



# Enrichment of the HIV reservoir in CD32+ CD4 T cells occurs early and is closely associated with immune checkpoint receptor expression

Genevieve E Martin  
*University of Oxford*



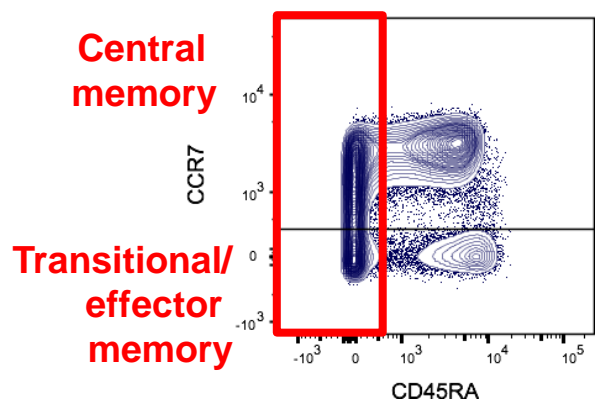
IAS HIV Cure & Cancer Forum  
Paris, France



# Background – what do we know about which cells comprise the reservoir?



## Memory compartments<sup>1,2</sup>



## Surface markers

Marker	Enrichment
Immune checkpoint receptors (PD-1, Lag-3 and TIGIT) <sup>1,3</sup>	2-3 fold
CD2 <sup>4</sup>	~ 6 fold
<b>CD32a<sup>5</sup></b>	<b>~1000 fold</b>

# CD32a is a marker of a CD4 T-cell HIV reservoir harbouring replication-competent proviruses

Benjamin Descours<sup>1\*</sup>, Gaël Petitjean<sup>1\*</sup>, José-Luis López-Zaragoza<sup>2,3,4</sup>, Timothée Bruel<sup>2,5</sup>, Raoul Raffel<sup>1</sup>, Christina Psomas<sup>6</sup>, Jacques Reynes<sup>6</sup>, Christine Lacabaratz<sup>2,3,4</sup>, Yves Levy<sup>2,3,4</sup>, Olivier Schwartz<sup>2,5</sup>, Jean Daniel Lelievre<sup>2,3,4</sup> & Monsef Benkirane<sup>1</sup>



## Aims

- Does CD32 expression differ pre- and post- ART?
- How does CD32 expression relate to reservoir size?
- Which CD4 T cells express CD32?



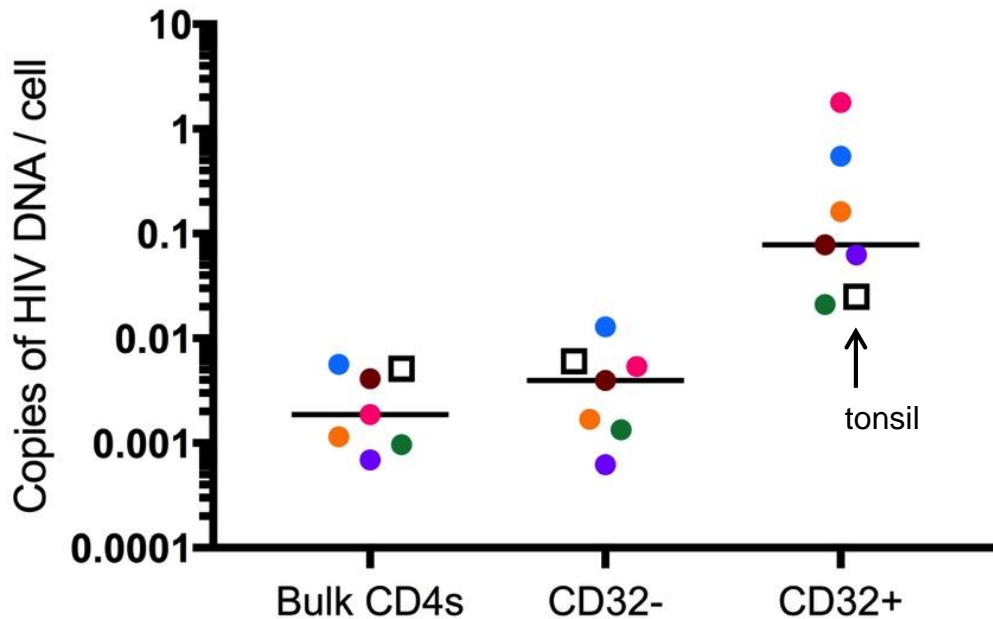
Treated primary HIV infection (PHI) cohort (n=300)

