

**ORAL ABSTRACT: OL-06**  
Tuesday, March 10, 2020

**COMBINED ACTIVE AND PASSIVE IMMUNIZATION IN SHIV-INFECTED RHESUS MONKEYS**

**Dan Barouch**  
*Beth Israel Deaconess Medical Center  
Boston, MA, USA*

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**Disclosures:**

Self: Research grant/grant pending Gilead Sciences, Inc,  
Janssen Therapeutics, Legend Biotech. Patents from  
Janssen

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# Combined Active and Passive Immunization in SHIV-Infected Rhesus Monkeys

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CROI 2020, Boston, MA  
March 10, 2020



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## Disclosures

- Janssen, Gilead, Sanofi, AVVI, SQZ

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## Question

**Can combined active and passive immunization together with an innate immune stimulant target the viral reservoir in ART-suppressed, SHIV-infected rhesus monkeys and control or delay viral rebound following ART discontinuation?**

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# nature Accelerated Article Preview

## LETTER

doi:10.1038/nature20583

### Ad26/MVA Therapeutic Vaccination with TLR7 Stimulation in SIV-Infected Rhesus Monkeys

Erica N. Borducchi, Crystal Cabral, Kathryn E. Stephenson, Jinyan Liu, Peter Abbink, David Ng'ang'a, Joseph P. Nkolola, Amanda L. Brinkman, Lauren Peter, Benjamin C. Lee, Jessica Jimenez, David Jetton, Jade Mondesir, Shanell Mojta, Abishek Chandrashekar, Katherine Molloy, Galit Alter, Jeff M. Gerold, Alison L. Hill, Mark G. Lewis, Maria G. Pau, Hanneke Schuitemaker, Joseph Hesselgesser, Romas Geleziunas, Jerome H. Kim, Merlin L. Robb, Nelson L. Michael and Dan H. Barouch

Borducchi et al. Nature 2016; 540:284-287

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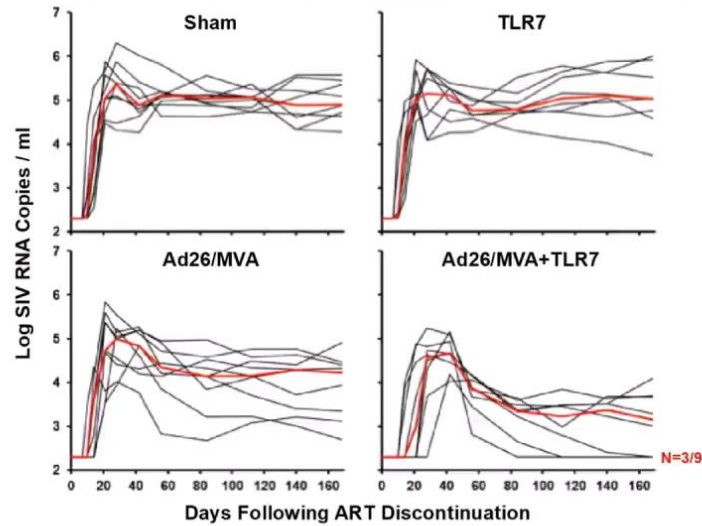
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### Ad26/MVA + TLR7 Agonist Vesatolimod Results in Virologic Control Following ART Discontinuation



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# ARTICLE

<https://doi.org/10.1038/s41586-018-0600-6>

## Antibody and TLR7 agonist delay viral rebound in SHIV-infected monkeys

Erica N. Borducchi<sup>1,4</sup>, Bryan Liu<sup>1,4</sup>, Joseph P. Nikolak<sup>1,4</sup>, Anthony M. Cadena<sup>1,4</sup>, Wen-Han Yu<sup>1</sup>, Stephanie Fischinger<sup>2</sup>, Thomas Broge<sup>3</sup>, Peter Abbink<sup>1</sup>, Noe B. Mercado<sup>1</sup>, Abishek Chandrasekar<sup>1</sup>, David Jetton<sup>1</sup>, Lauren Peter<sup>1</sup>, Katherine McMahan<sup>1</sup>, Edward T. Moseley<sup>2</sup>, Elena Bekerman<sup>3</sup>, Joseph Hesselgeser<sup>1</sup>, Wenjun Li<sup>1</sup>, Mark G. Lewis<sup>1</sup>, Galit Alter<sup>1</sup>, Roman Geleziunas<sup>3</sup> & Dan H. Baruch<sup>1,4\*</sup>

