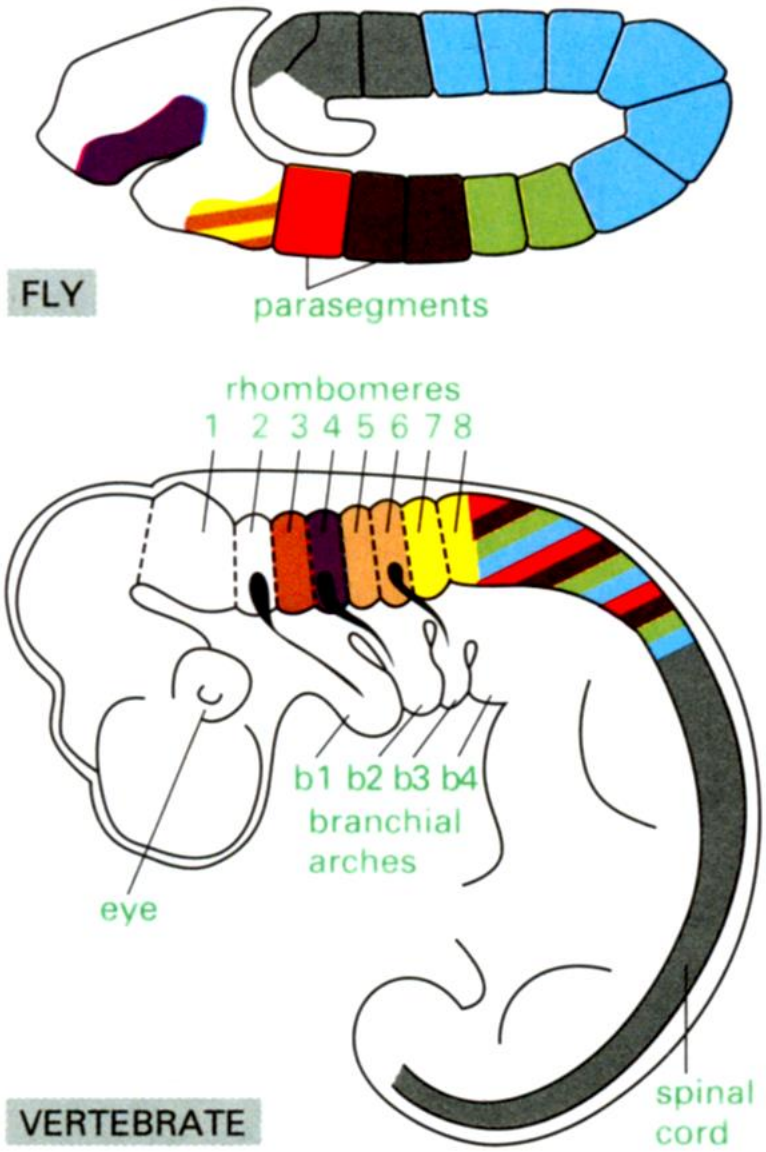


Geni omeotici

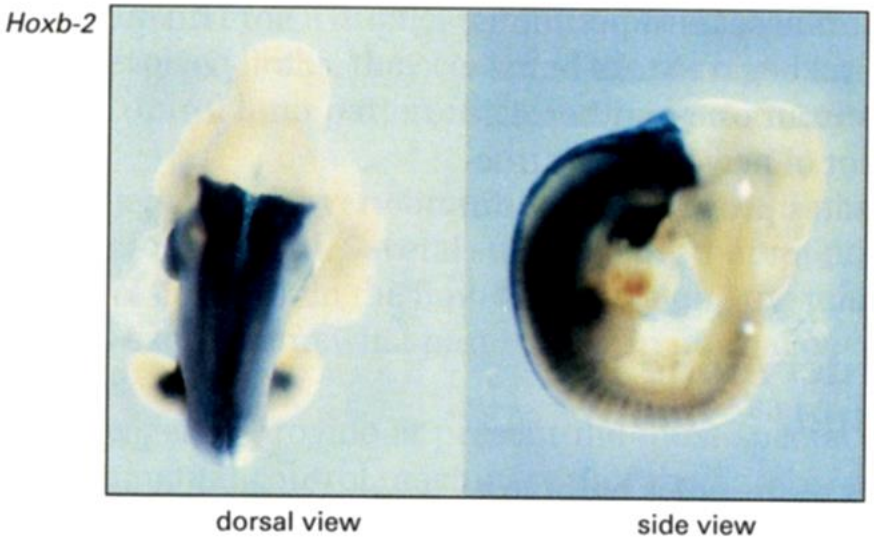
- Specificano l'organizzazione corporea
- Raggruppati in "clusters"

  (1 in Drosophila, 4 in vertebrati)
- Colinearità gene-posizione di espressione
- Fattori di trascrizione (homeobox)
- Sono geni regolatori ("master genes") che agiscono su più geni esecutori
- Specificano strutture simili, ma diverse nelle diverse specie (unghia/penna; dente/becco)

Corrispondenza tra le regioni del corpo di insetto e vertebrato definite dall’espressione di geni Hox

