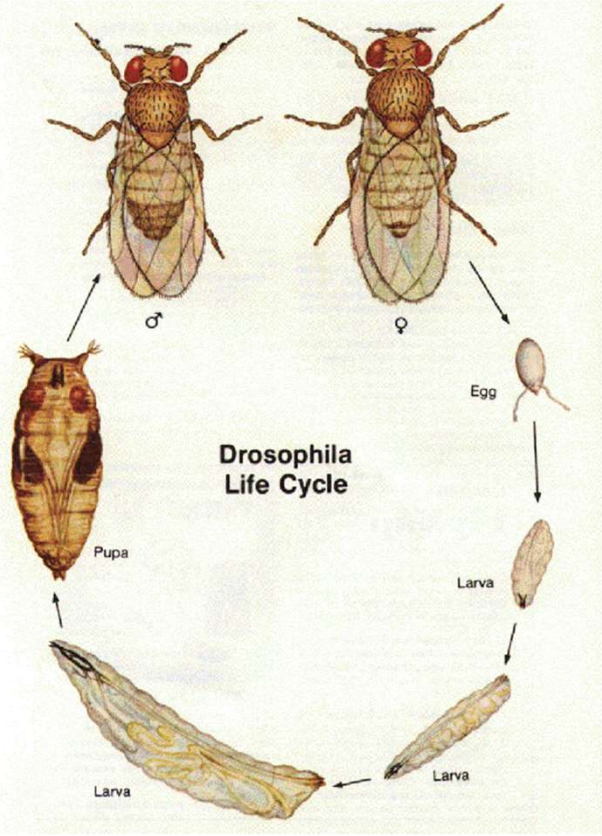
Maternal effect genes

1. These genes are present in the ovarian cell types such as the nurse cells and follicle cells and their expressions products are channeled into the oocytes in the form of mRNA after the egg is fertilized and laid.

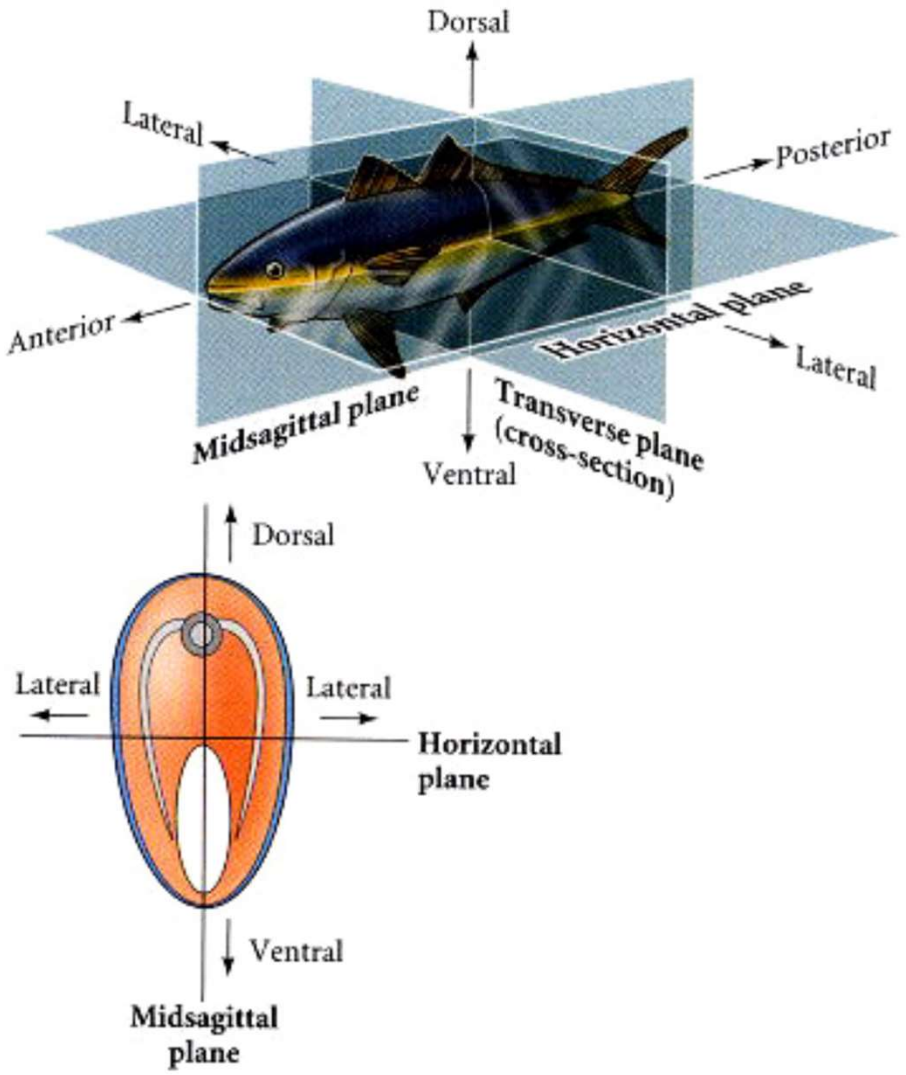
2. The patterning of the body plan is accomplished by performed mRNAs and proteins that are synthesized and laid down in the egg by the mother fly.

3. The genes responsible for the synthesis of these mRNAs are called maternal effect genes.

The anteroposterior axis of *Drosophila* embryo is patterned before the nuclei even begins to function. The nurse cells deposit mRNA in the developing oocyte, these mRNAs are apportioned to different regions of the cells.



The ***Drosophila*** **life cycle** consists of a number of stages: embryogenesis, three larval stages, a pupal stage, and (finally) the adult stage

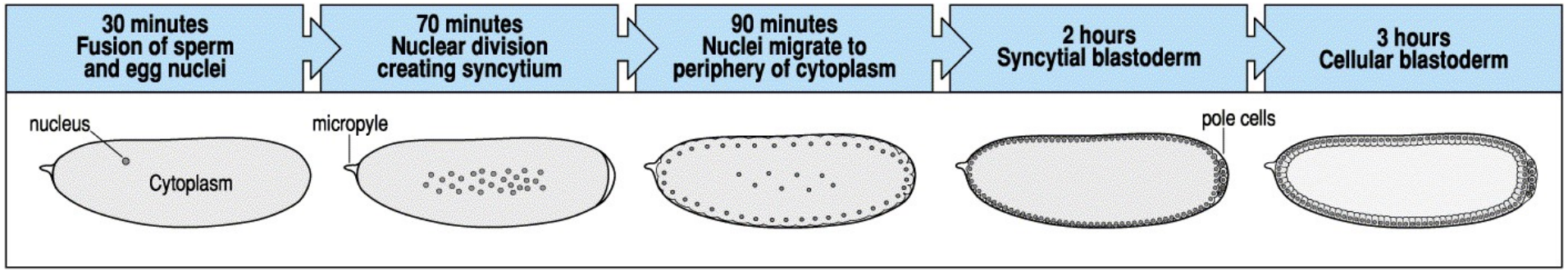


Early development of *Drosophila*

Rapid division
8 mins/division
9 divisions

13 divisions

asynchronous



Single cell

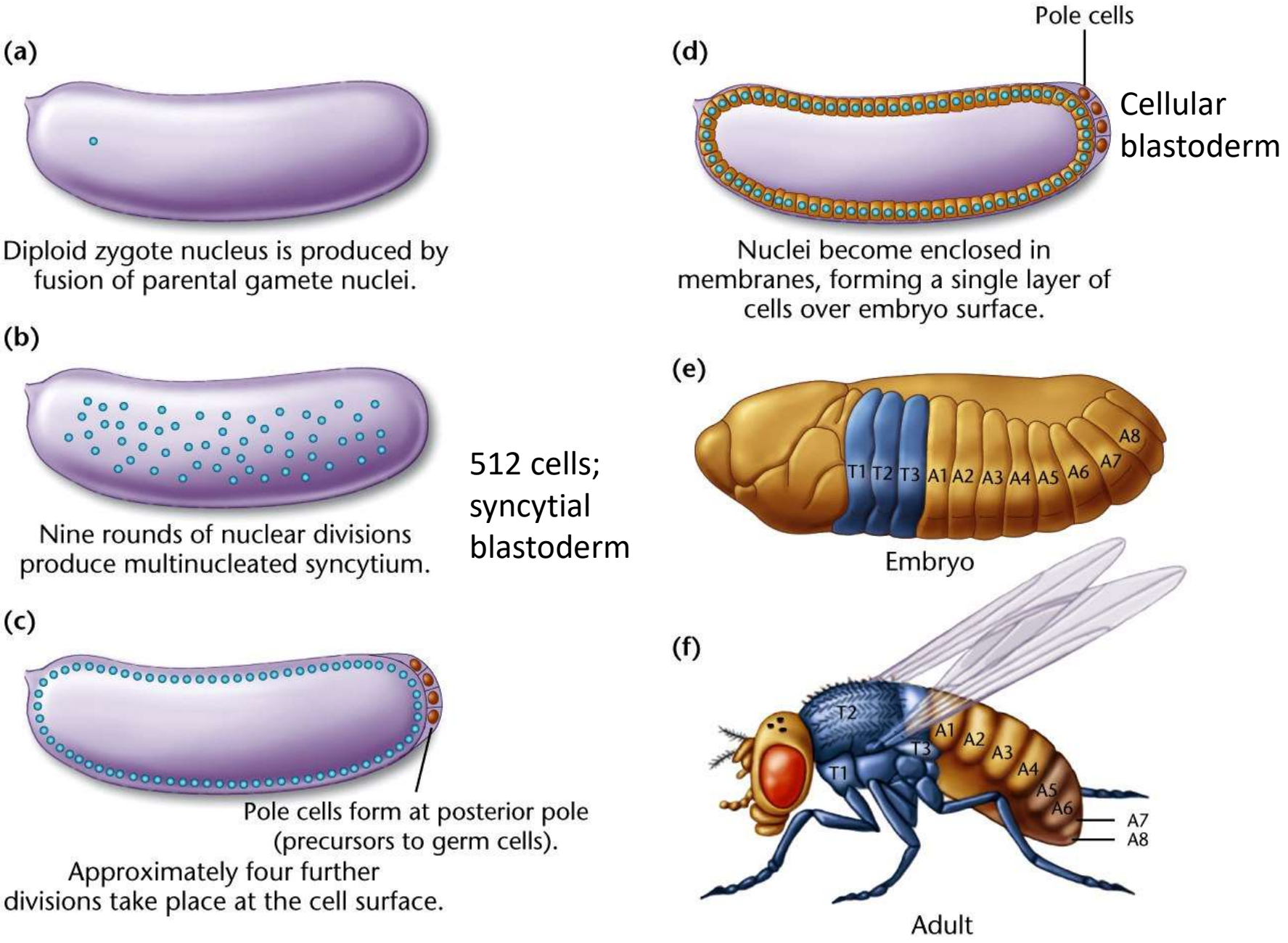


Figure 20-3 Essentials of Genetics, 6/e

Four maternal messanger RNAs are critical to formation of the anterior-posterior axis.

