Figure 22-42 Molecular Biology of the Cell 5/e (© Garland Science 2008)

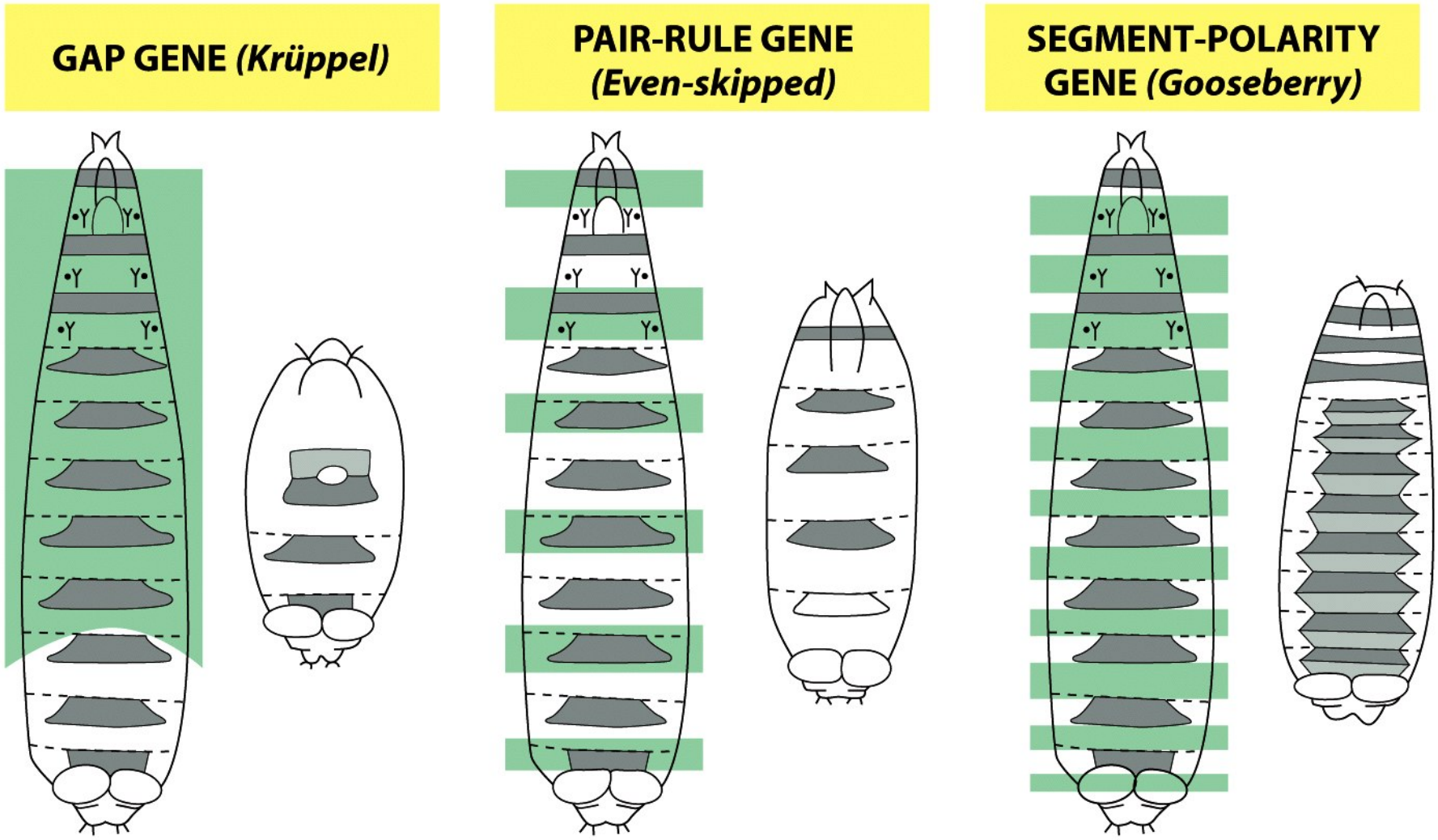
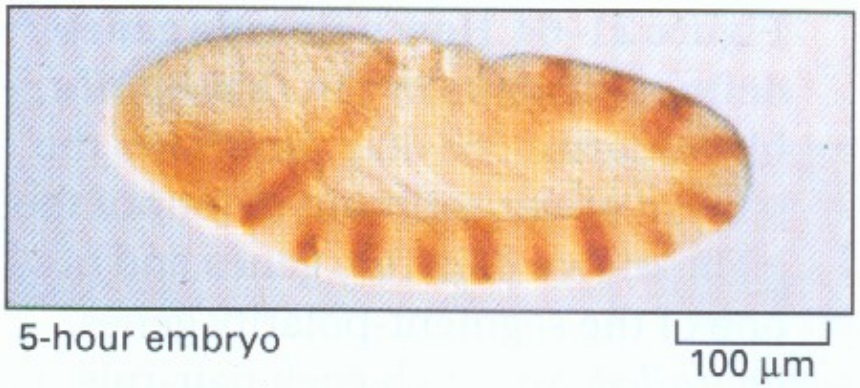
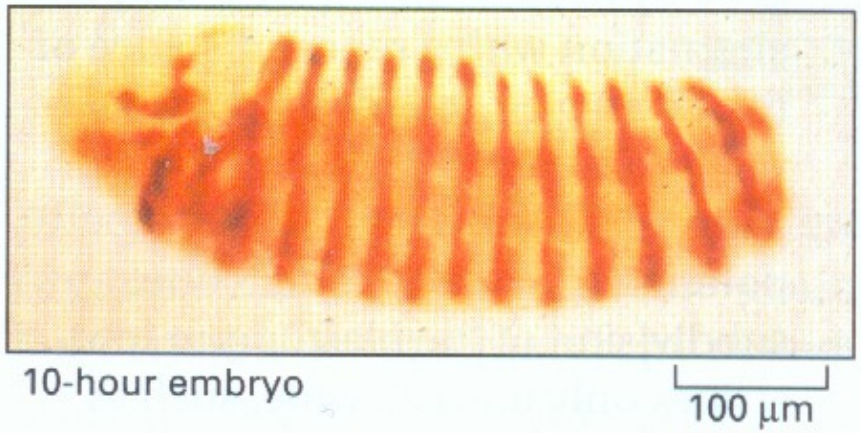
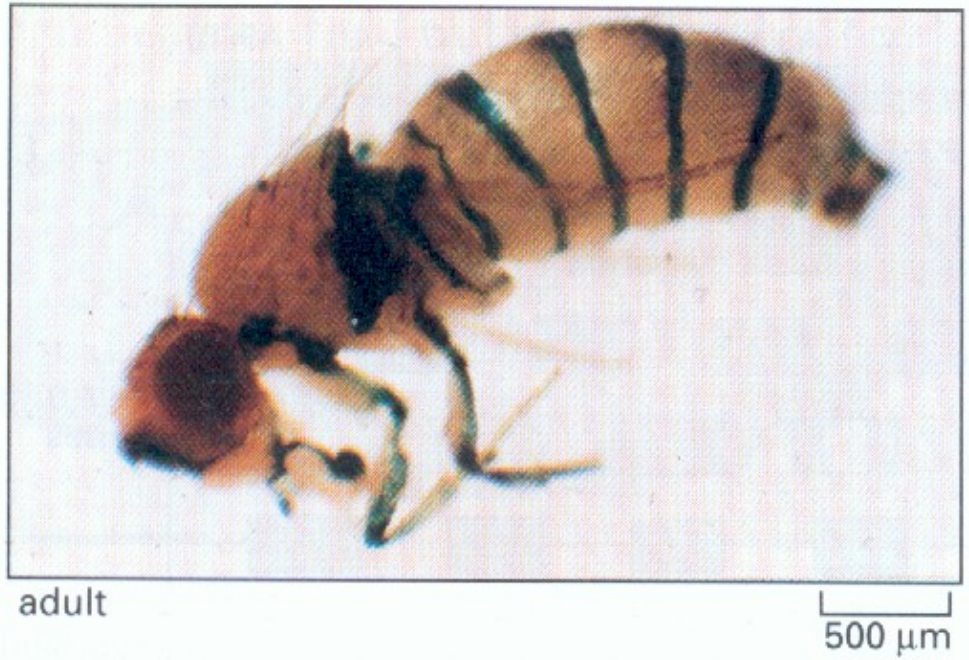


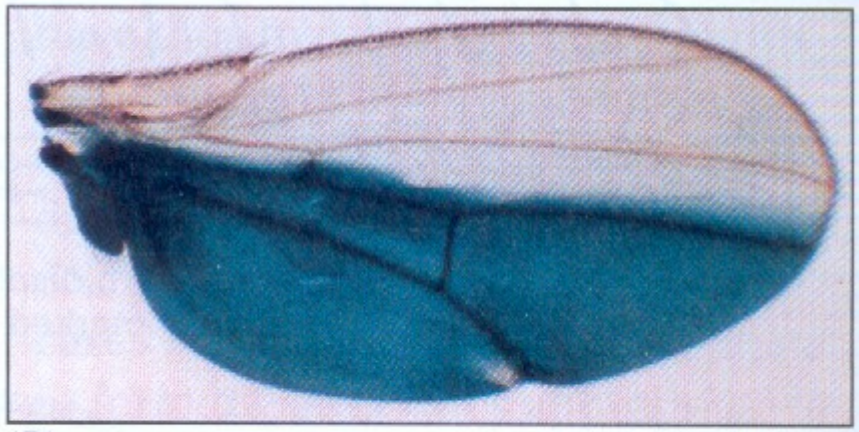
Figure 22-37 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Paikkatietoa

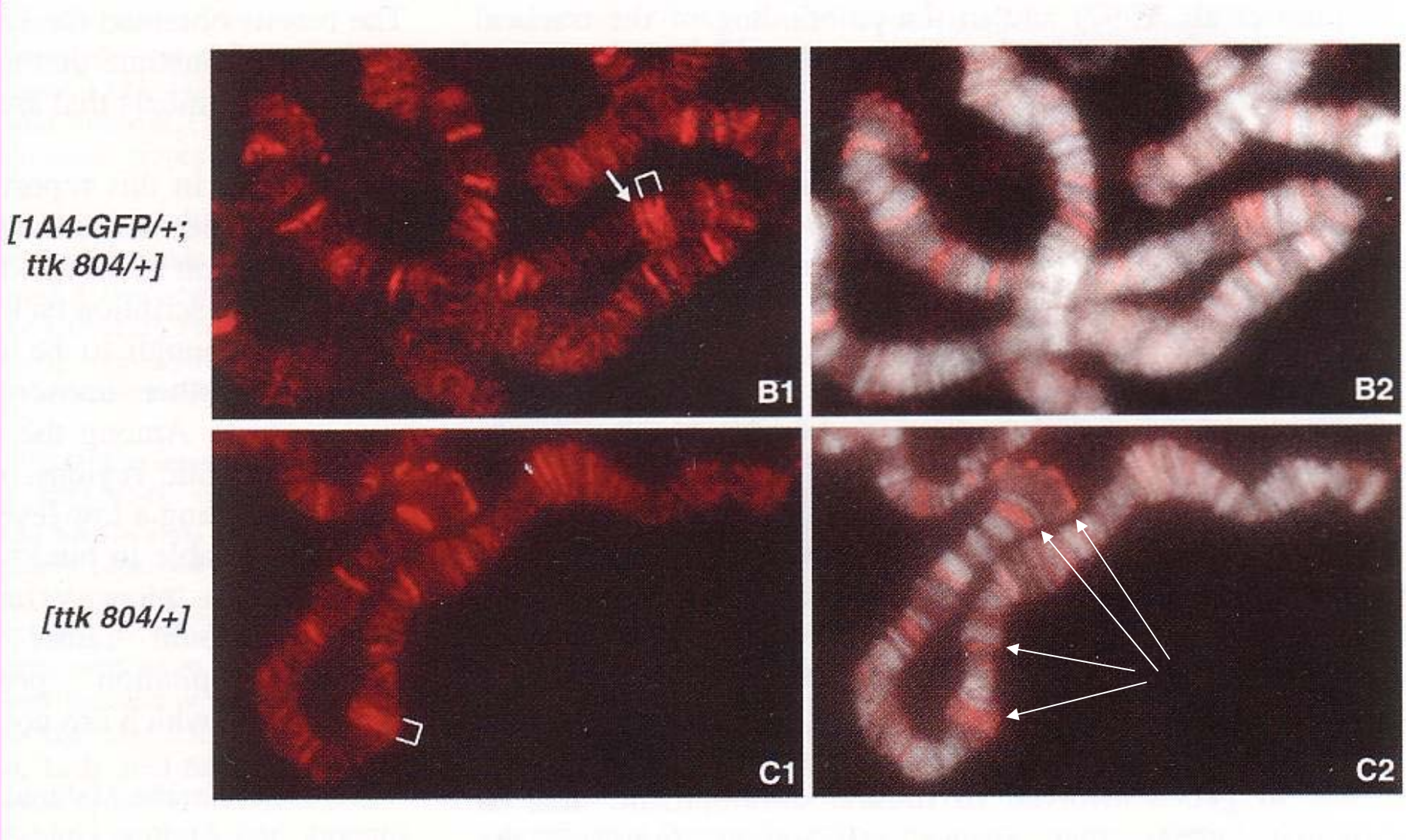






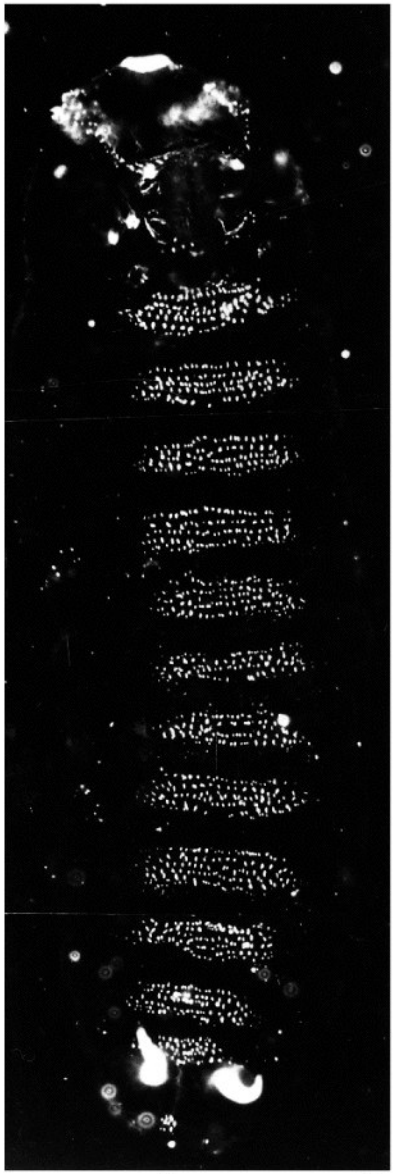


engrailed-geenin **ekspressio**



Engrailed –geenituotteen **vaikutus**

Engrailed –proteiini sitoutuu lukuisiin erityisiin sylkirauhaskromosomin kohtiin, toisin sanoen useiden geenien säätelyalueille (punaväri = engrailed-vasta-aine). Nimeltä tunnetaan 86 ”target-geeniä”, siiven, hengitysputkien, lihasten, hermoston ja silmän kehitysketjuista [Solano et al., **Development** April 2003]



