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CHARACTERIZATION OF RABBIT MONOCLONAL ANTIBODY CANDIDATES FOR THE DEVELOPMENT OF IMPROVED HEPATITIS B VIRUS (HBV) IMMUNOASSAY FOR THE DETECTION OF MUTATED SURFACE ANTIGENS

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Background:

Due to its mode of replication by reverse transcription of its pre-genomic RNA, HBV has a high rate of mutation relative to other DNA viruses. Amino acid substitutions have been described in all HBV DNA encoded viral proteins such as polymerase, nucleocapsid protein (HBcAg) and surface antigen (HBsAg). There are increasing concerns about the contribution of variant HBsAg to vaccine escape, immune prophylaxis failure and false negatives in serological HBV diagnosis or blood screening assays. The group-specific “a” determinant region (amino acids 124-147) has attracted most attention, not only because mutations in the “a” determinant were found in 10-20% vaccine escapes, but also because of the fact that high-affinity antibodies in response to this region have been used in most HBV diagnoses.

Method:

To address the needs of an improved immunoassay capable of detecting the major mutations in the “a” determinant regions, four potential rabbit monoclonal antibodies which exhibit a broad immunoreactivity and higher affinity to HBsAg mutant antigens were selected for further characterizations. The goal of the study is to identify a single or a few rabbit monoclonal antibodies that could replace the current panel of mouse monoclonal antibodies for the detection of the various HBsAg mutants.

Results:

The results from the Biacore analysis and the sandwich ELISA analysis demonstrated that the rabbit monoclonal antibodies, 99S9, 96S1, 99S1, and 99S6 have superior

sensitivities against the various HBsAg mutants compared to the mouse monoclonal antibodies.

Conclusion:

The study results also indicated that a single rabbit monoclonal antibody could substitute the multiple mouse monoclonal antibodies used in current assay development. Therefore, rabbit monoclonal antibodies may provide a tool for better detection of HBsAg variants.