Bicoid and **Hunchback**- Anterior to posterior gradient- Head and thorax formation

Nanos and **Caudal** – Posterior to anterior gradient - Abdominal segment formation

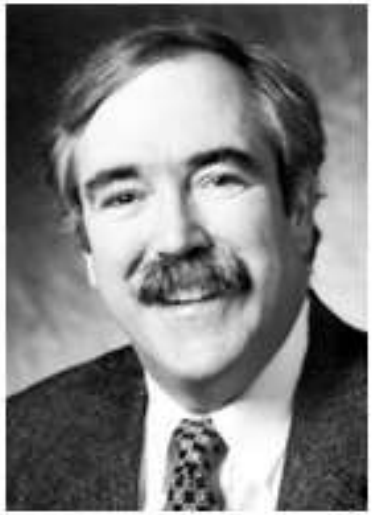
The Nobel Prize in Physiology or Medicine 1995

Edward B. Lewis

Prize share: 1/3

Christiane Nüsslein-Volhard

Prize share: 1/3

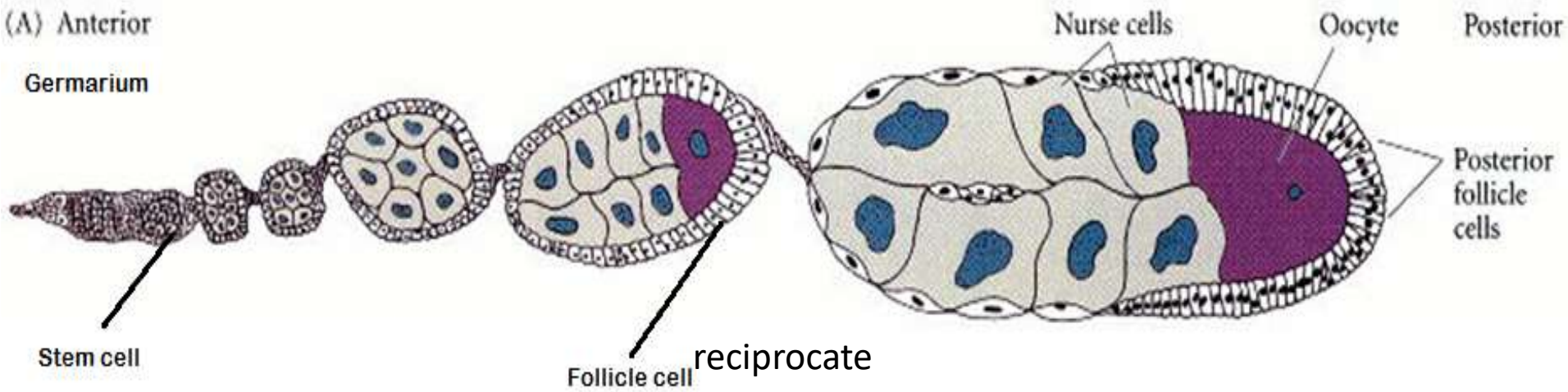


Eric F. Wieschaus

Prize share: 1/3

The Nobel Prize in Physiology or Medicine 1995 was awarded jointly to Edward B. Lewis, Christiane Nüsslein-Volhard and Eric F. Wieschaus *"for their discoveries concerning the genetic control of early embryonic development"*.

Oogenesis



reciprocate

Fig. 1 Development of Egg.

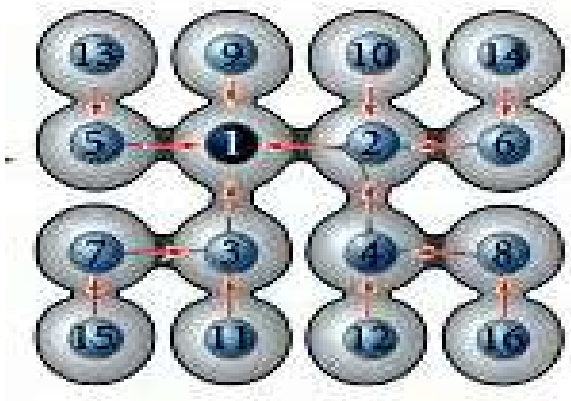


Fig. 2 One stem cell attach with four other cell.

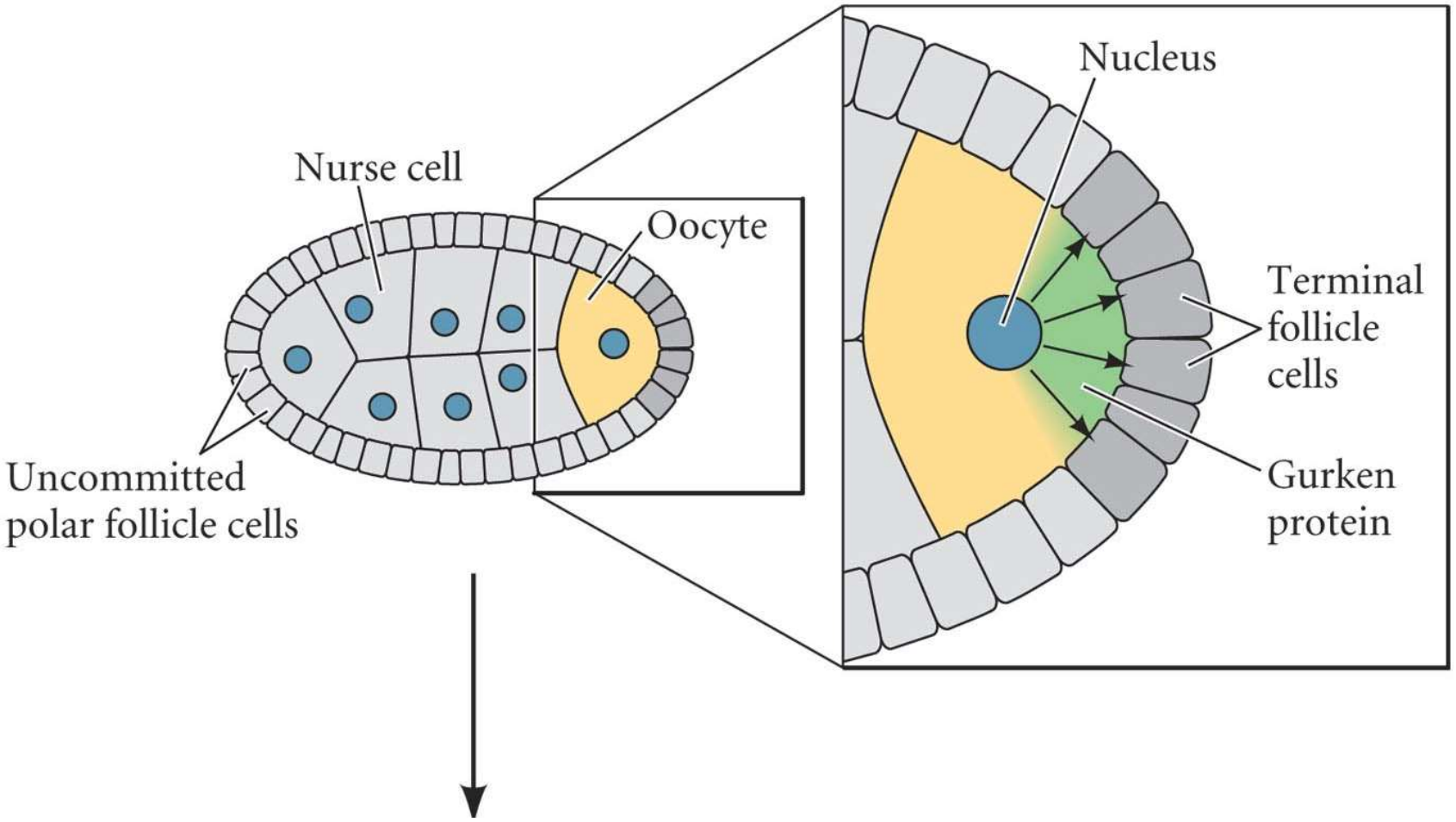
Oocyte moves into the posterior region of the egg chamber.

Nurse cells fill the anterior portion.

Oocyte nucleus moves to the terminal follicle cells and synthesizes **Gurken** protein.

Gurkein protein receptors are present in the follicel cells. The follicle cells after binding to Gurkein protein are differentiated to posterior follicle cells.

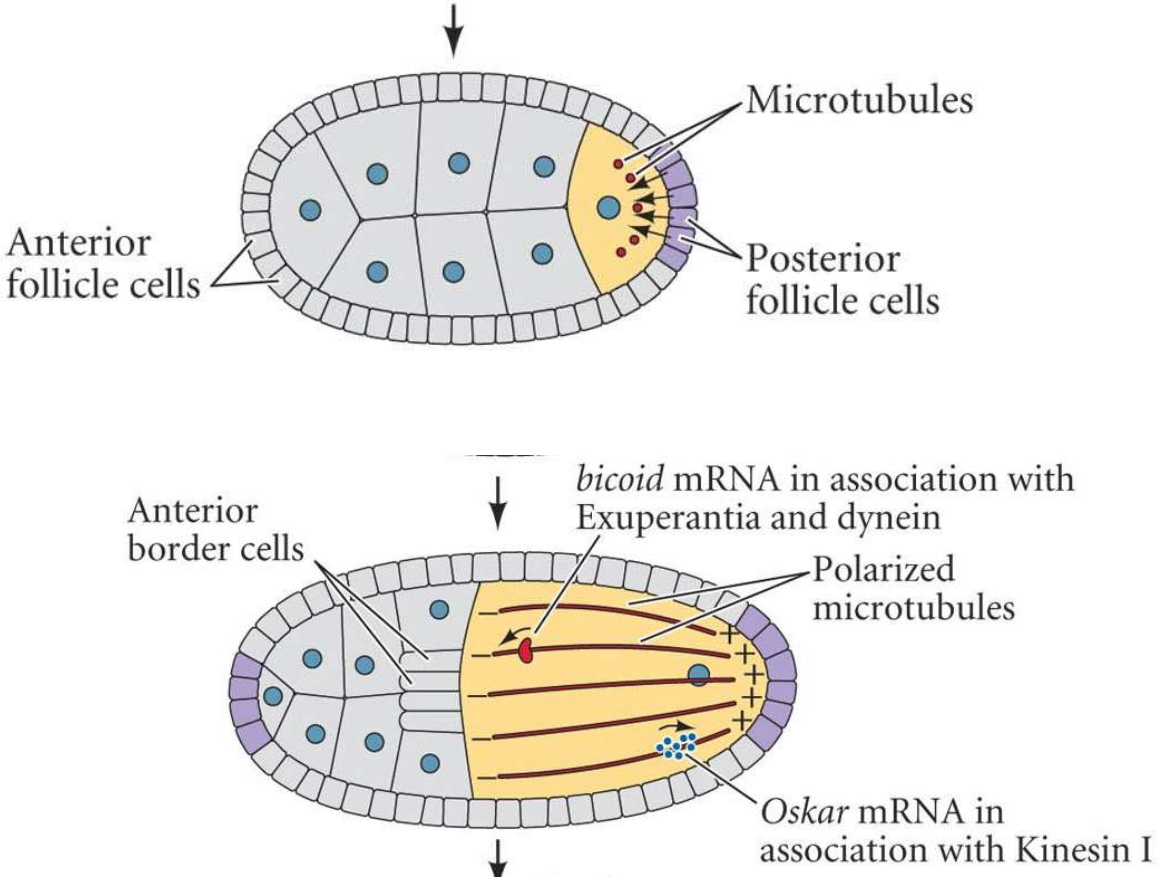
Gurken protein specifies the Anterior-Posterior axis of the *Drosophila* embryo during oogenesis



