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Epitope-based vaccines: SARS – a model

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In February 2003 The World Health Organization (WHO) announced that a new pathogen – a member of the coronavirus (CoV) family – is the cause of severe acute respiratory syndrome (SARS), a mysterious atypical pneumonia that emerged in China's Guangdong province three months earlier. Over the next weeks, the illness spread to more than two dozen countries in Asia, North America, South America, and Europe, resulting in over 8000 individuals becoming infected; 774 of which died. Currently, significant efforts in the area of SARS vaccine research are being made. Several neutralizing antibodies have been isolated and reported to prevent viral infection, mainly, via blocking the association between the viral spike protein and its cellular receptor, angiotensin converting-enzyme 2 (ACE-2). Here we report the first steps toward identifying a major neutralizing epitope of SARS-CoV, using an original reverse immunological approach. According to this approach, a neutralizing monoclonal antibody (mAb) serves as a template for the ultimate production of an epitope-based vaccine. In order to accomplish this task one must backtrack from the antibody of interest to its corresponding neutralizing epitope. Once identified, the epitope can be reconstituted and used to elicit antibodies with neutralizing activity characteristic of the original mAb. 80R [1], is a highly potent neutralizing human anti-SARS mAb directed against the viral spike protein and has been used to affinity select panels of mAb specific peptides from phage displayed random peptide libraries. "Mapitope" [2], a unique computer algorithm, uses these peptides as input and has enabled us to map the 80R epitope on the spike protein. In general, Mapitope prediction of an epitope is based on the notion that the panel of affinity selected peptides collectively represents the epitope of the mAb which they bind. More specifically, pairs of amino acids enriched in the peptide panels are taken to effectively represent surface accessible discontinuous pairs of residues of the epitope, juxtaposed in the antigen via protein folding. Two independent peptide-panels were analyzed against the crystalline structure of the receptor binding domain (RBD) of the SARS-CoV spike protein by Mapitope [3]. Three clusters (A, B and C) were predicted as potential epitopes. Cluster A ranked the highest, and is currently being considered for reconstitution and epitope based vaccine production.

References

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