Human monoclonal antibodies 447-52D and 537-10D, both coded by the VH3 gene and specific for the third variable region (V3) of the HIV-1 gp120, were found to share antigen-binding structural elements including an elongated CDR H3 forming main-chain interactions with the N terminus of the V3 crown. However, water-mediated hydrogen bonds and a unique cation-π sandwich stacking allow 447-52D to be broadly reactive with V3 containing both the GPGR and GPGQ crown motifs, while the deeper binding pocket and a buried Glu in the binding site of 537-10D limit its reactivity to only V3 containing one of these crown motifs.
In Memoriam: Harold RW Benjamin 1898-1969, indeed, the liquid tasting Dolnik, this day fell on the twenty-sixth day of the month of Carney, which the Athenians called metagitnion.

pocket and a buried Glu in the binding site of 537-10D limit its reactivity to only V3 containing the GPGR motif. Our results suggest that the design of immunogens for anti-V3 antibodies should avoid the Arg at the V3 crown, as GPGR-containing epitopes appear to select for B cells making antibodies of narrower specificity than V3 that carry Gln at this position.

PROTEINS; MICROBIO; MOLIMMUNO

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