Involvement of Gurken protein during formation of axis.

Posterior follicle cells reciprocate by producing a molecule that form active protein kinase A in the egg.

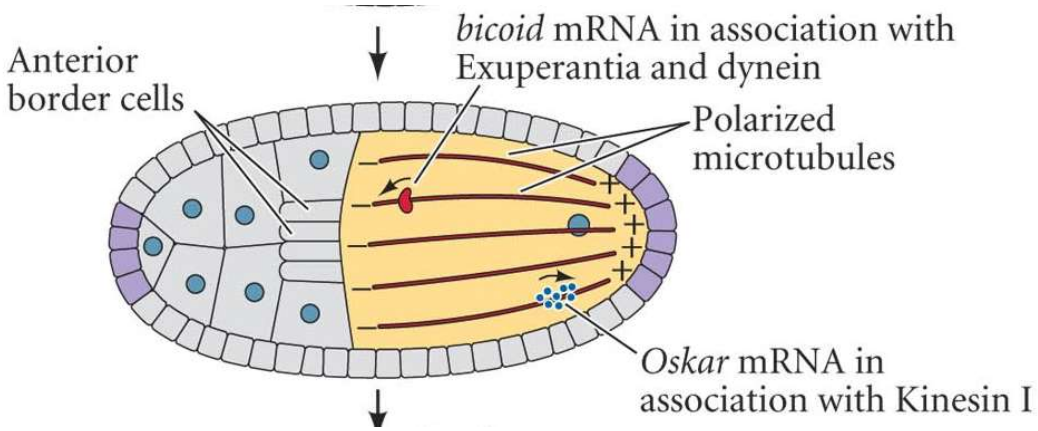
Protein kinase orient the microtubules such that the growing end is at the posterior



Bicoid message binds to non growing end of microtubule (bind to dynin, a motor protein)

Dynin moves the bicoid to anterior end of egg.

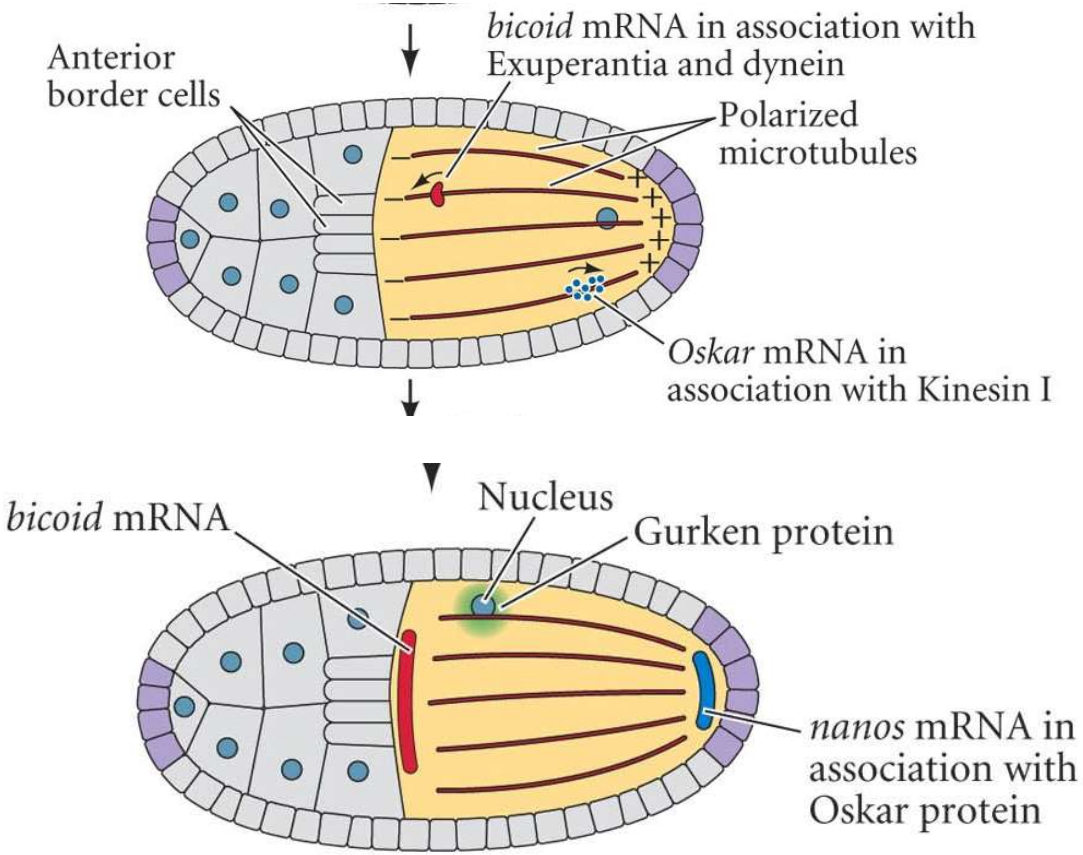
Bicoid mRNA contain a sequence in its 3'UTR that interact with Exuperantia and swallow proteins which tether this message to a dynein protein.



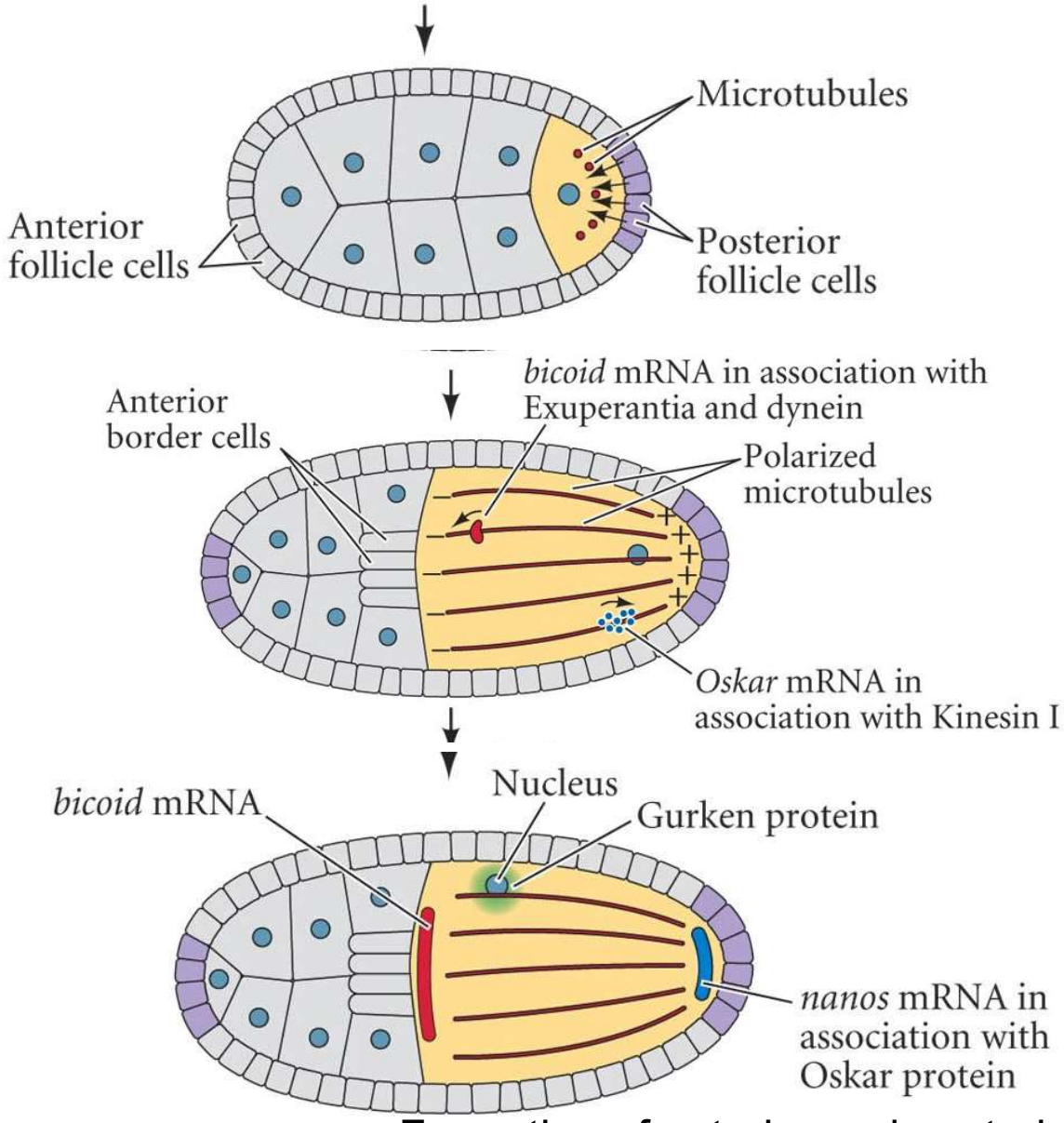
Oskar message becomes complexed with Kinesin I , (a moter protein that moves oskar to posterior end) and staufen protein. Staufen allows translation of oskar message to oskar protein.

Oskar protein binds to nanos message.

