**Enhanced Protection at the Site of Challenge of Rhesus Macaques That Receive PGT121 One Week Prior to Intravaginal Challenge With SHIV-SF162P3.**

Jeffrey R. Schneider[1], Flora Engelmann[2], Ann M Carias[2], Michelle Ash[1], Dan H. Barouch[3], Ron S. Veazey[4], Thomas J. Hope[2]
[1]Rush University, Chicago, IL, USA, [2]Northwestern University, Chicago, IL, USA [3]Harvard University, Boston, MA, USA, [4]Tulane National Primate Research Center, Covington, LA, USA

**Objective/Aim/Hypothesis**
In a recent study, rhesus macaques (RM) that got an intravenous (IV) infusion of the anti-HIV broadly neutralizing antibody(bNAb) PGT121, 24hrs prior to intravaginal challenge with SHIV-SF162P3, had distal site accumulation of virus 1-3 days after challenge. Using Cy5-labeled anti-HIV antibody VRC01 IV-injected into RMs we found that it takes antibodies ~1 week to achieve peak anatomical distribution in mucosal tissues. The aim of this study is to determine if giving antibodies more time to fully distribute can block distal site accumulation of virus following intravaginal challenge.

**Design/Approach/Methods**
Utilizing Cy5-labeled PGT121 and sham antibody DEN3, we compared -7 days (n=5) and -1 days (n=5) IV infusion prior to intravaginal challenge with SHIV-SF162P3 in RM and measured virus 48hrs after challenge. Tissue and plasma levels of viral RNA and DNA were detected using gag qPCR and antibody levels were measured through Cy5 fluorescence using deconvolution microscopy and a fluorometer. In addition we used RNA-Seq to probe for transcriptomic differences in animals that received antibody 1 week prior to challenge

**Results**
Whereas we detected viral RNA and DNA at the site of challenge in all the DEN3 and -1 day PGT121 RMs, we only detected viral DNA in 1/5 RMs in the -7 day PGT121 group. In a small subset of RMs in both the -7 and -1 day PGT121 groups, we detected viral DNA in the lymph nodes (LN) and viral DNA and RNA in the brain. In these tissues that were qPCR positive, PGT121 was also present. RMs that received DEN3 had no distal site accumulation of viral RNA or DNA. In the animals that received PGT121 1 week prior to challenge, there was a marked increase in the RNA-seq antiviral signature associated with the vaginal tissue 48hrs after challenge compared to animals that only received PGT121 1 day prior to challenge.

**Conclusions**
We have found that giving antibodies more time to distribute enhances protection at the site of challenge as shown both through a decrease in viral RNA and DNA as well as changes in antiviral transcriptomics. However there was still distal site accumulation of viral DNA and RNA 48 hours after challenge in a small subset of animals. Since this does not occur in DEN3-injected RMs, the early distal site accumulation of viral RNA and DNA in the LN and brain appears to be PGT121 dependent.