# Changes in the HIV-1 Reservoir in South African HIV+ to HIV+ Kidney Transplant Recipients

Poster #335

**Nokuzola Mbhele**[1], Natalie Howard[2], Gabriel Quiros[2], Jonathan Lochner[3], Edward Kankaka[4], Kathryn Manning[5], Alberto Bosque-Pardos[3], Elmi Muller[6], and Andrew D. Redd[2]

[1]Division of Medical Virology, Institute of Infectious Diseases and Molecular Medicine, University of Cape Town, Cape Town, South Africa. [2]Laboratory of Immunoregulation and Infectious Disease, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, USA. [3]Department of Microbiology, Immunology and Tropical Medicine, George Washington University, Washington, USA. [4]Research Department, Rakai Health Sciences Program, Rakai, Uganda. [5]Division of General Surgery, Department of Surgery, University of Cape Town, Cape Town, South Africa. [6]Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa

CROI Conference on Retroviruses and Opportunistic Infections

February 22 to 25, 2026 I Denver, Colorado

## BACKGROUND

- Antiretroviral therapy (ART) reliably suppresses plasma viremia but does not eliminate the need for lifelong treatment, nor has it led to substantial declines in HIV incidence, highlighting the urgent need for a Cure
- The reservoir persists despite effective ART, reflecting its stability and resistance to clearance, and immune system perturbations, whether caused by infection, inflammation or therapeutic interventions, have been shown to influence its size and composition
- Beyond persistent infection, PLWH disproportionately experience long-term complications such as chronic kidney disease, which can progress to end-stage renal disease requiring dialysis or kidney transplantation
- As access to kidney transplantation for PLWH has expanded, particularly in high-burden settings, the South African HIV+ to HIV+ transplant program has been shown to be highly successful and, in being so, raised important questions about how induction immunosuppression, particularly anti-thymocyte globulin (ATG), might influence the size and dynamics of the latent HIV-1 reservoir.

## OBJECTIVE

To examine changes in the HIV-1 latent reservoir among HIV+ to HIV+ kidney transplant patients who received ATG as immunosuppression induction therapy

## METHODS

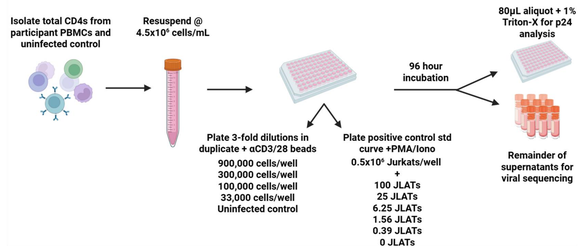
### Study Design

- Longitudinal cohort study using stored PBMC from kidney transplant recipients (N=21) enrolled in the HIV+ to HIV+ kidney transplant study at Groote Schuur Hospital, Cape Town, South Africa from 2008 – present.
- All recipients were on ART, clinically stable, and underwent standardized immunosuppression including ATG induction therapy.
- Local ethics committees approved the study

### Sampling

PBMC collected pre-transplant and at multiple post-transplant timepoints

### QUANTIFICATION OF THE TRANSLATIONAL-COMPETENT LATENT HIV-1 RESERVOIR – TRACER P24 ELISA




### DATA ANALYSIS - BAYESIAN MODEL A

$$\begin{cases} \alpha_j \sim \mathcal{N}(\mu_\alpha, \sigma_\alpha^2) \\ \beta_j \sim \mathcal{N}(\mu_\beta, \sigma_\beta^2) \\ \text{logit}(\lambda_j(t)) = \alpha_j + \beta_{\text{sex}} \cdot 1(\text{sex}_j = \text{female}) + \beta_j t \\ y_i \sim \text{Bernoulli}\left(1 - e^{-n_i \lambda_{j(i)}(t_i)}\right) \end{cases}$$

