## SUPPLEMENTAL INFORMATION

**Supplemental Table 1.** Time point summary

| Time Point | Description | Weeks Post-SHIV | Weeks Post-ART | Weeks Post-Transplant | Weeks Post-ART Withdrawal |
|---|---|---|---|---|---|
| Pre-SHIV | Prior to Infection | - | - | - | - |
| Acute SHIV | Early Infection | 1-4 | - | - | - |
| Chr SHIV | "Late" Infection | 21-26 | - | - | - |
| ART | cART Suppression | 28-34 | 3-8 | - | - |
| Pre-Tx | Pre-Transplant (on cART) | 42-57 | 16-32 | - | - |
| Ac Post-Tx I | Acute Post-Transplant #1 | 53-60 | 26-35 | 0 | - |
| Ac Post-Tx II | Acute Post-Transplant #2 | 56-63 | 29-38 | 2-4 | - |
| Post-Tx I | Late Post-Transplant #1 | 59-66 | 32-41 | 4-6 | - |
| Post-Tx II | Late Post-Transplant #2 | 62-72 | 35-47 | 9-12 | - |
| Post-Tx III | Late Post-Transplant #3 | 71-83 | 44-58 | 18-25 | - |
| ART WD I | Post cART Withdrawal #1 | 79-89 | N/A | 25-30 | 1-5 |
| ART WD II | Post cART Withdrawal #2 | 84-92 | N/A | 31-32 | 7-8 |
| Necropsy | End of Study | 81-97 | N/A | 33-44 | 9-20 |

**Supplemental Table 2.** Correlation between SHIV peak rebound and SHIV DNA or RNA in tissues at necropsy

| Outcome | SHIV DNA | p-value | rho value | FDR-corrected p-value |
|---|---|---|---|---|
| **Peak viral rebound** | Mesenteric Nodes | 0.0279 | 0.7857 | 0.0776 |
| | Iliac Nodes | 0.0154 | 0.8333 | 0.0776 |
| | Submandibular Nodes | 0.0279 | 0.7857 | 0.0776 |
| | Spleen | 0.0458 | 0.7381 | 0.0955 |
| | Colon | 0.0218 | 0.8095 | 0.0776 |
| | Tonsil | 0.0458 | 0.7381 | 0.0955 |
| | Lung | 0.0458 | 0.7381 | 0.0955 |
| | Liver | 0.0229 | 0.7785 | 0.0776 |
| | Adrenal | 0.0032 | 0.8879 | 0.0564 |
| | Kidney | 0.0045 | 0.8743 | 0.0564 |
| | Testis | 0.0082 | 0.8456 | 0.0681 |
| | Basal Ganglia | 0.0274 | 0.7638 | 0.0776 |
| | **SHIV RNA** | **p-value** | **rho value** | **FDR-corrected p-value** |
| | Mesenteric Nodes | 0.0107 | 0.8571 | 0.0536 |
| | Iliac Nodes | 0.0046 | 0.9048 | 0.038 |
| | Submandibular Nodes | 0.0368 | 0.7619 | 0.0886 |
| | Rectum | 0.0011 | 0.9524 | 0.0143 |
| | Tonsil | 0.0011 | 0.9524 | 0.0143 |
| | Thymus | 0.0274 | 0.7638 | 0.0886 |
| | Lung | 0.0107 | 0.8571 | 0.0536 |
| | Liver | 0.0387 | 0.7326 | 0.0886 |
| | Adrenal | 0.039 | 0.7319 | 0.0886 |
| | Prostate | 0.0229 | 0.7785 | 0.0886 |
| | Basal Ganglia | 0.0387 | 0.7326 | 0.0886 |