Nucleus and Gurken protein migrates along the microtubule.



Localized maternal mRNA sets up anterior and posterior poles

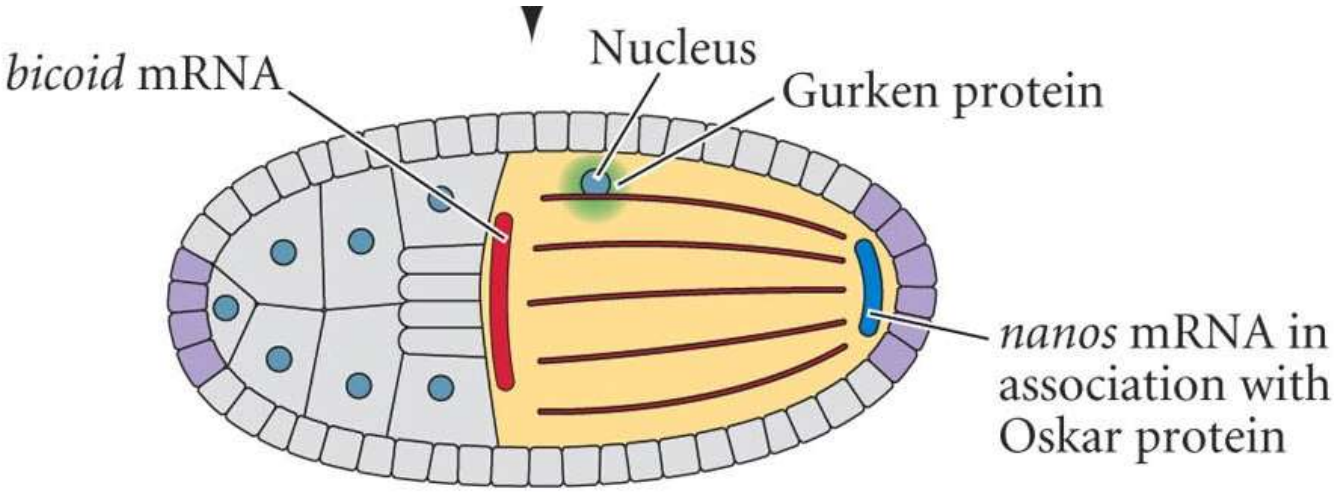


Formation of anterior and posterior axis.

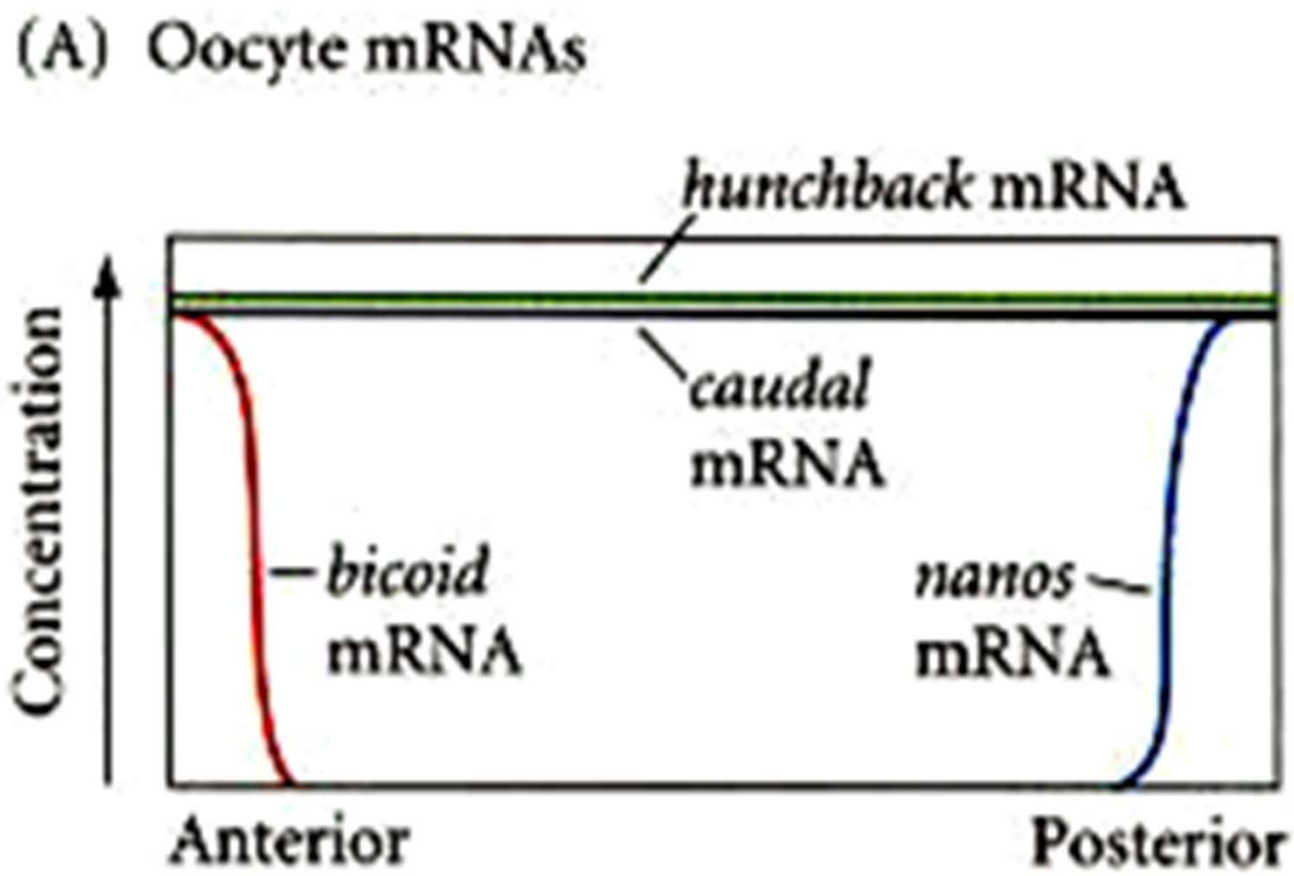
So, at completion of Oogenesis,

Bicoid is anchored at the anterior end of the oocyte.

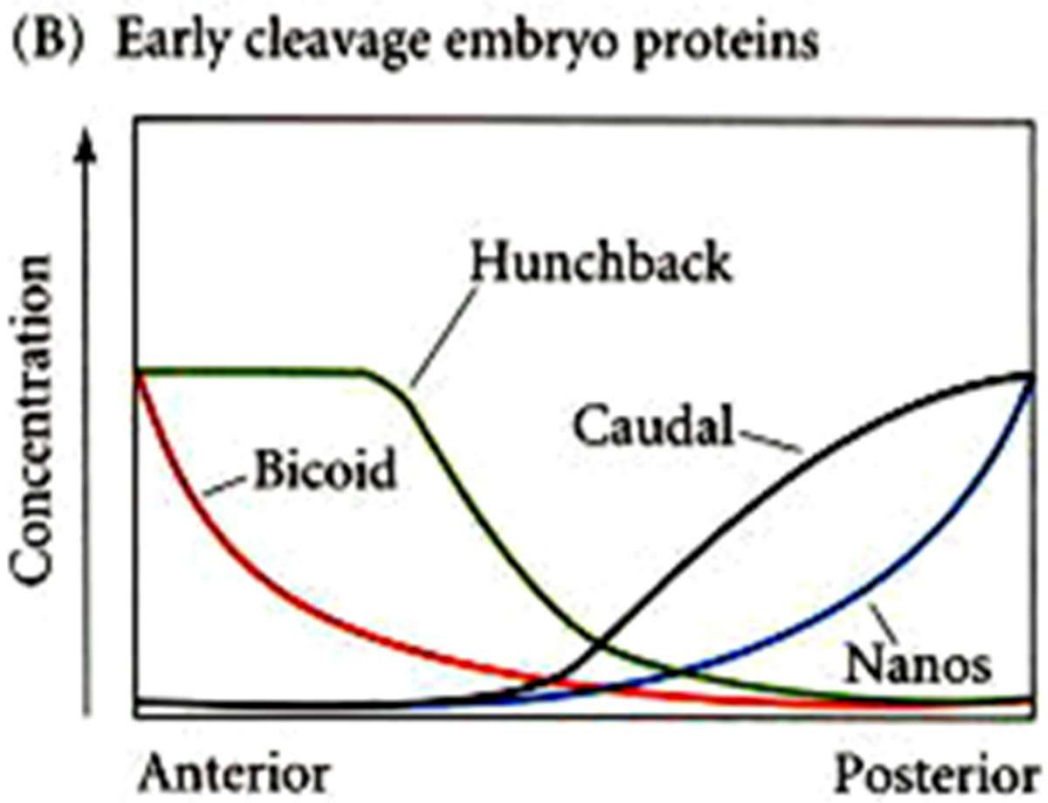
Nanos is tethered to the posterior end.



- The *bicoid* mRNAs are located in the anterior portion of the unfertilized egg, and are tethered to the anterior microtubules.
- The *nanos* messages are bound to the cytoskeleton in the posterior region of the unfertilized egg.
- The *hunchback* and *caudal* mRNAs are distributed throughout the oocyte.

