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ABSTRACT

“Objective” Clinical importance of the interleukin-28B gene encoding interferon (IFN)-λ3, which has antiviral effects, has been established in HCV infection but not in HBV infection. Thus, we measured IFN-λ3 levels in patients with HBV and investigated its clinical significance and association with nucleos(t)ide (NUC) analogue administration.

“Design” Serum IFN-λ3 level was measured in 254 patients with HBV with varying clinical conditions using our own high sensitivity method. The resulting values were compared with various clinical variables. In addition, cell lines originating from various organs were cultured with NUCs, and the production of IFN-λ3 was evaluated.

“Results” Higher serum IFN-λ3 levels were detected in the patients treated with nucleotide analogues (adefovir or tenofovir) compared with those treated with nucleoside analogues (lamivudine or entecavir). There were no other differences in the clinical background between the two groups. A rise in the serum IFN-λ3 levels was observed during additional administration of the nucleotide analogues. In vitro experiments showed that the nucleotide analogues directly and dose- dependently induced IFN-λ3 production only in colon cancer cells among the various tested cell lines that potentially produce IFN-λ3. Furthermore, the supernatant from cultured adefovir-treated colon cancer cells significantly induced IFN-stimulated genes (ISGs) and inhibited hepatitis B surface antigen (HBsAg) production in hepatoma cells, as compared with the supernatant from entecavir-treated cells.

“Conclusions” We discovered that the nucleotide analogues show an additional pharmacological effect by inducing IFN-λ3 production in GI cells, which further induces ISGs in hepatic cells and results in a reduction of HBsAg production. These findings provide novel insights for HBV treatment and suggest IFN-λ3 induction as a possible target.