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

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

**Memory compartments**¹,²

**Surface markers**

<table>
<thead>
<tr>
<th>Marker</th>
<th>Enrichment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune checkpoint receptors (PD-1, Lag-3 and TIGIT)¹,³</td>
<td>~2-3 fold</td>
</tr>
<tr>
<td>CD2⁴</td>
<td>~6 fold</td>
</tr>
<tr>
<td>CD32a⁵</td>
<td>~1000 fold</td>
</tr>
</tbody>
</table>

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

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Aims

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

**HEATHER**

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

**Total HIV DNA**

![Graph showing the relationship between total HIV DNA and % of CD4 T cells expressing CD32](image)

- $r = -0.0074$
- $p = 0.96$

**Time to viral rebound following treatment interruption**

![Graph showing time to viral rebound for CD32 low and high](image)

- CD32 low (below median)
- CD32 high (above median)

$n = 19$
CD32+ CD4 T cells have high levels of immune checkpoint receptor expression.
CD32+ CD4 T cells have a differentiated memory phenotype

\[n = 20\]

\[*** p<0.001, **** p<0.0001\]
• 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
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