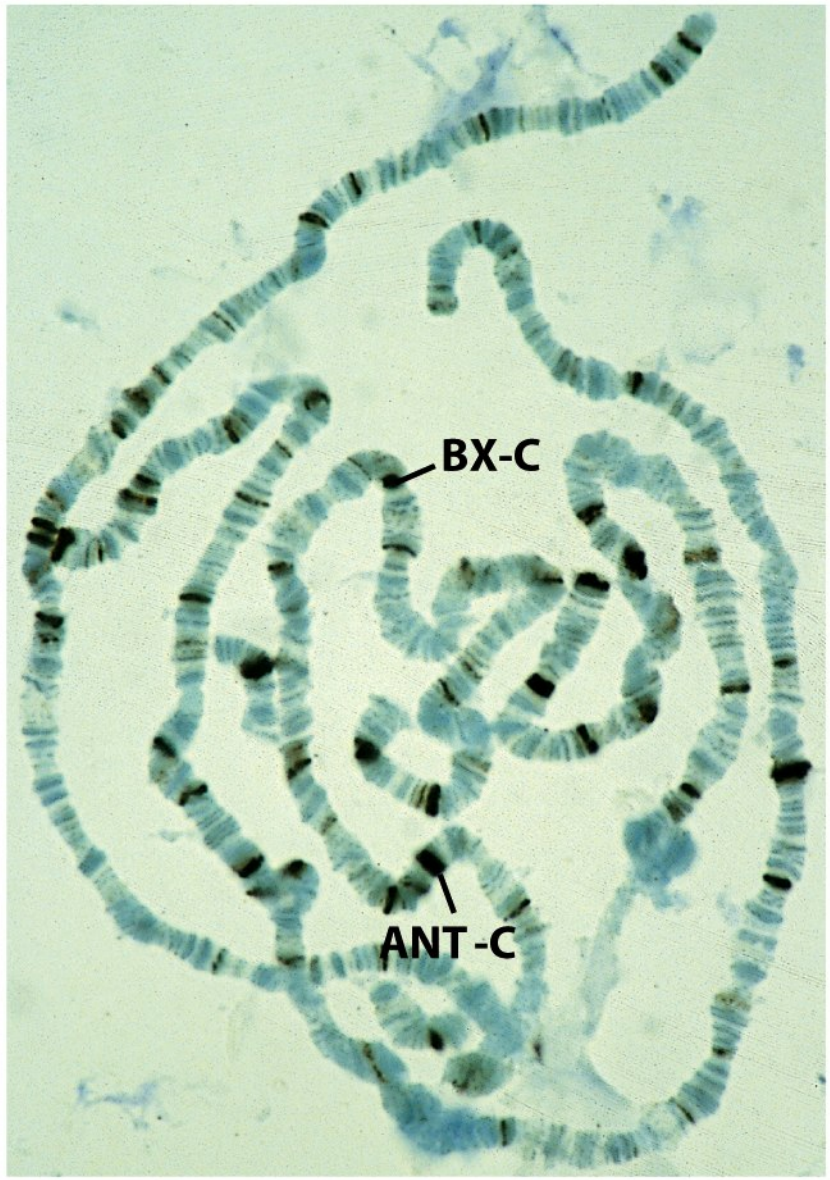


Figure 22-45 Molecular Biology of the Cell 5/e (© Garland Science 2008)

A. Extra sex combs mutantti

B. Polycomb-proteiinin situtuminen, sylkiruhaskromosomiin visualisoituna

Yli 60 sitoutumispaikkaa eli yli 60 säädeltävää geeniä

BX-C ja ANT-C selitetään ihan kohta >>>

CELL 1345

Homeoottiset selektorit

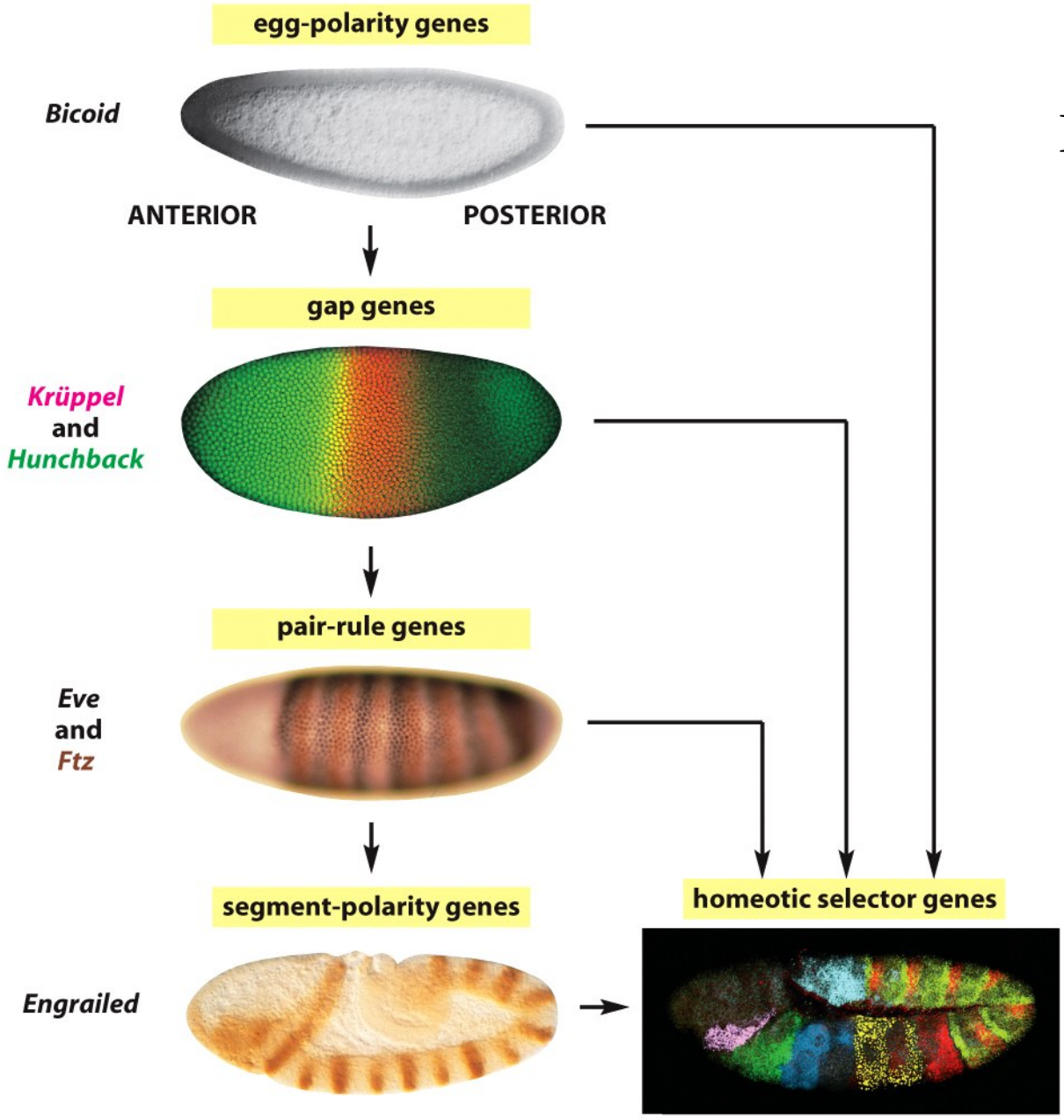


Figure 22-38 Molecular Biology of the Cell 5/e (© Garland Science 2008)

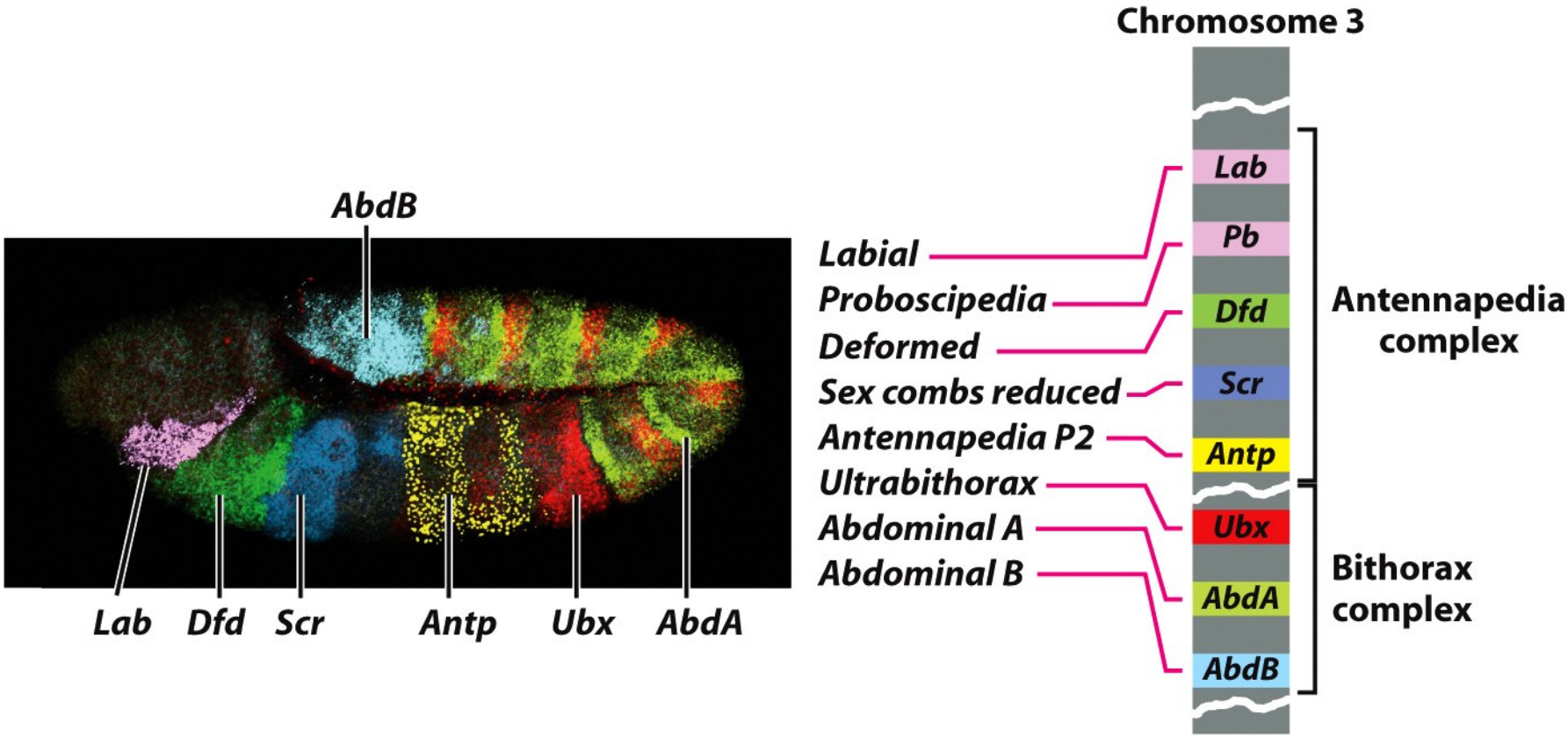
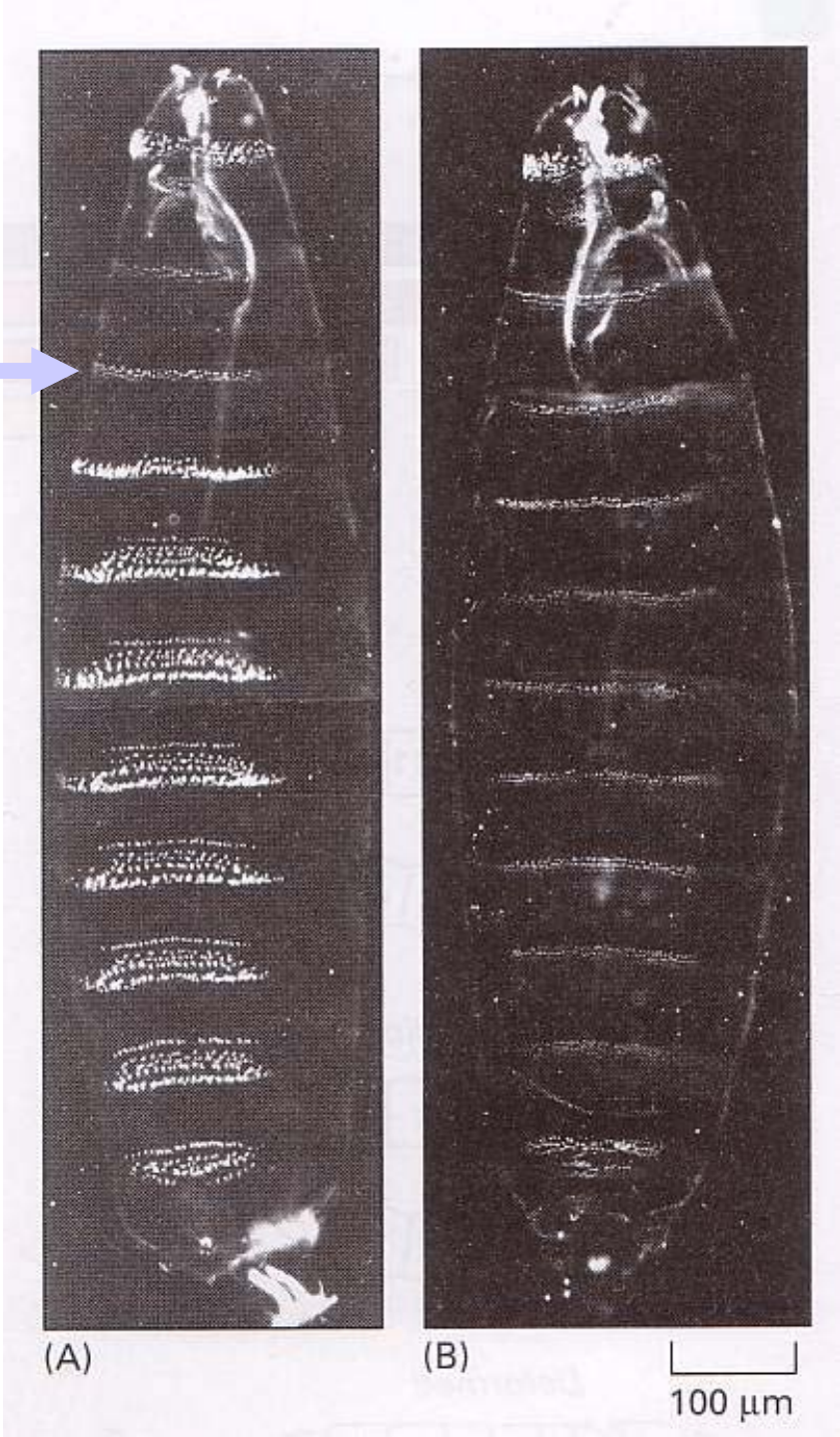