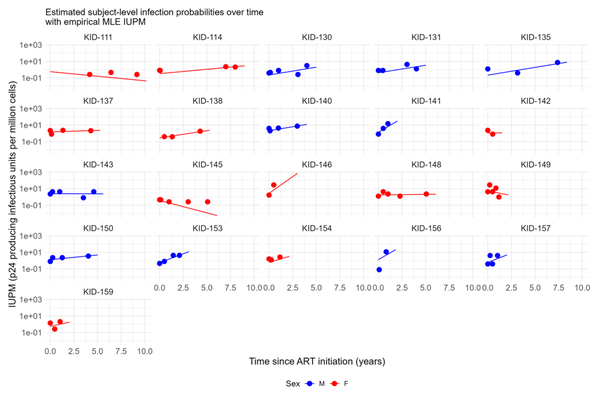
**Priors**

a ~ N(-15.5, 1.0)
b ~ N(0, 1.0)
$b_{sex}$ ~ N(0, 1.0)

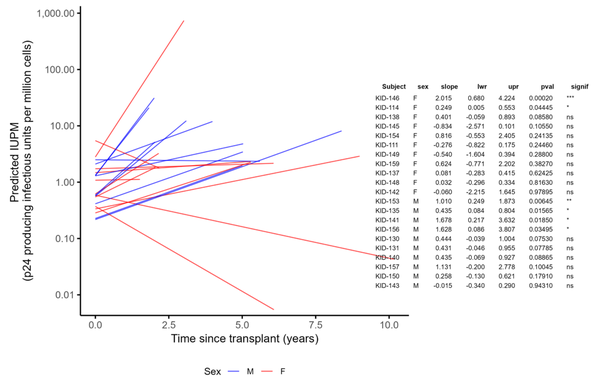
- $n_i$ = number of cells in well i (observed data)
- $y_i \in \{0,1\}$, positivity in well i (observed data)
- $l_j(t)$ = Probability that a well for individual *j* is positive at time *t* (Note: IUPM = l * 10^6)
- $a_j$ = intercept for individual *j*
- $b_{sex}$ = Population-level fixed effect of sex on the intercept
- $b_j$ = slope for individual *j*

## RESULTS

### SUBJECT-LEVEL PREDICTIONS



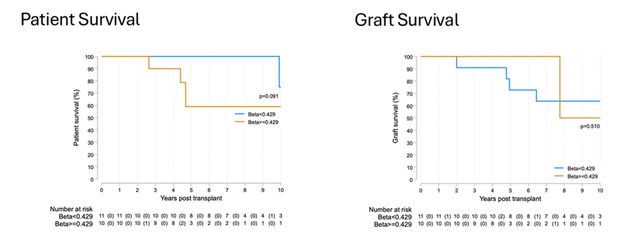

### COMBINED SUBJECT-LEVEL PREDICTIONS




| Subject | sex | slope | lwr | upr | pval | signif |
|---|---|---|---|---|---|---|
| KID-146 | F | 2.015 | 0.680 | 4.224 | 0.00020 | *** |
| KID-114 | F | 0.249 | 0.005 | 0.553 | 0.04445 | * |
| KID-138 | F | 0.401 | -0.059 | 0.893 | 0.08580 | ns |
| KID-145 | F | -0.834 | -2.571 | 0.101 | 0.10550 | ns |
| KID-154 | F | 0.816 | -0.553 | 2.405 | 0.24135 | ns |
| KID-111 | F | -0.276 | -0.822 | 0.175 | 0.24460 | ns |
| KID-149 | F | -0.540 | -1.604 | 0.394 | 0.28800 | ns |
| KID-159 | F | 0.624 | -0.771 | 2.202 | 0.38270 | ns |
| KID-137 | F | 0.081 | -0.283 | 0.415 | 0.62425 | ns |
| KID-148 | F | 0.032 | -0.296 | 0.334 | 0.81630 | ns |
| KID-142 | F | -0.060 | -2.215 | 1.645 | 0.97895 | ns |
| KID-153 | M | 1.010 | 0.249 | 1.873 | 0.00645 | ** |
| KID-135 | M | 0.435 | 0.084 | 0.804 | 0.01565 | * |
| KID-141 | M | 1.678 | 0.217 | 3.632 | 0.01850 | * |
| KID-156 | M | 1.628 | 0.086 | 3.807 | 0.03495 | * |
| KID-130 | M | 0.444 | -0.039 | 1.004 | 0.07530 | ns |
| KID-131 | M | 0.431 | -0.046 | 0.955 | 0.07785 | ns |
| KID-140 | M | 0.435 | -0.069 | 0.927 | 0.08865 | ns |
| KID-157 | M | 1.131 | -0.200 | 2.778 | 0.10045 | ns |
| KID-150 | M | 0.258 | -0.130 | 0.621 | 0.17910 | ns |
| KID-143 | M | -0.015 | -0.340 | 0.290 | 0.94310 | ns |

