Vaccine against Human Papilloma Virus inducing plantar warts

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Introduction
Human Papilloma Virus (HPV) is a family of non-enveloped double-stranded DNA virus, containing genomes of 7,800bp (1). Around 200 different types of HPV are classified, of which 118 are fully sequenced (2). HPV infects the skin and mucous membranes, and the cutaneous genotypes are responsible for common warts, planter warts, flat warts and genital warts (3). It is assumed that over 30% of the sexually active women and men are infected with HPV once in their life-time (4). This study focuses on HPV type 4 which causes plantar warts.

The aim was to find a single protein in HPV type 4 which is a suitable vaccine candidate considering both B-cell, class-I T-cell and class-II T-cell epitope. Germany was chosen as a suitable target population based on the assumption that Germany is a good representative of Western Europe and because it had a suitable allele sample size. The presented class-I T-cell epitopes cover HLA alleles corresponding to 89% of the selected target population and class-II T-cell epitopes corresponding to three distinct DR alleles.

Results and Conclusion

- The 3D structure of HPV type 4, hypothetical protein no. 3 was modeled using CPH-models and visualized in PyMol.
- Discontinuous B-cell epitopes for protein 3 were predicted by DiscoTop, and linear B-cell epitopes were predicted by BepiPred. Both the linear and discontinuous B-cell epitopes were visualized in PyMol on a 3D cartoon structure of the protein (figure 1).
- The results showed that the predicted B-cell epitopes were mainly located in loops and turns on the protein surface. This finding is in good agreement with most other known B-cell epitopes.
- The most prevalent HLA-A, HLA-B and HLA-DRB1 alleles in the German population were chosen using allelefrequency.net, and the most distinct alleles were selected by visual inspection of the motif logos using MHC motif viewer. The presented four HLA-A and four HLA-B alleles cover HLA alleles corresponding to 89% of the German population. Furthermore, the three most distinctive and prevalent HLA-DRB1 alleles were selected.
- NetMHCpan was used to predict potential cytotoxic T-cell epitopes on the selected four HLA-A and four HLA-B alleles. Similarly, NetMHCIIpan was used to predict potential T-helper epitopes on the selected three HLA-DRB1. The resulting predicted peptides were sorted by their binding affinities and by using a threshold of 0.426 to identify binding peptides. This threshold value corresponds to an IC50 value stronger than 50nM and is generally taken to define binding peptides.
- The smallest number of 15mer peptides was identified so that these peptides covered the presented four HLA-A, four HLA-B and the three HLA-DRB1 alleles.
- The six presented 15mer peptides all belong to the same HPV protein and thus a single protein could be identified as a potential vaccine candidate for both B-cell, class-I T-cell and class-II T-cell epitopes.