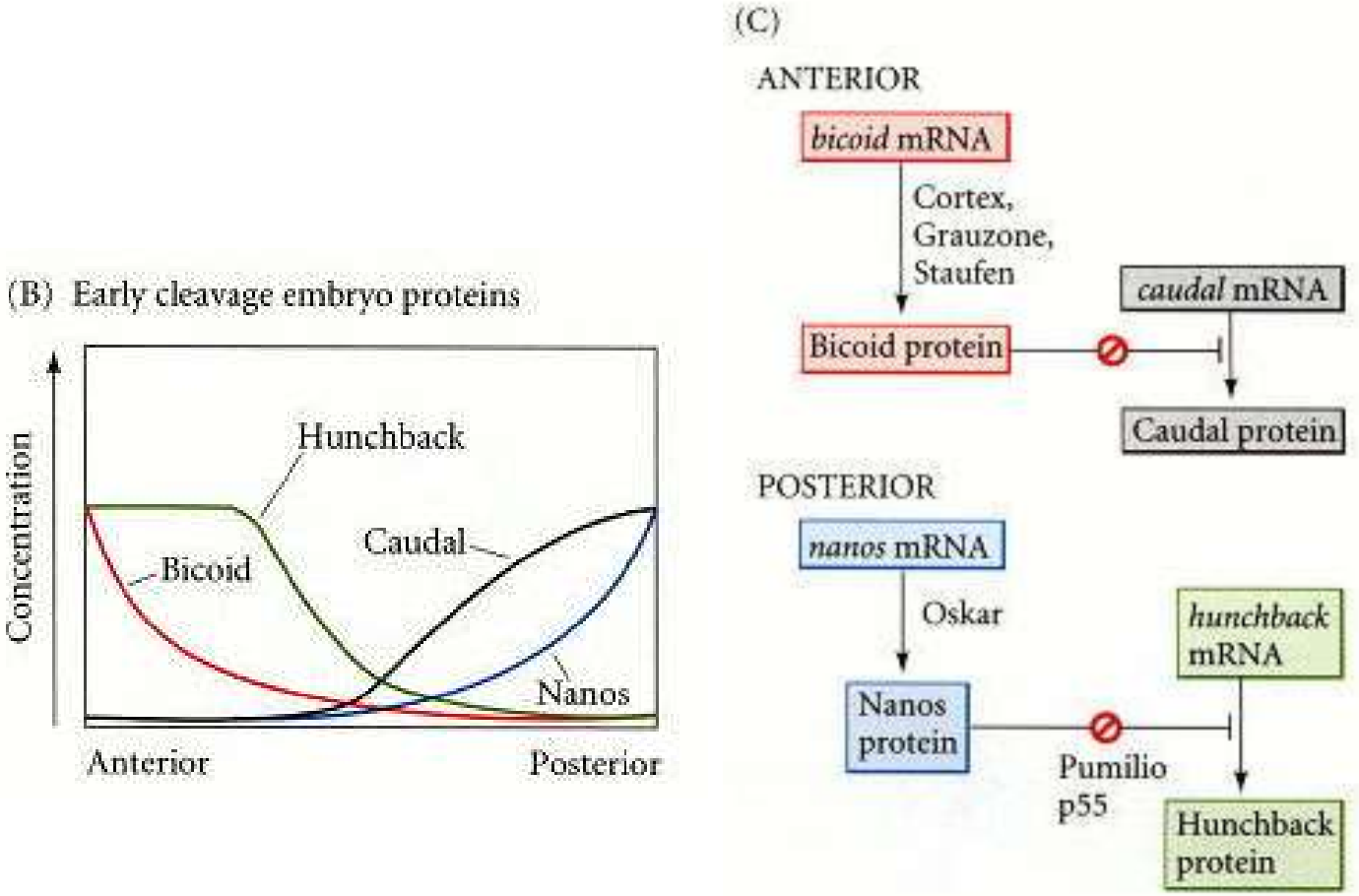


A model of anterior-posterior pattern generation by the *Drosophila* maternal effect genes. A) The *bicoid, nanos, hunchback,* and *caudal* messenger RNAs are placed in the oocyte by the ovarian nurse cells. The *bicoid* message is sequestered anteriorly. The *nanos* message is sent to the posterior pole



A model of anterior-posterior pattern generation by the *Drosophila* maternal effect genes.

Upon translation, the Bicoid protein gradient extends from anterior to posterior, and the **Nanos protein** gradient extends from posterior to anterior.



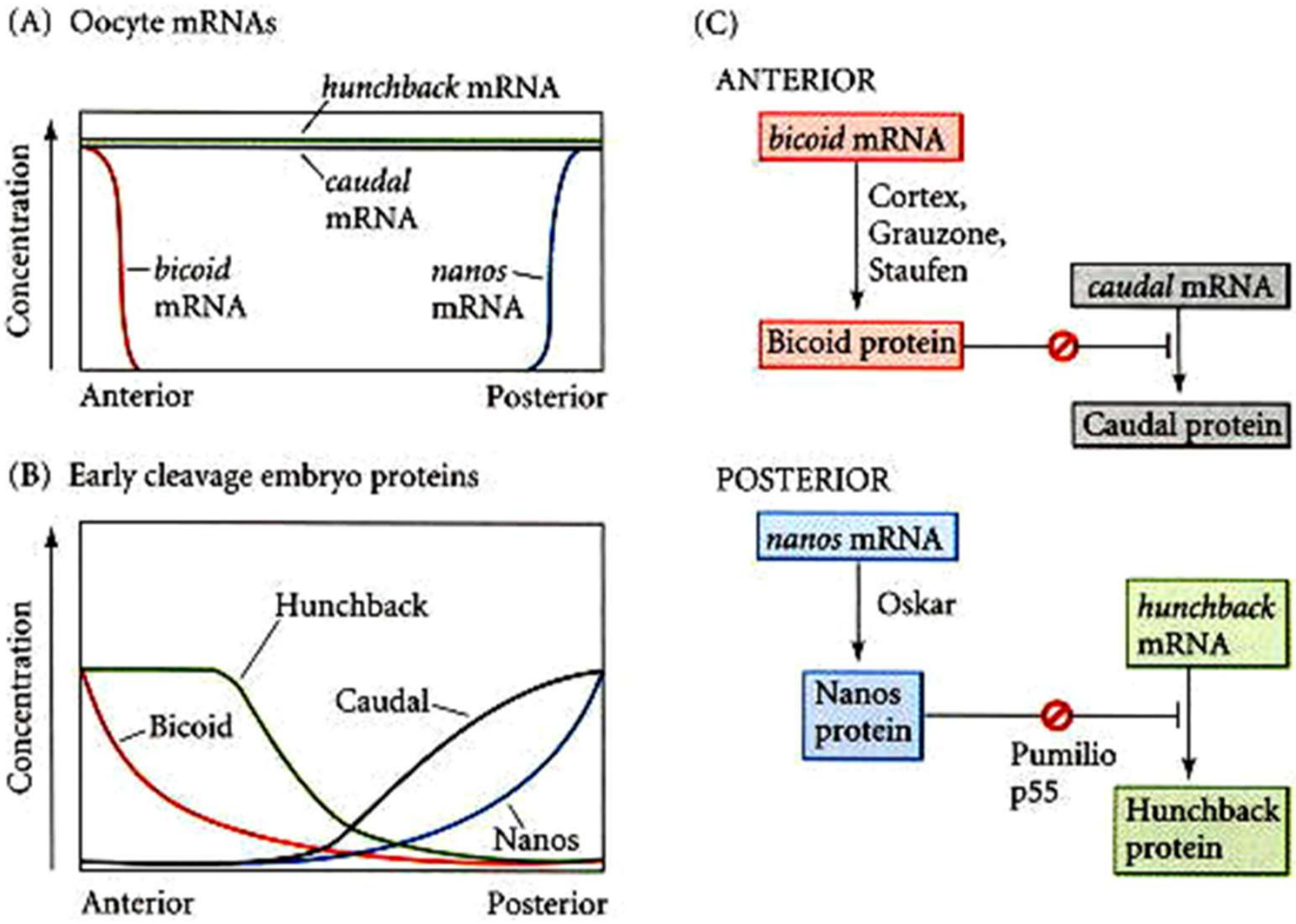
Translational gene regulation establishes the anterior-posterior patterning of the *Drosophila* embryo.

Bicoid prevents the translation of the *caudal* message (in the anterior).

Nanos inhibits the translation of the *hunchback* message (in the posterior)

This inhibition results in opposing Caudal and Hunchback gradients.

The Hunchback gradient is **secondarily strengthened** by the transcription of the *hunchback* gene in the anterior nuclei (since Bicoid acts as a **transcription factor** to activate *hunchback* transcription).



A model of anterior-posterior pattern generation by the *Drosophila* maternal effect genes. (A) The *bicoid, nanos, hunchback,* and *caudal* messenger RNAs are placed in the oocyte by the ovarian nurse cells. The *bicoid* message is sequestered anteriorly. The *nanos* message is sent to the posterior pole. (B) Upon translation, the Bicoid protein gradient extends from anterior to posterior, and the Nanos protein gradient extends from posterior to anterior. Nanos inhibits the translation of the *hunchback* message (in the posterior), while Bicoid prevents the translation of the *caudal* message (in the anterior). This inhibition results in opposing Caudal and Hunchback gradients. The Hunchback gradient is secondarily strengthened by the transcription of the *hunchback* gene in the anterior nuclei (since Bicoid acts as a transcription factor to activate *hunchback* transcription). (C) Parallel interactions whereby translational gene regulation establishes the anterior-posterior patterning of the *Drosophila* embryo.

Upon fertilization, these mRNAs can be translated into proteins.

At the anterior pole, the *bicoid* RNA is translated into Bicoid protein, which forms a gradient highest at the anterior.

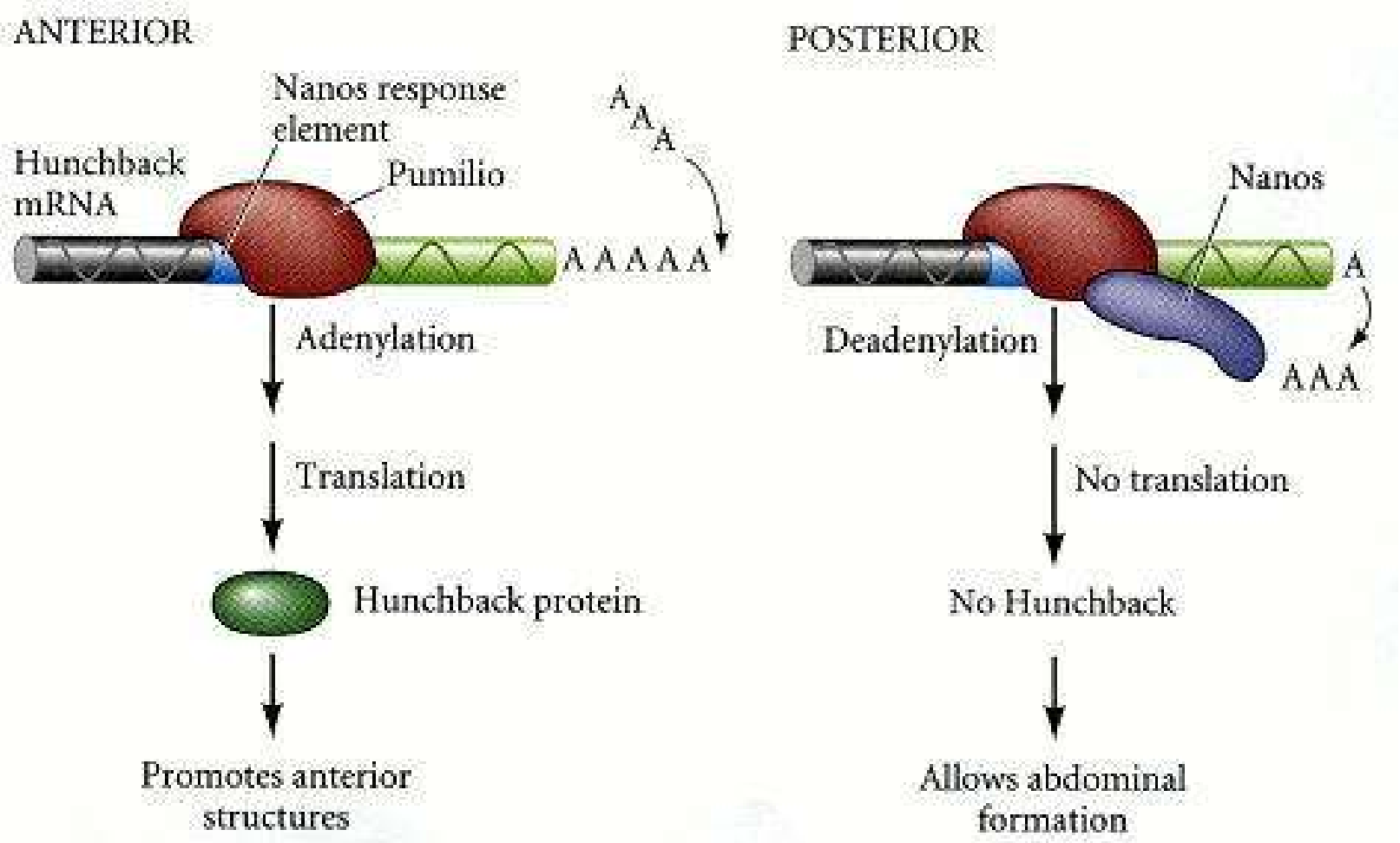
At the posterior pole, the *nanos* message is translated into Nanos protein, which forms a gradient highest at the posterior.

