Poster#: 339

KWAZULU-NATAL RESEARCH INSTITUTE FOR TUBERCULOSIS AND HIV

International AIDS Vaccine Initiative

Ragon Institute of MGH, MIT and Harvard

Acute HIV-1 Subtype C Infection is Associated with Rapid Changes in B-cell Subsets and Levels of CXCL13

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Background

HIV chronic infection (CI) is characterized by perturbations in B cell homeostasis, phenotype and function. There are limited data describing B cell dynamics during HIV acute infection (AI). Characterizing B cell subsets during AI might help define signatures that shape the humoral response in HIV infection.

Objective

- To describe the kinetics of B cell subsets upon HIV subtype C infection
- To determine if these changes influence development of BNAbs

Study Subjects and Laboratory Methods

- Eleven women who became HIV-1 infected during a longitudinal follow-up study in Durban South Africa were analyzed. Samples were analyzed at baseline (pre-infection) and weeks 1, 2, 4 and 12 post detection of HIV RNA
- Multicolor flow cytometry was used to identify B cell subsets based on expression of CD21CD27 on live CD19+ lymphocytes and defined as follows; activated memory (AM) CD27+CD21-, resting memory (RM) CD27+ CD21+, naïve cells (N) CD27-CD21+, tissue-like memory (TLM) CD27-CD21- and plasmablasts (PBs) CD27+CD38+ cells.
- Evolution of HIV-specific antibodies and changes in CXCL13 levels were determined by ELISA.

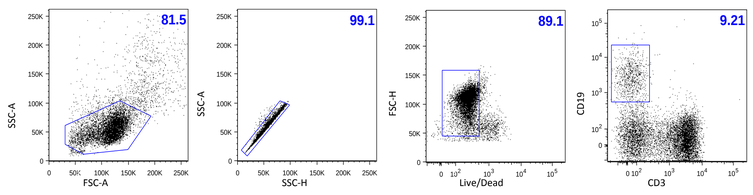


Figure 1a. Gating strategy used to identify B cells defined as CD19+ CD3- lymphocytes

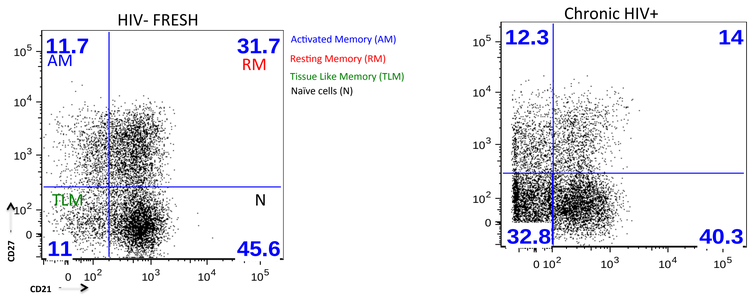


Figure 1b. B cell subsets defined by expression of CD27 and CD21 are disrupted in HIV infection {HIV – person (left) and HIV+ patient (right)}. Chronic infection is marked with elevated TLM cells and reduced RM cells.

Results.

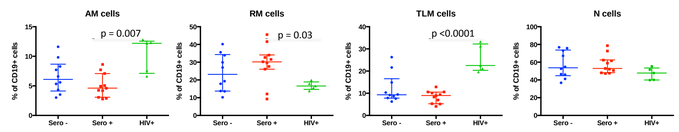


Figure 2. No significant differences in B cell subsets **at baseline** between women who remain seronegative (blue symbols) and those that seroconvert (red symbols). However, Significant differences are noted when B cell subsets from the negative groups are compared to those from chronically infected people.

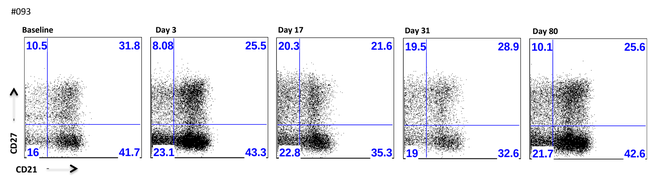


Figure 3a. There is rapid disruption of B cell subsets upon HIV infection characterized with an expansion of AM and TLM cells and a decline in RM and N cells

