<Further Development 12_07>

Gradients and Hox gene expression in *Xenopus*

The original orthogonal double-gradient model of induction comes from Saxén and Toivonen, and this is discussed in the accompanying essay on regional specification. Here, we will discuss the changing direction of Wnt expression and a model for the integration of temporal Hox gene expression, mesoderm involution, and the anterior-posterior patterning of the embryo.

I. Wnt signaling: Changing directions from Dorsoanterior to Ventroposterior

BMPs, FGFs, Wnts, and retinoic acid each contributes to the anterior-posterior axis; but they the ways they contribute are very complicated. This is because the pathways interact with one another. This cross-talk allows the pathways to have different roles in different places.

Consider the Wnt pathway for a moment (see Hikasa and Sokol 2013). Before gastrulation in *Xenopus*, the Wnt/b-catenin pathway is essential for the specification of *dorsoanterior* structures. Its target genes include *Noggin* and *Chordin* (which inhibit BMPs). But its target genes also include *Cerberus* and *Dickkopf*, two antagonists of the Wnt pathway. After gastrulation, these organizer genes are not activated by Wnts. Rather, the zygotic activation of Wnt8 causes the accumulation of b-catenin in the posterior and ventral regions (exactly the opposite of the earlier anterior/dorsal regions!) Here, the gene targets of Wnt signaling are Cdx, Vent, Meis, and Gbx. These genes have TCF-binding sites on their promoters and are directly controlled by the canonical Wnt pathway. Meanwhile, Wnt antagonists are expressed anteriorly.

The targets are not interchangeable. A plasmid reporter for *Siamois* (activated by Wnt pathway during organizer formation) is not activated by Wnt after gastrulation. What changes the targets of Wnt? There are several possible mechanisms. First, different homologues of the transcription factor TCF (which b-catenin binds to) might be available in a cell-specific manner. These different types of TCF work differently. Second, there may be cross-talk with other pathways. In some cases, these pathways work in parallel, each providing a context for the other. For instance, both BMP and Wnts are important in establishing ventroposterior gene expression. One of these ventroposterior genes, *Vent2*, has binding sites for both Smad1 and TCF (the major BMP- and Wnt-activated transcription factors) in its promoter. So it needs both of these pathways for maximum expression. In other cases, Fgf induces Wnt (as in the limb bud), such that both signals get made in the posterior of the embryo. And in a third case, Wnt can block the inactivation of Smad by other factors (such as Fgfs), thereby preserving the BMP signal. In zebrafish, the dorsoventral tissues are also patterned progressively, starting at the anterior and eventually ending at the posterior, by BMP signaling. Here, the FGF pathway (but not the Wnt pathway) localizes the activated BMP-induced Smad to the ventral vegetal region of the gastrula. The epiboly of the ectoderm is probably critical in moving the FGF-signaling region progressively posteriorly and vegetally (Hashiguchi and Mullins 2013)

II. Translating Time and Space: A Temporal Model for A–P Axis Hox Specification

Thus, the presence of numerous posteriorizing factors may interact to cause the expression of particular genes. Also, there appears to be, even in fish, a mechanism that combines dorsal-ventral specification with anterior-posterior specification. Durston and colleagues (2004. 2012) and Wacker et al. 2004) speculate that the different Hox genes are controlled by such an anterior-posterior clock such that certain Hox genes are turned on early (and these specify the anterior regions), while those Hox genes that happened to be turned on later specify the posterior regions (Figure 1). The Hox genes would be transiently expressed in the non-organizer mesoderm, and those genes that are expressed in the mesoderm at the time of its involution would become stabilized. In this way, different Hox genes are expressed in the notochord as it progresses into the embryo. This notochordal expression pattern would then influence the ectoderm above it to express Hox genes.

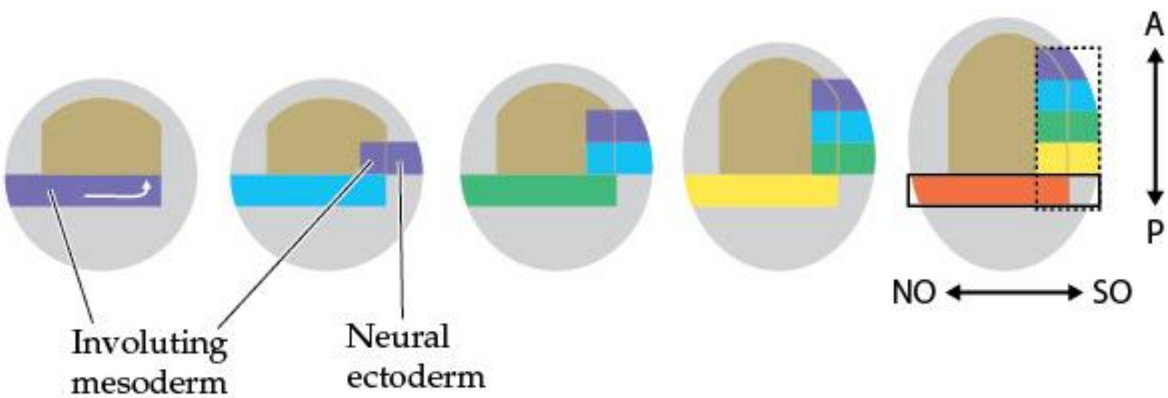

Figure 1 A space-time model of Hox gene expression. Hox-expressing tissue is represented by different colors, each of which represents a different set of Hox genes. Initially, the colored bar represents the non-organizer mesoderm in the wall of the late balstula. The later internal colored blocks at the dorsal side of the embryo represent the involuted dorsal mesoderm. The colored blocks next to them in the wall of the embryo represent the overlying neural ectoderm, which also comes to express Hox genes. (After Wacker et al. 2004.)

Literature Cited

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