Virological and immunological evaluation of individuals with spontaneous persistent viral control without ART.

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BACKGROUND

- HIV elite controllers (EC) maintain undetectable viral loads (<20 HIV RNA copies/ml) and normal CD4/CD8 counts without ART.

- Despite WHO guidelines recommending ART irrespective of CD4 count and viral load, there remains a lack of consensus on best clinical management for elite controllers.

- We have used detailed molecular and serological diagnostic assays to confirm HIV EC status amongst this group and evaluated markers of inflammation and HIV specific immune responses.

An observational study of 17 HIV Elite controllers attending a tertiary referral clinic in London between 2017-1019

Median Age (range)	**Gender (%)**	**Ethnicity (%)**	**Median time since HIV diagnosis (years)**	**Co-infection screen** (HTLV, *T palliidum*, Hep B, Hep C, EBV, HBV, CMV)	**Autoimmune screen** (antinuclear antibody, Anti-double-stranded DNA, Rheumatoid Factor, antimitochondrial antibody)
42 (37-54)	10 Female (59%) 7 Male (41%)	8 White (47%) 7 Black (41%) 2 Other (12%)	8 (1-12)	Negative for all	Negative for all

Table 1. Demographics and clinical descriptions of 17 EC.

NONE had any ART drug detectable in plasma.

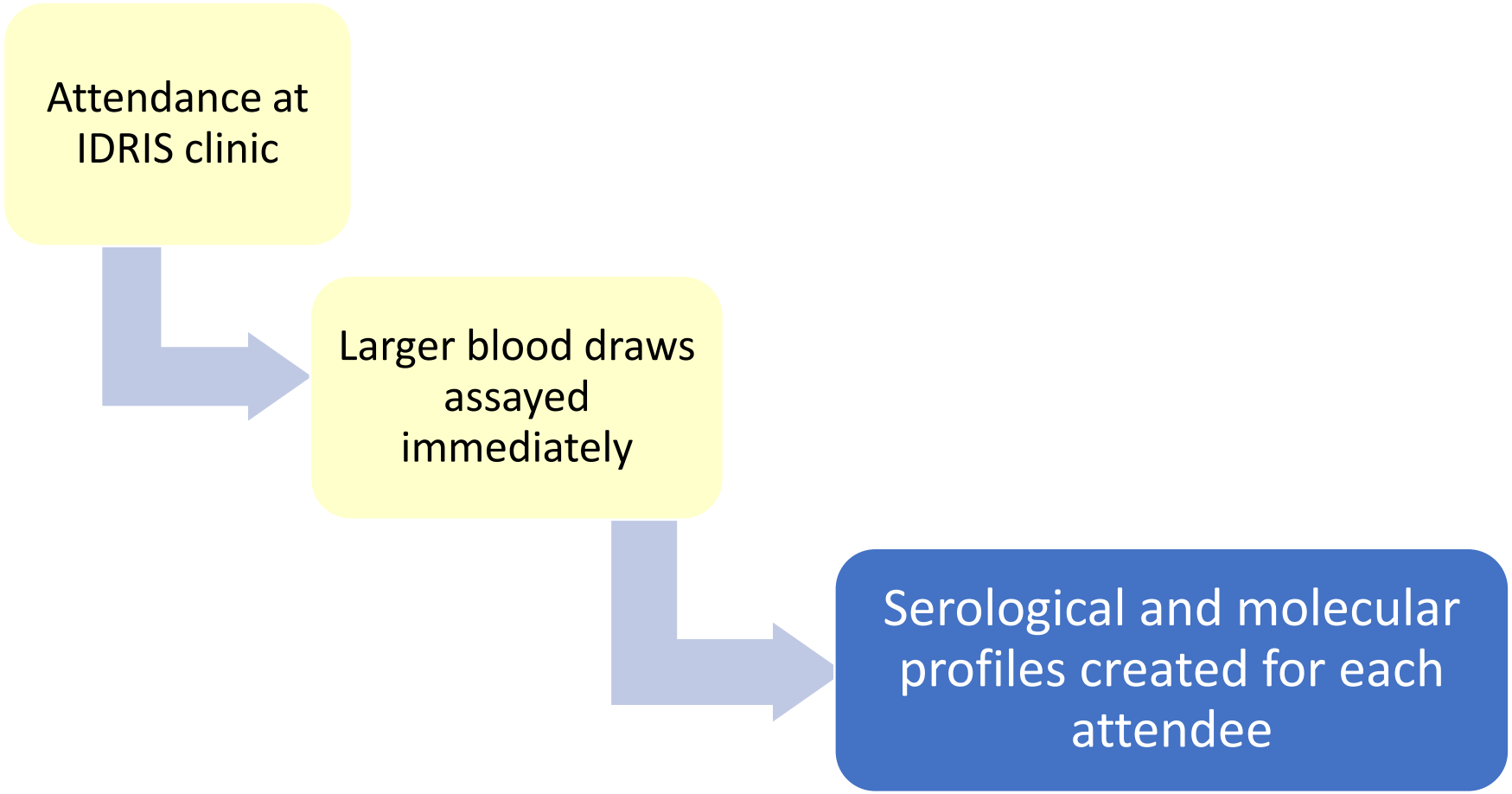
Research questions

- What is the molecular and serological evidence for HIV infection amongst EC?
- What are the levels of expression of T cell activation markers amongst EC ?
- Can we characterise CD8 T cell responses from EC?
- Is there evidence of increased inflammation measured by plasma cytokine levels in EC?

