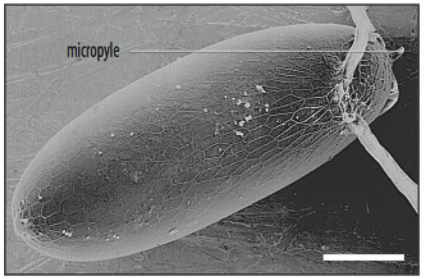
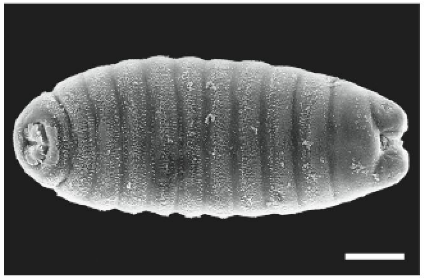
Model organisms and developmental biology

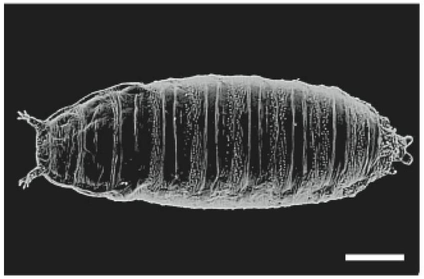
仲寒冰

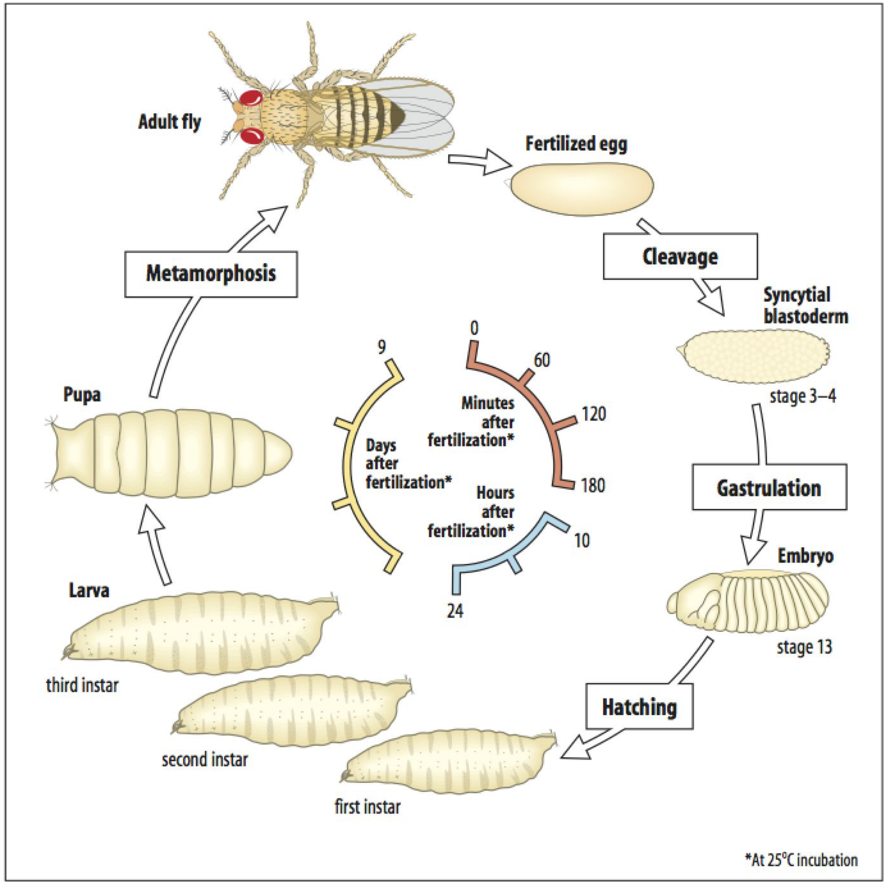
zhong.hb@sustc.edu.cn

Life cycle

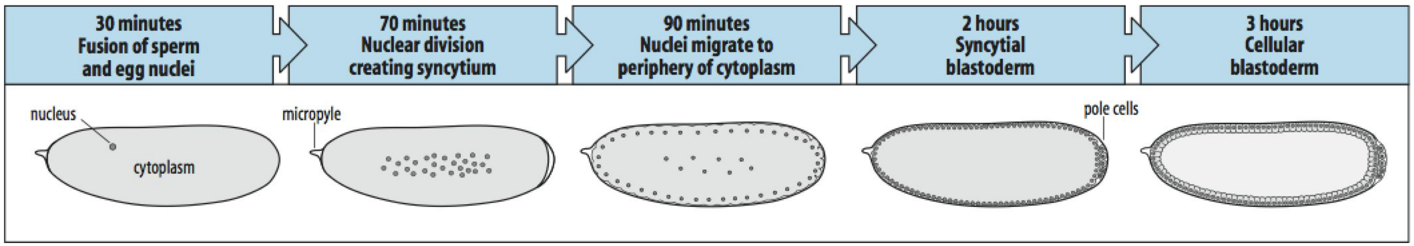

micropyle






Adult fly
Fertilized egg
Cleavage
Syncytial blastoderm
stage 3–4
Gastrulation
Embryo
stage 13
Hatching
first instar
second instar
third instar
Larva
Pupa
Metamorphosis
0
60
120
180
Minutes after fertilization*
10
24
Hours after fertilization*
9
Days after fertilization*
*At 25°C incubation

Cleavage

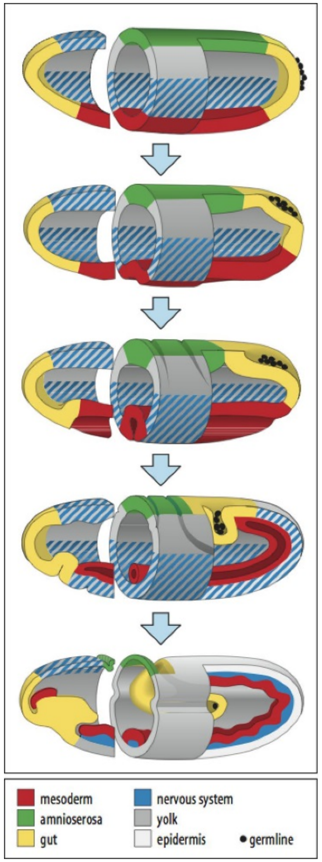


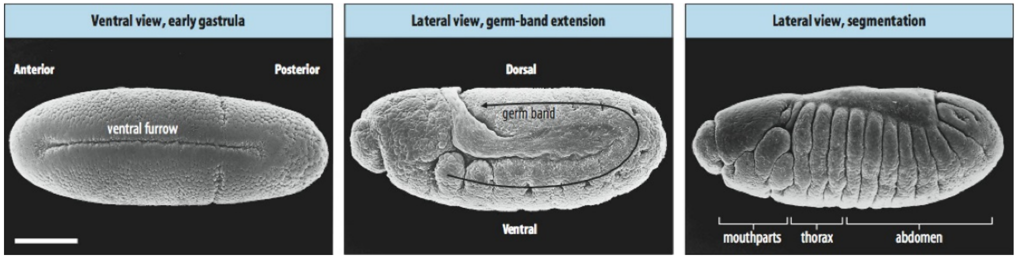
In the first 12 nuclear divisions, there is no cleavage of the cytoplasm. So a syncytium of about 6000 nuclei is formed.

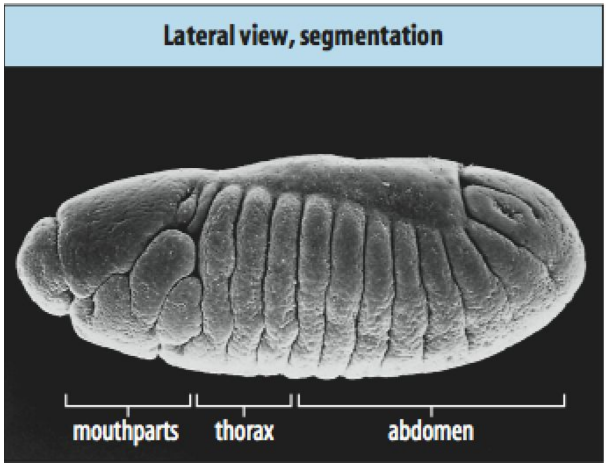
After 9 divisions, the nuclei move to the periphery to form the syncytial blastoderm.

Pole cells, potential germ cells.

