Retrovirology

Poster presentation

P19-45. Development of a therapeutic HIV vaccine comprised of autologous dendritic cells loaded with a mixture of lipopeptide HIV antigens

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Background

Clinical trials have shown that dendritic cell (DC)-based vaccines can induce antigen-specific immune responses as well as clinical responses in patients with stage IV cancer. In this study, a monocyte-derived DC vaccine pulsed with HIV antigen lipopeptides (LIPO5) was developed in preparation for a pilot vaccine clinical trial (DALIA) aimed at boosting the cellular immune response in chronic HIV infected patients on highly-active antiretroviral therapy (HAART).

Methods

Monocytes from six HIV-positive subjects on HAART were cultured with granulocyte macrophage-colony stimulating factor and interferon-α, loaded with LIPO5 peptides, and activated with lipopolysaccharide. LIPO5 is composed of five long immunogenic peptides of Gag p17 (17–35), Gag p24 (253–284), Nef (66–97), Nef (116–145), and Pol (325–355), which are covalently linked to a palmitoyl-lysylamide chain. DC vaccine development focused on establishing the method for monocyte isolation and establishing Quality Control (QC) release and characterization assays to assess the final vaccine product.

Results

We found that monocytes from HIV-positive subjects can be isolated by elutriation. LIPO5-loaded DC vaccines cultured from the isolated monocytes expressed 61.5 + 27.7% of CD14+, 94.0 + 3.6% of HLA-DR+/CD11c+, 94.8 + 2.5% of CD80+, 74.2 + 23.5% of CD83+, and 28.5 + 14.9% of Langerin. There was a strong proliferative response in allogeneic T cells cocultured with the LIPO5-loaded DC vaccine, as seen in a mixed lymphocyte reaction assay. Furthermore, the vaccine was able to elicit an HIV antigen-specific response by autologous T cells, as measured by intracellular IFN-γ staining. At least one peptide epitope response was induced per subject, in which the majority of the responses were CD8+ T cells and one was a CD4+ T cell response.

Conclusion

Collectively, these results paved the way for conducting a pilot DC vaccine clinical trial in HIV patients on HAART (BB-IND 13748).