Contribution ID: **532** Type: **Invited talk**

New Discoveries on HBV infection by Metabolomics

Thursday, 29 August 2019 10:30 (35 minutes)

Hepatitis B Virus (HBV) is a double stranded DNA virus and belongs to hepadnavirdae family. HBV infection causes a severe liver infectious disease and has become a global problem affecting human health. At least 250 million people are chronically infected with HBV, with an estimated 650,000 deaths per year from HBV associated hepatocellular carcinoma, mainly in Asia. Current clinical strategy is aimed at inhibiting the HBV replication. Research in HBV infection is also hindered by the factor that there is no great animal models. We employed metabolomics approach and investigated both human circulating metabolites and cell model. We found that HBV replication induces the promotions of central carbon metabolism, biosynthesis of nucleotides and total fatty acids; HBV up-regulates the biosynthesis of hexosamine and phosphatidylcholine through activating glutamine-fructose-6-phosphate amidotransferase 1 (GFAT1) and choline kinase α (CHKA), respectively. Furthermore, we demonstrate that GFAT1 and CHKA are two potential targets for treating HBV infection. To elucidate the relationship between HBV replication and host downstream lipid metabolism, we measured 10 classes of phospholipids in HBV infected patients and cells and we found that the levels of phosphatidylcholine (PC), phosphatidylethanolamine, and lyso-phosphatidic acid were increased in HBsAg (+) group compared with HBsAg (-), while phosphatidylserine, phosphatidylglycerol, phosphatidylinositol, and sphingomyelin were decreased, which were confirmed in HBV infected HepG2.2.15 cell line. We further evaluated the levels of enzymes of PC pathways and found that PCYT1A and LPP1 for PC synthesis were up-regulated after HBV infection. Moreover, the HBV replication was inhibited when PCYT1A and LPP1 were knocked down. These results indicated that the PC synthesis in HBV infected host are regulated by PCYT1A and LPP1, which suggests that PCYT1A, LPP1 could be new potential targets for HBV treatment.

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Session Classification: Metabolomics

Track Classification: Metabolomics