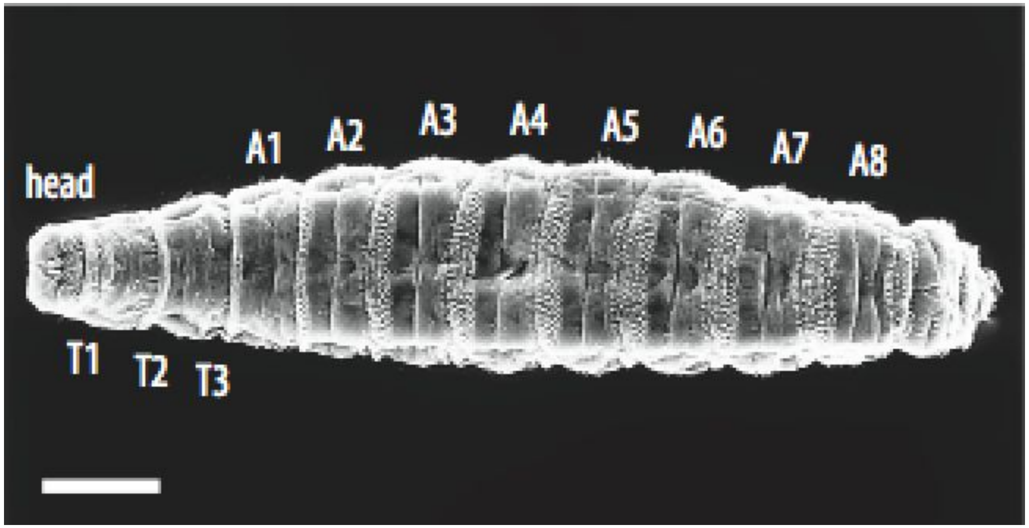
Gastrulation



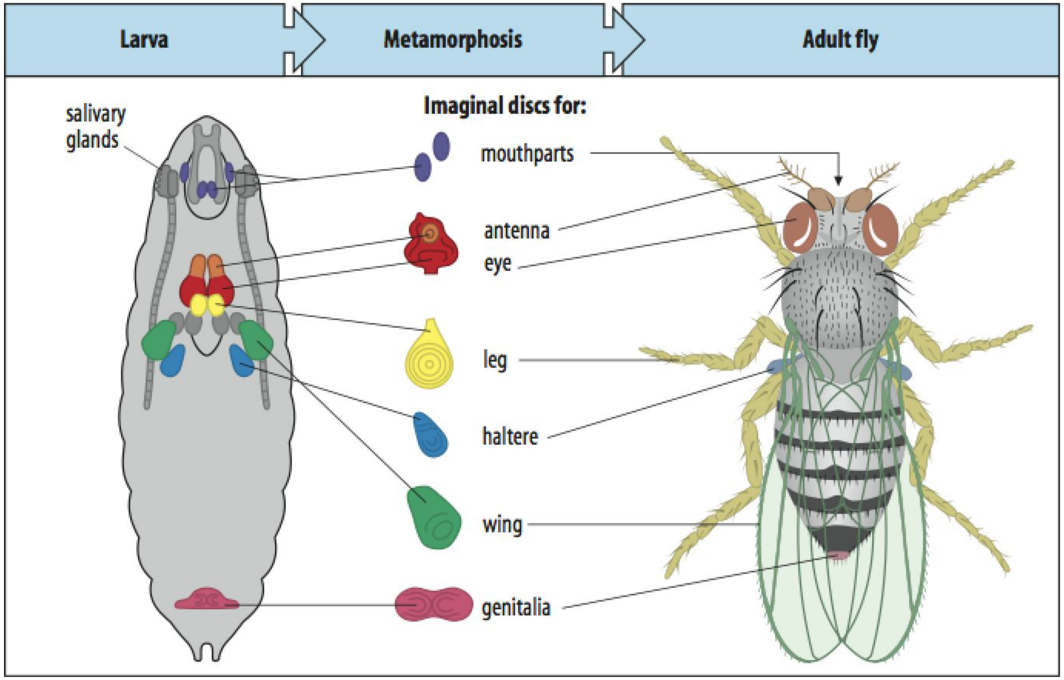




Hatching

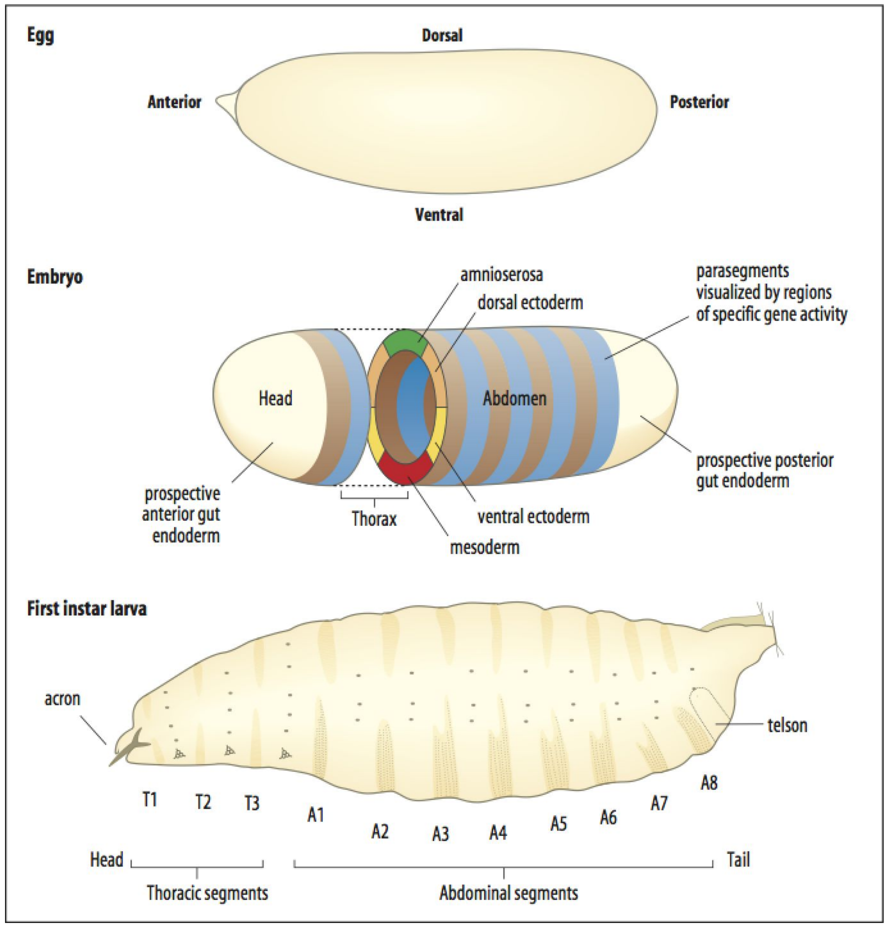


Metamorphosis

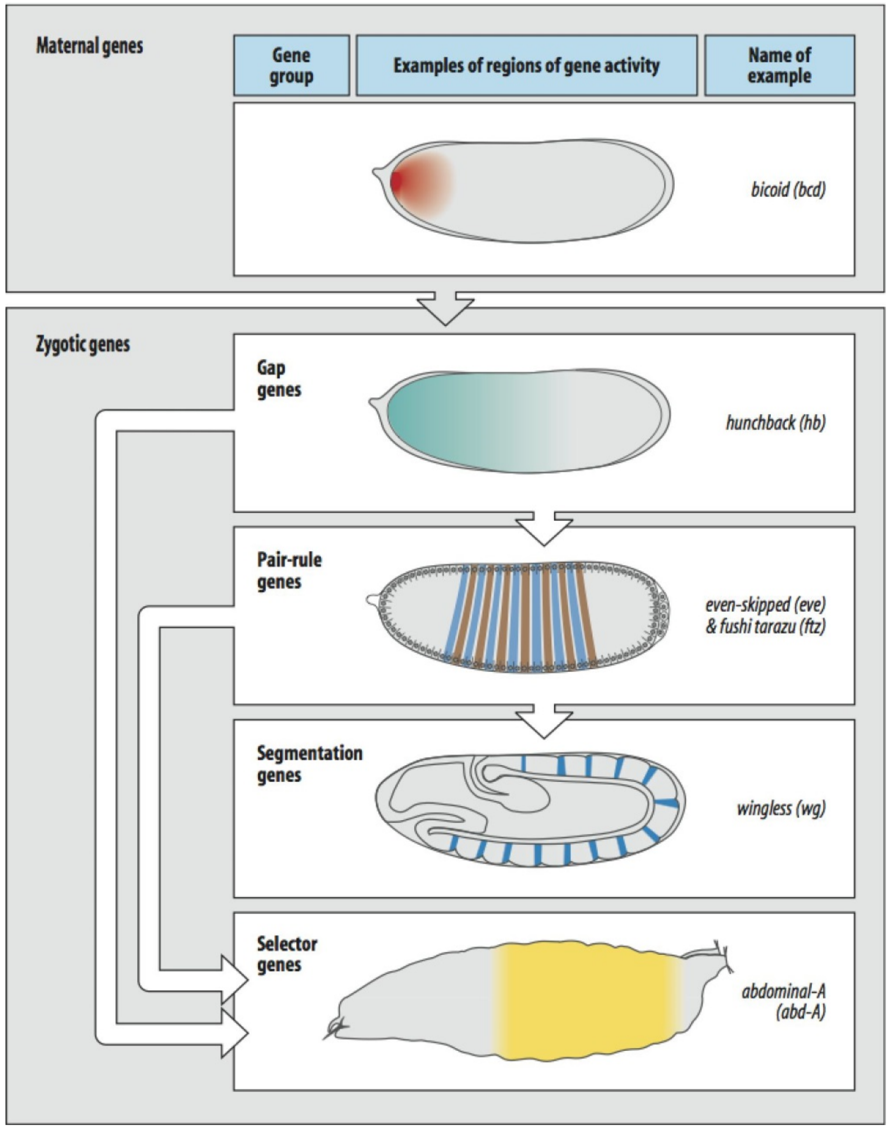


Imaginal discs: folded rudiments of organs

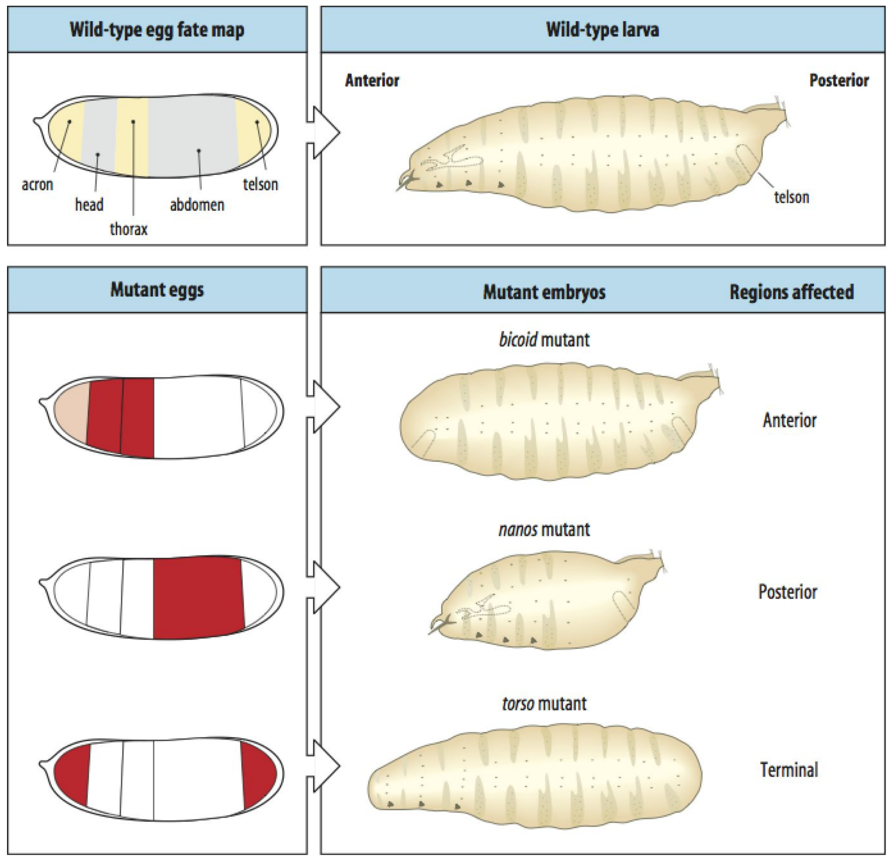
Patterning of the *Drosophila* embryo



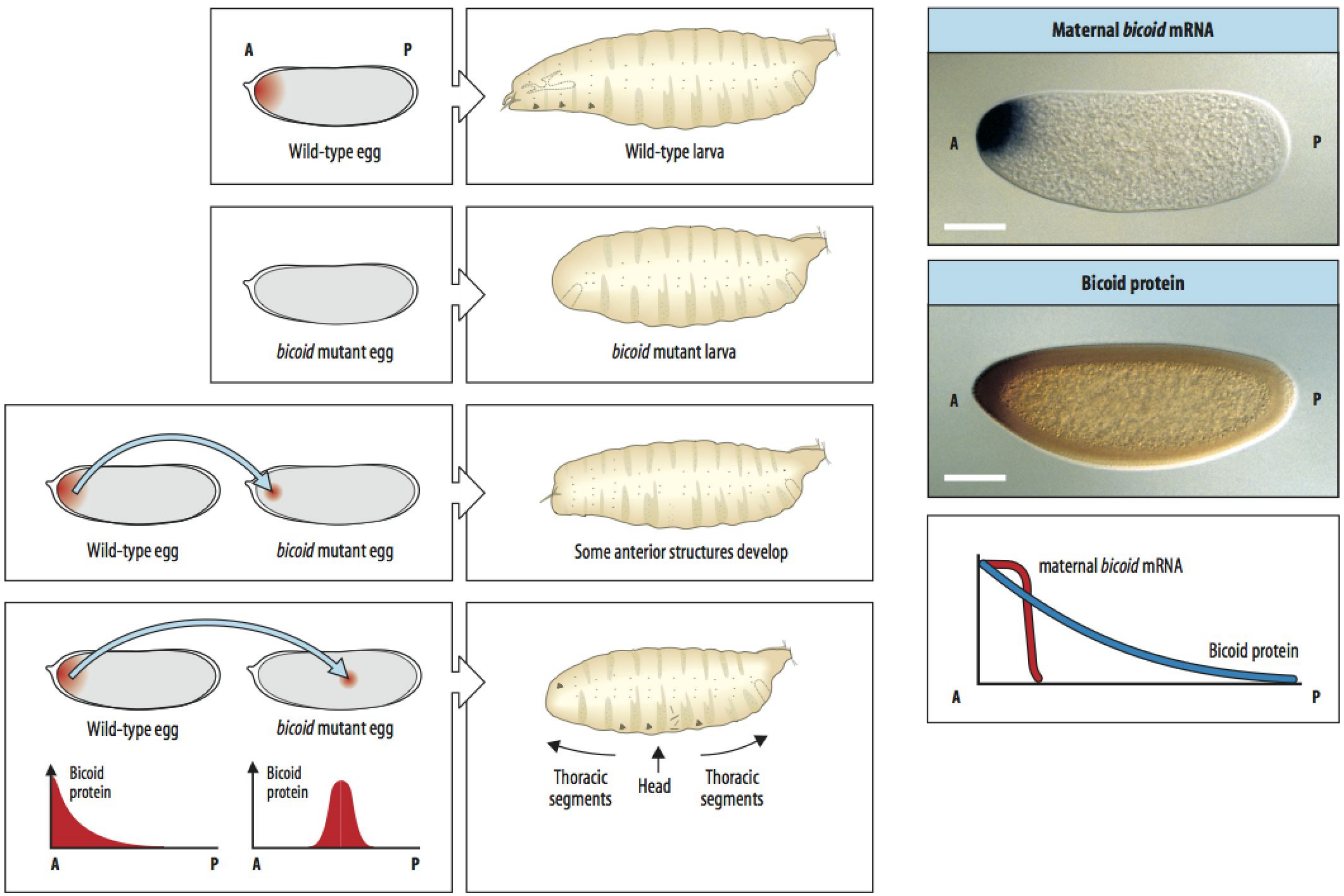
The sequential expression of different sets of genes establishes the body plan



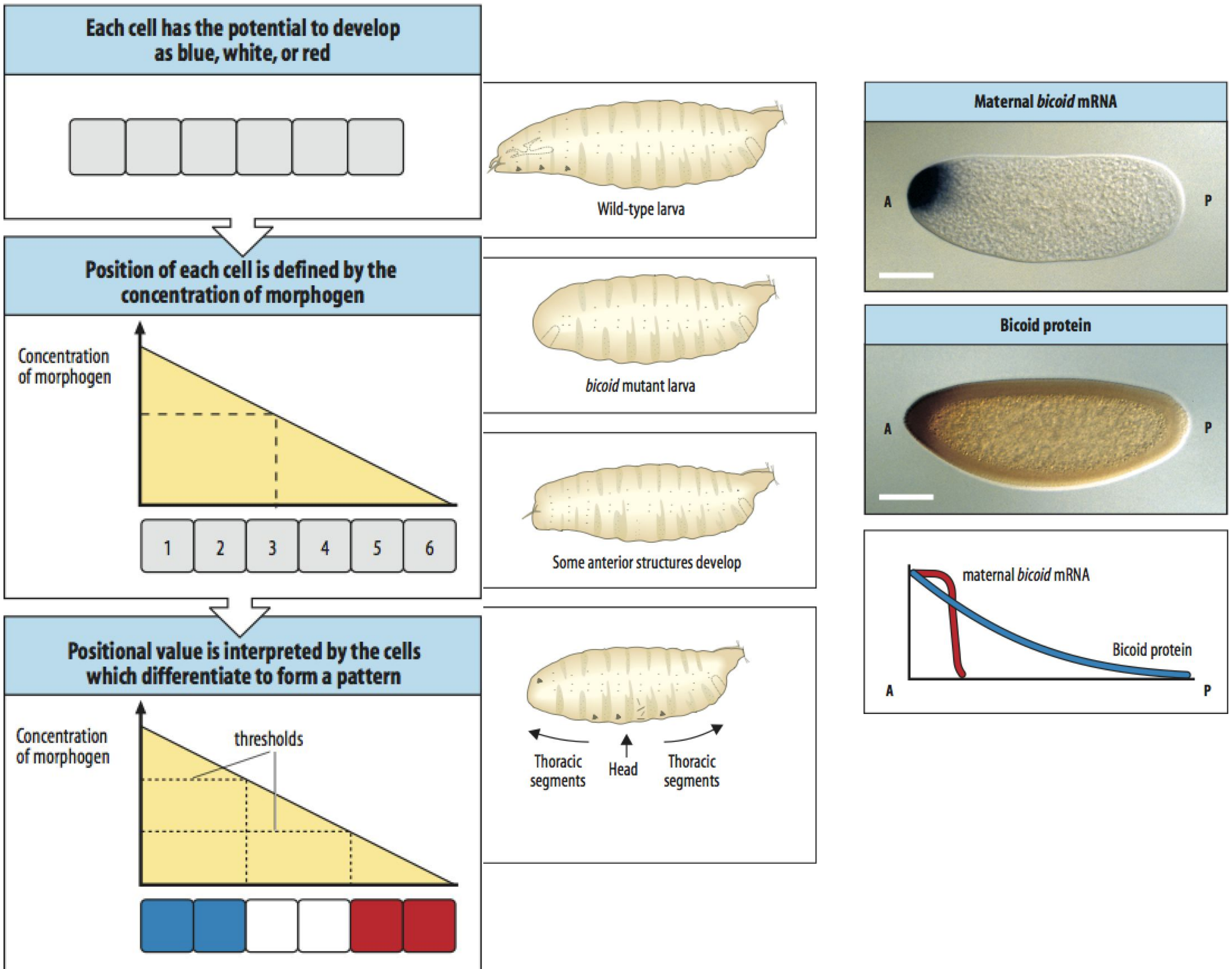
Maternal gene mutants



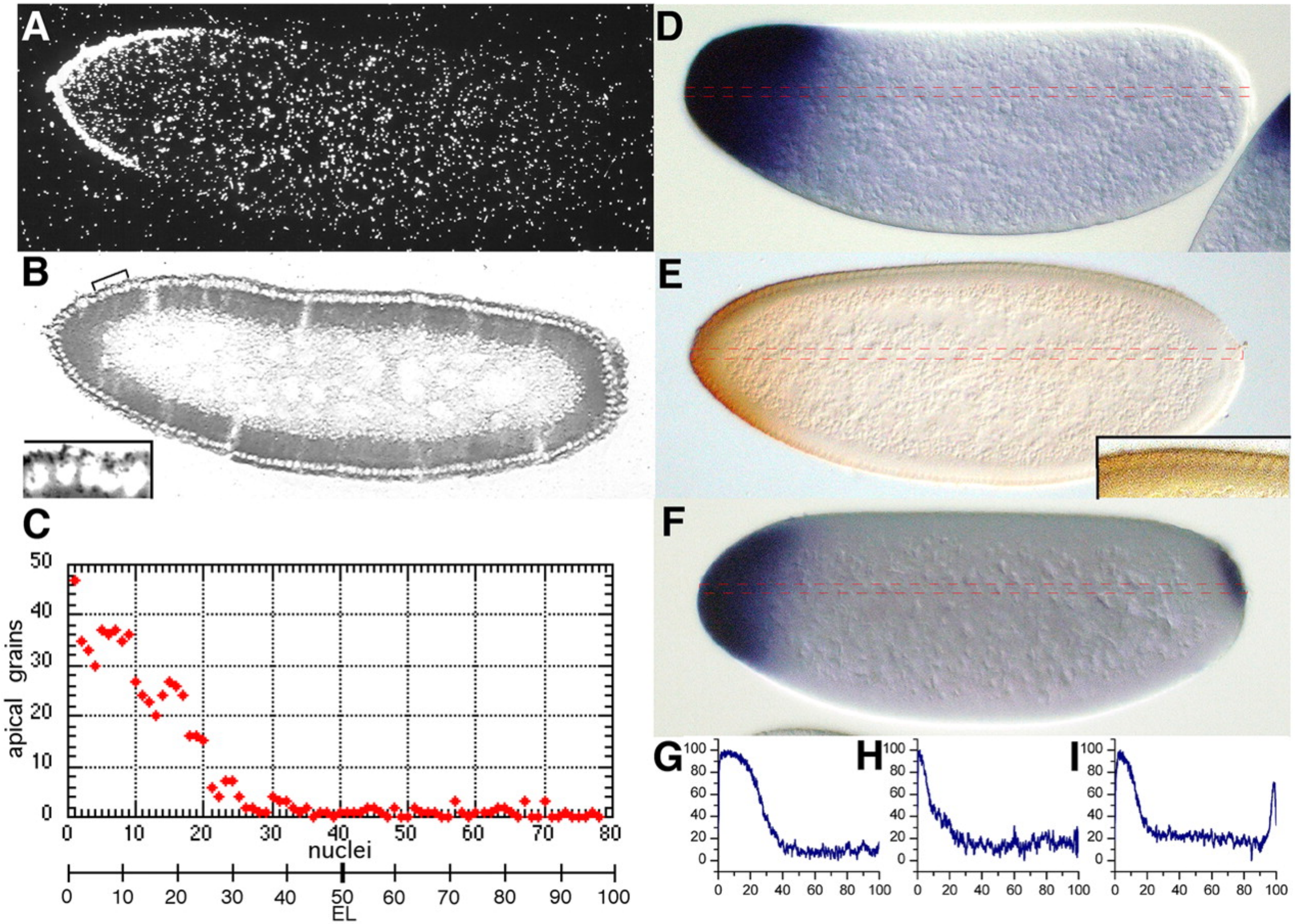
The *bicoid* gene is necessary for the development of anterior structures



The *bicoid* gene is necessary for the development of anterior structures

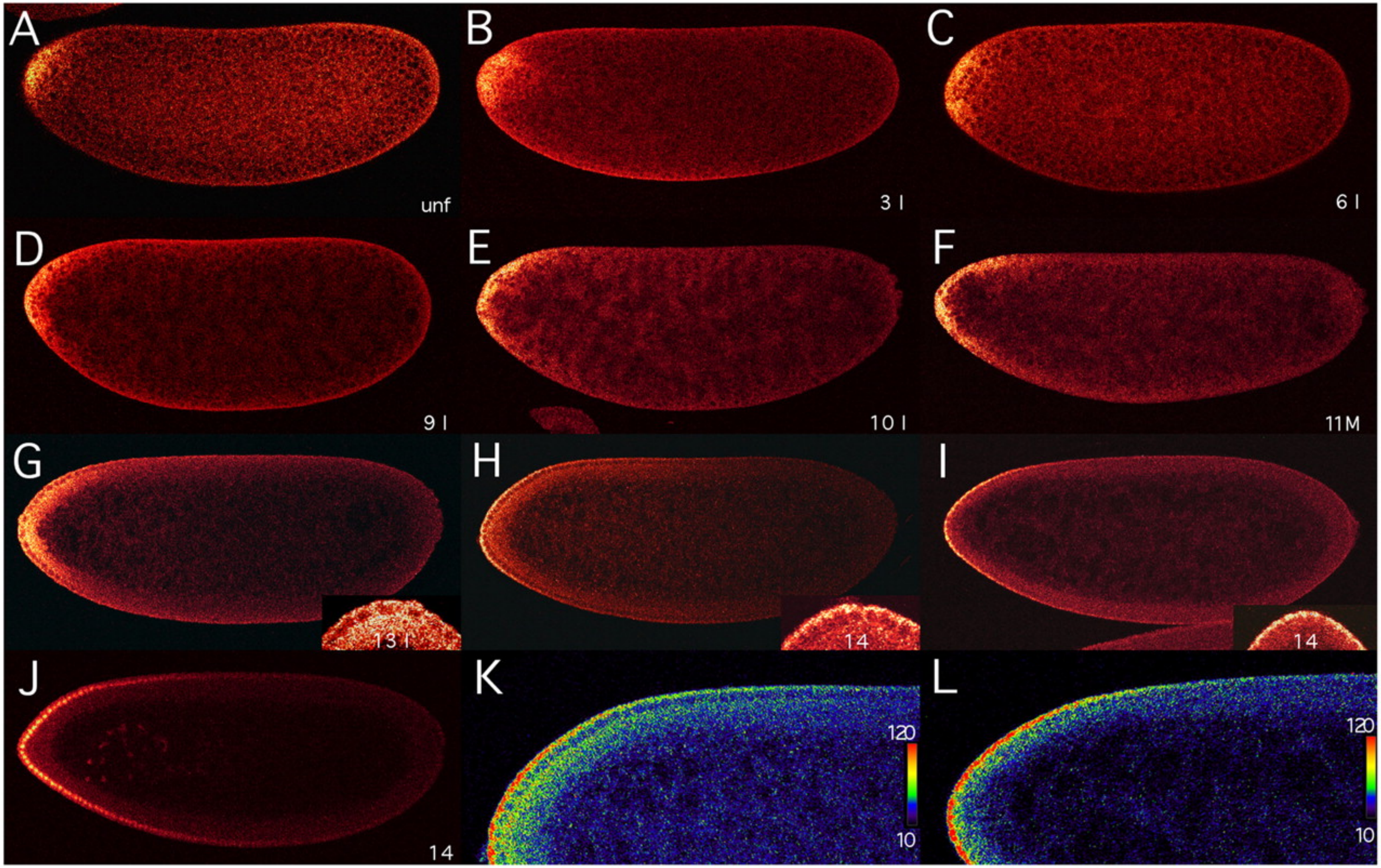


Visualization of the bcd mRNA gradient by established in situ hybridization methods.



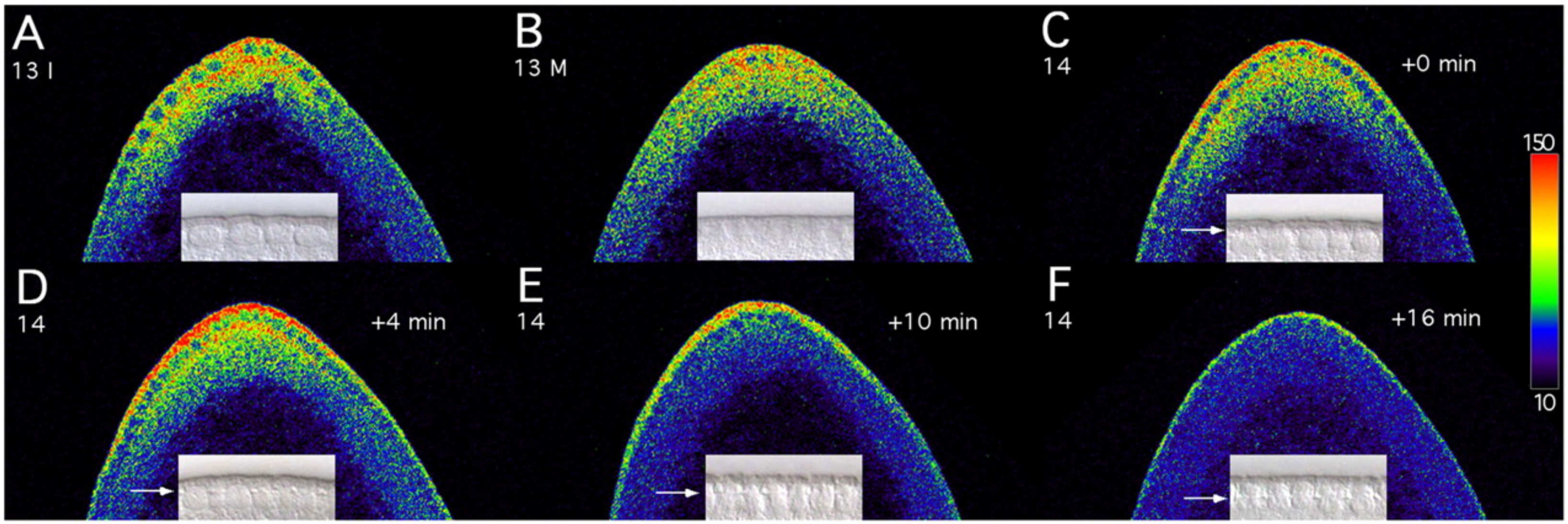
Spirov A et al. Development 2009;136:605-614

Formation of bcd mRNA gradient analyzed by confocal microscopy.



Spirov A et al. Development 2009;136:605-614

Transport of bcd mRNA from basal to apical nuclear periplasm, and its degradation during early nuclear cycle 14.