**Supplemental Table 3.** Significant correlations between B-cell, CD4+ T-cell, and SHIV-specific antibody parameters

| | Correlate | Time point | p-value | rho value | FDR-corrected p-value |
|---|---|---|---|---|---|
| **Total CD20$^+$ B-Cell Count** | Total CD4$^+$ Count | Ac Post-Tx I | 0.0107 | 0.8571 | 0.0723 |
| | | Ac Post-Tx II | 0.0003 | 0.9515 | 0.0074 |
| | | Post-Tx I | 0.0368 | 0.7619 | 0.1241 |
| | | Post-Tx II | 0.0218 | 0.8095 | 0.1176 |
| | | Post-ART II | 0.0067 | 0.9286 | 0.0607 |
| | | Necropsy | 0.0011 | 0.9524 | 0.0154 |
| | HIV GP120 Titer | Ac Post-Tx II | 0.0318 | 0.7509 | 0.1225 |
| | | Post-Tx I | 0.0318 | 0.7509 | 0.1225 |
| **Total CD4$^+$ T-Cell Count** | Total CD20$^+$ AUC pre-ART WD | Pre-Tx | 0.0694 | 0.6905 | 0.1874 |
| | | Ac Post-Tx I | 0.0107 | 0.8571 | 0.1446 |
| | | Ac Post-Tx II | 0.0107 | 0.8571 | 0.1446 |
| | | Post-Tx I | 0.0694 | 0.6905 | 0.1874 |
| | | Post-Tx II | 0.0218 | 0.8095 | 0.1508 |
| | | Post-Tx III | 0.0279 | 0.7857 | 0.1508 |
| | | Post ART I | 0.0279 | 0.7857 | 0.1508 |
| | | Necropsy | 0.0694 | 0.6905 | 0.1874 |
| | HIV-1 gp120 Titer AUC pre-ART WD | Ac Post-Tx II | 0.0694 | 0.6905 | 0.1874 |
| | | Post-Tx I | 0.0576 | 0.7143 | 0.1874 |
| | Total CD20$^+$ AUC post-ART WD | Ac Post-Tx II | 0.0107 | 0.8571 | 0.1446 |
| | | Post-Tx I | 0.0279 | 0.7857 | 0.1547 |
| | | Post-Tx II | 0.0458 | 0.7381 | 0.1547 |
| | | Post-Tx III | 0.0218 | 0.8095 | 0.1547 |
| | | Post ART I | 0.0368 | 0.7619 | 0.1547 |
| | | Necropsy | 0.0022 | 0.9286 | 0.0603 |
| | HIV-1 gp120 Titer AUC post-ART WD | Ac Post-Tx II | 0.0368 | 0.7619 | 0.1547 |
| | | Post-Tx III | 0.0458 | 0.7381 | 0.1547 |

**Supplemental Table 4.** Correlation between SHIV peak viral rebound and PD1 expression at each time point

| Outcome | PD1$^+$ T-cell subset | Time point | p-value | rho value | FDR-corrected p-value |
|---|---|---|---|---|---|
| **Peak Viral rebound** | CD8 Naïve | Pre-Tx | 0.02793 | 0.78571 | 0.09076 |
| | | Ac Post-Tx II | 0.01538 | 0.83333 | 0.07269 |
| | | Post-Tx III | 0.00724 | 0.88095 | 0.07269 |
| | | Post-ART I | 0.01071 | 0.85714 | 0.07269 |
| | | Necropsy | 0.00456 | 0.90476 | 0.07269 |
| | CD8 CM | Pre-Tx | 0.00456 | 0.90476 | 0.07269 |
| | | Ac Post-Tx II | 0.02793 | 0.78571 | 0.09076 |
| | | Post-Tx III | 0.02793 | 0.78571 | 0.09076 |
| | | Necropsy | 0.01538 | 0.83333 | 0.07269 |
| | CD8 EM | Pre-Tx | 0.02793 | 0.78571 | 0.09076 |
| | | Ac Post-Tx II | 0.03676 | 0.76190 | 0.11243 |
| | | Post-Tx I | 0.00456 | 0.90476 | 0.07269 |
| | | Post-Tx II | 0.01071 | 0.85714 | 0.07269 |
| | | Post-Tx III | 0.02178 | 0.80952 | 0.09076 |
| | | Post-ART I | 0.01538 | 0.83333 | 0.07269 |
| | | Post-ART II | 0.00675 | 0.92857 | 0.07269 |
| | | Necropsy | 0.01538 | 0.83333 | 0.07269 |

**Supplemental Table 5.** Boolean analysis of immune checkpoint protein expression on T cells following in control and transplanted animals.

