

# Relationship between HIV-specific T-cell response functionality and HIV persistence:

## Relevance in the context of cure strategies

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# Background

- A **functional HIV-specific T-cell response** is key to controlling the infection.
- **Current cure strategies under study** involve:
  - **enhancing HIV-specific T-cell response**
  - **reducing HIV reservoirs**
  - **improving cell functionality** through different strategies, including the use of **PD-1 blockers**

## Objective

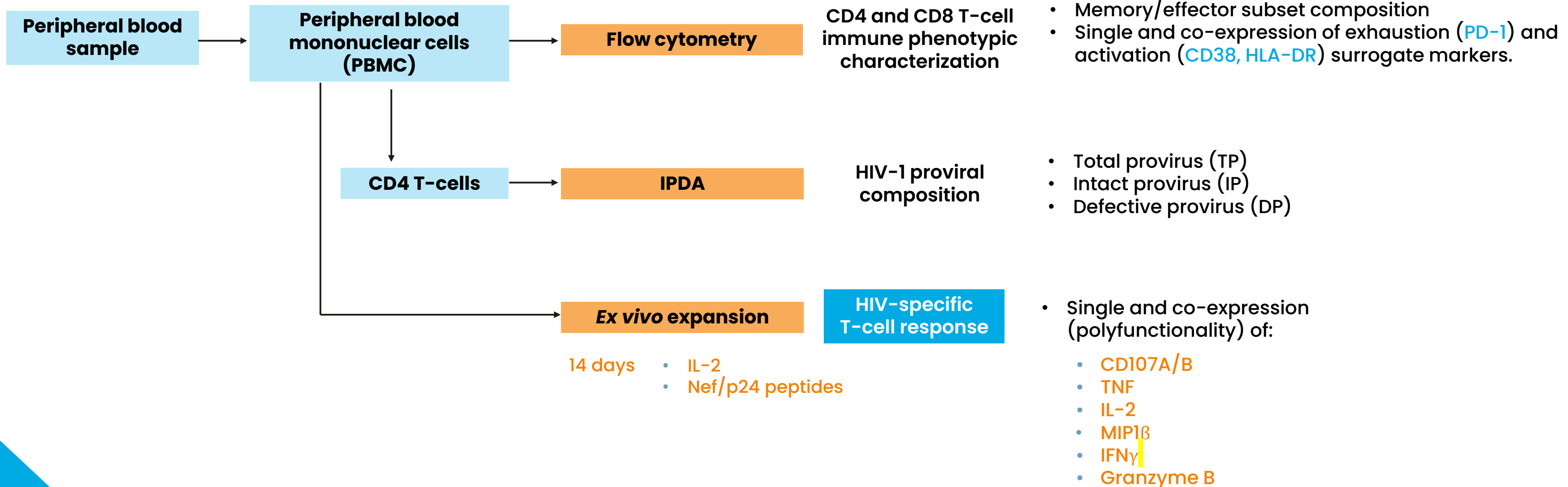
To evaluate, *ex vivo*, the magnitude and functionality of the HIV-specific response and its relation with viral persistence and immune markers associated with activation and exhaustion, and the HIV reservoir.

# Methods

1. Informed consent signature
2. Peripheral blood sample collection
3. Gathering of clinical data

\* Undetectable viral loads for two years.

Enrollment of 9 individuals living with HIV with undetectable viral load  $\geq$  2 years



