# *Tuberculosis promotes the persistence of genetically-intact HIV in people with HIV and Tuberculosis*

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## BACKGROUND

**There is no cure for HIV** because the virus persists in a reservoir of HIV-infected CD4+ T cells.

***Mycobacterium tuberculosis (Mtb)*** is the causative agent of tuberculosis (TB).

**People living with HIV are 16 times more likely to develop TB disease** than the general population. (WHO, 2024)

**TB disease is responsible for one in four HIV related deaths** each year. (WHO,2024)

**Our study examines the HIV proviral landscape and the mechanisms of viral persistence in people experiencing both *Mtb* and HIV infections.**

## AIMS

1. To characterise differences in the HIV proviral landscape of people living with HIV and those living with HIV and *Mtb*
2. To characterise the HIV proviral landscape at the site of the coinfection
3. To investigate the effects of the TB-associated microenvironment on the anti-HIV CD8+ T cell response

## HYPOTHESIS

Concurrent infection with *Mtb* will impair immune-mediated viral control leading to an increased number of replication-competent HIV DNA sequences.

## METHODS

### Study Participants

**Aim 1.** 10 participant cohort from Argentina.

PBMCs from people living with HIV

PBMCs from people living with HIV/TB

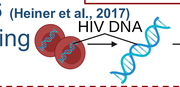
**Aim 2.** 1 participant living with HIV and TB

PBMCs

Cells derived from tuberculous pleural effusion (PEMCs)

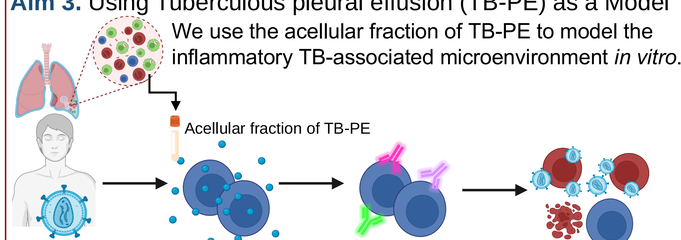
**Study approach: FLIPS** (Heiner et al., 2017)

Near full-length sequencing individual proviruses.




**Aim 3.** Using Tuberculous pleural effusion (TB-PE) as a Model

We use the acellular fraction of TB-PE to model the inflammatory TB-associated microenvironment *in vitro*.




CD8+ T cells from donors living with HIV are stimulated with HIV peptides +/- TB-PE

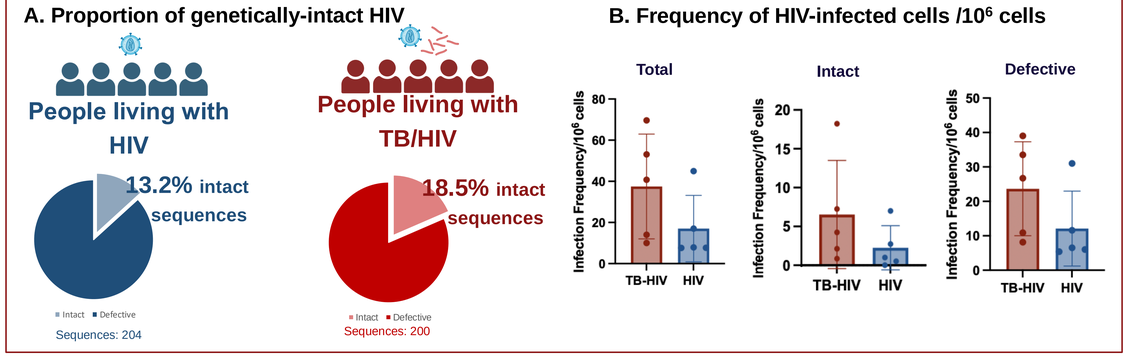
CD8+ T cell functionality is assessed by quantification of CD107a/b, TNF-α, and IFN-γ

CD8+ T cell cytotoxicity is also quantified by coculture with autologous HIV-infected CD4+ T cells

