

Induction of Novel CD8⁺ T Cell Responses During Chronic Untreated HIV-1 Infection by Therapeutic Immunization

Henrik Klopper¹, Ingrid Karlsson¹, Jesper Bonde¹, Mette Thorn¹, Lasse Vinner¹, Anders Pedersen², Betina Andresen¹, Julie Hentze¹, Gregers Gram¹, Inge M. Svane³, Jan Gerstoft⁴, Gitte Kronborg⁵, Anders Fomsgaard¹

¹SSI, ²University of Copenhagen, ³University Hospitals of Herlev, ⁴Copenhagen and ⁵Hvidovre, Denmark

To investigate the potential to induce additional CTL immunity during chronic HIV-1 infection we selected infrequently targeted or subdominant conserved HLA-A*0201-binding epitopes. These immune silent epitopes were modified as anchor-optimized peptides to improve immunogenicity and delivered on autologous monocyte-derived dendritic cells (MDDCs) together with 3 T_{CD4} epitopes to 12 treatment-naïve HLA-A*0201⁺ HIV-1 infected individuals. New T cell responses specific for one or more epitopes were induced in all 12 individuals as detected by IC-FACS (IFN- γ , TNF- α , IL-2) and/or pentamer labelling. No severe adverse effects were observed and no overall change in viral load or CD4⁺ T cell counts. This shows the possibility to generate new T cell responses in chronically HIV-1-infected individuals and redirect immunity to target new multiple and rationally selected subdominant CTL epitopes. Further optimization with additional epitopes and delivery could lead to responses able to better control viral replication, prevent disease and limit spread in the population.