DEVELOPMENT

Polymerase stalling gets genes in sync

Two cells that receive the same signals do not necessarily show identical responses — a result of intrinsic stochasticity in gene expression. How is this variability dealt with in situations in which precise patterns of gene activation are important? A recent study suggests a mechanism that can reduce variability in the onset of transcriptional activation in the *Drosophila melanogaster* embryo and may contribute to the precision of the developmental programme.

Chance differences in the recruitment of RNA polymerase II (RNAPII) to promoters are a key source of stochasticity in eukaryotic gene expression. One way to decrease this variability might be through the pre-loading of RNAPII at promoters so that target genes are poised for simultaneous activation in different cells. Boettiger and Levine investigated this possibility in the context of *D. melanogaster* embryogenesis, which, with its rapid transitions between gene expression patterns, provides a good setting for exploring mechanisms of transcriptional precision.

The authors carried out *in situ* hybridization to analyse target genes of key developmental regulatory proteins using probes that corresponded to intronic regions and could therefore detect nascent transcripts. To get a clear picture of the variability between cells in the timing of transcriptional onset, they used a semi-automated computational method to obtain quantitative measures of gene expression in large numbers of embryos. By looking at genes that are activated at a range of times and positions during embryogenesis, Boettiger and Levine distinguished two classes of developmental genes: the first class showed synchronous expression, in which all of the cells began to express the transcript within a short time frame (2–3 minutes), whereas the second class showed stochastic onset, in which transcriptional activation occurred over a much longer period (sometimes more than 20 minutes) in different cells. These two classes had not been distinguished before, probably because of the smaller numbers of embryos examined in previous studies. Strikingly, the genes that showed synchronous expression were associated with stalled RNAPII, whereas the genes that showed stochastic onset were not.

RNAPII stalling is clearly not required at all developmental genes, but Boettiger and Levine argue that that stalling and the resulting synchronous expression at genes with key regulatory roles may contribute to reproducibility in the developmental process.

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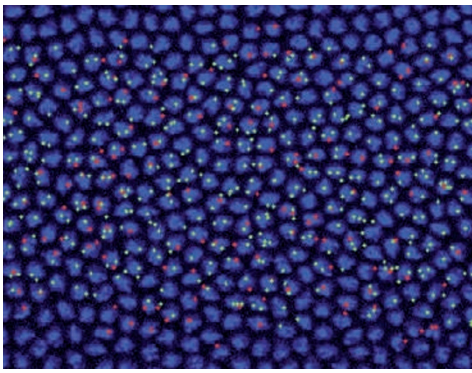
ORIGINAL RESEARCH PAPER Boettiger, A. N. & Levine, M. Synchronous and stochastic patterns of gene activation in the *Drosophila* embryo. *Science* **325**, 471–473 (2009)



Drosophila melanogaster embryos stained for two mesodermal genes, *Mes4* (a non-stalled gene, stained red) and *Mes2* (a stalled gene, in green). At this stage, *Mes4* still shows patchy, stochastic activation, whereas *Mes2* shows uniform expression in most nuclei. Image courtesy of A. Boettiger, University of California, Berkeley, USA.