



# 29,清华,基因

本模板有完整的思路及框架，更贴近实用

汇报人： 时间： 2020



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# 29.1 Introduction

Development begins with a single fertilized egg, but gives rise to cells that have different developmental fates. The problem of early development is to understand how this asymmetry is introduced: how does a single initial cell give rise within a few cell divisions to progeny cells that have different properties from one another? The means by which asymmetry is generated varies with the type of organism. The egg itself may be homogeneous, with the acquisition of asymmetry depending on the process of the initial division cycles, as in the case of mammals. Or the egg may have an initial asymmetry in the distribution of its cytoplasmic components, which in turn gives rise to further differences as development proceeds, as in the case of *Drosophila*

# 29.1 Introduction

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## 29.2 Fly development uses a cascade of transcription factors

**Homeotic genes** are defined by mutations that convert one body part into another; for example, an insect leg may replace an antenna.

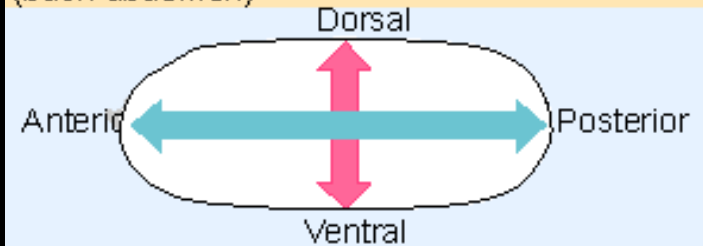
**Segmentation genes** are concerned with controlling the number or polarity of body segments in insects.

## 29.3 A gradient must be converted into discrete compartments

Figure 29.1 Gradients in the egg are translated into segments on the anterior-posterior axis and into specialized structures on the dorsal-ventral axis of the larva, and then into the segmented structure of the adult fly.

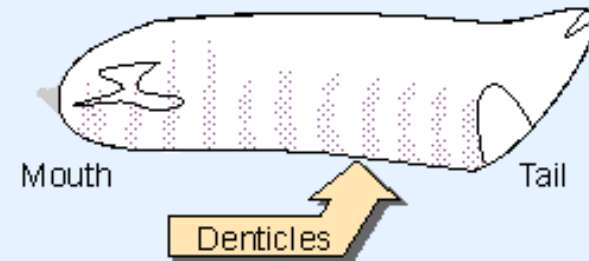
### The egg

Polarities are established along anterior-posterior (head-tail) axis and dorsal-ventral (back-abdomen)



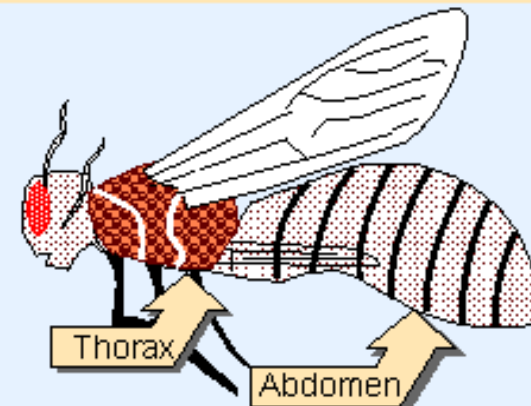
### The larva

Mouth parts are at anterior, tail parts at posterior. Bands of denticles extend from the ventral side, and identify segmentation units along the anterior-posterior axis



### Adult fly

Segmented structure has 3 thoracic segments & 8 abdominal segments



## 29.3 A gradient must be converted into discrete compartments

Figure 29.2 The early development of the *Drosophila* egg occurs in a common cytoplasm until the stage of cellular blastoderm.

Fertilized egg  
has two nuclei



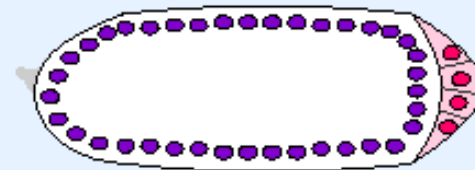
Divisions 1-8 (90 min)

Nuclei divide in common cytoplasm (syncytium). Nuclei in polar plasm (pink) become germ cell precursors.



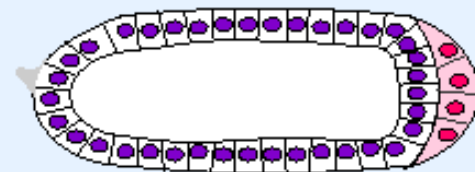
Syncytial blastoderm (150 min)

Nuclei migrate to periphery and divide; 4 further divisions occur (in close but not perfect synchrony).



Cellular blastoderm (195 min)

Membranes surround nuclei to form monolayer of ~6000 somatic cells.



## 29.4 Maternal gene products establish gradients in early embryogenesis

**Morphogen** is a factor that induces development of particular cell types in a manner that depends on its concentration.

## 29.4 Maternal gene products establish gradients in early embryogenesis

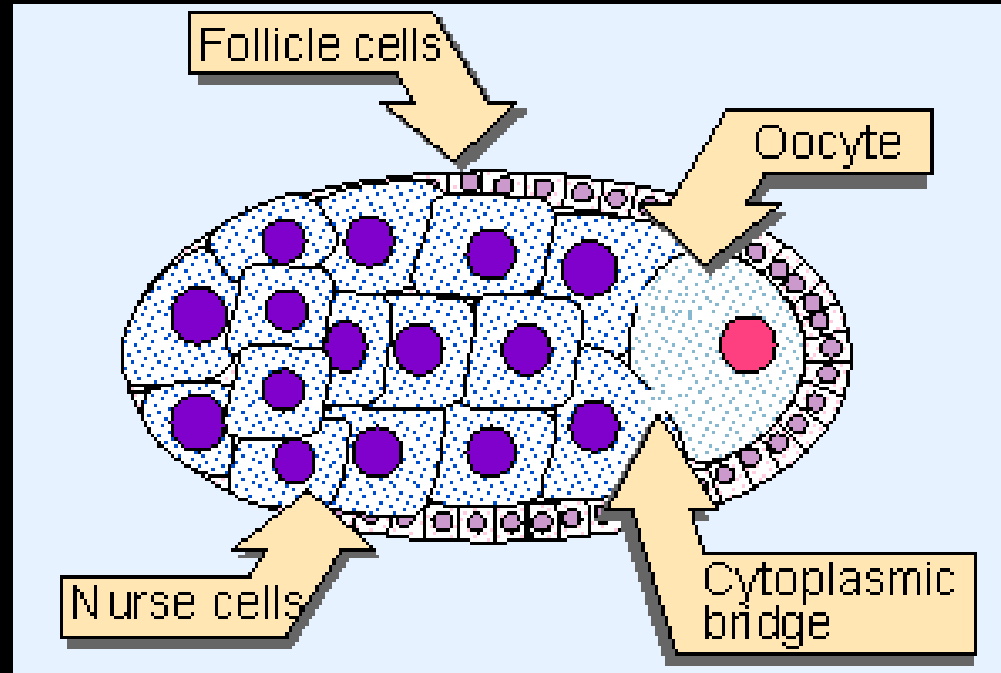


Figure 29.3 A *Drosophila* follicle contains an outer surface of follicle cells that surround nurse cells that are in close contact with the oocyte. Nurse cells are connected by cytoplasmic bridges to each other and to the anterior end of the oocyte. Follicle cells are somatic; nurse cells and the oocyte are germline in origin.

## 29.4 Maternal gene products establish gradients in early embryogenesis

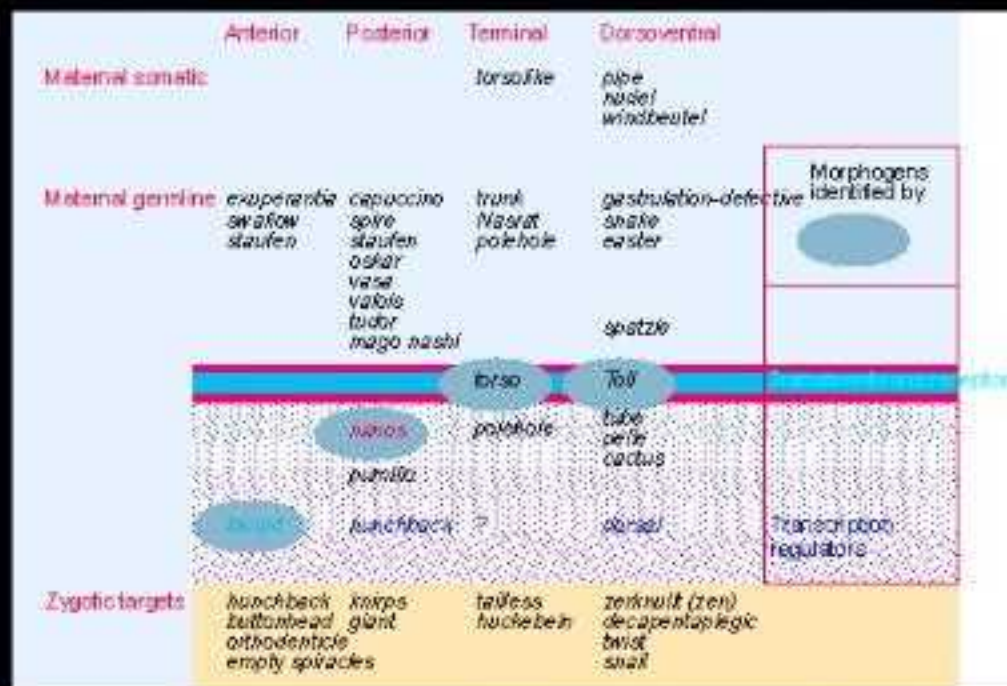


Figure 29.4 Each of the four maternal systems that functions in the egg is initiated outside the egg. The pathway is carried into the egg, where each pathway has a localized product that is the morphogen. This may be a receptor or a regulator of gene expression. The final component is a transcription factor, which acts on zygotic targets that are responsible for the next stage of development.

