

THE INSIGHT INTO THE HUMAN LIVER PROTEOME

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The Human Liver Proteome Project (HLPP) is a large-scale international collaborative initiative now focusing on the proteomic analysis of the human liver in its different conditions. In the past five years, we have set up standard operating procedures, optimized the strategies of the proteomic analysis and investigated the proteomes of the Chinese fetal liver tissues, French adult liver tissues and Chinese adult liver tissues in turn.

Recently, after analyzing the proteome from the Chinese adult liver tissues, which comprised of 6,788 identified proteins in 95% confidence with at least two peptides matching, we turn to the proteomic analysis of the different organelles as well as the different kinds of liver cells. We succeeded in identifying 5882 proteins with 2 peptides or more in 95% confidence from plasma membrane, nucleus, cytoplasm, mitochondria, rough endoplasmic reticulum and smooth endoplasmic reticulum in human liver cells, which will be compared with those proteins identified from the human liver tissues. As well, 4969 proteins were identified from the same organelles of the mouse liver. Furthermore, we optimized the approach of the extracorporeal liver perfusion and cell sorting and obtained the purified mouse hepatic parenchymal cells, in which, 2216 proteins were identified with at least 2 peptides in 99% confidence.

In order to effectively enrich the low-abundance proteins, especially those with modifications, we developed several new methods, which were obviously more useful, such as dephosphorylation of phosphopeptides by cerium oxide and specific capture of phosphopeptides on MALDI mass spectrometry. In addition, on the basis of our past results of the protein-protein interactions, we expanded the number of the baits. So far, we totally found 1732 unique protein-protein interactions by screening the human liver cDNA library with the yeast two hybrid. Meanwhile, a protein array of about 5000 unique liver ORFs was screened by yeast two hybrid mating method and 1632 protein-protein interactions were discovered. Of them, 1270 interactions were verified by yeast retransformation assay.

Key words: Human Liver Proteome/ organelle/ protein-protein interaction