Figure 22-44 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Homeoottiset selektorigeenit

Villi

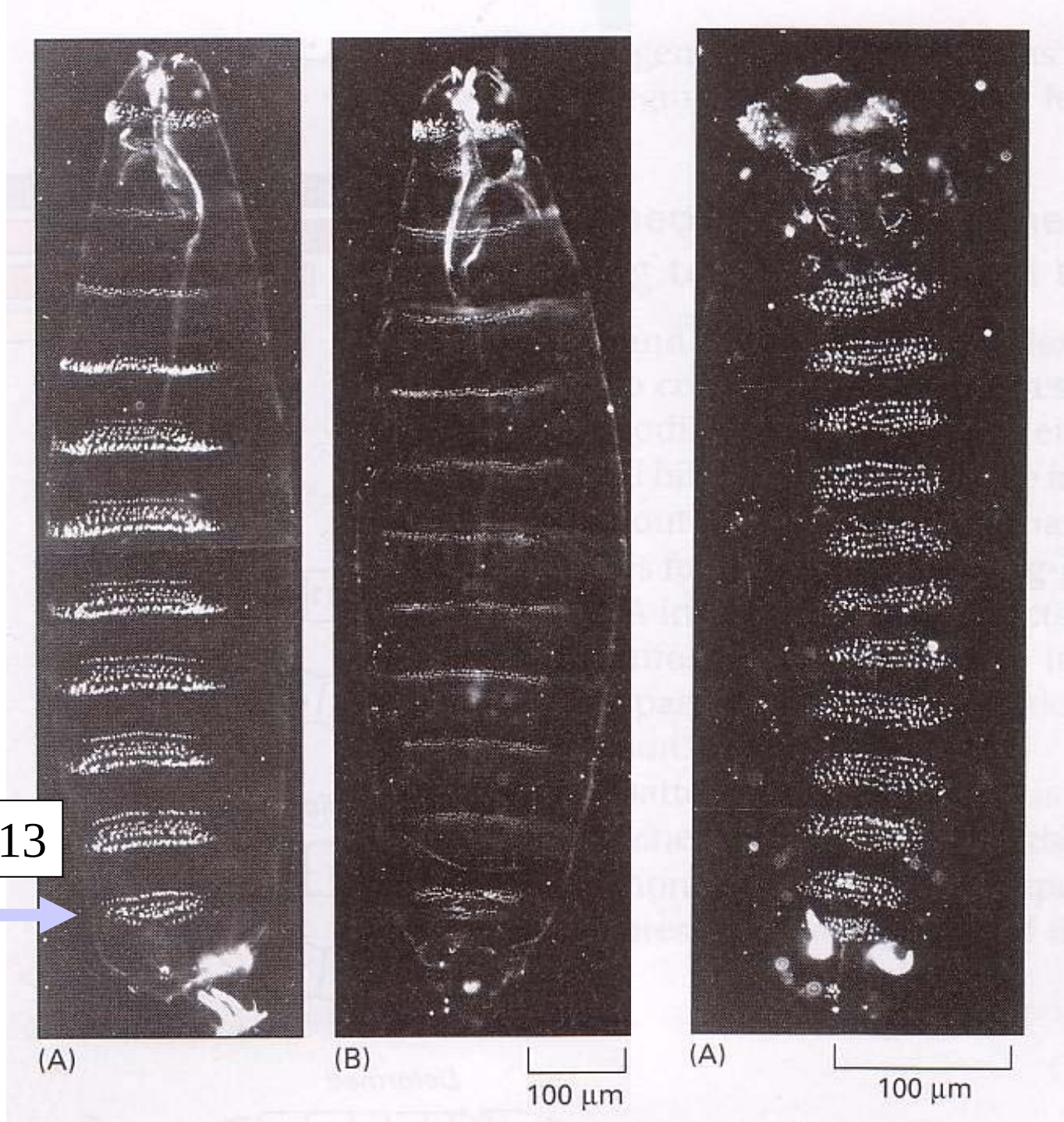
#5



Suurin osa bithorax-kompleksista poistettu

Kaikki segmentit suunnilleen samanlaisia kuin #5

Kaikki segmentit ovat kuitenkin syntyneet mutta eivät erilaistu!



#13

Extra sex combs -mutantti

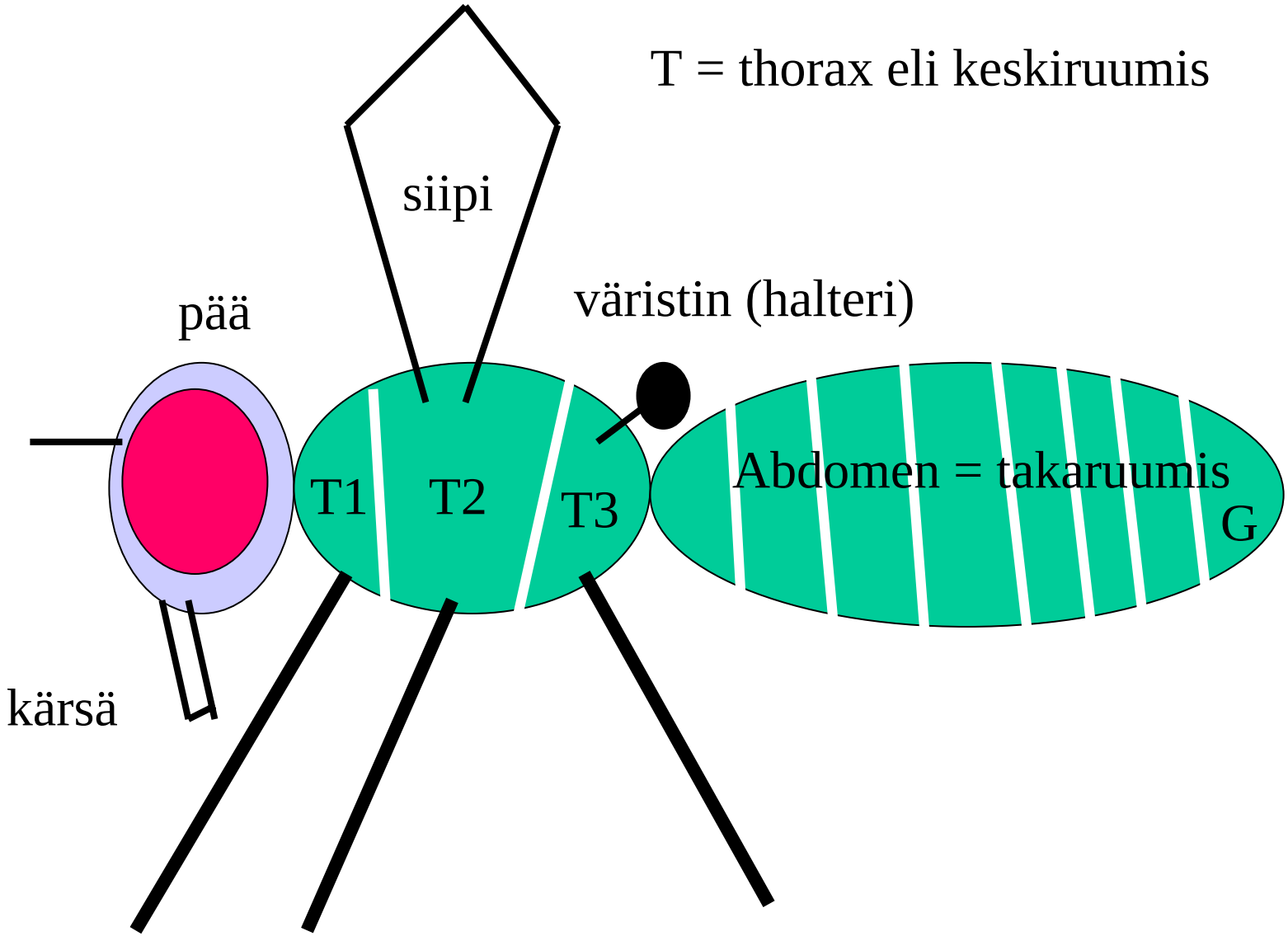
Kaikki segmentit takimmaisen abdominaali-segmentin kaltaisia!

Homeoottiset selektorigeenit löydettiin katselemalla aikuisia kärpäsiä!

Antennapedia -mutantti

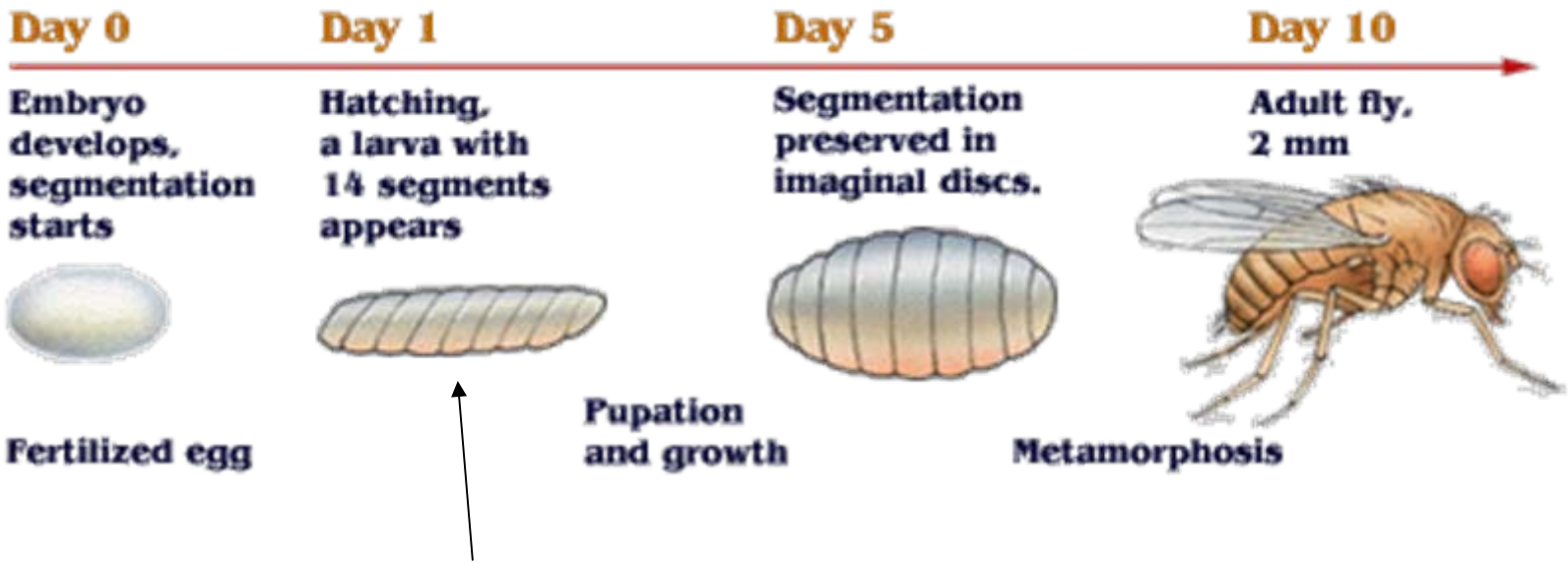
Kaksoismutantti *bithorax-postbithorax*. **T3 > T2**

abdominal-B mutantti: genitaalien aiheesta onkin tullut jalka



Aikuisen hyönteisen (kärpäsen) pääosat (jaokkeet)

Homeoottiset selektorigeenit?