Longitudinal follow up

Sampled at 1 year post-ART initiation



# HIV DNA is enriched in CD32+ CD4 T cells from patients treated during primary HIV infection



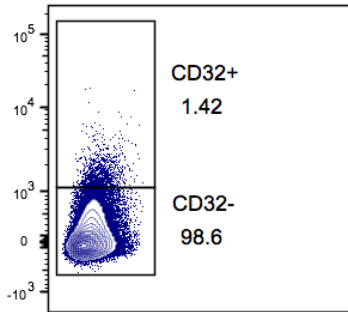
Median enrichment 69-fold  
(range 16-333)

Also observed in tonsillar  
tissue (n=1)

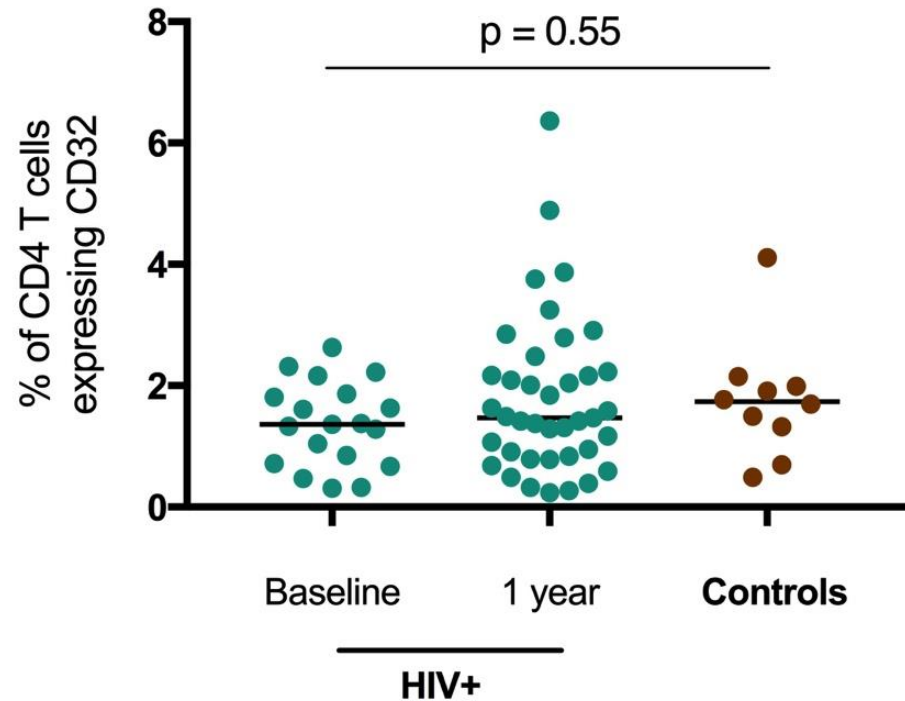
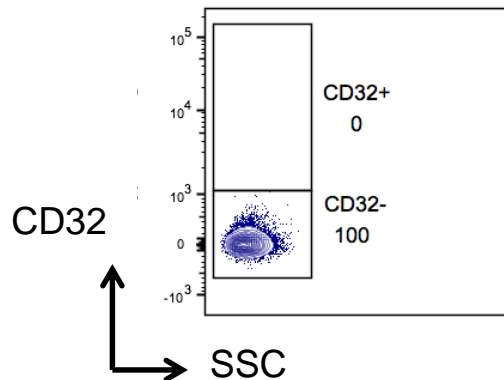


