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In vitro activation of monocyte-derived dendritic cells with HIV antigens induces specific T cell response in HIV-seronegative individuals

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Despite 20 years of effort, the design of an effective HIV-1 vaccine still remains an enormous challenge. In this scenario, new immunological approaches must be considered. Dendritic cells-based vaccines have been widely used in cancer therapy showing interesting successful results. In 2004, Lu et al. described large reductions on virus load in untreated HIV-infected patients immunized with autologous DC pulsed with inactivated viruses. Although encouraging, these results showed sustained virus reductions in only half of vaccinees.

Based on that same vaccine model, we evaluated, in vitro, the use of alternative HIV products, rather than autologous virus, in order to optimize the Mo-DC antigenic presentation and increase the range of therapeutic success.

Monocytes from HIV-serodiscordant couples were differentiated in vitro into dendritic cells, pulsed with a pool of aldrithiol-2-inactivated HIV-1 subtypes or the HIV-1_{IIIB} p55Gag protein and then cultured with autologous lymphocytes for 7 days. At day 7, the culture received a boost of fresh Mo-DCs pulsed with the same antigens. The T lymphocyte immunological response was determined by proliferation assay, IFNγ production and cellular activation. The Mo-DC phenotype and function were also evaluated.

Mo-DCs were shown to be fully matured and activated ($CD11c^{+}HLA\text{-}DR^{hi}CD86^{hi}CD80^{hi}CD83^{+}$; high CCL3 and low IL-10 secretion) in both antigen-pulsing protocols. IFNγ production by CD4+ and CD8+ T lymphocytes, as well as the percentage of $CD38^{+}$ cells, was always higher when stimulated with pulsed Mo-DCs compared to the non-pulsed cells stimulation. The T lymphocyte proliferation of pulsed Mo-DCs was also significant greater compared to the non-pulsed condition, being slightly higher in p55Gag-pulsed cells.

Both pulsed Mo-DC conditions elicited in vitro detectable HIV-specific cellular immune responses in HIV-negative subjects, which suggest that strategies using antigen-pulsed DCs may be more effective than immunizations with antigen alone.

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