Transcriptional control of the mitotic regulator *string,* in *Drosophila*

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by

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ABSTRACT

Before morphogenesis can begin, positional information must be in place to direct the complex array of cellular processes. In a *Drosophila* embryo the transcription factors encoded by the patterning genes are expected to provide this information. However, the genes regulated in this manner, to bring about morphogenesis, have so far been elusive. One potential candidate is *string*, a homologue of the mitotic initiator *cdc25* from *Schizosaccharomyces pombe*. Early in embryogenesis a complex spatio-temporal pattern of *string* transcription partitions the embryo into mitotic domains which delineate larval organ primordia. The complexity and timing of *string* transcription, at such an early stage, suggests that this morphogenetic event is regulated by the patterning genes.

If *string* is integrating patterning gene information it is anticipated that the promoter may be comprised of many position specific elements (PSE's), each defining individual mitotic domains. To test this, promoter fragments from the *string* gene were used in *lacZ* reporter constructs to look for these PSE's. Initial constructs failed to identify any such elements. However, the addition of a proximal *stg* promoter fragment, to these constructs, allowed the identification of some *stg* regulatory regions that activated transcription in specific domain-like patterns. In particular, PSE's for cycle 14 domains 1, 2, and 21, were identified as well as distinct PSE's for different subsets of domains N and M.

The PSE's that activated transcription in domains 1 and 2 were defined to a region of 1.4kb by further construct generation and a detailed analysis of the regulation of mitotic domain 2 was undertaken. The early patterning genes *buttonhead (btd)* and *snail (sna)* were found to be required for the transcriptional regulation of domain 2, and their products were shown bind specifically to the defined 1.4kb region.

This work has demonstrated that *string* is a downstream target of the patterning genes, making a direct connection between patterning information and morphogenesis, which suggests that mitotic timing forms an independent and important part of morphogenesis.