## 29.5 Anterior development uses localized gene regulators

Figure 29.5 Translation of a localized mRNA generates a gradient of protein as the products diffuse away from the site of synthesis.

mRNA is localized at anterior end



mRNA is translated

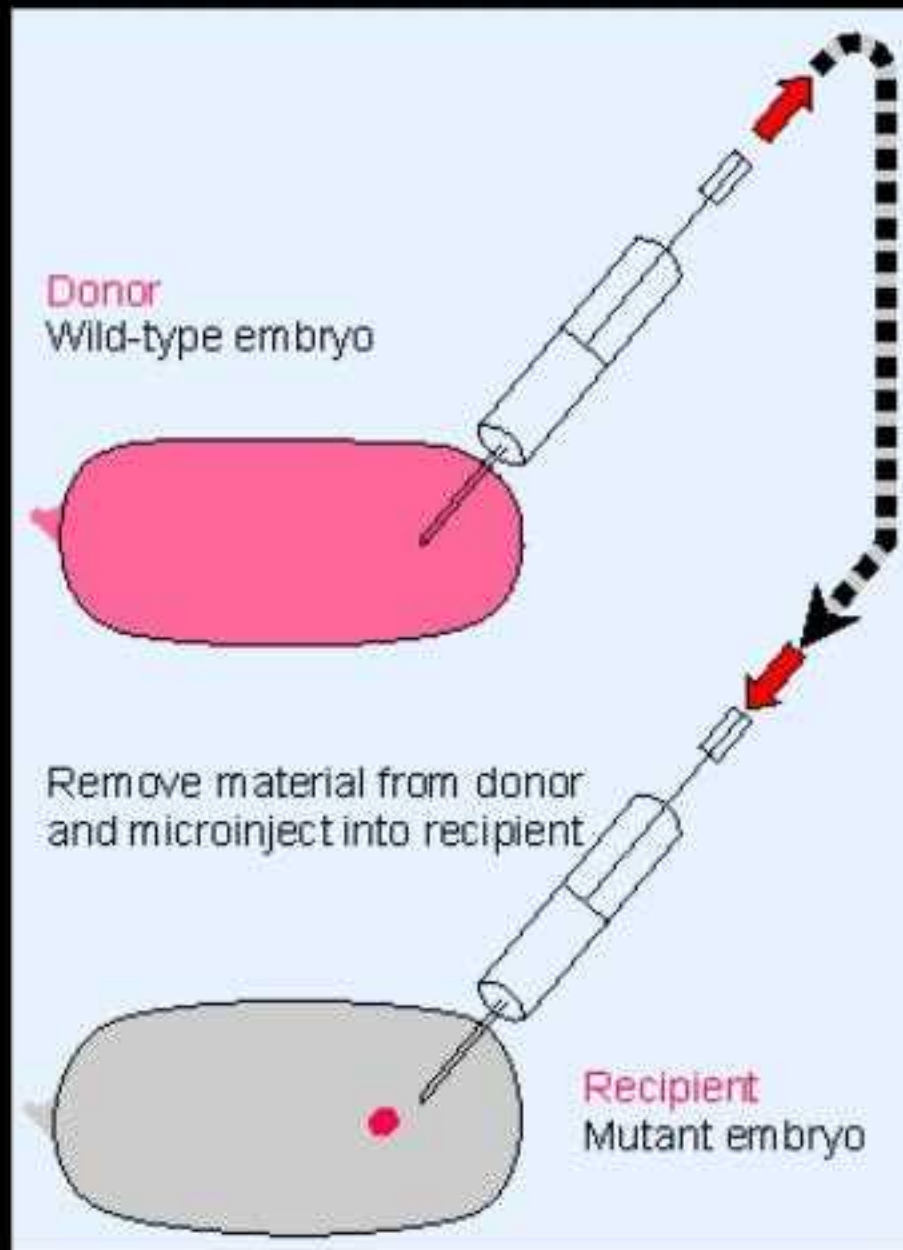


Protein diffuses from site of synthesis



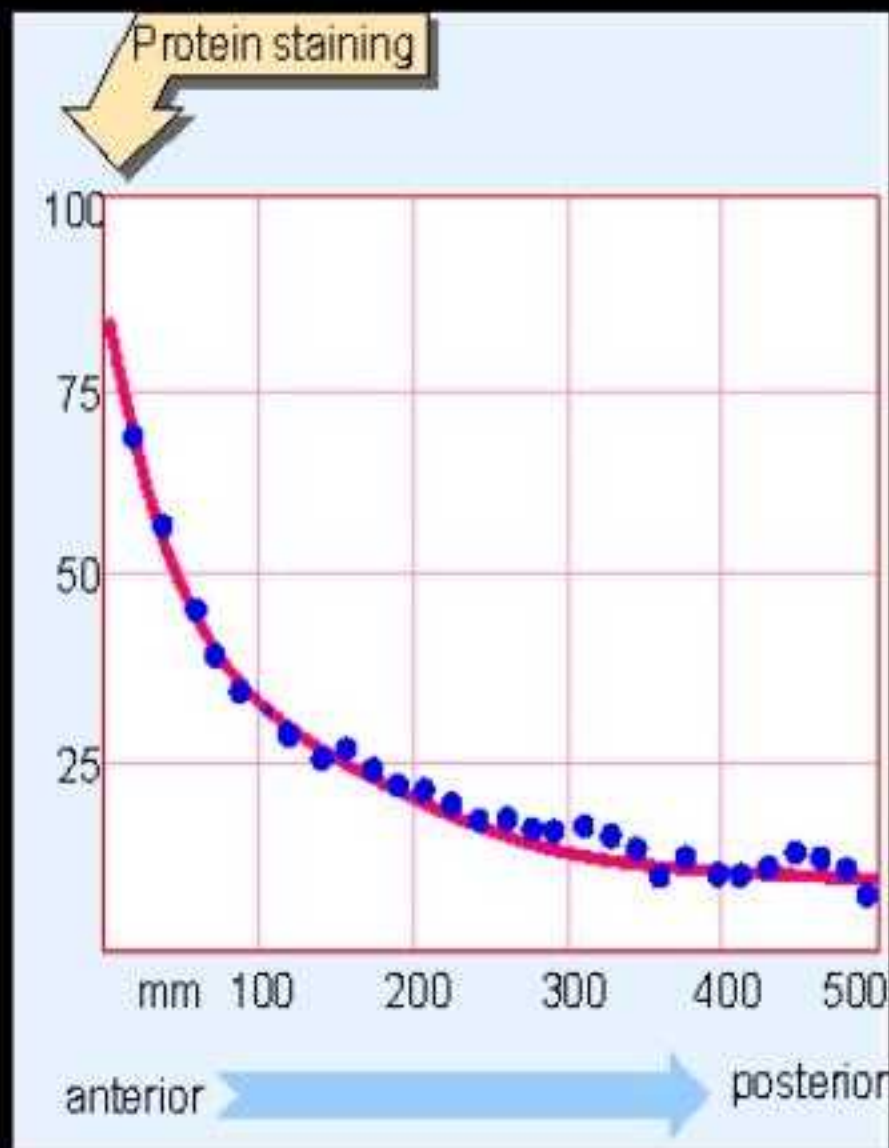
## 29.5 Anterior development uses localized gene regulators

Figure 29.6 Mutant embryos that cannot develop can be rescued by injecting cytoplasm taken from a wild-type embryo. The donor can be tested for time of appearance and location of the rescuing activity; the recipient can be tested for time at which it is susceptible to rescue and the effects of injecting material at different locations.



