

SPECIAL BIOCHEMISTRY SEMINAR

Exhaustive Protein Interaction Mapping: DrosoMan, a human-fly case study in cancer cell signaling

Marcela Núñez, Ph.D.

Project Leader, Scientific Projects,
Hybrigenics Services SAS, Paris, France
www.hybrigenics-services.com

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Abstract

Protein interaction mapping has proven instrumental for the delineation and understanding of cancer signaling pathways, both in *Homo sapiens* and model organisms. We have published a drosophila protein interaction map centered on fly orthologs of human cancer-related and signaling proteins¹.

We now report the completion of the cognate human interaction map using the same high-throughput, domain-based yeast two-hybrid (Y2H) technology. 149 human homologs of the 102 drosophila proteins, including 29 human oncogenes and tumor suppressors², were used as entry points to screen a highly complex, random-primed placenta cDNA library comprised of 10 million independent fragments in yeast. In order to strictly parallel the drosophila study, the same domains were selected as baits on human orthologs, resulting in 230 different screens. To ensure reproducible and exhaustive Y2H results, the library was screened at saturation using an optimized mating procedure that allowed for testing on average 50 million interactions per screen, corresponding to a 5-fold coverage of the library. As a consequence, multiple, independent fragments of the same interactant could be isolated, enabling the delineation of a minimal interacting domain and the computation of a confidence score.

The features of the drosophila and human parallel interaction maps were compared. Orthology relationships were combined with Y2H data and the conservation of interaction networks across evolution was examined. Experimentally determined interacting domains were also systematically confronted to known functional domains in both species, pointing to a significant enrichment of domains involved in protein binding. Finally, both experimental protein interaction maps were extended by including protein interaction data from the literature. We believe that this protein interaction map centered on human cancer signaling pathways will be an invaluable resource for researchers in the field.