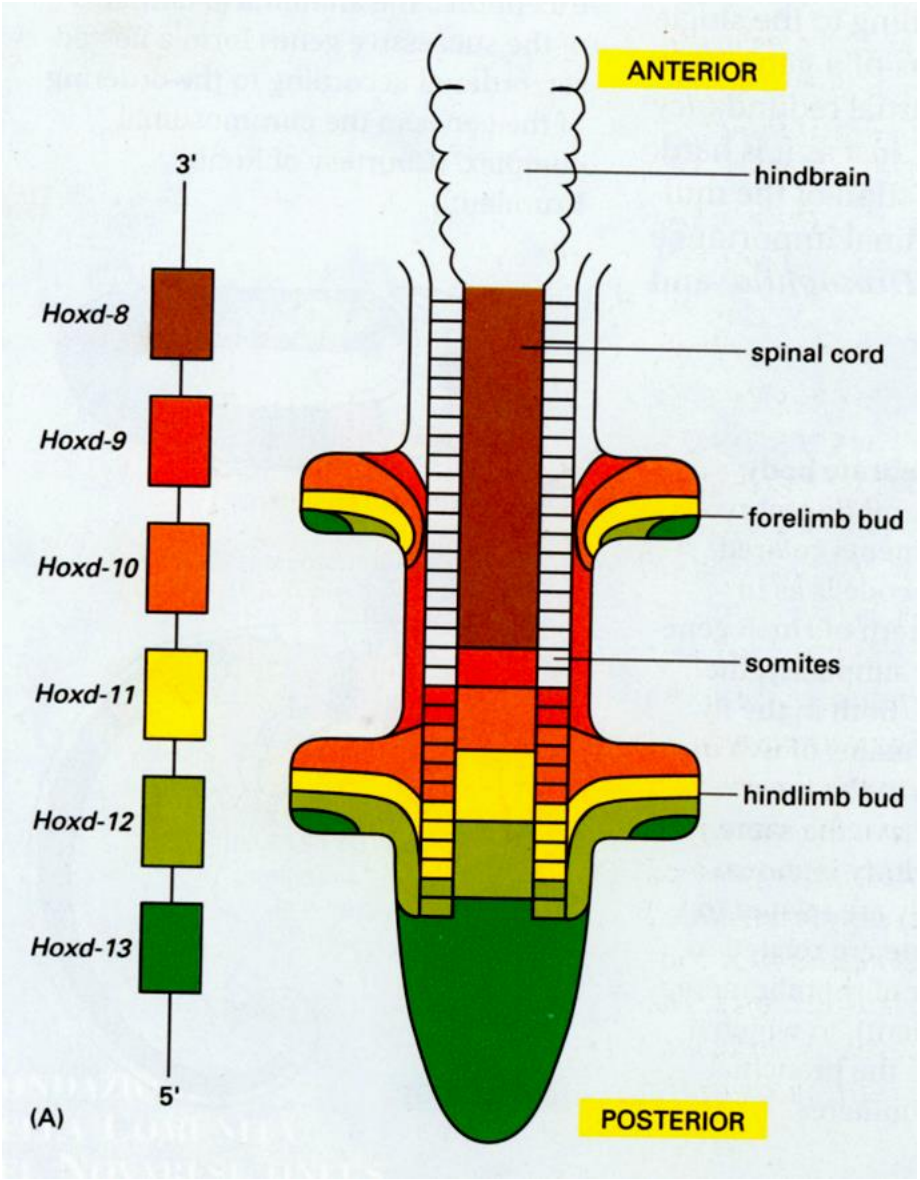


Espressione di geni omeotici nel topo

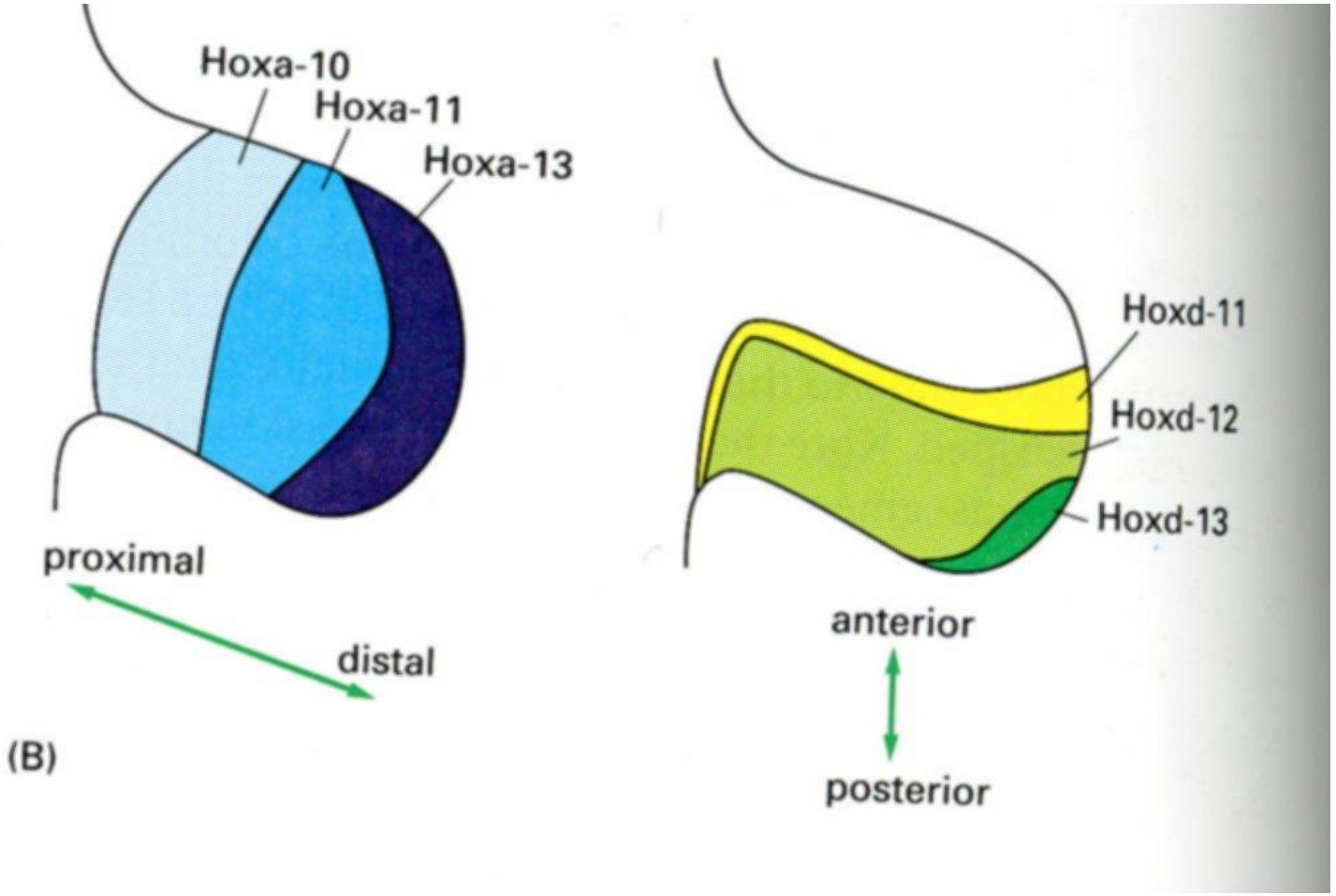


Profilo di espressione dei geni Hox nell'abbozzo dell'arto (mammifero)

(topo: asse ant-post)



Espressione di geni Hox nell'arto (uccello: assi prox-dist e ant-post)



Espressione ectopica di geni Hox nel topo → difformità scheletriche

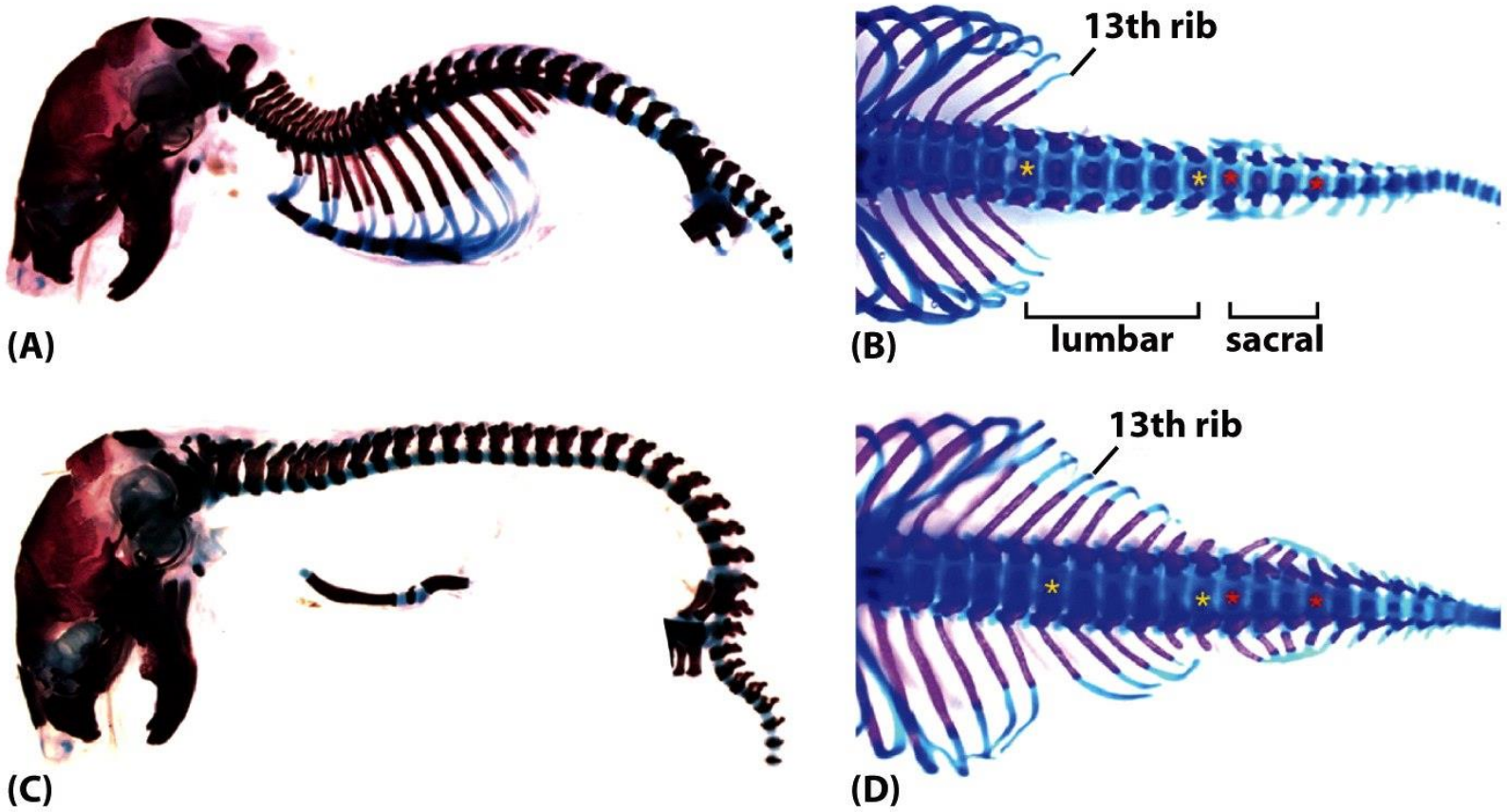


Figure 22-48 *Molecular Biology of the Cell* (© Garland Science 2008)

