Titel des Beitrags: Hepatitis B virus impairs TLR9 expression and function in plasmacytoid dendritic cells.

Abstract: Plasmacytoid dendritic cells (pDCs) play a key role in detecting pathogens by producing large amounts of type I interferon (IFN) by sensing the presence of viral infections through the Toll-Like Receptor (TLR) pathway. TLR9 is a sensor of viral and bacterial DNA motifs and activates the IRF7 transcription factor which leads to type I IFN secretion by pDCs. However, during chronic hepatitis B virus (HBV) infection, pDCs display an impaired ability to secrete IFN-? following ex vivo stimulation with TLR9 ligands. Here we highlight several strategies used by HBV to block IFN-? production through a specific impairment of the TLR9 signaling. Our results show that HBV particle internalisation could inhibit TLR9- but not TLR7-mediated secretion of IFN-? by pDCs. We observed that HBV down-regulated TLR9 transcriptional activity in pDCs and B cells in which TLR9 mRNA and protein levels were reduced. HBV can interfere with TLR9 activity by blocking the MyD88-IRAK4 axis and Sendai virus targeting IRF7 to block IFN-? production. Neutralising CpG motif sequences were identified within HBV DNA genome of genotypes A to H which displayed a suppressive effect on TLR9-immune activation. Moreover, TLR9 mRNA and protein were downregulated in PBMCs from patients with HBV-associated chronic hepatitis and hepatocellular carcinoma. Thus HBV has developed several escape
mechanisms to avoid TLR9 activation in both pDCs and B lymphocytes, which may in turn contribute to the establishment and/or persistence of chronic infection.