Spirov A et al. Development 2009;136:605-614

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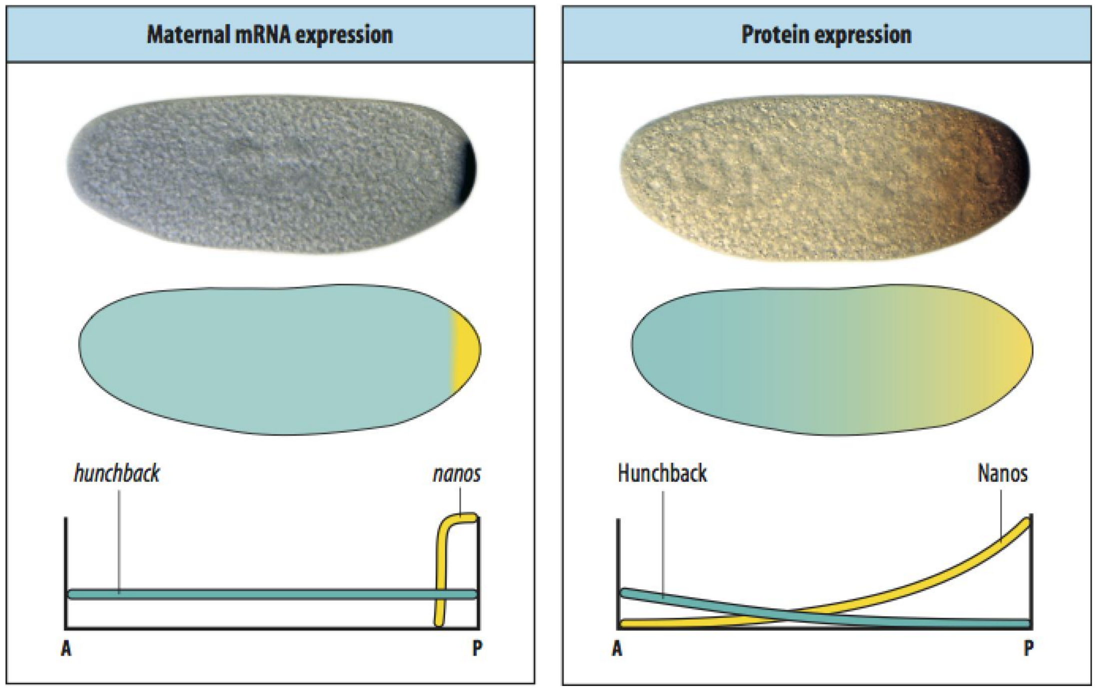
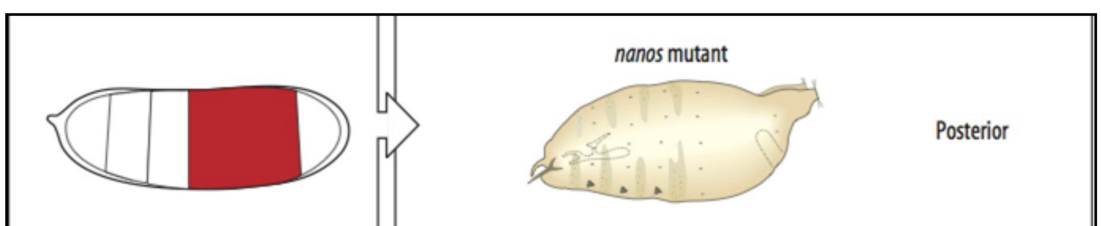
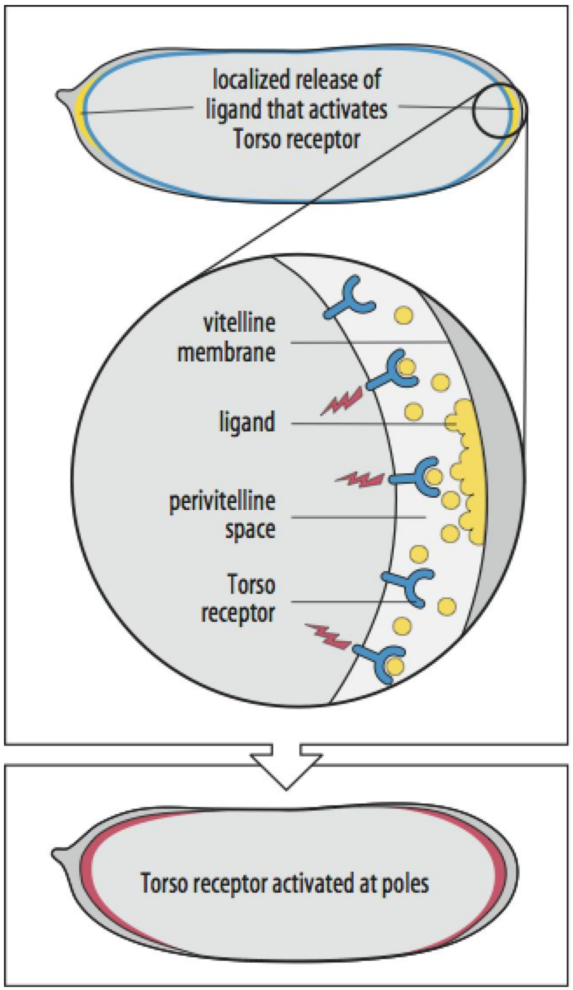
Establishment of a maternal gradient of Hunchback protein



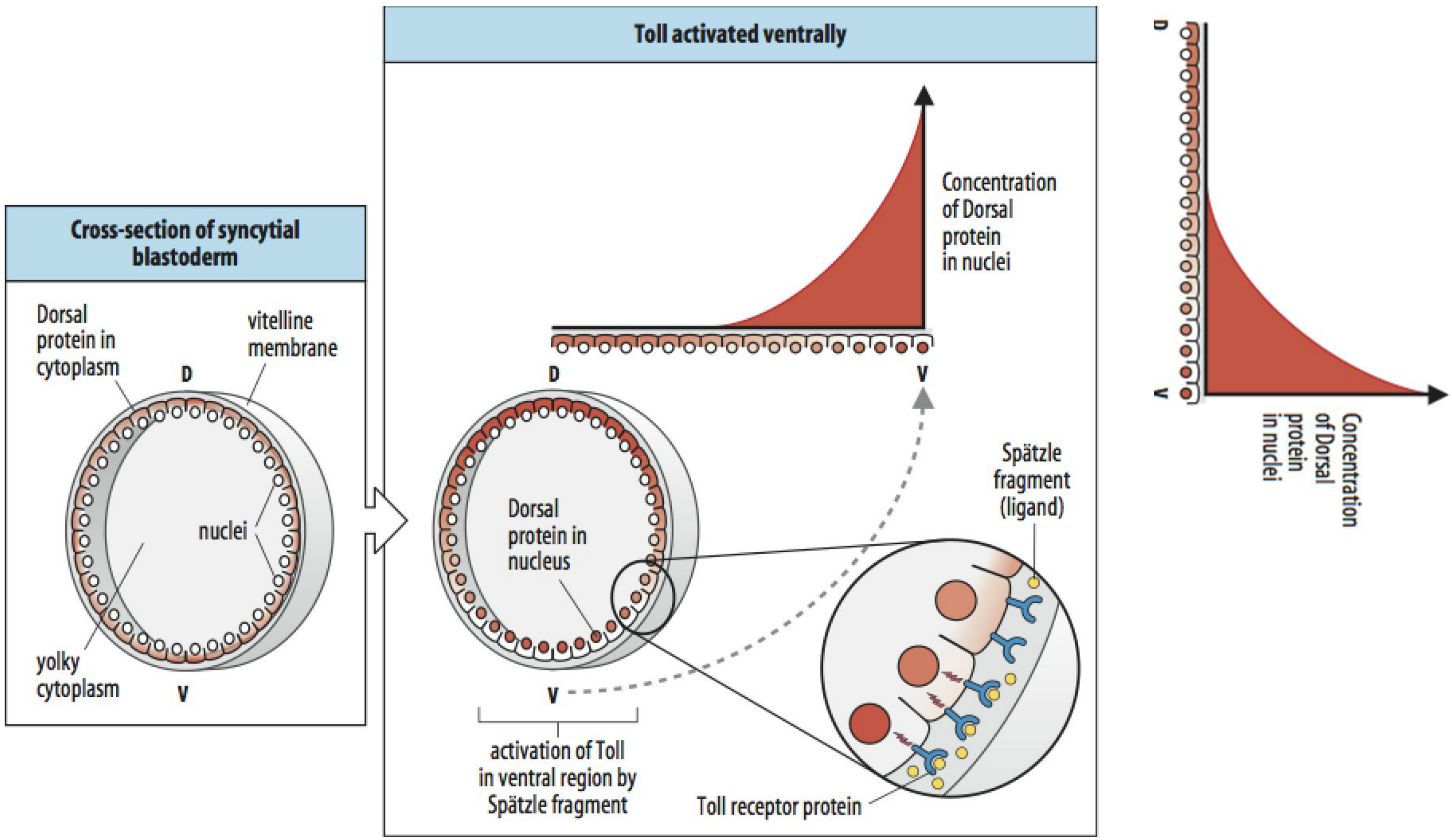


The receptor protein Torso is involved in specifying the terminal regions of the embryo

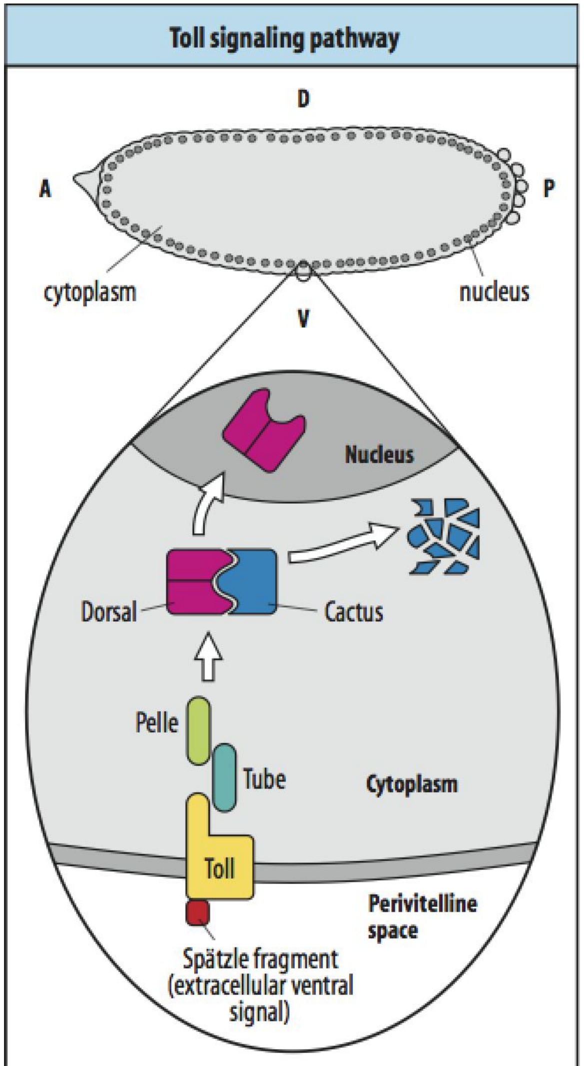


- The receptor Torso is present throughout the fertilized egg.
- The ligand, a fragment of Trunk protein, is present at the ends of the fertilized egg.
- Torso-like is localized at the ends of the fertilized egg.

Toll protein activation results in a gradient of intranuclear Dorsal protein



The Toll signaling pathway



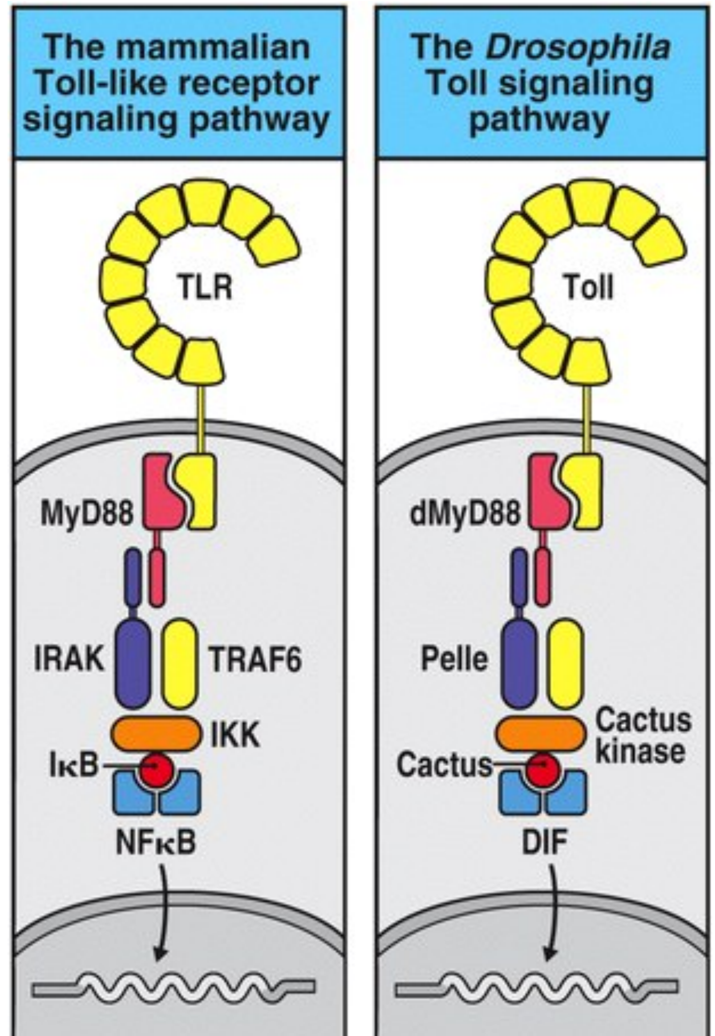


Figure 15-4 Immunobiology, 6/e. (© Garland Science 2005)

The Nobel Prize in Physiology or Medicine 2011

Bruce A. Beutler

Jules A. Hoffmann

Photo: The Rockefeller University

Ralph M. Steinman

The Nobel Prize in Physiology or Medicine 2011 was divided, one half jointly to Bruce A. Beutler and Jules A. Hoffmann *"for their discoveries concerning the activation of innate immunity"* and the other half to Ralph M. Steinman *"for his discovery of the dendritic cell and its role in adaptive immunity"*.

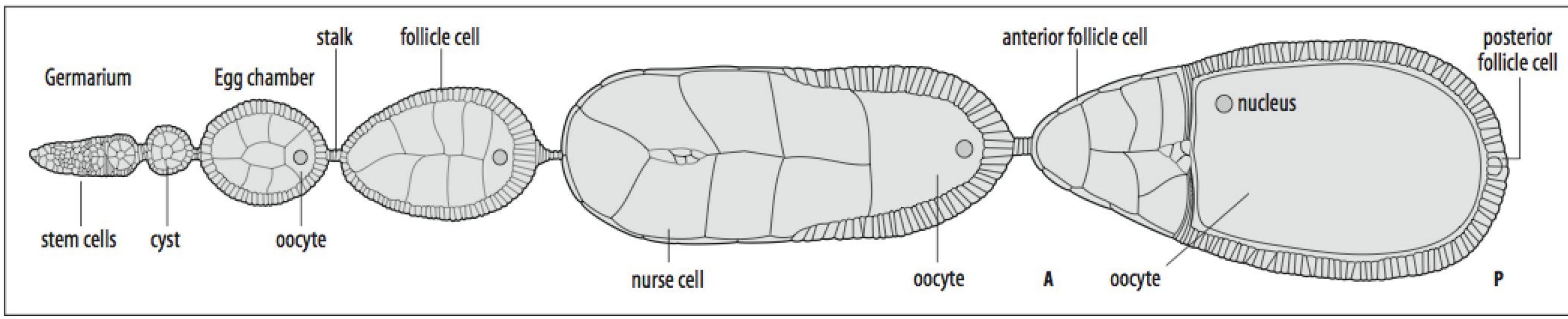
Milestones in the discovery of Toll-like receptor

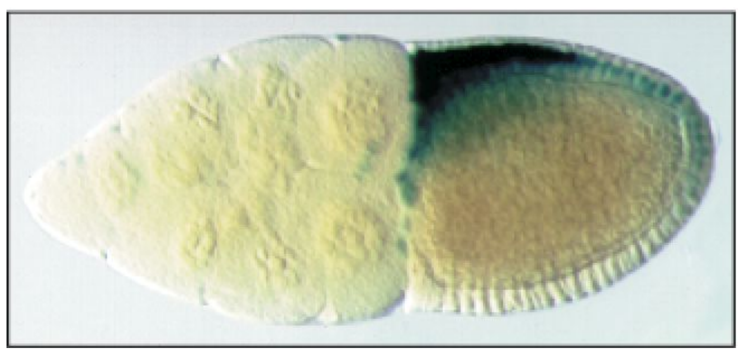
- 1980年，Nusslein-Volhard等在研究果蝇胚胎发育过程中发现有一个基因决定着果蝇的背腹分化，将其命名为Toll基因。
- 1988年，Hashimoto等人发现Toll基因编码一种跨膜蛋白质，并阐明了Toll蛋白的结构。
- 1991年，Gay等人发现，Toll蛋白在结构上与哺乳动物中一种天然免疫功能分子—白细胞介素受体1（IL-1）具有同源性：二者的细胞质部分相似。
- 1994年，Nomura等人首先报道了人中的Toll样受体。
- 1996年，Jules A. Hoffmann和他的同事们发现Toll在果蝇对真菌感染的免疫中起着重要作用，从而确立了Toll的免疫学意义。
- 1997年，Charles Janeway和Ruslan Medzhitov阐明了一种Toll样受体（后来被命名为TLR4）能够激活与适应性免疫有关的基因。
- Bruce A. Beutler随后发现TLR4能够探测LPS（脂多糖）的存在。后来他们又发现，如果使小鼠中的TLR4突变而丧失功能，小鼠不会对LPS起反应。

Common intracellular signals in Drosophila

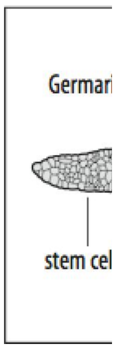
Common intercellular signals used in *Drosophila*		
Family and examples	**Receptors**	**Examples of roles in development**
Hedgehog family		
Hedgehog	Patched	Patterning of insect segments Positional signaling in insect leg and wing discs
Wingless (Wnt) family		
Wingless and other Wnt proteins	Frizzled	Insect segment and imaginal disc specification (Wingless) Other Wnts have roles in development
Delta and Serrate		
Transmembrane signaling proteins	Notch	Roles at many stages in development Specification of oocyte polarity
Transforming growth factor-α (TGF-α) family		
Gurken, Spitz, Vein	EGF receptor (receptor tyrosine kinase) One only in *Drosophila*, known as DER or Torpedo.	Polarization of the oocyte Eye development, wing vein differentiation (see Chapter 9)
Transforming growth factor-β (TGF-β) family		
Decapentaplegic	Receptors act as heterodimers of type I (e.g. Thick veins) and type II (e.g. Punt) subunits Serine/threonine kinases	Patterning of the dorso-ventral axis and imaginal discs
Fibroblast growth factor (FGF) family		
A small number of FGF homologs (e.g. Branchless)	FGF receptors (receptor tyrosine kinases) Two in *Drosophila*, e.g. Breathless	Migration of tracheal cells (see Chapter 9)

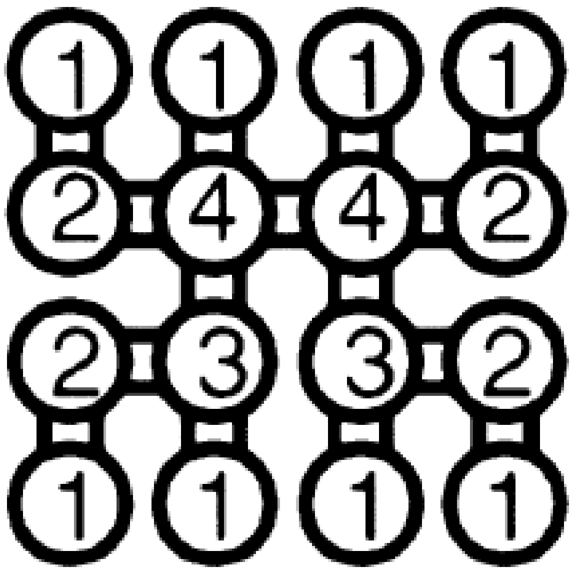
Localization of maternal determinants during oogenesis

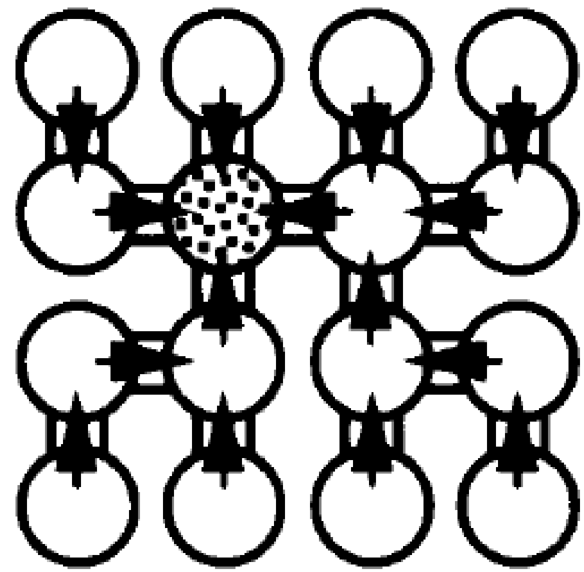


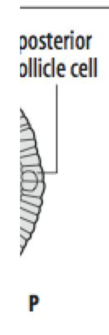


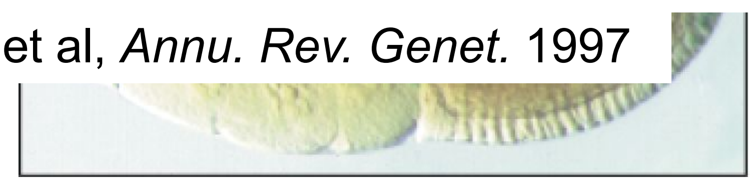
Localization of maternal determinants during oogenesis





