CD32 is enriched on CD4+ T-cells with a T-follicular phenotype in gut-associated lymphoid tissue

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Presented on behalf of Dr John Thornhill

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The presenting author has no conflict of interest to declare
Abstract no. O18
Background

- The HIV reservoir is the barrier to cure
- Latently infected cells are rare
- What do we know about where the HIV reservoir is?

Anatomical sites

CD4 T cell subsets
- T-follicular helper
- Memory subsets

Cell surface markers
- PD-1

References:
1. Chun TW et al. (2008), JID, 197:714-720
2. Estes et al. (2017), Nature Medicine, 23:1271-1276
3. Chomont N et al. (2009), Nature, 15:893-901
5. Fromentin R et al. (2016), PLOS Pathogens, e1005761
Background

- T-follicular helper (TFH) cells
  - CD4 T cells
  - Tissue resident
  - Provide B cell help
  - Preferential HIV reservoir$^{1-2}$

- CD32 was recently identified as a marker of an enriched HIV reservoir$^3$

Is CD32 expression on CD4 T cells related to TFHs in gut associated lymphoid tissue (GALT)?

References:
Methods

HIV infected individuals treated on ART → Terminal ileum (TI) and rectal biopsies at colonoscopy → Collagenase digestion → Reservoir size (qPCR for HIV DNA)

Immunophenotyping (flow cytometry)
<table>
<thead>
<tr>
<th></th>
<th>Primary HIV infection (n=18)</th>
<th>Chronic HIV infection (n=1)</th>
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<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18 (100%)</td>
<td>1 (100%)</td>
</tr>
<tr>
<td><strong>Age (years; median [IQR])</strong></td>
<td>34.5 [27 – 45.3]</td>
<td>48</td>
</tr>
<tr>
<td><strong>Time between estimated date of seroconversion and ART (weeks; median [IQR])</strong></td>
<td>8.0 [7.0 – 13.7]</td>
<td>297</td>
</tr>
<tr>
<td><strong>Baseline CD4 T cell count (cells/µL; median [IQR])</strong>*</td>
<td>473 [438 – 632]</td>
<td>1320</td>
</tr>
<tr>
<td><strong>Baseline CD8 T cell count (cells/µL; median [IQR])</strong>*</td>
<td>900 [712 – 1225]</td>
<td>-</td>
</tr>
<tr>
<td><strong>Baseline HIV RNA (log_{10} copies/mL; median [IQR])</strong></td>
<td>5.6 [4.6 – 6.1]</td>
<td>3.1</td>
</tr>
<tr>
<td><strong>Baseline CD4:CD8 ratio (median [IQR])</strong>*</td>
<td>0.51 [0.40 – 0.81]</td>
<td>-</td>
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<tr>
<td><strong>Method for diagnosing primary HIV infection</strong></td>
<td></td>
<td></td>
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<tr>
<td>Antigen positive (p24 or PCR) but antibody negative</td>
<td>3</td>
<td>-</td>
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<tr>
<td>Negative test with 6 months of positive test</td>
<td>11</td>
<td>-</td>
</tr>
<tr>
<td>Recent incidence testing algorithm (based on antibody avidity)</td>
<td>4</td>
<td>-</td>
</tr>
</tbody>
</table>
HIV DNA is higher in gut-associated lymphoid tissue than in the periphery

\[ n=16 \text{ (gut samples)} \]
Kruskall-Wallis test \( p=0.003 \); pairwise comparisons shown

The frequency of CD32+ CD4 T cells is similar across anatomical sites

\[ n=18 \text{ (gut samples)} \]
Kruskall-Wallis test

Overall \( p = 0.70 \)
**T-follicular helper cells (TFH) in GALT have higher CD32 expression than non-TFH cells**

- **T-follicular helper cells (TFH) are defined by the co-expression of CXCR5 and PD-1.**

- **CD32+ CD4 T cells in GALT express high levels of the TFH markers Bcl-6 and ICOS, as well as the activation marker HLA-DR.**
CD32 expression may correlate with reservoir size in GALT, but not in PBMCs

**Terminal ileum**

\[ r = 0.46 \]
\[ p = 0.05 \]

**Rectum**

\[ r = 0.50 \]
\[ p = 0.03 \]

**Peripheral blood**

\[ r = 0.17 \]
\[ p = 0.32 \]
• CD32 is expressed at similar levels on CD4 T cells from GALT and in the periphery

• CD32+ CD4 T cells in GALT exhibit a T-follicular helper cell phenotype

• The expression of CD32 on TI and rectal CD4 T cells may relate to the size of the HIV reservoir in these compartments
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