

ABSTRACT #87 ¹ SIV DNA Vaccine Co-delivered with Plasmid Expressing RANTES Induce Antigen Specific Cellular Immune and Lead to Suppression of SIVmac251 Replication

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A major challenge in the development of an effective vaccine for HIV is to improve protection. RANTES (regulated on activation normal T-cell expressed and secreted), acting primarily as a chemoattractant and as an activator of leukocytes, is a natural candidate for modulating immune responses. In this study, we utilized RANTES to improve SIV DNA vaccine protective efficacy in macaques model. Groups of six rhesus macaques were immunized at weeks 0, 8, 12 and 24 with 1.5mg of SIVgag, SIVenv and SIVpol (DNA group) or 1.5mg of SIVgag, SIVenv and SIVpol coinjected with 1.5mg of RANTES (DNA +RANTES group) by electroporation. We observed 16,489 SFC and 9,379 SFC antigen-specific IFN- γ -producing effector T cells per million PBMCs for macaques immunized with DNA or DNA co-injected with RANTES respectively. Subsequently, using CFSE staining and flow cytometry, we found an average 40% and 17.2% simian immunodeficiency virus antigen-specific proliferating CD8⁺ T cells in the DNA group or DNA co-injected with RANTES group respectively. Furthermore, the profile of these cells revealed more effector memory than central memory cells. After rhesus macaques were challenged with SIVmac251, the vaccine group that included co-injection of RANTES had suppressed viral infection. In addition, we studied a series of gene expression by DNA microarray. 109 genes were significantly different in expression in the DNA compared to the DNA+RANTES treated group after the fourth immunization. These genes are being assessed in more detail to ascertain the profile of the immune response when RANTES is co-delivered which also resulted in an enhanced ability to suppress viral replication. In conclusion, co-immunization with simian immunodeficiency virus DNA-based vaccines co-injected with RANTES immune adjuvant by electroporation delivery can lead to suppression of viral replication.