Bicoid protein inhibits the translation of the *caudal* RNA, allowing Caudal protein to be synthesized only in the posterior of the cell.

Conversely, Nanos protein, in conjunction with Pumilio protein, binds to *hunchback* RNA, preventing its translation in the posterior portion of the embryo.

Bicoid also elevates the level of Hunchback protein in the anterior of the embryo by binding to the enhancers of the *hunchback* gene and stimulating its transcription.

The result of these interactions is the creation of four protein gradients in the early embryo



Control of *hunchback* mRNA translation by Nanos.
In the anterior of the embryo, Pumilio protein binds to the Nanos Response Element (NRE) in the 3´ UTR of the *hunchback* message, and the message is polyadenylated normally.
This **polyadenylated message can be translated into Hunchback protein.**

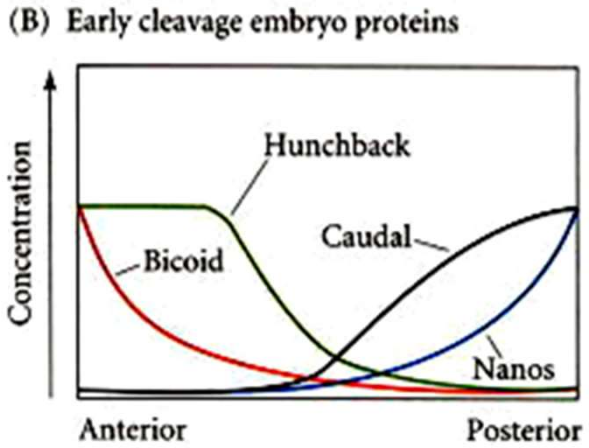
In the posterior of the embryo, where **Nanos protein** is found, Nanos binds to Pumilio to cause the **deadenylation of the *hunchback* message**. This prevents the translation of the *hunchback* message

An anterior-to-posterior gradient of Bicoid protein

An anterior-to-posterior gradient of Hunchback protein

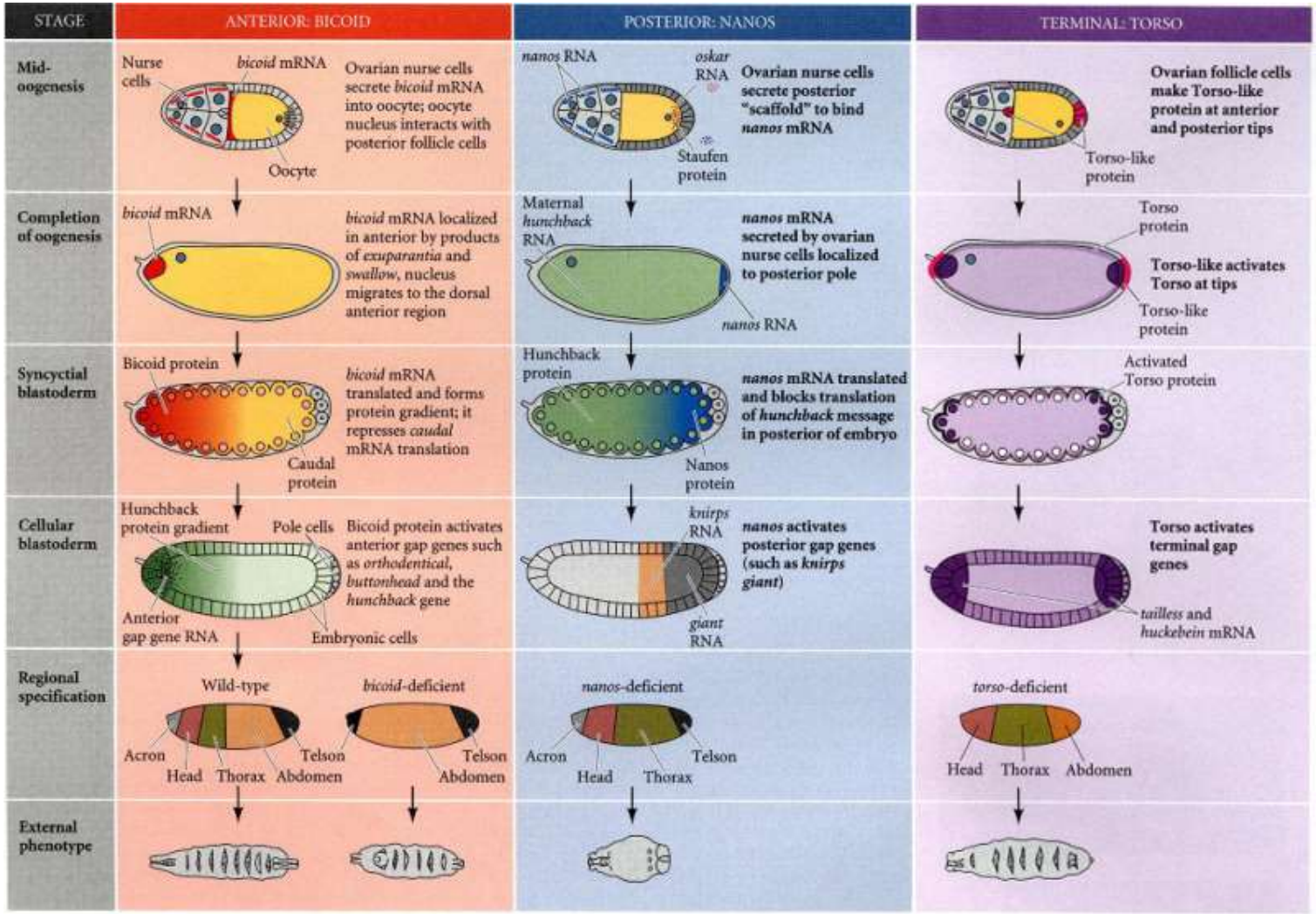
A posterior-to-anterior gradient of Nanos protein

A posterior-to-anterior gradient of Caudal protein



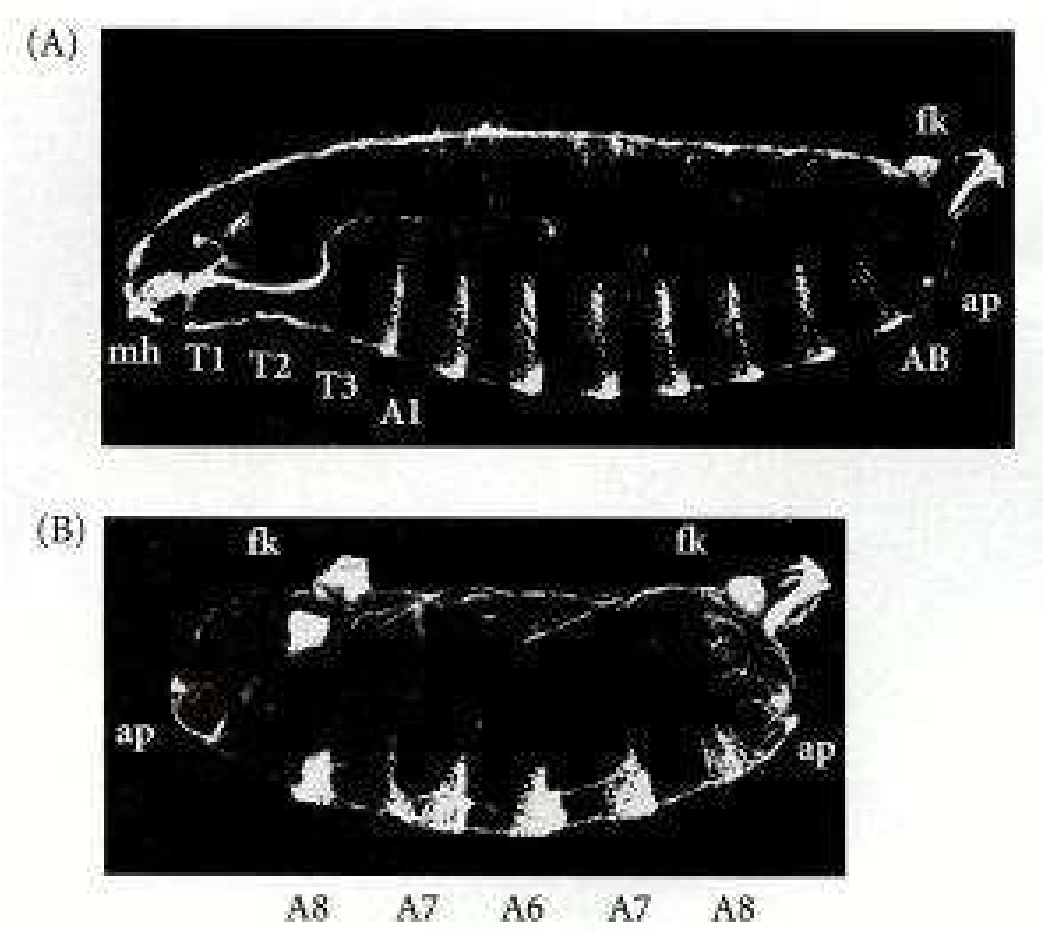
The Bicoid, Hunchback, and Caudal proteins are **transcription factors** whose relative concentrations can activate or repress particular zygotic genes.