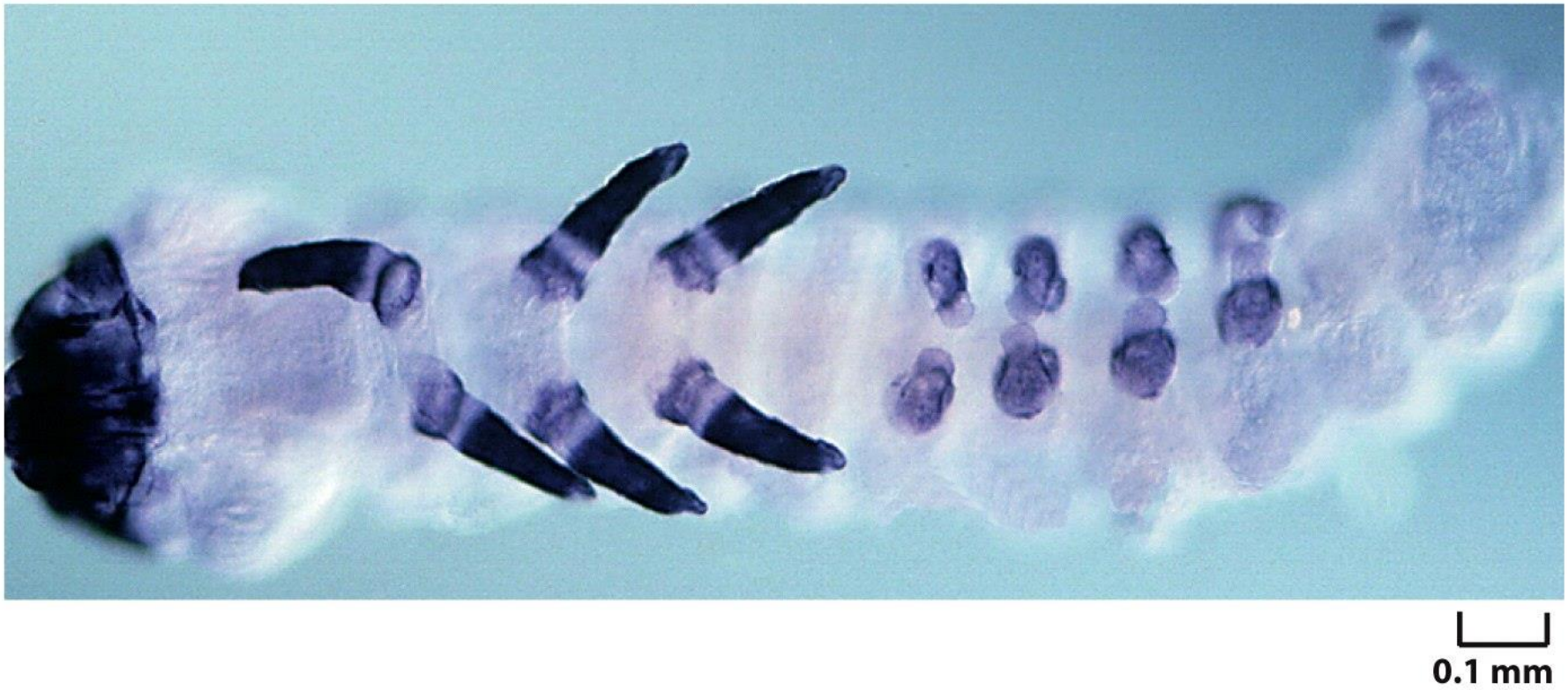


Figure 22-52b *Molecular Biology of the Cell* (© Garland Science 2008)