| | Subset | CTLA4 | PD1 | SLAM | TIGIT | Post-Tx I | Post-Tx II | Necropsy |
|---|---|---|---|---|---|---|---|---|
| **CD8$^+$ T-Cells** | Naïve | + | + | + | + | | | ↗ |
| | | - | + | + | + | | ↗ | ↗ |
| | | - | - | + | + | | ↗ | ↗ |
| | | - | + | + | - | | ↗ | ↗ |
| | | - | + | - | + | | | ↗ |
| | | - | - | + | - | ↗ | ↗ | ↗ |
| | | - | + | - | - | | ↗ | ↗ |
| | | - | - | - | + | | ↗ | ↗ |
| | | - | - | - | - | · | ↘ | ↘ |
| | CM | - | + | + | + | · | ↗ | · |
| | EM | - | + | - | + | ↘ | · | · |
| | | - | - | - | - | ↗ | · | · |
| **CD4$^+$ T-cells** | Naïve | - | + | + | + | · | ↘ | · |
| | | - | + | + | - | ↘ | ↘ | · |
| | | - | + | - | - | | ↘ | · |
| | | - | - | + | - | | ↘ | · |
| | | - | - | - | - | · | ↗ | · |
| | CM | - | + | + | + | · | ↘ | · |
| | | + | + | - | + | | | ↗ |
| | | + | - | - | + | | ↗ | ↗ |
| | | - | + | + | - | ↘ | ↘ | ↘ |
| | | + | - | - | - | | | ↗ |
| | | - | + | - | - | | ↘ | ↘ |
| | | - | - | - | + | | ↗ | ↗ |
| | | - | - | - | - | · | ↗ | · |
| | EM | + | + | - | + | · | · | ↗ |
| | | - | + | - | - | ↗ | | · |
| | | - | - | - | - | · | ↗ | · |

Statistically significant differences are indicated by black arrows. Up arrows indicate an increase in transplanted animals relative to untransplanted controls. Up and down arrows indicate an increase or decrease in transplanted animals relative to untransplanted controls, respectively. Statistical analysis was performed using a Mann-Whitney test ($p \leq 0.05$). Gray arrows: near-significant p-values. CM: Central Memory T-Cells; EM: Effector Memory T-Cells.

**Supplemental Table 6.** Correlation between peak viral rebound and ICP combined expression of immune checkpoint proteins on T cell subsets

| Outcome | T-Cell Subset | CTLA4 | PD1 | SLAM | TIGIT | Post-Tx I | | | Post-Tx II | | | ART WD I | | | Necropsy | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | rho | p-value | FDR p-value | rho | p-value | FDR p-value | rho | p-value | FDR p-value | rho | p-value | FDR p-value |
| Peak Viral Rebound | CD8 Naïve | - | + | + | + | 0.8929 | 0.0123 | 0.1374 | | | | | | | 0.8095 | 0.0218 | 0.1945 |
| | | - | - | + | + | 0.8929 | 0.0123 | 0.1374 | | | | | | | 0.9286 | 0.0022 | 0.0654 |
| | | + | - | - | + | | | | 0.8975 | 0.0061 | 0.0909 | | | | | | |
| | | + | + | - | - | | | | | | | | | | 0.8051 | 0.0159 | 0.1470 |
| | | - | + | + | - | | | | | | | | | | 0.9286 | 0.0022 | 0.0654 |
| | | - | + | - | + | | | | | | | | | | 0.9762 | 0.0004 | 0.0354 |
| | | + | - | - | - | -0.8524 | 0.0148 | 0.1470 | | | | | | | | | |
| | | - | + | - | - | | | | | | | | | | 0.9048 | 0.0046 | 0.0735 |
| | | - | - | + | - | | | | | | | | | | 0.7857 | 0.0279 | 0.2138 |
| | | - | - | - | + | 0.8571 | 0.0238 | 0.2058 | | | | | | | 0.8743 | 0.0045 | 0.0735 |
| | | - | - | - | - | | | | | | | | | | -0.9524 | 0.0011 | 0.0612 |
| | CD8 CM | - | + | + | + | 0.9643 | 0.0028 | 0.0677 | | | | | | | | | |
| | | + | + | - | + | | | | | | | 0.9429 | 0.0167 | 0.1688 | | | |
| | | - | - | - | - | | | | | | | | | | -0.8571 | 0.0107 | 0.1305 |
| | CD8 EM | + | - | + | + | | | | 0.8090 | 0.0275 | 0.2138 | | | | | | |
| | | - | - | - | - | | | | | | | | | | 0.8333 | 0.0154 | 0.1470 |
| | CD4 Naïve | - | + | - | + | | | | | | | | | | 0.9271 | 0.0009 | 0.1574 |

