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A multiscale view of protein-protein interactions

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Abstract

High-throughput proteomics has allowed for the drafting of large protein-interaction networks (PPIN) and systems biology devotes a constant effort in the statistical analysis of these. Accurate descriptions of these assemblies must reflect the cellular context in which they usually operate and the many factors that may have conditioned their evolution. The detailed analysis of a particular cellular function may benefit from the study of smaller and accurately selected sub-networks, containing high confidence interactions resulting from the cross-mapping of multiple sources of information for the nodes (proteins) such as tissue-specific expression data, gene expression data, domain profiles and structural information. Analysis of these SNKs provides the basis for the identification of fundamental components of the network and of specific pathways associated with the studied phenomenon that can be targeted to speed-up experimental screening and design new experiments. We will present an application to the study of specific interactions involving Cdc42 activity increases during Natural Killer (NK) cell immune surveillance, and predicted network components to perturb by RNA interference. The downstream consequences on cytotoxic vesicle polarization of knockdown with two RNAi show a strong reproducible effect on Cdc42 activity. By reducing further the scale of details analysed in a given PPIN, we focus only on special proteins in the network, like the multi-partner ones, called 'hubs'. In particular, we concentrated on protein hubs that have a 3D-structure and on the characterization of their conformational dynamics and flexibility of the multiple interfaces.

Biography

Franca Fraternali received her PhD in Physical Chemistry from the University of Naples, working on characterization of protein conformational dynamics by molecular simulations techniques. During her PhD she worked in collaboration with Prof. W.F. van Gunsteren at the Polytechnic of Zurich (ETH) and developed implicit solvent models for use in molecular dynamics. She has hold post-doctoral positions at prestigious Institutions like ETH, the Institute Pasteur in Strasbourg and the European Molecular Laboratories in Heidelberg (EMBL). In 2000 she obtained a staff position in the Mathematical Biology Division of the National Institute for Medical Research (NIMR) MRC in London. Since 2005 she has established her own group at King's College within the Randall Division.