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ANTIGENIC PROPERTIES OF WILD-TYPE AND MUTANT HEPATITIS B VIRUS SURFACE ANTIGENS

Objectives. To study the effect of sequence heterogeneity on the antigenic properties of hepatitis B surface antigen (HBsAg).

Methods. A series of plasmids was constructed for the expression in *Hansenula polymorpha* of subtypes *ayw1*, *adw2* and *adw4*, as well as 'vaccine escape' mutants *adw2-N126* (Asn-for-Thr substitution at amino acid position 126) and *adw2-R145* (Arg-for-Gly at position 145). Each of the expressed recombinant HBsAg variants was purified and tested by enzyme immunoassay with 66 monoclonal antibodies (MAbs) specific for different determinants. The subtype of each recombinant HBsAg except for *adw2-R145* variant was confirmed by additional testing with five well characterized determinant specific MAbs.

Results. Fifty-two (78.8%) of the 66 MAbs reacted with subtype *ayw1*, 42 (63.6%) with *adw4* and 62 (93.9%) with *adw2*. Surprisingly, the *adw2-N126* mutant showed reactivity with 56 MAbs (84.8%). This finding suggests that the N126 mutation does not have a profound effect on the antigenic property of HBsAg *adw2*. However, mutant *adw2-R145* only immunoreacted with 26 (39.4%) MAbs. This observation suggests that the R145 mutation significantly affected the epitope composition of subtype *adw2*. Twenty (30.3%) out of the 66 MAbs immunoreacted with all five HBsAg variants. This observation suggests that despite sequence heterogeneity, all of the variants used in this study share a common epitope(s). Eighteen (27.3%) MAbs immunoreacted with four HBsAg variants except the *adw2-R145* mutant. Therefore, the substitution of Arg for Gly essentially reduces the number of common antigenic epitopes between the *adw2-R145* and the wild type *adw2*.

Conclusions. The data obtained in this study demonstrates that the HBsAg sequence heterogeneity may have a significant effect on the antigenic properties of this antigen. However, different HBsAg vaccine escape mutants may be affected by mutations to different degrees.

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