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Therapeutic efficacy of combined active and passive immunization in ART-suppressed, SHIV-infected rhesus macaques

Victoria Walker-Sperling

Laboratory of Dan Barouch, Beth Israel Deaconess Medical Center, Harvard Medical School
Boston, Massachusetts

Disclosure: I have no financial relationships with any ineligible companies.

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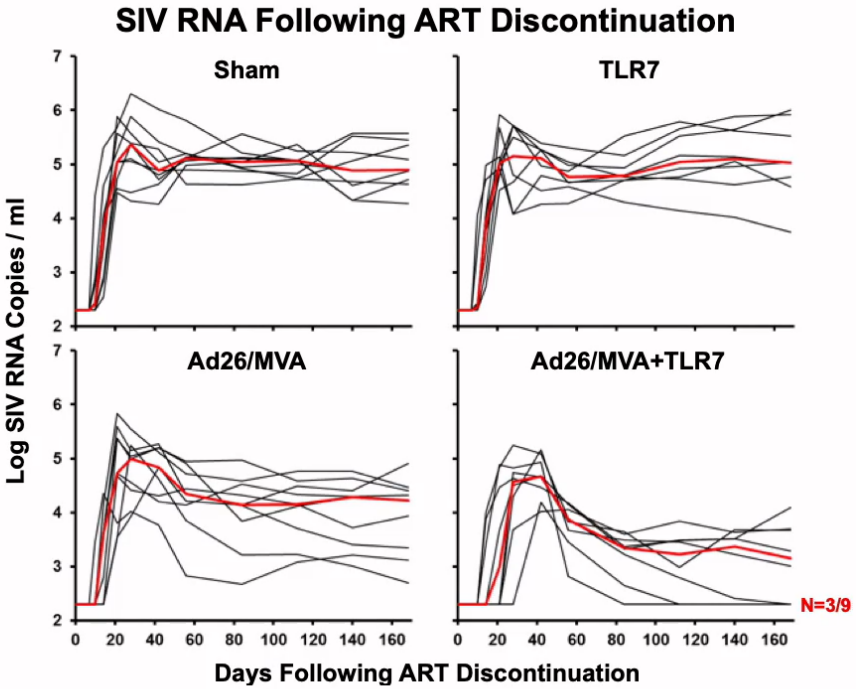
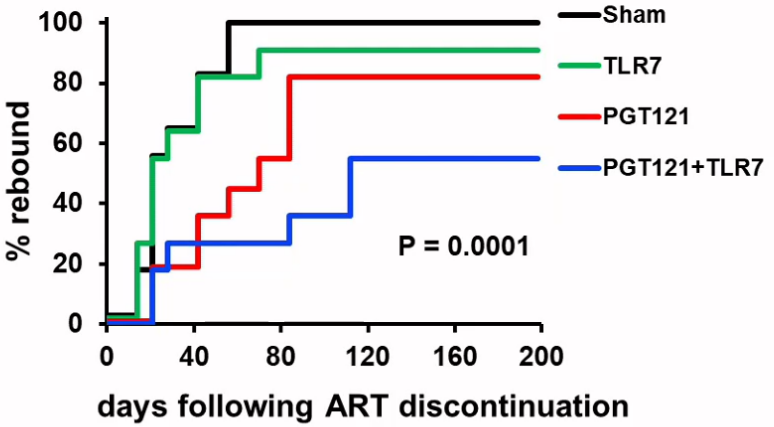
SIV+ Rhesus macaques have lower set point viral loads post-treatment interruption when treated with Ad26/MVA and a TLR7 agonist



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

Delay of viral rebound in SHIV+ Rhesus macaques treated with a TLR7 agonist and antibody PGT121