**Supplemental Table 7.** Correlation between post-transplant microbial translocation markers and serum cytokine levels

| Microbial Translocation Marker | Cytokine | Time point | p-value | rho value | FDR-corrected p-value |
|---|---|---|---|---|---|
| **CRP** | LBP | Ac Post-Tx I | 0.0048 | -0.9747 | 0.1831 |
| **sCD14** | IL2 | ART WD I | 0.0028 | 0.9643 | 0.1715 |
| | LBP | Necropsy | 0.0045 | 0.8743 | 0.1715 |
| **Zonulin** | LBP | Ac Post-Tx I | 0.0004 | 0.9461 | 0.0143 |
| | | Ac Post-Tx II | 0.0229 | 0.7785 | 0.158 |
| | | Post-Tx I | 0.0396 | 0.7306 | 0.2312 |
| | | Post-Tx II | 0.0195 | 0.7904 | 0.1485 |
| | | Post-Tx III | 0.0007 | 0.9341 | 0.0172 |
| | | ART WD I | 0.0045 | 0.8743 | 0.0857 |
| | | Necropsy | 0.0075 | 0.8503 | 0.0946 |
| | MCP-1 | Ac Post-Tx I | 0.0154 | 0.8333 | 0.1299 |
| | | Ac Post-Tx II | 0.0154 | 0.8333 | 0.1299 |
| | TGFa | Post-Tx I | 0.0067 | -0.9286 | 0.0946 |
| | | Post-Tx II | 0.0129 | -0.8608 | 0.1299 |
| | IL10 | Ac Post-Tx II | 0.0002 | 0.9581 | 0.0135 |
| | IL8 | Post-Tx I | 0.0458 | -0.7381 | 0.2488 |

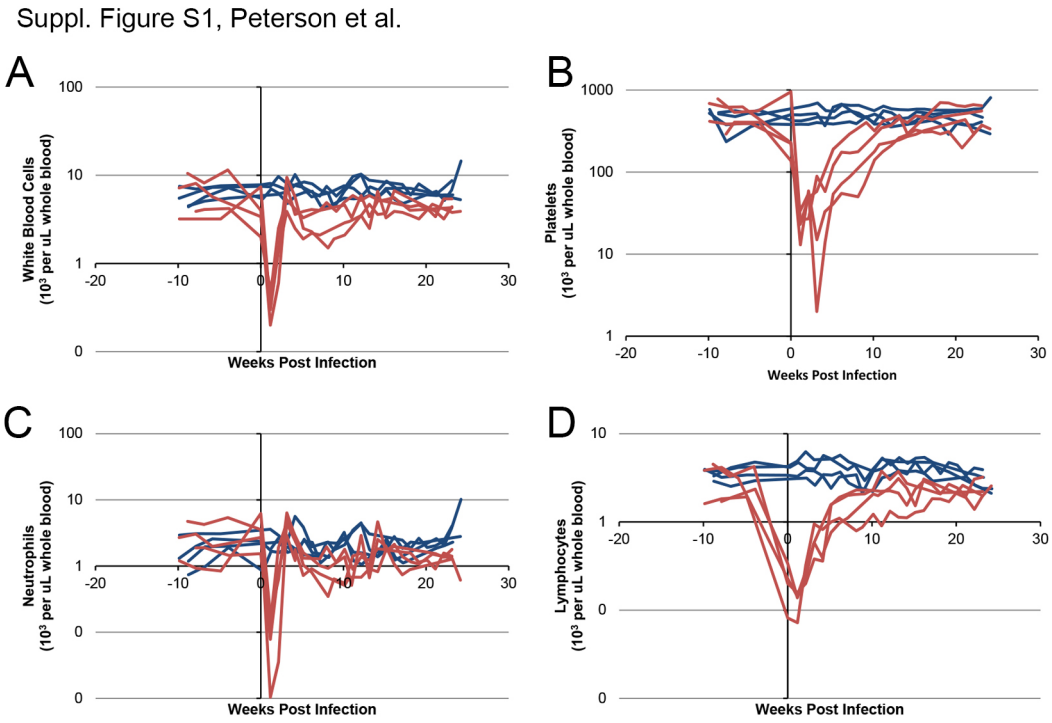
**Supplemental Table 8.** Correlation between post-transplant serum cytokine expression and T cell subsets homeostasis.

