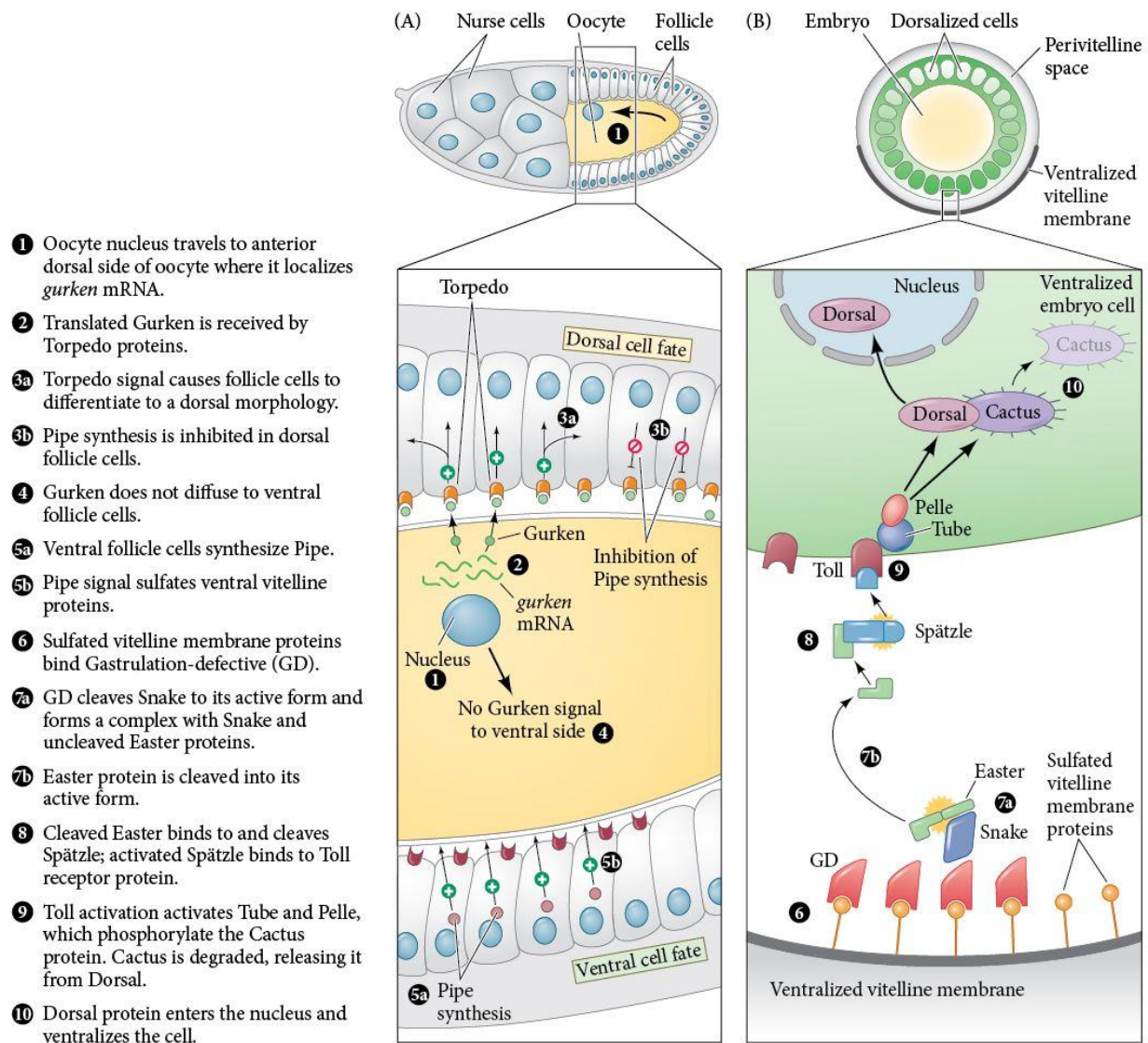


Torpedoes Away: The Downstream Signaling Events

The activated Torpedo receptor protein activates Mirror, a transcription factor that represses expression of the *pipe* gene (Andreu et al. 2012; Fuchs et al. 2012). As a result, Pipe is made only in the ventral follicle cells (Figure 1A; Sen et al. 1998; Amiri and Stein 2002). Pipe protein modifies the ventral vitelline envelope by sulfonating its proteins. This allows the Gastrulation-defective protein to bind to the vitelline envelope (only in the ventral region) and to recruit other proteins to make a complex that will cleave the Easter protein into its active protease form (Figure 1B; Cho et al. 2010, 2012). Easter then cleaves the Spätzle protein (Chasan et al. 1992; Hong and Hashimoto 1995; LeMosy et al. 2001), and the cleaved Spätzle protein is the ligand that binds to and activates the Toll receptor on the membrane of the embryo. It is important that the cleavage of Spätzle be limited to the most ventral portion of the embryo. This is accomplished by the secretion of a protease inhibitor from the follicle cells of the ovary. This can inhibit any small amounts of proteases that might be expected on the margins (Hashimoto et al. 2003; Ligoxygakis et al. 2003).

Toll protein is a maternal product that is evenly distributed throughout the cell membrane of the egg (Hashimoto et al. 1988, 1991), but it becomes activated only by binding Spätzle, which is produced only on the ventral side of the egg. The ventral Toll receptors bind the mature Spätzle protein, and the membrane containing activated Toll protein undergoes endocytosis. Signaling from the Toll receptor is believed to occur in these cytoplasmic endosomes rather than on the cell surface (Lund et al. 2010). Therefore, the Toll receptors on the ventral side of the egg are transducing a signal into the egg, whereas the Toll receptors on the dorsal side are not. This localized activation establishes the dorsal-ventral polarity of the oocyte.



After F. van Eeden and D. St Johnston 1999, *Curr Opin Genet Dev* 9: 396-404; Y.S. Cho et al. 2010, *Curr Biol* 20: 1133-1137.

Figure 1 Generating dorsal-ventral polarity in *Drosophila*. (A) The nucleus of the oocyte travels to what will become the dorsal side of the embryo. The *gurken* genes of the oocyte synthesize mRNA that becomes localized between the oocyte nucleus and the cell membrane, where it is translated into Gurken protein. The Gurken signal is received by the Torpedo receptor protein made by the follicle cells (see Figure 1 in Further Development 9.3, online). Given the short diffusibility of the signal, only the follicle cells closest to the oocyte nucleus (i.e., the dorsal follicle cells) receive the Gurken signal, which causes the follicle cells to take on a characteristic dorsal follicle morphology and inhibits the synthesis of Pipe protein. Therefore, Pipe protein is made only by the ventral follicle cells. (B) The ventral region, at a slightly later stage of development. Sulfated proteins on the ventral region of the vitelline envelope recruit Gastrulation-defective (GD), which in turn complexes with other proteins, initiating a cascade that results in the cleaved Spätzle protein binding to the Toll receptor. The resulting cascade ventralizes the cell.

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