**Figure 1.** Translationally competent units per million CD4 cells (TCUPM) quantified with the ultrasensitive tracer p24 ELISA revealed a significant increase in the translationally competent reservoir across the cohort, with six individuals showing significant increases in their latent reservoir, and no individuals showing significant declines

### KAPLAN-MEIER ANALYSES OF LATENT RESERVOIR SLOPES




| | Patient Survival Lower Beta<0.429 | Patient Survival Higher Beta>=0.429 |
|---|---|---|
| 1-Year | 100% | 100% |
| 3-Year | 100% | 90% (95% CI 47 – 99%) |
| 5-Year | 100% | 59% (95% CI 16 - 86%) |

| | Graft Survival Lower Beta<0.429 | Graft Survival Higher Beta>=0.429 |
|---|---|---|
| 1-Year | 100% | 100% |
| 3-Year | 90% (95% CI 51-99%) | 100% |
| 5-Year | 72% (95% CI 37-90%) | 100% |

**Figure 2.** Kaplan-Meier analyses examining slopes of change in the latent reservoir suggest a trend whereby individuals with increasing reservoirs may have reduced patient survival (p=0.09), whereas those with lower or stable beta values appear more prone to graft failure

## CONCLUSIONS

- As a group, the translationally competent reservoir was increasing in this cohort of HIV+ to HIV+ kidney transplant recipients, and six individuals showed significant increases
- No participants in the cohort exhibited significant declines in their HIV-1 reservoir
- ATG-associated changes in the HIV reservoir were linked to distinct trends in patient and graft survival
- ATG induction provides a unique opportunity to study how immune perturbations influence latent reservoir dynamics and may help to better define the underlying immunological mechanisms of reservoir maintenance

### SUMMARY

ATG is a therapy routinely used in kidney transplantation to prevent the body from rejecting a new organ. In a group of people living with HIV and kidney failure, this therapy showed that dormant HIV cells can be “reset,” offering a chance to eliminate the virus. We found that, overall, the amount of dormant HIV temporarily increased after transplantation. When we looked at clinical outcomes, the findings suggest there may be a trade-off between how the immune system controls HIV and how well the graft survives, which warrants further investigation. Studying this immune “reset” gives us a unique opportunity to understand how dormant HIV behaves and could help guide future strategies aimed at targeting and clearing it

## REFERENCE

1. Muller, E., et al., Kidney transplantation in HIV positive patients: current practice and management strategies. Transplantation, 2021. 105(7): p. 1492.

2. Benner, S.E., et al., The effect of induction immunosuppression for kidney transplant on the latent HIV reservoir. JCI insight, 2022. **7**(21): p. e162968.

## ACKNOWLEDGEMENTS

### FUNDING

1. Division of Intramural Research, NIAID, NIH, and by the U.S.-South Africa Program for Collaborative Biomedical Research , NIH and South African Medical Research Council)

2. National Research Foundation, South Africa

### AUTHOR CONTACT INFORMATION

nokuzola.mbhele@uct.ac.za