

ABSTRACT #30 Live attenuated SIV: Characterising the Role of Vaccine Persistence in Protection Neil Almond¹, Neil Berry¹, Hannah Tudor¹, Wendy Kleibeuker², Mark Page³, Mark Robinson¹, William Elsley, Debbie Ferguson¹, Debbie Smith¹, Richard Stebbings¹, Bo LI⁴, Maria Manoussaka, Bep Klaver², Martin Cranage⁴, Atze Das², Ben Berkhout¹² Division of Retrovirology, NIBSC, Potters Bar EN6 3QG¹², Laboratory of Experimental Virology, Academic Medical Centre of the University of Amsterdam, Amsterdam¹³, Division of Retrovirology, NIBSC, Potters Bar EN6 3QG, St George's University of London, London⁴

Live attenuated SIV confers potent protection in the macaque model for HIV/AIDS. However, the mechanism for this superior protection has not been fully elucidated. We propose that the persistence of the vaccine is a crucial factor in this protection, as it enables other anti-viral responses to contribute, in addition to adaptive immunity. The development of a conditional live attenuated SIV that is absolutely dependent on the presence of the antibiotic doxycycline to replicate in vitro has provided the opportunity to investigate this question of vaccine persistence in the macaque model. Inoculation of the doxycycline-dependent vaccine (SIVrtTA) resulted in infection of all 12 Indian derived rhesus macaques. The kinetics of virus replication were attenuated compared with infection with wild-type SIVmac239. Peak viremia was also lower than that observed for the attenuated SIVmac239 Δ nef. Vaccination for 6 months resulted in alterations in the frequency of lymphocyte sub-populations, as well as the development of antiviral immune responses. Removal of the doxycycline for 8 weeks prior to challenge resulted in a reduction of virus signal from lymphoid tissues by immuno-histochemistry and a reversal of selected changes that occurred following vaccination. Vaccination with SIVrtTA conferred partial protection against intravenous challenge with wild-type SIVmac239 virus. These data indicate that the doxycycline-dependent attenuated SIV will be an extremely valuable tool that will allow the characterization of the responses arising from the persistent replication of the vaccine and contribute to the protection observed.