| T cell count AUC | Cytokine | Time point | p-value | rho value | FDR-corrected p-value |
|---|---|---|---|---|---|
| **Naïve $CD4^+$** | TGFa | Ac Post-Tx II | 0.0279 | 0.7857 | 0.2358 |
| | | Post-Tx I | 0.0341 | 0.8214 | 0.2358 |
| | | Post-Tx II | 0.0229 | 0.8233 | 0.2358 |
| | MCP-1 | Ac Post-Tx I | 0.0022 | -0.9286 | 0.0848 |
| | | Ac Post-Tx II | 0.0011 | -0.9524 | 0.0848 |
| | IL8 | Ac Post-Tx II | 0.0107 | 0.8571 | 0.2036 |
| | | Post-Tx I | 0.0107 | 0.8571 | 0.2036 |
| | LBP | Post-Tx III | 0.0195 | -0.7904 | 0.2358 |
| | | Necropsy | 0.0138 | -0.8144 | 0.2104 |
| | VEGF | Post-Tx II | 0.0333 | -0.8857 | 0.2358 |
| | IL10 | Ac Post-Tx II | 0.0265 | -0.7665 | 0.2358 |
| **Total $CD8^+$** | MCP-1 | Post-Tx I | 0.0218 | -0.8095 | 0.2364 |
| | | Post-Tx III | 0.0154 | -0.8333 | 0.2364 |
| | | ART WD I | 0.0218 | -0.8095 | 0.2364 |
| | IL8 | Post-Tx III | 0.0022 | 0.9286 | 0.1696 |
| | | Post-Tx I | 0.0218 | 0.8095 | 0.2364 |
| | IL15 | Post-Tx III | 0.0167 | -0.9429 | 0.2364 |
| | VEGF | Necropsy | 0.0167 | 1 | 0.2364 |
| **EM $CD4^+$ $Ki67^+$** | MCP-1 | Ac Post-Tx I | 0.0107 | 0.8571 | 0.2036 |
| | | Ac Post-Tx II | 0.0022 | 0.9286 | 0.1696 |
| | IL8 | Ac Post-Tx II | 0.0154 | -0.8333 | 0.2337 |
| | | Post-Tx I | 0.0107 | -0.8571 | 0.2036 |
| | LBP | Necropsy | 0.0093 | 0.8383 | 0.2036 |

