

High-throughput Proteomics

Proteomics is the study of the function of all expressed proteins. It includes the analysis of expression, localization, interaction and ultimately the function of each protein. Proteomics is based on Genomics. It uses the information about potential and verified ORF's generated by genomics approaches and the advances in automation to create and analyze huge complements of protein. In contrast to DNA and RNA, where every fragment behaves biochemically like any other, proteins possess unique properties which make the analysis of genomic complements of proteins much more difficult.

I will describe two studies done with the same proteomic method: creating a fusion library of all the genome of the budding yeast and analyzing it.

The first experiment¹ tried to determine the abundance of proteins during log phase in the budding yeast. Protein product was observed for around 70% of ORF's cloned. The abundances found vary from 50 to more than 10^6 proteins per cell. We will also look into a method to discover spurious ORF's as a complement method to the comparative genomics approach.

The second experiment² used fusions with GFP to determine sub cellular localization of proteins. Micrographs of each strain were taken and analyzed for localization. After determination of the sub cellular localization of more than 4,500 proteins, they tried to determine the correlation between localization and mRNA co-expression. They also created a map of interactions between cellular components based on the localization data and on protein-protein interaction data from GRID. They show how one can use the knowledge about localization together with other biological knowledge of a certain protein to understand the protein's function and activity.

Last, we will look at an article³ which tries to devise the relationship between mRNA abundance and Protein abundance. It shows that post transcriptional regulation and protein specific degradation disturb the correlation between mRNA and protein levels. They show that in some modules there is "Translation on Demand"; mRNA levels are high relative to protein amounts so that in time of need there is no need for transcription but only for enhanced translation. The importance of this article is that it shows how one can use the extensive knowledge we have today to create a more accurate information of the cell's control mechanisms.

For conclusion I will briefly review future prospects for Proteomics.

¹ Global analysis of protein expression in yeast, Ghaemmaghami S, Huh WK, Bower K, Howson RW, Belle A, Dephoure N, O'Shea EK, Weissman JS. Nature 2003 Oct 16;425(6959):737-41

² Global analysis of protein localization in budding yeast, Huh WK, Falvo JV, Gerke LC, Carroll AS, Howson RW, Weissman JS, O'Shea EK. Nature 2003 Oct 16;425(6959):686-91.

³ Post-transcriptional expression regulation in the yeast *Saccharomyces cerevisiae* on a genomic scale, Beyer A, Hollunder J, Nasheuer HP, Wilhelm T, Mol Cell Proteomics. 2004 Nov;3(11):1083-92