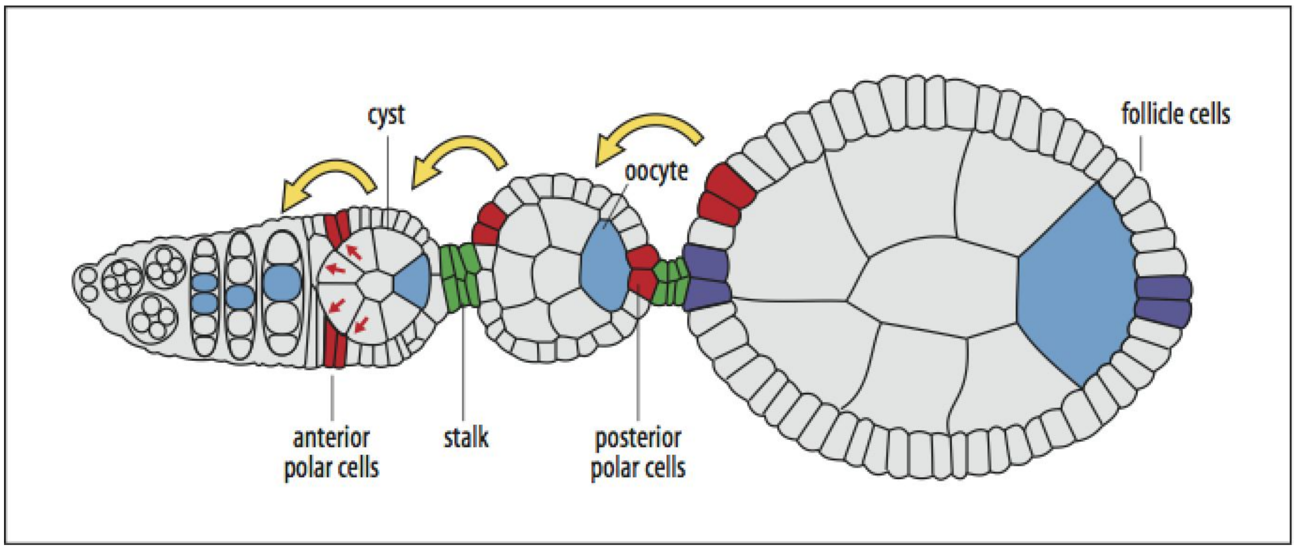




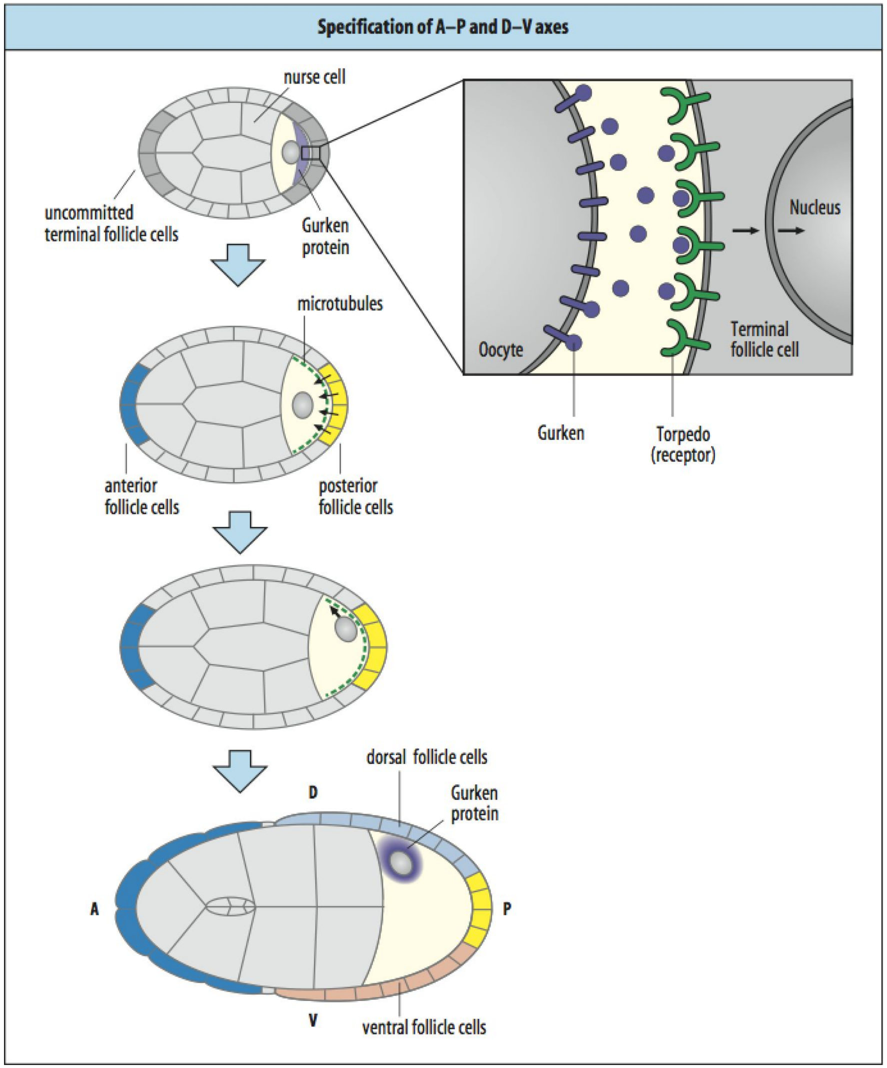


de Cuevas et al, *Annu. Rev. Genet.* 1997

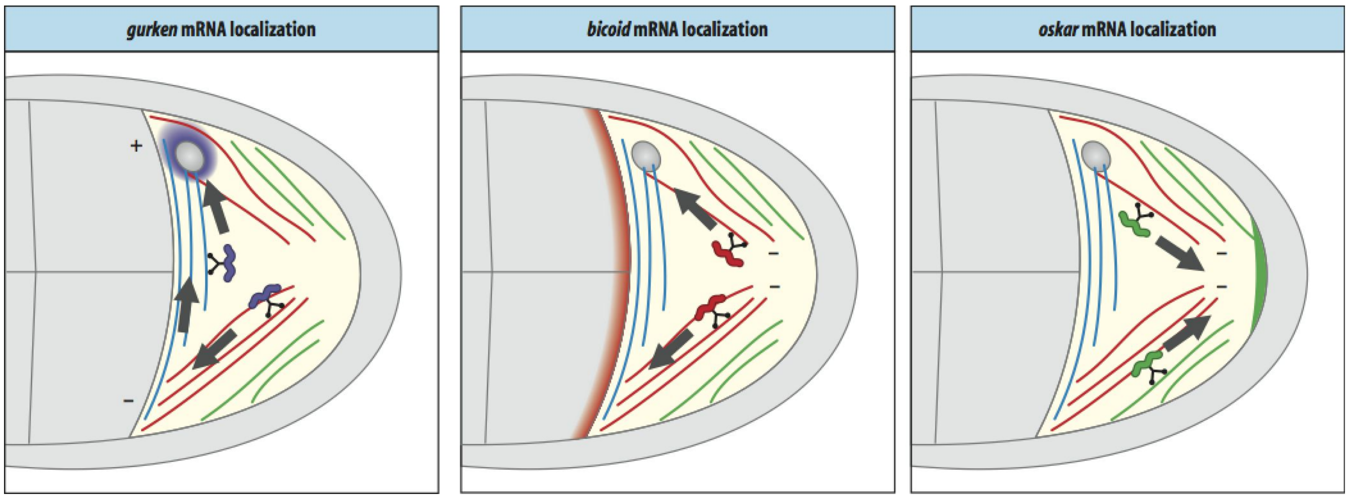
Signals from older to younger egg chambers initially polarize the oocyte



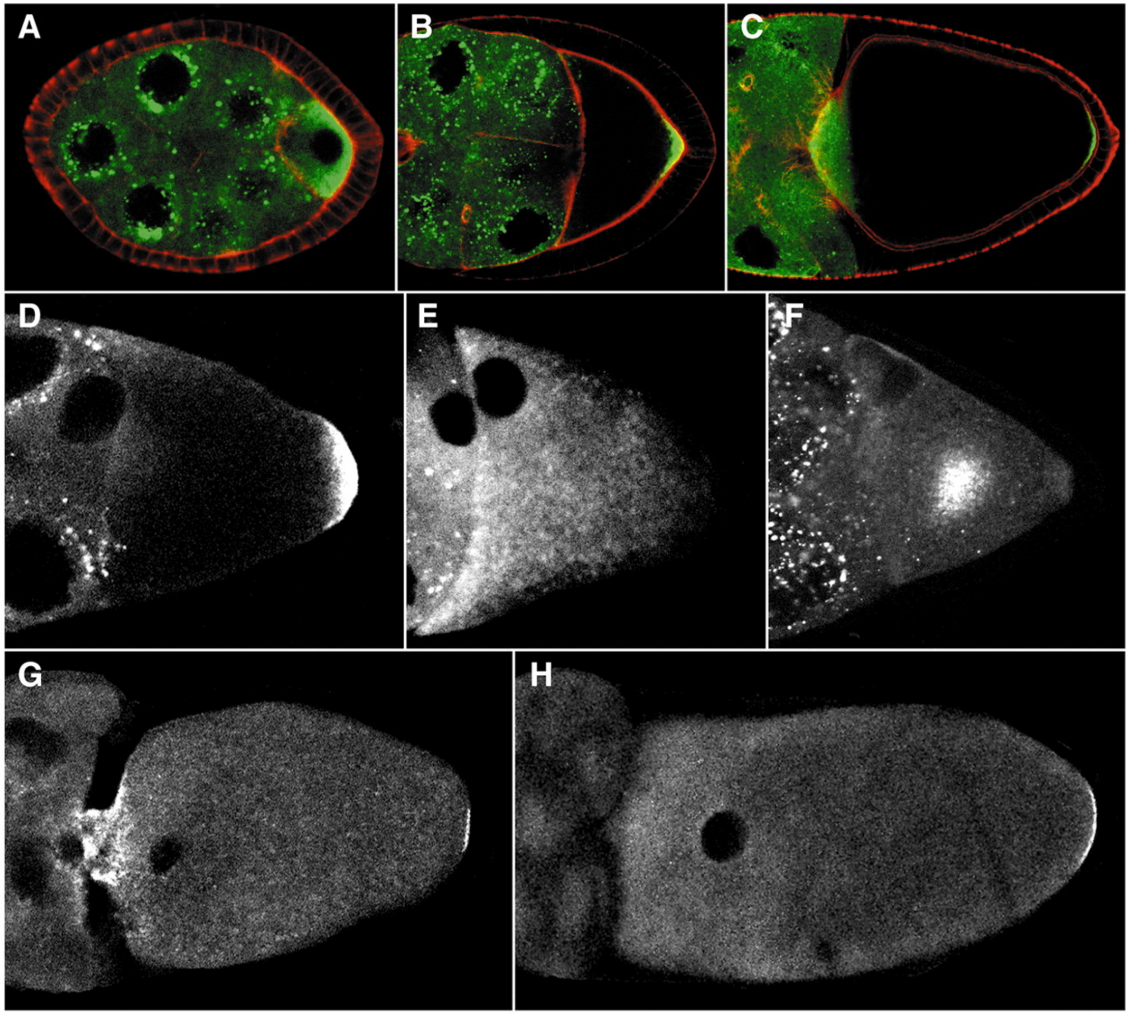
Specification of the AP and DV axes during oogenesis



bicoid, oskar and *gurken* mRNAs are localized by transportation along microtububles

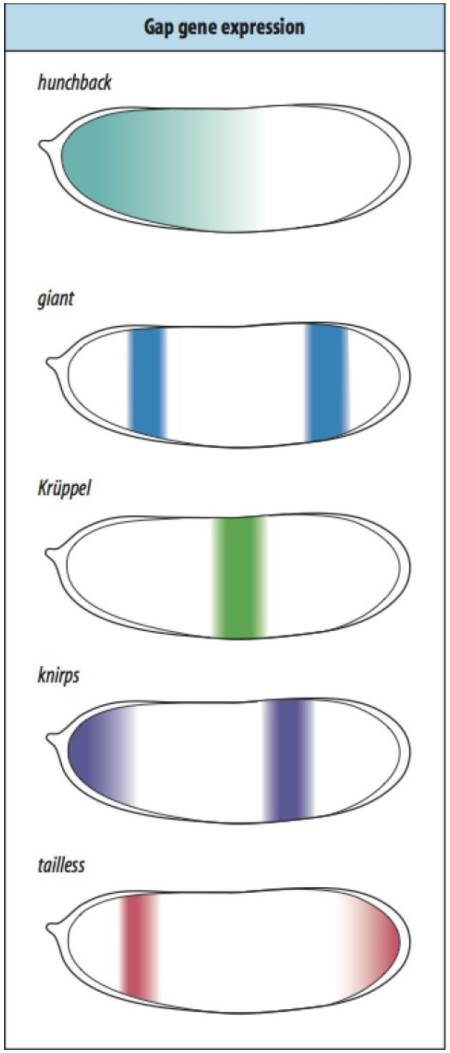


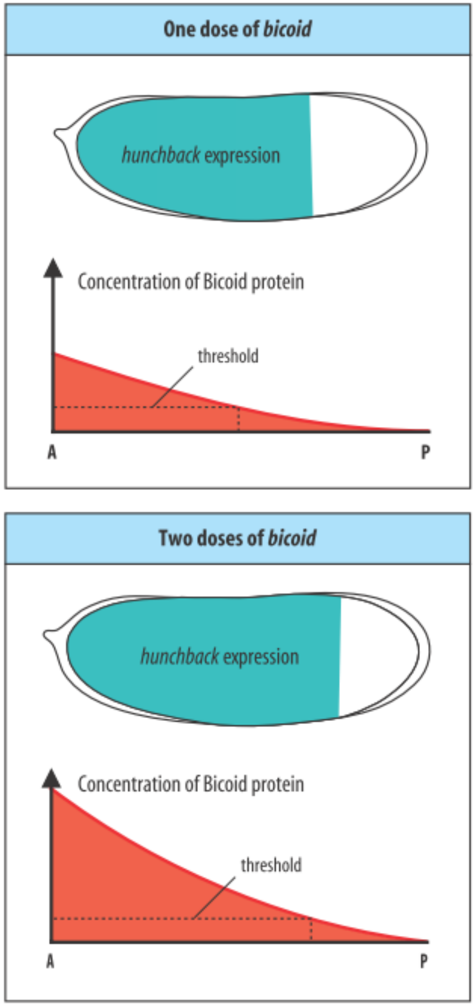
Localization of GFP-Staufen



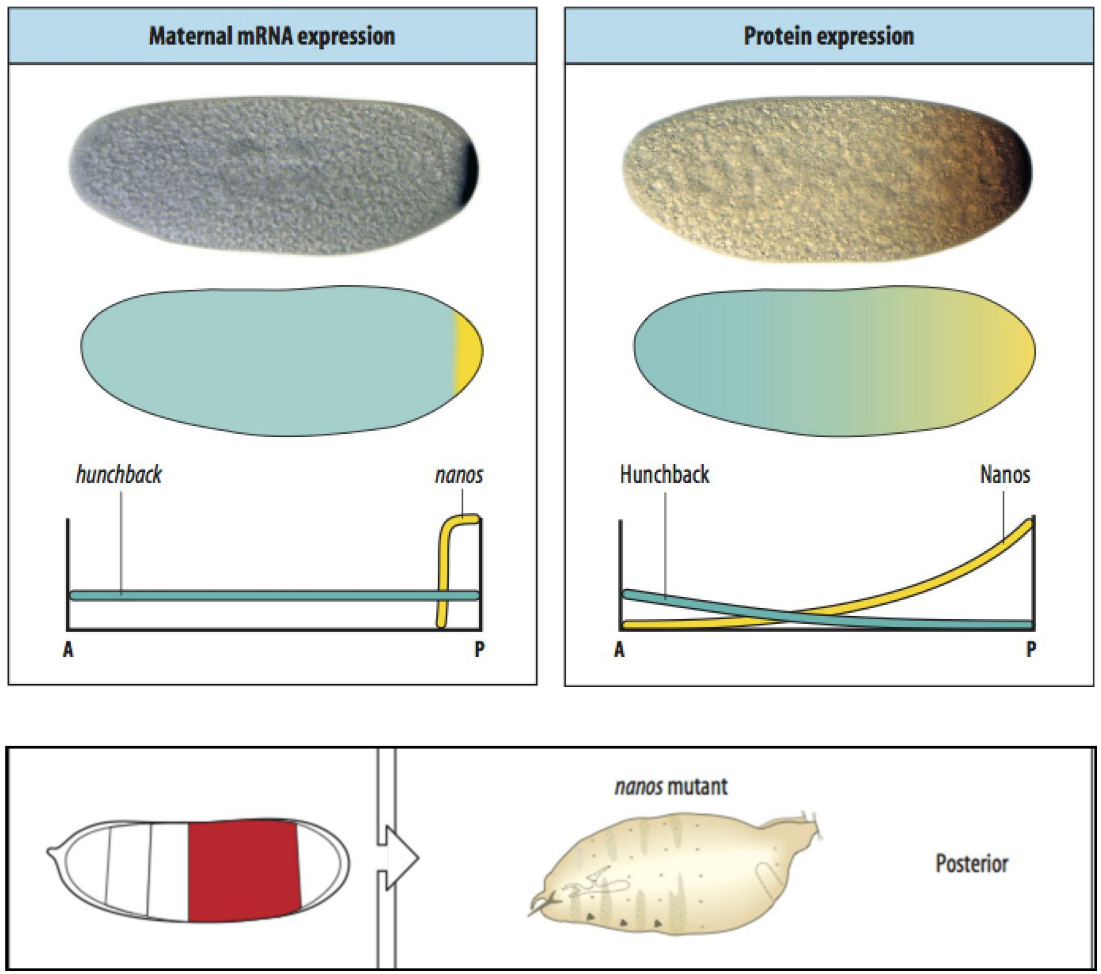
Martin S G et al. Development 2003;130:4201-4215

The expression of gap genes and the control of *hunchback* zygotic expression by *bicoid*

