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GENE EXPRESSION

One size does not fit all for transcriptomes

Cells of a particular cell type, in both multicellular and unicellular organisms, are remarkably uniform in size. This indicates that cell size is not just sensed but tightly regulated, yet little is currently known about the causes and consequences of changes in cell size. However, a new transcriptomic profiling study has identified novel genes whose expression varies in response to alterations in cell size.

Gerald Fink's laboratory previously showed that one major determinant of cell size, chromosomal ploidy, is linked to subtle shifts in gene expression. However, the relative influences of ploidy versus cell size were unresolved. In their latest work, the authors used RNA–seq to compare, in unprecedented detail, the transcriptomes of small, haploid *Saccharomyces cerevisiae* yeast cells with their larger, tetraploid counterparts, and they dissected the specific role of cell size in gene regulation.

Although the expression of most genes was unaffected, a subset of genes was reproducibly up- or downregulated between haploid–tetraploid pairs. This gene subset included *FLO11* (also known as *MUC1*), which was previously shown by the authors to be highly repressed in tetraploid versus haploid cells. Crucially, mutant haploid strains of various cell sizes recapitulate the observed gene expression changes in the absence of differences in ploidy, demonstrating that cell size, rather than merely cell ploidy, influences expression of these genes.

This set of differentially expressed genes was highly enriched for cell-surface protein-coding genes, which might reflect the altered ratio of cell volume to surface area as a function of cell size. But what drives these gene expression alterations? The authors analysed the functions of the genes that are repressed by an enlarged cell size (by looking at gene ontology classes) in addition to the transcription factor binding motifs of these genes. These analyses suggested that mitogen-activated protein kinase pathways that function in mating and filamentation could be involved in this differential gene expression. Indeed, yeast strains that were deficient for the transcriptional repressor *dig1* or the kinases *kss1* and *fus3* within these pathways were defective for cell-size-regulated gene repression, implicating the protein products of these genes as key transducers of cell size signalling. However, the mechanisms of cell-size-induced gene upregulation remain unclear, as do the functional consequences of the observed changes in mRNA levels.

The differentially expressed genes identified in this study seem to be reporters rather than controllers of cell size, as mutations in these genes do not themselves alter cell size. Given that cell size and ploidy disruptions have been linked to cancer and neurological diseases, it will be interesting to see whether cell surface genes are similarly regulated in higher organisms.

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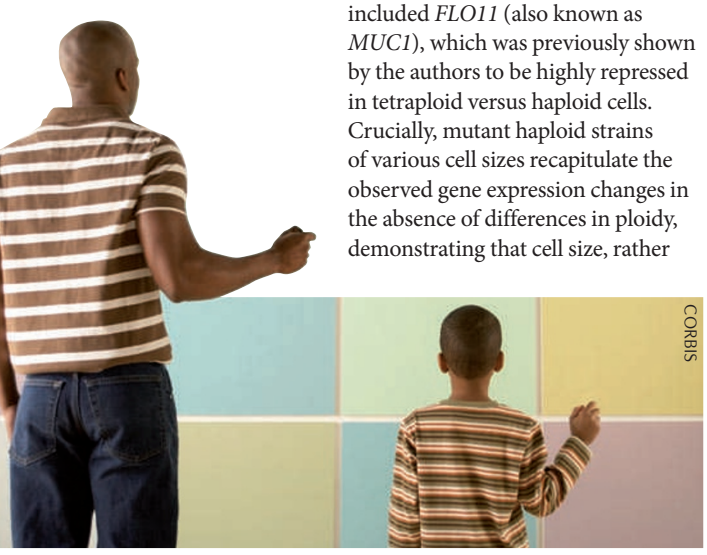

CORBIS

ORIGINAL RESEARCH PAPER Wu, C.-Y. *et al.* Control of transcription by cell size. *PLoS Biol.* **8**, e1000523 (2010)
FURTHER READING Saucedo, L. J. & Edgar, B. A. Why size matters: altering cell size. *Curr. Opin. Genet. Dev.* **12**, 565–571 (2002)