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Development of A Novel Dendritic cell/Macrophage-Targeting Vaccine Approach Against Human Immunodeficiency Virus (HIV)

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Background:

Introduction: The development of an effective vaccine against HIV infection remains a global priority. Dendritic cell (DC)-based HIV immunotherapeutic vaccine is a promising approach which aims at optimizing the HIV-specific immune response using primed DCs to promote and enhance both the cellular and humoral arms of immunity.

Objective:

Since the Ebola virus envelope glycoprotein (EboGP) has strong DC-targeting ability, we investigated whether EboGP could be able to direct HIV particles towards DCs efficiently, and promote potent HIV-specific immune responses *in vivo*.

Methods:

We first produced EboGP-pseudotyped HIV VLPs by co-transfecting a HIV Gag/Pol expression plasmid (CMV-Gag/Pol) and the plasmids encoding EboGP and/or HIVgp into HEK 293T cells. Then these produced EboGP-pseudotyped HIV VLPs were used "infect" human monocyte-derived dendritic cells (MDDCs) and macrophages (MDMs), and vaccinated into BALB/C mice for monitoring host immune responses.

Results:

Results: Our results indicate that the incorporation of EboGP into virus-like particles (VLPs) enhances their ability to target human MDDCs and MDMs. Furthermore, we investigated the effect of EboGP on HIV immunogenicity in mice, and the results revealed a significantly stronger HIV-specific humoral immune response when immunized with EboGP-pseudotyped HIV VLPs compared with those immunized with non-pseudotyped HIV VLPs. In addition, our study has revealed that splenocytes harvested from mice immunized with EboGP-pseudotyped HIV VLPs secreted increased levels of MIP-1α and IL-4 upon stimulation with HIV Env and/or Gag peptides compared with those harvested from mice immunized with non-pseudotyped HIV VLPs.

Conclusion:

Conclusion: Collectively, this study provides evidence for the first time that the presence of EboGP in HIV VLP enhances its DCs/MDMs targeting ability and can significantly induce robust host immune responses in mouse model. Further optimization of this strategy will lead us to investigate its potential

either as therapeutic vaccine (used for *in vivo* administration, and/or by priming DCs *in vitro*) or as a preventive vaccine strategy.