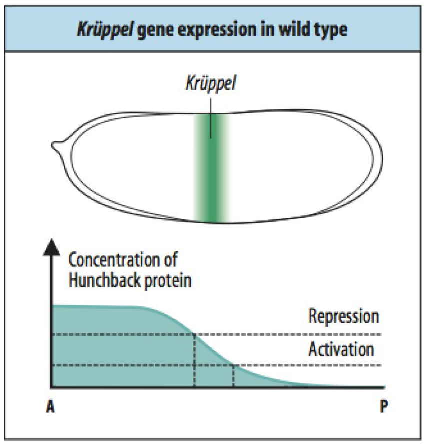


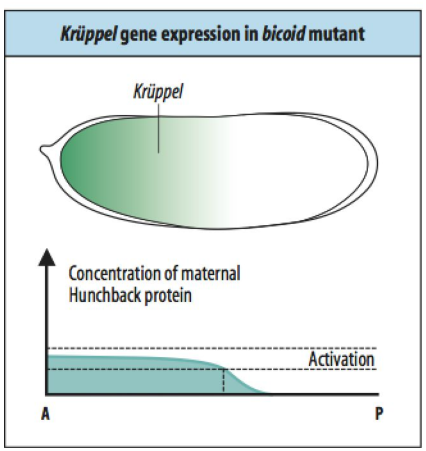


Establishment of a maternal gradient of Hunchback protein

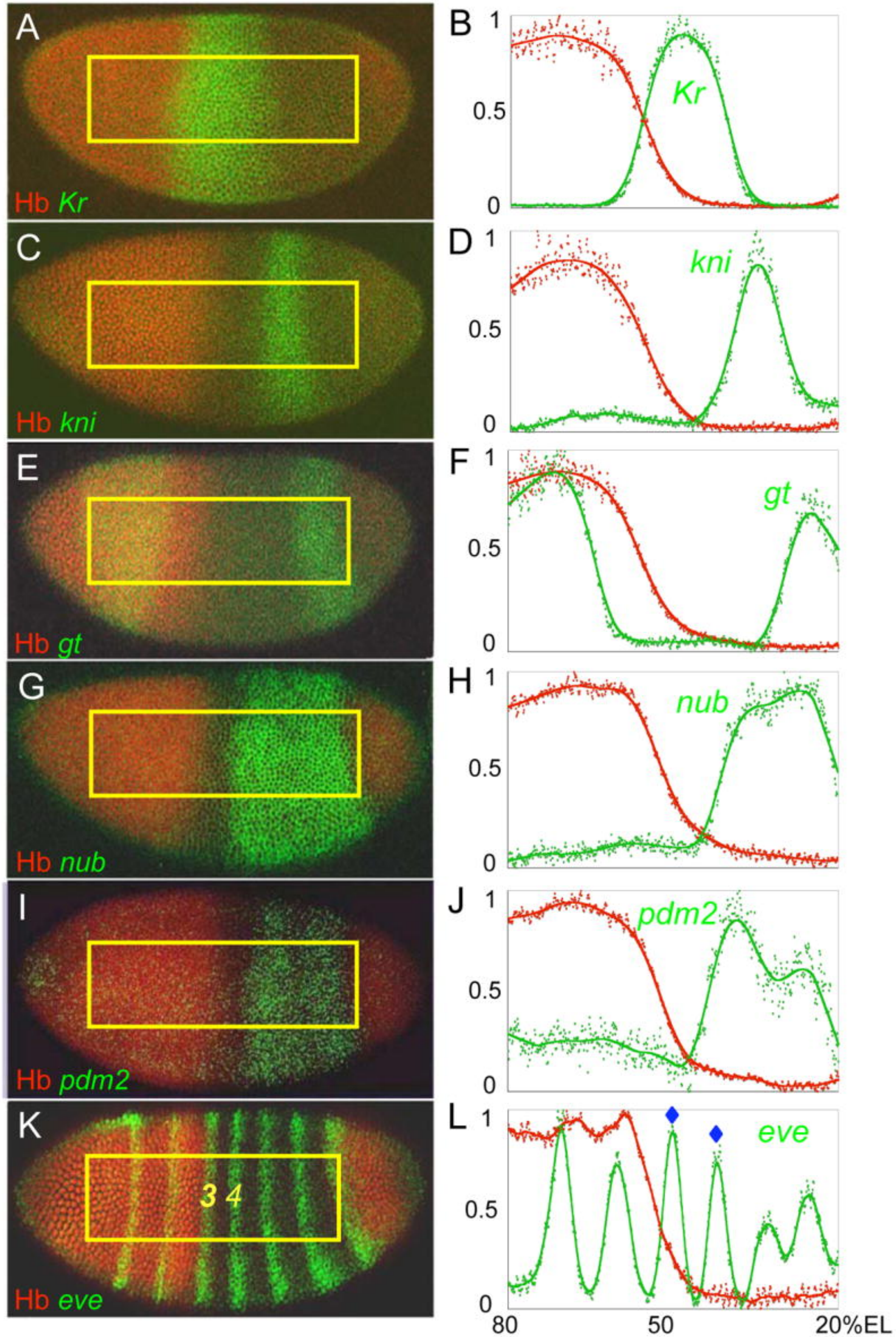


Hunchback specifies *kruppel* gene activity



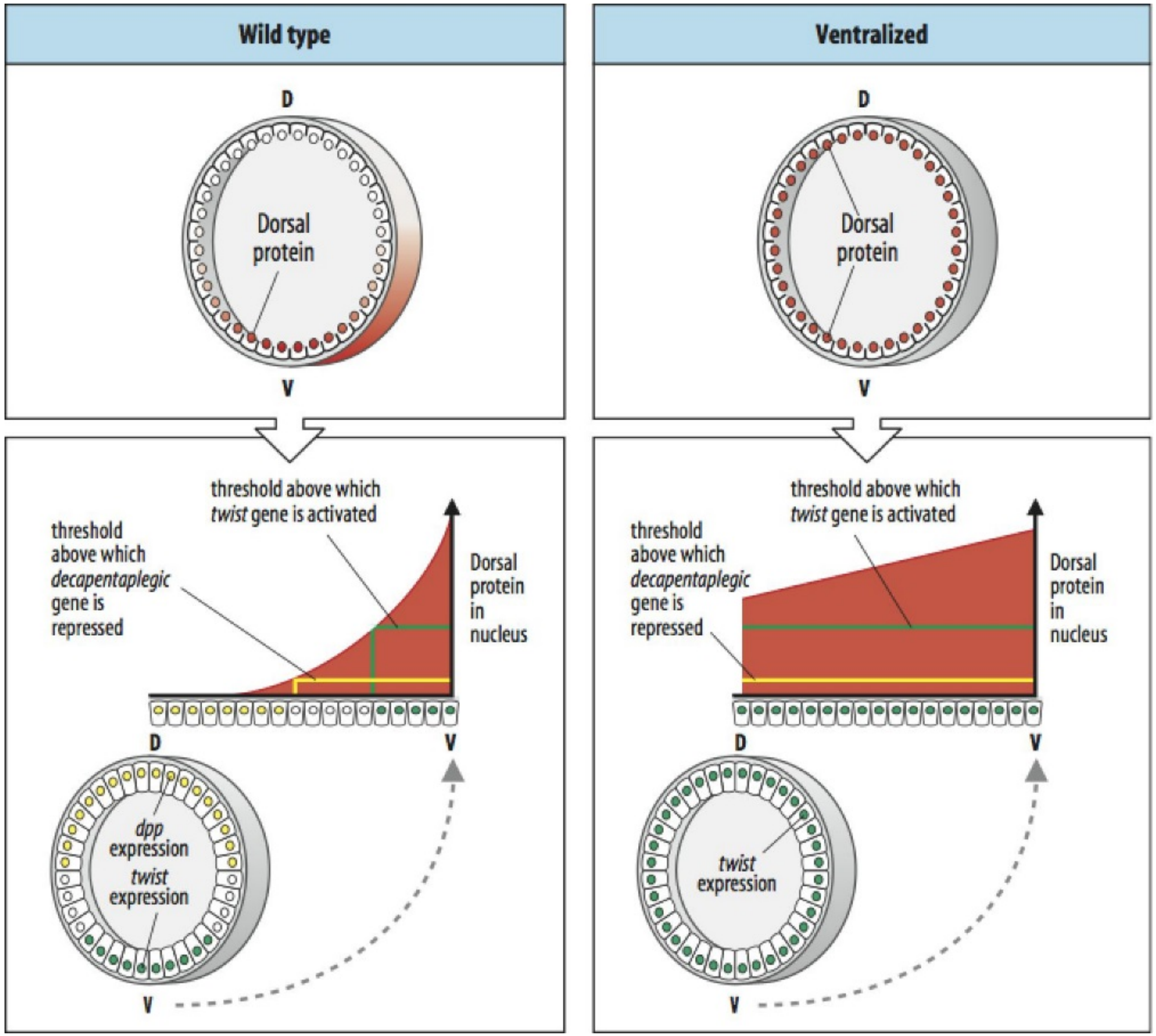


Hu ' gene activity

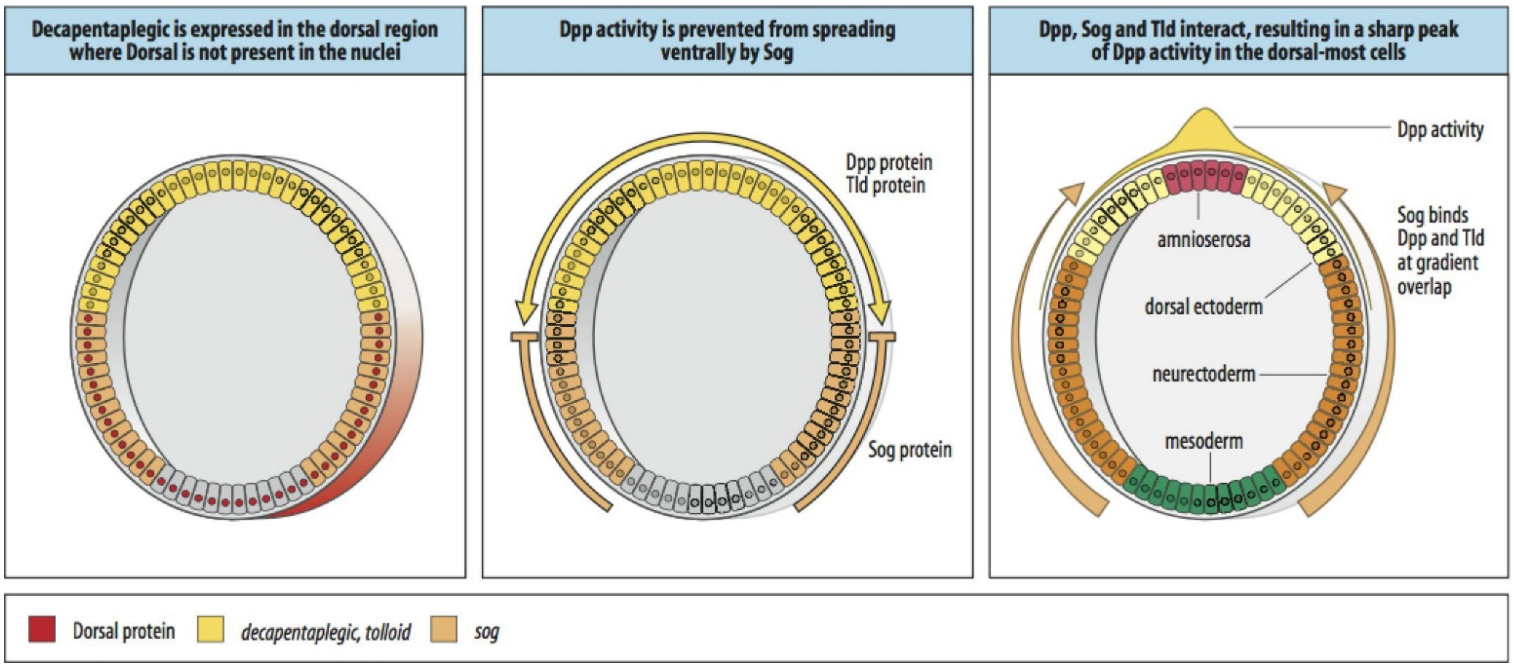


Yu and Small, *Curr Biol*, 2008

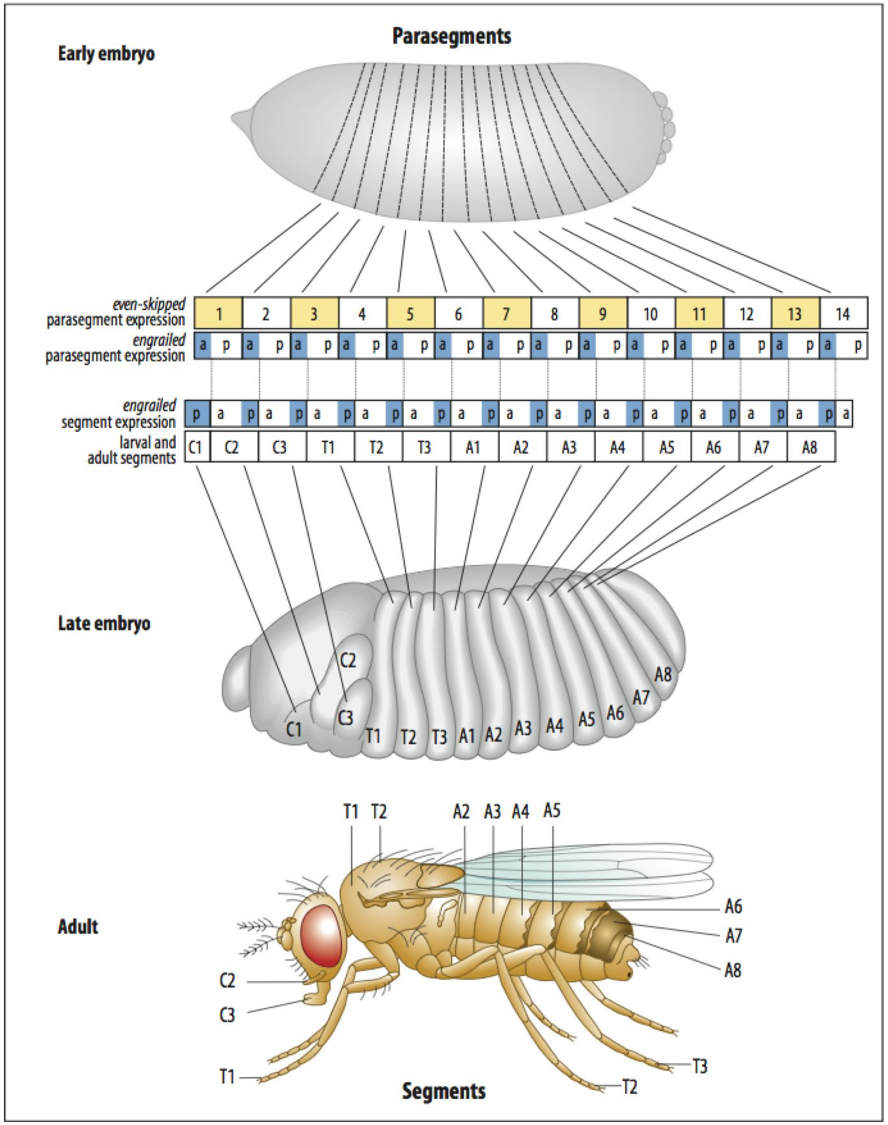
The nuclear gradient in Dorsal protein is interpreted by the activation of other genes



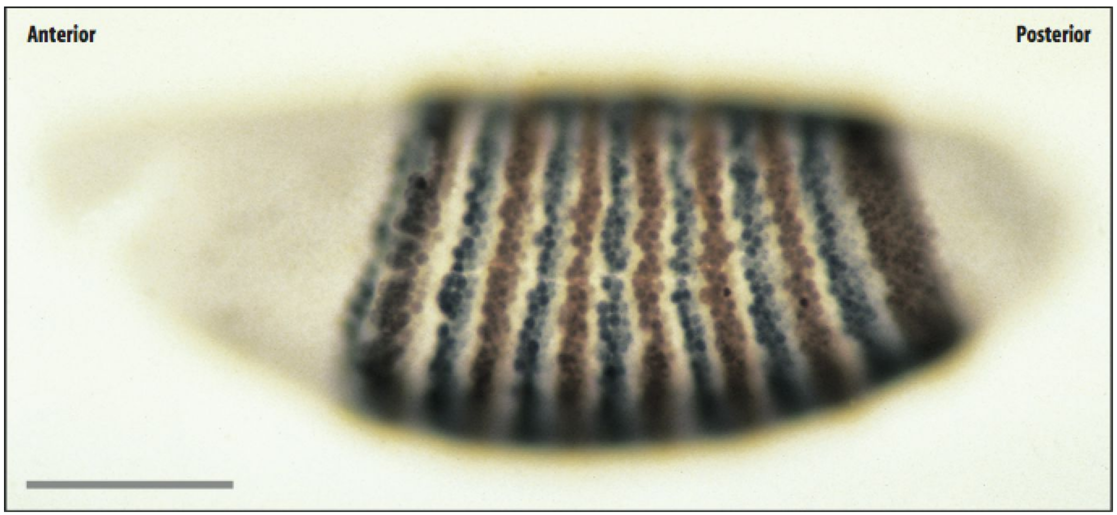
Dpp protein activity is restricted to the dorsal-most region of the embryo by the antagonistic activity of the Short gastrulation protein



