THE PROTEOMINER AND THE FORTYNINERS: SEARCHING FOR GOLD NUGGETS IN THE PROTEOMIC ARENA

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The present lecture will cover modern aspects of combinatorial ligand libraries (CLL), as used for analyzing the “low-abundance proteome” in association with mass spectrometry. First, the capturing properties of baits of different lengths (from single amino acid to hexa-peptides) are described, to show that a plateau is rapidly reached above a tetra-peptide in length, thus confirming the validity of having adopted hexapeptides for the considered application. The mechanism of interaction with proteins from very complex proteomes and the ability to decrease the dynamic concentration range is demonstrated with the help of mass spectrometry analysis. Examples are given on how treatment with CLLs dramatically improves the detectability of peptides in mass spectrometry analysis and permits one to detect a very large number of proteins as compared with control, untreated samples. The use of complementary libraries is discussed with the aim to discover additional low-abundance species that escaped the first library. The lecture will end by discussing the possibility to discover extremely rare gene products, and the quantitative aspect of the technology when associated with mass spectrometry. Some insights on the applications for hidden, low-abundance biomarkers are also presented. The samples to be dealt with: the cytoplasmic proteome of the red blood cell, egg white proteomics, cerebrospinal fluid, human sera and urines. Last, but not least, the use of CLLs for the discovery of a large number of previously undetected host proteins in recombinant DNA products.

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