Chimigen® HIV: A Novel Dendritic Cell Receptor-Targeted Multi-Antigen HIV Vaccine

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Background

Chimigen® Platform Technology has been used to design a novel dendritic cell (DC) receptor-targeted HIV vaccine that incorporates multiple HIV-1 antigens and is capable of inducing antigen-specific cellular and humoral immune responses for prophylactic and early intervention therapeutic applications. Chimigen® HIV Vaccine contains the HIV-1 antigens Gag, Env, Tat, Rev, Vpr and Vpu.

Chimigen® Vaccines are chimeric recombinant fusion proteins of selected antigen(s) and specific xenotypic (murine) antibody fragments including the Fc region. These chimeric molecules bind to specific receptors on DCs and other antigen presenting cells for antigen uptake. They are processed through both proteasomal and endosomal pathways and presented to T cells through MHC class I and class II molecules, stimulating cellular and humoral immune responses against the chosen antigens.

Methods

Chimigen® HIV Vaccine was expressed in Sf9 insect cells and purified. E*x vivo* immune responses were evaluated by DC-binding experiments and antigen presentation assays (APA) using human peripheral blood mononuclear cell-derived DCs. Evaluation of immune responses to the vaccine *in vivo* were performed in Sprague Dawley rats.

Results

The binding and APAs showed that Chimigen® HIV Vaccine binds to human immature DCs in a dose-dependent manner, induces $CD4^+$ and $CD8^+$ T cell activation and proliferation, and promoted increased production of IFN-γ and TNF-α from both $CD4^+$ and $CD8^+$ T cells. Furthermore, B cells stimulated with vaccine-loaded DCs were found to produce antigen-specific IgM antibodies. Evaluation of the mmune responses *in vivo* in Sprague Dawley rats confirmed that all antigenic components of the HIV vaccine are immunogenic and induce both HIV-specific cell-mediated and humoral immune responses. Th1 immune responses were predominant, with IFN-γ cytokine responses prevalent over IL-4 production in rat splenocytes, and IgG2A serum antibody titres dominant over IgG1 antibodies.

Conclusions

This study established safety and “proof of concept” and therefore, shows potential for development as a prophylactic/early intervention therapeutic vaccine against HIV infections.

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