Oral Session VII

Retrovirus and Hepadnavirus Infections

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Mechanism of Action of Antiviral Agents Targeted Against Duck Hepatitis B Virus Supercoiled DNA. SA Locarnini, S Bowden, Guo Ning, G Tachedjian, Xin Hong and J Newbold. Virology Department, Fairfield Hospital, Fairfield, Victoria, 3078, Australia; and Department of Microbiology and Immunology, UNC School of Medicine, Chapel Hill, North Carolina, USA.

Hepatitis B virus (HBV) supercoiled DNA (SC DNA) is the main transcriptional template for hepadnaviral replication and is the major replicative intermediate most resistant to therapy with conventional antiviral agents such as the interferons and nucleoside analogues (ganciclovir). To further characterize hepadnaviral SC DNA, we have examined the structure of the duck HBV minichromosome (ie. the SC DNA and its association with cellular histones) derived from hepatocyte nuclei of congenitally infected ducks. Analysis of the duck hepatocyte chromatin on agarose gels after digestion with micrococcal nuclease revealed classical nucleosome laddering with a core nucleosome fragment size of 200 bp. In contrast, analysis of the DHBV minichromosome following micrococcal nuclease digestion showed a different pattern of nucleosome banding on a background of significant viral DNA smearing. Treatment of ducks with the SC DNA active agent nalidixic acid, resulted in significant changes in viral SC DNA generation and processing, confirming that DHBV SC DNA has a different structural organisation from that of its host cell chromatin and that it is a potentially useful target for antiviral drug design.