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

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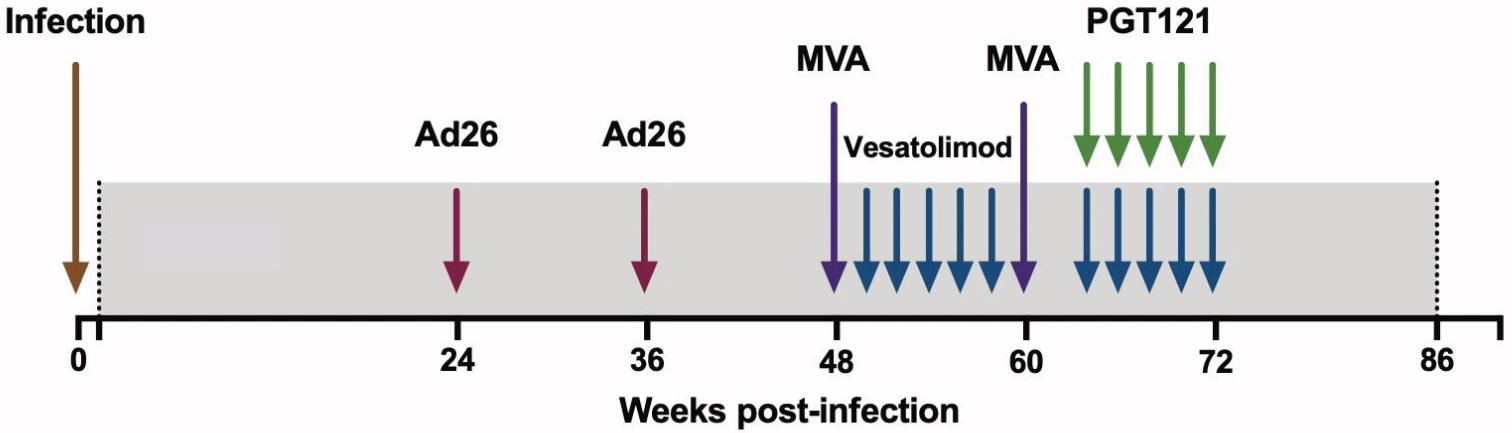
Project Objective:

- To determine if giving ART-suppressed SHIV-infected macaques a TLR7 agonist (vesatolimod) with **both** Ad26/MVA vaccination **and** PGT121 treatment will result in more frequent positive outcomes than either alone.

- 51 Rhesus macaques infected intrarectally with SHIV-SF162P3 and treated from D9 onward with preformulated, daily ART (TDF, FTC, DTG).
  - Group 1: Ad26/MVA + PGT121 + Vesatolimod (N=12)
  - Group 2: Ad26/MVA + Vesatolimod (N=12)
  - Group 3: PGT121 + Vesatolimod (N=12)
  - Group 4: Sham (N=15)



