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A bioinformatics tool for epitope-based vaccine design that accounts for human ethnic diversity: Application to emerging infectious diseases

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ABSTRACT

Background: Peptide vaccination based on multiple T-cell epitopes can be used to target well-defined ethnic populations. Because the response to T-cell epitopes is restricted by HLA proteins, the HLA specificity of T-cell epitopes becomes a major consideration for epitope-based vaccine design. We have previously shown that CD4+ T-cell epitopes restricted by 95% of human MHC class II proteins can be predicted with high-specificity.
Methods: We describe here the integration of epitope prediction with population coverage and epitope selection algorithms. The population coverage assessment makes use of the Allele Frequency Net Database. We present the computational platform Predivac-2.0 for HLA class II-restricted epitope-based vaccine design, which accounts comprehensively for human genetic diversity.
Results: We validated the performance of the tool on the identification of promiscuous and immunodominant CD4+ T-cell epitopes from the human immunodeficiency virus (HIV) protein Gag. We further describe an application for epitope-based vaccine design in the context of emerging infectious diseases associated with Lassa, Nipah and Hendra viruses. Putative CD4+ T-cell epitopes were mapped on the surface glycoproteins of these pathogens and are good candidates to be experimentally tested, as they hold potential to provide cognate help in vaccination settings in their respective target populations.
Conclusion: Predivac-2.0 is a novel approach in epitope-based vaccine design, particularly suited to be applied to virus-related emerging infectious diseases, because the geographic distributions of the viruses are well defined and ethnic populations in need of vaccination can be determined ("ethnicity-oriented approach"). Predivac-2.0 is accessible through the website http://predivac.biosci.uq.edu.au/.

1. Introduction

Q3 Emerging infectious diseases (EIDs) caused by major families of viruses are increasing in frequency, causing a high disease burden and mortality world-wide [1,2]. Epitope-based vaccines (EVs) make use of short antigen-derived peptide fragments that are administered to be presented either to T-cells (as T-cell epitopes in association with HLA molecules), or B-cells (as B-cell epitopes) [3]. While CD8+ cytotoxic T-cells generally recognize intracellular peptides displayed by HLA class I molecules, CD4+ T-helper cells generally recognize peptides from the extracellular space, displayed by HLA class II molecules (CD4+ T-cell epitopes). Traditional vaccines against EIDs are difficult to produce due to the need for culturing pathogenic viruses *in vitro*. By contrast, EVs have a number of advantages: (i) biosafety: no *in vitro* culturing requirement; (ii) bioprocessing: large-scale production can be carried out economically and rapidly; (iii) selectivity: precise activation of immune response by selecting conserved or immunodominant epitopes, and epitopes

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