The stage is now set for the activation of zygotic genes in those nuclei that were busily dividing while this gradient was being established.

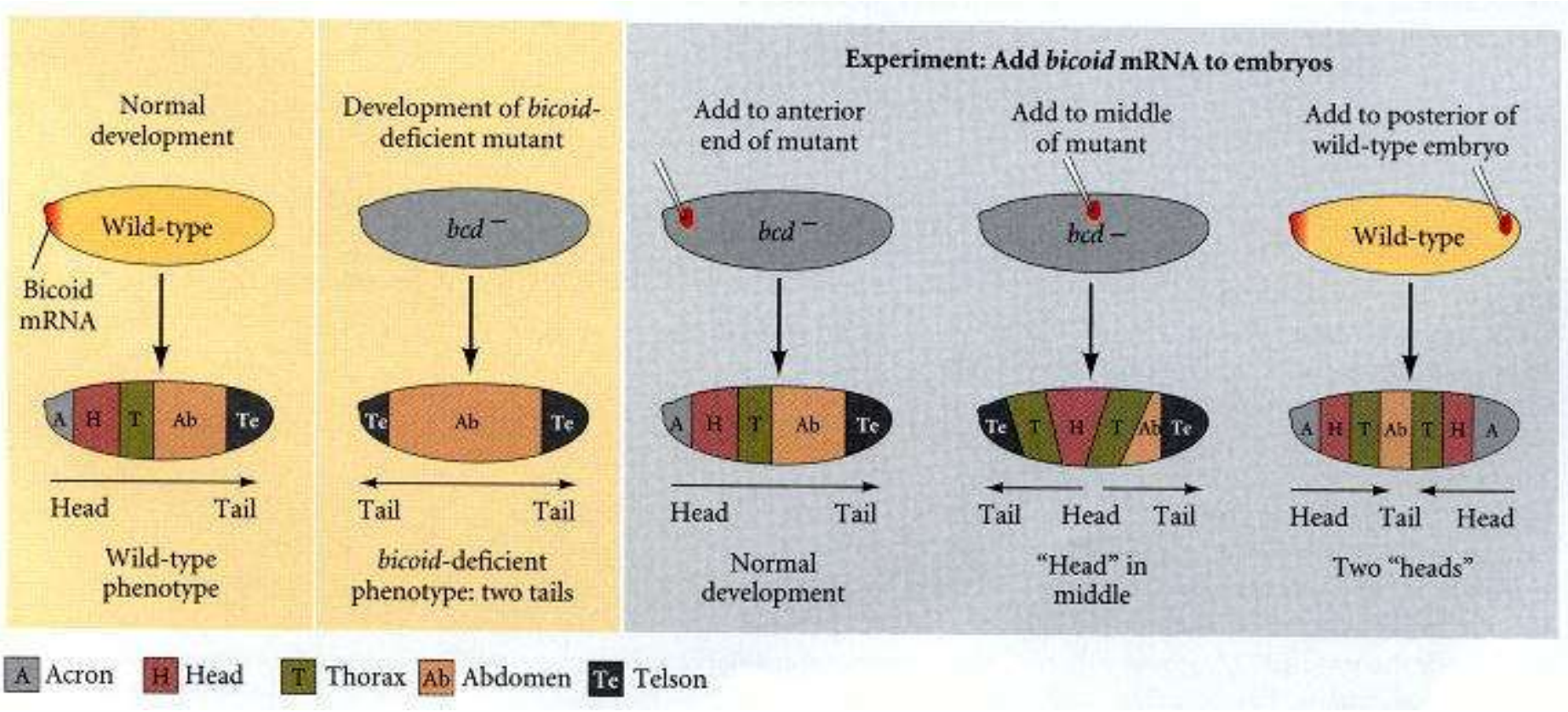


Three independent genetic pathways interact to form the anterior-posterior axis of the *Drosophila* embryo. In each case, the initial asymmetry is established during oogenesis, and the pattern is organized by maternal proteins soon after fertilization. The realization of the pattern comes about when the localized maternal proteins activate or repress specific zygotic genes in different regions of the embryo

Gene	Mutant phenotype	Proposed function and structure
Anteriro Group		
bicoid (*bcd*)	Head and thorax deleted, replaced by inverted telson	Graded anterior morphogen; contains homeodomain; represses caudal
exuperantia (*exu*)	Anterior head structures deleted	Anchors bicoid mRNA
swallow (*swa*)	Anterior head structures deleted	Anchors bicoid mRNP
Posteriro Group		
nanos (*nos*)	No abdomen	Posterior morphogen; represses hunchback
tudor (*tud*)	No abdomen, no pole cells	Localization of Nanos
oskar (*osk*)	No abdomen, no pole cells	Localization of Nanos
vasa (*vas*)	No abdomen, no pole cells; oogenesis defective	Localization of Nanos
valois (*val*)	No abdomen, no pole cells; cellularization defective	Stabilization of the Nanos localization complex
pumilio (*pum*)	No abdomen	Helps Nanos protein bind hunchback message
caudal (*cad*)	No abdomen	Activates posterior terminal genes
Terminal Group		
torso (*tor*)	No termini	Possible morphogen for termini
trunk (*trk*)	No termini	Transmits Torsolike signal to Torso
fs(1)*Nasrat*[*fs*(1)*N*]	No termini; collapsed eggs	Transmits Torsolike signal to Torso
fs(1)*polehole*[*fs*(1)*ph*]	No termini; collapsed eggs	Transmits *Torsolike* signal to *Torso*



Phenotype of a strongly affected embryo from a female deficient in the bicoid gene. (A) Wild-type cuticle pattern. (B) Bicoid mutant. The head and thorax have been replaced by a second set of posterior telson structures



Schematic representation of the experiments demonstrating that the *bicoid* gene encodes the morphogen responsible for head structures in *Drosophila.*

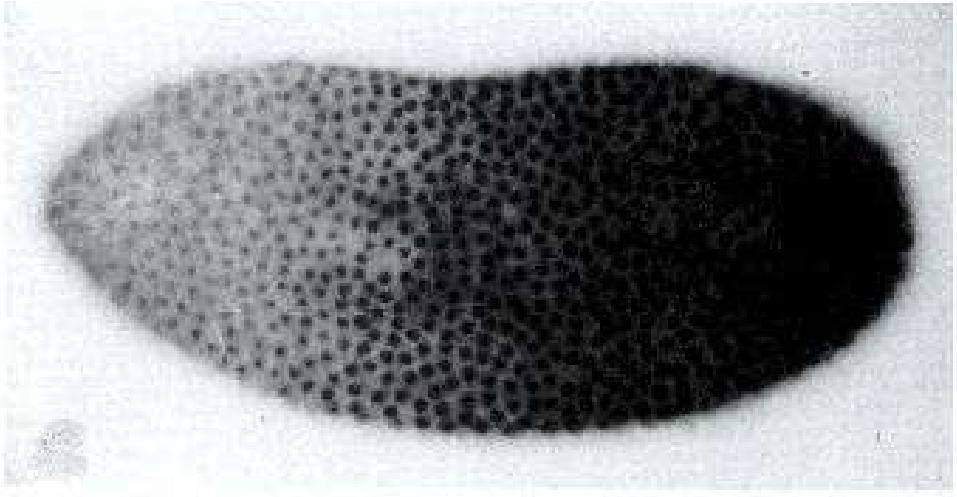
The phenotypes of *bicoid*-deficient and wild-type embryos are shown at the sides. When *bicoid*-deficient embryos are injected with *bicoid* mRNA, the point of injection forms the head structures.

When the posterior pole of an early-cleavage wild-type embryo is injected with *bicoid* mRNA, head structures form at both poles.

Bicoid acts in two ways to specify the anterior of the *Drosophila* embryo.

First, it acts as a repressor of posterior formation. It does this by binding to and suppressing the translation of *caudal* RNA, which is found throughout the egg and early embryo.

The Caudal protein is critical in specifying the posterior domains of the embryo, and it activates the genes responsible for the invagination of the hindgut.



Gradient of **Caudal protein** in the syncitial blastoderm of a wild-type *Drosophila* embryo.

The protein (stained darkly) enters the nuclei and helps specify posterior fates

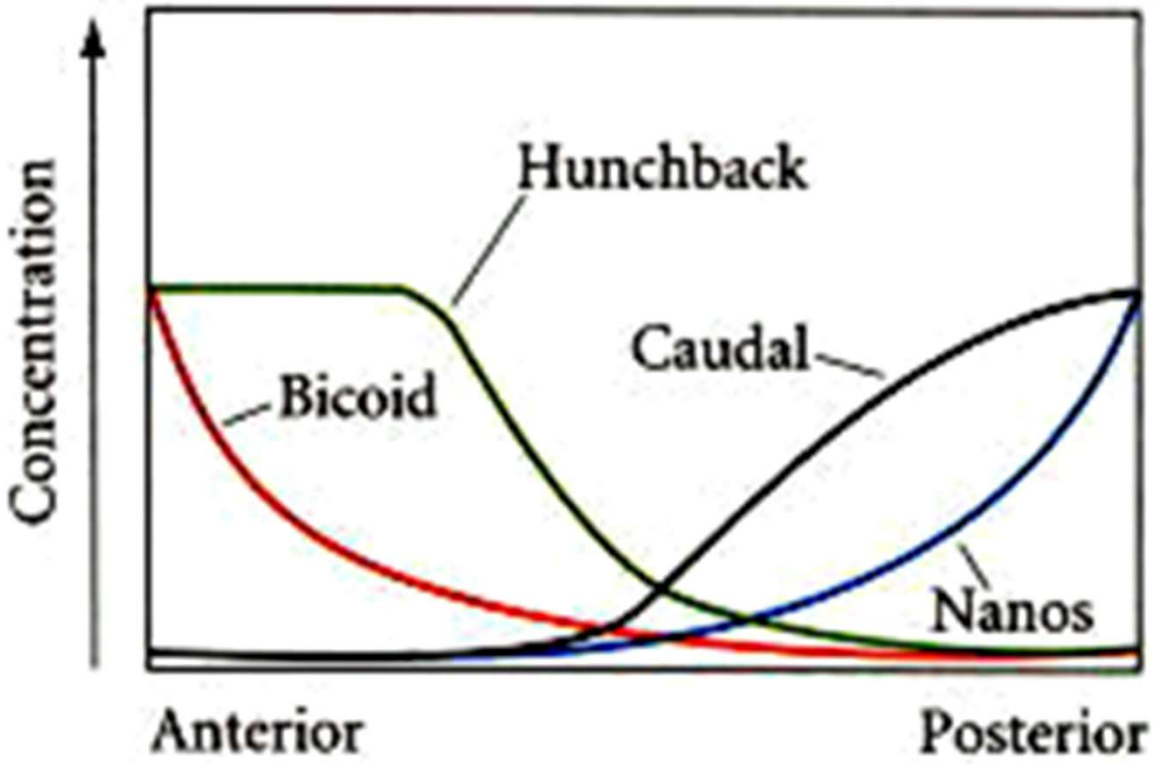
The posterior organizing center: localizing and activating nanos.
The Nanos protein forms a gradient that is highest at the posterior end.
Nanos functions by inactivating *hunchback* mRNA translation .

