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Inhibition of Human Hepatitis B Virus DNA Polymerase (HBV DNAP) and Duck Hepatitis B Virus DNA Polymerase (DHBV DNAP) by Triphosphates of Thymidine Analogs. P.-Z. Tao*, B. Löfgren+, R. Datema‡, and B. Oberg‡, Department of Virology, Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences, Beijing, P. R. China*, Department of Medical Microbiology, University of Lund, Lund, Sweden+ and Department of Antiviral Therapy, Research & Development, Astra Alab AB, Södertälje, Sweden‡.

It has been well documented that hepadnavirus has a unique reverse transcription mechanism in its genomic replication cycle. This involves the viral DNAP which contains both DNA-dependent DNA polymerase (DNAP) and RNA-dependent DNA polymerase (RT) activities. The viral polymerase is a potential target for chemotherapy against hepatitis B. In order to compare sensitivities of different enzyme preparations towards inhibitors we have used HBV DNAP from human serum and DHBV DNAP both from duck serum and liver (RT activity). Triphosphates of thymidine analogs have been tested for their inhibitory activities against these enzymes with the intention both to explore differences between these enzymes and structural requirements for inhibitors. The results showed that with the inhibitors tested HBV DNAP was the most sensitive enzyme, followed by DHBV DNAP from liver (RT), and DHBV DNAP from serum being the least sensitive. Kinetic studies with DHBV DNAP from serum showed the triphosphate of 5-propenyl-araU to be a competitive inhibitor (Kis = 0.12 μM) with respect to dTTP and preliminary data indicated that it did not substitute for dTTP as a substrate.

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The Effect of Ribavirin on Hepatitis B Virus Induced Suppression of Bone Marrow Progenitor Cells In Vitro. H.N. Steinberg and J.B. Zeldis. Charles A Dana Research Institute and Thorndike Laboratory, Beth Israel Hospital and Harvard Medical School, Boston, MA. 02215.

Exposure of human bone marrow cells to hepatitis B virus (HBV) containing sera or purified viral particles results in the suppression of progenitor cell proliferation and differentiation as measured by the decrease in erythroid (CFU-E; BFU-E), granulocyte-macrophage (CFU-GM), and lymphocyte (CFU-TL) colony formation in vitro. The degree of bone marrow suppression is related to the multiplicity of infection and the time of exposure to the virus. The HBV suppression of erythroid colony formation is completely reversed by the addition of 0.1 to 2.5 ug/ml ribavirin to the cultures. Inhibiton of CFU-E by HBV continues to be observed in culture treated with either with acyclovir or AZT. Our studies suggest the utility of the human bone marrow-HBV assay to screen agents with potential activity against HBV.