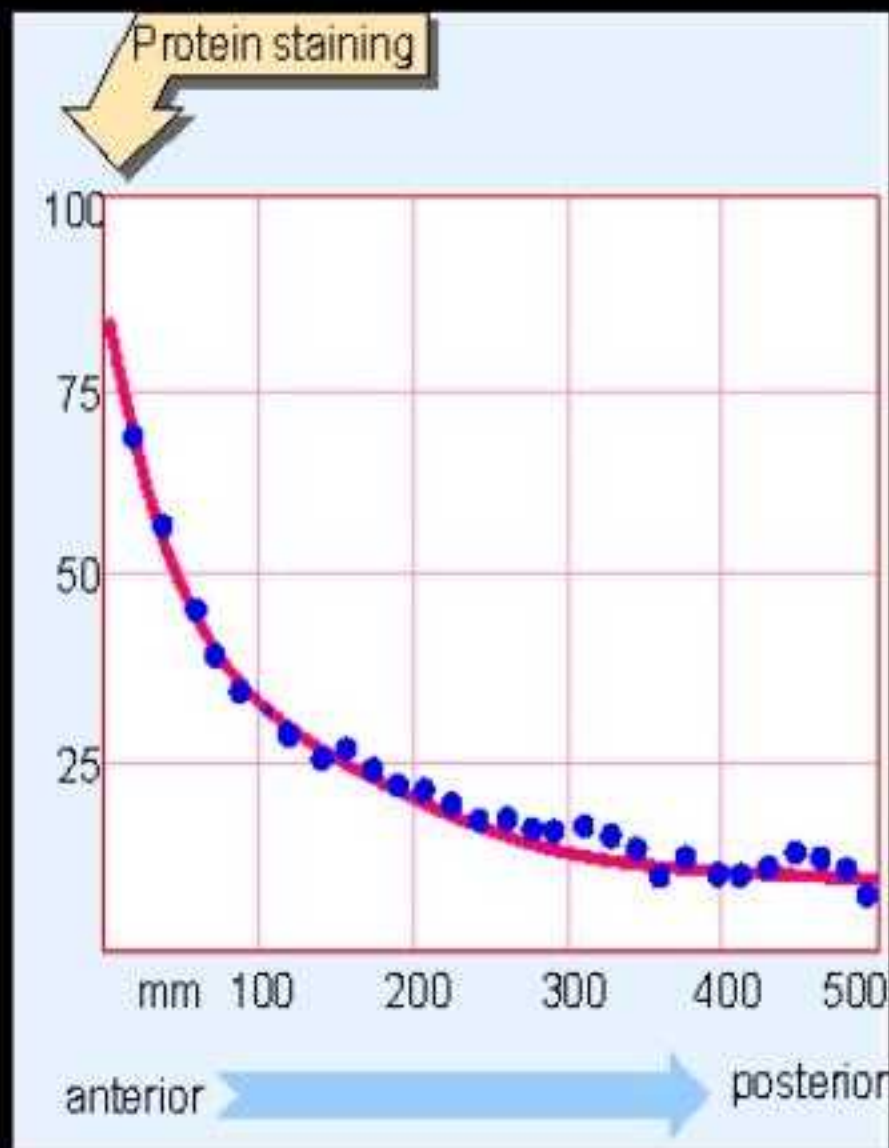
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Figure 29.7 Bicoid protein forms a gradient during *D. melanogaster* development that extends for ~200 mm along the egg of 500 mm.



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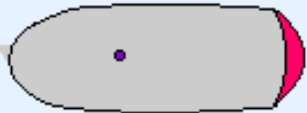







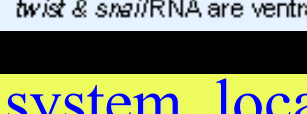
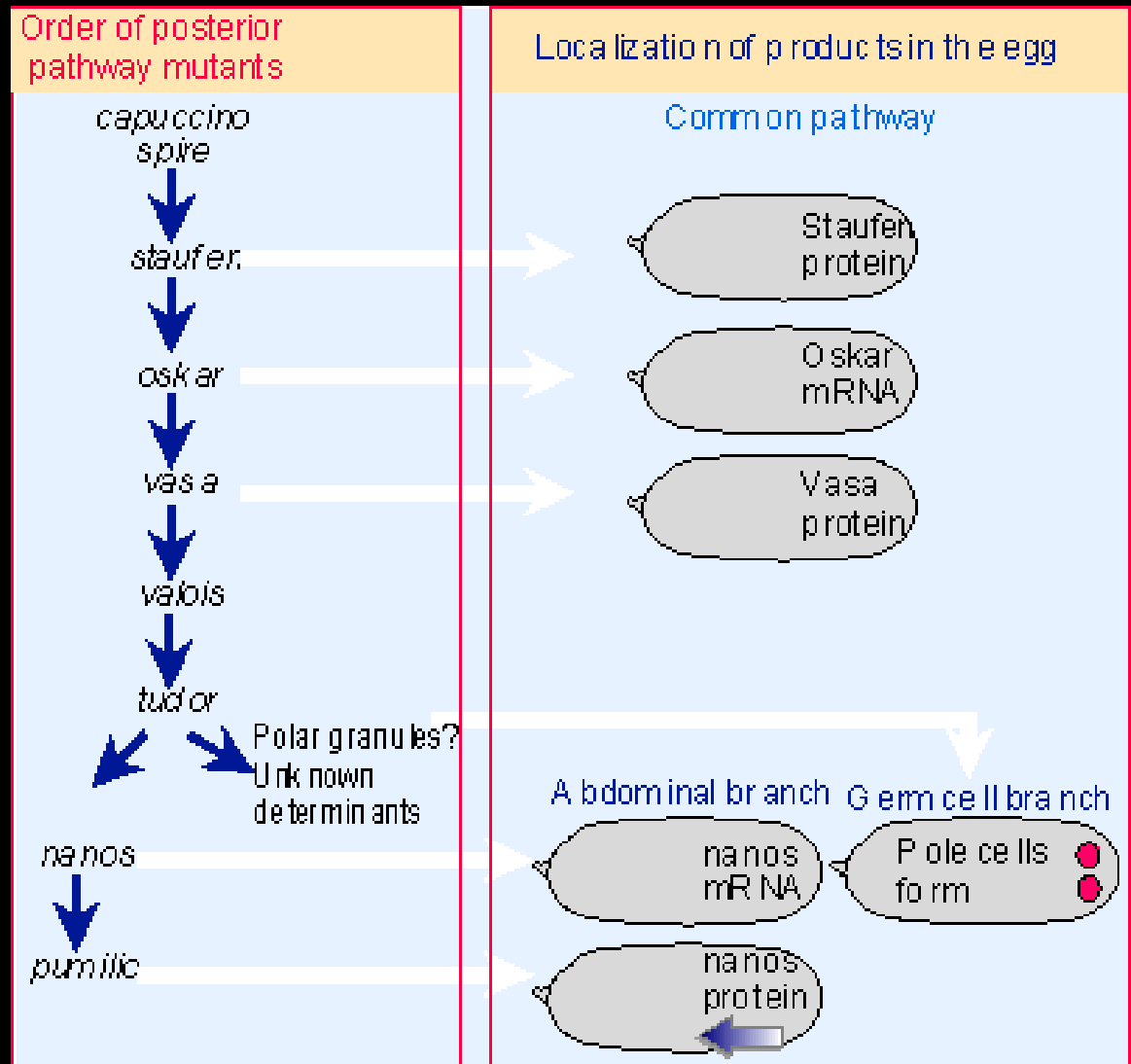
	Anterior system	Posterior system	Dorsal-ventral system
<b>Egg</b> Products transported or activated by nurse or follicle cells	<i>bicoid</i> RNA is anterior 	<i>hunchback</i> RNA is ubiquitous; <i>nanos</i> RNA is posterior 	Toll protein is ubiquitous; spatzle protein (and therefore Toll) is activated ventrally 
<b>Syncytial blastoderm</b> Maternal RNAs are translated	<i>bicoid</i> protein forms gradient 	<i>nanos</i> protein is in posterior half 	dorsal protein is cytoplasmic 
<b>Cellular blastoderm</b> Zygotic RNAs are transcribed	<i>hunchback</i> RNA fills anterior region 	stripes of <i>knirps</i> & <i>giant</i> RNA 	<i>dpp</i> & <i>zen</i> RNA are dorsal 
			<i>twist</i> & <i>snail</i> RNA are ventral 

Figure 29.17 In each axis-determining system, localized products in the egg cause other maternal RNAs or proteins to be broadly localized at syncytial blastoderm, and zygotic RNAs are transcribed in bands at cellular blastoderm.

# 29.6 Posterior development uses another localized regulator

Figure 29.8 The posterior pathway has two branches, responsible for abdominal development and germ cell formation.



# 29.6 Posterior development uses another localized regulator

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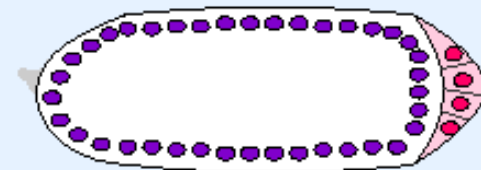
Divisions 1-8 (90 min)

Nuclei divide in common cytoplasm (syncytium). Nuclei in polar plasm (pink) become germ cell precursors.



