“Elucidation of the innate immune activation against Hepatitis B virus and its molecular mechanism of action”

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This study aims to identify the potential pathway of the host innate immune system in recognizing HBV upon infection. We did the microarray analysis the liver tissues upon HBV infection. Our results demonstrated that cGAS is among the host viral nucleic acid sensing pathway that are upregulated and activated during the HBV infection. To further investigate the response of hepatic cells to HBV, we investigated if the co-culture of the hepatocytes and non-parenchymal cells will lead to the release of cytokines which indicates that the host innate immune system has been activated. To further clarify the role of the cGAS/STING pathway in such immune activation, we have established a human macrophages cell line (THP-1) lacking the cGAS expression. The qPCR have confirmed that the 80% mRNA knockdown for cGAS in the cell line constructed. In the preliminary result of the co-culture experiment, we found that the cGAS knock down THP-1 failed to secret the relevant cytokines when co-cultured with the HBVtransfected hepatocytes compared to the wild type. Reproducibility and repeatability of the experimental result obtained in this study will further confirm our hypothesis. To identify the possible pathogen associated molecular patterns of the HBV viral DNA that activate innate immune responses, we constructed the 11 viral DNA fragments of the viral DNA coding for its ORF of PreS1, PreS2, S, P, Pre-core, core, X protein, and etc. we found that full length viral genome as well the PreS1 (Pre-surface protein 1), PreS2 (Pre-surface protein 2) and Surface protein triggered the up-regulation of the IFN-β, IL6, IL-1 and IL-10 expression in the real-time qPCR analysis. This has indicated that the viral DNA containing the sequence of the viral surface protein could possibly be the important Pathogen-associated molecular patterns (also known as PAMPs) that activate innate immune responses.

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