Therapeutic vaccines

PE43

Monocyte-derived DC electroporated with mRNAs encoding both specific HIV antigens and DC adjuvants are able to improve T-cell functionality

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Background: In the context of therapeutic vaccination of HIV-infected patients, we have tested in vitro a combination of mRNA sequences that fulfil two main objectives. On the one hand, a specific T cell activation immunogen mRNA that focuses the response onto the most vulnerable targets in the HIV viral proteome and on the other hand, a previously tested stimulus (TriMix: a mixture of CD70+CD40L+caTLR4 mRNAs) for appropriate activation of antigen presenting cells (DCs).

Methods: DCs were generated from peripheral blood monocytes (MDDC) from chronically HIV infected patients by incubation with GM-CSF and IL-4. These cells were electroporated with TriMix (15 µg) and/or HIVACAT (20 µg) mRNA, with their respective controls. After that, DCs were cocultured with autologous PBMCs for up to 6 days. In addition, the maturation profile of MDDCs (CD80, CD83, CD86, CCR7) was analyzed by FACS 24h after electroporation. Functional analysis was performed using different techniques: 25-multiplex Luminex assay, T cell proliferation by CFSE and IFN-γ ELISPOT at different time points.

Results: Increased expression of CD80, CD83 and CCR7 was observed on MDDCs upon electroporation with TriMix mRNA. Functionally, mRNA electroporated MDDCs were able to stimulate T cells from HIV-infected individuals on cART in vitro. In fact, MDDCs electroporated with both HIV antigens and TriMix, induced higher T-cell activation than their respective separated components or whole AT2-inactivated virus in terms of both IFNγ secretion and proliferation. Other Th1, Th2 and proinflammatory cytokines showed a similar profile secretion pattern. Finally, a higher proportion of stimulated CD8+ T cells, than of CD4+ T cells, was detected.

Conclusions: mRNA electroporation of MDDCs improved their maturation status and was able to enhance HIV specific T cells responses. Our results suggest that this mRNA combination could be considered for a HIV therapeutic vaccination approach.