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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**Introduction**

Current therapy for HIV infection is based on combined antiretroviral treatment (cART). HIV-infected patients who are currently treated with cART show stabilized disease with no clinical progression. However, cART should be maintained for life, since it is not able to eradicate the infection by itself (1). In this regard, several antigenic molecules, administration routes and strategies have been employed so far with limited success. The most promising results up to date were obtained in a clinical trial in HIV-infected patients based on administration of autologous dendritic cells pulsed with HIV viral particles (2), a strategy known as ‘ex vivo modification of DCs’, indicating that DC-based vaccines offer a promising strategy for therapeutic vaccination. Unfortunately, although a reduction of 90-95% of viral replication in HIV-infected patients was demonstrated, ‘functional cure’ (a 100% reduction) was not achieved and in addition, the use of ex vivo modification of DCs is technically a challenge for widespread use and a very costly strategy. For that reason the current mRNAs, under development, constitute and interesting tool to test in vitro their implication in DC differentiation and T cell function.

**Material and Methods**

- DCs were generated from peripheral blood monocytes (moDCs) from chronic HIV infected patients by incubation with GM-CSF and IL-4. These cells were electroporated with 15μg of TRIMIX (CD40L-CD70-caTLR4) (3) and/or 20μg of HIVACAT immunogen (4), with their respective controls. After that, co-culture with autologous PBMCs were maintained up to 6 days. Additionally maturation profile was conducted 24h after moDCs electroporation using different moAbs (CD80, CD83, CD86, CCR7 and CD69).
- Functional analysis were performed using several techniques: 25-multiplex Luminescence 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 TrImmX 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 TrImmX, 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.

**Conclusion**

mRNA Electroporation of DCs (HIVACAT+TrImmX) improved their maturation status and was able to enhance HIV specific T cells responses. Taking advantages of these features: directly administration to the patient without the need to modify DCs ex vivo and cost-effective, our results suggest that this mRNA combination should be considered in HIV therapeutic vaccine approaches.

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**References**