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A census of yeast protein-protein interactions

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Mar Alba

Abstract

Genome-wide yeast two-hybrid screening has provided a census of protein-protein interactions in *Saccharomyces cerevisiae*.

Significance and context

Uetz and colleagues present results from two exhaustive two-hybrid screens to detect protein-protein interactions in *Saccharomyces cerevisiae* (baker's yeast). The work is very important as it provides a strategy for obtaining comprehensive protein-protein interaction data with which to construct a map of direct molecular interactions (and, by extension, pathways) in yeast. It provides a precedent for similar techniques to be applied to other genomes, such as that of *Caenorhabditis elegans*. The first screen involves construction of an array of the roughly 6,000 open reading frames (ORFs) known to be in the yeast genome, fused to the Gal4 transcriptional activation domain. This array is then screened against 192 ORFs fused to the Gal4 DNA-binding domain. Positive results from the 192 screens represent putative protein-protein interactions resulting from the two ORF-encoded proteins interacting to drive transcription. The second screen is a high-throughput analysis of an activation domain fusion library (similar to the one used for the array) against a DNA-binding domain library (similar to the 192 probes used against the array). As these libraries theoretically contain all yeast proteins, this screen represents a complete assessment of all possible interacting pairs.

Key results

The implications of this research are twofold. First, the work is a major breakthrough in the systematic study of protein-protein interactions of an organism, especially with respect to the use of array technology. Second, a large list of putative interactions for yeast has been generated and made publicly available. The array-screening technique appears to be more successful than the total library screening in that more interactions are detected: 45% of the proteins form interacting pairs (a total of 281 pairs) in contrast to only 8% of the estimated 5,345 proteins in the library screening (a total of 692 pairs). In addition, the arraying technique has the advantage that elements have fixed positions, so that positive interactions are immediately identified, and results from different screens can be compared. The array method is much more labor- and material-intensive, however, limiting the number of screens that can be performed.

Links

The results of the screens can be accessed online from Curagen's GeneScape Portal homepage.

Reporter's comments

Uetz *et al.* present exciting results based on developments using the well established yeast two-hybrid technology. It is important to note, however, that great variability in the strength and reproducibility of the interactions is observed in both the array and the library screening experiments, suggesting that the results should be interpreted with caution. Further experiments will be needed to confirm the interactions detected by the two-hybrid analysis.

Table of links

Nature

GeneScape Portal

References

1. Uetz P, Giot L, Cagney G, Mansfield TA, Judson RS, Knight JR, Lockshon D, Narayan V, Srinivasan M, Pochart P, et al: A comprehensive analysis of protein-protein interactions in *Saccharomyces cerevisiae*. Nature. 2000, 403: 623-627. 0028-0836