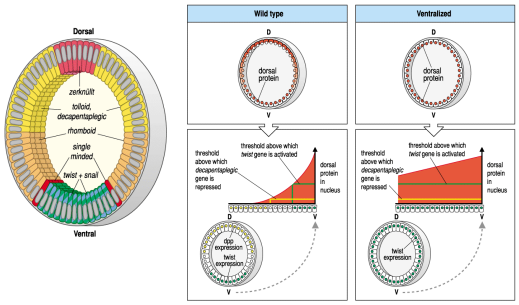
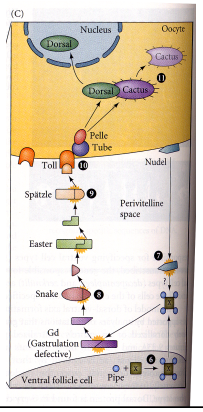
Notes on Dorsal-Ventral Patterning

Dorsal-Ventral Patterning depends on a gradient of the morphogen Dorsal, which acts as both an activator and repressor of transcription

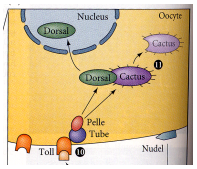


The Dorsal gradient results from a complicated protease cascade that results in localized activation of the Toll receptor. But it's still not known just how the initial asymmetry in D-V patterning is established.

This pathway is also important in the innate immune response in both insects and in mammals.



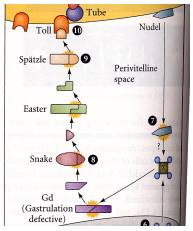
Toll is found everywhere in the oocyte plasma membrane. But it's only *active* on the ventral side:



Toll signaling activates the Pelle ser/thr kinase. This leads to phosphorylation of Cactus, causing its release from Dorsal. Dorsal can then enter the nucleus.

Why is Toll only active on the ventral side?

The Toll ligand is Spätzle. Spätzle becomes activated following cleavage by a serine protease cascade similar to the one used in blood clotting:



Cleaved Spätzle is found only on the ventral side of the egg. This explains why Toll is only active ventrally. On the other hand:

Why is Spätzle only active on the ventral side?

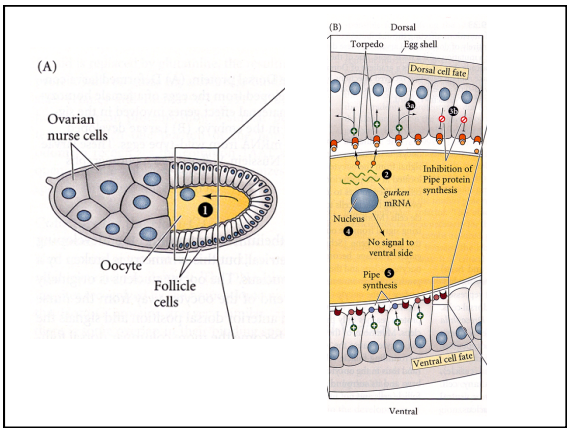
It turns out that the entire protease cascade leading to Toll activation is active only ventrally--but it's been very hard to determine why. In fact, we still don't completely understand this.

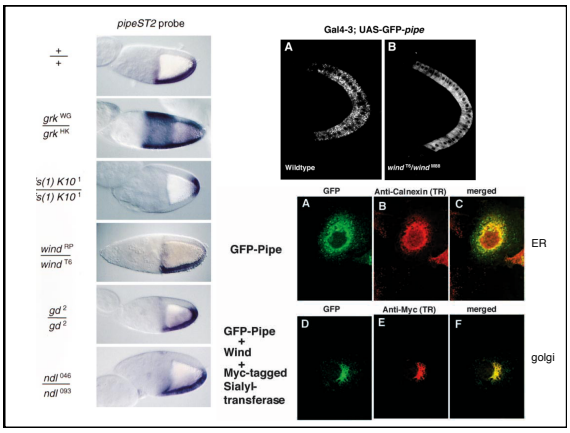
The dorsally located oocyte nucleus signals to dorsal follicle cells via the EGF-receptor pathway. This causes transcription of the *pipe* gene to be repressed. Thus, *pipe* is only produced in ventral follicle cells.

Pipe is the only clearly localized member of the dorsal/ventral patterning genes. It encodes a 2-O-sulfotransferase. However, we do not know all of its substrates or how it initiates the ventral localization of the protease cascade.

Recent work shows that at least some Pipe substrates are components of the vitelline membrane.

Sulfation of eggshell components by Pipe defines dorsal-ventral polarity in the Drosophila embryo.
Zhang Z, Stevens LM, Stein D.Curr Biol. 2009 Jul 28;19(14):1200-5.PMID: 19540119

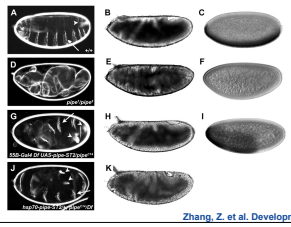




But:

Recent work shows that in the presence of uniformly distributed Pipe, there is still some D-V polarity. So Pipe may not be the only determinant.

Residual DV polarity in embryos from females expressing Pipe-ST2 uniformly around the DV circumference of the follicular epithelium



Zhang, Z. et al. Development 2009;136:2779-2789

Key concepts in dorsal/ventral patterning:

- ultimately depends on a *morphogen gradient* of a nuclear-localized transcription factor (Dorsal)
- takes place by *localized activation* of a globally expressed receptor