Multiple routes to achieve sex-chromosome dosage compensation in our cells

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Correct gene expression dosage is vital for normal cell function and homeostasis. As a biochemical entity, the cell must maintain tolerable stoichiometric relationships of its functional gene products, a necessity that is particularly obvious for multimeric proteins. Chromosomal copy number variation (CNV) leads to imbalance of hundreds of genes in a single sweep and is poorly tolerated by the cell system. Indeed, most aneuploidies arising in the germline result in early embryo lethality, and CNVs are common genomic alterations in cancer cells. The X chromosome is a remarkable exception in this context, as female cells naturally carry two X copies while male cells cope with one – challenging our cells to balance X-gene expression correctly in each sex. Here, I will discuss new and surprising insights into how our cells resolve this fundamental challenge, achieving correct sex-chromosome dosage balance both in relation to the diploid autosomal gene expression networks, and between the two sexes.