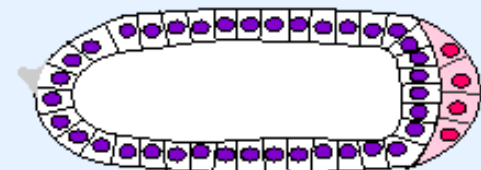
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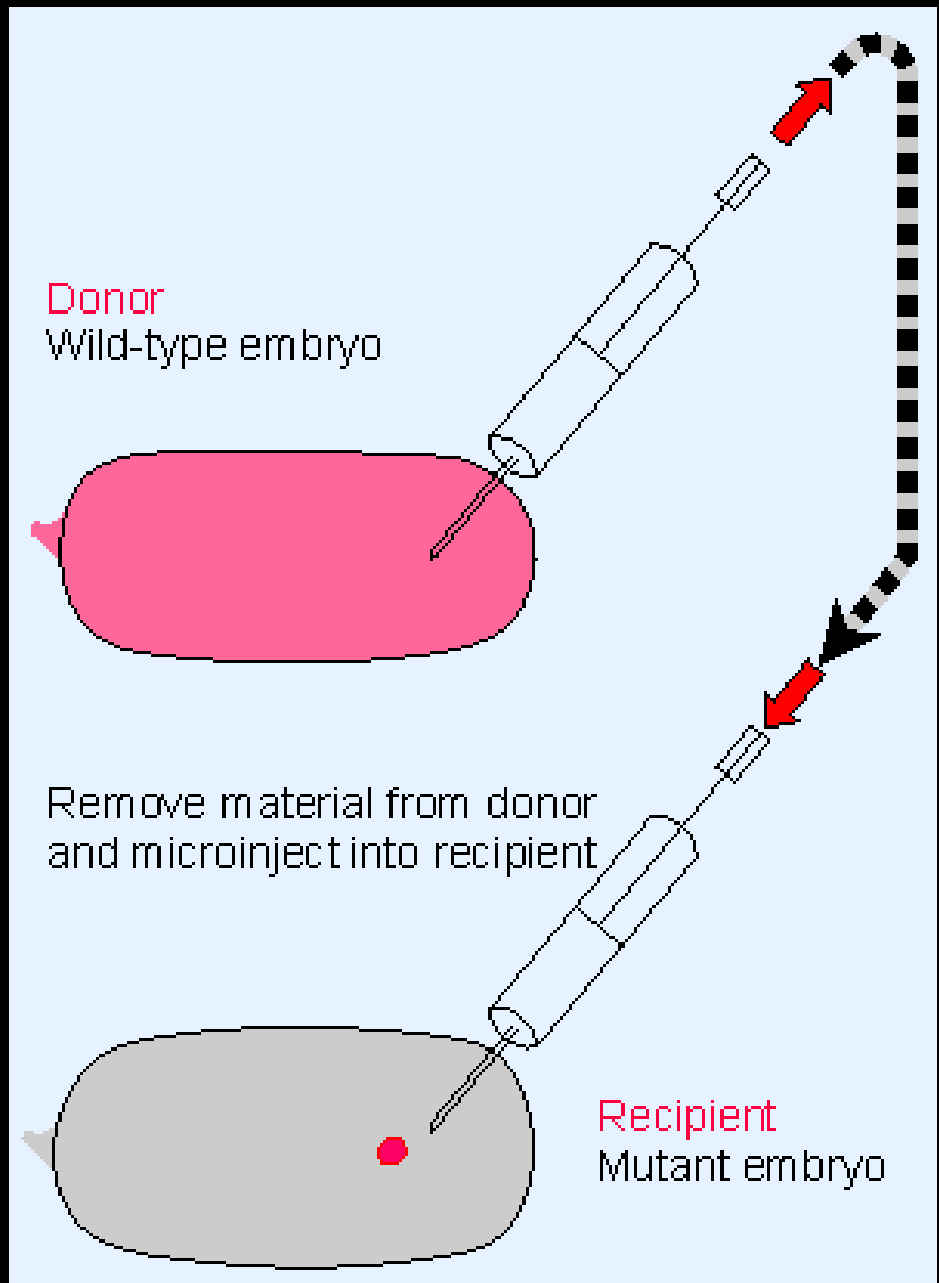
Cellular blastoderm (195 min)

Membranes surround nuclei to form monolayer of ~6000 somatic cells.



## 29.6 Posterior development uses another localized regulator

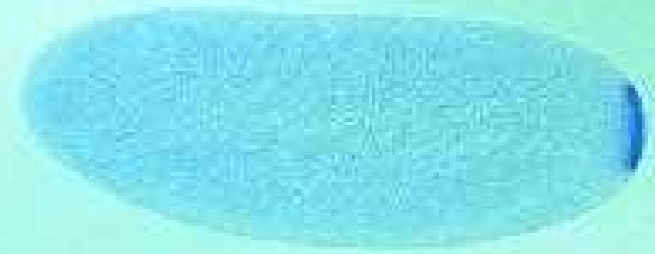
Figure 29.6 Mutant embryos that cannot develop can be rescued by injecting cytoplasm taken from a wild-type embryo. The donor can be tested for time of appearance and location of the rescuing activity; the recipient can be tested for time at which it is susceptible to rescue and the effects of injecting material at different locations.



## 29.6 Posterior development uses another localized regulator

Figure 29.9 nanos products are localized at the posterior end of a *Drosophila* embryo. The upper photograph shows the tightly localized RNA in the very early embryo (at the time of the 3rd nuclear division). The lower photograph shows the spreading of nanos protein at the 8th nuclear division. Photographs kindly provided by Ruth Lehmann.

nanos RNA is localized at the posterior end at the 3rd division

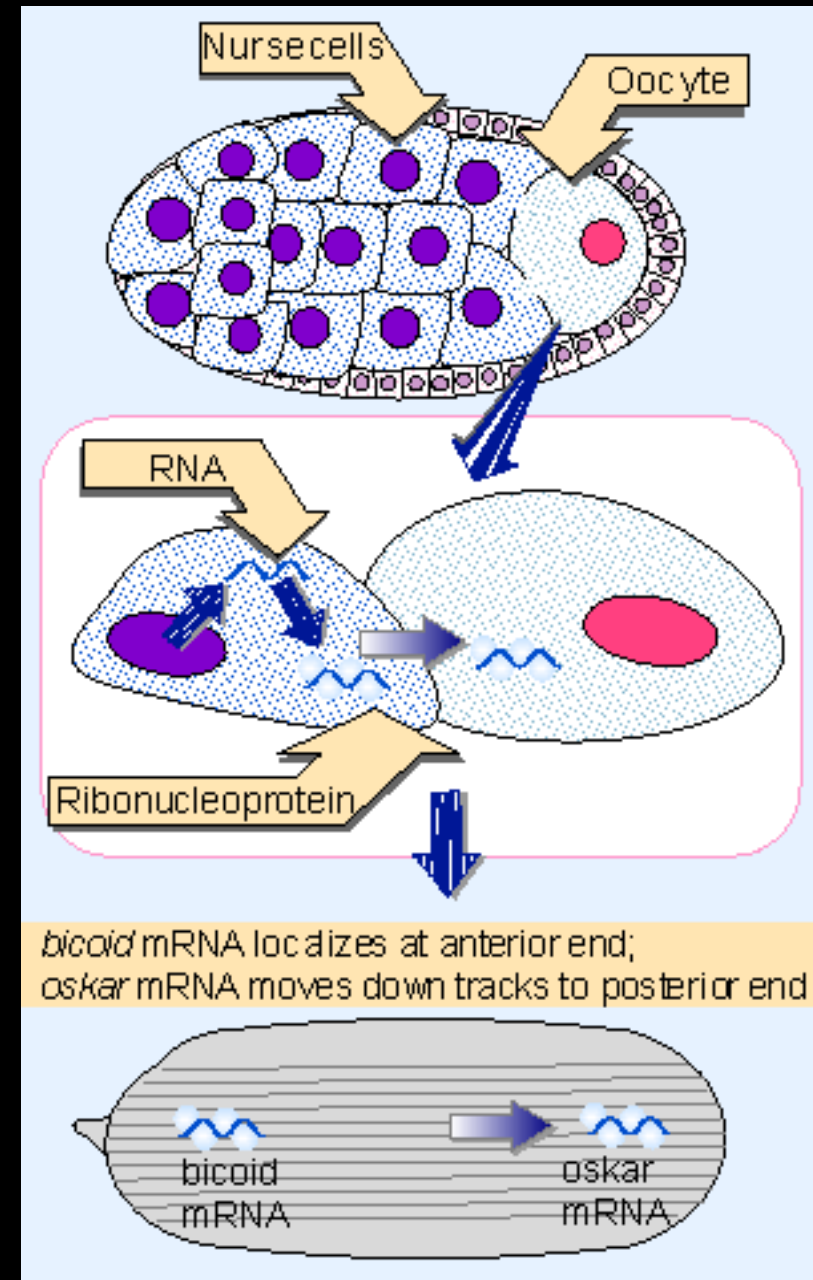


nanos protein spreads from the posterior end at the 8th division



## 29.7 How are mRNAs and proteins transported and localized?

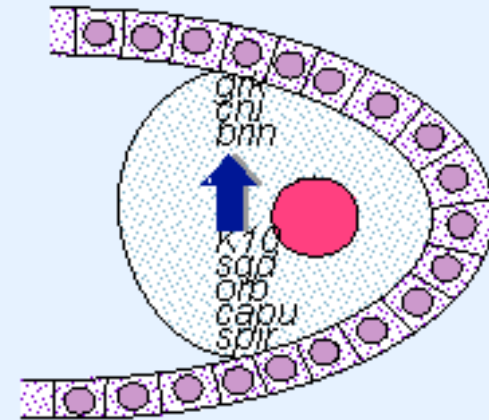
Figure 29.10 Some mRNAs are transported into the *Drosophila* egg as ribonucleoprotein particles. They move to their final sites of localization by association with tracks that may be either either microtubules or actin filaments.