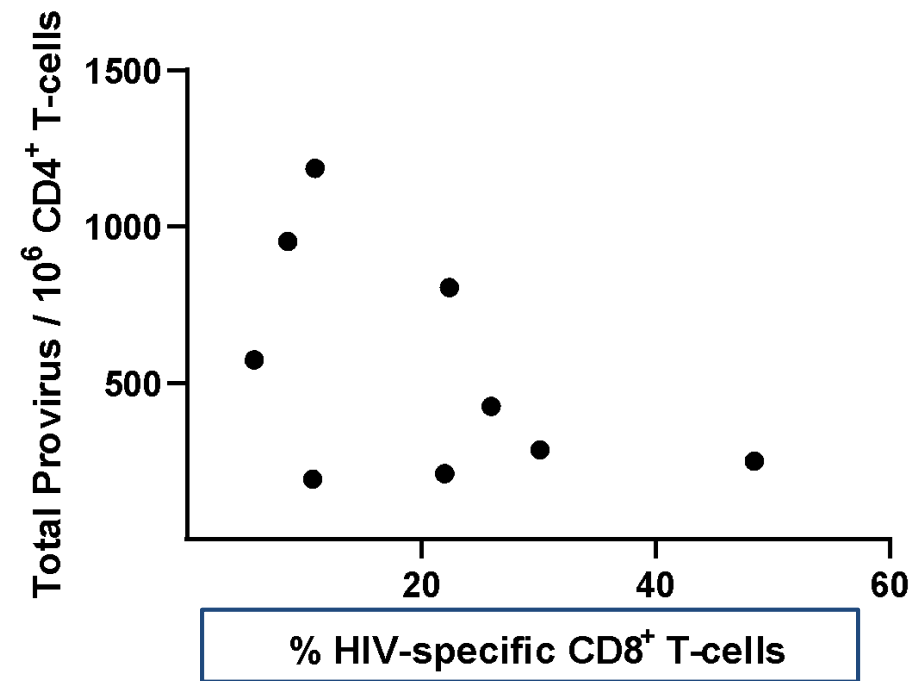
# Clinical characteristics

<b>Women</b> (n, %)	<b>Age*</b> (years)	<b>CD4 counts*</b> (cells/ $\mu$ L)	<b>CD4/CD8 ratio*</b>	<b>Known time living with HIV*</b> (years)	<b>Time with undetectable viral loads*</b> (years)
4 (44.4%)	30 (23-48.5)	772 (656.5-1128)	0.96 (0.64-1.489)	22 (12-25.5)	14 (6.5-18.75)

\*median, interquartile range (R1-R3).

