

Retargeting of HIV reverse transcriptase to MHC class II processing improves its immunogenicity

Latanova Anastasia^{1,2}, Starodubova E^{1,2}, Petkov S², Kuzmenko Y¹, Krotova O^{1,3}, Isaguliants M^{2,3} and Karpov V¹

¹RAS, Russia

²Karolinska Institutet, Sweden

³DI Ivanovsky Institute of Virology, Russia

Currently tested multi-gene DNA vaccines towards HIV fail to induce a strong immune response against reverse transcriptase (RT) which is a key enzyme in the viral escape from drugs. Design of DNA-vaccine against HIV, specifically against drug resistant virus variants, requests a considerable enhancement of RT-specific immune response. MHC class II targeting of RT by fusion with signals of lysosome targeting of lysosome-associated membrane protein I, fragment of invariant chain and the minimal Gly-Ala repeat of EBNA1 tested previously somewhat improved the cellular, but not the humoral immune response to RT. To further strengthen its immunogenic performance, we N-terminally fused RT to the leader sequence of nonstructural protein 1 (NS1) of TBE. The NS1-RT chimera was detected both on the surface of transfected cells and in the cell culture medium. BALB/c mice were immunized with RT gene chimera by intradermal injection followed by electroporation, and immune response was assessed by serology, IFN-g/IL-2 Fluorospot, ICCS for IFN-g, IL-2; and ELISA for perforin and granzyme B. NS1-RT chimeric gene induced a potent Th2-tilted immune response manifested by strong dual IFN-gamma/IL-2 production and secretion of perforin and granzyme B by murine splenocytes stimulated with RT-peptides. Moreover, mice response by high anti-RT antibody production reaching 80000 for IgG and 1000 for systemic IgA. Thus retargeting of RT processing and presentation by turning it into secretable protein resulted in strong potentiation of RT-specific immune response.

aalatanova@gmail.com