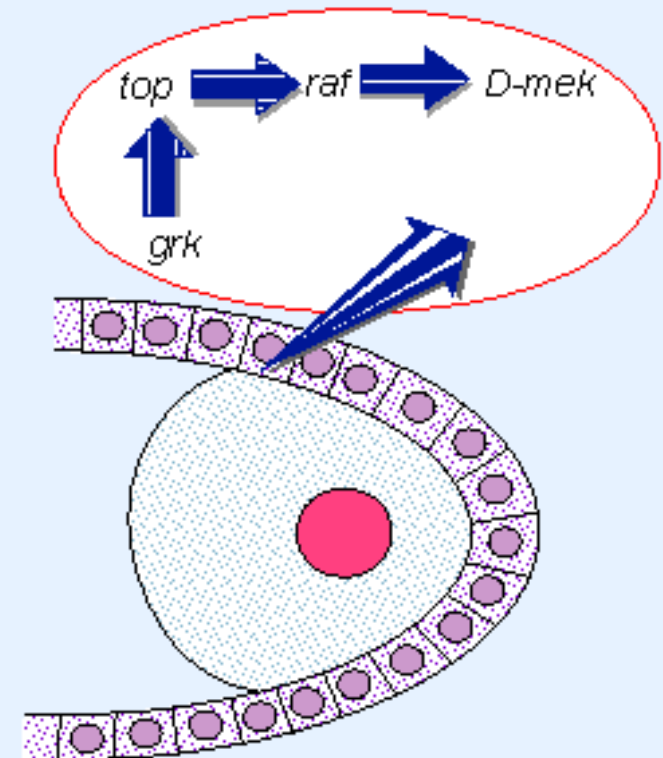
## 29.8 Dorsal-ventral development uses localized receptor-ligand interactions

Figure 29.11 Dorsal and ventral identities are first distinguished when *grk* mRNA is localized on the dorsal side of the oocyte. Synthesis of Grk activates the receptor coded by *torpedo*, which triggers a MAPK pathway in the follicle cells.

Dorsal localization of *grk* mRNA in oocyte



Activation of *torpedo* pathway in dorsal follicle cells



# 29.8 Dorsal-ventral development uses localized receptor-ligand interactions

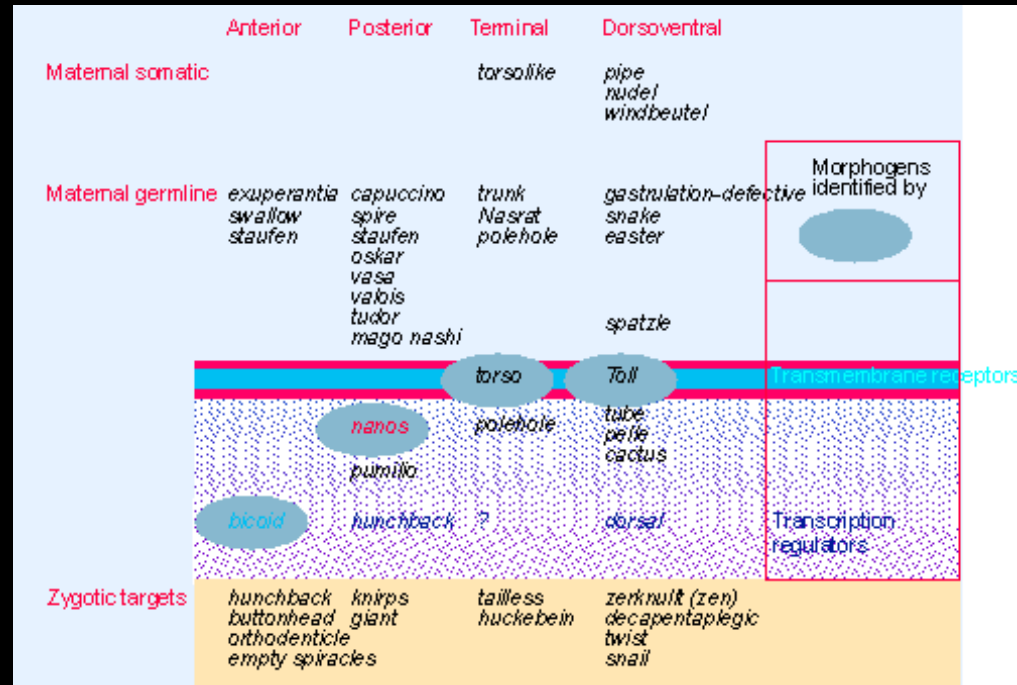
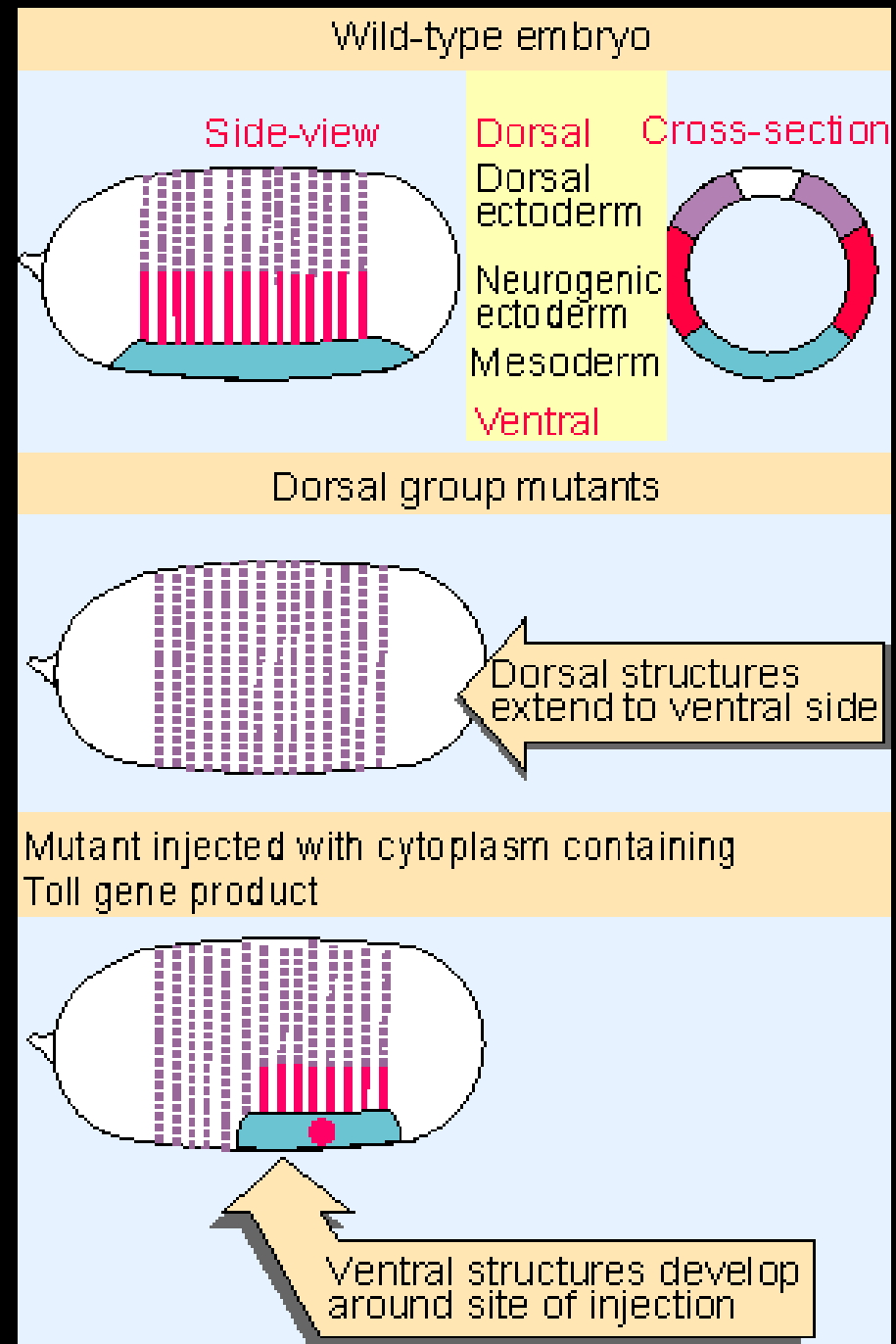