The latent viral reservoir is the critical barrier for the development of a cure for HIV-1 infection. Previous studies have shown direct antiviral activity of potent HIV-1 Env-specific broadly neutralizing antibodies (bNAbs) administered when antiretroviral therapy (ART) was discontinued, but it remains unclear whether bNAbs can target the viral reservoir during ART. Here we show that administration of the V3 glycan-dependent bNAb PGT121 together with the Toll-like receptor 7 (TLR7) agonist vesiculinoid (GS-9620) during ART delayed viral rebound following discontinuation of ART in simian-human immunodeficiency virus (SHIV)-SF162P3-infected rhesus monkeys in which ART was initiated during early acute infection. Moreover, in the subset of monkeys that were treated with both PGT121 and GS-9620 and that did not show viral rebound after discontinuation of ART, adoptive transfer studies and CD8-depletion studies also did not reveal virus. These data demonstrate the potential of bNAb administration together with innate immune stimulation as a possible strategy for targeting the viral reservoir.

Borducchi et al. Nature 2018; 563:360-364

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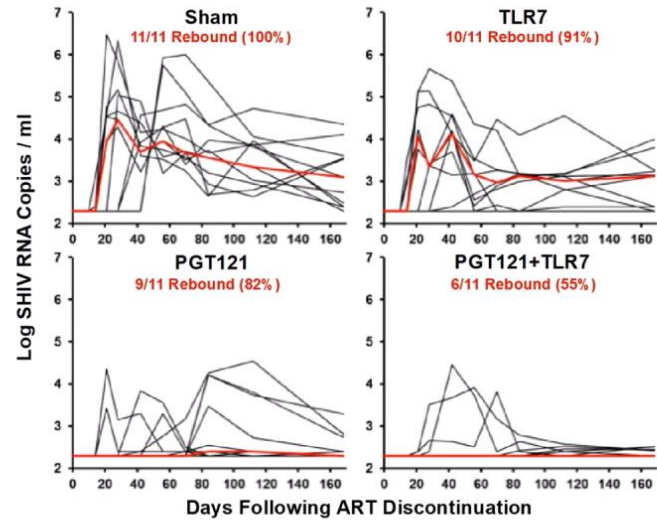
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### PGT121 + TLR7 Agonist Vesatolimod Results in Delayed Viral Rebound Following ART Discontinuation



Borducchi et al. Nature 2018; 563:360-364

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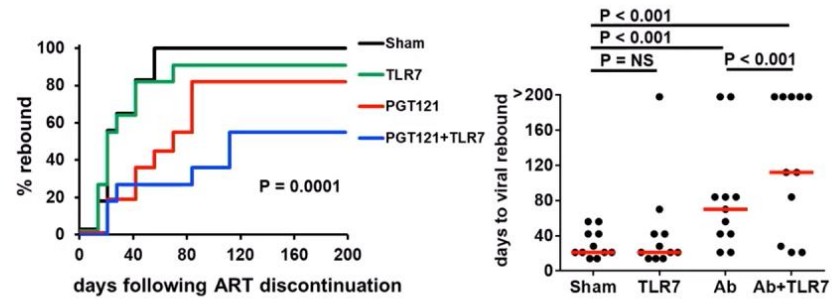
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## Combined Active and Passive Immunization in ART-Suppressed, SHIV-Infected Rhesus Monkeys

- This study builds on our prior studies of Ad26/MVA+VES or PGT121+VES in rhesus monkeys
- 51 rhesus monkeys infected IR with SHIV-SF162P3
- Preformulated daily ART initiated on day 9 (TDF, FTC, DTG)
- Vaccine: Ad26 prime, MVA boost expressing SHIV Env/Gag/Pol
- bNAb: 5 infusions of PGT121
- TLR7 agonist: Vesatolimod (VES)
  
- Group 1: Ad26/MVA + PGT121 + VES (N=12)
- Group 2: Ad26/MVA + VES (N=12)
- Group 3: PGT121 + VES (N=12)
- Group 4: Sham (N=15)