I geni della segmentazione sono interscambiabili attraverso le specie

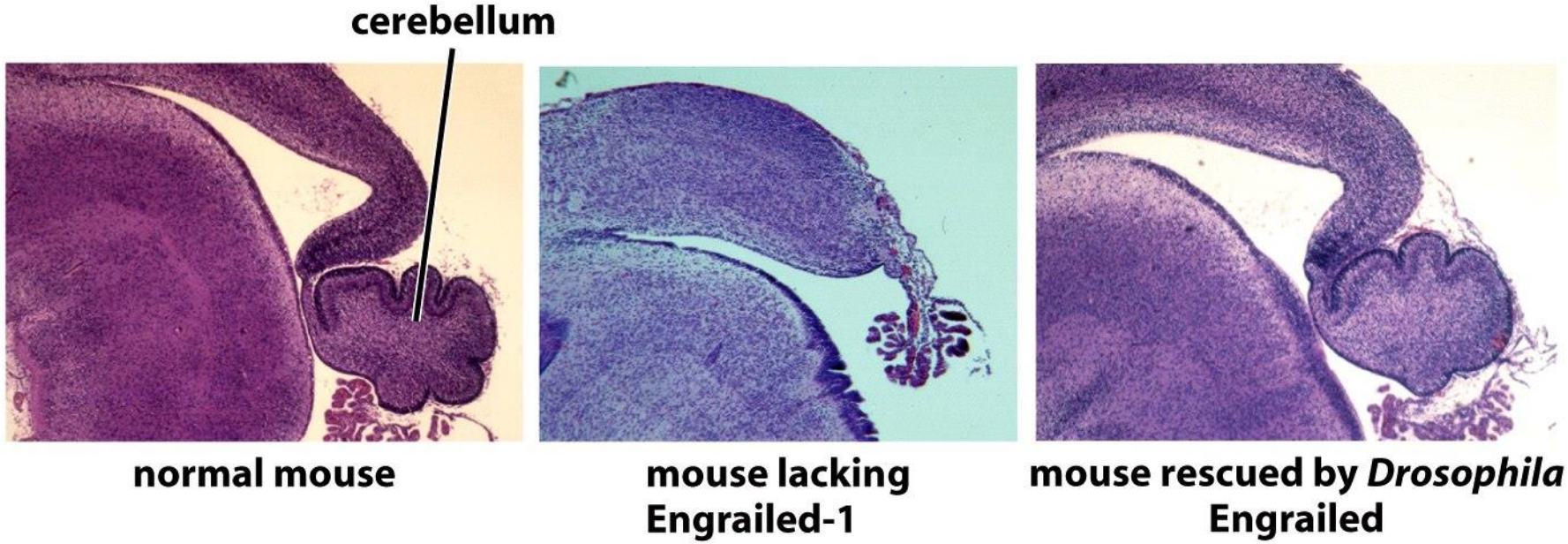
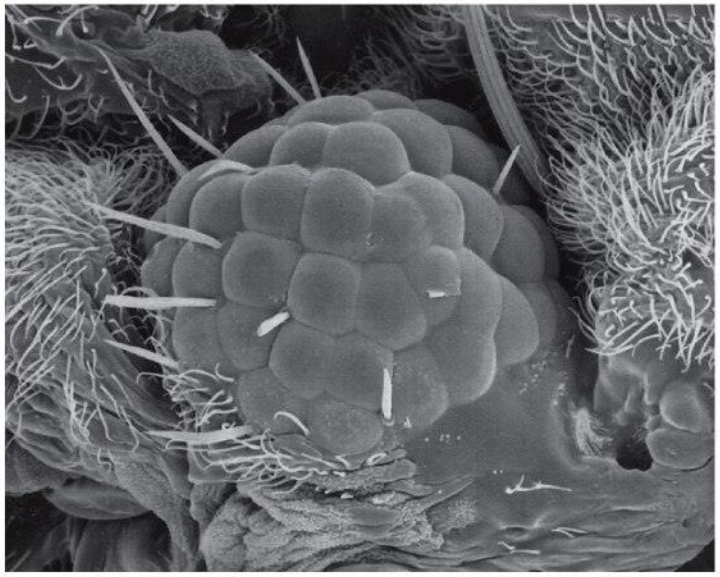
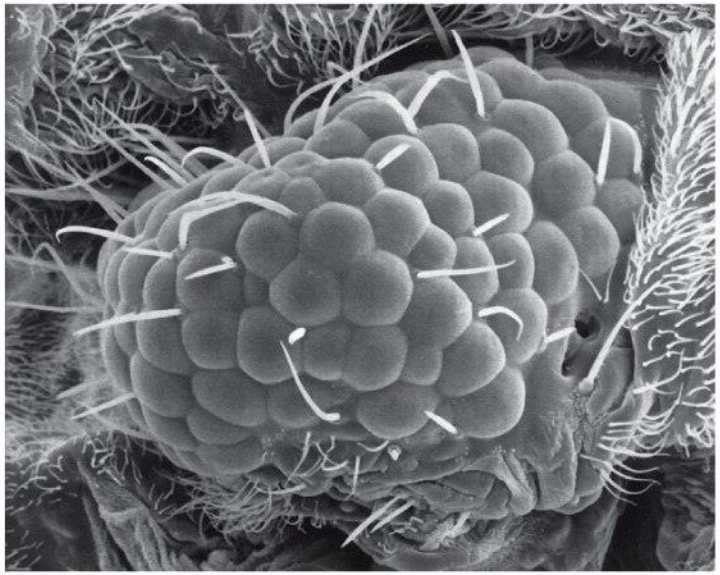
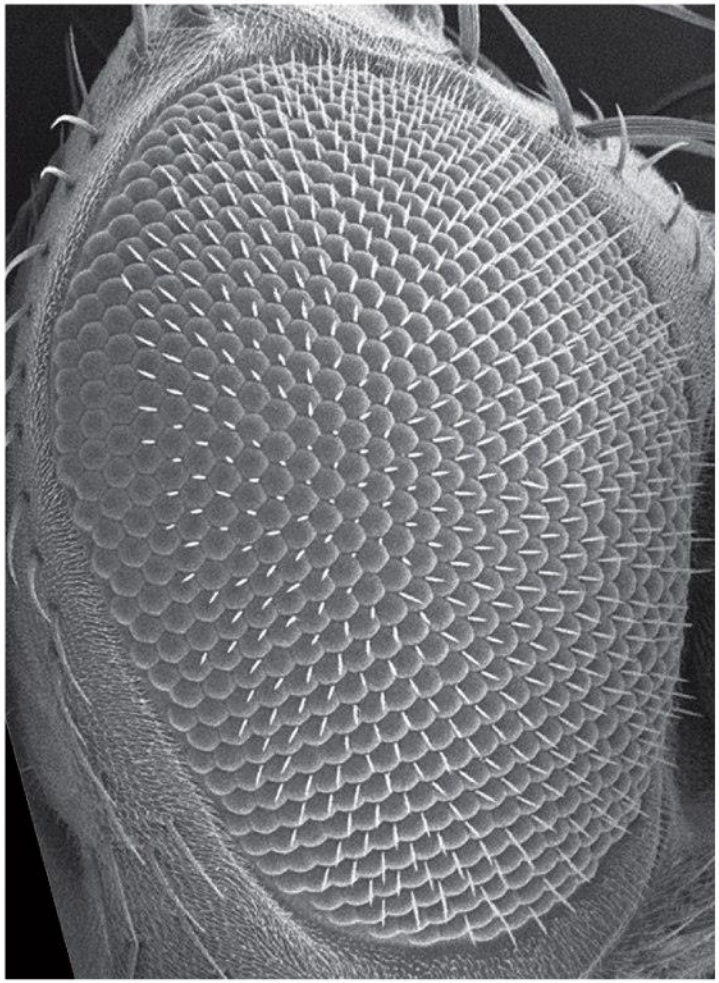


Figure 22-2a *Molecular Biology of the Cell* (© Garland Science 2008)





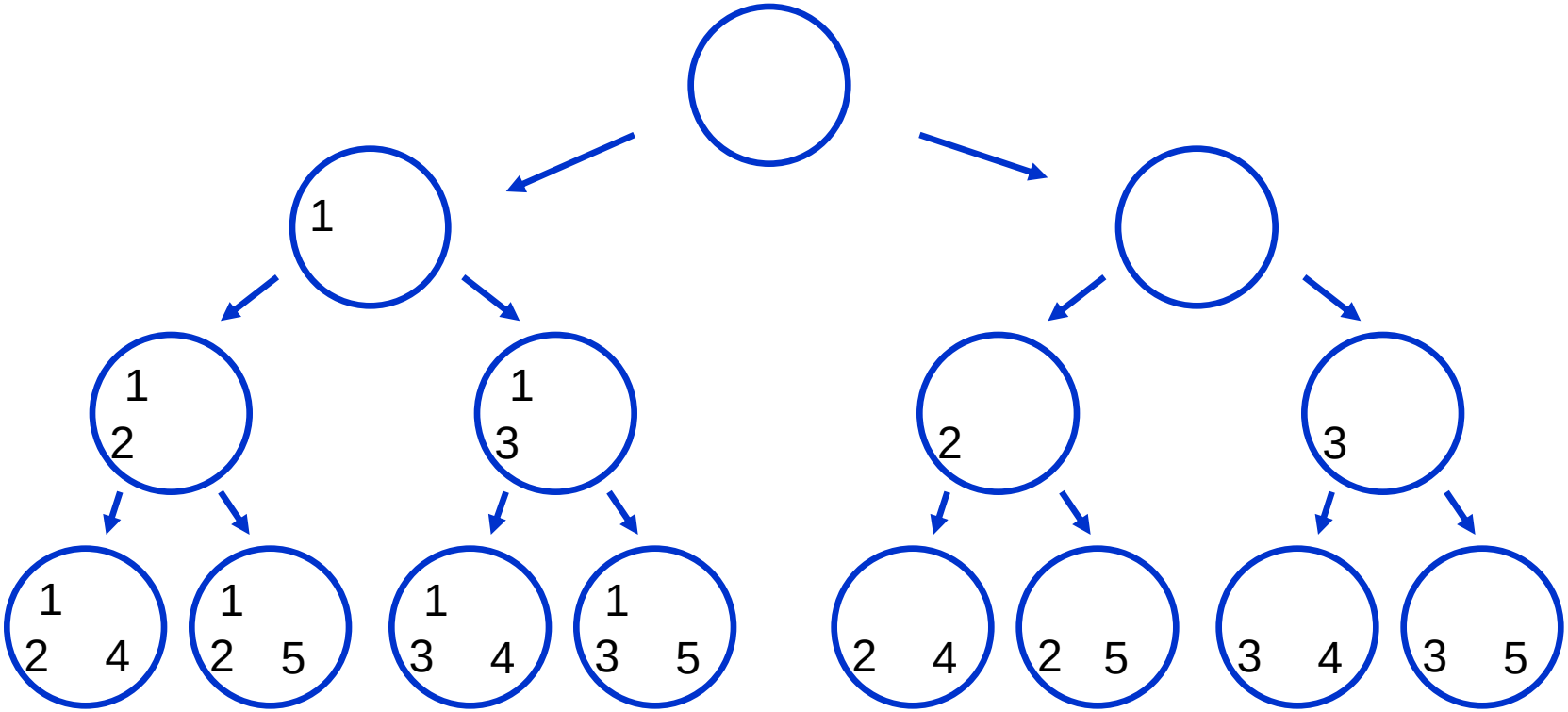


50 μm

Geni del mollusco e del topo omologhi a eyeless inducono formazione di occhio su zampa