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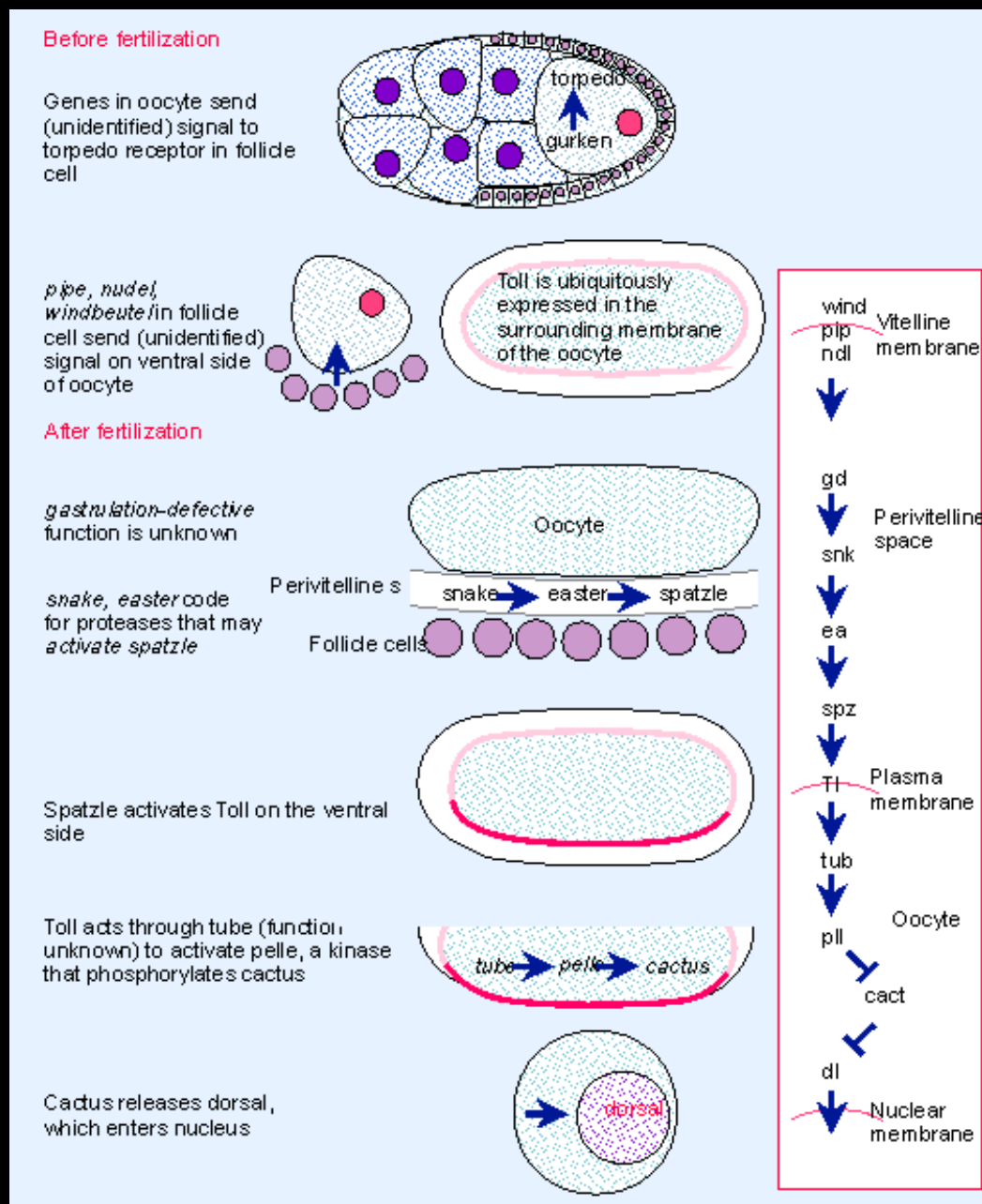
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Figure 29.12 Wild-type *Drosophila* embryos have distinct dorsal and ventral structures. Mutations in genes of the dorsal group prevent the appearance of ventral structures, and the ventral side of the embryo is dorsalized. Ventral structures can be restored by injecting cytoplasm containing the Toll gene product.



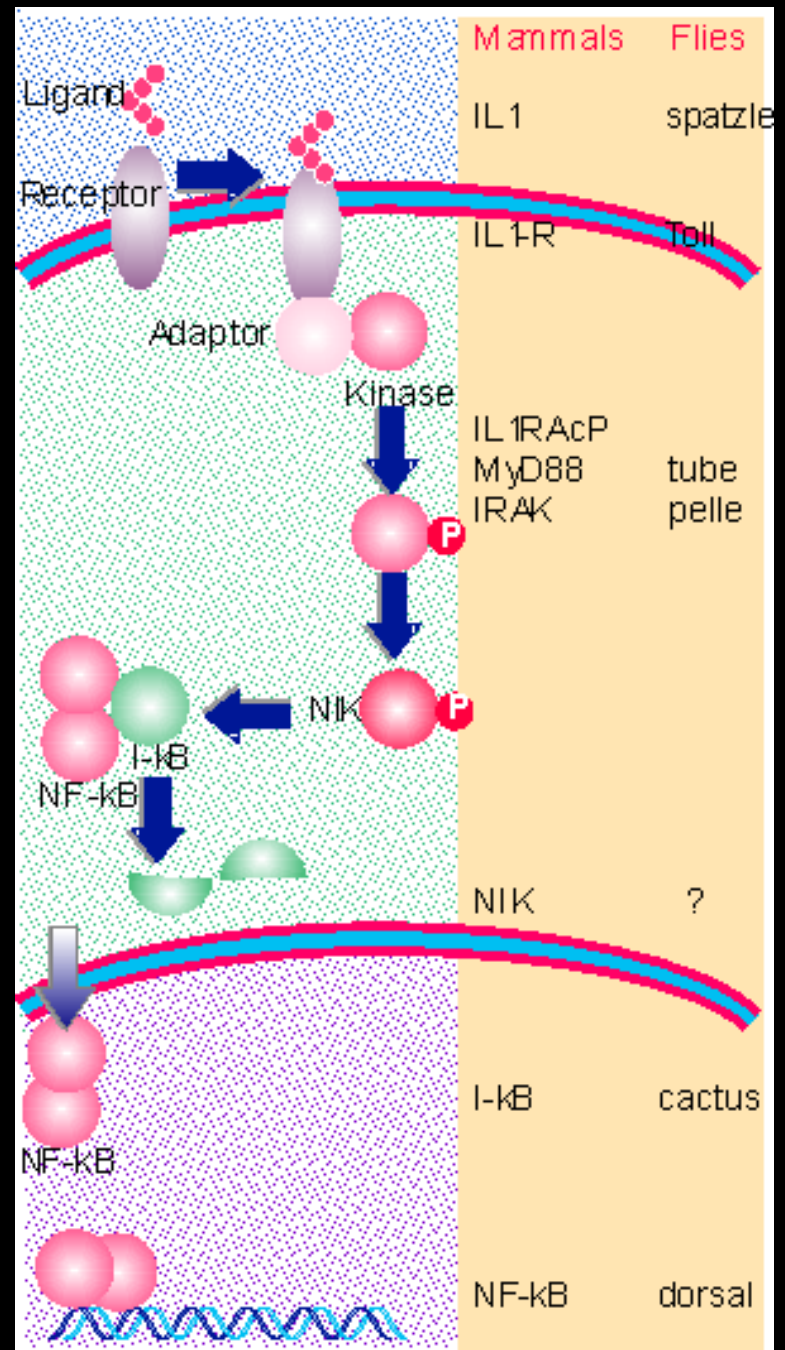
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Figure 29.13 The dorsal-ventral pathway is summarized on the right and shown in detail on the left. It involves interactions between follicle cells and the oocyte. The pathway moves into the oocyte when spatzie binds to Toll and activates the morphogen. The pathway is completed by transporting the transcription factor dorsal into the nucleus.



