

Keys to the molecular basis of specific protein interactions

Madrid, 19th January 2010 – The prestigious journal *Proceedings of the National Academy of Science USA (PNAS)* publishes today the first extensive study on the influence of evolution on the sequences of interacting proteins. This research was carried out by Antonio Rausell and David Juan, from the Spanish National Cancer Research Centre (CNIO), and Florencio Pazos, from the Spanish National Centre for Biotechnology (CNB-CSIC), under the direction of Prof. Alfonso Valencia, Head of the CNIO's Structural Biology and Biocomputing Programme.

In the article, the authors present a detailed analysis of the large number of known protein complexes obtained by experimental methods to show how the corresponding protein families evolve to fit with their specific protein partners. The computational methodology developed by the authors permits tracing, with great accuracy, the corresponding changes in the amino acid sequences that underlie the delicate balance of interactions in the signalling pathways that control most biological processes. This new bioinformatics approach opens exciting possibilities for the direct manipulation of the protein binding sites, and can be considered a key step for the redesign of signalling pathway and cellular signal transmission. This line of research will be followed up in the context of the ENFIN international systems biology consortium.

Furthermore the quantitative study of the protein interaction surfaces suggests that the differential interaction with molecular partners can change very fast over evolutionary time and is present in a large number of protein families. One of the practical implications of this work is that it would be important to take into account this new information about the organization of proteins' functional sites when interpreting the consequences of mutations discovered in ongoing cancer genome projects.

Protein interactions and ligand binding: From protein subfamilies to functional specificity. Antonio Rausell, David Juan, Florencio Pazos and Alfonso Valencia. *PNAS* published online before print January 19, 2010, doi:10.1073/pnas.0908044107

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