The relationship between parasegments and segments

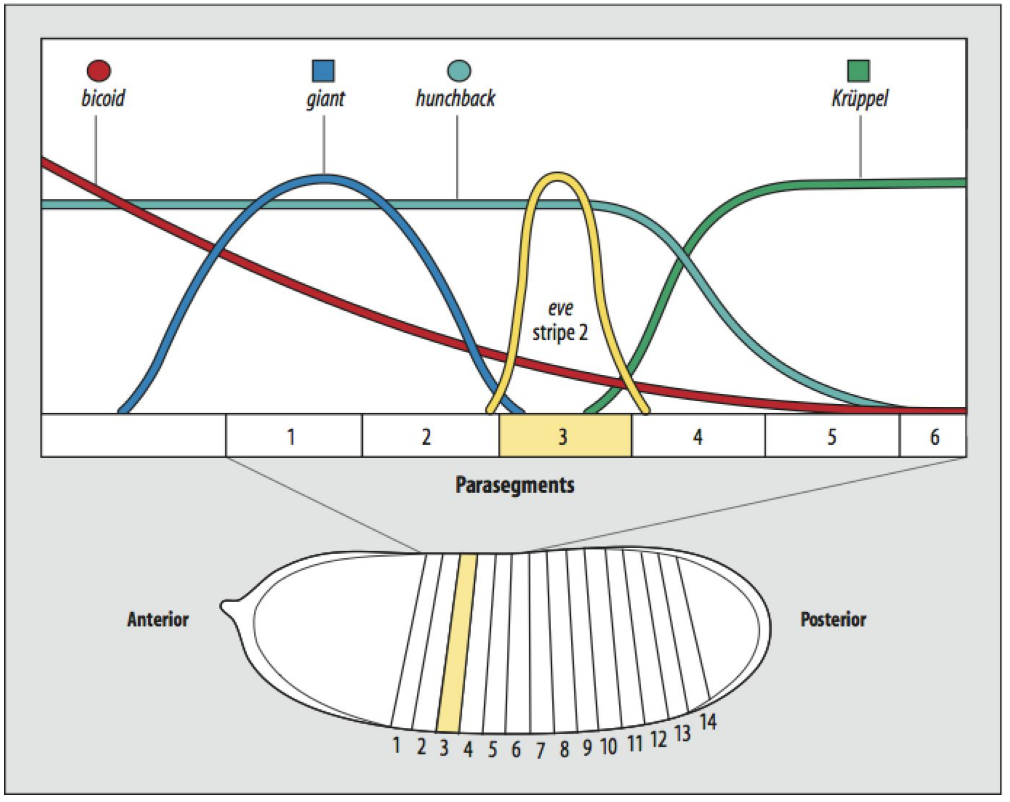


The expression pattern of pair-rule genes

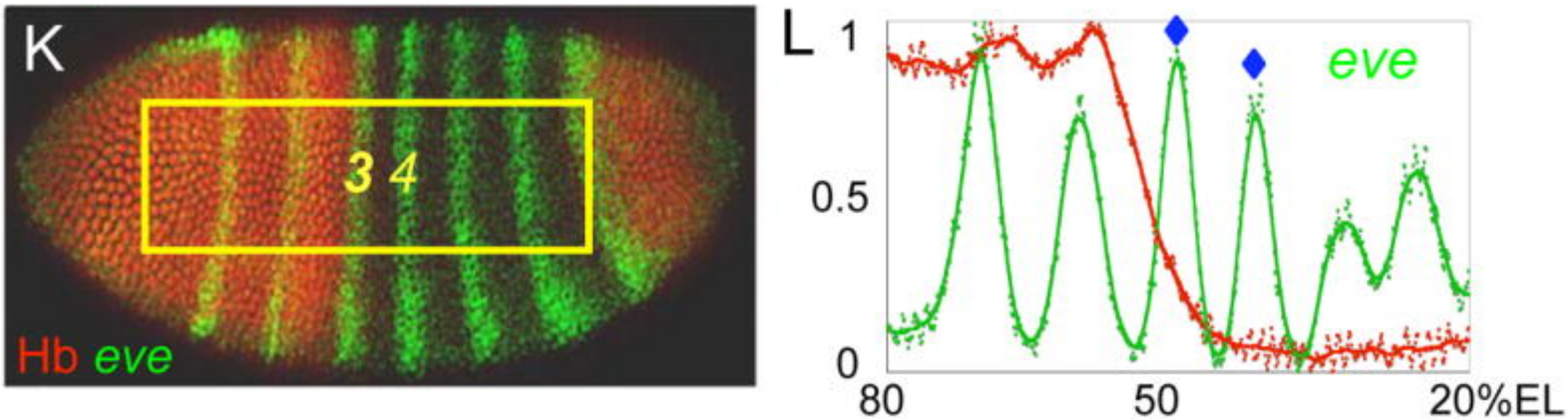


Blue, *even-skipped*
Brown, *fushi tarazu*
Each stripe is a few cells wide

The specification of the second *even skipped* (*eve*) stripe by gap genes

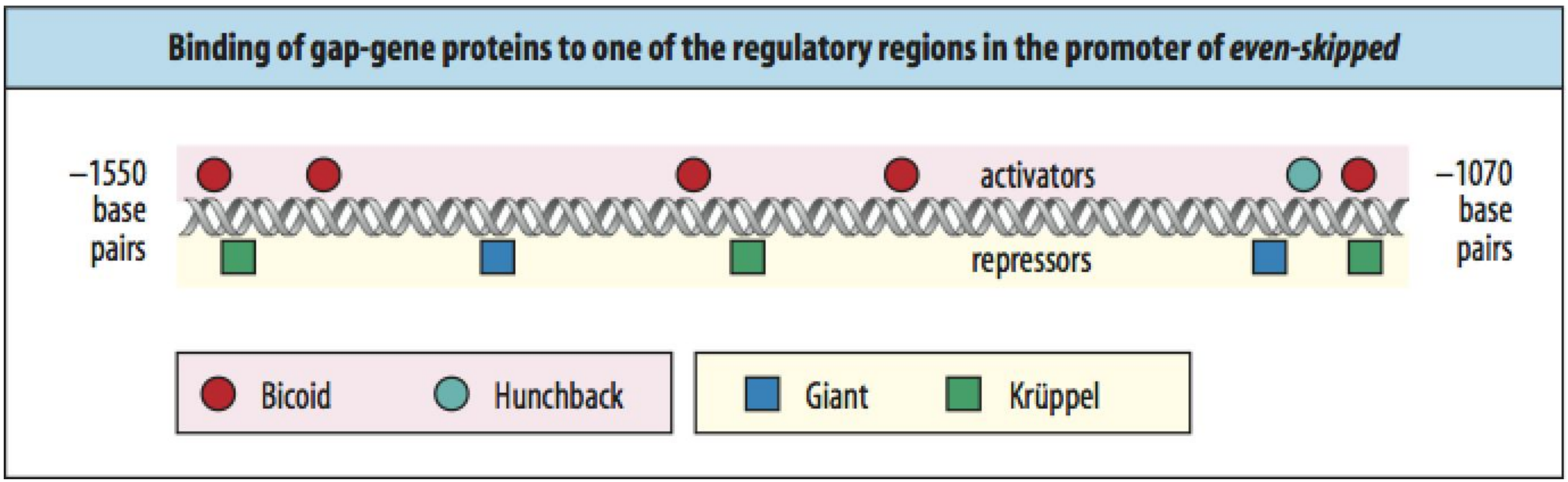


Positioning of the third and fourth *eve* stripes by the Hunchback gradient

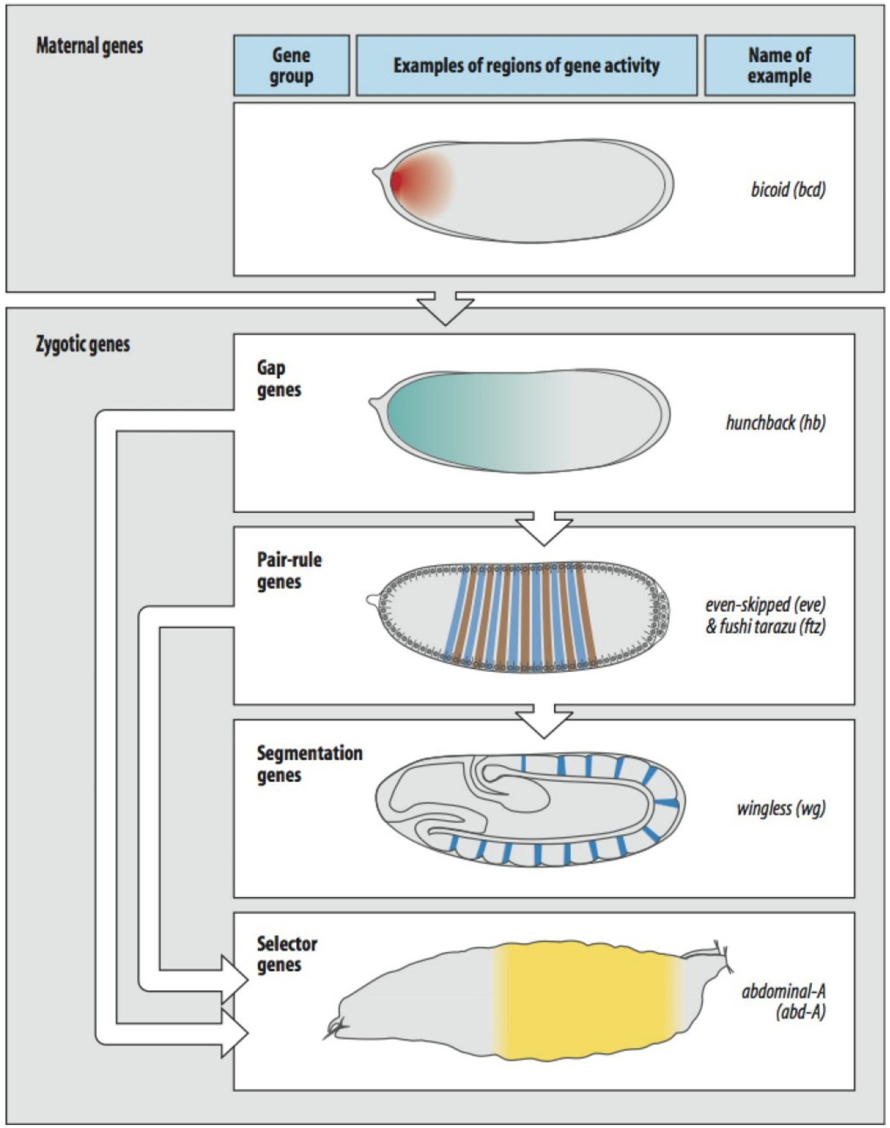


Yu and Small, *Curr Biol*, 2008

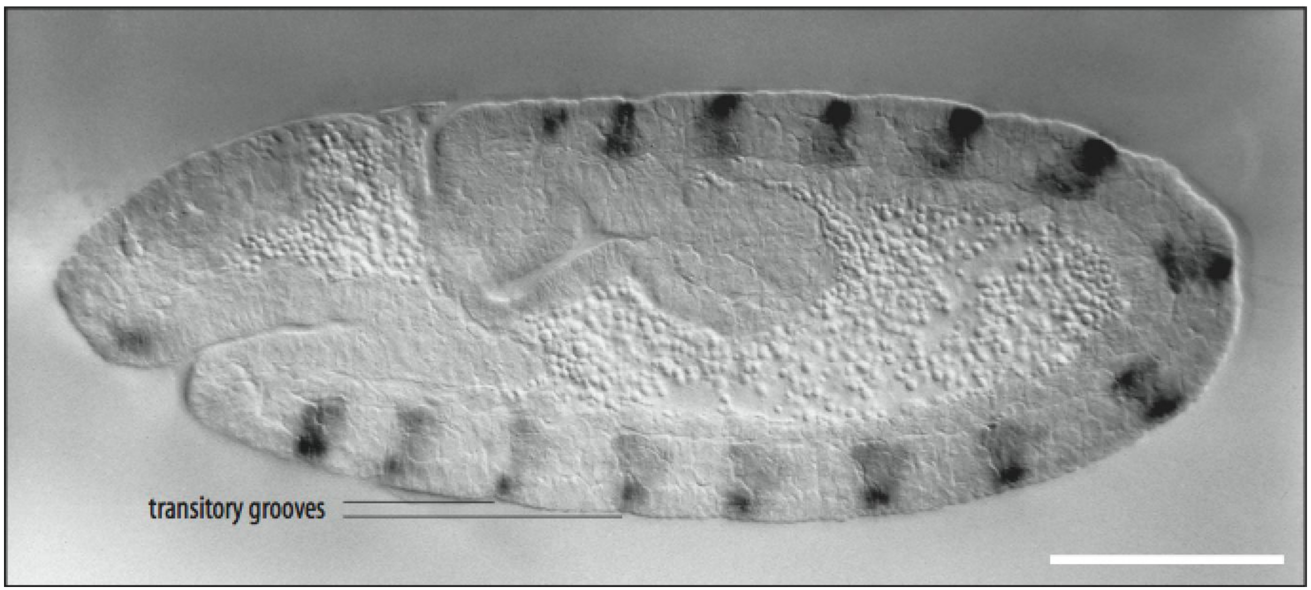
The binding sites which are involved in expression of the second *eve* stripe



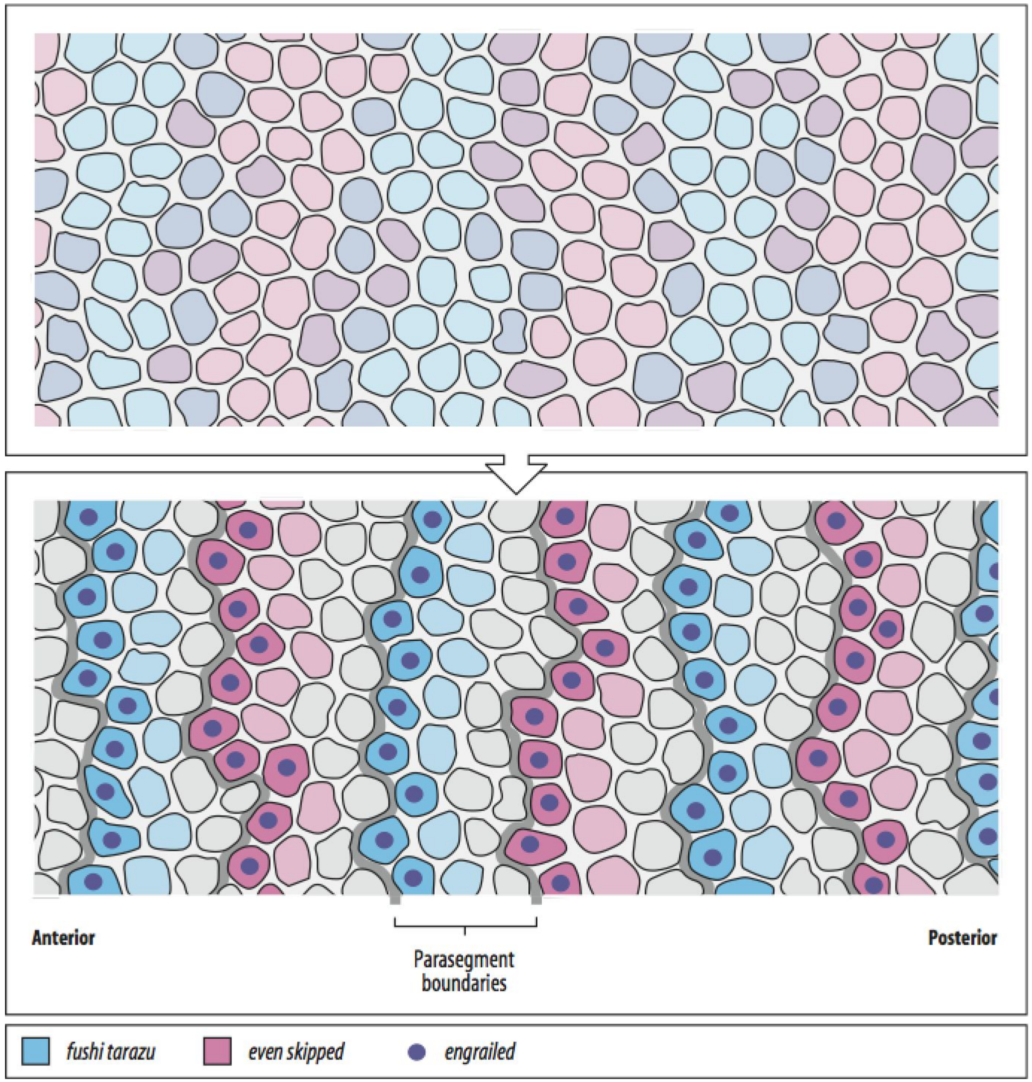
The sequential expression of different sets of genes establishes the body plan



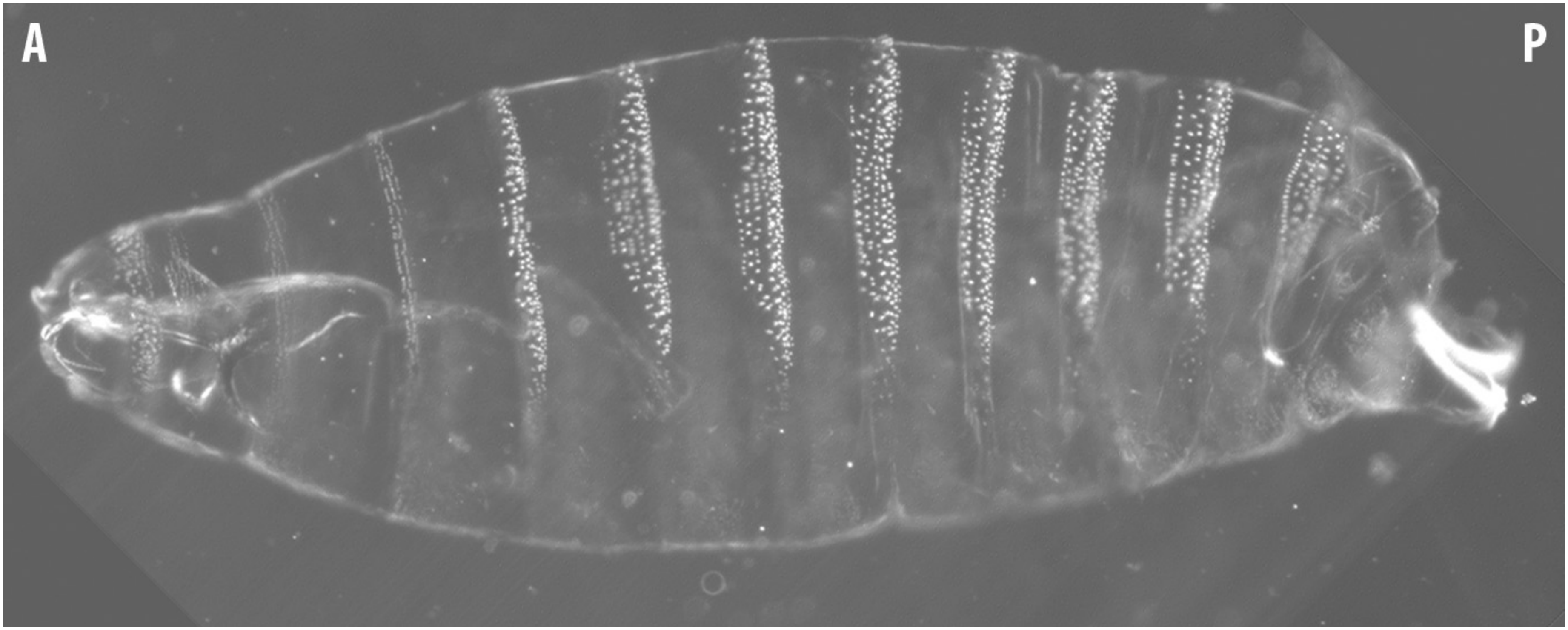
The expression of the *engrailed* gene in a late (stage 11) *Drosophila*



The expression of *fushi tarazu*, *even skipped*, and *engrailed*



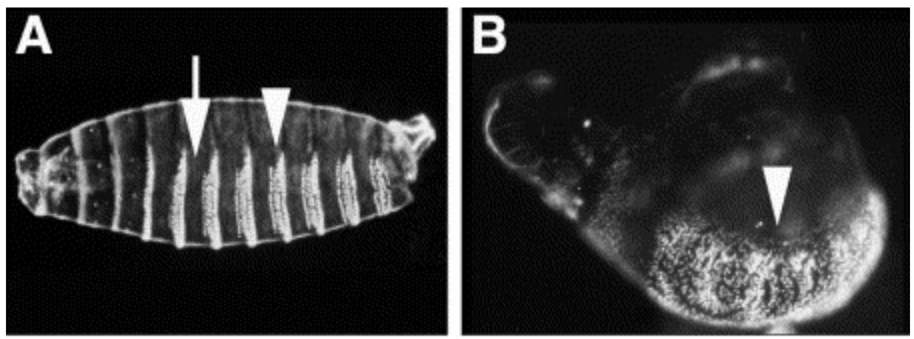
The characteristic patterns of denticles on each segment



Goodman et al, *Development*, 2006

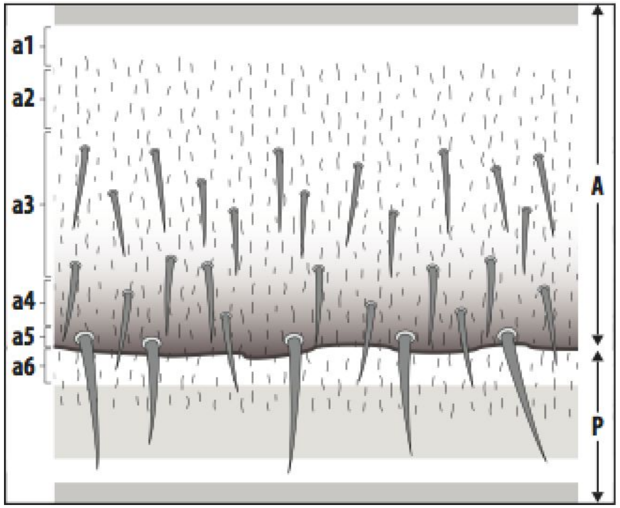
A *wg* (*wingless*) mutant embryo lacks all smooth cuticle