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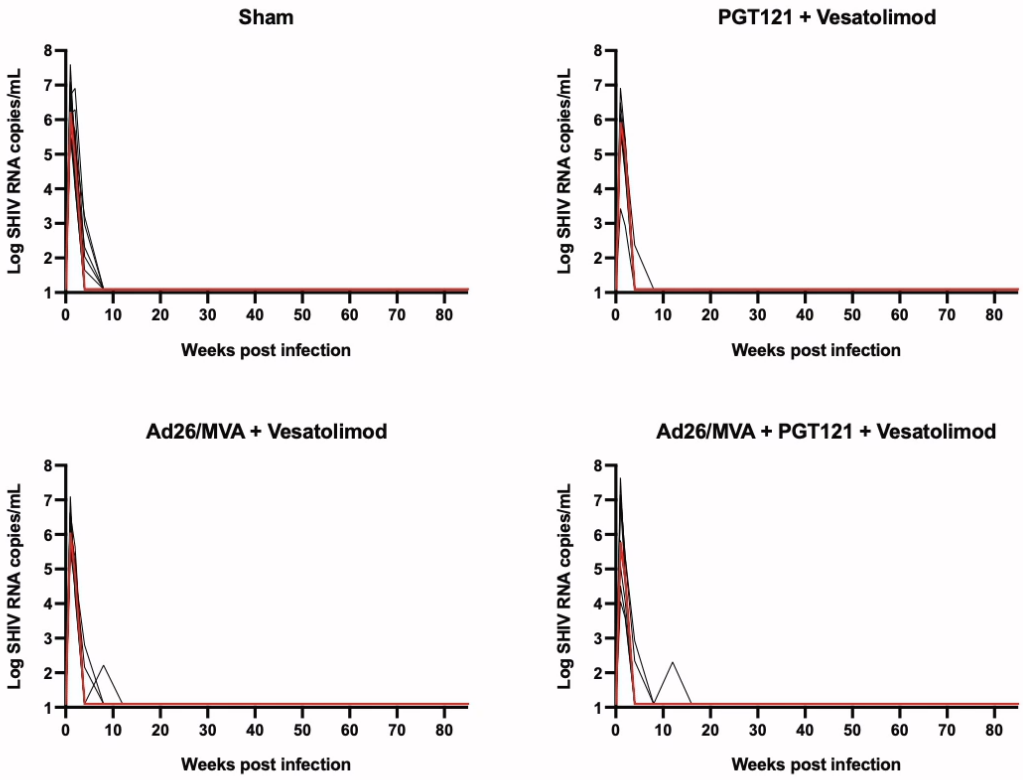
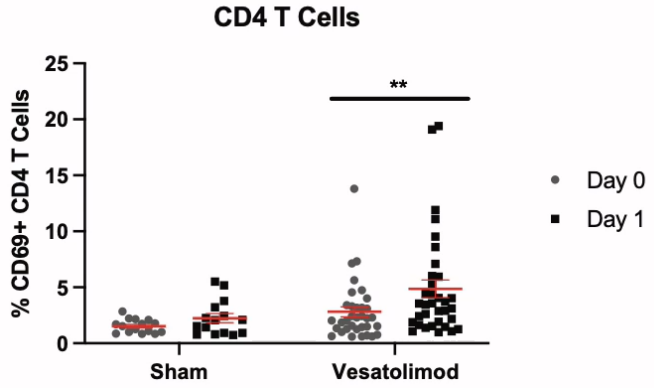
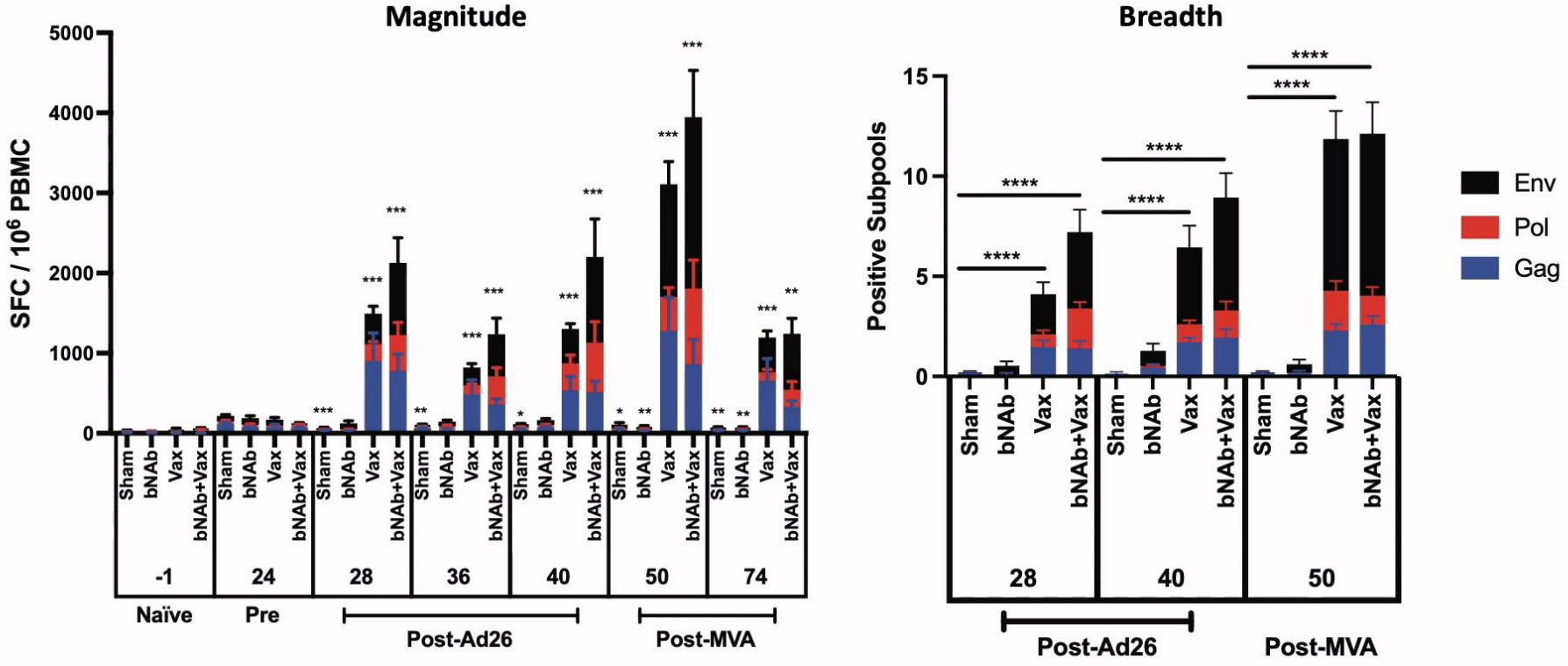
All animals were fully suppressed during treatments and prior to cART discontinuation despite significant vesatolimod-induced activation of CD4 T cells





