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Fly screen

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Identifying and dissecting the interactions between proteins is important in understanding fundamental physiological functions in all organisms. In the November 6 Sciencexpress, L. Giot and colleagues at CuraGen Corporation report a high-throughput yeast two-hybrid screen in *Drosophila* that provides global and local views of protein interaction networks that have relevance to the design of small molecule drugs for treatment of human diseases such as cancer, heart disease, and diabetes. In addition, detailed examination of protein interactions in transcription, splicing, signal transduction, calcium regulation, and cell cycle regulation gives insights into novel members of protein networks that have relevance to the wider scientific community (*Sciencexpress* 2003, DOI:10.1126/science.1090289).

Giot *et al.* performed high-throughput cloning of the entire *Drosophila* transcriptome by designing polymerase chain reaction primers to the 5' and 3' ends of 14,202 predicted open-reading frames and cloned relevant products into both DNA-binding domain (bait) and DNA-activation domain (prey) two-hybrid vectors. In total, 11,282 clones were screened between bait and prey pools and against two cDNA libraries, and over 90% of the resultant 63,093 diploid clones were matched to predicted transcripts and coding domain sequences in the Berkley Drosophila Genome Project Sequence and Annotation Databases. A locus-based map identified 4679 proteins and 4780 interactions with high confidence. Statistical analysis indicated a small-world network for *Drosophila* - reflecting biological and hierarchical organization - displaying both local and global connectivity.

"While [the] global analysis meets with the expectation that interactions within a compartment would be observed more frequently than those between compartments, it is gratifying that this is seen quantitatively in the two-hybrid network generated by high-throughput means. The two-hybrid network maintains a signature of cellular topology," the authors conclude.

Giot was joined by J.S. Bader, C. Brouwer, and A. Chaudhuri (all also at CuraGen Corporation) as primary authors of this paper.

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