Retrovirology

BioMed Central

Poster presentation

Open Access

Replication kinetics and persistence of a conditionally live attenuated SIV (SIVrtTA) *in vivo* confers protection against SIVmac239 wild-type challenge in a rhesus macaque model

Neil Berry*[1], Atze Das[2], Mark Page[1], Hannah Tudor[1], Mark Robinson[1], Ruby Quartey-Papafio[1], William Elsley[1], Deborah Ferguson[1], Bo Li[1], Wendy Kleibeuker[2], Bep Klaver[2], Maria Manoussaka[3], Richard Stebbings[1], Martin Cranage[3], Ben Berkhout[2] and Neil Almond[1]

Address: [1]NIBSC, Division of Retrovirology, Health Protection Agency, South Mimms, Herts, EN6 3QG , UK, [2]Laboratory of Experimental Virology, Department of Medical Microbiology, Center for Infection and Immunity Amsterdam (CINIMA), Academic Medical Center of the University of Amsterdam, Meibergdreef 15, 1105 AZ Amsterdam, The Netherlands and [3]Division of Cellular and Molecular Medicine, St. George's University of London, London, SW17 0RE, UK

* Corresponding author

from Frontiers of Retrovirology: Complex retroviruses, retroelements and their hosts
Montpellier, France. 21-23 September 2009

Published: 24 September 2009

Retrovirology 2009, **6**(Suppl 2):P13 doi:10.1186/1742-4690-6-S2-P13

This abstract is available from: http://www.retrovirology.com/content/6/S2/P13

Vaccination with live attenuated SIV confers potent protection against wild-type SIV challenge in the SIV/macaque model of HIV. Although safety concerns preclude the direct application of this vaccine approach in humans, a clearer understanding of its mechanism of protection may lead to the development of novel AIDS vaccines. A novel live attenuated SIVmac239 Δnef vaccine (SIVrtTA), dependent on doxycycline administration for replication, has been evaluated *in vivo* and its ability to protect against pathogenic SIV challenge determined. Two groups of six Indian rhesus macaques (Groups A and B) were vaccinated with SIVrtTA with an oral doxycycline dosing regime for 6 months. In Group A, doxycycline was stopped for 8 weeks before wtSIVmac239 challenge. A third group was vaccinated with a conventional SIVmac239Δnef vaccine. In the presence of doxycycline, all 12 macaques receiving SIVrtTA were infected exhibiting peak SIV RNA levels ($\log_{10}$ 3-5 SIV RNA copies/ml) which declined in all macaques but persisted at higher levels in three SIVrtTA vaccinates. Levels of virus replication measured by independent qRT-PCR and qDNA PCR assays were lower in SIVrtTA vaccinates compared with the SIVmac239Δnef vaccine which peaked in the $\log_{10}$ 4-6 SIV RNA copies/ml range. No escape from doxycycline dependence was identified. Upon challenge with wild-type SIVmac239 and compared with naive challenge controls (Group D), a significant vaccine effect was observed in all three vaccine groups, assessed by the comparative reduction of circulating viral RNA in plasma. Naive wtSIVmac239 challenge controls exhibited ~7 $\log_{10}$ SIV RNA copies/ml at peak which persisted beyond the acute infection phase. This compared with all three vaccine groups where post wtSIVmac239 viral RNA levels were markedly reduced among SIVrtTA vaccinates with a more pronounced vaccine effect among Group A vaccinates. Viral RNA was un-detectable in one SIVrtTA vaccinate (Group A) and in the 2 $\log_{10}$ range in another (Group B). The highest levels of protection in SIVrtTA vaccinates correlated with an enhanced persistence of SIVrtTA as circulating viral RNA in the immediate post-acute infection vaccine period. Retrospective sequence analysis recovered from SIVrtTA vaccinates indicated a selection of sequence variants in the LTR promoter region and the Tat and rtTA genes that do not affect doxycycline control but which may have influenced replication *in vivo*. Vaccination with SIVrtTA induced a marked vaccine effect which will enable

the role of viral persistence to be evaluated in this vaccination strategy. SIVrtTA represents a new tool to develop and design novel AIDS vaccines.