ABSTRACT #86  Effects of pre-existing adenoviral immunity on mucosal inflammation in rhesus macaques following vaccination with Ad5-gag/pol/nef  Katherine Masek Hammerman, Angela Carville, Keith G. Mansfield, Dan H. Barouch 1, Division of Comparative Pathology, New England Primate Research Center, Southborough, MA 01772, Division of Primate Resources, New England Primate Research Center, Southborough, MA 01772, Divisions of Comparative Pathology and Primate Resources, New England Primate Research Center, Southborough, MA 01772, Division of Vaccine Research, Beth Israel Deaconess Medical Center, Boston, MA 02215

Post-hoc analysis from the recently concluded Merck STEP trial suggested an increased rate of HIV transmission among adenovirus type 5 (Ad5) seropositive volunteers who received the Ad5gag/pol/nef vaccine (Ad5-g/p/n). Moreover, HIV transmission risk was greatest among seropositive, uncircumcised vaccinees. The mechanism of the potential enhanced HIV transmission in seropositive vaccinees is unknown. Here, we test the hypothesis that pre-existing immunity to Ad5 alters inflammatory and target cell populations at mucosal sites of HIV transmission in Ad5-g/p/n vaccinees. In an initial pilot study, Ad5 seronegative young adult male rhesus macaques were inoculated intranasally with a replication competent Ad5 empty vector (n=2) to generate pre-existing immunity, or were sham treated (n=2), and then all four animals were vaccinated intramuscularly with replication-incompetent Ad5-g/p/n. Blood was collected to confirm seroconversion and samples of mucosa were collected by biopsy from the colorectum, duodenum, penis and prepuce at baseline and again before and after each vaccination. Animals were sacrificed 14 days after receiving IM Ad5-g/p/n and full necropsy was performed. Formalin-fixed sections of colorectum, duodenum, penis and prepuce from pilot animals and from Ad5 naïve, unvaccinated male controls (previously collected; n=6) were evaluated by light microscopy and immunohistochemistry for inflammation and characterization of immune cell populations at each mucosal site. Histologically, seropositive animals had a trend toward increased CD3+ inflammation in the lamina propria of the colorectum and the submucosa of the penis and prepuce relative to seronegative and unvaccinated controls. Cell populations at other sites were similar between groups. A larger study is presently underway to confirm and extend these results.