Retrovirology

Poster presentation

P19-07. Development of a protective HIV/SIV vaccine based on a self-boosting cytomegalovirus vector

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Background

Human cytomegalovirus (HCMV) is a ubiquitous herpesvirus responsible for asymptomatic, dormant, lifelong infection in healthy individuals. HCMV frequently reactivates inducing a strong, mucosally-oriented immune response. These features of HCMV provide advantages over other viral vectors investigated to date as HIV vaccine candidates. Therefore, we hypothesize that an HCMV-based vaccine can elicit safe and protective HIV-specific immunity in humans. Cytomegaloviruses are highly species-specific viruses and generally restricted in their ability to infect even closely related hosts. Therefore, to test our hypothesis, we propose to use rhesus cytomegalovirus (RhCMV), a non-human primate cytomegalovirus, as a vaccine vector to induce protective immunity to simian immunodeficiency virus (SIV) in cynomolgus macaques (CM). RhCMV is considered the best animal model for HCMV, and SIV pathogenesis in CM closely mimics HIV/AIDS pathogenesis in humans.

Methods

Phase 1: To determine if CMV sero-positive CM can be re-infected with RhCMV and to evaluate immunogenicity of the vector. Phase 2: Construction of RhCMV expressing codon-optimized SIV antigens gag, pol, env and Nef-Tat-Rev fusion protein, and assess the levels and pattern of SIV antigen expression and growth *in vitro*. Phase 3: Compare the *in vivo* growth and immunogenicity of these vectors and their ability to confer protection following a multi-low dose mucosal challenge with pathogenic SIVmac239 in CM.

Results

Phase 1: To differentiate RhCMV from endogenous cynomolgus CMV, a recombinant RhCMV expressing green fluorescent protein (RhCMV-EGFP) has been constructed. Six CMV seropositive adult CM were subcutaneously inoculated with live RhCMV-EGFP and two animals were inoculated with UV-inactivated RhCMV-EGFP. Four CM serve as control animals. Currently we are in the process of evaluation of clinical and immunological responses to the vaccine vector (RhCMV) and to EGFP.

Conclusion

This RhCMV-based SIV vaccine study will address key issues of the immunogenicity, protective efficacy and self boosting-capacity of this herpesvirus vector.