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Vaccinia protein-protein interactions

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Abstract

The availability of the complete sequence of the vaccinia virus genome has enabled a comprehensive two-hybrid analysis in yeast of virus protein-protein interactions.

Significance and context

Genome-wide studies of putative protein-protein interactions are useful not only for identifying protein complexes but also for gaining information on which components are part of the same molecular pathway. These studies are usually carried out, as in this paper, by the yeast two-hybrid technique. Two vector constructs, one containing the Gal4 activation domain fused to an open reading frame (ORF) and the other containing the Gal4 DNA-binding domain fused to another ORF, are used to detect interactions between the two ORF-encoded proteins. Interaction of these proteins brings the Gal4 activation and DNA-binding domains together, which results in the activation of expression of a reporter gene. In a genome-wide assay, all possible pairs of ORFs are assessed. The physical association of a protein of unknown function with another protein whose function is known can be used to predict the function of the former and thus speed up the functional annotation of 'unknowns'. McCraith *et al*. provide the first example of this approach applied to the study of putative interactions between proteins encoded by a large viral genome, that of vaccinia virus.

Key results

A total of 266 predicted ORFs in the vaccinia genomic sequence were screened against each other using the two-hybrid system, and 37 protein-protein interactions were detected. Many of the complexes detected include proteins involved in viral DNA replication, transcription and virion formation. Problems are encountered in the study of viral membrane proteins because of their lack of solubility. Some of the interactions identified are new and make good cases for further experimental testing. For example, a putative replication complex involving three proteins - DYR, DSR and A20R - is identified.

Reporter's comments

This work sets an excellent precedent for similar studies with other large viruses such as herpesviruses. The number of interacting pairs detected is disappointingly low, however, and some of these may be artifactual as the proteins may be expressed at different times during viral infection. In addition to virus protein-protein interactions, many virus proteins interact with cellular proteins during infection. The study of such interactions at a genomic scale is still difficult to tackle, but may be possible in the near future.

Table of links

Proceedings of the National Academy of Sciences of the United States of America

References

1. McCraith S, Hotzman T, Moss B, Fields S: Genome-wide analysis of vaccinia virus protein-protein interactions. Proc Natl Acad Sci U S A. 2000, 97: 4879-4884. 0027-8424