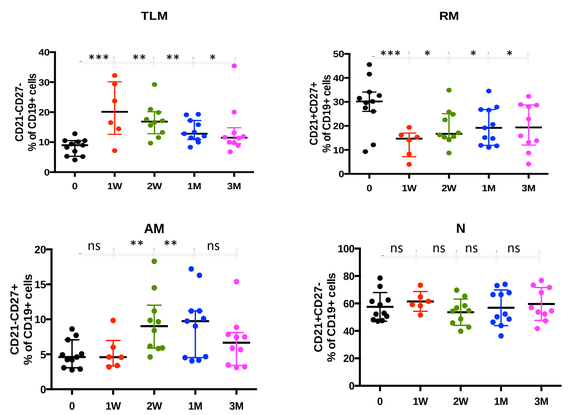


Figure 3b. Expansion of TLM and contraction of RM cells is very rapid, is significantly different from baseline by 1 week post infection (PI) and does not revert to baseline 3 months PI. Changes in AM cells only become statistically significant 2 weeks PI and normalize by 3 months PI.

Outcome	Effect of Log VL on outcome (per 1 log increase) Effect estimate (standard error)	p-value
Plasmablasts (PBs)	0.095 (0.049)	0.0633
Activated Memory (AM)	0.004 (0.026)	0.8721
Resting Memory (RM)	-0.063 (0.017)	**0.0008**
Naïve Cells (N)	-0.002 (0.007)	0.7732
Tissue Like Memory (TLM)	0.075 (0.018)	**0.0002**

Table 1. Changes in B cell subsets are driven by viral loads.

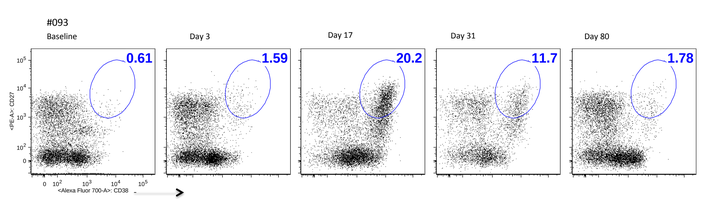


Figure 4a. Plasmablasts (PBs) were identified by gating for CD27+ CD38+ cells.

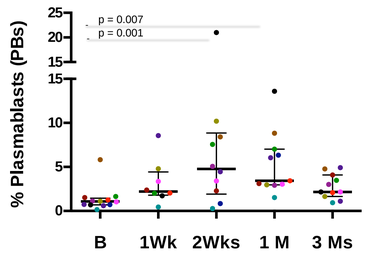


Figure 4b. Summary of PBs kinetics over-time. Changes were significant at 2 weeks and 1 month PI. Peak PBs was transient and variable with a median peak day of 17 daysPI (range 7-32 days). Frequency of PBs expansion was also variable with a median of 7.1% (range 1.9-20.2%)

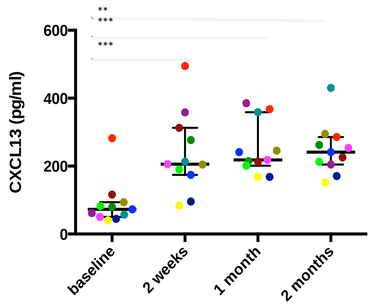


Figure 5a. CXCL13 chemokine levels increase significantly upon HIV infection

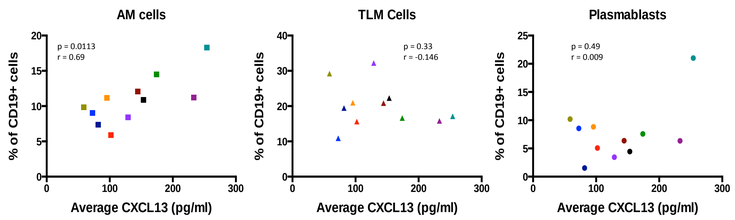


Figure 5b. Positive association between CXCL13 and levels of AM cells.

Summary:

1. TLM and AM cells expand rapidly upon HIV infection while RM cells decline.
2. CXCL13 chemokine levels increase significantly upon HIV infection.
3. CXCL13 chemokine levels correlate positively with AM cells

Remaining Questions:

1. Is the initial PB peak composed of HIV specific B cells?
2. How do changes in B cell subsets and CXCL13 chemokine influence development of BNAbs

References

1. Moir S and Fauci A.S 2009, 2013