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## Study Schedule

- **Week 0: SHIV-SF162P3 IR**
- **Week 1: ART initiation**
  
- **Week 24, 36: Ad26-SHIV Env/Gag/Pol**
- **Week 48, 60: MVA-SHIV Env/Gag/Pol**
  
- **Week 64-72: PGT121 every 2 weeks x 5 infusions**
  
- **Week 50-72: VES every 2 weeks x 10 doses**
  
- **Week 86: ART discontinuation**

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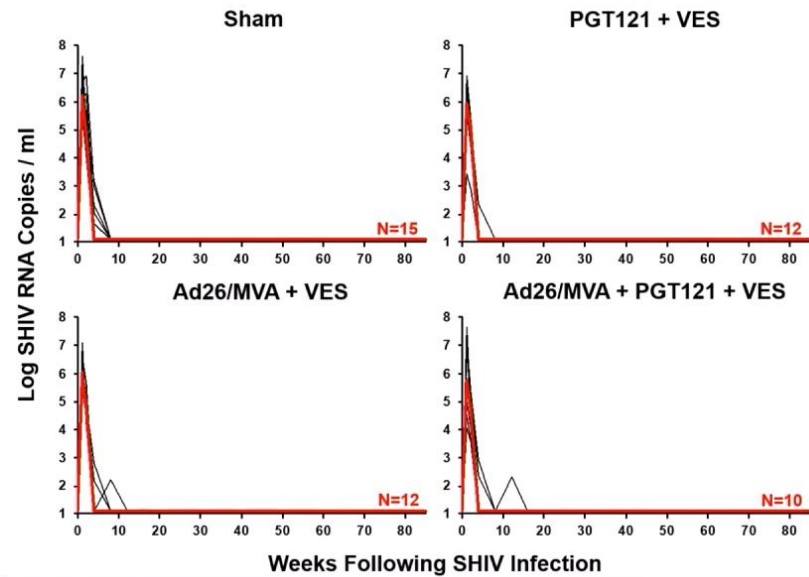
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### SHIV RNA Following Infection and ART Suppression



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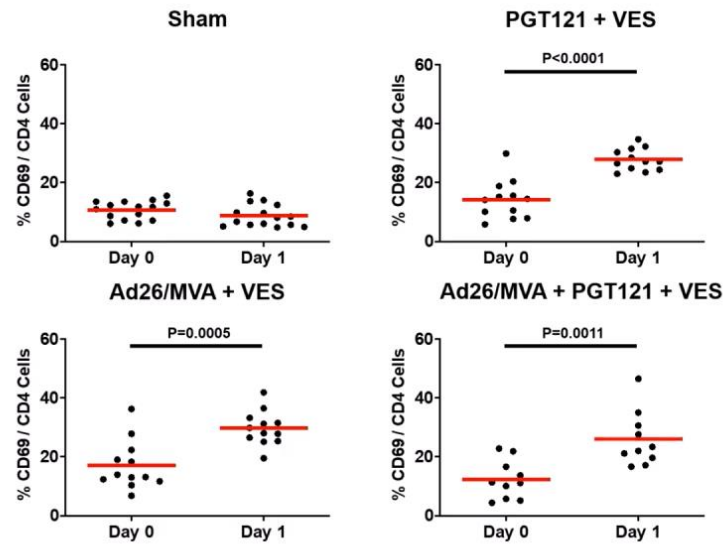
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### CD4 T Cell Activation Following VES Administration



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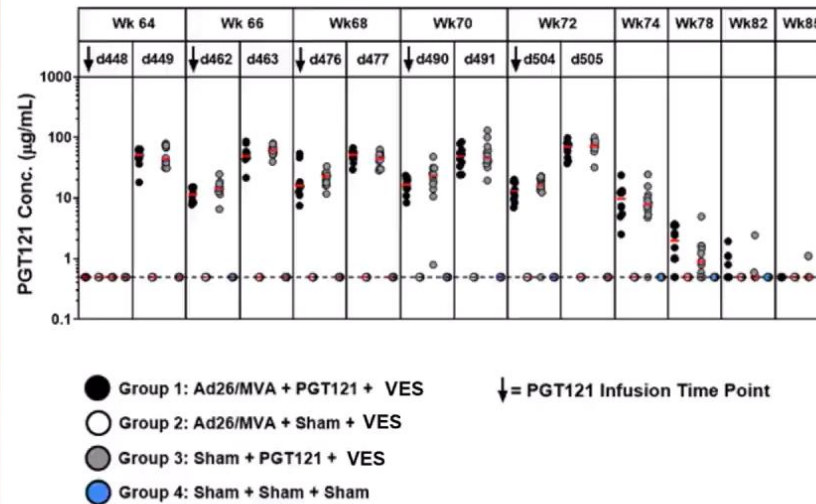
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### PGT121 Pharmacokinetics Following PGT121 Infusions



