

Bioinformatic analysis of HIV-specific T cell responses against variant epitopes reveals restricted T cell receptor promiscuity

Ilka Hoof¹, Carina L Pérez^{2,3}, Rasmus K L Gustafsson⁴, Morten Nielsen¹, Ole Lund¹, Annika C Karlsson^{2,3}

¹Center for Biological Sequence Analysis, Department of Systems Biology, Technical University of Denmark, Lyngby, Denmark

²Department of Microbiology, Cell Biology, and Tumor Biology, Karolinska Institutet, Stockholm, Sweden

³Department of Virology, The Swedish Institute of Infectious Disease Control, Stockholm, Sweden

⁴Division of Neurology, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

HIV-1 specific CD8⁺ T lymphocyte (CTL) responses play a key role in limiting viral replication. The high mutation rate of HIV, however, poses a tremendous problem for the control of virus replication. Even though CTLs recognize epitope variants, this cross-reactivity has not been quantitatively investigated in a genetically diverse population. Employing a bioinformatic binding-prediction method, we compared HLA-matched immune responses against tested and autologous epitope sequences from 1517 patient-peptide pairs to quantify determinants of recognition. Epitopes recognized in ELISPOT studies were found to be significantly more similar to the autologous virus than those that did not elicit a response. A single substitution in the presented peptide decreased the chance of a CTL response by 50%. Substitutions at positions that are important for recognition were particularly likely to result in lack of recognition. The presented data demonstrates a highly restricted promiscuity of HIV-1 specific T cells in the recognition of variant epitopes.