

ABSTRACT #74 ₁ Live Attenuated SIV: Pathology of GALT During Acute Infection.

Deborah Helen Ferguson, Debbie A. Smith₁, Richard Stebbings₂, Emily Liefoghe₂, Bo Li₁, Neil Berry, Mark Page₁, Neil Almond_{1,2,1} Retrovirology, National Institute of Biological Standards and Control, South Mimms, Potters Bar EN6 3QG₂, Biotherapeutics, National Institute of Biological Standards and Control, South Mimms, Potters Bar EN6 3QG Infection with pathogenic HIV and SIV results in severe loss of CD4⁺ CCR5⁺ memory T cells in GALT. If attenuated SIV vaccines deplete the same subset then it may contribute to the potent protection obtained with these vaccines. Pairs of cynomolgus macaques infected with the Δ nef attenuated vaccine SIVmacC8 were sacrificed 3, 7, 10, 21 and 127 days after infection. At necropsy, a range of tissues including intestinal samples were taken for immunohistochemical analyses and isolation of lymphocytes. FACS analyses demonstrated transient loss of CD4⁺CCR5⁺ lymphocytes from the small intestine during the acute phase of disease followed by apparent recovery of these cells by day 127. No loss was seen in blood, spleen, thymus and lymph nodes. Immunohistochemical analyses of tissues for CCR5⁺ cells mirrored this pattern. Staining disappeared over days 10-21pi, before returning to both lamina propria and lymphoid follicles in the small intestine by day 127pi. Immunostaining for SIV envelope in the small intestine at these times revealed hazing across follicular germinal centres and specific staining of infected cells within lamina propria. Evidence for apoptosis increased between days 3-21pi. Fas and FasL staining peaked at day 3pi in both lamina propria and follicles. Immunostaining for CD68, CD123, CD11c, CD86 revealed a marked increase in both frequency and intensity of staining between days 3-10pi that was mainly but not exclusively within the lamina propria. This staining was not present at days 21 or 127dpi. The changes in intestinal cell populations during the acute phase of infection with SIVmacC8 along with induction of innate responses could contribute to the protection observed with this attenuated SIV vaccine against wild type virus challenge.