

## LINKS FOR WEB YEAST GENOMICS

Gene Ontology:  
<http://www.geneontology.org>

## Shaping up the genome

Many yeast mutations result in qualitative changes in morphology, but can this be practically quantified for discovering gene function? Ohya *et al.* have devised a quantitative screen for morphological phenotypes and they show that these phenotypes correlate with function. They demonstrate how this information can be applied to the collection of yeast mutants to predict the roles of genes of unknown function.

The authors have previously produced a database of digital images of every non-essential yeast mutant. In each image the cell wall, the cytoskeleton and the nuclear DNA are stained simultaneously, allowing quantitative data to be extracted. From this they have now defined 254 statistically reliable parameters that reflect morphology at different stages of the cell cycle.

They found that 2,378 of the 4,718 available deletion strains differed from the wild type in at least one parameter, and that 247 of the 254 parameters identified differences in at least one strain. Importantly, 544 genes of unknown function showed a morphological phenotype, representing about half of the unassigned genes in the genome.

To test for correlations between morphology and function the authors used the **Gene Ontology** functional annotation of the genome. Each gene for which a function is known is assigned to one or more of 1,452 functional groups. They compared each of these groups with all 254 parameters and found that 260 of the functional groups showed significant correlation with at least one morphological phenotype.

Conversely, the authors tested

each morphological class for enrichment with the genes that are associated with any one specific function. They found that 109 of the 254 morphological traits were associated with a functional annotation. Together, these results show that morphological data can be used to predict the functions of unassigned genes.

The power of such a method can be improved by studying more than one morphological trait at the same time. For example, the authors found two morphological traits that were associated with genes annotated as being involved in DNA repair. They then retrieved all the other non-essential genes in the genome that shared both traits and so identified several more candidate genes. These were then further characterized for sensitivity to the DNA-damaging reagent hydroxyurea. Interestingly, the morphological characteristics of wild-type cells that had been treated with hydroxyurea were similar to those of the untreated DNA-repair mutants. This indicates that correlations between chemically induced

and mutant phenotypes could be used to predict the chemical targets of drugs. Wild-type cells that have been treated with a particular drug can be assessed for morphological traits, and the mutants with similar characteristics can be identified. It is likely that the molecular targets of the genes that are deleted in these mutants are the same as the targets of the drug.

The methods demonstrated in this study can now be systematically applied to all of the 544 genes of unknown function that show a morphological phenotype, and hopefully they will lead to the identification of function in many cases. This will further close the gap in our knowledge of the functions that are encoded by the yeast genome.

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**ORIGINAL RESEARCH PAPER** Ohya, Y. *et al.* High-dimensional and large-scale phenotyping of yeast mutants. *Proc. Natl Acad. Sci. USA* **102**, 19015–19020 (2006)

**WEB SITE**

**Saccharomyces cerevisiae Morphological Database:** <http://scmd.gi.k.u-tokyo.ac.jp>