Figure 22-2b *Molecular Biology of the Cell* (© Garland Science 2008)

Schema del modello combinatoriale desunto da studio delle mutazioni omeotiche

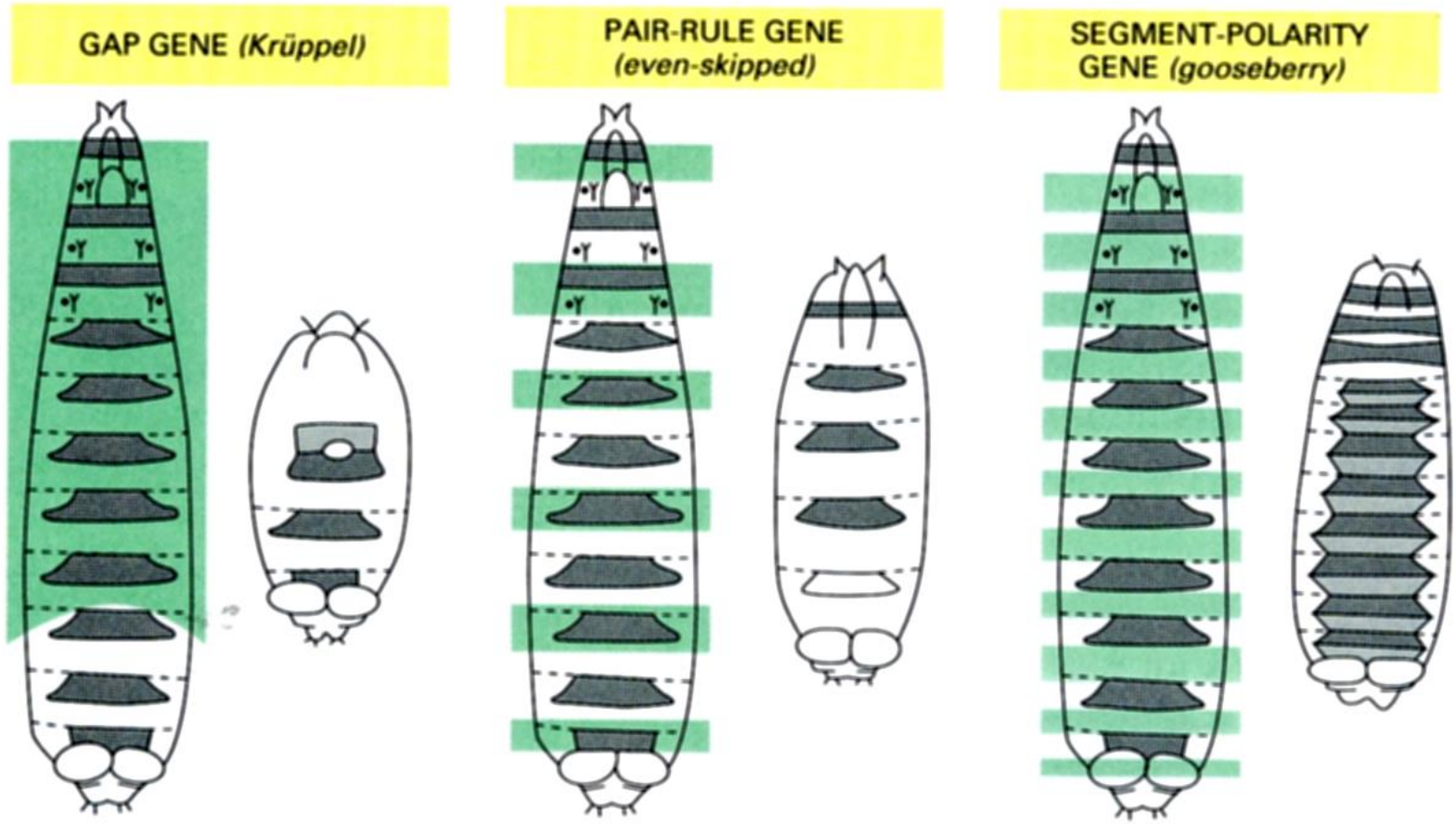


Compartimentalizzazione del corpo

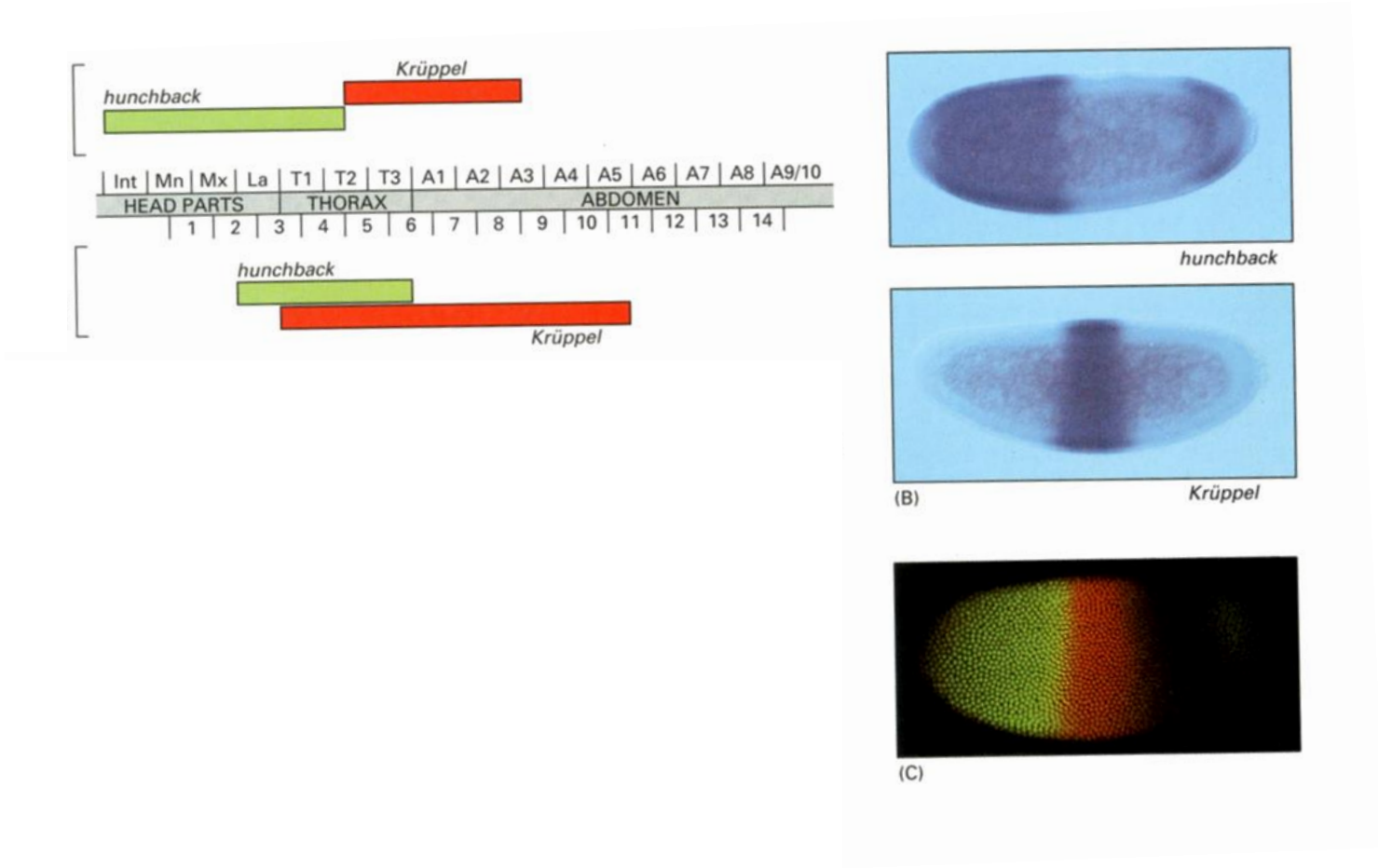
Graduale nel tempo:

- Geni della polarità o degli assi corporei
  ant-post e dorso-ventr
- Geni della segmentazione
  geni gap
  geni di coppia
  geni di compartimentazione del segmento
- Geni dell'identità del segmento corporeo
  geni omeotici

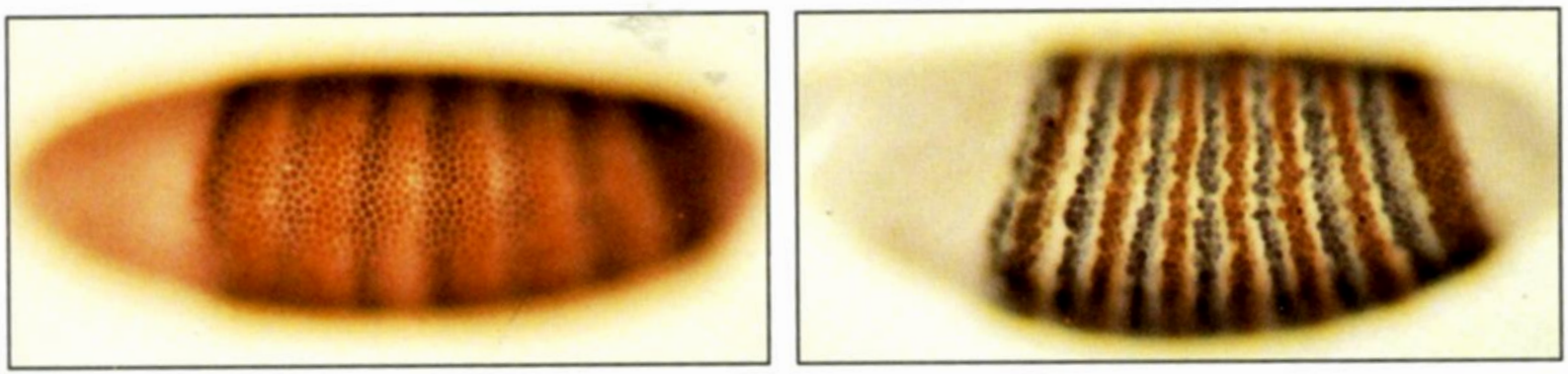
Compartimentalizzazione del corpo



Espressione di geni gap mutati



Genesi del piano corporeo (Drosophila)

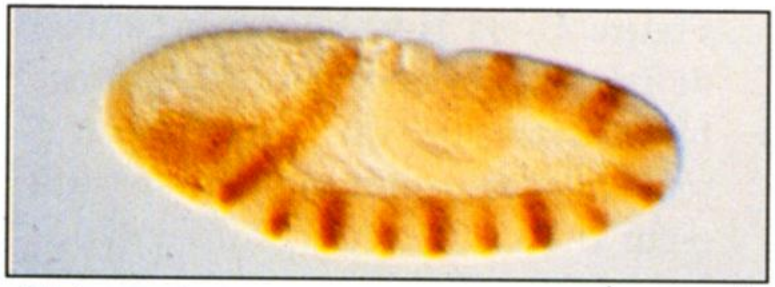


3 hours after fertilization

3½ hours after fertilization

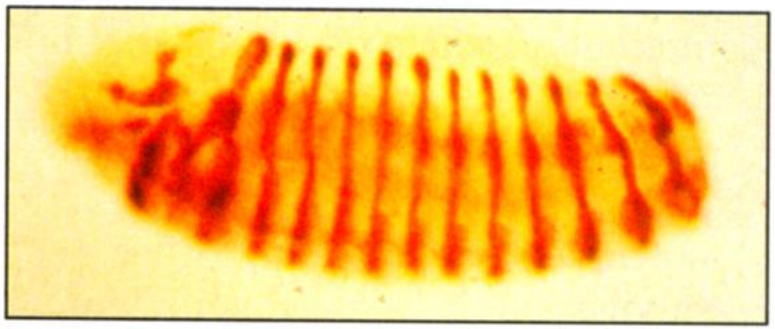
Drosophila I. Genesis of the Body Plan

Sviluppo della Drosophila:espressione di un gene della classe segmentale



5-hour embryo

100 µm



10-hour embryo

100 µm

adult

500 µm

La mutazione omeotica antennapedia

Gene omeotico

- Contiene una “homeobox”, che codifica per l’omeodominio (61 aminoacidi basici, sequenza che si lega a DNA)

- Fattore transattivante, che agisce sulle sequenze regolatorie di più geni, attivando un programma di sviluppo complesso

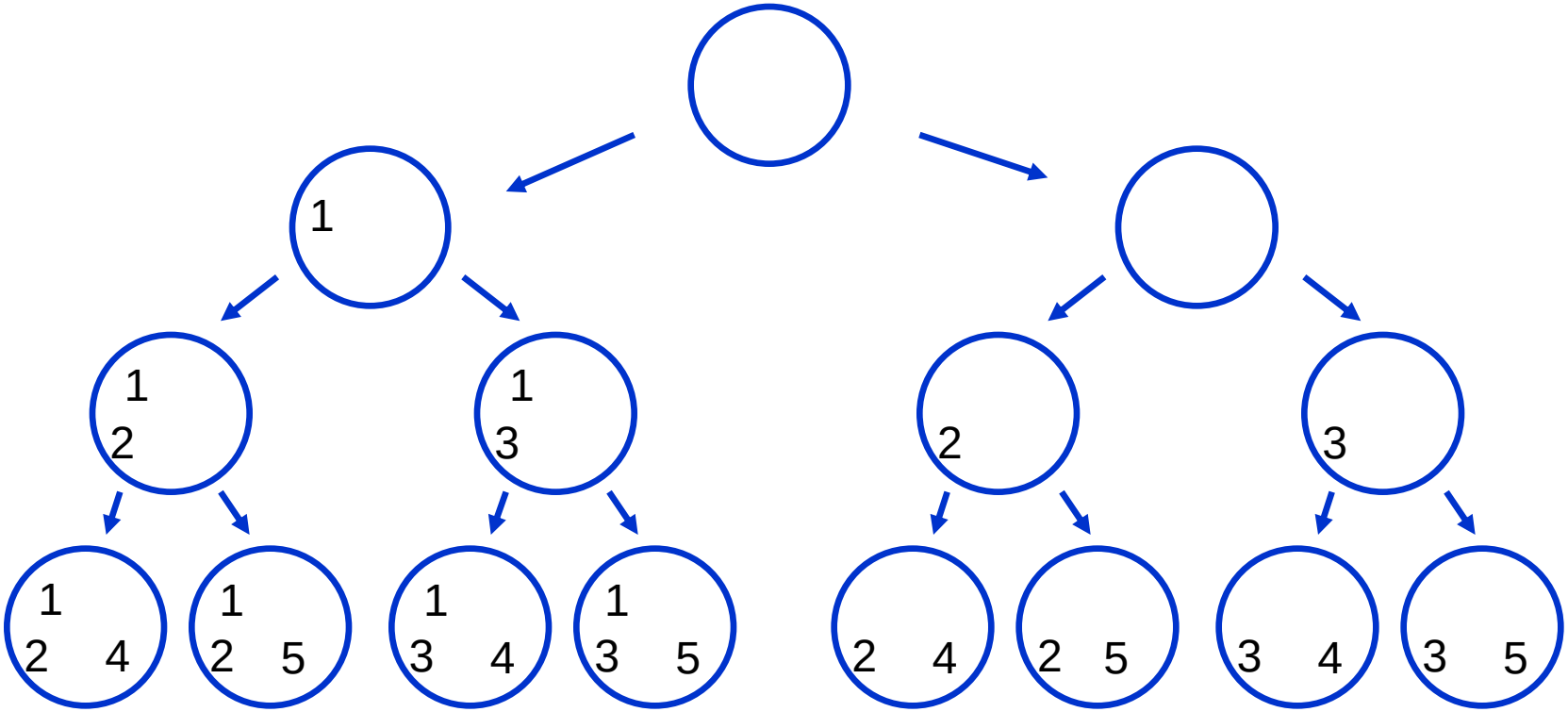
Geni omeotici

- Il più spettacolare esempio del mantenimento nell'evoluzione del meccanismo/macchinario di controllo dello sviluppo
- Il modello corporeo si determina con lo stesso meccanismo per tutti gli organismi.