3 toukkavaihetta

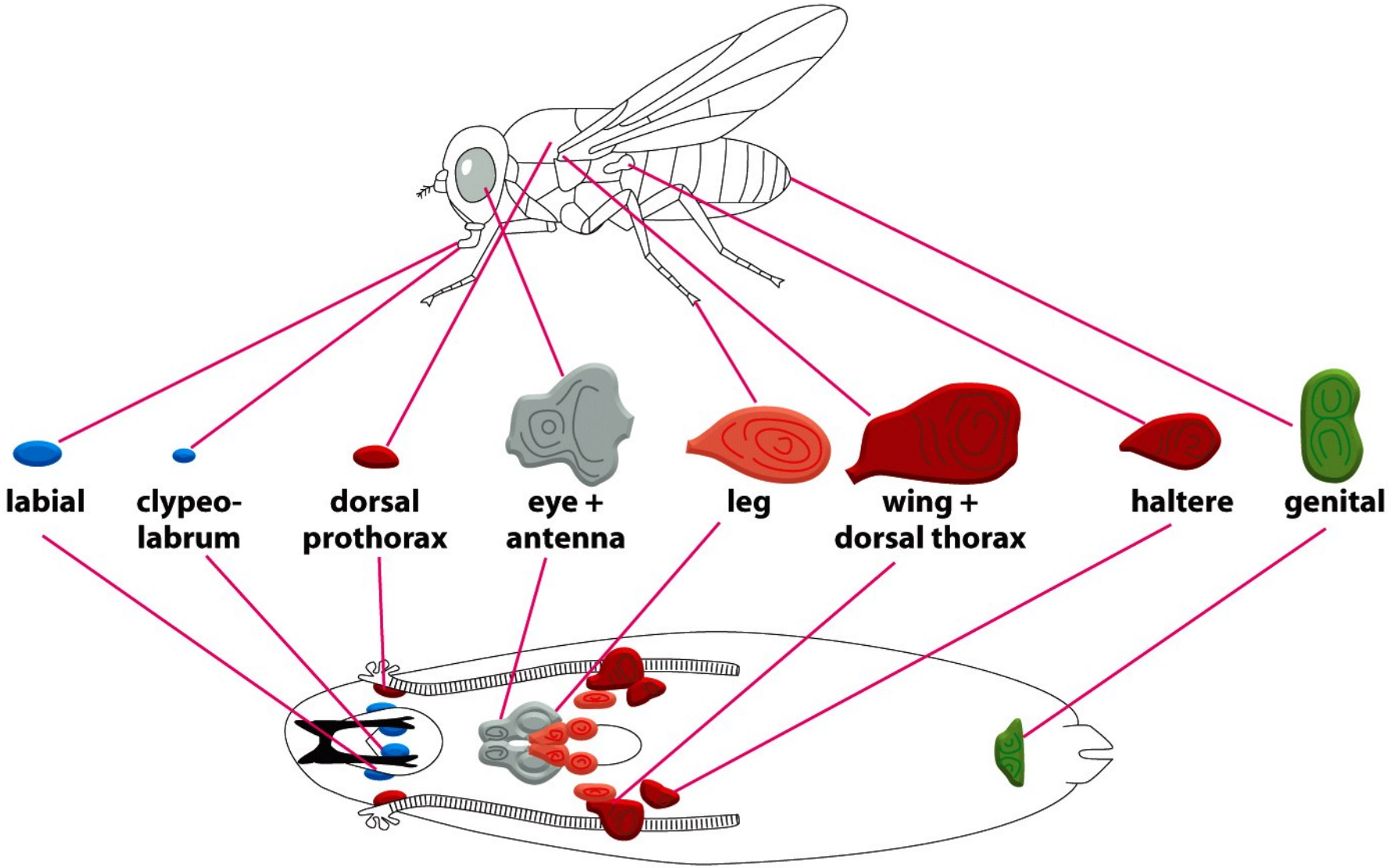


Figure 22-51 Molecular Biology of the Cell 5/e (© Garland Science 2008)

CELL 1350

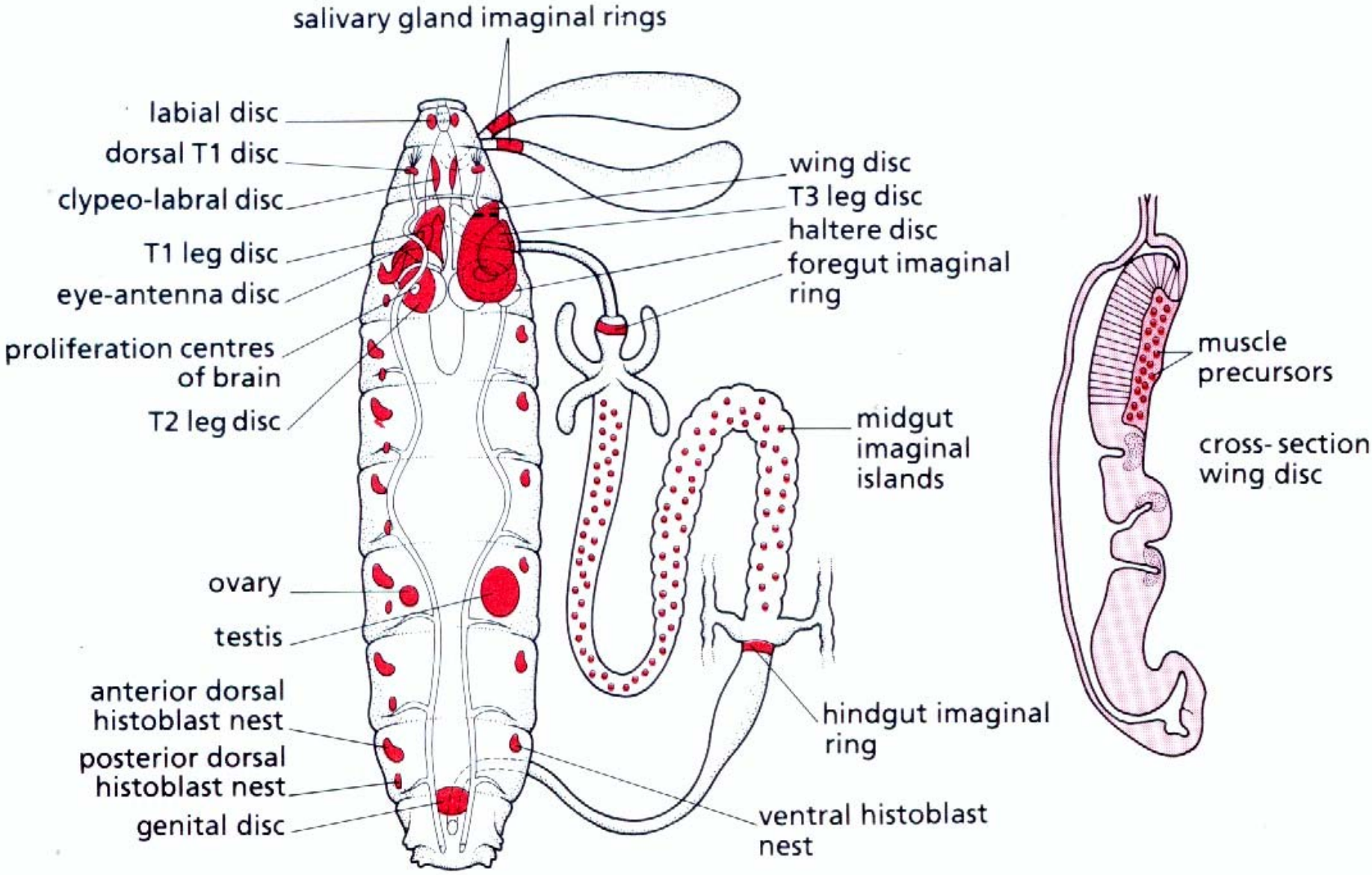


Figure 1.7 The origin of the adult cells (red).

CELL 1350

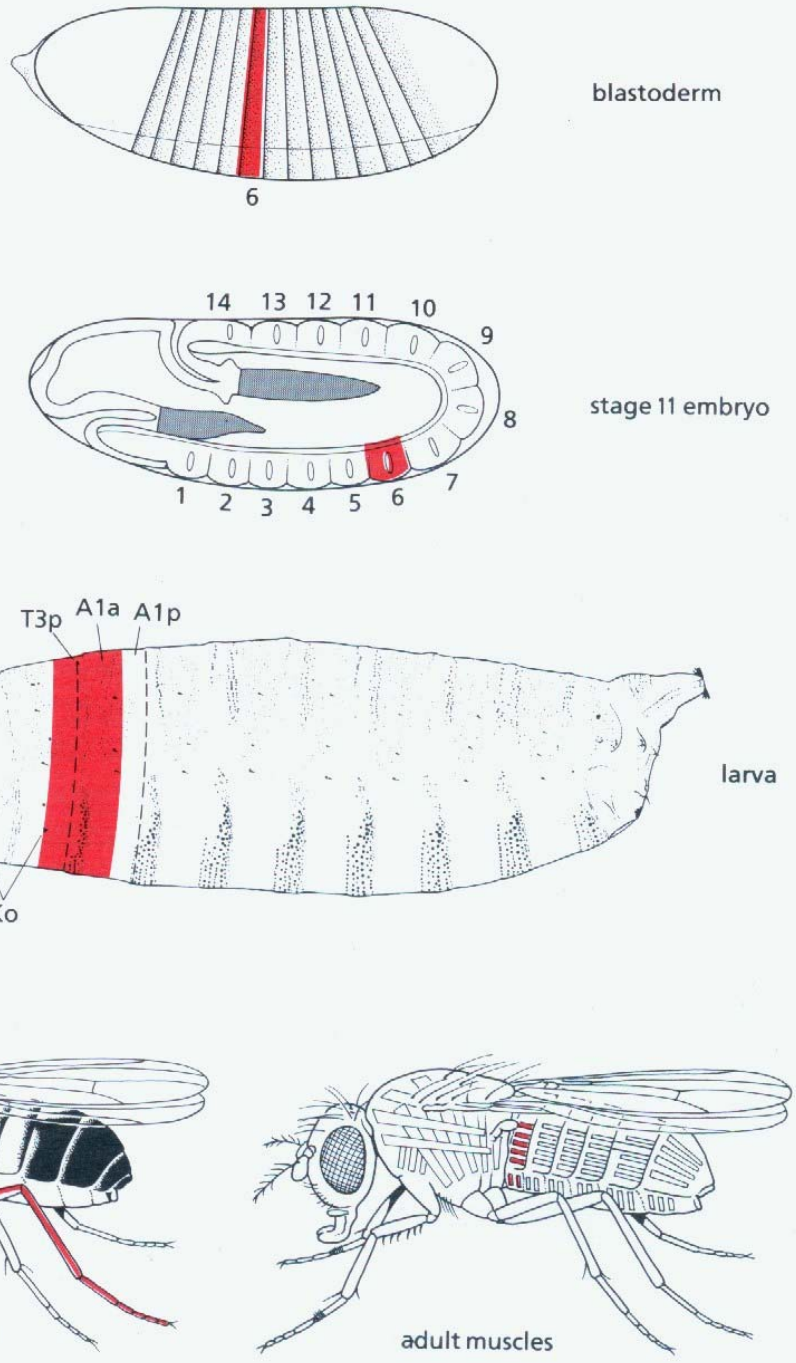
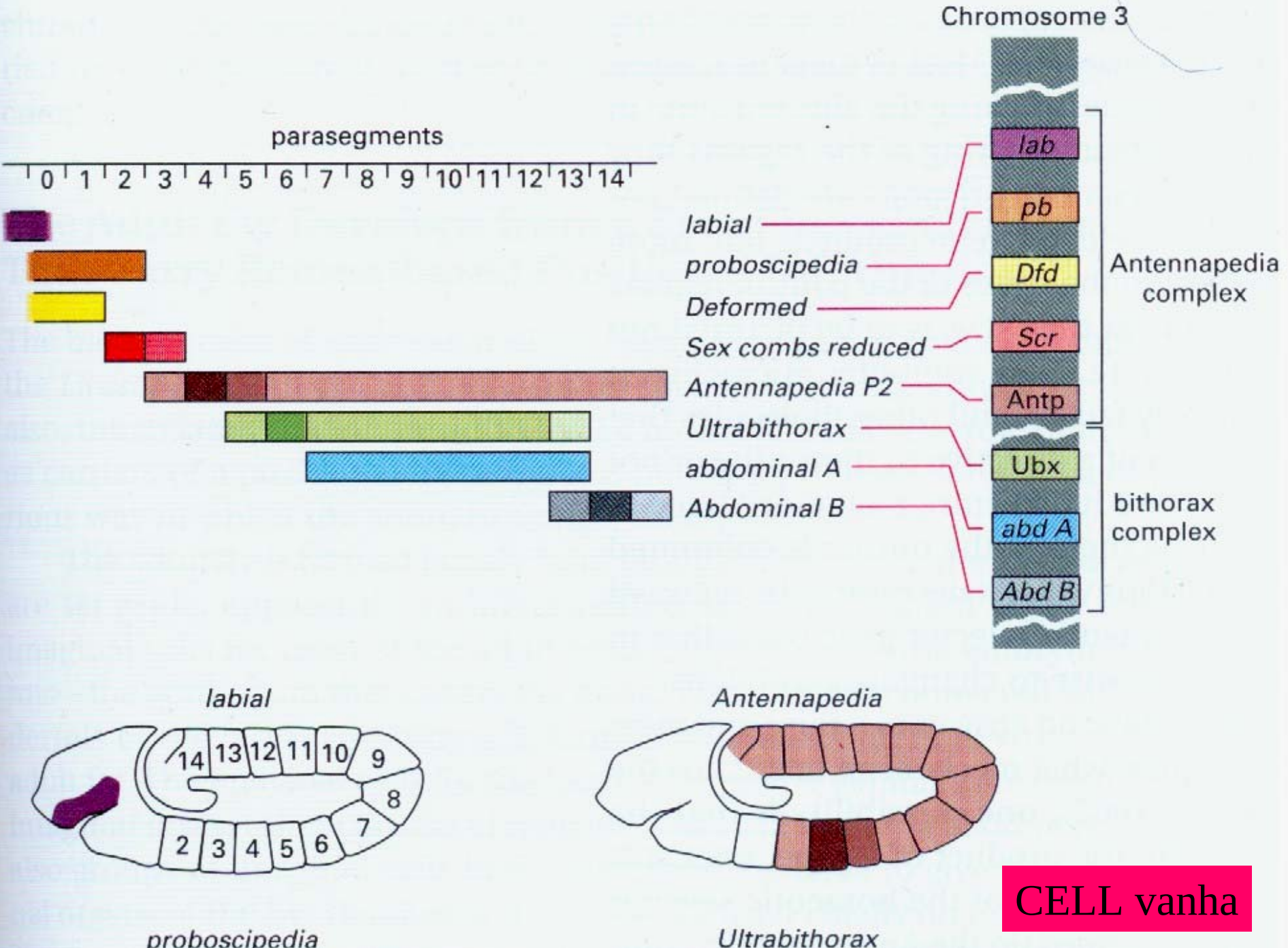


