

Axis Specification in Sea Urchin Embryos

In the sea urchin blastula, the general cell fates (ectoderm, endoderm, skeletogenic mesenchyme, etc.) line up along the animal-vegetal axis—an axis that is established in the egg cytoplasm prior to fertilization. The animal-vegetal axis also appears to structure the future anterior-posterior axis, with the vegetal region sequestering those maternal components necessary for posterior development (Boveri 1901; Maruyama et al. 1985).

In most sea urchins, the dorsal-ventral and left-right axes are specified after fertilization, but the manner of their specification is just now beginning to be understood. Lineage tracer dye injected into one blastomere at the 2-cell stage demonstrated that, in nearly all cases, the oral pole of the future oral-aboral (mouth-anus; ventral-dorsal) axis lies 45° clockwise from the first cleavage plane as viewed from the animal pole (Cameron et al. 1989). The oral-aboral axis appears to form through the activation of the *Nodal* gene in the oral (but not in the aboral) ectoderm during gastrulation.

The role of *Nodal* was discovered through the classic “find it, lose it, move it” mode of experimentation described in Chapter 4 (Duboc et al. 2004). Researchers cloned a sea urchin *Nodal* gene and, using in situ hybridization, demonstrated that Nodal protein becomes expressed in the presumptive oral ectoderm at about the 60-cell stage. Nodal then becomes prominent on one side of the blastula, and this side becomes the oral (mouth) side of the gastrula. When the researchers prevented translation of the *Nodal* message, development was normal until the mesenchyme blastula stage—but the larvae never obtained bilateral symmetry, the archenteron did not bend to one side to form the mouth, and the skeletogenic mesenchyme did not separate into the two sets of spicule-forming skeleton cells. Moreover, genes usually activated in the oral ectoderm were not expressed. Conversely, when researchers induced ectopic expression of the *Nodal* gene throughout the ectoderm, all of the ectoderm appeared to become oral. Thus, Nodal appears to be crucial in establishing the oral ectoderm.

The difference in Nodal gene appears to be initiated by local difference in the translation of the maternal messenger for the Panda protein (Haillot et al 2015). Panda is a TGF-β family member related to the vertebrate gene, *Lefty*, and it inhibits Nodal synthesis. Knocking out Panda and its receptors leads to an extremely ventralized phenotype, due to the expression of Nodal throughout the embryo. The expression difference appears to be augmented by a small difference in the redox state of the ectoderm: the prospective oral side of the embryo has a higher mitochondrial respiration rate than the prospective aboral side (Coffman and Davidson 2001; Nam et al. 2007), and this helps activate the transcription factors that activate *Nodal*.

While *Nodal* expression during gastrulation establishes the oral-aboral axis of the larva, the right-left axis of the larva appears to be established by Nodal signaling *after* gastrulation, in the early larval stages (Duboc et al. 2005). At that time, *Nodal* expression moves to the future right side of the larva.ⁱ Importantly, it is expressed in the right coelomic pouch where it appears to restrict the pouch's growth, thus allowing the adult sea urchin to arise solely from the left coelomic pouch. Inhibiting Nodal signaling results in the formation of an imaginal rudiment (a pouch whose cells form the adult urchin) on both sides of the larva, leading to twin urchins, whereas forcing *Nodal* expression on both sides of the embryo prevents either pouch from developing into an imaginal rudiment. Thus,

although there is no right-left partitioning of the *adult* sea urchin body, the distinguishing of left and right sides is critical for sea urchin development.

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ⁱ As we will see in subsequent chapters, Nodal initiates a pathway that determines the left-right axis in vertebrates as well. However, in vertebrates, Nodal specifies the left side rather than the right side as in echinoderms