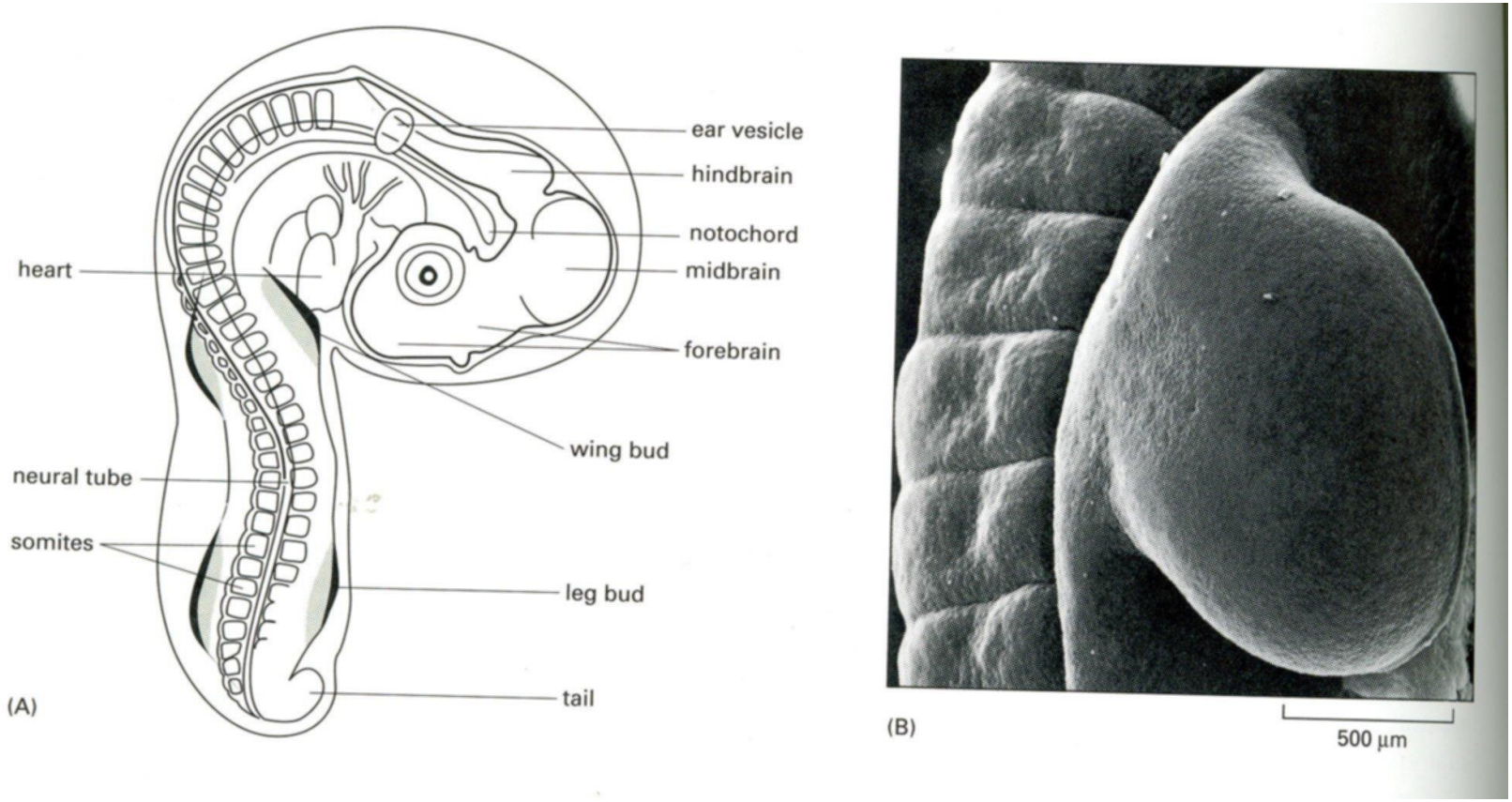
  (andando dal più semplice al più complesso, aumentano solo la complessità e il numero dei geni coinvolti)

La mutazione omeotica antennapedia

Schema del modello combinatoriale desunto da studio delle mutazioni omeotiche



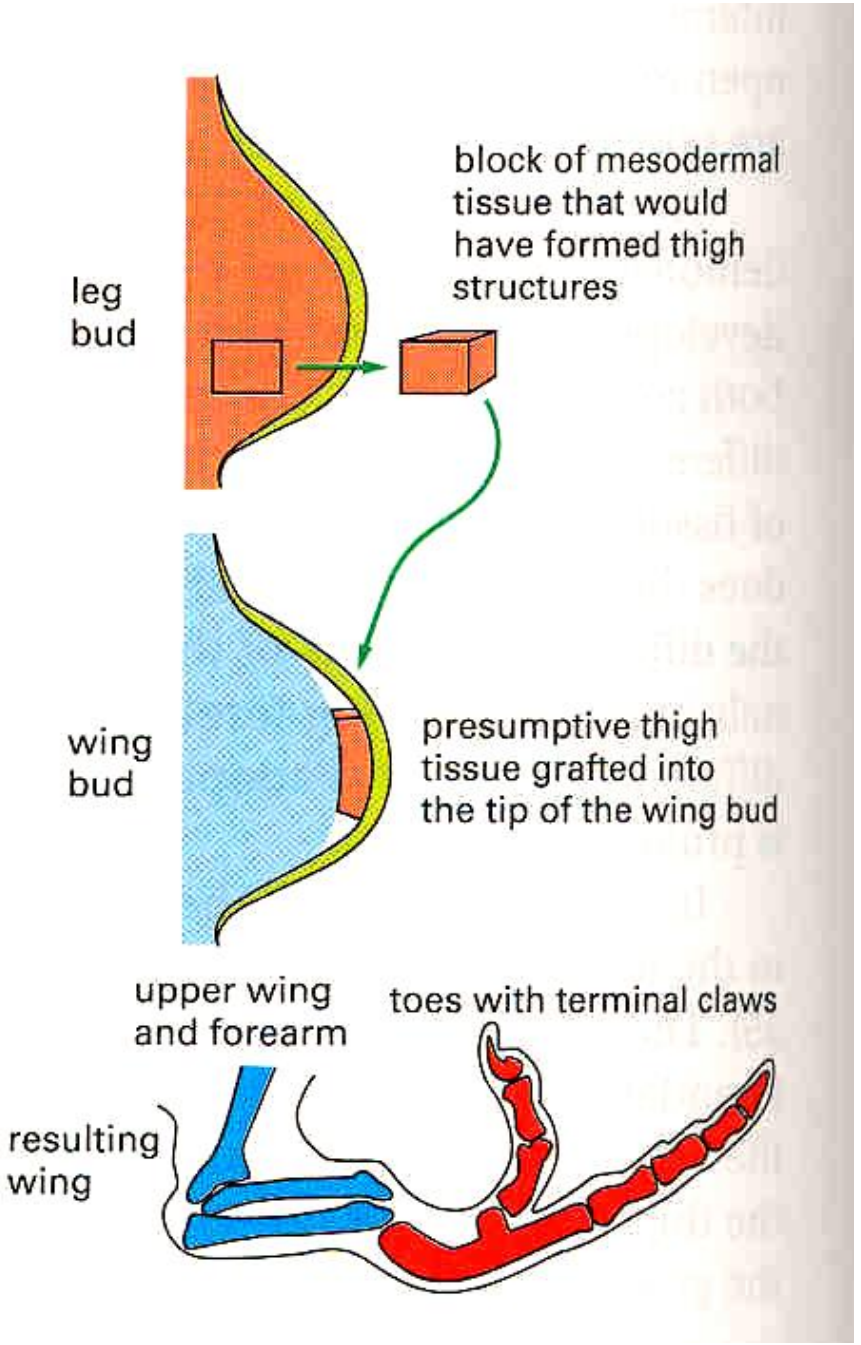
Abbozzi degli arti (uccello)



