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Identification by Phage Display and Characterization of Two Neutralizing Chimpanzee Monoclonal Antibodies to the Hepatitis E Virus Capsid Protein

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Abstract

Two monoclonal antibodies (MAbs) against the ORF2 protein of the SAR-55 strain of hepatitis E virus (HEV) were isolated by phage display from a cDNA library of chimpanzee (Pan troglodytes) g1/k antibody genes. Both MAbs, HEV#4 and HEV#31, bound to reduced, denatured open reading frame 2 (ORF2) protein in a Western blot, suggesting that they recognize linear epitopes. The affinities (equilibrium dissociation constants, Kd) for the SAR-55 ORF2 protein were 1.7 nM for HEV#4 and 5.4 nM for HEV#31. The two MAbs also reacted in an enzyme-linked immunosorbent assay with recombinant ORF2 protein from a heterologous HEV, the Meng strain. Each MAb blocked the subsequent binding of the other MAb to homologous ORF2 protein in indirect competition assays, suggesting that they recognize the same or overlapping epitopes. Radioimmunoprecipitation assays suggested that at least part of the linear epitope(s) recognized by the two MAbs is located between amino acids 578 and 607. MAbs were mixed with homologous HEV in vitro and then inoculated into rhesus monkeys (Macaca mulatta) to determine their neutralizing ability. Whereas all control animals developed hepatitis (elevated liver enzyme levels in serum) and seroconverted to HEV, those receiving an inoculum incubated with either HEV#4 or HEV#31 were not infected. Therefore, each MAb neutralized the SAR-55 strain of HEV in vitro.

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