

# HIGHLIGHTS

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## FUNCTIONAL GENOMICS

# Fully functional

The ultimate goal of functional genomics is to determine the function of every gene in a given organism. To this end, systematic projects have begun to knock out all of the genes in some organisms whose genomes have been sequenced. *Saccharomyces cerevisiae* has led the way, and Giaever *et al.* now report in *Nature* the creation and initial functional analysis of strains that, collectively, are deleted for 96% of this yeast's genes. This pioneering analysis substantially enhances our knowledge of yeast biology.

Using mitotic recombination, the authors deleted the complete coding sequence of 96% of all annotated yeast ORFs. The function of each deleted gene was assayed in several growth conditions, and, because of the unique 20-nucleotide molecular barcode included in the deletion cassette, all deletion strains could be analysed in parallel. The more important a gene was for growth under a given condition, the quicker the strain in which it had been deleted diminished in culture, so that genes could be ranked in the order of their importance for growth under a specific condition.

The authors tested the fitness of their deletion strains on media that contained different amino acids and carbon sources, when osmolarity, pH and salinity were altered, and in the presence of an antifungal agent. In each case, new genes were identified. For example, ten new genes were found to be involved in growth on galactose. This was quite a surprise,

given that galactose metabolism is among the best-studied pathways in yeast.

Another surprising finding was that the expression of many genes that were important for growth in a given medium didn't change under these conditions; conversely, expression of those that were not required, did change.

Fitness profiling of a collection of yeast deletion strains was also carried out by Steinmetz *et al.* who focused on mitochondrial genes. Having identified 466 genes that are important for mitochondrial function, they used genomic map positions to identify human orthologues that are linked with heritable diseases.

These results have important implications for expression profiling studies that have not been confirmed by functional data, as they indicate that fitness profiling can refine expression profiling data. This approach provides systematic, unbiased information about gene function and marks the beginning of a fully functional era of genomics. It will make those who work on other organisms for which full genome sequences are available pursue their deletion projects even more zealously.

Magdalena Skipper

## References and links

**ORIGINAL RESEARCH PAPERS** Giaever, G. *et al.* Functional profiling of the *Saccharomyces cerevisiae* genome. *Nature* **418**, 387–391 (2002) | Steinmetz, L. M. *et al.* Systematic screen for human disease genes in yeast. *Nature Genet.* **31**, 400–404 (2002)

**FURTHER READING** Grünenfelder, B. & Winzler, E. A. Treasures and traps contained in genome-wide data sets: case examples from yeast. *Nature Rev. Genet.* **3**, 653–661 (2002)