# The percentage of CD32+ CD4 T cells is similar between HIV+ individuals and healthy controls

## Stain



## Isotype control

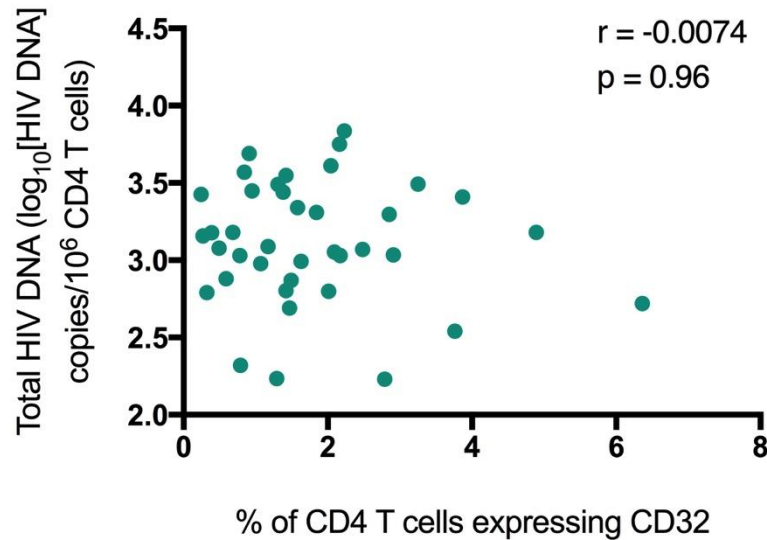




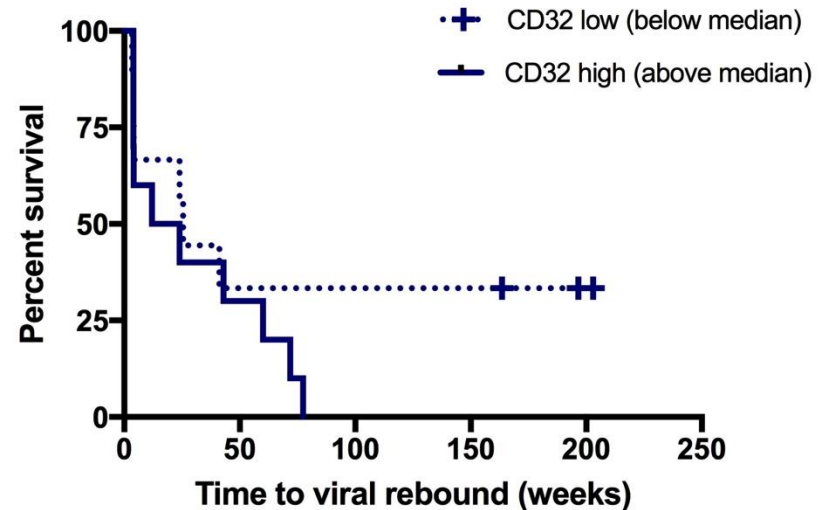
The percentage of CD32+ CD4 T cells does not appear to be a surrogate of overall reservoir size



### Total HIV DNA



### Time to viral rebound following treatment interruption

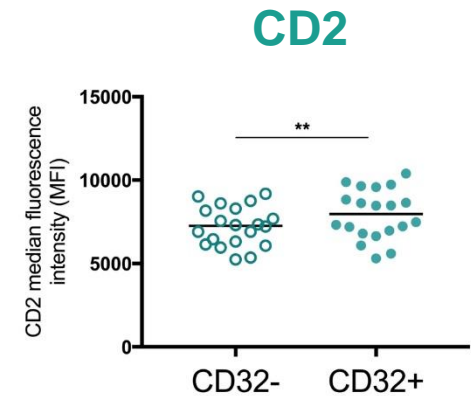
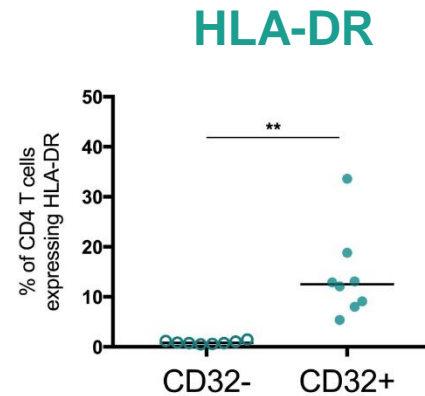
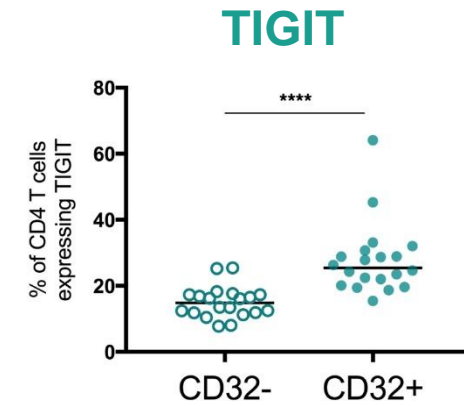
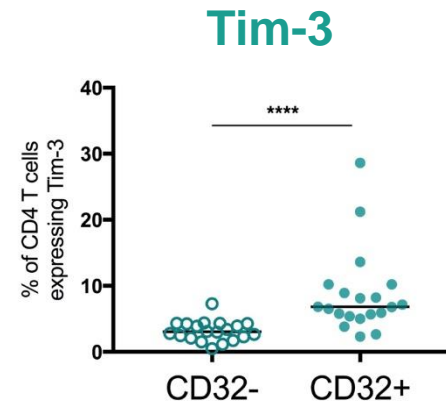
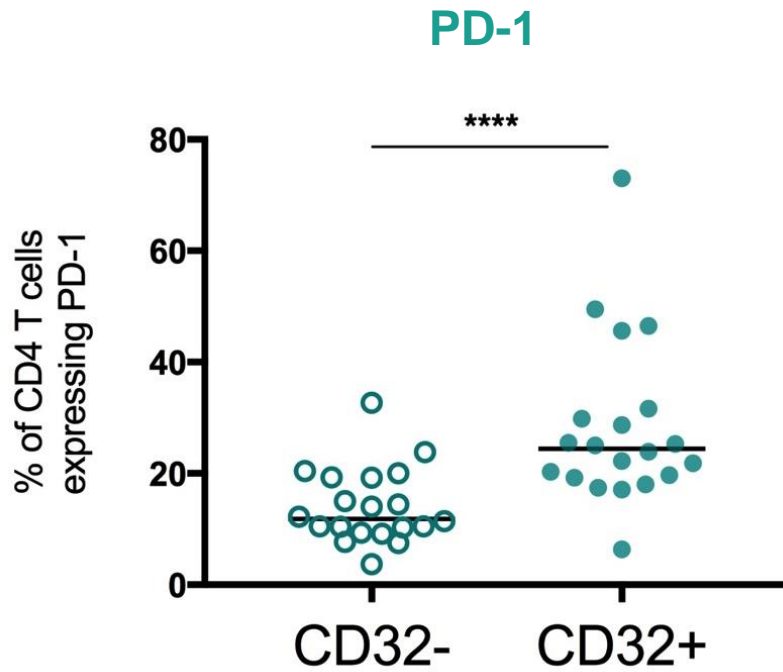


