IN BRIEF

SPLICING

Noisy splicing drives mRNA isoform diversity in human cells

Pickrell, J. K. *et al. PLoS Genet.* **6**, e1001236 (2010)

By deep RNA sequencing in human cells, the authors identified many low-abundance transcript isoforms that use previously unannotated splice junctions. These junctions are not evolutionarily conserved, and most of the low-abundance isoforms seem to arise owing to splicing errors. Errors are caused by 'mistakes' in exon recognition or splice site choice, so the authors predict that splicing noise will vary among organisms with different splicing machinery. This could partially account for differences in levels of alternative splicing among organisms.

EVOLUTION

Hsp90 and environmental stress transform the adaptive value of natural genetic variation

Jarosz, D. F. & Lindquist, S. *Science* **330**, 1820–1824 (2010)

Drosophila Piwi functions in Hsp90-mediated suppression of phenotypic variation

Gangaraju, V. K. *et al. Nature Genet.* 26 Dec 2010 (doi:10.1038/ng.743)

HSP90 is proposed to facilitate rapid evolutionary adaptation by buffering the phenotypic manifestation of genetic variation. In this model, HSP90 acts until environmental stresses overwhelm its chaperone functions, thus revealing potentially adaptive phenotypic variation. To determine the extent of this mechanism, Jarosz and Lindquist studied 102 genetically diverse yeast strains in 100 different growth conditions, in the presence or absence of Hsp90 inhibition. They found that Hsp90 can either buffer or, conversely, potentiate the phenotypic outcome of genetic variation at over 100 loci, thus confirming the broad role of Hsp90 in determining the adaptive value of genetic variation. To uncover mechanistic detail of HSP90's buffering functions, Gangaraju *et al.* used *Drosophila melanogaster*, in which eye outgrowths (the phenotypic output of ectopic Kr^{If1} expression) are usually repressed by HSP90 function. They found that HSP90 functions in a complex with PIWI (the piRNA-interacting protein) and that overexpression of PIWI lessened the eye outgrowth frequency in HSP90-inhibited flies. This suggests that PIWI-mediated transcriptional silencing could assist HSP90 in buffering the phenotypic expression of genetic variants.

CHROMATIN

Transcriptional activation of polycomb-repressed genes by ZRF1

Richly, H. *et al. Nature* **468**, 1124–1128 (2010)

How is the repression of developmental genes by Polycomb complexes relieved? This study shows that when differentiation is initiated in human cells, zuotin-related factor 1 (ZRF1) binds to monoubiquitylated histone H2A (H2Aub) and specifically displaces Polycomb repressive complex 1 (PRC1) from genes involved in differentiation. The authors show that H2Aub is required for stable maintenance of PRC1 at chromatin and suggest that ZRF1 and PRC1 might compete for this mark. Furthermore, they find that ZRF1 cooperates with deubiquitylases, which might facilitate gene activation.