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IDENTIFICATION OF DIFFERENTIAL PROTEINS IN LIVER CELLS UPON DEPLETION OF PROHIBITIN

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Liver diseases afflict more than 10% of the world population. Although in most cases hepatopaties present slow progression, the risk factors are known and the population at risk is monitorized, the prognostic of patients with severe liver damage is poor. Development of efficient therapies greatly depends on a better understanding of the molecular pathogenesis of liver diseases and in the identification of biomarkers allowing early diagnosis. Prohibitin (PHB) plays a central role in the maintenance of liver homeostasis since, in the hepatocyte, it participates in essential cellular pathways including cell signalling, apoptosis, cell survival and proliferation, through the regulation of central proteins involved in these processes by means of protein-protein interaction mechanisms. Recent studies suggest that PHB impairment participate in the inflammatory reaction associated to both acute and chronic liver diseases as well as in the progression of liver fibrosis, common alterations to most pathological conditions in human liver disorders. In the last few years evidences have been accumulated that support the implication of PHB in the etiopathogenesis of non-alcoholic steatohepatitis (NASH), liver fibrosis and cirrhosis, and hepatocellular carcinoma (HCC). In this work we have investigated the molecular mechanisms underlying the participation of PHB in the progression of liver diseases. PHB was impaired in PLC human liver cancer cells using specific siRNAs and differential proteins relative to control PLC cells were detected in various subcellular fractions by DIGE analysis. Decyder analyses revealed 76 and 25 differential spots in the cytosolic and microsomal fractions respectively. Differential spots were then analyzed by nanoLC-ESI-MS/MS and 35 unique proteins were identified. Besides, further functional analyses indicate deregulation of the proteasome system in addition to alterations in mitochondrial and endoplasmic reticulum integrity in liver cells in response to PHB deficiency in liver cells.