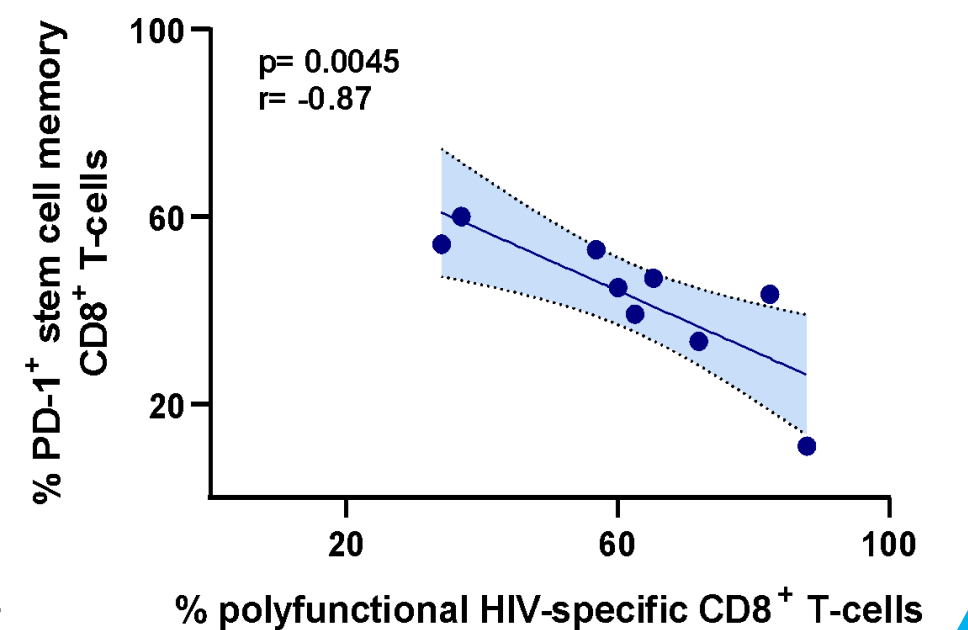
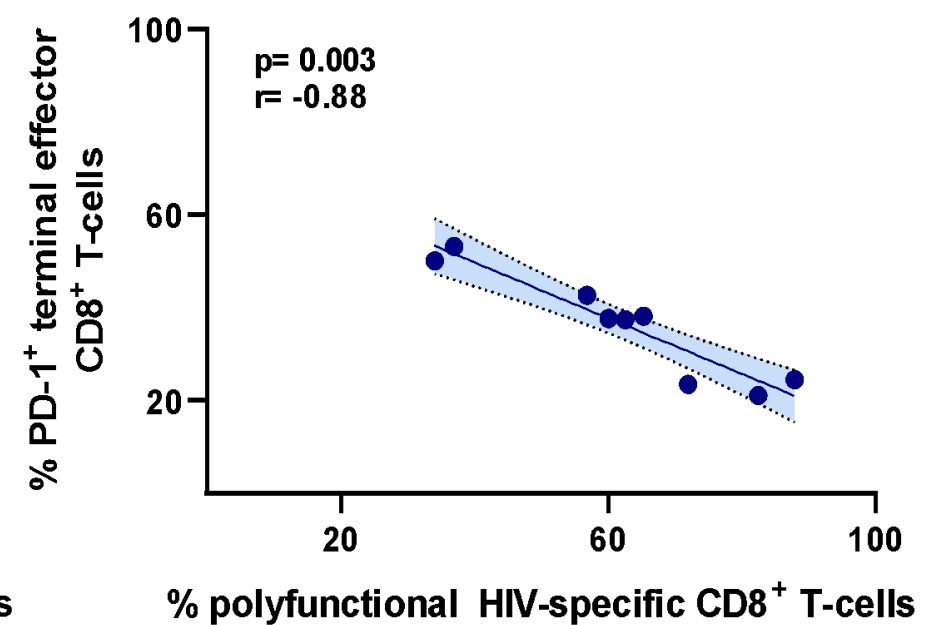
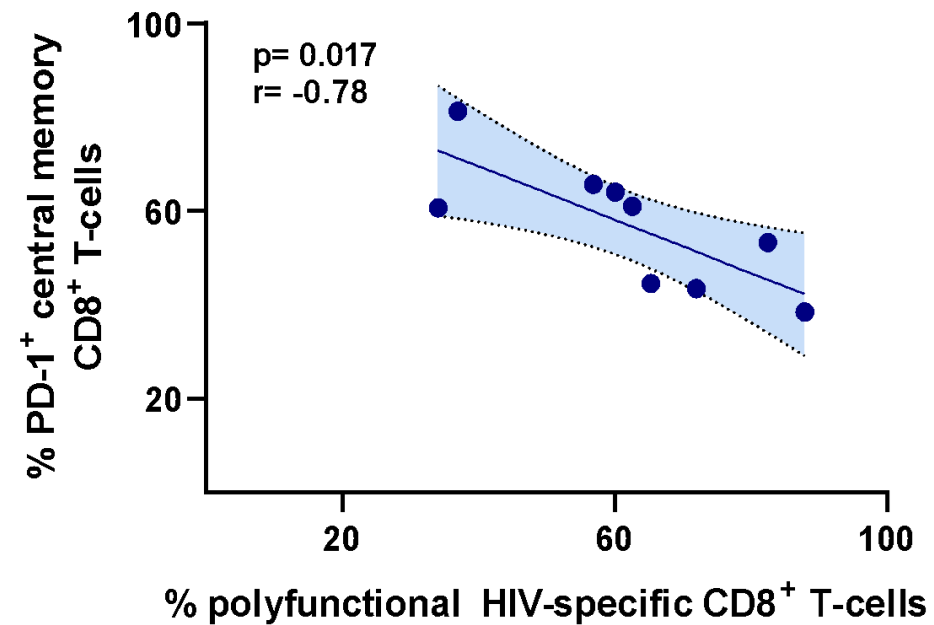
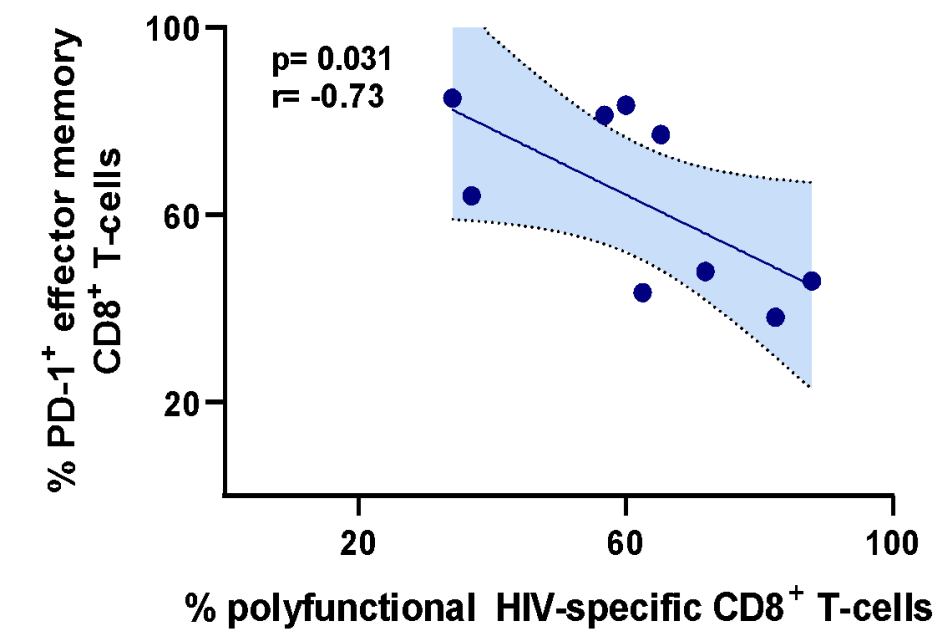
# HIV-specific CD8<sup>+</sup> T-cell response characterization

