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Co-Incubation with core proteins of HBV and HCV leads to modulation of human Dendritic Cells

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Hepatitis B and C (HBV and HCV) are hepatotropic viruses in humans with approximately 350and 170 million chronic carriers respectively. Since both viruses have similar modes of transmission, many people are co-infected. Co-infection is common in intravenous drug users, HIV-positive individuals and transplant recipients. Compared to mono-infected patients, co-infected patients exhibit exacerbated liver cirrhosis, hepatocellular carcinoma and liver failure. Some of the pathogenic effects may be attributed in part to the structural core proteins of both viruses – ones that have displayed immuno-modulatory properties. Yet, the effects of their combined interaction on the human immune system remain a mystery. We aimed to elucidate the combined effects of HBV and HCV core proteins on human dendritic cells' (DCs) ability to present antigens and stimulate antigen-specific T cells. We observed that when DCs, differentiated from human peripheral blood monocytes, were co-incubated with both core proteins, IL-10 productionwas dramatically enhanced, IL-6, TNF-α and IL-12 productionwas significantly reduced, and HLA-DR expressionwas down-regulated. This instant functional and phenotypic modulation of DCs induced by a combination of HBV and HCV core proteins can allow them to behave like tolerizing DCs, inefficiently presenting antigens to CD4+ T cells and even suppressing induction of the cellular immune response. These results reveal an important mechanism by which HBV and HCV synergistically induce immune tolerance early in infection that may be instrumental in establishing chronic, persistent infections.

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