The Human Liver Proteome Project

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The Human Liver Proteome Project (HLPP) was the first HUPO initiative organized around an organ. HLPP was launched in October 2002 under the leadership of Professor Fuchu He, director of the recently established Beijing Proteome Research Center, Beijing, China. This center also serves as the headquarters for HLPP management and coordination. Co-chairs from Europe and the United States joined He in leading this initiative: Professor Christian Bréchot, director of the Institut National de la Santé et de la Recherche Médicale (INSERM), Paris, France, recently replaced by Dr. José Mato, director of Centro de Investigación Cooperativa en Biociencias (CIC bio)GUNE, Bilbao, Spain, and Professor Laura Beretta, associate member at the Fred Hutchinson Cancer Research Center, Seattle, Washington. HLPP has received strong support from the National Institutes of Health and from governments, mainly from the Chinese government.

The scientific objectives of HLPP are to characterize the proteome of the healthy human liver (expression profiling, cellular localization, post-translational modifications, and protein-protein interactions) and to develop tools for its study (sample banking, ORFeome, antibodies). The information and tools that are generated by this international effort will be available to the scientific community with the hope that these will help us to understand, diagnose, and treat liver diseases more effectively.

At the 2005 HLPP workshop held at the Airlie Center, Virginia, initial targets for HLPP were identified as follows: 1) identification of 5,000 individual proteins in the normal human liver, 2) availability of antibodies against these 5,000 proteins, and 3) determination of the presence of these 5,000 proteins in plasma. The aim of these targets is to generate sufficient knowledge of the normal liver and resources to allow the study of liver diseases and biomarker discovery. As learned during the 2006 workshops held in Bilbao, Spain, and in Long Beach, California, immediately prior to the HUPO 5th Annual World Congress, major progress has been made toward these goals (1). A major achievement was made on the construction of the human normal liver proteome expression profile, with well over 5,000 proteins identified. The list of proteins and associated information will be publicly available soon, in the PRoteomics IDEntifications (PRIDE) database at the European Bioinformatics Institute. Efforts to associate the identified proteins with subcellular organelles and with the different liver cell types are underway. Studies to determine their presence in plasma are also ongoing. Establishment of a liver antibody bank has been one of the priorities of HLPP from the beginning of the initiative. An antibody knowledge database will be constructed with information on the availability of antibodies against the proteins identified in the reference samples. Future directions are to prioritize proteins for production of antibodies unavailable to date.

The past 4 years have generated extensive information on the normal liver proteome. The next phase of the project is to use this information to perform functional studies and further understand the biology of the liver. To that end, groups of proteins associated with specific functions (e.g. detoxification, endoplasmic reticulum stress, lipid metabolism, liver development, liver regeneration), and groups of proteins with similar post-translational modifications (e.g. phosphoproteome, glycoproteome) will be characterized in greater detail.

Finally, plans are to expand the initiative from the study of the normal liver to the study of liver diseases. Liver diseases affect a large percentage of the general population worldwide, and there is an urgent need to identify non-invasive means to diagnose chronic liver diseases such as fibrosis, steatosis, and cancer. Collaborative studies focusing on mouse models of liver diseases and on biomarker discovery have been recently initiated among HLPP participants.

Additional information on HLPP structure and activities can be obtained at the HUPO web page and in the newly launched HLPP Newsletter (www.hupo.org/research/hlpp/).

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REFERENCE