HIGHLIGHT ADVISORS

MICHAEL AKAM
UNIVERSITY OF CAMBRIDGE, UK

SEAN B. CARROLL
UNIVERSITY OF WISCONSIN, USA

NANCY J. COX
UNIVERSITY OF CHICAGO, USA

SUSAN FORSBURG
UNIVERSITY OF SOUTHERN CALIFORNIA, USA

RALPH J. GREENSPAN
THE NEUROSCIENCES INSTITUTE, CALIFORNIA, USA

YOSHIHIDE HAYASHIZAKI
RIKEN GENOMIC SCIENCES CENTER, JAPAN

MARK JOBLING
UNIVERSITY OF LEICESTER, UK

PETER KOOPMAN
UNIVERSITY OF QUEENSLAND, AUSTRALIA

LEONID KRUGLYAK
FRED HUTCHINSON CANCER RESEARCH CENTER, USA

BARBARA MEYER
UNIVERSITY OF CALIFORNIA, BERKELEY, USA

JOHN QUAKENBUSH
THE INSTITUTE FOR GENOMIC RESEARCH, USA

JANET ROSSANT
MOUNT SINAI HOSPITAL, TORONTO, CANADA

MARC VIDAL
DANA-FARBER CANCER INSTITUTE, BOSTON, USA

VIRGINIA WALBOT
STANFORD UNIVERSITY, USA

DETLEF WEIGEL
MAX PLANCK INSTITUTE FOR DEVELOPMENTAL BIOLOGY, GERMANY

PHIL ZAMORE
UNIVERSITY OF MASSACHUSETTS, USA

LEONARD I. ZON
CHILDREN'S HOSPITAL, BOSTON, USA

NETWORK BIOLOGY

A protein network of one's own proteins

Network biology has taken off with the advent of high-throughput, parallel data collection and analysis. The term interactome has been coined to describe an organism's total set of protein–protein interactions, and interactome maps have been created for many model organisms. Knowing all protein–protein interactions is seen as a crucial prerequisite to understanding how cells function and the general principles that govern this function. Importantly, such information should also help us to understand disease processes. Two recent reports provide the first experimentally derived description of a human protein–protein interaction network. The network, although preliminary, is a useful resource and provides interesting insights into the nature of protein–protein interactions on a global scale.

Two groups led by Erich Wanker and by Marc Vidal used similar high-throughput, stringent yeast two-hybrid strategies and identified 3,186 and ~2,800, mostly novel, protein–protein interactions, respectively. The data sets were each evaluated for technical and biological false positives. Whereas the former were dealt with rigorously, using co-affinity purification and pull-down assays, the authors admit that the latter are more difficult to deal with. To this end, Vidal's group compared their interactions with other known biological relationships such as expression correlation, shared gene ontology or phenotype annotation. Wanker's group used orthologous interactions as well as topological and gene ontology criteria to develop a confidence-scoring system to evaluate the biological relevance of the interactions. They also compared the human interaction network with 22 human regulatory pathways from the Kyoto Encyclopedia of Genes and Genome, KEGG. The authors mapped 150 human proteins to KEGG pathways and using more stringent criteria mapped 66 of those to specific pathways.

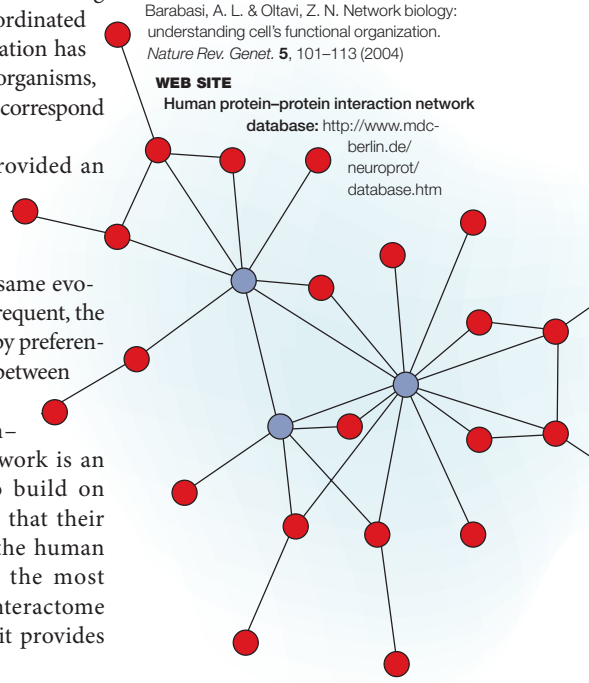
The human interaction network seems to have scale-free properties. Most proteins are separated by only a few links, indicating that the network has 'the small world property'. The network is also hierarchical, showing local clusters that are coordinated by hubs. Similar organization has been observed in model organisms, in which hubs are likely to correspond to essential proteins.

Vidal's group also provided an insight into how the interactome might evolve. Because interactions between proteins of the same evolutionary class are more frequent, the network seems to evolve by preferentially adding interactions between lineage-specific proteins.

The human protein–protein interaction network is an invaluable resource to build on (Vidal's group estimate that their data set reveals 1% of the human interactome). Perhaps the most exciting aspect of an interactome map in humans is that it provides direct information about molecular processes that are related to disease.

The interaction network is a template onto which other information will need to be superimposed. Determining the location and the timing of the interactions, and their regulation, are just some of the challenges that lie ahead.

Magdalena Skipper



References and links

ORIGINAL RESEARCH PAPERS Stelzl, U. *et al.* A human protein–protein interaction network. *Cell* 1 September 2005 (doi:10.1016/S0092867405008664) | Rual, J.-F. & Venkatesan, K. *et al.* Towards a proteome-scale map of the human protein–protein interaction network. *Nature* 28 September 2005 (doi:10.1038/nature04209)

FUTHER READING Cusick, M. *et al.* Interactome: gateway into systems biology. *Hum. Mol. Genet.* 26 August 2005 (doi:10.1093/hmg/ddi326) | Barabasi, A. L. & Oltavi, Z. N. Network biology: understanding cell's functional organization. *Nature Rev. Genet.* **5**, 101–113 (2004)

WEB SITE

Human protein–protein interaction network database: http://www.mdc-berlin.de/neuroprot/database.htm

© 2005 Nature Publishing Group