ABSTRACT #44 [1] **Identification of MHC heterozygote advantage in SIV-infected Mauritian cynomolgus macaques** Shelby L O'Connor, Jennifer J Lhost[1], Ann M Detmer[2], Randall C Johnson[2], Roger W Wiseman, Caitlin E MacNair[2], Julie A Karl[2], Justin M Greene[13], Benjamin J Burwitz[2], Benjamin N Bimber, Simon M Lank[2], Thomas C Friedrich[2], Mary Carrington[41], David H O'Connor[11] Department of Pathology and Laboratory Medicine, University of Wisconsin-Madison, Madison, WI 53706[2], Wisconsin Primate Research Center, University of Wisconsin-Madison, Madison, WI 53706, Laboratory of Genomic Diversity, NCI-Frederick, Frederick, MD 21702[43], SAICFrederick, NCI, Frederick, MD 21702 Characterizing the breadth of a successful CD8-T lymphocyte (CD8-TL) immune response to HIV is challenging. The diversity of host Major Histocompatibility Complex (MHC) alleles and infecting viral sequence among HIV+ patients confounds immunological assays designed to characterize antiviral CD8-TL responses. Although many of these challenges can be minimized by studying MHC-defined macaques infected with a known strain of Simian immunodeficiency virus (SIV), these analyses are limited because *in vitro* measurements of immunological activity directed at a limited number of epitopes do not necessarily represent the *in vivo* immune response. In contrast, the effect of CD8-TL breadth on disease outcome can be evaluated *in vivo* by comparing viral loads in MHC homozygous or heterozygous macaques infected with a known strain of SIV. In this study, we examined viral loads in MHC homozygous and heterozygous Mauritian cynomolgus macaques (MCM) infected with SIVmac239. We found that the average chronic phase viral load in MHC heterozygous MCM was approximately 100-fold lower than in MHC homozygous MCM. Notably, viral loads in 7 out of 8 MHC homozygous MCM at one year post infection were greater than 5 x 10^4 copies/ml, independent of MHC genotype. In contrast, viral loads in 3 out of 5 MHC heterozygous MCM at one year post infection were less than 4 x 10^3 copies/ml, even though many of the MHC alleles were shared between the homozygous and heterozygous cohorts. The consistently high viral loads in MHC homozygous MCM suggest that the reduced breadth of CD8-TL responses contributed to a lack of viremic control. By using this unique non-human primate model of SIV infection, we now provide comprehensive *in vivo* evidence that the breadth of the CD8-TL response plays a key role in suppressing plasma viremia.