N 409 PREDICTION OF HELPER T-CELL ANTIGENIC SITES FROM THE PROTEIN SEQUENCE.
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We have used a data base of 23 known immunodominant helper T-cell antigenic sites, located on 12 proteins, to systematically develop an optimized algorithm for predicting T-cell antigenic sites from the amino acid sequence. The algorithm is based on the amphipathic helix model, in which antigenic sites are postulated to be helices with one face predominantly polar and the opposite face predominantly apolar. Such amphipathic structures can form when the polarity of residues along the sequence varies with a regular period and hence, can be identified by methods that detect periodic variations in properties of a sequence. We examined two such methods: a Fourier transform and a least squares fit of a sinusoid. Different hydrophobicity scales and other model parameters were examined. An algorithm was tested by comparing the predicted amphipathic segments with the locations of the known T cell sites, and calculating the probability of getting this number of matches by chance alone. The optimum algorithm uses the Fauchere-Pliska hydrophobicity scale and a least squares fit of a sinusoid to detect periodic variation in the sequence of hydrophobicity values. By applying this algorithm, 18 of the 23 known sites are identified with a high degree of significance ($p<0.001$). The success of the algorithm supports the hypothesis that stable amphipathic helices are fundamentally important in determining immunodominance. This approach may be of practical value in designing synthetic vaccines aimed at T cells.

N 410 SITE-SPECIFIC ALTERATION OF POLIOVIRUS ANTIGENS. Guy S. Page and Marie Chow, MIT Cambridge, MA 02139
The poliovirus capsid is composed of four proteins, three of which are assembled on the external surface, the fourth lying internally in association with genomic RNA. As part of an effort to understand the interaction of the external proteins with the host immune system we have analyzed amino acid substitutions in the capsid proteins of 65 poliovirus variants that show resistance to neutralizing antibodies. Amino acid changes were found in all three of the external capsid proteins, and group into three limited areas. These groups define the locations and partial compositions of the Polio Type I antigens. To extend the description of the antigens and study antibody interactions in more detail, we are selectively altering the antigens and neighboring regions using oligonucleotide directed mutagenesis on infectious cloned viral cDNA.

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N 411 SYNTHETIC ANTIBODIES WITH KNOWN 3-D STRUCTURE, Andreas Plückthun*, Rudi Glockshuber, Jörg Stadlmüller, and Arne Skerra, Genzentrum der Universität München, Max-Planck-Institut für Biochemie, Am Klopferspitz, D-8033 Martinsried, W-GERMANY

The genes encoding the variable domains (V_H and V_L) of the phosphorylcholine binding antibody McPC603 were obtained by DNA synthesis. In addition, we constructed genes encoding the variable and the appropriate constant domains of each chain in order to directly express the exact F_{ab} fragment whose crystal structure is known. The design of the synthetic genes took into consideration the facile replacement of gene fragments (e.g. the hypervariable loops) as well as current knowledge about efficient expression. We have investigated purifications of the cloned gene products from bacterial expression systems and are comparing their efficiency in obtaining large amounts of protein. The essence of antibody architecture is a framework of fairly constant residues and hypervariable loops (complementary determining regions, CDR) that contain the antigen recognition sequences to a great variety of antigens. The particularly well studied antibody combining site of McPC603 is used by us as a model system for quantitatively investigating factors that contribute to efficient hapten binding, subunit interactions, as well as for the potential of stabilizing a transition state through the controlled modification of the protein.