# HIERARCHICAL CLUSTERING SHOWS B-CELL PERTURBATIONS INDEPENDENT OF HIV-2 VIRAEMIA

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**Emil Johansson**[1*], Priscilla F. Kerkman[2,3], Lydia Scharf[4], Jacob Lindman[5], Zsófia Ilona Szojka[1], Fredrik Månsson[6], Antonio Biague[7], Patrik Medstrand[6], Hans Norrgren[5], Marcus Buggert[8], Annika C. Karlsson[4], Mattias N.E. Forsell[2,†], Joakim Esbjörnsson[6,9†], Marianne Jansson[1,†] and the SWEGUB CORE Group

[1]Department of Laboratory Medicine, Lund University, Lund, Sweden, [2]Department of Clinical Microbiology, Umeå University, Umeå, Sweden. [3]Department of Medical Microbiology, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands, [4]Department of Laboratory Medicine, Karolinska Institutet, Stockholm, Sweden. [5]Department of Clinical Sciences Lund, Lund University, Lund, Sweden. [6]Department of Translational Medicine, Lund University, Lund, Sweden. [7]National Laboratory for Public Health, Guinea-Bissau, [8]Department of Medicine Huddinge, Karolinska Institutet, Stockholm, Sweden. [9]Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom, [†]These authors have contributed equally to this work.

## BACKGROUND

Time to AIDS in HIV-2 infection is approximately twice as long compared to in HIV-1 infection[1]. Still, and despite reduced viraemia, HIV-2 infected individuals display signs of chronic immune activation[2]. In HIV-1 infected individuals, the expansion of hyperactivated B-cells, characterized by the expression of the transcription factor T-bet, is driven by continuous antigen exposure[3]. However, the contribution of viraemia to B-cell perturbations in HIV-2 infected individuals remains largely unexplored.

Here we set out to determine if B-cell hyperactivation is viraemia dependent during HIV-2 infection, as it has been described for HIV-1 infection, and if aviraemic individuals display signs of virus replication in tissue.

## METHODS

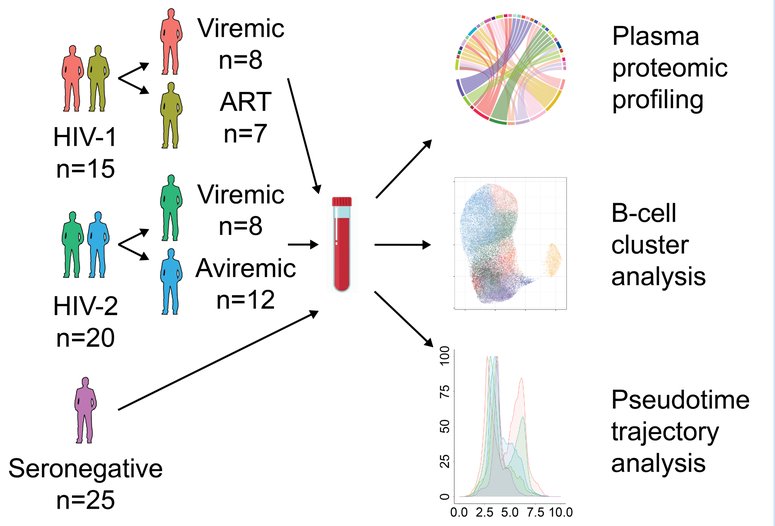


**Figure 1. Flow cytometry and mass spectrometry-based profiling of study participants.** Study participants were enrolled from an occupational cohort in Guinea-Bissau. B-cells were immunophenotyped using flow cytometry and blood plasma was profiled using mass-spectrometry based-proteomics. Tissue damage was assessed using differentially expressed proteins and a previously published list of tissue-enriched genes[4].

## CONCLUSIONS

Aviraemic HIV-2 infected individuals display elevated frequencies of hyperactivated T-bet$^{high}$ B-cells.

Hyperactivated T-bet$^{high}$ B-cells are located at the terminal end of the pseudotime trajectory.

