Retrovirology

Poster presentation

P17-20. Lentiviral vector-based vaccine against SIV infection and simian AIDS

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Background

AIDS vaccination has a pressing need for more potent vaccination vectors capable of eliciting strong, diversified and long-lasting cellular immune responses against HIV. Lentiviral vectors have a proven efficiency not only as gene delivery vehicles for gene therapy applications but also as vaccination tools. This is likely due to their ability to transduce non-dividing cells, including dendritic cells, enabling a sustained endogenous antigen presentation and thus the induction of high proportions of specific cytotoxic T cells and long-lasting memory T cells.

Methods

The protective efficacy of a lentiviral vector based vaccine was assessed in the SIVmac251/cynomolgus macaques model.

Results

Our prime-boost vaccination strategy using lentiviral vectors pseudotyped with a glycoprotein G from two non-cross-reactive VSV serotypes elicited robust and broad cellular immune responses against the vector-encoded antigen, SIV GAG. Vaccination conferred strong protection against a massive intra-rectal challenge with SIVmac251 as evidenced both by the reduction of viremia at the peak of primo-infection (a mean of over 2 log10 fold reduction) and the full preservation of the central memory CD4+ T cells during the acute phase. Although vaccinees continued to display lower viremia than control macaques during the early chronic phase, these differences were not statistically significant by day 50 post-challenge. This encouraging pilot prophylactic trial gave the proof-of concept for the strong potential of the lentiviral vector system for vaccination. Various optimizations were successfully tested in mice to increase the immunogenicity of our vaccine. An improved vaccine – with a codon-optimized sequence encoding 2 viral antigens, GAG together with NEF, under the control of a promoter devoid of associated enhancer activity and injected via the intramuscular route – is being evaluated in a therapeutic setting, in viremic rhesus monkeys.

Conclusion

Gene transfer vectors derived from HIV-1 appear as promising candidates for vaccination against HIV-1 infection.