METHODS

- Serological profiling by western blotting.
- Molecular profiling by single copy assays (RNA /ml) and (DNA/10^5 PBMCs) targeting integrase gene and qualitative DNA assays targeting LTR/pol and gag/int.
- Immune activation markers measurement (CD4, CD8, CD25 and HLA-DR) by flow cytometry.
- HIV specific CD8 T-cell responses using a pool of gag, env, nef and vif peptides in an IFN-γ ELISPOT.
- Plasma cytokines measurements by (IL-2,IL-6, TNF-α, MIP-1β, CRP) by mesoscale Vplex platform.

EC WERE IDENTIFIED THROUGH ATTENDANCE AT SPECIALIST TERTIARY REFERALL CLINIC .



EC can present as serologically positive or serologically indeterminate

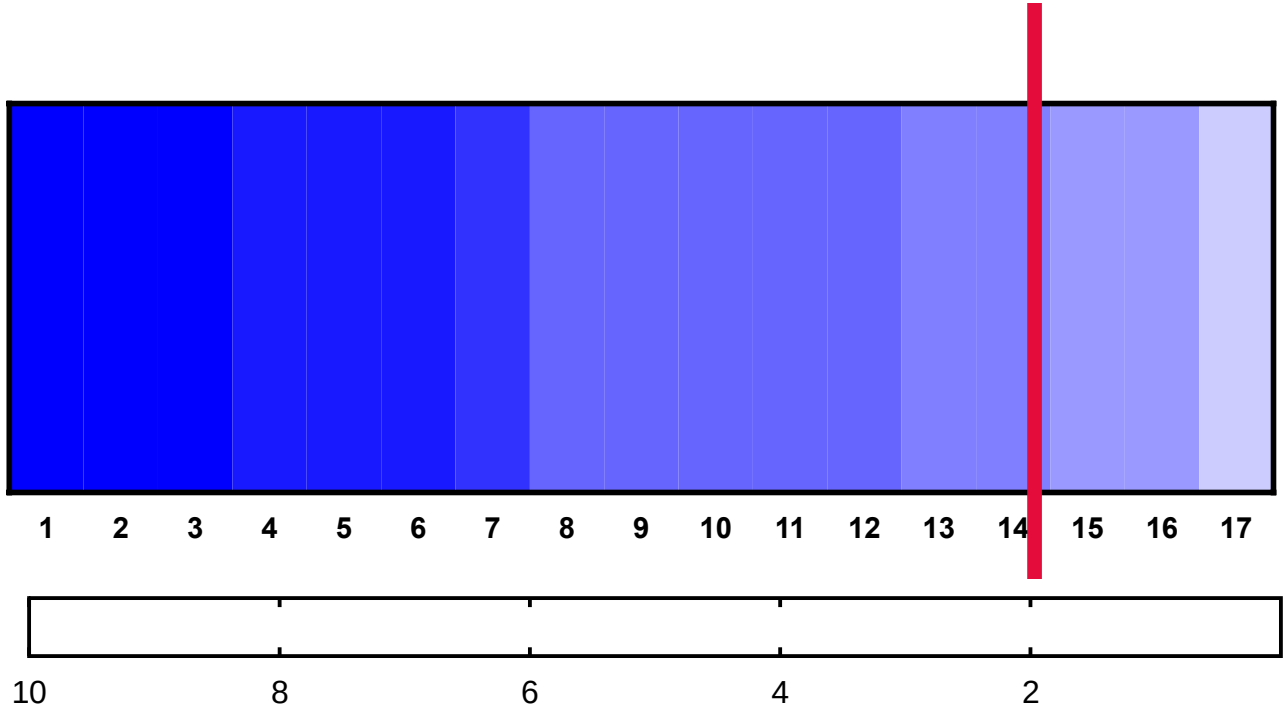
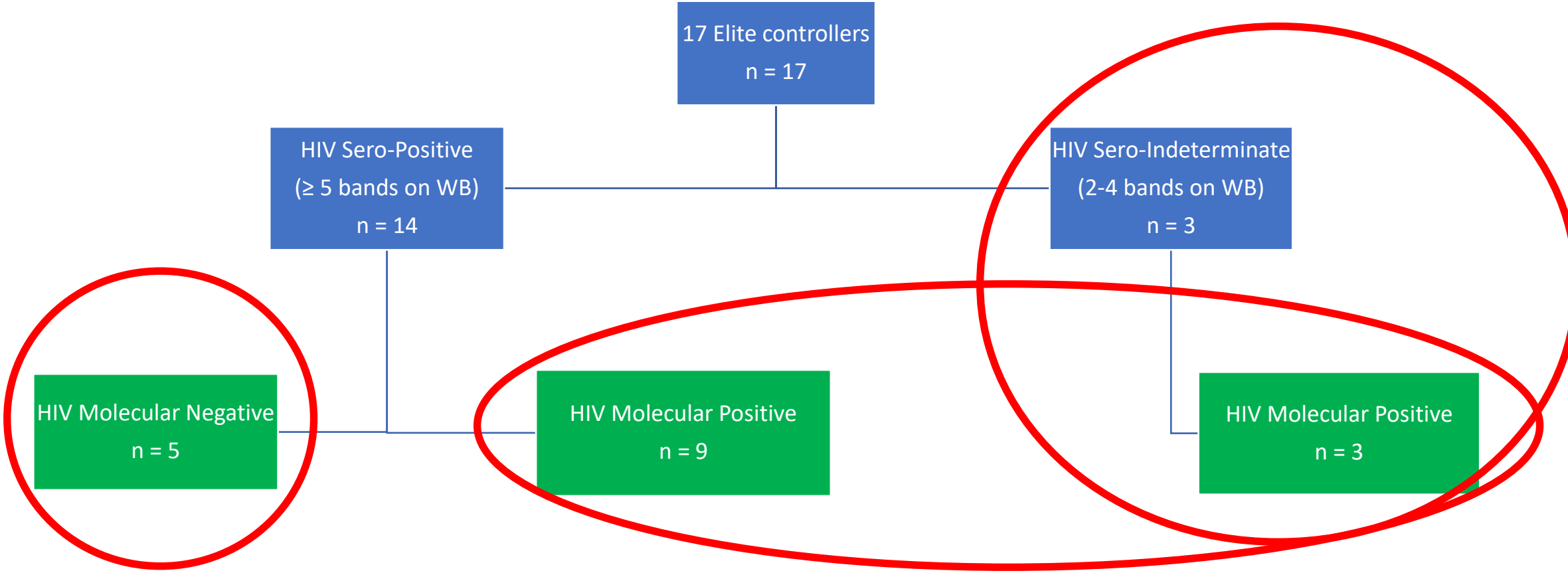