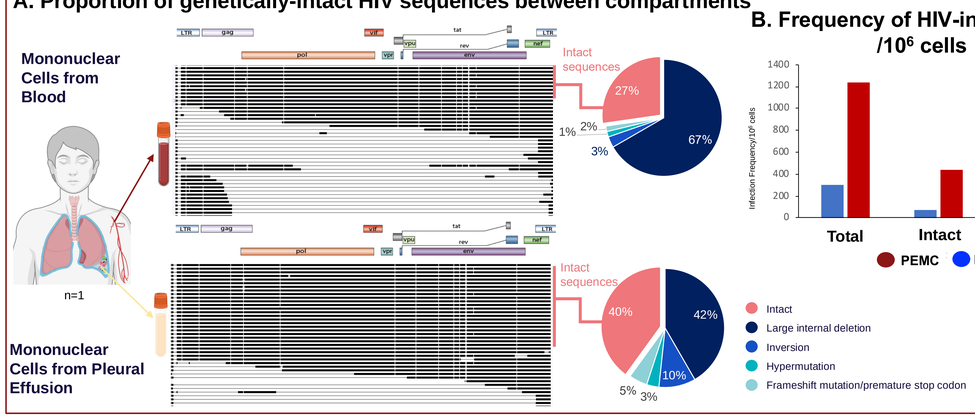
**Coinfection with *Mtb* impairs CD8+ T cell-mediated viral control resulting in a higher proportion of genetically-intact HIV proviruses.**

## RESULTS

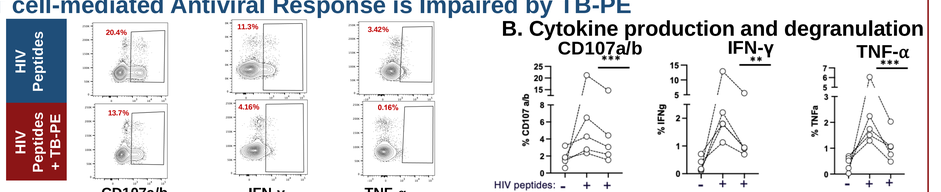
### Result 1. There is a higher proportion of genetically-intact HIV in people living with HIV and TB.



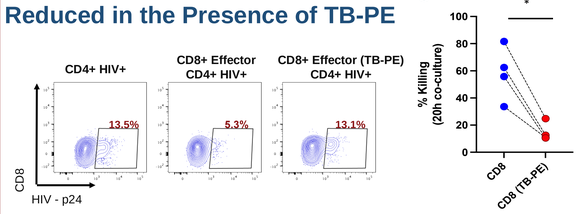

### Result 2. There is a higher proportion of genetically-intact provirus at the site of the coinfection.




### Result 3. CD8+ T cell-mediated Antiviral Response is Impaired by TB-PE




### Result 4. CD8+ T cell-mediated Killing Capacity is Reduced in the Presence of TB-PE




HIV specific CD8+ T cells (n=4; each dot represents one donor) were stimulated with HIV peptides in the presence or absence of TB-PE and then co-cultured with HIV infected autologous CD4+ T cells. TB-PE treated CD8+ T cells showed reduced capacity to kill infected CD4+ T cells by quantification of HIV-p24 ($p<0.05$).

## CONCLUSIONS

**These results indicate that concurrent TB and HIV leads to a higher frequency of cells infected with genetically-intact HIV provirus.**

**Furthermore, our results indicate that co-infection with *Mtb* inhibits the effector functionality and killing capacity of HIV-specific CD8+ T cells, resulting in a higher frequency of cells containing genetically-intact HIV proviral DNA at the site of the coinfection.**

**Our study highlights the importance of understanding the immunological effects of coinfection to inform immune-mediated curative approaches and to improve clinical outcomes for all people living with HIV.**

## REFERENCES

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World Health Organisation, 2024. Tuberculosis Factsheet. Accessed: 22nd February, 2025.

## STATISTICS

Unpaired t-test with Welch's correction for unequal SD.

Mann-Whitney Test

*p<0.05, ** p<0.01, ***p<0.001

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