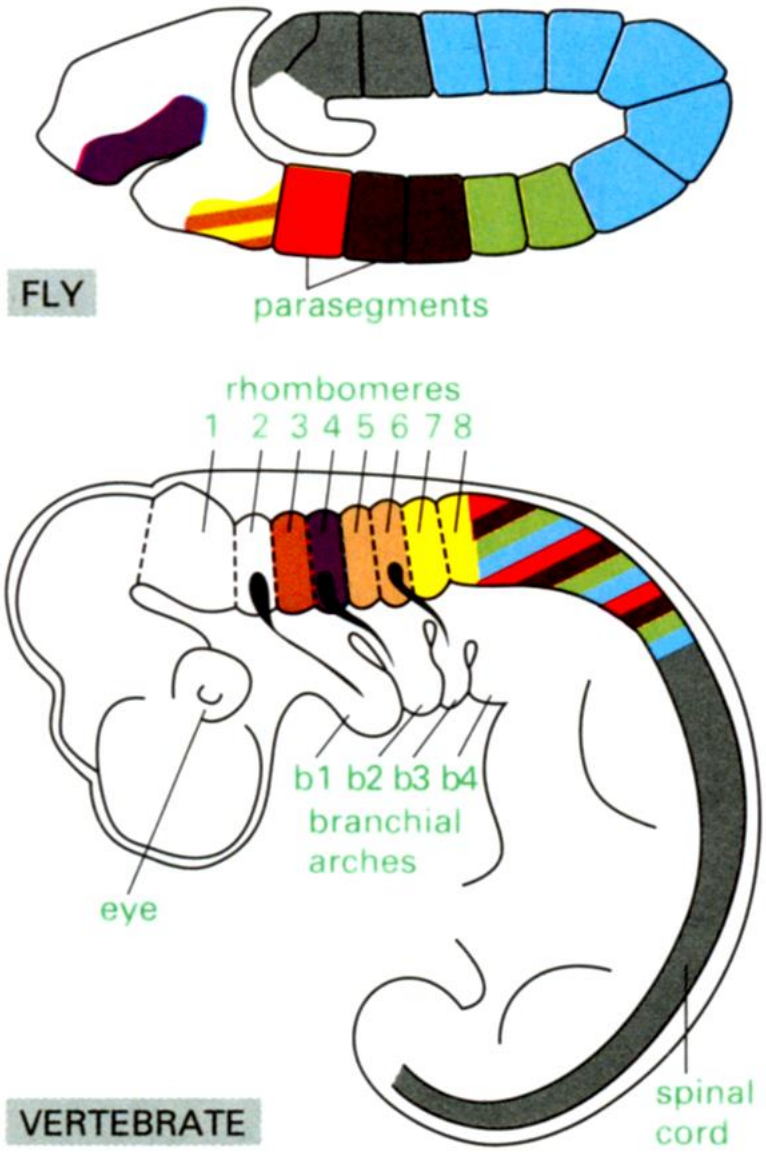
La determinazione avviene per tappe successive

1. identità dell'arto
2. segmenti dell'arto

meccanismo combinatoriale

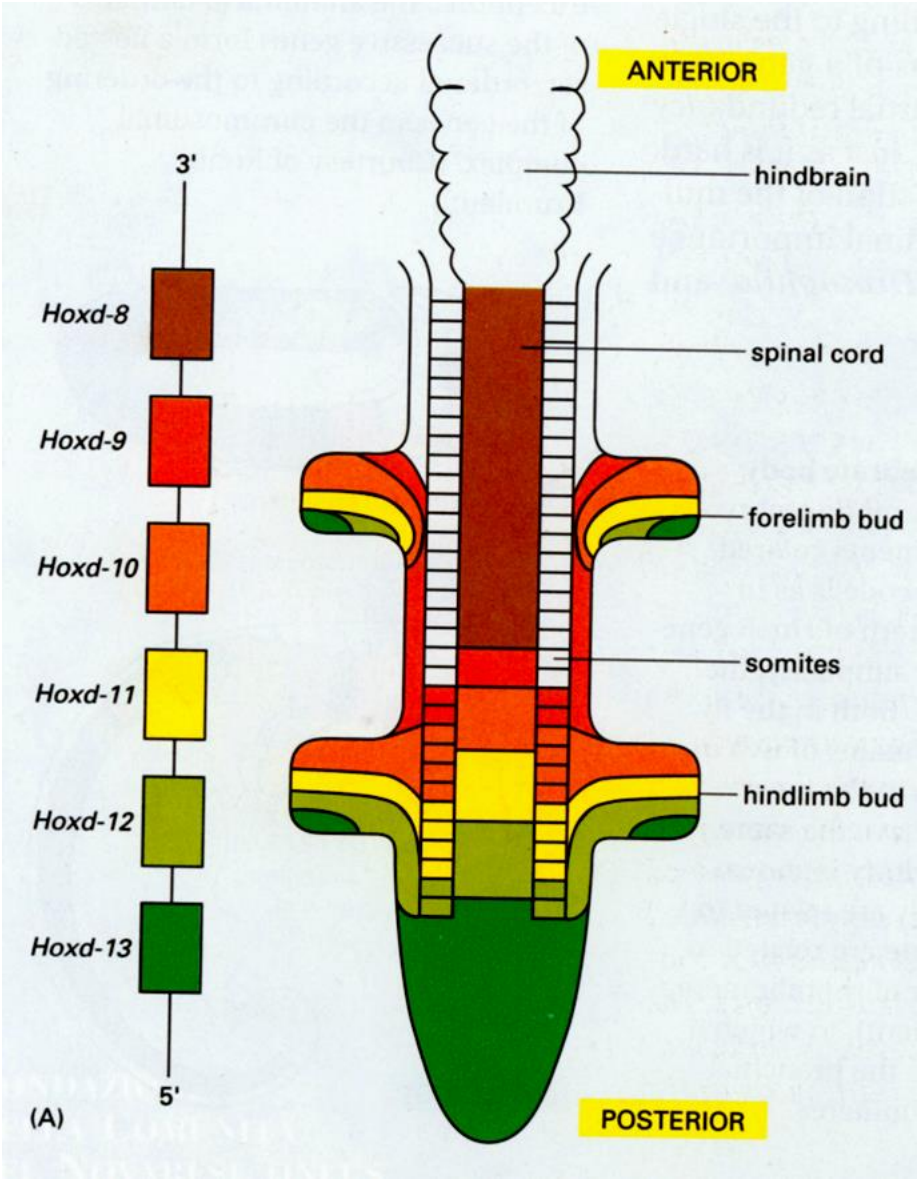


Espressione di geni Hox (confronto Drosophila-vertebrato)



Profilo di espressione dei geni Hox nell'abbozzo dell'arto (mammifero)

(topo: asse ant-post)



Espressione di geni Hox nell'arto (uccello: assi prox-dist e ant-post)