Aviraemic HIV-2+ individuals also display colon tissue damage, suggesting virus replication and antigen release

## RESULTS

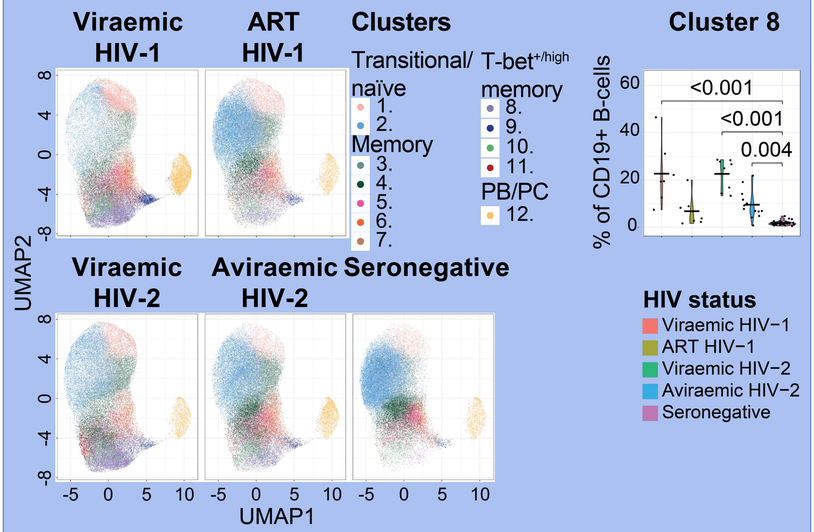


**Figure 2. Aviraemic HIV-2 infected individuals display elevated frequencies of hyperactivated T-bet$^{high}$ B-cells.** A) Consensus hierarchical cluster analysis of flow cytometry data, using the FlowSOM algorithm, identified 12 clusters of B-cells. B) Frequencies of cluster 8, containing T-bet$^{high}$CD95$^{+}$CD27$^{int}$ hyperactivated B-cells, was elevated among both viraemic and aviraemic HIV-2 infected individuals.

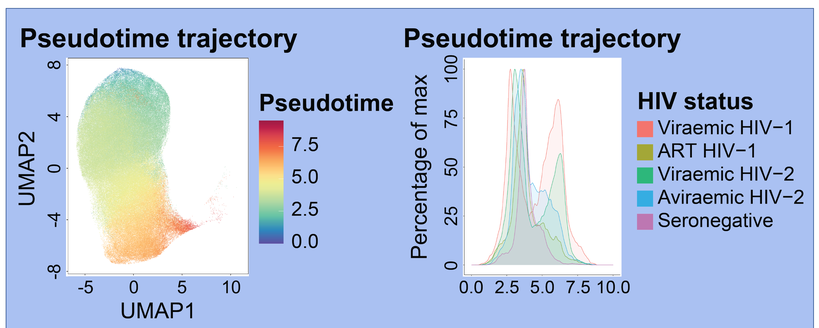


**Figure 3. Hyperactivated T-bet$^{high}$ B-cells are located at the terminal end of a pseudotime trajectory.** A) UMAP plot displaying the differentiation of B-cells from transitional B-cell to hyperactivated T-bet$^{high}$ B-cells along a pseudotime trajectory, created using the slingshot algorithm. B) Density plot demonstrating the enrichment of B-cells from HIV infected individuals at the terminal end of the pseudotime trajectory.

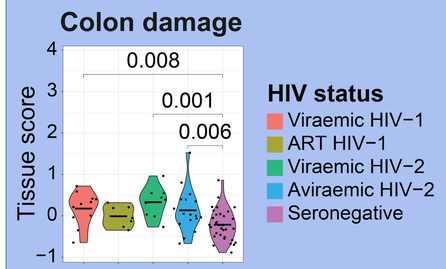


**Figure 4. Viraemic and aviraemic HIV-2 infected individuals displays signs of colon tissue damage.** Viraemic and aviraemic HIV-2 infected individuals have elevated plasma levels of proteins predicted to have leaked from sigmoid colon, suggesting ongoing replication.

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## References

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**Contact information:** emil.johansson@med.lu.se