## Relationship with proviral composition: Total HIV-proviruses



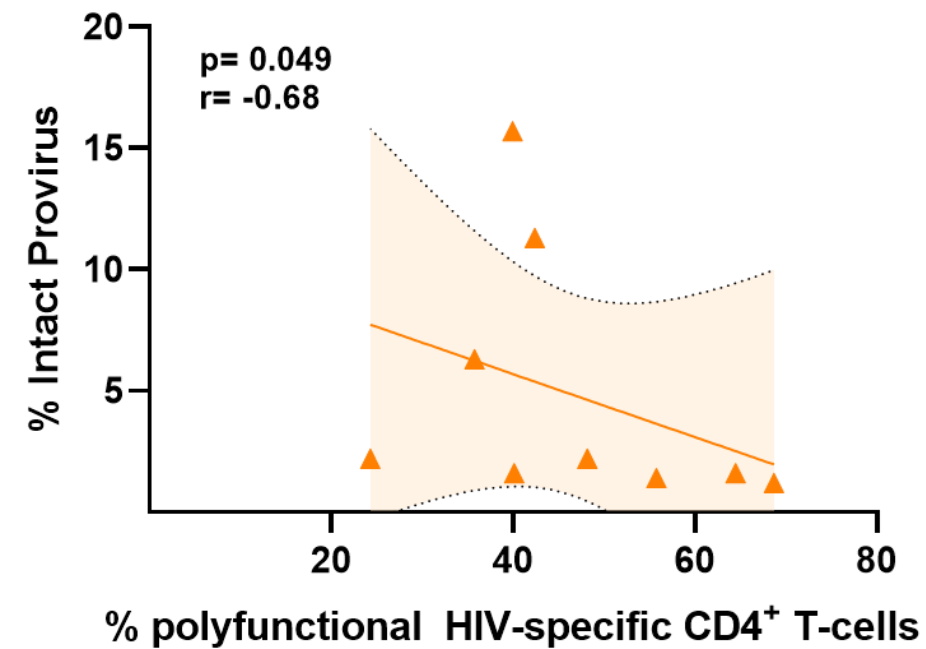
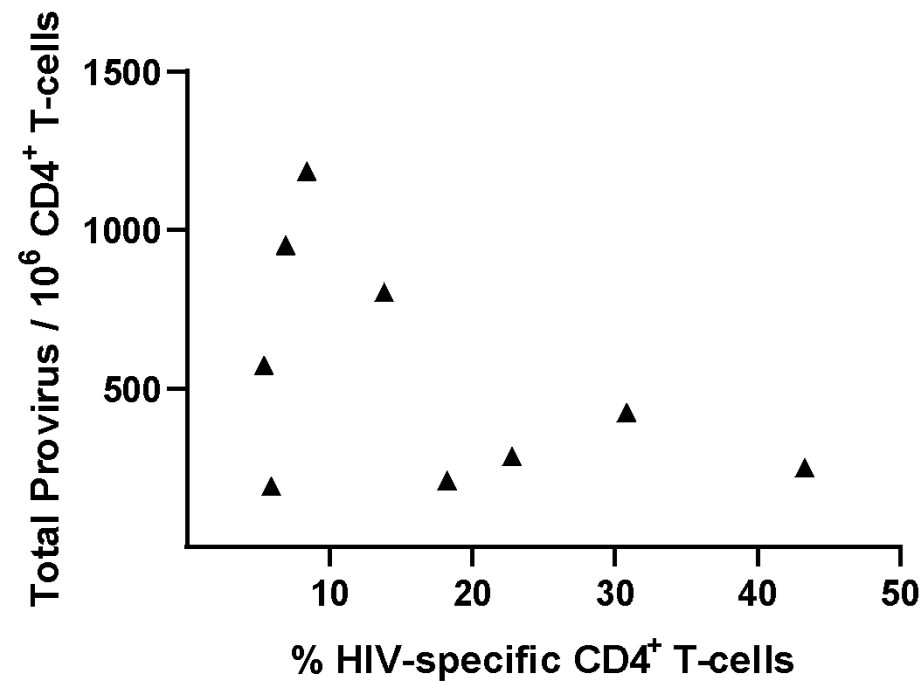
**Total provirus** = proviral HIV-DNA per million CD4<sup>+</sup> T-cells

