ABSTRACT #40 [1] **Influence of FCγ -receptor polymorphisms on efficacy of antibody-mediated lymphocyte depletion in rhesus macaques** Samantha L Finstad, Guanglan Zhang[2], Caitlyn Linde[1], Alexander Muik[1], Fabian Hermann[1], Valerie Evans, Maurus de la Rosa[1], Roland Zahn[1], Thaidra Gaufin[3], Keith Reimann[113], Cristian Apetrei, Christopher Miller[4], Joseph McCune[5], Louis Picker[6], Ronald Veazey[2], Vladimir Brusic, Norman Letvin[1], Joern Schmitz[17] Division of Viral Pathogenesis, Beth Israel Deaconess Medical Center, Boston, MA[21], Cancer Vaccine Center, Dana-Farber Cancer Institute, Boston, MA, Tulane National Primate Research Center, Tulane University Health Sciences Center,, Covington, LA[43], California National Primate Research Center, Davis, Davis, CA, Division of Experimental Medicine, University of California, San Francisco, CA[65], Vaccine and Gene Therapy Institute, Oregon Health and Science University, Portland, OR[7], Tulane National Primate Research Center, Tulane University Health Sciences Center, Covington, LA The *in vivo* application of monoclonal antibodies (mAbs) in nonhuman primates has enhanced our understanding of correlates of immune protection. However, the *in vivo* efficacy of mAbs in nonhuman primates is variable. Investigations in humans treated with mAbs have shown that functional variability may depend, at least in part, on polymorphisms of Fcgreceptors. We investigated polymorphisms of Fcγ RI, Fcγ RIIA, Fcγ RIIB, and Fcγ RIIIA by sequencing of cDNA in rhesus monkeys (RM) treated with different lymphocyte-depleting mAbs (anti-CD20, anti-CD8, or anti-CD4). Eighty-nine rhesus monkeys treated with anti-CD20 (Rituximab), anti-CD8 (cM-T807), anti-CD4 (OKT4a), or control antibody were examined. Animals were bred and housed at different primate centers; therefore, they represent a heterogeneous pool of unrelated animals. Depending on the duration of lymphocyte depletion, animals were stratified into two groups: efficiently- and inefficiently-depleted. As in humans, we found Fcγ RI was highly conserved in RM. Two polymorphisms resulting in amino acid changes were observed in Fcγ RIIB and 3 in Fcγ RIIIA. Surprisingly, extensive polymorphisms in Fcγ RIIA were identified. Protein modeling indicated that several polymorphisms cluster in a region that might directly interact with an antibody. Following comparison of polymorphism frequencies between efficiently- and inefficiently lymphocyte-depleted animals, we set a threshold of >20% difference as an indicator for biological relevance. Our results demonstrated overrepresentation of specific polymorphisms in Fcγ RIIA in inefficiently lymphocyte-depleted animals following anti-CD20, anti-CD4 and anti-CD8 mAb treatments. In addition, overrepresentation of Fcγ RIIIA 265V and 269V were also associated with inefficient depletion of lymphocytes following anti-CD8 mAb treatment but not anti-CD20 or anti-CD4 treatment. In contrast, Fcγ RIIB polymorphisms did not play a role in mAb-mediated lymphocyte depletion. However, as the correlations between the efficacy of antibody-mediated lymphocyte depletion and Fcγ-receptor polymorphisms were moderate, it remains unclear whether rhesus monkeys should be preselected to increase the number of animals that would likely be efficiently depleted following mAb treatment.