Figure 1.6 The origin and fate of parasegment 6 (red).

CELL 1350


Chromosome 3
parasegments
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
labial
proboscipedia
Deformed
Sex combs reduced
Antennapedia P2
Ultrabithorax
abdominal A
Abdominal B
lab
pb
Dfd
Scr
Antp
Ubx
abd A
Abd B
Antennapedia complex
bithorax complex
labial
14 13 12 11 10 9 8 7 2 3 4 5 6
Antennapedia
proboscipedia
Ultrabithorax

CELL vanha

Homeoottiset selektorit

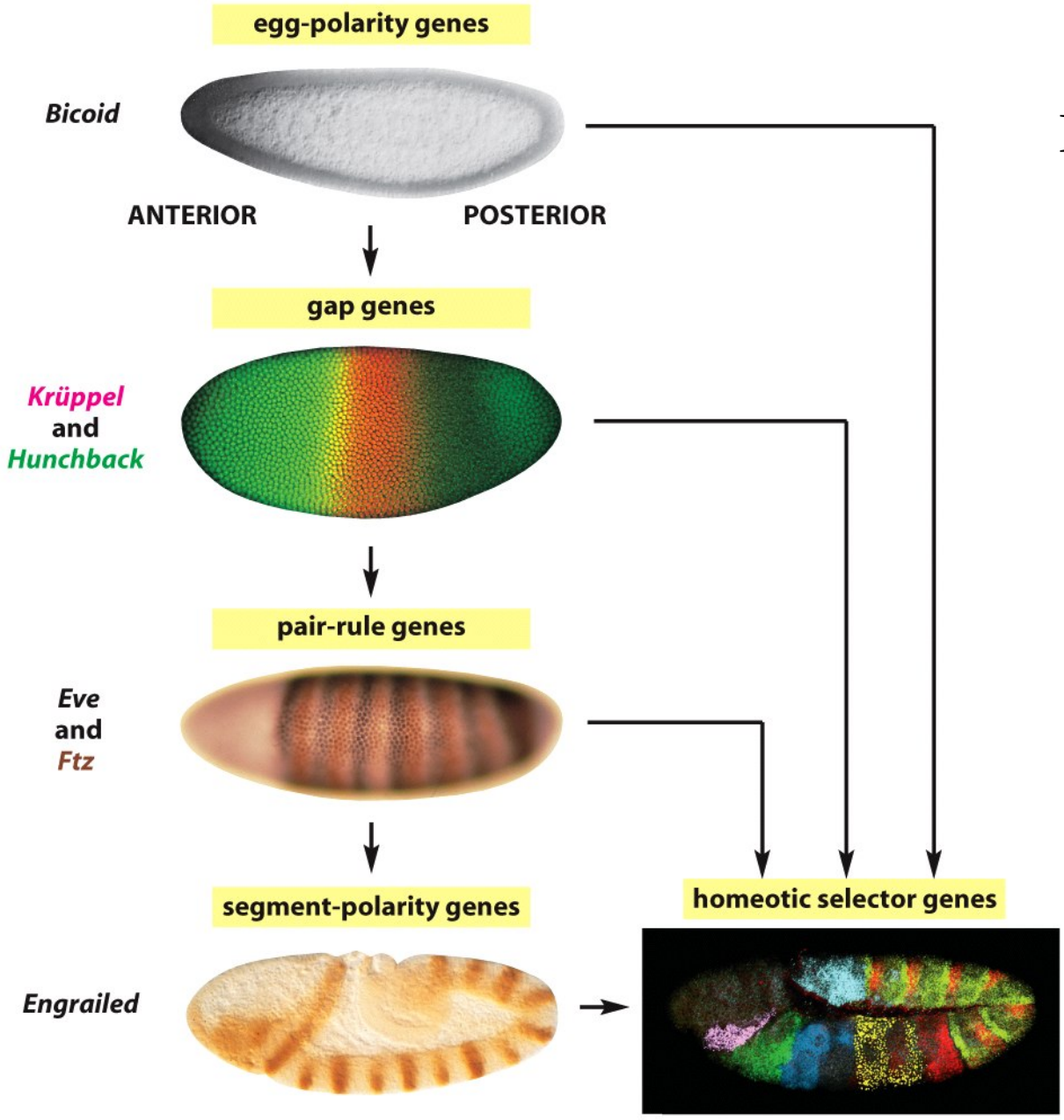


Figure 22-38 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Miten munasta tulee ... eläin

Polaarisuus määräytyy munaan jo ennen hedelmöitystä (***bicoid***)

Segmentaatio (jaokkeellisuus) etenee kolmessa vaiheessa

gap -geenit, joita on noin kuusi (*hunchback*, *Krüppel*, ***knirps***, *tailless*)

parisääntögeenit (pair-rule), vähintään kahdeksan (mm. ***even-skipped***)

segmentin napaisuus -geenit (segment polarity), yli kymmenen (esim. ***engrailed***)

Seuraava askel on universaali:
homeoottiset selektorigeenit reagoivat paikkatietoon kaikilla eläimillä

HOMEOTIC SELECTOR GENES AND THE PATTERNING OF THE ANTEROPOSTERIOR AXIS

CELL 1341

The Hox Code Specifies Anterior–Posterior Differences

CELL 1342

Homeotic Selector Genes Code for DNA-Binding Proteins That Interact with Other Gene Regulatory Proteins

CELL 1342

The Homeotic Selector Genes Are Expressed Sequentially According to Their Order in the Hox Complex

CELL 1343

The Hox Complex Carries a Permanent Record of Positional Information

CELL 1344

The Anteroposterior Axis Is Controlled by *Hox* Selector Genes in Vertebrates Also

CELL 1344

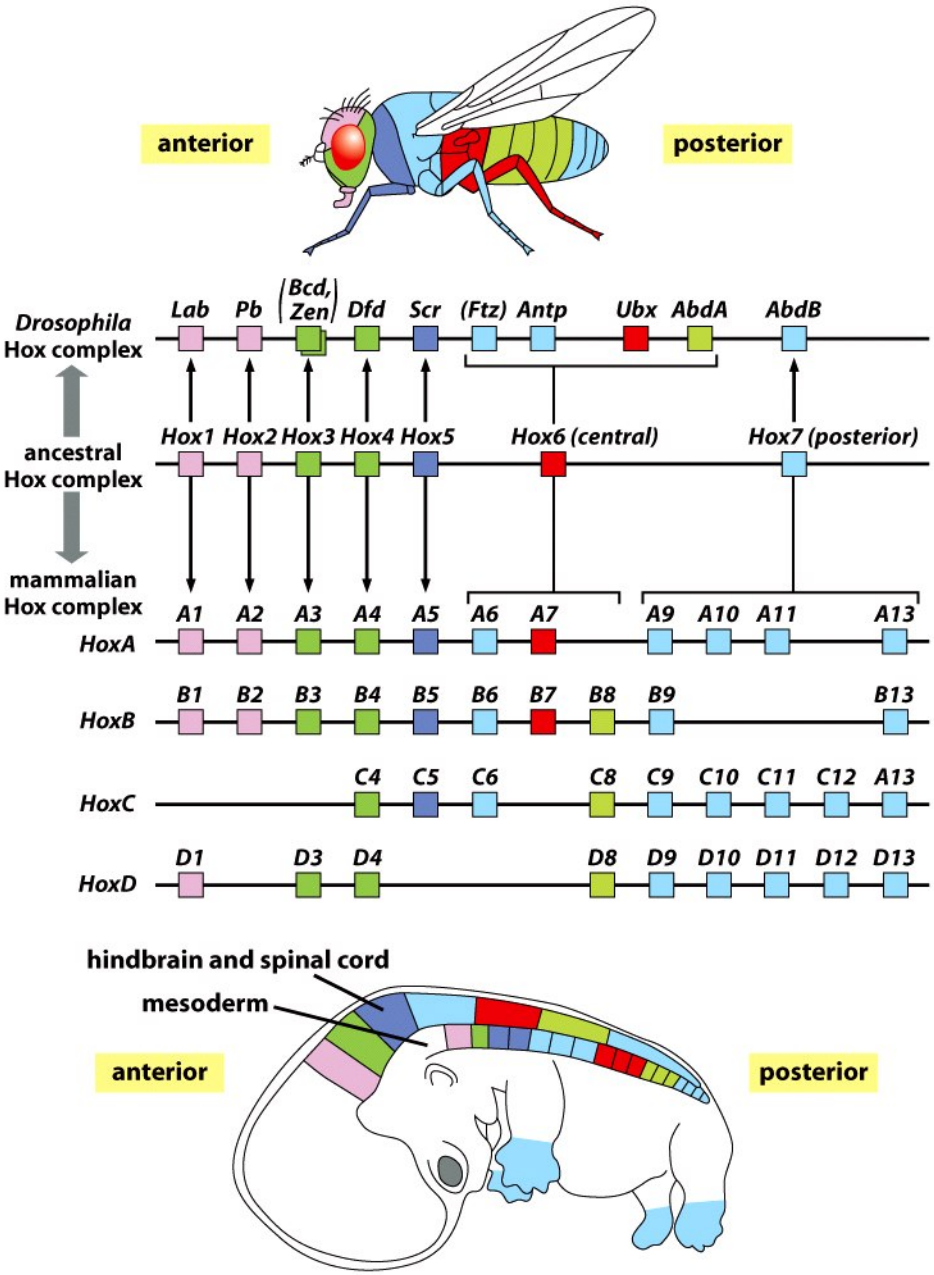


Figure 22-46 Molecular Biology of the Cell 5/e (© Garland Science 2008)

kärpänen

alkueläin (siis monisoluinen, ei mikään protista, vaan esim *Hydra*)

hiiri (= ihminen)

CELL 1346

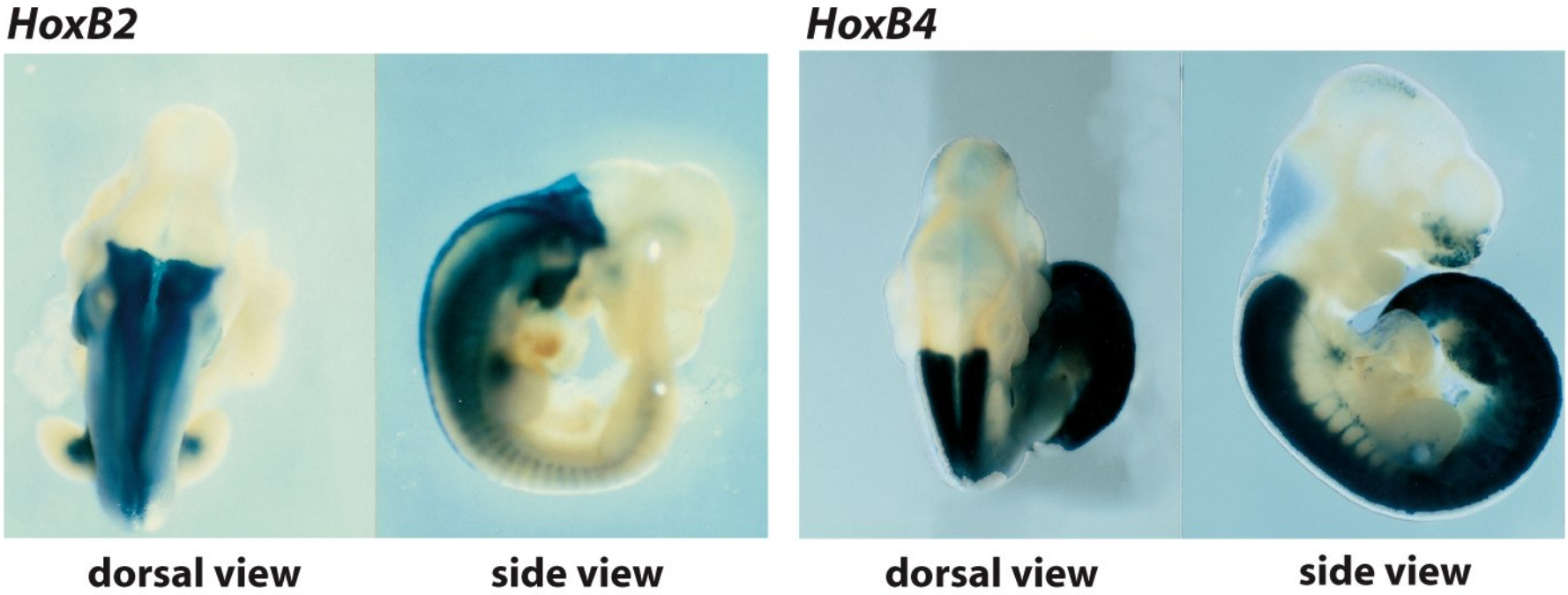


Figure 22-47 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Hiiren alkio: kahden *Hox*-geenin ekspressio

