HLA-BINDING PEPTIDE AFFINITY PREDICTION AND T CELL-MEDIATED RESPONSE

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BACKGROUND.

Human leukocyte antigen (HLA) allele and supertype peptide binding motif scanning of viruses are routinely used to predict conserved peptides that may trigger cross-reactive HLA class I and/or class II restricted T cell responses. Yet, "good" HLA-binding peptide affinity does not necessarily translate into a "good" T cell-mediated response that can control infections for example with pandemic and seasonal influenza strains. Aside HLA polymorphisms other important factor that affects the T cell-mediated response is the quality of T-cell receptor interaction with the HLA/peptide complex. The design and use of a combined affinity- and structure-based prediction approach permits to take steric and topological effects of TCR contact residues on TCR binding affinity into consideration when evaluating peptides for further candidate vaccine testing.

METHODS.

Influenza HA peptide-HLA class I binding candidates were predicted by integrating NetCTL[1]. Homology models of selected candidate peptides were docked to HLA-B*4405 and DM1-TCR followed by three-stage molecular dynamics simulation[2].

RESULTS.

Molecular docking of H1N1 HA influenza peptides bound to HLA-B*4405 docking as ligand to DM1-TCR produced H5N1 HA cross-reactive epitope candidates suitable as multivalent peptide in influenza A vaccine development. Most mutations that accumulated between the analyzed HA sequences of 2004 H5N1 and 2009 H1N1 did not appear to affect DM1 TCR recognition of HLA-B*4405 presented epitope candidates.

CONCLUSIONS.

In a future pandemic it is therefore expected that apart from a few mutated epitopes, heterologous immunity mediated by pre-existing cross-reactive T cell responses to seasonal influenza virus will ameliorate its severity and extent. While it is possible to successfully infer potential differences in recognition and cross-reactivity for a few alleles, here HLA-B*4405, an extension to population level is limited. The bottom line in *in silico* inference of epitope candidates that may induce a broad T cell response is data.

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