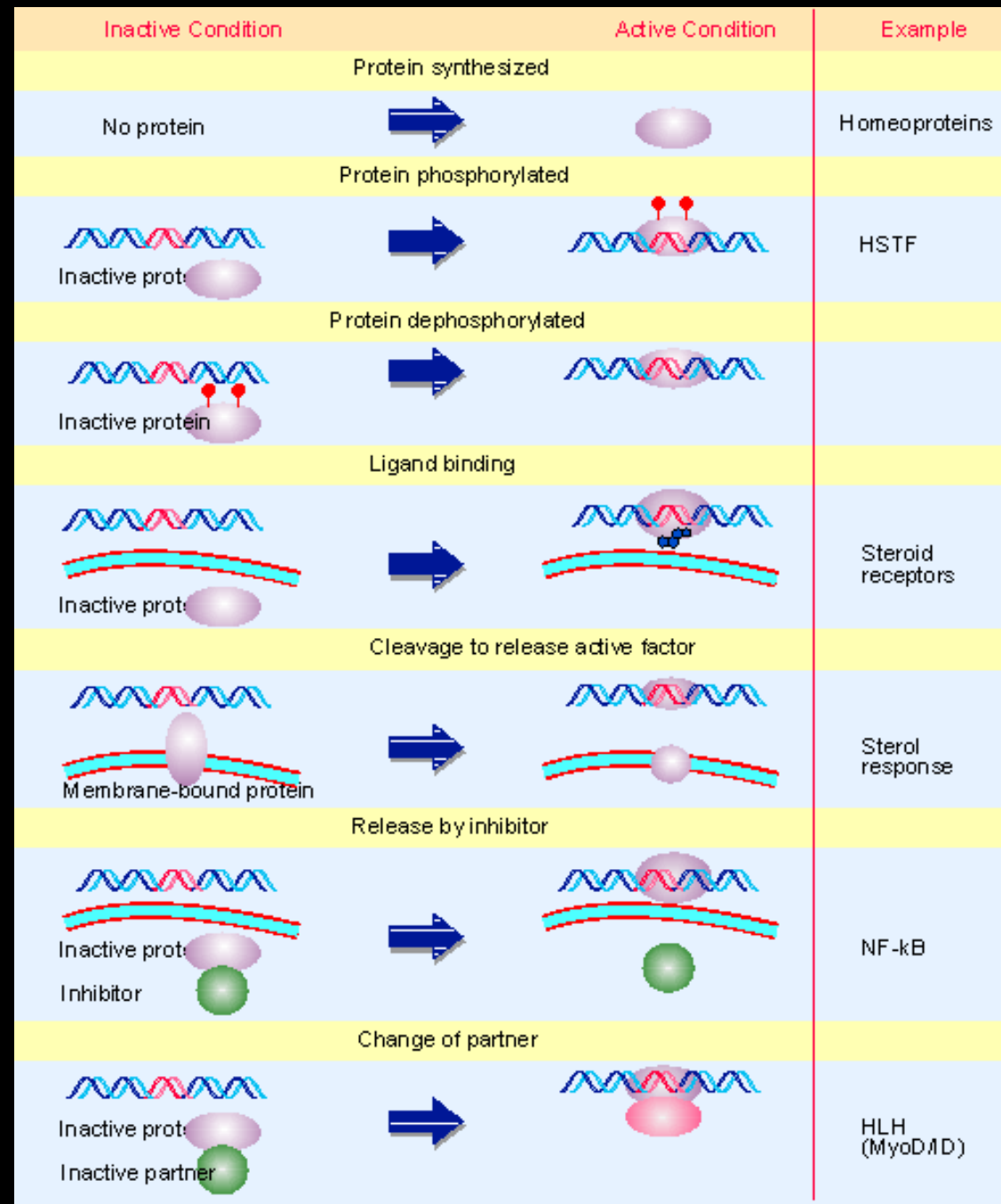
# 29.8 Dorsal-ventral development uses localized receptor-ligand interactions

Figure 29.14 Activation of IL1 receptor triggers formation of a complex containing adaptor(s) and a kinase. The IRAK kinase activates NIK, which phosphorylates I- $\kappa$ B. This triggers degradation of I- $\kappa$ B, releasing NF- $\kappa$ B, which translocates to the nucleus to activate transcription.



# 29.8 Dorsal-ventral development uses localized receptor-ligand interactions

Figure 21.2 The activity of a regulatory transcription factor may be controlled by synthesis of protein, covalent modification of protein, ligand binding, or binding of inhibitors that sequester the protein or affect its ability to bind to DNA.



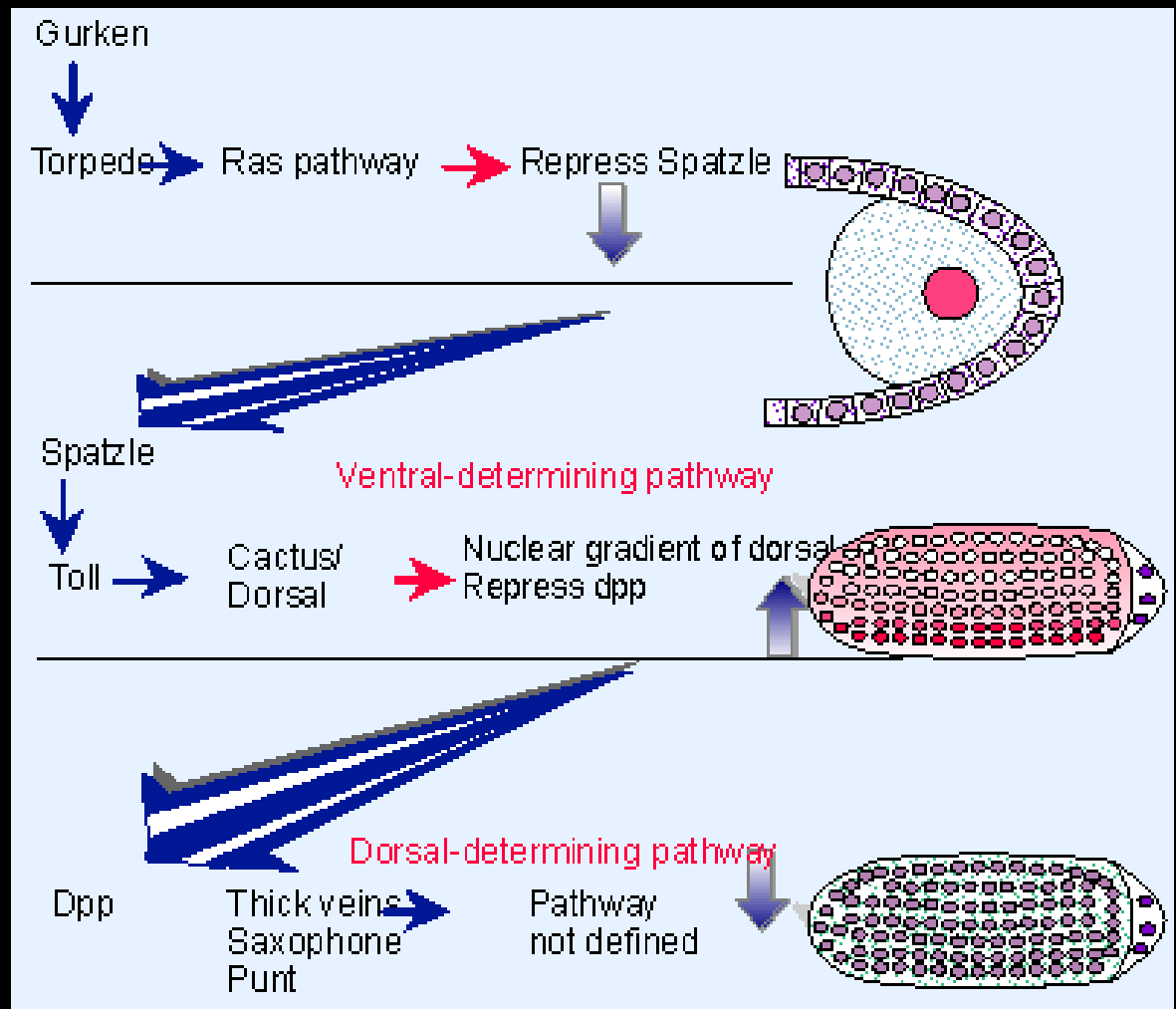
## 29.8 Dorsal-ventral development uses localized receptor-ligand interactions

Figure 29.15 Dorsal protein forms a gradient of nuclear localization from ventral to dorsal side of the embryo. On the ventral side (lower) the protein identifies bright nuclei; on the dorsal side (upper) the nuclei lack proteDorsal protein forms a gradient of nuclear localization from ventral to dorsal side of the embryo. On the ventral side (lower) the protein identifies bright nuclei; on the dorsal side (upper) the nuclei lack protein and show as dark holes in the bright cytoplasm.



# 29.8 Dorsal-ventral development uses localized receptor-ligand interactions

Figure 29.16  
Dorsal-ventral  
patterning  
requires the  
successive  
actions of  
three localized  
systems.



