**In Vitro and In Vivo anti-HBV Activities of the New Cyclophilin Inhibitor STG-175**

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**Results**

Fig 1: STG-175 decreases HBV entry by preventing the binding of the viral envelope to the NTCP receptor

![Diagram of viral entry](image)

Primary hepatocytes (A) or NTCP-positive Huh7 cells (B) (triplicate) were exposed to purified HBV (AD38) for 4 h in the presence of increasing concentrations of DSMO or STG-175. Drugs were added together with the virus. Cells were washed, trypsinized and analyzed for HBV entry by measuring by ELISA amounts of HBV core in cell lysates. C. NTCP-positive Huh7 cells were exposed to fluorescent recombinant HBV S envelope (HBVpreS2-2/48min-X-FITC (100 μM)) for 1 h in the presence of increasing concentrations of DSMO or STG-175 (triplicate). Drugs were added together with the FITC HBV envelope peptide. Cells were washed and analyzed by FACS.

**Materials and Methods**

We evaluated both in vitro and in vivo the anti-HBV inhibitory potency of the new cyclophilin inhibitor STG-175, which previously demonstrated high efficacy against HCV.

**Conclusions**

By demonstrating that the new cyclophilin inhibitor STG-175 exhibits potent anti-HBV activities both in vitro and in vivo, our findings strongly indicate that STG-175 represents an attractive drug partner for IFN-free direct-acting antiviral regimens for the treatment of hepatitis B.

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**Fig 3: The combination of STG-175 and ETV exhibits synergistic anti-HBV effects**

HepAD38 (A), HepDE19 (B) or HepDES19 (C) cells (triplicate) were treated with increasing concentrations of STG-175 combined either with STG-175 or entecavir (ETV) as described in Figure 2. Antagonistic, additive and synergistic effects were analyzed by quantification of intrahepatic HBV DNA by qPCR. Cell viability was analyzed by CalFluor assay while additive and synergistic effects were analyzed by the MacSynergy program. This program is based on the Bliss independence model that is triggered by the following equation: 

\[ E_F = E_x + E_y - (E_x \times E_y) \]

where \( E_x \) is the additive effect of drugs x and y as predicted by their individual effects, \( E_x \) and \( E_y \).

**Fig 4: STG-175 inhibits HBV replication in transgenic mice**

HBV transgenic C57Bl/6 mice (S/37/B/6) mice containing a single genomic transgene 1.3 HBV genome copy (serotype ayw) and reproducing the virus replication cycle from gene expression through virion release) were treated daily for 3 weeks as indicated in the figure. Users were collected at the end of treatment and HBV DNA levels were quantified by qPCR while liver HBsAg and HBeAg levels were quantified by ELISAs.