wg

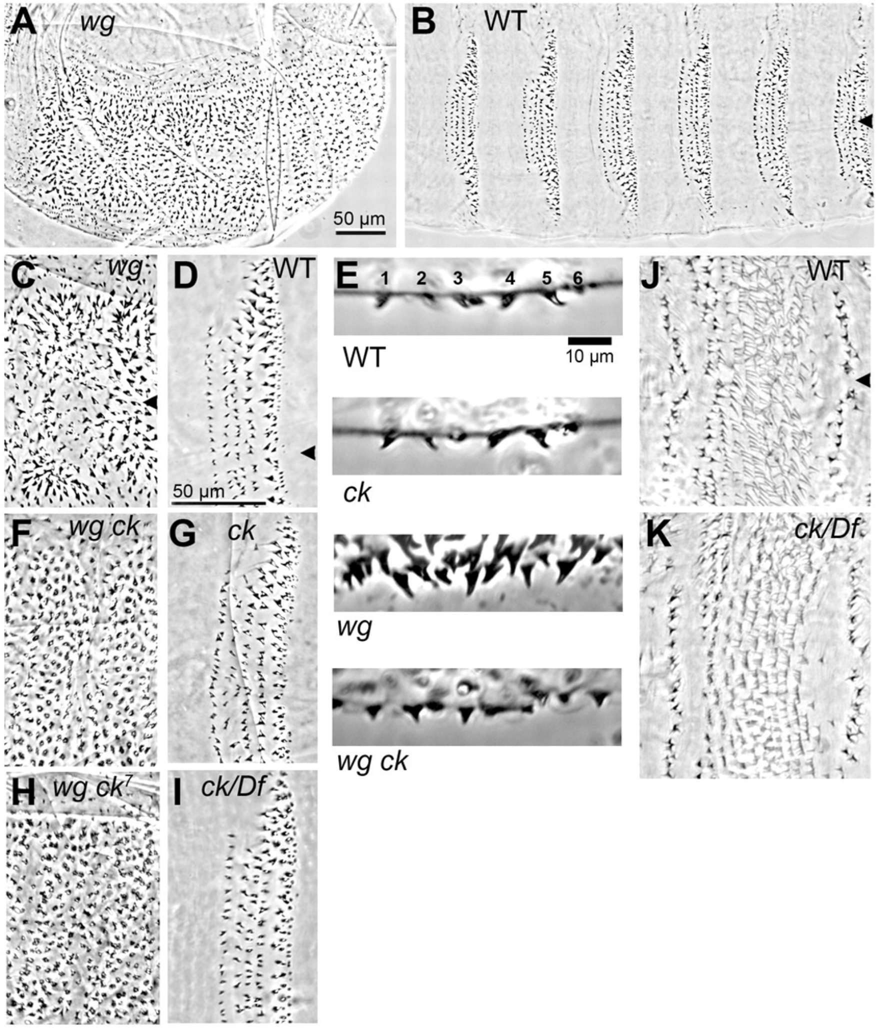


Tolwinski et al (Eric Wieschaus lab), *Developmental cell*, 2003

The detailed pattern of epidermis



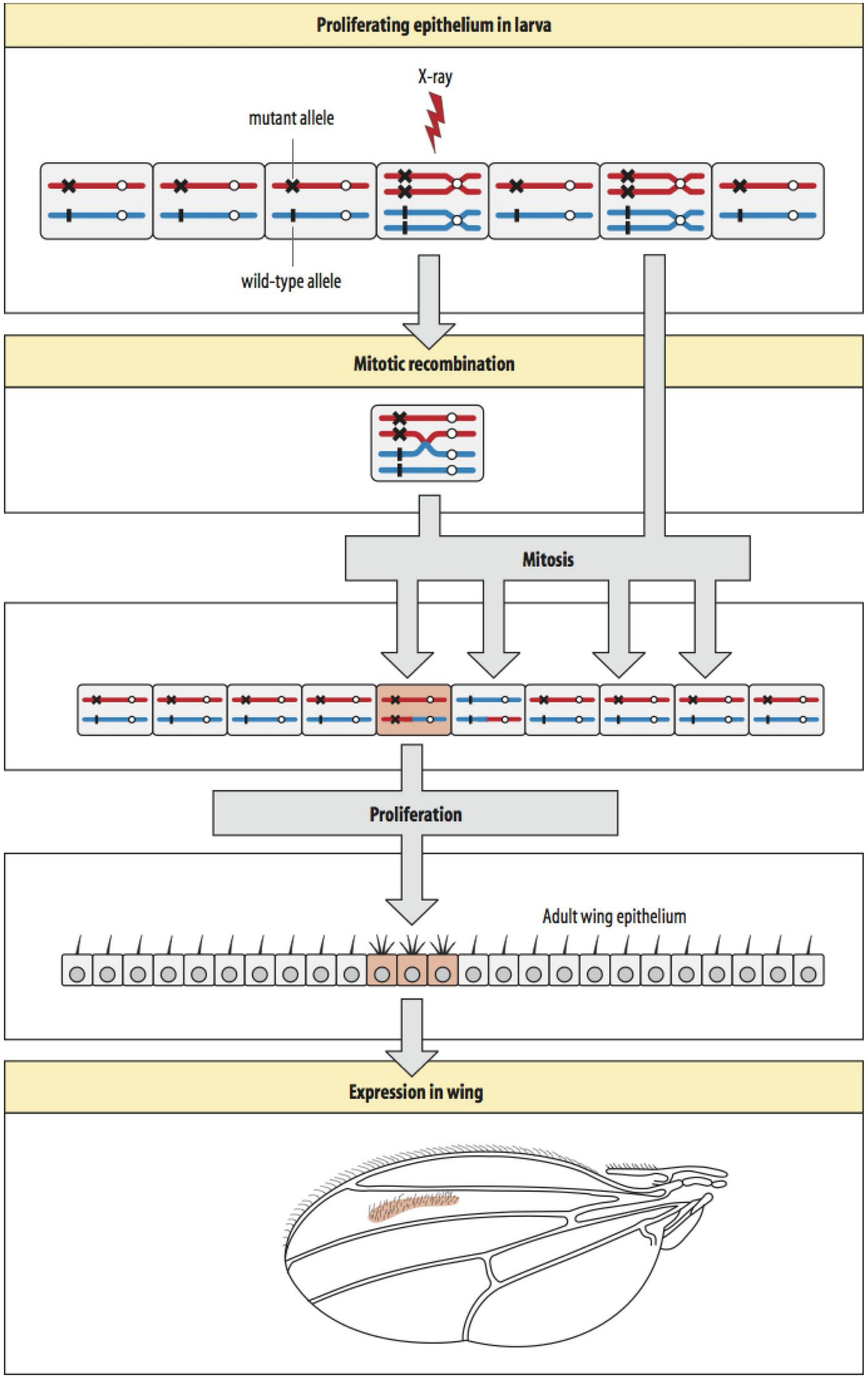
Mutations in *ck* disrupt denticle morphology in a Wg-dependent manner.



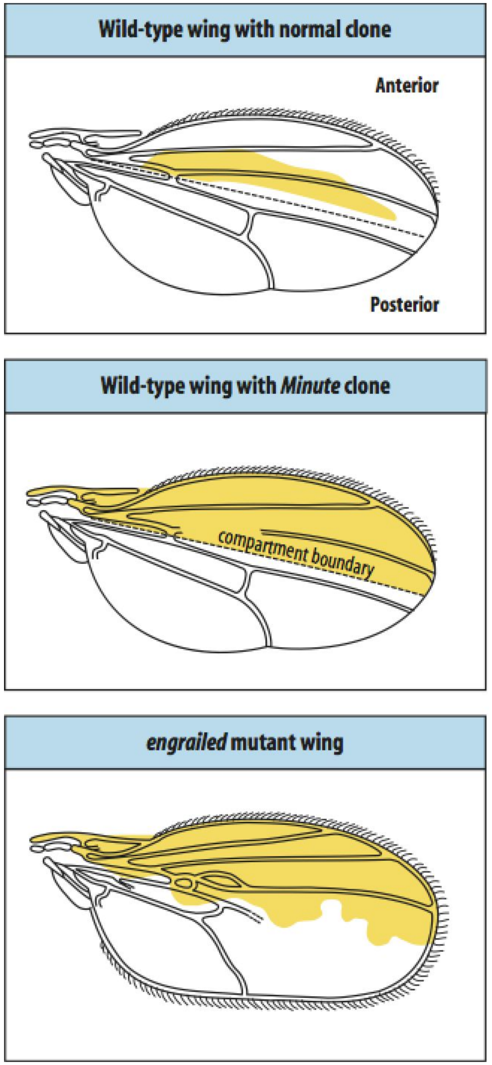
Bejsovec A , and Chao A T Development 2012;139:690-698

Genetic mosaics and mitotic recombination

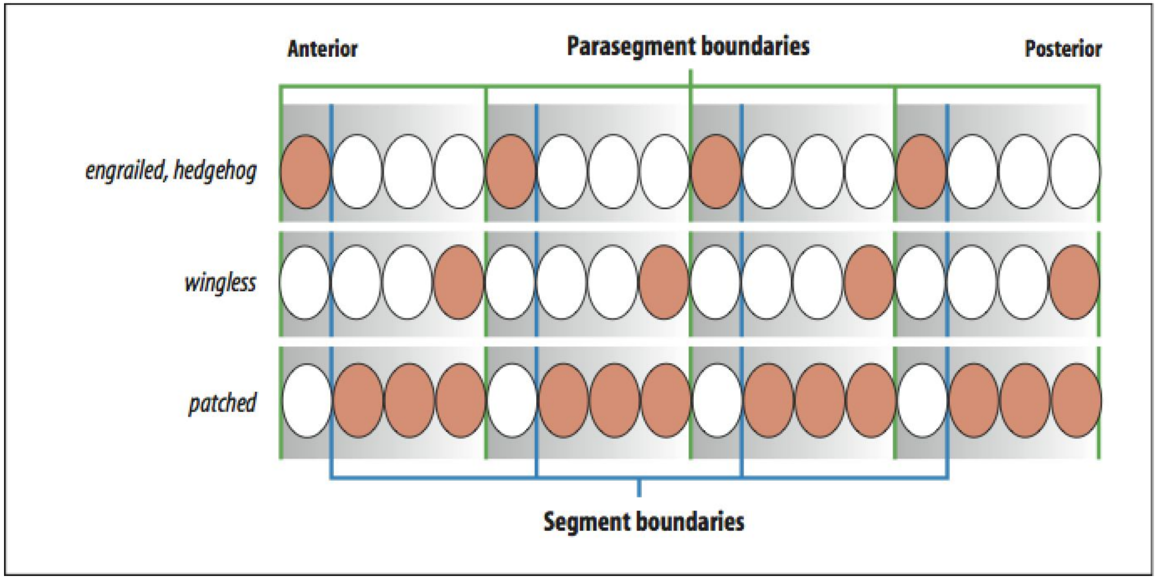
Minute technique



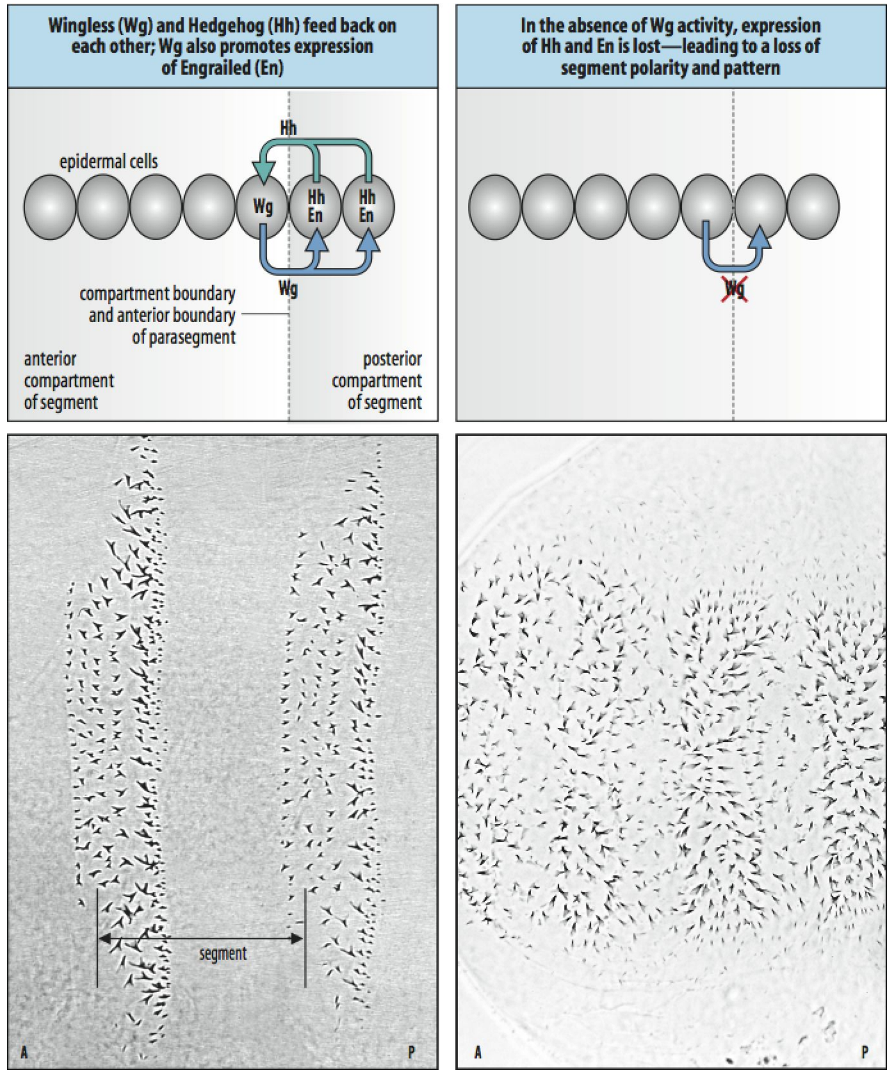
Marked cell clones demonstrates the boundary between anterior and posterior compartments in the wing



The domains of expression of the segmentation genes



Interactions between hedgehog, wingless, and engrailed genes at the compartment boundary control denticle patterns



Homeosis

- In 1894, William Bateson coined the word “homeosis”. He gave a surprisingly broad definition of the term as a type of variation in which “something has been changed into the likeness of something else.”

- In 1790, Goethe (歌德) had already described the “homeotic” phenomenon. In 1869 Masters made more extensive studies in plants and termed it “metamorphy”.

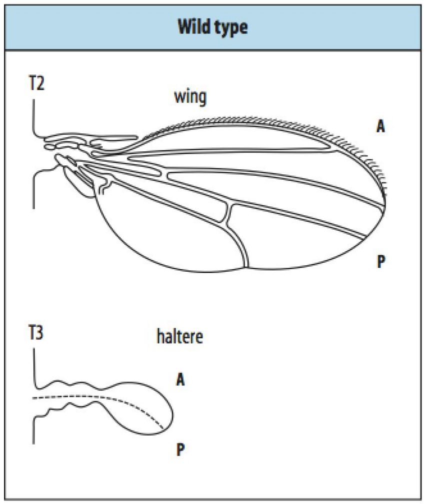
- However, as metamorphy had quite different meanings in other branches of biology, Bateson proposed “homeosis” as a more specific and useful term, and this name has certainly stood the test of time.

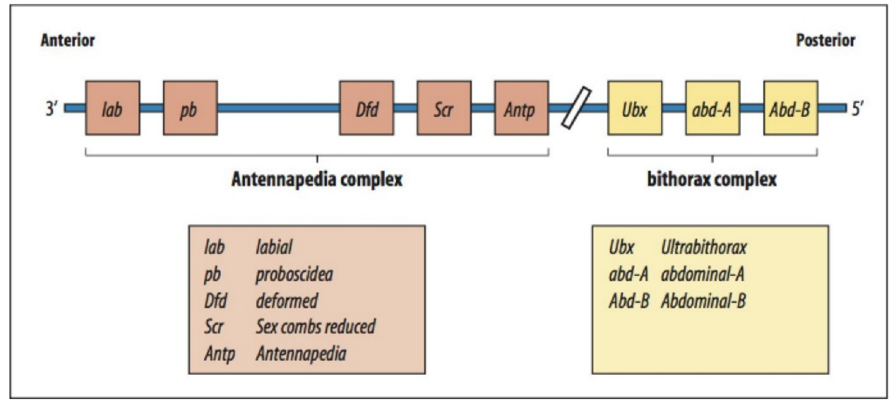
Homeotic mutants

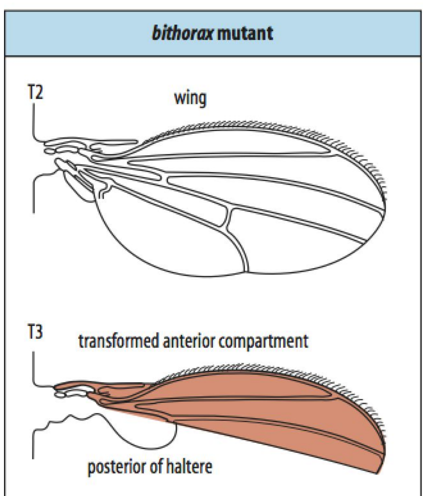
- Bridges described a homeotic mutant *bithorax (bx)* in drosophila. (Somewhat of a misnomer as the number of thoracic segments is not affected; rather, there is a conversion, albeit weakly, of the third segment into the second, producing flies that have a small second pair of wings in place of the halteres.)

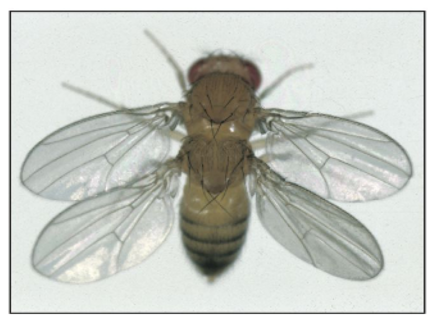
- In 1919, Bridges found another mutant *bithoraxoid (bxd)*, which fully complemented *bx* mutants. *bithorax-dominant (bxD*) failed to complement either *bx* or *bxd*.

The HOM-C complex and homeotic transformation of the wing and haltere





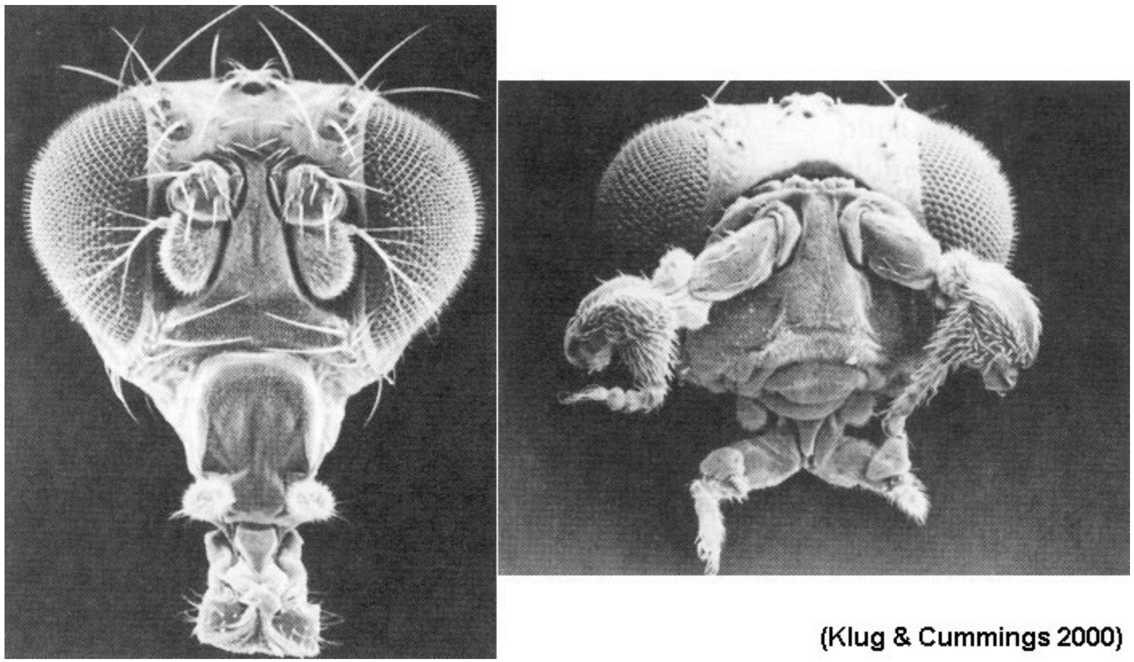




Bithorax and *postbithorax* double mutant

Antennapedia homeotic mutant in *Drosophila*

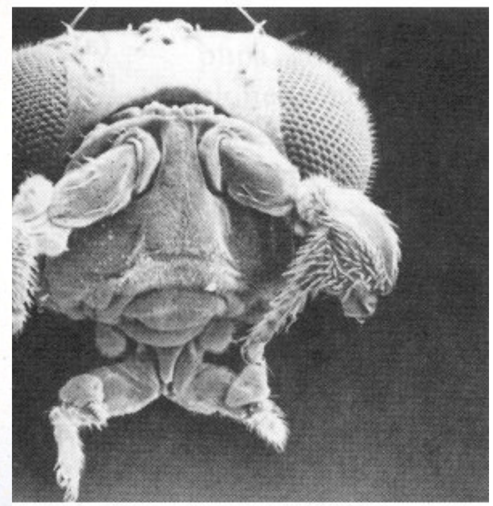
Wild-type *Drosophila* have a pair of imaginal discs that differentiate as antennae (left).
The ***Antp*** mutant causes these discs to differentiate as legs (right)



(Klug & Cummings 2000)

Antennapedia homeotic mutant in *Drosophila*

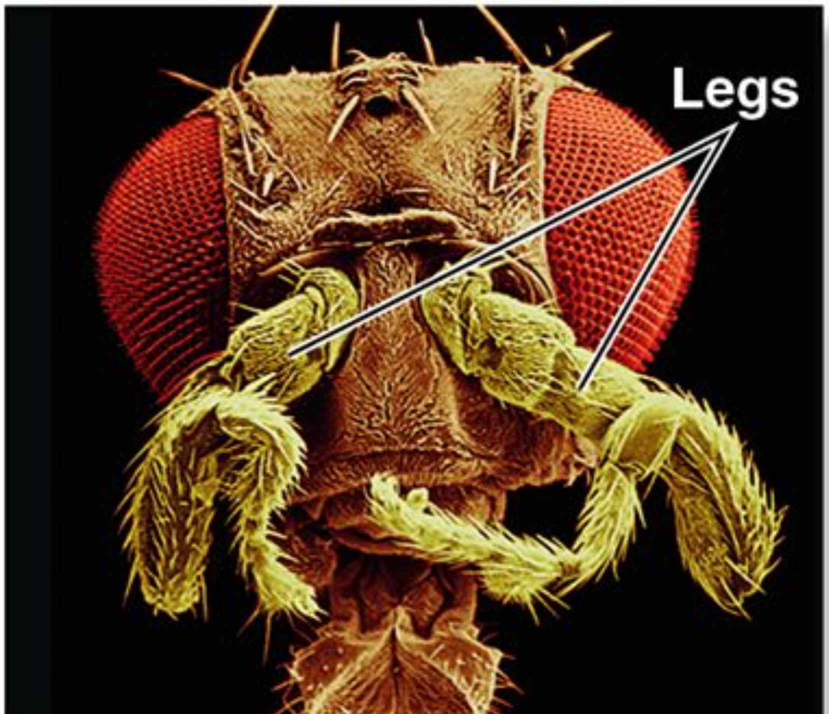
Wild-type *Drosophila* have a pair of imaginal discs that differentiate as antennae (left). The ***Antp*** mutant causes these discs to differentiate as legs (right)



