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Drug Target Discovery Through Protein-Protein Interaction Database

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While Human Genome Projects have produced a tremendous amount of important data about the genome, it does not, on its own, provide information about how these genes and their products, the proteins, function in disease. Realizing that the answer to finding new targets that can reverse the effects of disease may lie in the interaction between proteins, not just the over-expression or under-expression of the genes, researchers began to study the function of different genes and proteins. It seems logical to identify and describe all the genes and proteins, and correlate them with disease, then identify the function, and from there, identify new drug targets. Finding a drug target that safely regulates disease without affecting normal function has proved very challenging by using current genomics approaches. Further complicating matters is that even when a protein is identified that controls cell function, it does not act alone. It is typically one part of a complex cascade of proteins (known as a signaling pathway) that in concert produces a physiologic effect. And in each cell, there exist many possible signaling pathways that can lead to a variety of physiologic outcomes. In treating disease, it may be possible to modify a signaling pathway other than the defective one and still improve the health of the cell. After bioinformatics researchers identify a cell protein that is implicated in a particular disease, researchers build peptide chains that can bind to a domain on another protein. Next, the computers determine the peptide chains to be interacted and synthesized. The strengths of the interactions are then measured. Strong affinity correlates with strong interaction; thus a pharmaceutical made to inhibit or enhance those interactions might alleviate some symptoms of a particular disease. Specific software then may allow pharmaceutical companies to analyze data in proteomics company's databases. The bioinformatics team creates protein interaction maps. Computational chemists then can design drugs that mimic the structure of particular peptide chains that are known to bind with one particular domain, but not with others.

To characterize the functions of unknown genes in large scales, protein-interaction partners can be screened by using the modified yeast two-hybrid system which allowing one-stop screening with reduced frequencies of false positives. A system allowing efficient and large-scale gene cloning strategy, which is based on the double-stranded break repair process in yeast has been developed. And a system for the large-scale test, which is based on the yeast mating method, has also been developed. This could establish the protein networking-map for identification of upstream and down stream genes and for determination of the functions of the proteins providing key proteins for further study as well as for the best target for anticancer drugs.

Exploring targets on the genomic scale