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Prediction of B-cell epitopes – "Step 1" for rational vaccine design

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The classical paradigms for effective vaccines simply do not comply with HIV. Therefore, alternative strategies must be developed in order to produce a prophylactic AIDS-vaccines. Whereas the correlates of sterilizing immunity are not well understood, there is an ever-growing consensus that cross-reactive and neutralizing antibodies are an essential component of the desired immune response against HIV. A possible scheme for rational vaccine design could consist of three steps. Step 1 would be to identify a potent cross-reactive neutralizing antibody and use it as a template of sorts to backtrack and discover its corresponding epitope. Step 2 would then be to reconstitute the epitope as an effective immunogen. Step 3 would be to determine the most effective means to implement the reconstituted As a first step towards this reversed immunological approach we have developed a means to predict the epitope corresponding to monoclonal antibodies of interest. For this the antibody is used to screen combinatorial phage display peptide libraries thus generating panels of peptides that correspond in some fashion to the epitope of the antibody being studied. These peptides, along with the atomic coordinates of the corresponding antigen are then used as input data for computational prediction of the epitope on the surface of its antigen by means of the algorithm – "Mapitope". The output of Mapitope is a number of epitope candidates ranked according to their likelihood of best representing the bona fide epitope of the mAb. The Mapitope prediction of the neutralizing epitope corresponding to the b12 human monoclonal antibody will be presented. Here we have been able to predict the main core of the epitope and support this prediction with experimental data and additional Mapitope analyses of the competing antibodies, m14 and b6.