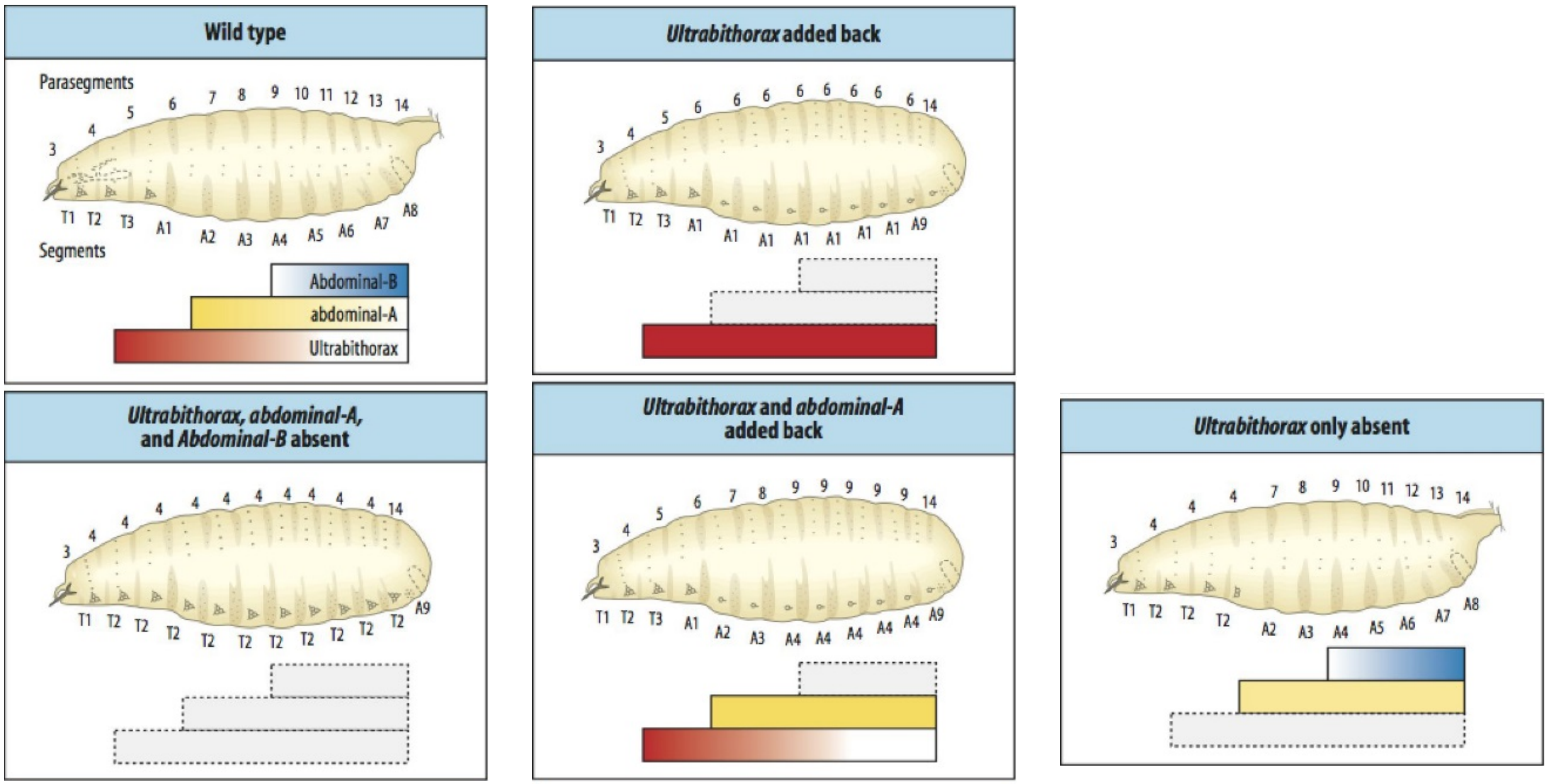
(Klug & Cummings 2000)

Antennapedia homeotic mutant in _Drosophila_

Wild-type *Drosophila* have a pair of imaginal discs that differentiate as antennae (left). The ***Antp*** mutant causes these discs to differentiate as legs (right)



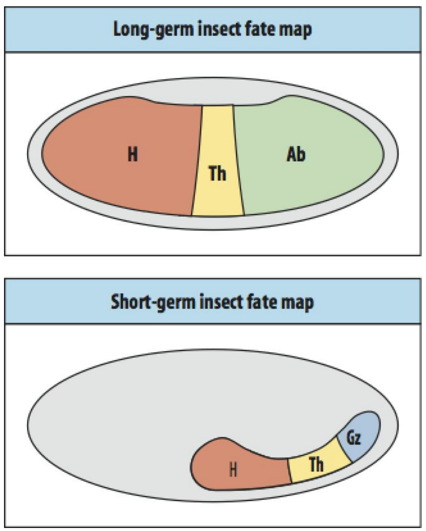
The spatial expression pattern of the bithorax complex genes



Summary

- 1. Maternal factors set up the framework.
- 2. The half life of the factors are short (From fertilized egg to cellular blastoderm is about 3 hours).
- 3. The range of a certain signal is short (several lines of cells).
- 4. The regulation has hierarchy. Then a single gene mutation can induce dramatic change.
- 5. Read the table of main genes.

Some insects use different mechanisms for patterning the body plan

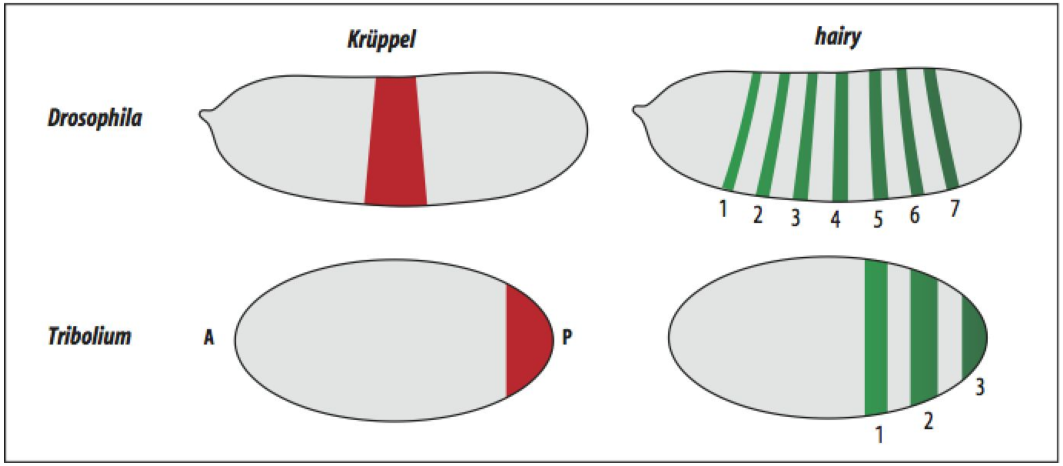


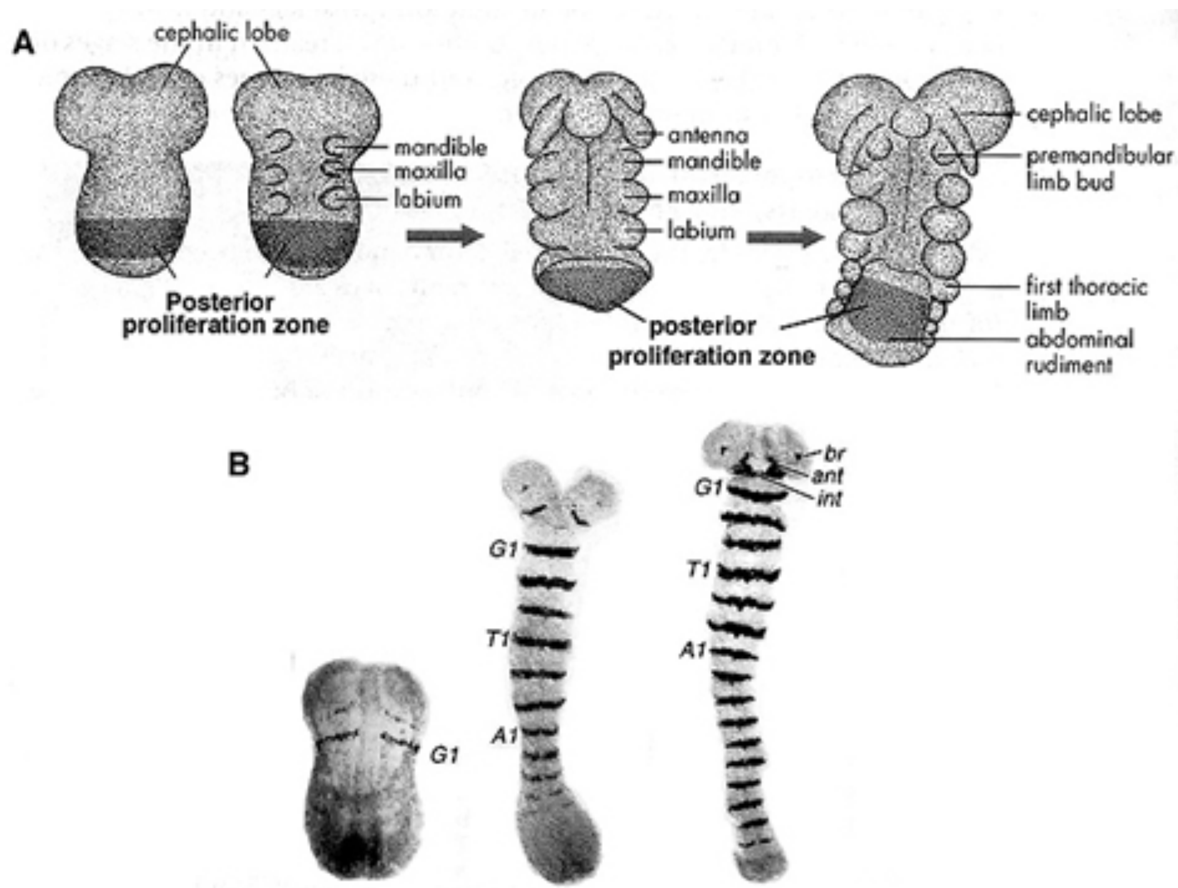
The red flour beetle (*Tribolium castaneum*)

Gz, growth zone

Germ band = ventral blastoderm

Gap and pair-rule gene expression in long-germ and short-germ insects at the time of germ-band formation



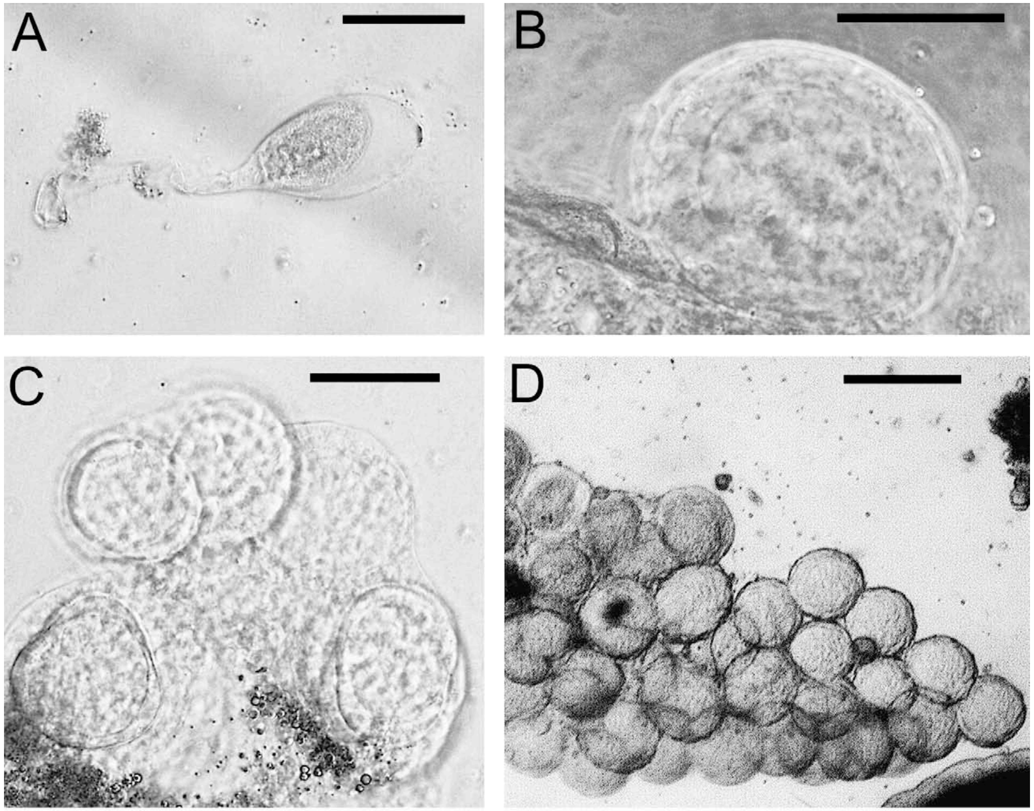


(A) The posterior proliferation zone of the *Petrobius*, a wingless thysanuran.
(B) In situ hybridization of *engrailed* shows the segmentation of the short germ band beetle, *Tribolium*.

Polyembryony: The Parasitic Wasps

- The female parasitic wasp deposits her egg inside the egg of another species. However, the wasp egg divides holoblastically.
- Moreover, instead of differentiating a body axis, the cells of the parasitic embryo divide repeatedly to become a mass of undifferentiated cells called a **polygerm**.
- As the polygerm grows, it splits into dozens (sometimes thousands, depending on the species) of discrete groups of cells. Each of these groups of cells becomes an embryo!
- The polyembryonic wasp *Copidosoma floridanum* produces up to 2000 individuals from a single fertilized egg (Grbic et al., 1996; 1998).
- This ability of an egg to develop into a mass of cells that routinely forms numerous embryos is called **polyembryony**. Polyembryony is characteristic of certain insect groups and certain mammalian species, such as the nine-banded armadillo, whose eggs routinely form identical quadruplets.

Developmental stages of *C. koehleri* inside the host



A, Egg (scale bar 50 um). B, Primary morula (scale bar 100 um). C, Early polymorula (scale bar 100 um). D, Late polymorula (scale bar 100 um). Segoli et al, Arthropod Structure & Development, 2009.

Comparative Embryology Ⅱ

——the four principles of Karl Ernst von Baer (1828)

Karl Ernst von Baer

Ernst Haeckel, *The evolution of man*, 1903

Alien (1979)

Edit

Trivia

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The alien's habit of laying eggs in the chest (which later burst out) was inspired by spider wasps, which are said to lay their eggs "in the abdomen of spiders." This image gave Dan O'Bannon nightmares, which he used to create the story. But spider wasps (pompilidae) lay eggs on their prey, not inside them, after which the wasp maggots simply snack on the sting-paralyzed spiders. O'Bannon may instead have been thinking of either ichneumon wasps or braconid wasps. The ichneumon drills a single egg into a wood-boring beetle larva, whereas braconids inject eggs inside certain caterpillars. Both result in fatal hatch-outs more alike to O'Bannon's alien.

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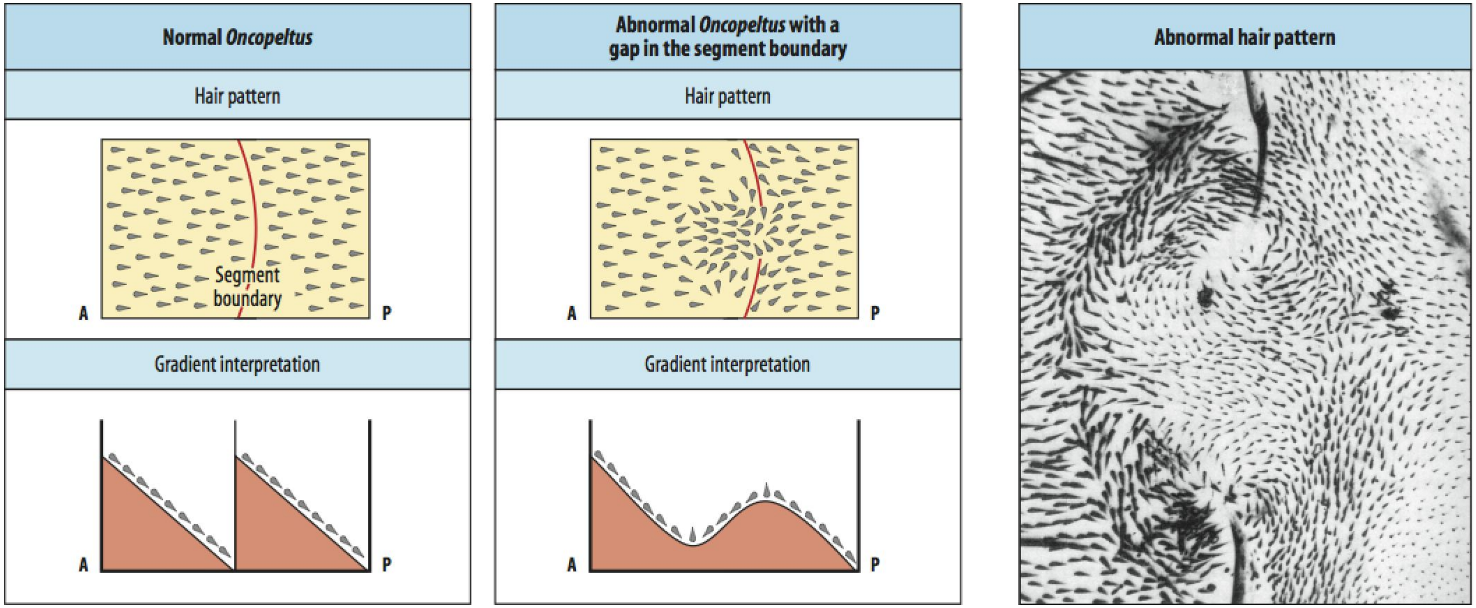
Gradients could specify polarity in the segments of Oncopeltus



Gut Microbiota from Twins Discordant for Obesity Modulate Metabolism in Mice

Vanessa K. Ridaura,[1] Jeremiah J. Faith,[1] Federico E. Rey,[1] Jiye Cheng,[1] Alexis E. Duncan,[2,3] Andrew L. Kau,[1] Nicholas W. Griffin,[1] Vincent Lombard,[4] Bernard Henrissat,[4,5] James R. Bain,[6,7,8] Michael J. Muehlbauer,[6] Olga Ilkayeva,[6] Clay F. Semenkovich,[9] Katsuhiko Funai,[9] David K. Hayashi,[10] Barbara J. Lyle,[11] Margaret C. Martini,[11] Luke K. Ursell,[12] Jose C. Clemente,[12] William Van Treuren,[12] William A. Walters,[13] Rob Knight,[12,14,15] Christopher B. Newgard,[6,7,8] Andrew C. Heath,[2] Jeffrey I. Gordon[1*]

The role of specific gut microbes in shaping body composition remains unclear. We transplanted fecal microbiota from adult female twin pairs discordant for obesity into germ-free mice fed low-fat mouse chow, as well as diets representing different levels of saturated fat and fruit and vegetable consumption typical of the U.S. diet. Increased total body and fat mass, as well as obesity-associated metabolic phenotypes, were transmissible with uncultured fecal communities and with their corresponding fecal bacterial culture collections. Cohousing mice harboring an obese twin's microbiota (Ob) with mice containing the lean co-twin's microbiota (Ln) prevented the development of increased body mass and obesity-associated metabolic phenotypes in Ob cage mates. Rescue correlated with invasion of specific members of Bacteroidetes from the Ln microbiota into Ob microbiota and was diet-dependent. These findings reveal transmissible, rapid, and modifiable effects of diet-by-microbiota interactions.