Pegylated Interferon Lambda efficiently suppresses HDV productivity and shows comparable ability to induce ISGs as peg-IFNα in HBV/HDV co-infected humanized mice

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Background: The interferon system plays a fundamental role in countering viral infections. Like interferon-alpha (IFNα), interferon-lambda (IFNλ) induces antiviral activity in hepatocytes. Because its receptor is largely restricted to cells of epithelial origin, IFNα may induce an antiviral state via the activation of interferon stimulated genes (ISGs), while showing fewer side effects. Although IFNα was reported to suppress HBV replication in vitro and in HBV-transgenic mice, the impact of IFNα on hepatitis Delta virus (HDV) infection has not been investigated.

Aim of the study was to determine the antiviral effect of peg-IFNα on HDV productivity and to explore its ability to induce the innate immune system of the human hepatocytes compared to peg-IFNα in human liver-chimeric uPA/SCID mice.

Methods: Chronic HBV/HDV co-infected mice were treated either with peg-IFNα (PEG-IFNα-1 and PEG-IFNα-2) or peg-IFNλ for 4 weeks (Figure 1A). Viremia and ISG levels were determined by qRT-PCR, intrahepatic genomic and antigenomic HDV-RNA by using a novel qRT-PCR assay and HDAg by immunohistochemistry.

Peg-IFNα provoked the reduction of HDV and HBV viremia and circulating HBsAg

Conclusions:

Similarly to IFNα, IFNλ efficiently suppressed HDV productivity (viremia, intrahepatic HDV-RNA levels and amounts of HDAg-positive cells) and strongly enhanced the innate immune responses of the human hepatocytes. However, the self-induction of IFNα genes was unique and underlay the diverse capacities of these IFNs to trigger distinct antiviral pathways, which may prove useful for the development of more effective therapeutic concepts.