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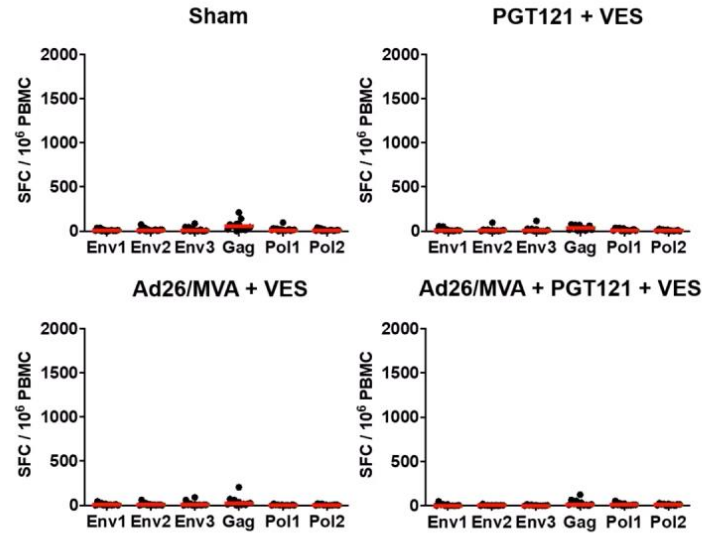
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### ELISPOT Prior to Vaccination (Week 24)



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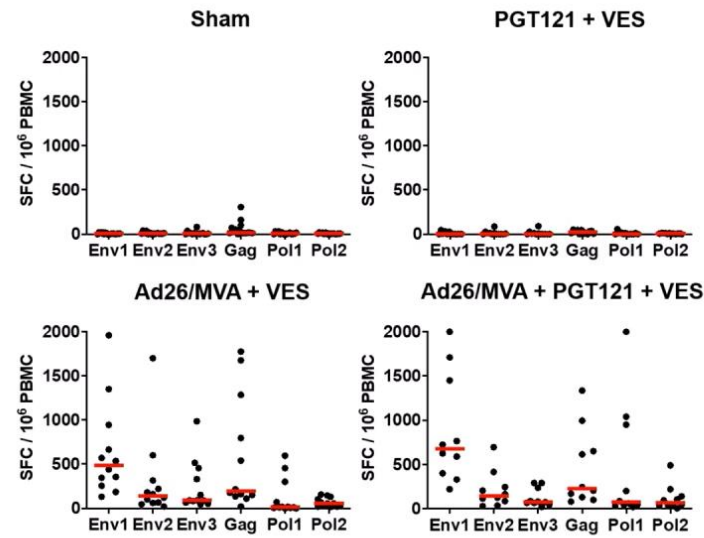
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### ELISPOT Following Ad26/MVA Vaccination (Week 62)



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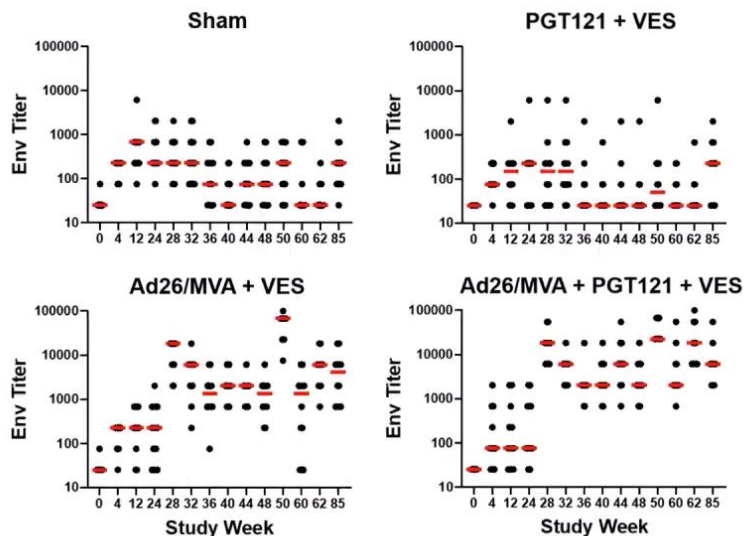
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### Env ELISA Titers Following Ad26/MVA Vaccination