CELL 1346

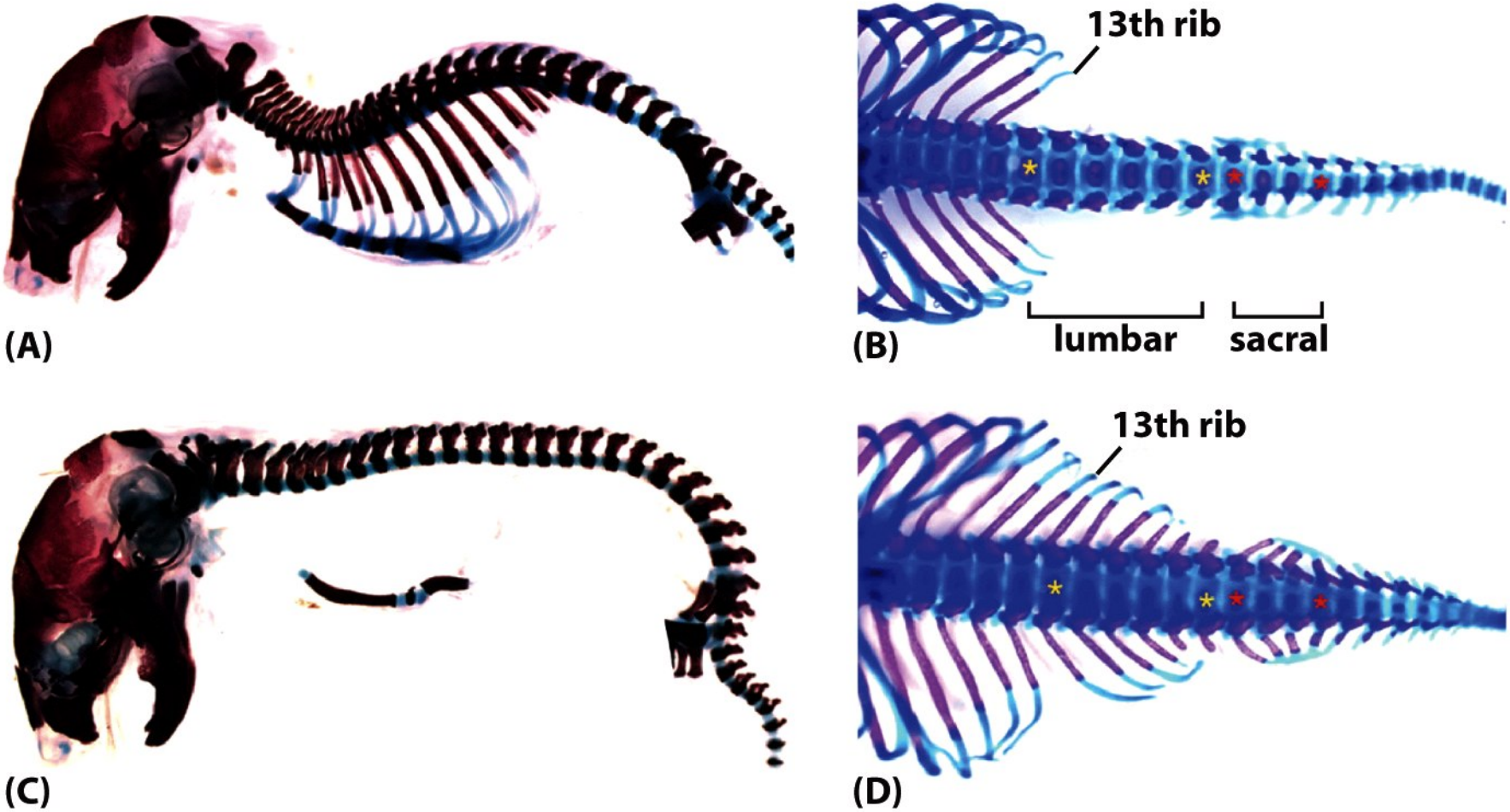


Figure 22-48 Molecular Biology of the Cell 5/e (© Garland Science 2008)

CELL 1347

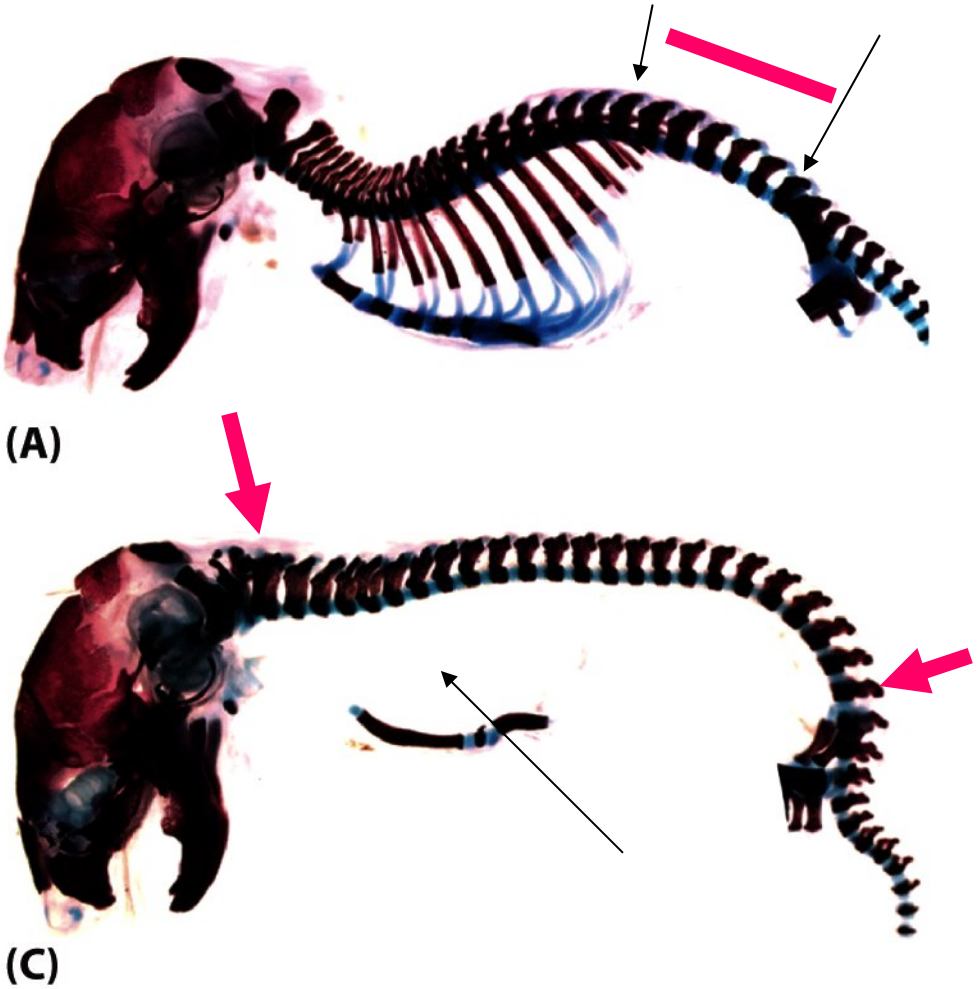
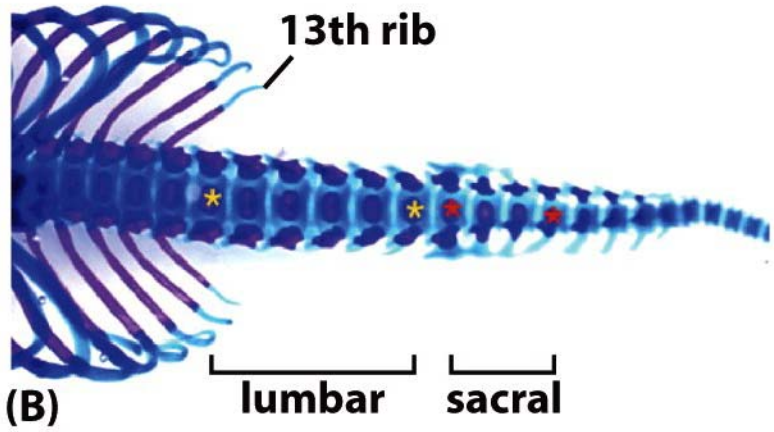
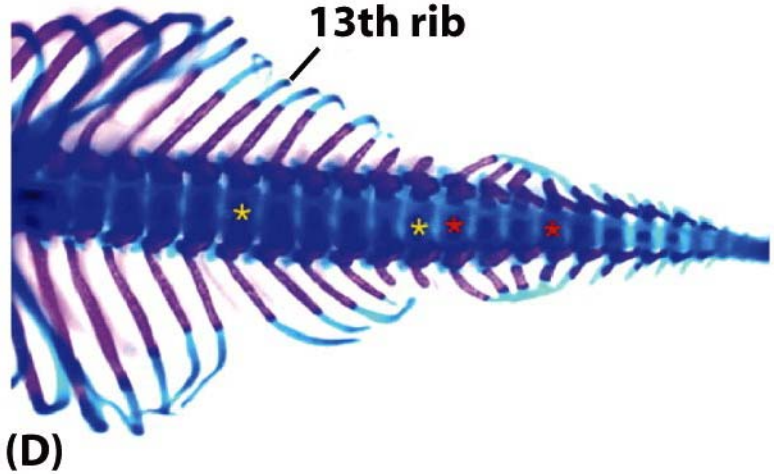


Figure 22-48 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Figure 22–48 Control of anteroposterior pattern by *Hox* genes in the mouse. (A,B) A normal mouse has about 65 vertebrae, differing in structure according to their position along the body axis: 7 cervical (neck), 13 thoracic (with ribs), 6 lumbar (bracketed by *yellow* asterisks in (B)), 4 sacral (bracketed by *red* asterisks in (B)), and about 35 caudal (tail). (A) shows a side view; (B) shows a dorsal view; for clarity, the limbs have been removed in each picture. (C) The *HoxA10* gene is normally expressed in the lumbar region (together with its paralogs *HoxC10* and *HoxD10*); here it has been artificially expressed in the developing vertebral tissue all along the body axis. As a result, the cervical and thoracic vertebrae are all converted to a lumbar character. (D) Conversely, when *HoxA10* is knocked out along with *HoxC10* and *HoxD10*, vertebrae that should normally have a lumbar or sacral character take on a thoracic character instead. (A and C, from M. Carapuço et al., *Genes Dev.* 19:2116–2121, 2005. With permission from Cold Spring Harbor Laboratory Press; B and D, from D.M. Wellik and M.R. Capecchi, *Science* 301:363–367, 2003. With permission from AAAS.)

CELL 1347





character. (D) Conversely, when *HoxA10* is knocked out along with *HoxC10* and *HoxD10*, vertebrae that should normally have a lumbar or sacral character take on a thoracic character instead. (A and C, from M. Carapuço et al., *Genes Dev.* 19:2116–2121, 2005. With permission from Cold Spring Harbor Laboratory Press; B and D, from D.M. Wellik and M.R. Capecchi, *Science* 301:363–367, 2003. With permission from AAAS.)

Calvin Bridges löysi *bithorax*-mutantin vuonna 1915. Mutaatio muunsi halterin (väristin) vähän siipimäisemmäksi kuin se on.

Homeoottinen tarkoittaa sitä, että mutaatio muuttaa jonkin osan jonkun toisen osan kaltaiseksi (hede>emi, jalka> siipi, *etc*.)

Ed Lewis alkoi tutkia *bithorax*ia vuonna 1946. Geenipä olikin tosi vaikea, ja varhainen molekyylibiologia ei tukenut tutkimusta lainkaan, päinvastoin, sotki ajattelua pahasti. Doktriini oli:

yksi geeni, yksi proteiini

Lewis ei hellittänyt. Lopulta hänen mallinsa oli varsin monimutkainen, ettei juuri kukaan jaksanut edes ajatella sitä. Noin vuonna 1980 myös Lewis itse oli leikillisesti sanottuna täysin pihalla. Mikään kartoitus ei vienyt lähemmäksi selitystä.