Ad26/MVA vaccination significantly increases the magnitude and breadth of cell-associated IFNγ responses



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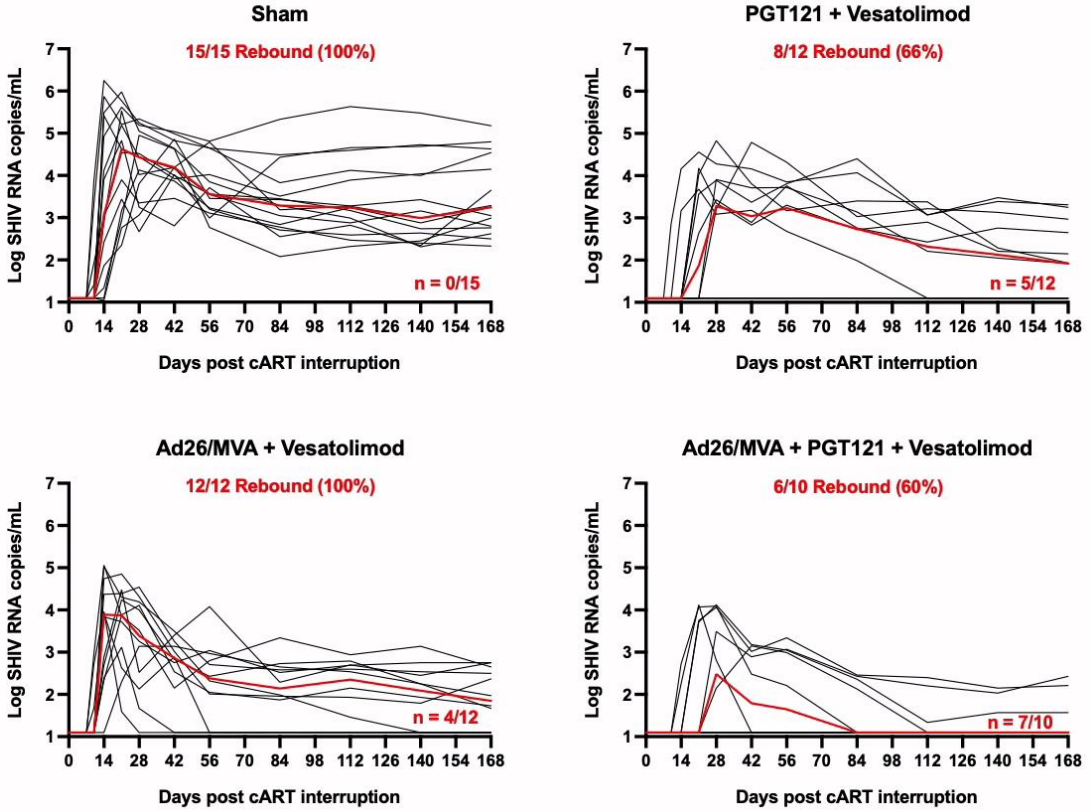
Treatment with the triple combination resulted in the least amount of rebound and highest frequency of virologic control of the three groups



