GENE REGULATION

Compensation culture

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Dosage compensation ensures that there are equal levels of X-linked gene products in males and females. In *Drosophila melanogaster*, this is achieved by doubling the transcript levels of X-linked genes in males. The process requires the association on the X chromosomes of the male-specific lethal (MSL) complex, or dosage-compensation complex. Now, three independent reports present the results of chromosome-wide analyses of several MSL proteins. Using chromatin immunoprecipitation combined with high-throughput DNA microarray detection, the chromosome-wide binding of the *D. melanogaster* MSL complex to the single male X chromosome is detailed with unprecedented resolution, providing new insights into the dosage-compensation process.

Peter Becker's group investigated how the MSL complex identifies and binds the X chromosome in fly embryos using high-resolution genomic tiling arrays. They found that just over half the annotated genes on the X chromosome were bound by the complex. Preferred targets were essential genes, and the greatest compensation was seen for genes that bound high levels of the MSL complex. Notably, genes,

rather than intergenic regions, were favoured by the complex, which bound most strongly to the 3' end of the transcription units. The authors proposed a model in which individual genes that are under selective pressure to equalize dosage between the sexes have evolved targeting signals to attract the MSL complex.

Peter Park, Mitzi Kuroda and colleagues also determined the X-chromosome-specific binding pattern of the MSL complex in two male cell lines and in embryos, again using high-resolution genomic tiling arrays. Similarly to Becker's group, the authors found that the MSL complex recognizes and preferentially binds to genes rather than intergenic regions; the binding is also biased towards the 3' end of the transcription units. The same gene sequences can be clearly bound or unbound by the MSL complex, depending on cell type, indicating that MSL targeting cannot be explained by sequence alone. The authors proposed that the MSL complex selectively targets most X-linked genes, but only within the context of active transcription.

Asifa Akhtar and colleagues mapped the distribution of MSL1, a component of the MSL complex, in *D. melanogaster* embryos and larvae using an expression array that represented more than 10,000 annotated fly genes. They found that most MSL1-bound genes were expressed early in embryogenesis.

In larvae, the recruitment of MSL1 did not rely solely on transcription on the X chromosome. Moreover, many genes on the X chromosome seemed to be dosage compensated without direct MSL1 binding. The authors therefore suggested that the MSL complex might also regulate transcription of X-linked genes at a distance in larvae.

Taken together, these papers raise new questions about dosage-compensation selectivity and highlight the need for further investigation into selectivity determinants, while helping to redefine current models of dosage compensation. Given that the vertebrate X chromosome has also been shown to be subject to activating dosage compensation, lessons that have been learned from studying fruitflies could also help to understand dosage compensation in other species.

Sharon Ahmad, Assistant Editor,
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ORIGINAL RESEARCH PAPERS

Gillfillan, G. D. *et al.* Chromosome-wide gene-specific targeting of the *Drosophila* dosage compensation complex. *Genes Dev.* 17 March 2006 (doi:10.1101/gad.1399406) | Alekseyenko, A. A. *et al.* High-resolution ChIP-chip analysis reveals that the *Drosophila* MSL complex selectively identifies active genes on the male X chromosome. *Genes Dev.* 17 March 2006 (doi:10.1101/gad.100206) | Legube, G. *et al.* X-chromosome-wide profiling of MSL-1 distribution and dosage compensation in *Drosophila*. *Genes Dev.* 17 March 2006 (doi:10.1101/gad.377506)

FURTHER READING Schübeler, D. Dosage compensation in high resolution: global up-regulation through local recruitment. *Genes Dev.* 17 March 2006 (doi:10.1101/gad.1423006)

"...helping to redefine current models of dosage compensation."