# 29.8 Dorsal-ventral development uses localized receptor-ligand interactions

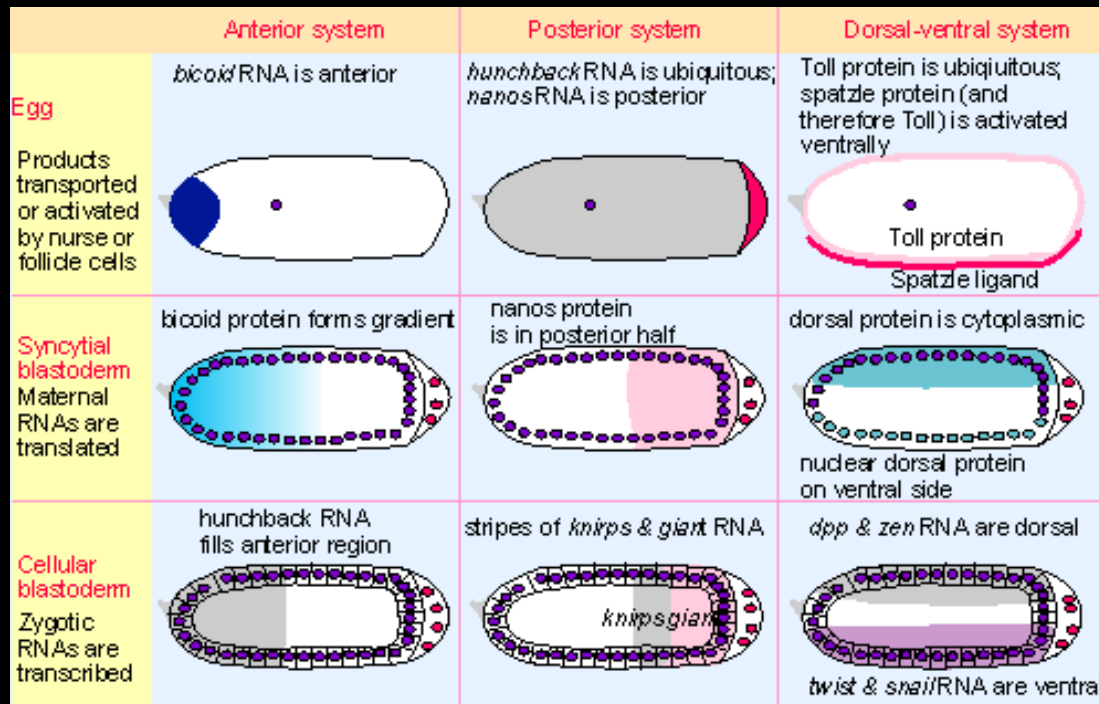
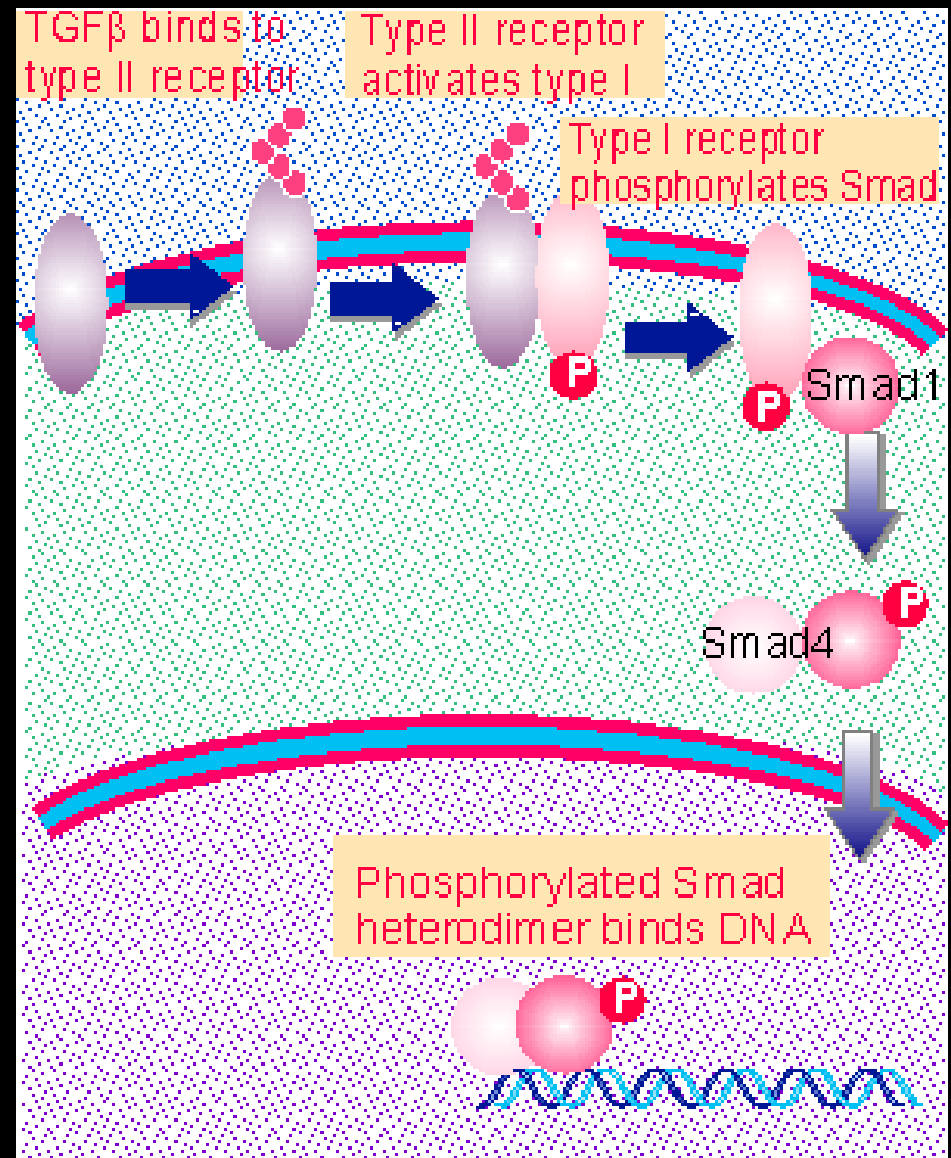


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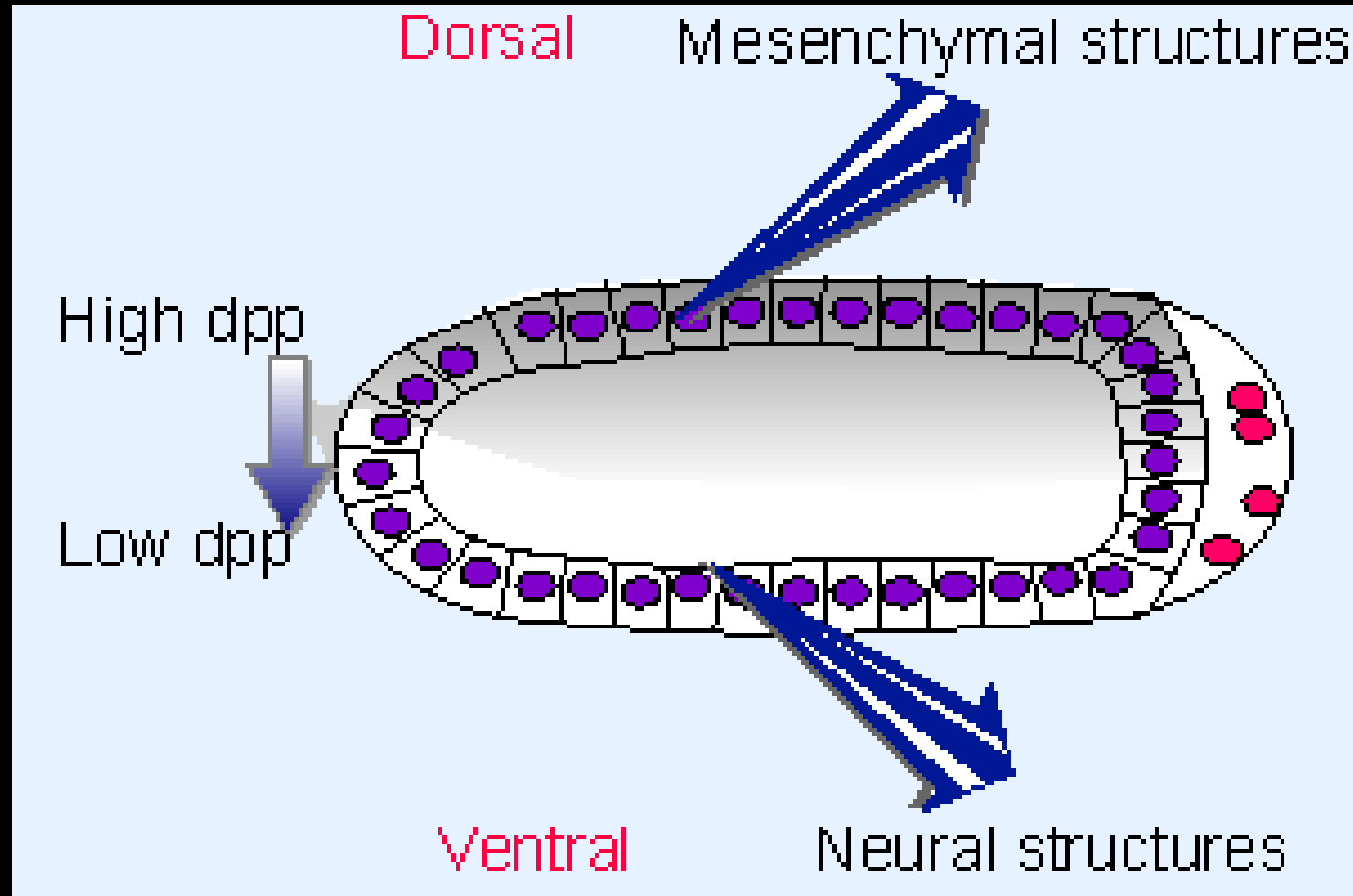
## 29.9 TGF/BMPs are diffusible morphogens

Figure 26.35 Activation of TGF $\beta$  receptors causes phosphorylation of a Smad, which is imported into the nucleus to activate transcription.



# 29.9 TGF/BMPs are diffusible morphogens

Figure 29.18  
The morphogen dpp forms a gradient originating on the dorsal side of the fly embryo. This prevents the formation of neural structures and induces mesenchymal structures.



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