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TRANSCRIPTION

Shadow enhancers confer robustness

Many developmental genes contain multiple enhancers that drive apparently redundant patterns of transcription, but what are the functions of these various regulatory elements? A new study in *Drosophila* species indicates that secondary, 'shadow' enhancers, which are distant from promoter regions, confer phenotypic robustness to environmental and genetic perturbations.

IMAGE100

Frankel, Stern and colleagues identified two secondary enhancers (*Z* and *DG2*) that lie upstream of three known enhancers in the *shavenbaby* (*svb*) gene, which encodes a transcription factor. To examine the function of these new enhancers, they generated a deficiency strain in which both enhancers were removed. First-instar larvae from the deficiency strain that developed at an optimal temperature showed only subtle trichome (hair) abnormalities. There was a clear overlap between the expression patterns driven by *Z* and *DG2* and the previously identified *svb* enhancers, suggesting that the mild phenotype of the deficiency larvae might be because the primary enhancers drive sufficient levels of *svb* transcription under optimal developmental conditions.

One possibility is that secondary enhancers contribute to phenotypic robustness. The authors tested this hypothesis: deficiency larvae that developed at extreme temperatures produced significantly fewer trichomes than control embryos that developed at intermediate temperatures. The loss of trichomes in the deficiency strain could be rescued by a transgene carrying the *svb* cDNA under the control of the *Z* enhancer, further supporting the idea that these enhancers contribute to robustness against environmental perturbations.

Do the *svb* shadow enhancers also buffer against genetic variability? The authors crossed the deficiency strain into a background heterozygous for a null allele of *wingless*, a gene required for normal trichome development. This resulted in reduced trichome number compared with control larvae. The authors suggest that apparently redundant enhancers in other developmental genes could confer similar functions and that secondary enhancers might be maintained by selection for robustness against environmental and genetic variability. Uncovering the molecular mechanisms that contribute to this developmental buffering will be the next step forward.

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ORIGINAL RESEARCH PAPER Frankel, N. *et al.* Phenotypic robustness conferred by apparently redundant transcriptional enhancers. *Nature* 30 May 2010 (doi:10.1038/nature09158)