n = 19





# CD32+ CD4 T cells have high levels of immune checkpoint receptor expression



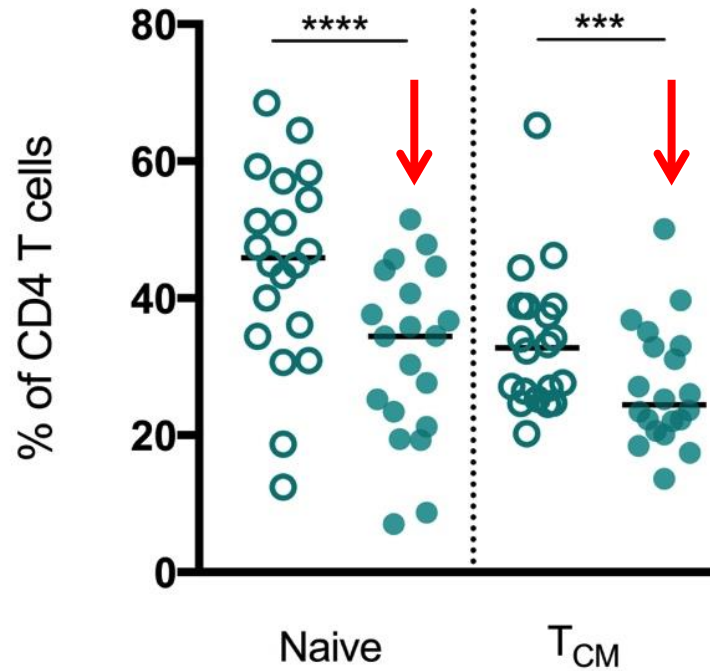
\*\* p<0.01, \*\*\*\* p<0.0001



# CD32+ CD4 T cells have a differentiated memory phenotype



- CD32- (HIV+)
- CD32+ (HIV+)



n = 20  
\*\*\* p<0.001, \*\*\*\* p<0.0001





- Demonstrate enrichment of the HIV reservoir in CD32+ CD4 T cells during treated PHI
- CD32 expression does not reflect overall reservoir size
- CD32 is co-expressed with other markers of the reservoir (and HLA-DR)
- CD32+ CD4 T cells have a differentiated memory phenotype



# Acknowledgments



We thank the participants of HEATHER and SPARTAC



**John Frater**  
Matthew Pace  
Chan Phetsouphanh  
Morgane Gossez  
Jodi Meyerowitz  
Emily Hopkins  
Helen Brown  
Natalia Olejniczak

Paul Klenerman  
Christian Willberg



**Sarah Fidler**  
John P Thornhill  
Carolina Herrera  
Kristin Kuldane  
Heather Lewis



Kholoud Porter  
Wolfgang Stöhr



Nneka Nwokolo  
Sathya Visvendra  
Rhian Bull



Julie Fox  
John Cason  
Teresa Solano



HEATHER Investigators  
SPARTAC Trial Investigators  
CHERUB Collaboration



Funded by:

