MiRNA146a IS A KEY COMPONENT OF IMMUNNOSUPRESSIVE ENVIRONMENT OF HEPATOCYTES CHRONICALLY INFECTED WITH HBV

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Hepatitis B virus (HBV) causes acute hepatitis and can lead to chronic liver inflammation, often resulting in hepatocellular carcinoma. Known as a "stealth virus," HBV can evade recognition by the immune system. Plasmacytoid dendritic cells (pDCs), robust producers of type I and III interferons (IFNs),[1] which are crucial for HBV clearance.,[1] However, miRNA146a, an immunosuppressive and proliferative miRNA in hepatocytes, modulates pDCs by silencing TRAF6 and IRAK1/4 proteins.[2]

We hypothesize that HBV-infected hepatocytes produce miRNA146a within extracellular vesicles (EVs)[3], which can deliver miRNA146a into pDCs and inhibit their functions.[4] Indeed, the supernatant from HBV-producing cells contained higher levels of miRNA146a than supernatant from noninfected cells and inhibited TLR9 agonist-induced IFNα production by model pDC cell line Gen2.2. We further demonstrated the functional role of miRNA146a in IFNα downregulation by using a miRNA146a inhibitor. Supernatant collected from miRNA146a inhibitor-treated HBV-producing cells showed decreased levels of miRNA146a and did not inhibit IFNα production in Gen2.2 cells.

Since miRNA146a levels may be altered by HBV infection in patients and interfere with the immune responses, targeting this miRNA could be of significant therapeutic interest.

Acknowledgement
The work was supported by the project National Institute of Virology and Bacteriology (Programme EXCELES, ID Project No. LX22NPO5103) – Funded by the European Union – Next Generation EU.

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