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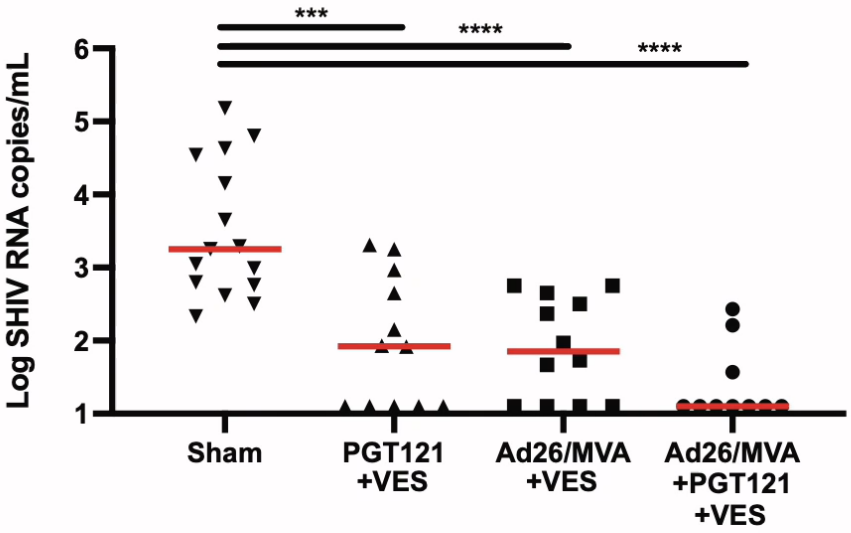
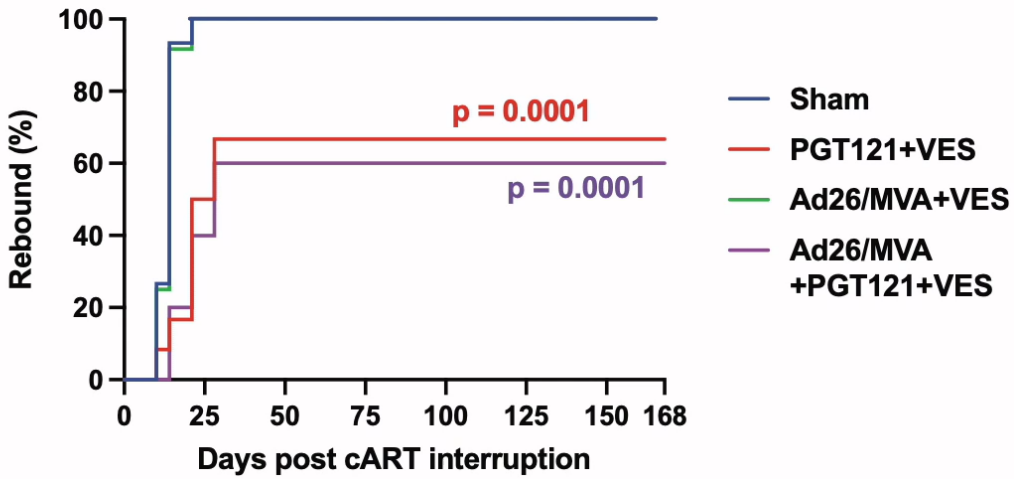
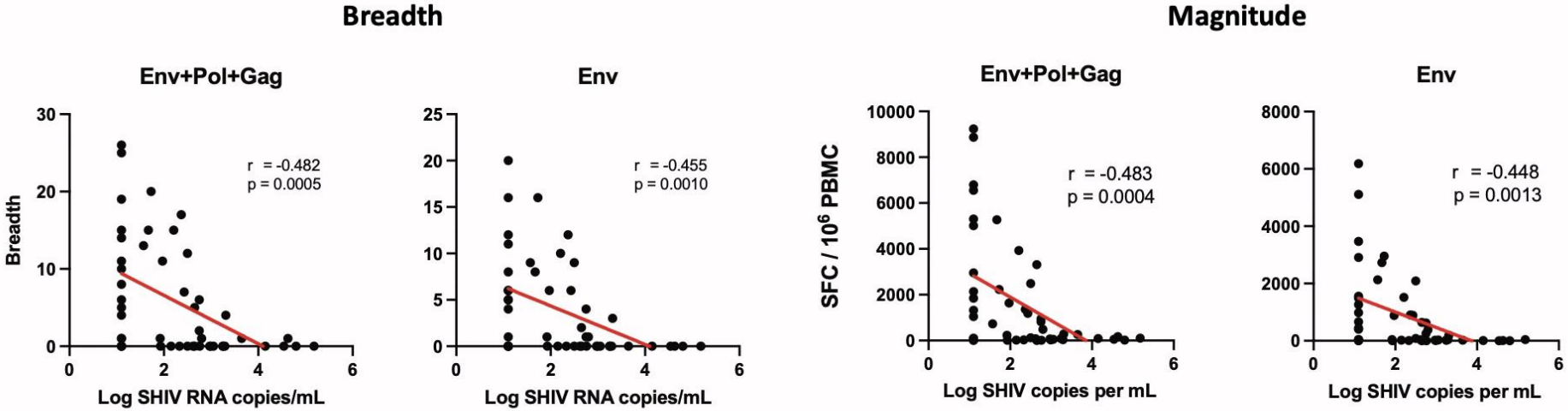
All interventions significantly reduced the set-point viral load compared to sham treatment and PGT121 treatment significantly lowered the likelihood of and increased the time to viral rebound





Larger breadth and greater magnitude of cellular IFNg responses correlate with set-point viral load



Conclusions

- The combination of vesatolimod, Ad26/MVA vaccination, and PGT121 administration resulted in 70% of animals exhibiting virologic control.
  - Four animals did not rebound & three controlled post-rebound.
- Combining passive and active immunization with vesatolimod resulted in more improved outcomes than either alone.

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