Retrovirology

Poster presentation

P18-09. Persistent virological benefit in SIV-infected macaques upon therapeutic vaccination upon vaccination with DNA vectors

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Background

Antiretroviral treatment leads to a reduction of virus-specific immune responses. We hypothesized that DNA vaccination during ART can increase effective virus-specific immune responses and contribute to a 'functional cure', while the virus remains suppressed.

Methods

SIVmac251-infected Indian rhesus macaques treated with ART during the chronic phase of infection were vaccinated intramuscularly using needle/syringe method (IM) or *in vivo* electroporation (EP) with optimized DNA vectors producing the majority of SIVmac239 proteins. Immune responses were monitored by flow cytometry. Animals were released from ART and plasma viral loads were monitored.

Results

Therapeutic immunization by the IM route effectively induced recall responses able to reduce viremia by 0.9 log upon ART release in ~half of the animals. Long-term virus reduction (3–4 years follow-up) was observed in several vaccinated animals, while none of the controls survived, supporting the potency of the vaccine-induced recall responses. DNA delivery via EP induced significantly higher recall responses (up to 5% of SIV-specific T cells in blood). These responses appeared rapidly, were broad (all antigens) and robust in DNA vaccinated animals but not in controls. Vaccination led to the induction of SIV-specific $CD4^+$ and $CD8^+$ T cells with EM and CM phenotype & polyfunctional cells. Cellular immune responses were found both in blood and in BAL, indicating induction of recall responses also at mucosal sites. Repeated vaccination by 2nd round of therapeutic vaccination showed a persistent virological benefit with additional >1 log10 reduction in viremia after release from ART.

Conclusion

DNA vaccination during ART is able to boost potent, efficacious, and long-lasting antigen-specific recall immune responses and has the advantage of repeated administration. Using the more efficient electroporation as DNA delivery method greatly improves immunogenicity in therapeutic vaccination. These data support the concept of adding DNA therapeutic vaccination to the HAART regimen to boost the HIV-specific immune responses.