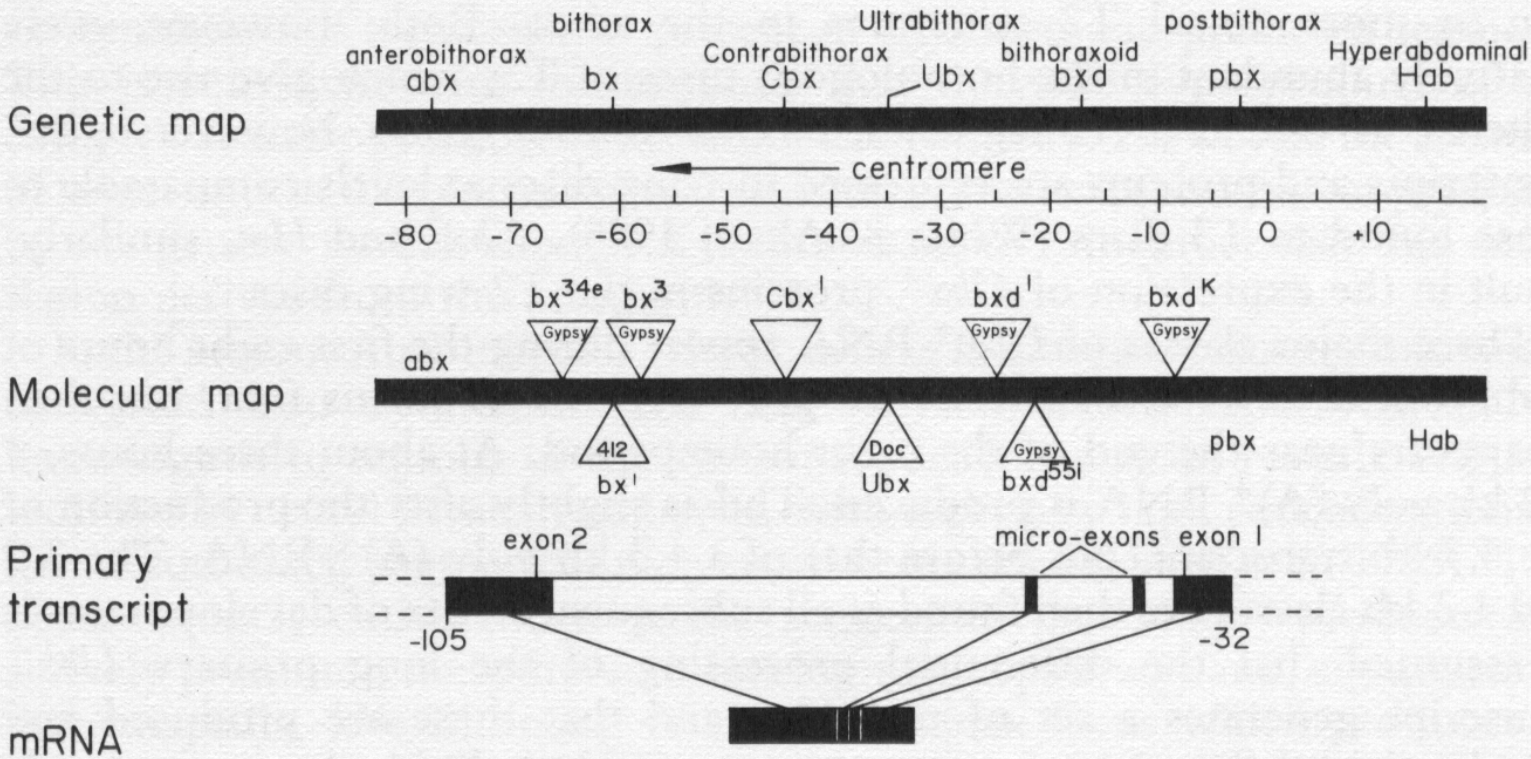


Figure 2.12 A comparison of the genetic and molecular maps of the left half of the Bithorax Complex of *Drosophila melanogaster* and the primary transcript and mRNA produced by the *Ubx*$^+$ region. The triangles denote DNA insertions (data of Bender *et al.* 1983b). Updated versions of these maps are available in Hogness *et al.* (1985), while the right half of the complex has been mapped by Bender *et al.* (1985) and Karch *et al.* (1985).

John & Miklos (1988) The eukaryote genome in development and evolution. Allen & Unwin

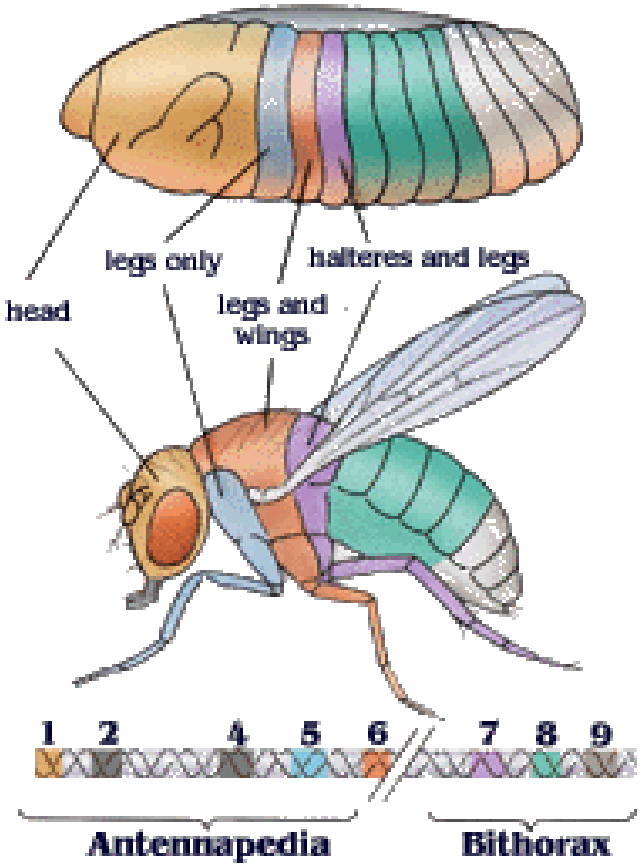
Mutta sitten alkoi molekyyligenetiikan aikakausi.

1982 alkaen muutamat laboratoriot yrittivät toista tietä: *bithorax*-kompleksin (***BX-C***) kimppuun iskettiin juuri keksityllä geenin kloonaamis- ja sekvensointikonstilla. Nimiä ei enää mainita, koska niitä on niin paljon.

Ed Lewis sai Nobelinsa vuonna 1995

Me voimme opetella oleelliset asiat homeoottisista selektorigeeneistä hyvin helpolla tavalla, mikä ei vähennä innostus-kiihtymystä.

Vasta tässä vaiheessa löytyy jotakin, mikä on yhteistä kaikille eläimille myös morfologisessa mielessä!



Aikuisen kärpäsen ja embryon välissä on kolme toukkavaihetta ja kotelovaihe.

Kotelovaiheessa tapahtuu metamorfoosi.

Ekologialtaan toukka ja aikuinen kuuluvat kokonaan eri maailmoihin!

Aikuista hyönteistä ei voida tehdä toukasta!

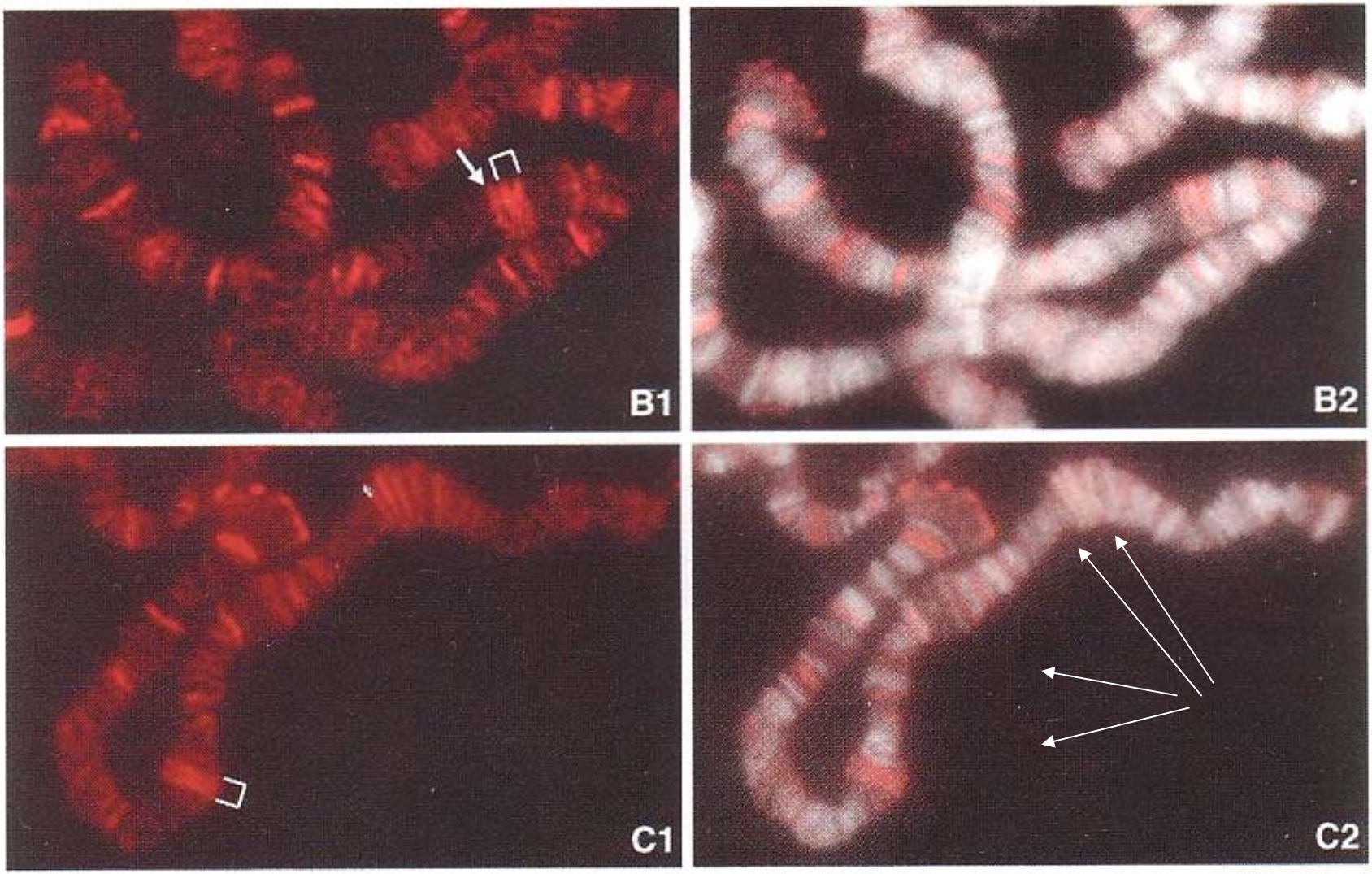
Aikuinen tehdään embryovaiheen lopulla sivuun pannuista aihioista, **imaginaalidiskeistä**

No miten nämä *imaginal diskit* saadaan ***tietämään*** ja ***muistamaan*** tehtävänsä kolmen toukkavaiheen yli?

Homeotic Selector Genes Are Essential for the Memory of Positional Information in Imaginal Disc Cells

The cells of one imaginal disc look like those of another, but grafting experiments show that they are in fact already regionally determined and nonequivalent. If one imaginal disc is transplanted into the position of another in the larva and the larva is then left to go through metamorphosis, the grafted disc is found to differentiate autonomously into the structure appropriate to its origin: a wing disc will give wing structures, a haltere disc, haltere structures, regardless of its new site. This shows that the imaginal disc cells are governed by a memory of their original position. By a more complex serial grafting procedure that lets the imaginal disc cells proliferate for an extended period before differentiating, it can be shown that this cell memory is stably heritable (with rare lapses) through an indefinitely large number of cell generations.

The homeotic selector genes are essential components of the memory mechanism. If, at any stage in the long period leading up to differentiation at metamorphosis, both copies of a homeotic selector gene are eliminated by induced somatic recombination from a clone of imaginal disc cells that would normally express that gene, those cells will differentiate into incorrect structures, as though they belonged to a different segment of the body. These and other observations indicate that each cell's memory of positional information depends on the continued activity of the homeotic selector genes. This memory, furthermore, is expressed in a cell-autonomous fashion—each cell appears to maintain its state individually, depending on its own history and genome.