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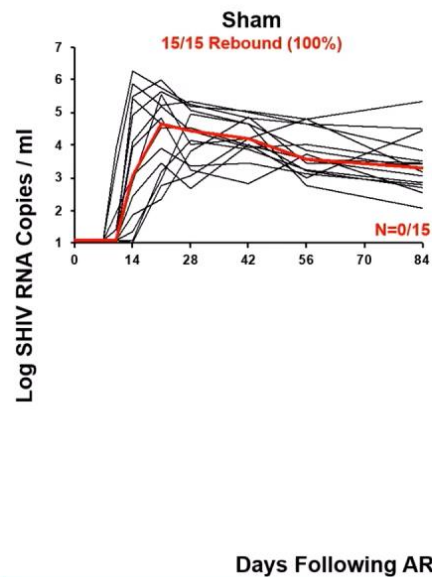
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### SHIV RNA Following ART Discontinuation



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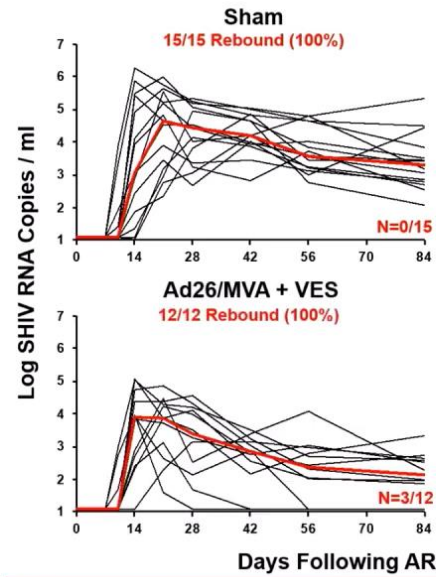
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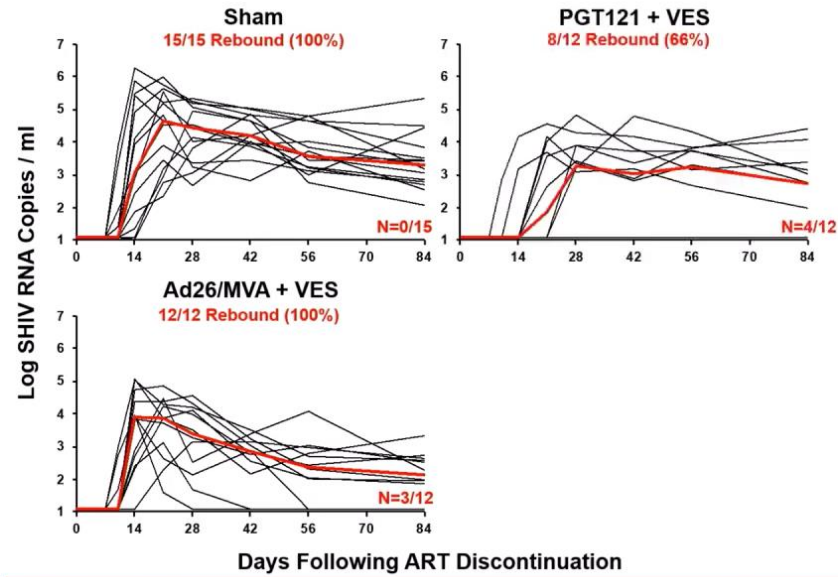
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### SHIV RNA Following ART Discontinuation



