Transcriptional Precision in the Drosophila Embryo

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The dorsal-ventral patterning of the Drosophila embryo is controlled by Dorsal, a sequence-specific transcription factor related to mammalian NF-kB. The Doresal protein is distributed in a broad nuclear gradient in the precellular embryo. This Dorsal gradient controls dorsal-ventral patterning by regulating at least 50 target genes in a concentration-dependent manner. Dorsal target enhancers that are regulated by low levels of the gradient contain fixed arrangements of binding sites for Dorsal and additional transcription factors that help pattern the embryo.

Whole-genome ChIP-chip assays permitted the efficient identification of over 60-70 Dorsal target enhancers. Surprisingly, between a third and a half of all Dorsal target genes appear to contain "shadow enhancers", secondary enhancers that produce patterns of gene expression which overlap those produced by the primary enhancers. For example, the brinker gene is regulated by a 5' primary enhancer as well as a 3' shadow enhancer located within the intron of a neighboring gene. We propose that shadow enhancers help ensure the precision and reproducibility of gene expression during development.

Once Dorsal binds to its target enhancers (and shadow enhancers), it appears to regulate gene expression by triggering the release of an active, but stalled form of RNA Pol II at the core promoter. The stalled Pol II generally maps between +20 bp and +50 bp downstream of the transcription start site. Most developmental control genes expressed during embryogenesis contain stalled Pol II. Based on studies of heat shock genes it is likely that the stalled Pol II renders Dorsal target genes "poised" for rapid induction by transient signals, such as FGF and Notch.

What is the purpose of shadow enhancers and paused Pol II? Preliminary studies suggest that these mechanisms are used to produce rapid, synchronous bursts of gene expression in the early Drosophila embryo. Genes lacking shadow enhancers and paused Pol II display stochastic patterns of gene activation. We propose that transcriptional synchrony helps ensure the coordinate deployment of the genetic networks controlling embryogenesis.