**Supplemental Table 9.** Correlation between post-transplant microbial translocation markers and T cell subsets

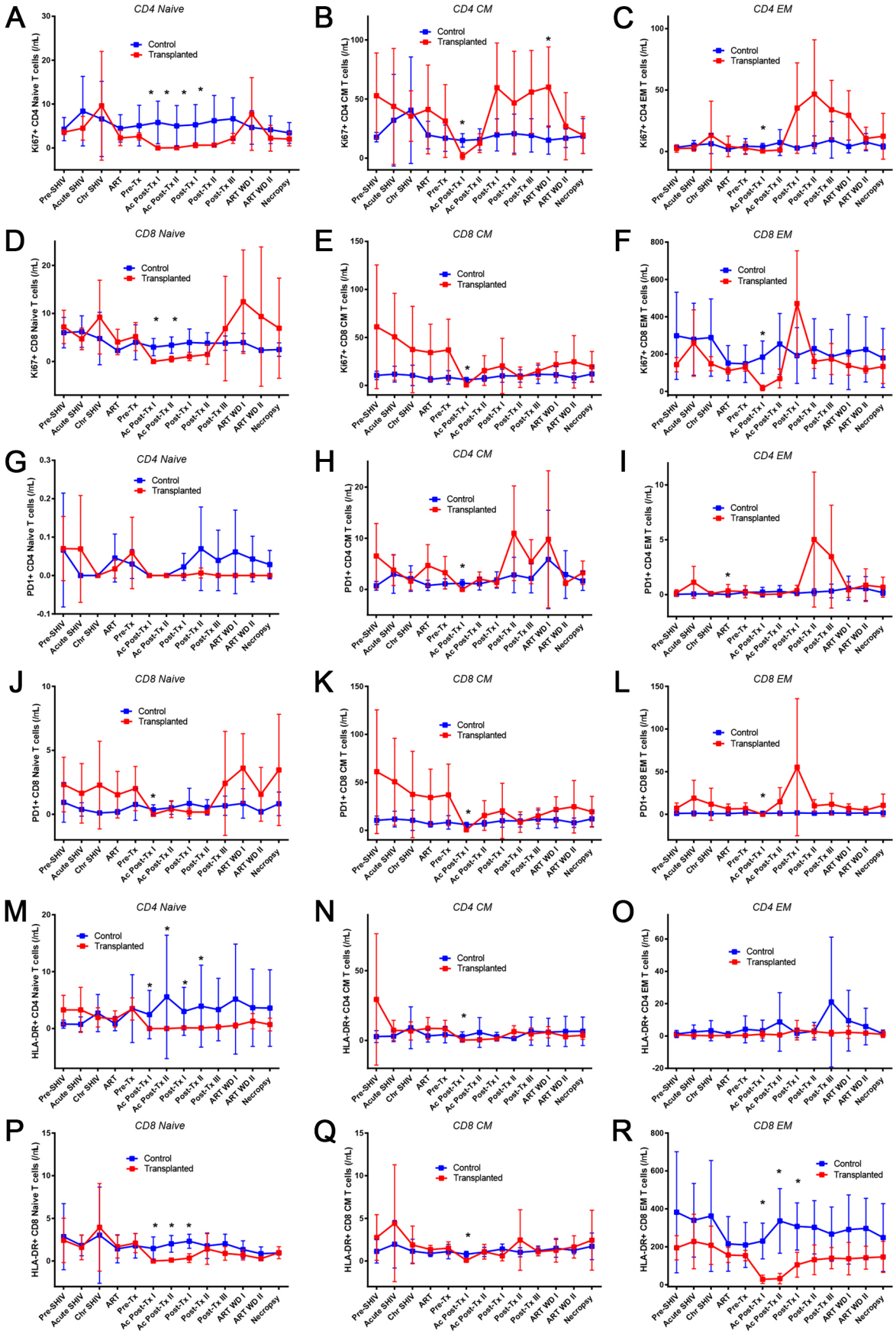
| AUC T cell subset | Microbial Marker | Timepoint | p-value | rho value | FDR-corrected p-value |
|---|---|---|---|---|---|
| **Total CD4$^+$** | Zonulin | Necropsy | 0.0004 | -1 | 0.019 |
| **CD8 CM PD1$^+$** | sCD14 | Ac Post-Tx I | 0.0148 | 0.8524 | 0.2305 |
| | | Post-Tx I | 0.0269 | 0.8108 | 0.2305 |
| | | Post-Tx II | 0.048 | 0.7857 | 0.2305 |
| | | ART WD I | 0.0034 | 0.919 | 0.0825 |
| | Zonulin | Ac Post-Tx I | 0.048 | 0.7857 | 0.2305 |
| | | Post-Tx I | 0.0028 | 0.9643 | 0.0825 |
| | | Post-Tx II | 0.0341 | 0.8214 | 0.2305 |
| | LPS | ART WD I | 0.048 | -0.7857 | 0.2305 |
| | | Necropsy | 0.048 | -0.7857 | 0.2305 |
| **CD8 Naive SLAM$^+$** | sCD14 | ART WD I | 0.0048 | 0.9747 | 0.2313 |
| **CD4 Naive SLAM$^+$** | sCD14 | Post-Tx III | 0.0048 | 0.9747 | 0.2313 |
| **Total CD4 SLAM$^+$** | sCD14 | Post-Tx III | 0.0048 | 0.9747 | 0.2313 |