Engrailed –geenituotteen ***vaikutustapa***

Engrailed –proteiini ***sitoutuu*** lukuisiin erityisiin sylkirauhaskromosomin kohtiin, toisin sanoen ***useiden geenien säätelyalueille*** (punaväri = engrailed-vasta-aine). Nimeltä tunnetaan 86 ”target-geeniä”, siiven, hengitysputkien, lihasten, hermoston ja silmän kehitysketjuista [Solano et al., **Development** Apr 2003]

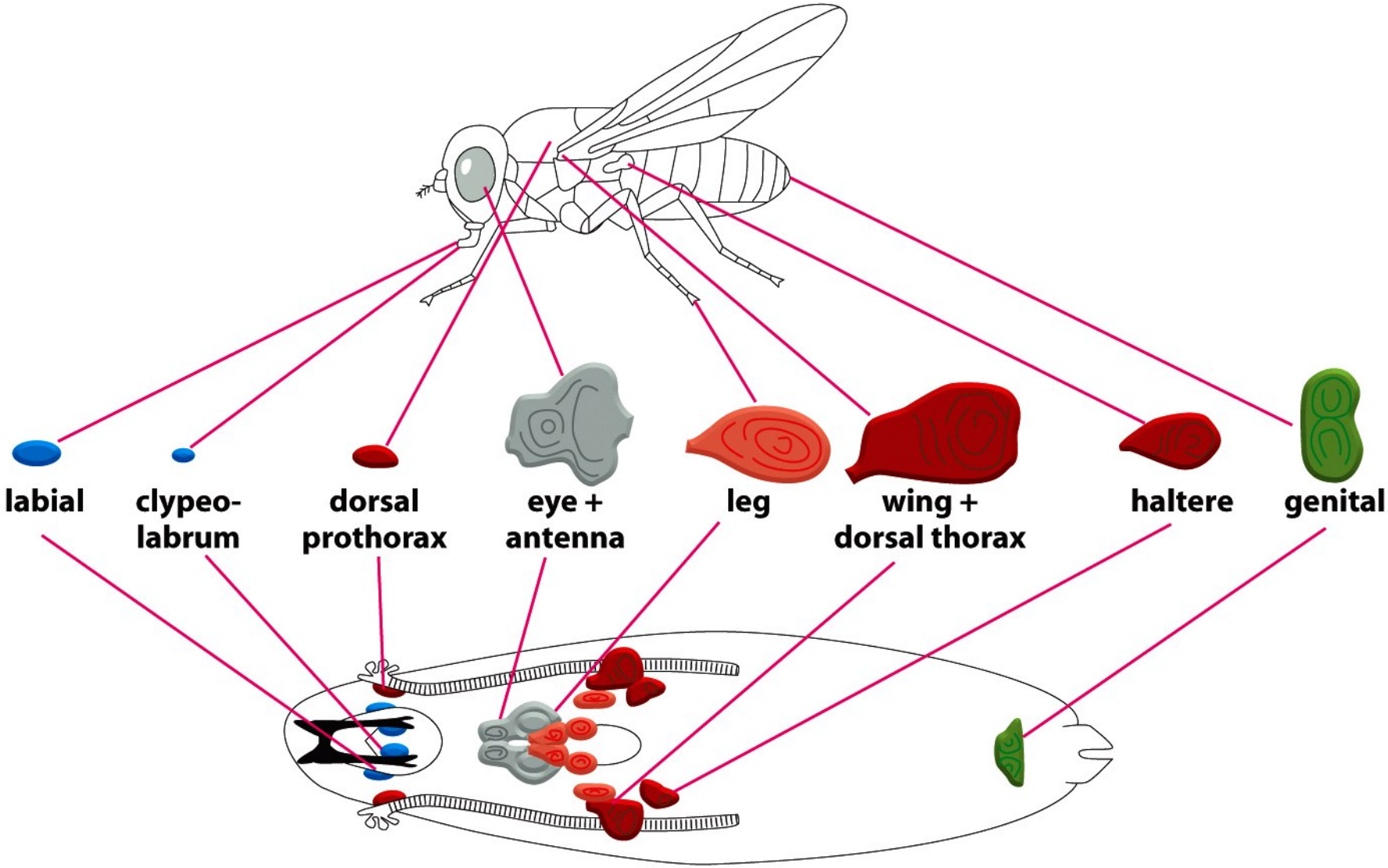
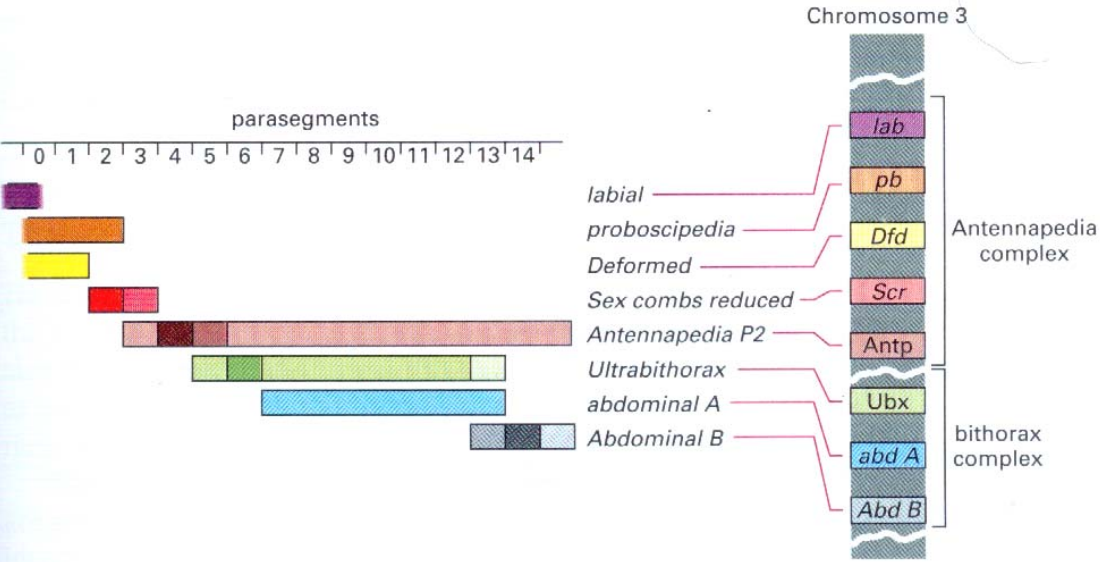
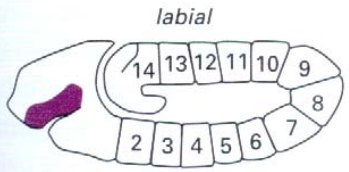
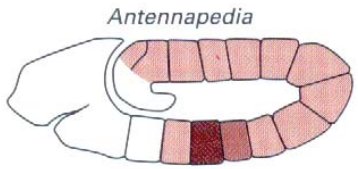
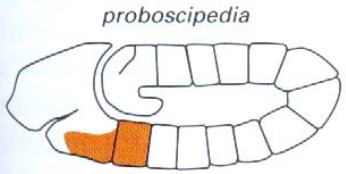


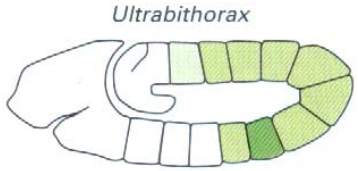
Figure 22-51 Molecular Biology of the Cell 5/e (© Garland Science 2008)

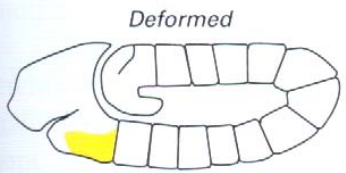


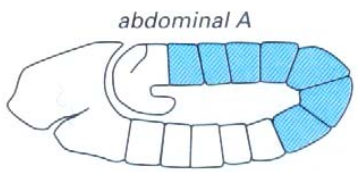


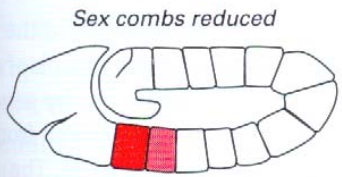


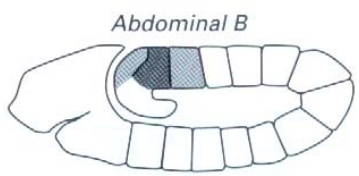










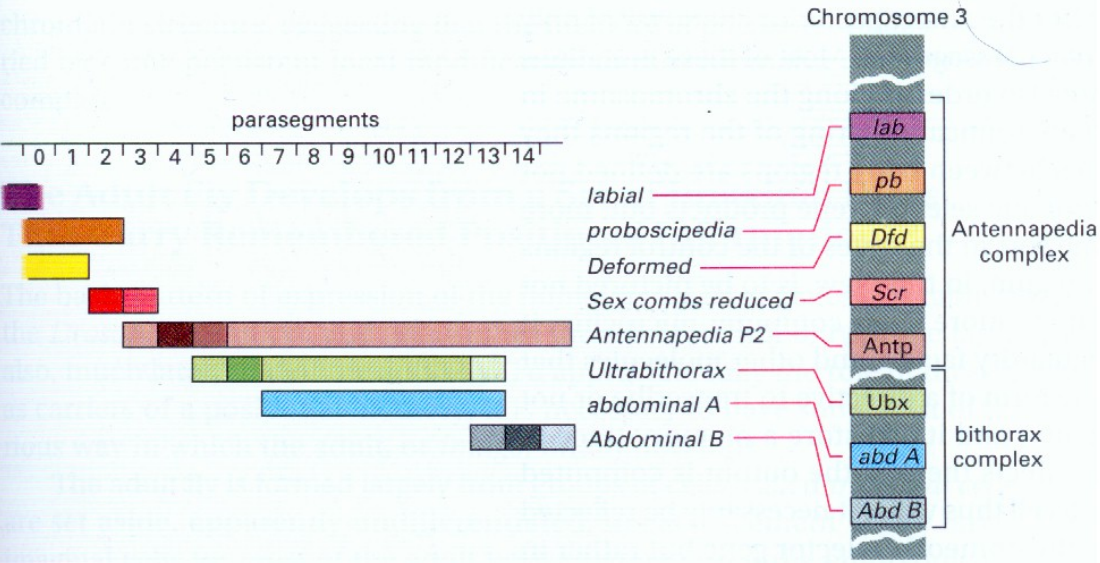


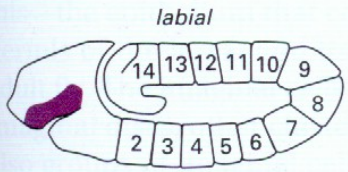
HOM-kompleksin geenit ja niiden toimialueet embryossa

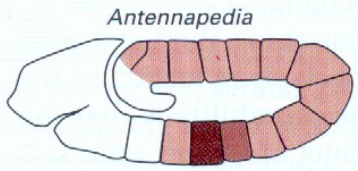
Segmentaatio määrää toimialueen (transkription säätely)

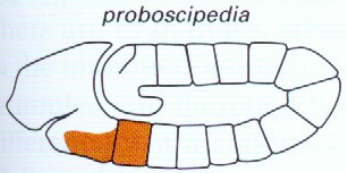
Geeni transkriboidaan ja tulkitaan proteiiniksi

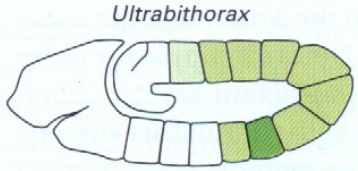
Proteiini tekee tehtävänsä: tallettaa saamansa paikkatiedon ja kertoo sen alueensa tumissa kaikille ***kiinnostuneille*** geeneille

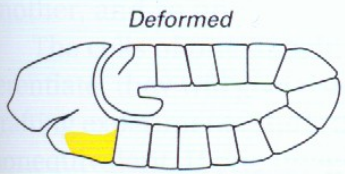


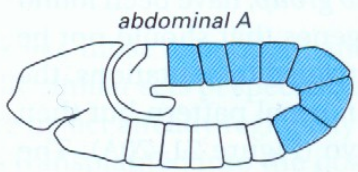


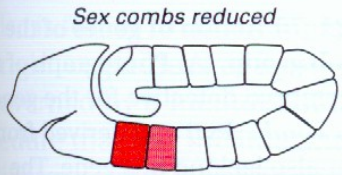


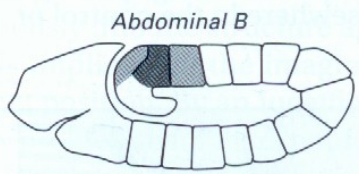


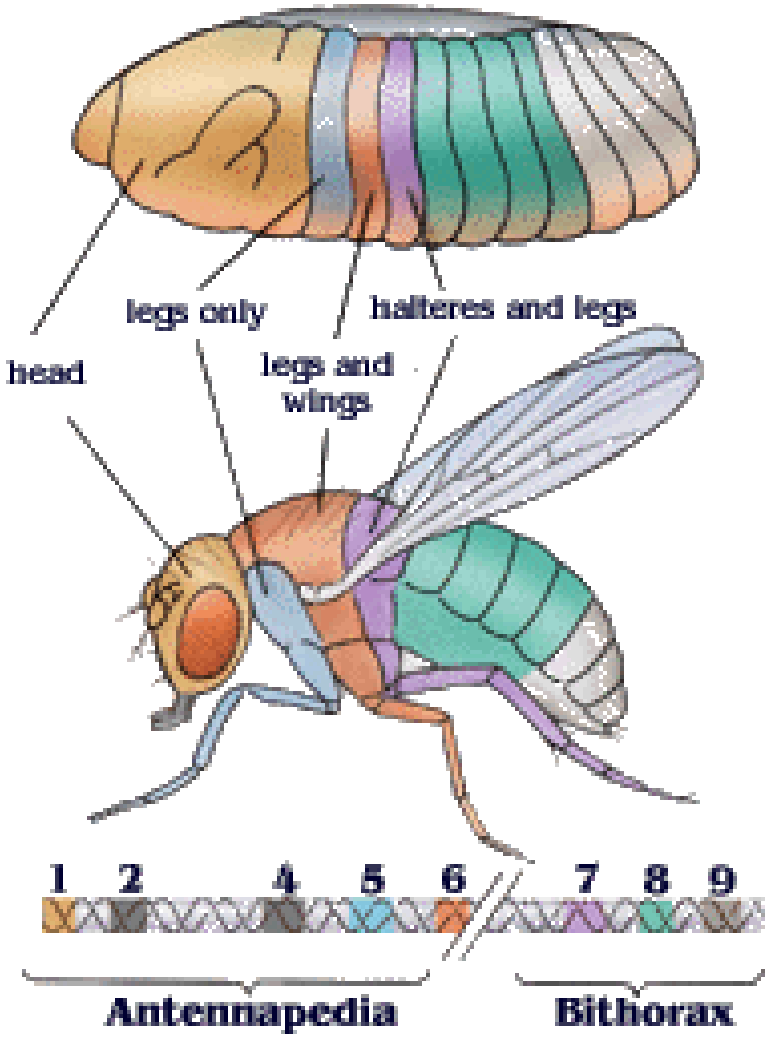












Kaikista näistä geeneistä löytyi **homeoboksi**

Figure 22-42 Molecular Biology of the Cell 5/e (© Garland Science 2008)