Retrovirology

Poster presentation

P03-11. DNA vaccination with IL-12 lowers viral replication following SIVmac251 challenge

LA Hirao*[1], L Wu[1], AS Khan[2], A Dai[1], J Karl[3], S Lank[3], R Wiseman[3], D O'Connor[3], D Watkins[3], N Miller[4], MR Betts[1], NY Sardesai[2], JD Boyer[1] and DB Weiner[1]

Address: [1]Pathology, University of Pennsylvania, Philadelphia, PA, USA, [2]VGX Pharmaceuticals, The Woodlands, US, [3]University of Wisconsin-Madison, Madison, WI, USA and [4]NIAID, Bethesda, MD, USA

* Corresponding author

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Background

DNA vaccines have previously not been potent enough to generate immunity in macaques, nor capable of impacting a pathogenic SIV challenge. This study examines the magnitude and phenotype of immune responses induced by an optimized SIV vaccine delivered by electroporation (EP) with or without plasmid IL-12 and the ability of these responses to impact viral replication in a SIVmac251 challenge. The impact of macaque haplotypes on virus control was also examined.

Methods

Two groups (n = 6) of Chinese rhesus macaques were immunized with consensus SIVmacgag, env, and pol with (DNA+12) or without (DNA) plasmid IL-12. All animals were extensively haplotyped for potentially protective alleles. Cellular responses were evaluated by IFN-γ ELISpot, CFSE proliferation and ICS for polyfunctionality. Animals were rested 8 months before an intra-rectal, high-dose SIVmac251 challenge.

Results

Viral loads were followed out 35 weeks post-infection and area under the curve analysis revealed that the DNA and the DNA+12 group had a significant reduction in viral loads over the course of the study compared to the naive group (ANOVA: p = 0.035 and 0.037, respectively). A more dramatic vaccine effect was seen early in infection, at week 12, with the DNA+12 group having a 1.5 log decrease in viral loads compared to the naive group. DNA and DNA+12 immunization also prevented sustained $CD4^+$ T cell loss. Two animals in the DNA+12 group and one in the DNA group had a MHC haplotype associated with control. Interestingly, differences in viral loads in these animals were not evident until late in infection and no single immune parameter appeared to be consistently enhanced in these controller animals.

Conclusion

This study demonstrates the efficacy of DNA vaccination with plasmid IL-12 in impacting viral replication following challenge. These data have clear importance for the DNA vaccine platform as well as the T cell approach to HIV vaccine development.