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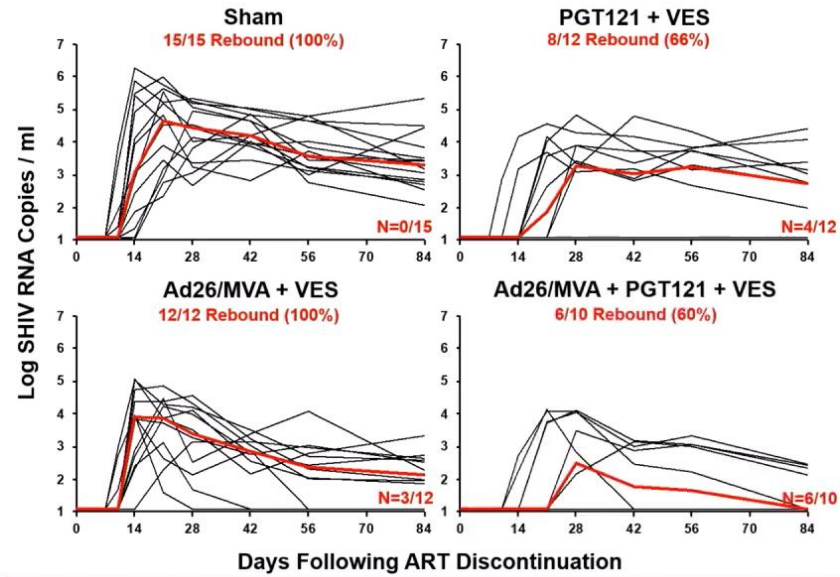
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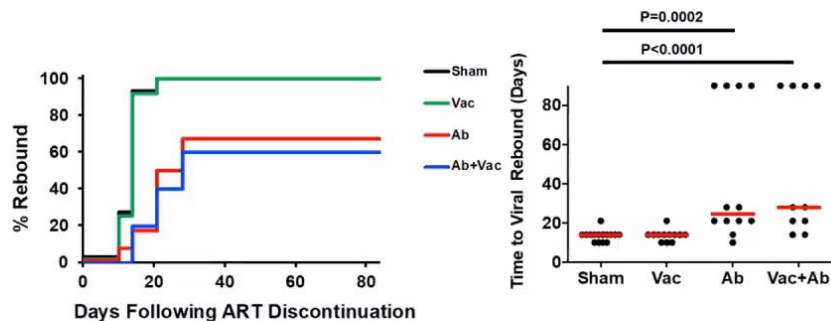
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### SHIV RNA Following ART Discontinuation



Group vs Sham	Log-Rank Test	Cox Proportional Hazard Model	Weibull Survival Model
Vac+VES	P=0.8749	HR=0.904, P=0.887	HR=0.955, P=0.906
Ab+VES	P=0.0001	HR=0.037, P<0.001	HR=0.046, P<0.001
Ab+Vac+VES	P=0.0001	HR=0.027, P<0.001	HR=0.035, P<0.001

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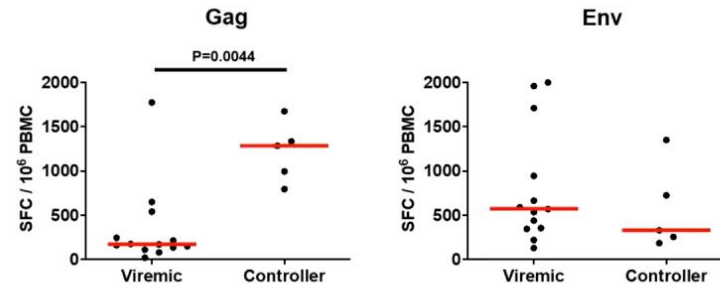
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### Gag-Specific ELISPOT Responses Correlate with Post-Rebound Virologic Control in Ad26/MVA+VES Monkeys



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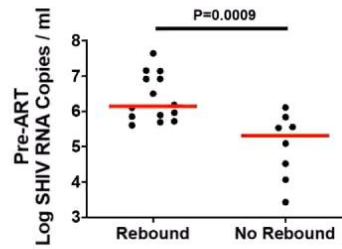
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### Lower Pre-ART Viral Loads Correlate with Lack of Viral Rebound in PGT121+VES Treated Monkeys



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## Ongoing Work

- Follow-up through day 140 following ART discontinuation
- IPDA assays to assess viral reservoir
- CD8 depletion studies and adoptive transfer studies to assess virologic control vs. clearance

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## Conclusions

- Active immunization + VES resulted in post-rebound virologic control, whereas passive immunization + VES resulted in delayed viral rebound in a subset of monkeys
- Combined active and passive immunization + VES resulted in both delayed viral rebound and post-rebound virologic control, suggesting additive effects
- Taken together, these data suggest a mechanistic basis of humoral and cellular immunologic targeting of the viral reservoir in “shock-and-kill” strategies
- Efficacy of PGT121 + VES in monkeys that initiated ART during chronic infection will be presented in today’s 2:30-4:00 pm poster session (Joe Nkolola, Poster #4549)

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[dbarouch@bidmc.harvard.edu](mailto:dbarouch@bidmc.harvard.edu)



#virtualCROIQandA

(be sure to include presenter's name in question)

Get information about the virtual CROI 2020 by following this link  
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**CROI**  
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## CROI 2020: Live Webcast Schedule

Sunday, March 8, 2020

9:00 AM-12:25 PM ET

12:25 PM-1:40 PM ET

2:00 PM-4:00 PM ET

5:00 PM-7:00 PM ET