**SUPPLEMENTAL FIGURES**

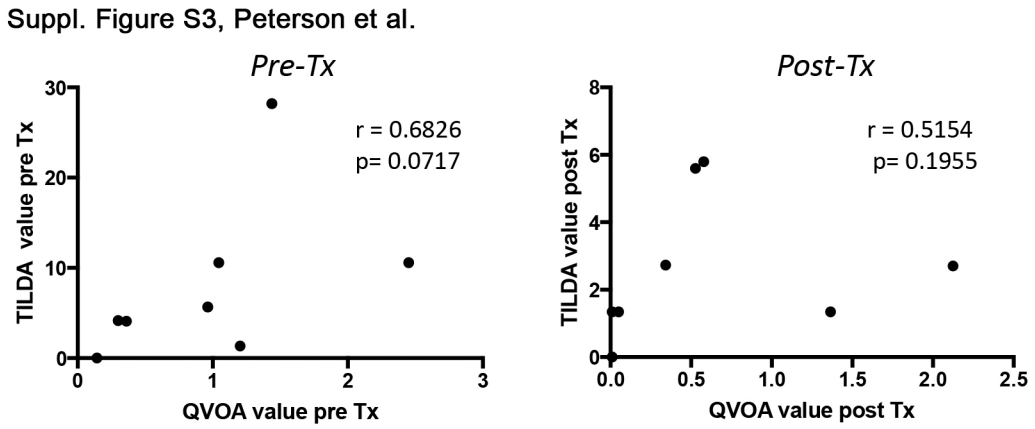



**Supplemental Figure 1. Hematologic Recovery Following Autologous Transplantation in SHIV+, cART-Suppressed Macaques.** At the indicated days post transplantation, total white blood cell (**A**), Platelet (**B**), Neutrophil (**C**), and Lymphocyte counts (**D**) were measured by CBC from transplanted (red lines), and untransplanted control animals (blue lines).

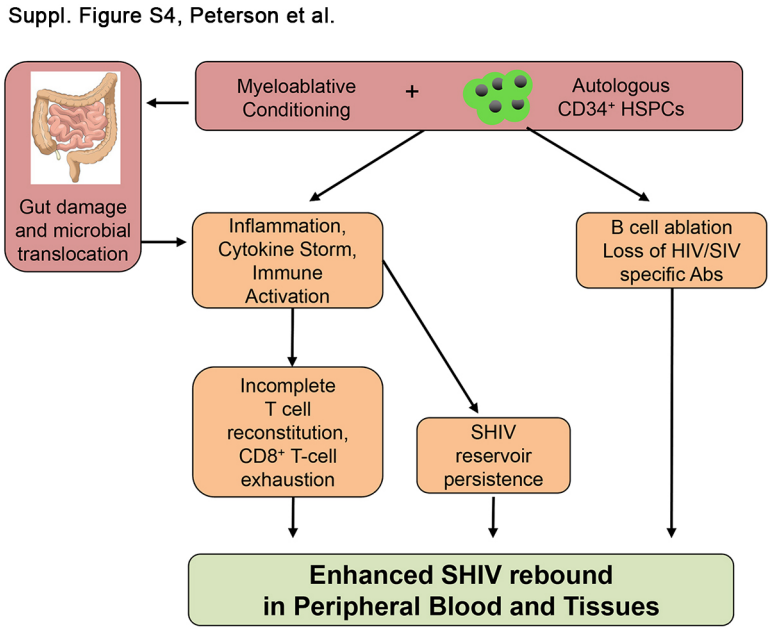
Suppl.Figure 2, Peterson et al.



**Supplemental Figure 2. Absolute cell count measurements of peripheral T-cell activation and proliferation.** At the indicated time points, flow cytometry was used to analyze batched PBMC samples for expression of activation/proliferation/exhaustion markers Ki67 **(A-F)**, PD1 **(G-L)**, and HLA-DR **(M-R)**. Shown are the percentages expressing the indicated marker in CD4+ and CD8+ naïve, central memory (CM), and effector memory (EM) subsets. CBC measurements were used to calculate absolute cell counts.




**Supplemental Figure 3. Lack of correlation between TILDA and QVOA assays before and after transplantation.** At pre-transplant (left panel) and post-transplant time points (right panel), correlations were calculated between TILDA and QVOA measurements of viral reservoir size. Each point represents measurements from one of the eight control or transplanted animals shown in Figure 8.




**Supplemental Figure 4. Model for enhanced viral rebound in transplanted animals.** Following myeloablative conditioning and autologous transplantation in SHIV+, cART-suppressed animals, peripheral blood cell counts are significantly impacted, and gut damage is induced (red boxes). Cytopenia and gut damage trigger an intense but incomplete regeneration of the hematopoietic system, including decreased anti-SHIV antibody titers in peripheral blood (orange boxes). Following cART withdrawal, these factors combine to facilitate enhanced viral rebound in transplanted animals, relative to untransplanted SHIV+ controls.