## Relationship between polyfunctionality and PD-1 expression



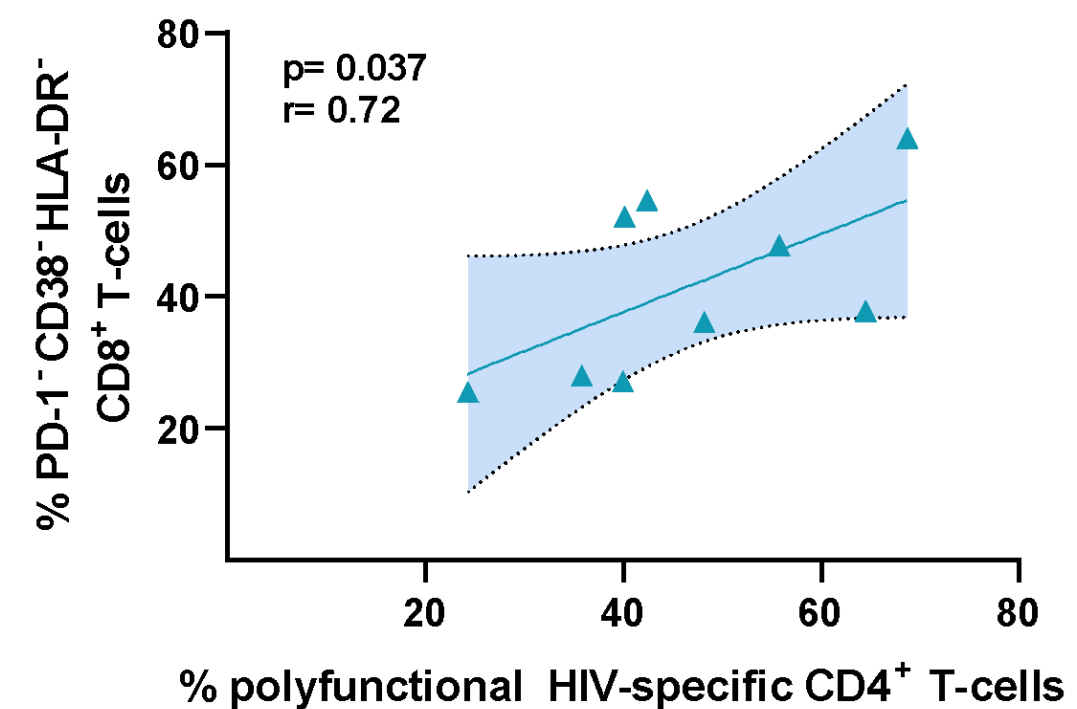
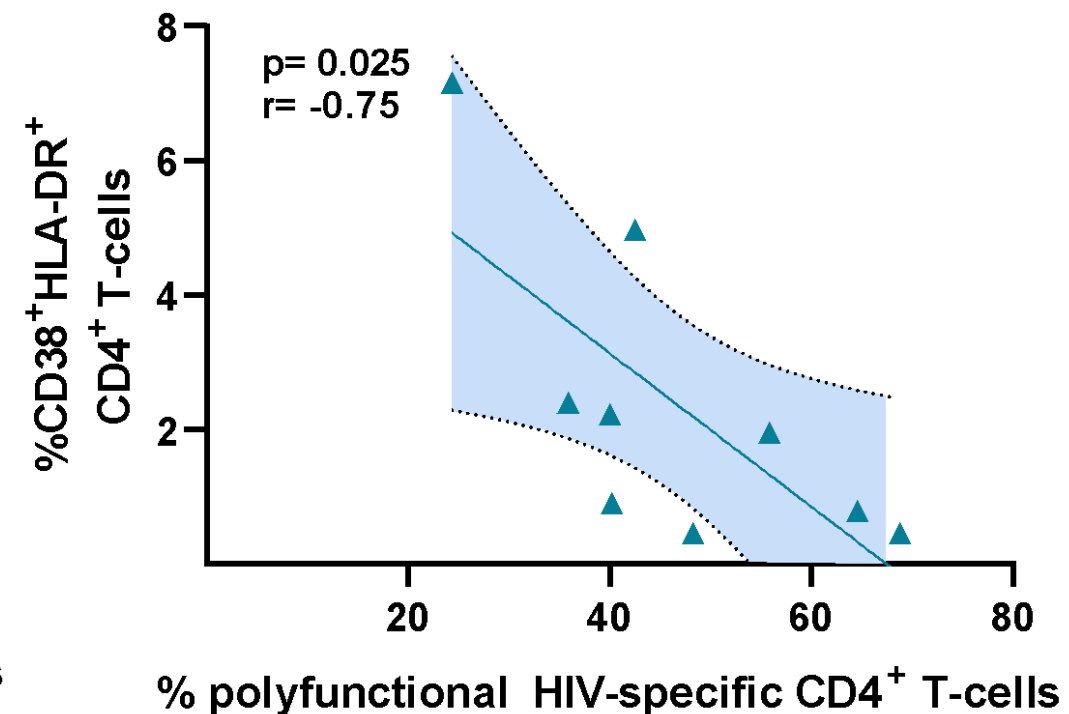
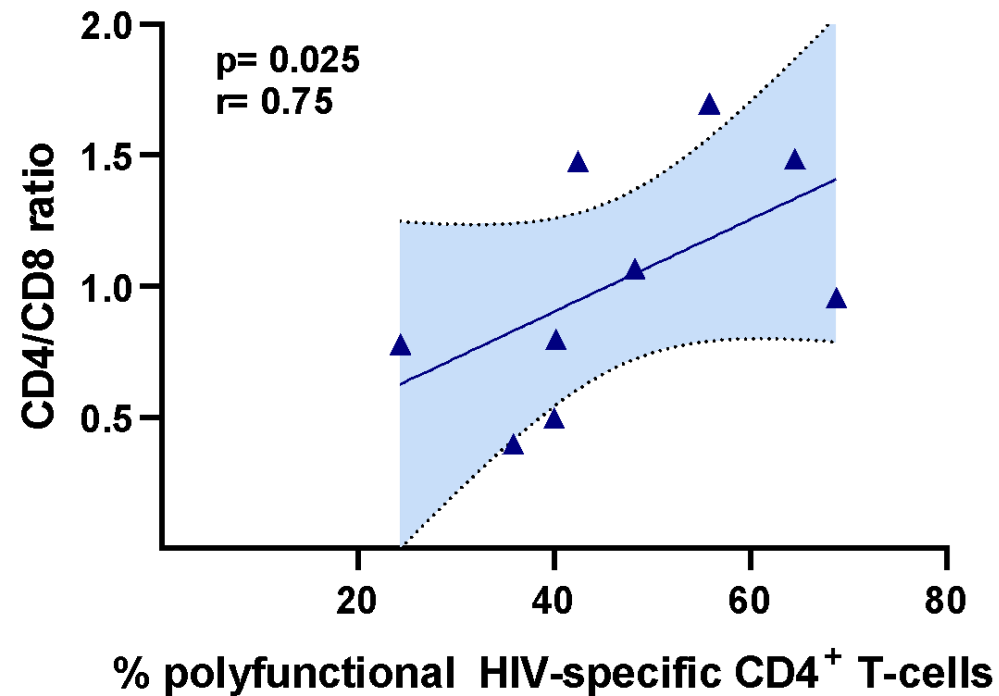
# HIV-specific CD4<sup>+</sup> T-cell response characterization

## Relationship between polyfunctionality and proviral composition



➤ Role of polyfunctionality in the elimination of intact proviruses

## Relationship between polyfunctionality and immune activation



# Conclusions and perspectives

- A **lower PD-1 expression** is associated with **improved HIV-specific T-cell polyfunctionality**.
- An effective **CD4-CD8 collaboration** could contribute to **reduce the intact viral reservoir** (relevant for viral rebound).
- These results reinforce the **negative impact of immune activation and exhaustion** on T-cell response functionality.

Potential benefit of **PD-1 blocking strategies** to **enhance the HIV-specific response**.

# Thank you so much!



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