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Hepatitis B Virus DNA and RNA Circulating in the Blood of Distinct Groups of Carriers

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The nucleic acid serodiagnosis of HBV infection usually is restricted to the determination of HBV DNA and considered to amount to the determination of virus particles. Recently, circulating HBV DNA and RNA in the blood were identified as potential new diagnostic markers. In this study, assays for the identification were refined and used for the description of HBV infection stages. Specifically, a combination assay was developed for the identification of differentially polyadenylated RNA (full-length RNA and truncated RNA, fRNA and trRNA). It was shown that the patterns of circulating viral DNA and RNA represent the respective patterns in the liver.

Furthermore, it was shown that HBV expression in leucocytes does not remarkably contribute to the observed patterns of circulating viral nucleic acids. Hence, the involved assays appear to be representative of liver infection stages. Groups of patients subjected to the analysis of circulating HBV nucleic acids included cancer patients under chemotherapy, cryptically infected HCC patients,

and infants of HBV infected mothers. It could be shown that circulating HBV RNA constitutes a valuable marker to monitor the induction of HBV expression following chemotherapy, the expression of HBV in cryptically infected individuals, including newborns. For the newborns with circulating trRNA as the sole single marker, an early stage of infection is suggested. For monitoring lamivudine therapy, PCR assays were developed addressing segments of viral DNA synthesized successfully during viral replication. The obtained results were consistent with the known chain terminator activity of the drug and demonstrated an excess of non-polyadenylated over polyadenylated viral RNA indicative of a rapid removal of the polyA tail of packaged pregenome. As the main result of lamivudine therapy monitoring, an apparent lasting production of nucleocapsids containing early replication intermediates was observed. It is suggested that the analysis of circulating HBV nucleic acids as a non-invasive procedure has the capacity to reduce the need for taking liver biopsies.

An application of the results in serum serodiagnosis appears to be useful for monitoring the progress of lamivudine therapy, identifying newborns with occult HBV infection and adults with late stage of chronic infection.