The posterior organizing center is defined by the activities of the *nanos* gene. The *nanos* RNA is produced by the ovarian nurse cells and is transported into the posterior region of the egg (farthest away from the nurse cells).

The *nanos* message is bound to the cytoskeleton in the posterior region of the egg through its 3´ UTR and its association with the products of several other genes (***oskar, valois, vasa, staufen,*** **and** ***tudor****) .*

If *nanos* or any other of these maternal effect genes are absent in the mother, **no embryonic abdomen** forms.

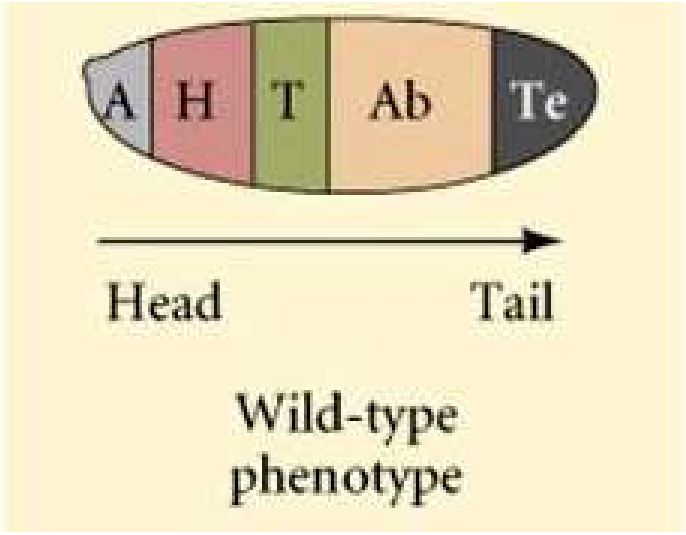
The Bicoid protein activates *hunchback* gene transcription in the anterior part of the embryo, while the Nanos protein inhibits the translation of *hunchback* RNA in the posterior part of the embryo.



The terminal gene group

In addition to the anterior and posterior morphogens, there is third set of maternal genes whose proteins generate the **extremes of the anterior-posterior axis.**

Mutations in these terminal genes result in the loss of the unsegmented extremities of the organism: the **acron** and the most anterior head segments and the **telson** (tail) and the most posterior abdominal segments

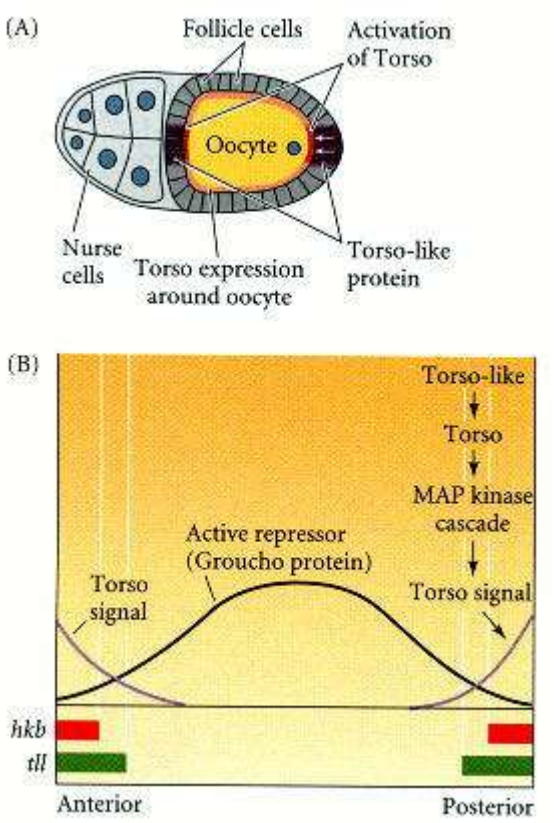


A Acron H Head T Thorax Ab Abdomen Te Telson

A critical gene here appears to be ***torso***, a gene encoding a receptor tyrosine kinase.
The embryos of mothers with mutations of the *torso* gene have neither acron nor telson, suggesting that the two termini of the embryo are formed through the same pathway.

The *torso* RNA is synthesized by the ovarian cells, deposited in the oocyte, and translated after fertilization.

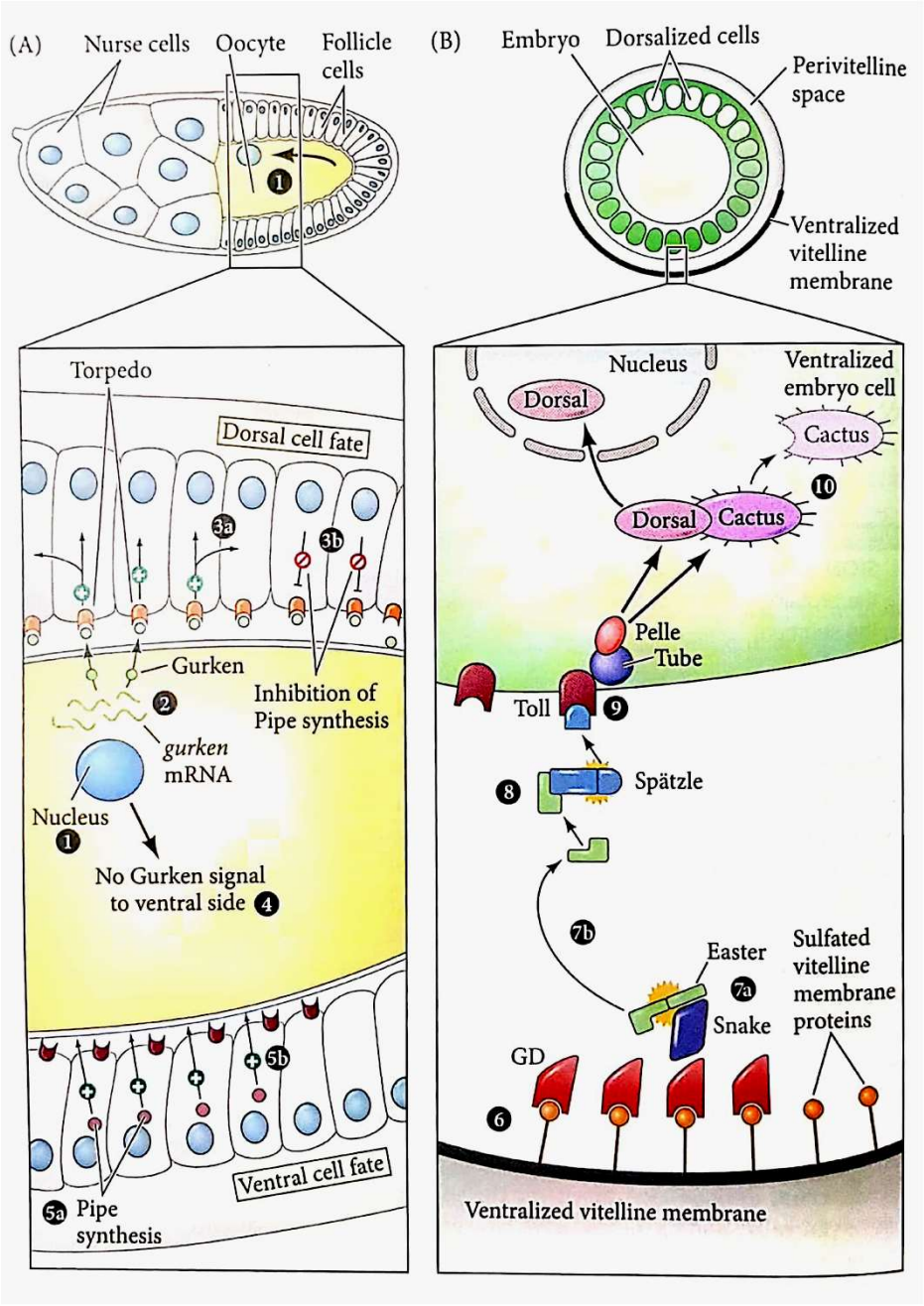
The transmembrane Torso protein is not spatially restricted to the ends of the egg, but is evenly distributed throughout the plasma membrane



Formation of the unsegmented poles by *torso* signaling.

(A) Torso-like protein is expressed by the follicle cells at the poles of the oocyte. Torso protein is expressed around the entire oocyte. Torso-like activates torso protein at the poles .

(B) (B) Inactivation of the transcriptional suppression of *huckebein* (*hkb*) and *tailless* (*tll*) genes. The *torso* signal antagonizes the Groucho protein. Groucho acts as a repressor of *tailless* and *huckebein* expression. The gradient of Torso protein is thought to provide the information that allows *tailless* to be expressed further into the embryo than *huckebein.*



1. Oocyte nucleus travels to anterior . dorsal side of oocyte where it localizes gurken mRNA.
2. gurken messages are translated. Gucken is received by Torpedo proteins during mid--oogenesis.
3a. Torpedo signal causes follicle cells to differentiate to a dorsal morphology.
3b. Synthesis of Pipe is inhibited in dorsal follicle cells.
4. Gurken does not diffuse to ventral side.
5a. Ventral follide cells synthesize Pipe.
5b. Pipe signal sulfates ventral vitelline proteins
6. Sulfated vitelline membrane proteins bind gastrulation defective (GD)
7a. GD splits the Snake protein to its active form and forms a complex with snake and uncleaved Ester protein.
7b. Activated Easter splits
8. Cleaved Ester binds to and cleaves Spatzle; activated Spatzle binds to Toll receptor protein.
9. Toll activation activates Tube and Pelle, which phosphorylate the Cactus protein. Cactus is degraded. releasing it from Dorsal.
10. Dorsal protein enters the nucleus and ventralizes the cell.

Dorso ventral polarity