Figure 1. Western Blotting profiles (number of bands detected)

EC can categorised as molecular positive and molecular negative

Molecular profiling by single copy assays (RNA /ml) and (DNA/10^5 PBMCs) targeting integrase gene and qualitative DNA assays targeting LTR/pol and gag/int.



12/17 EC are molecular positive and 5/17 are molecular negative

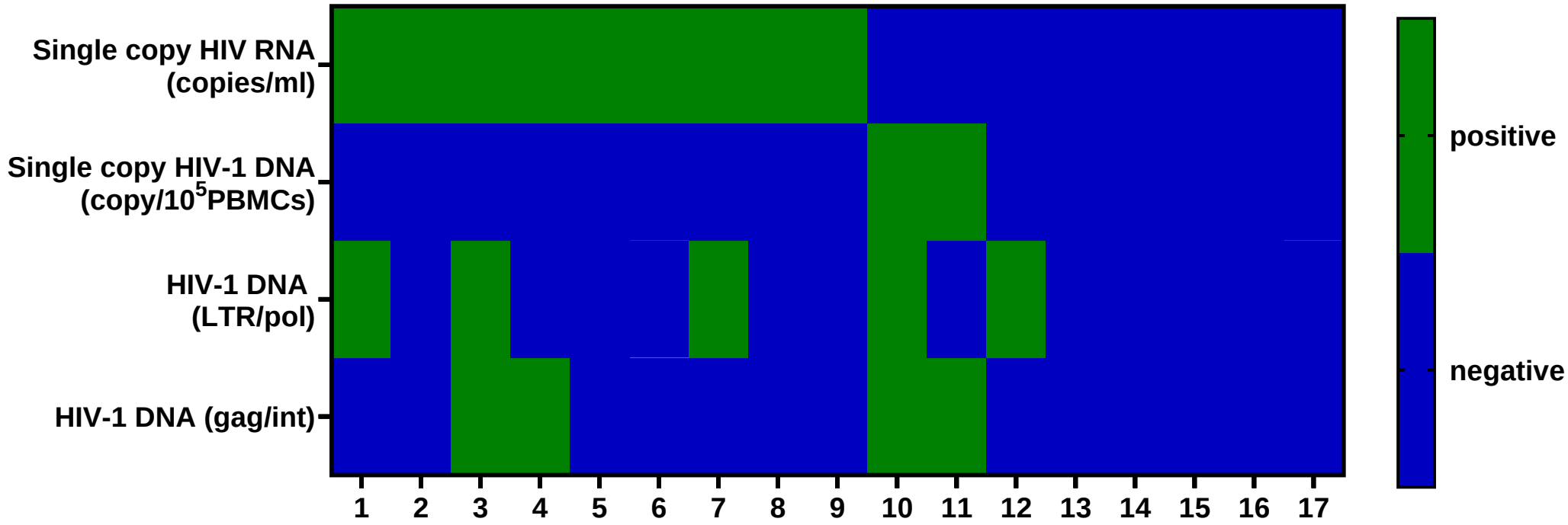


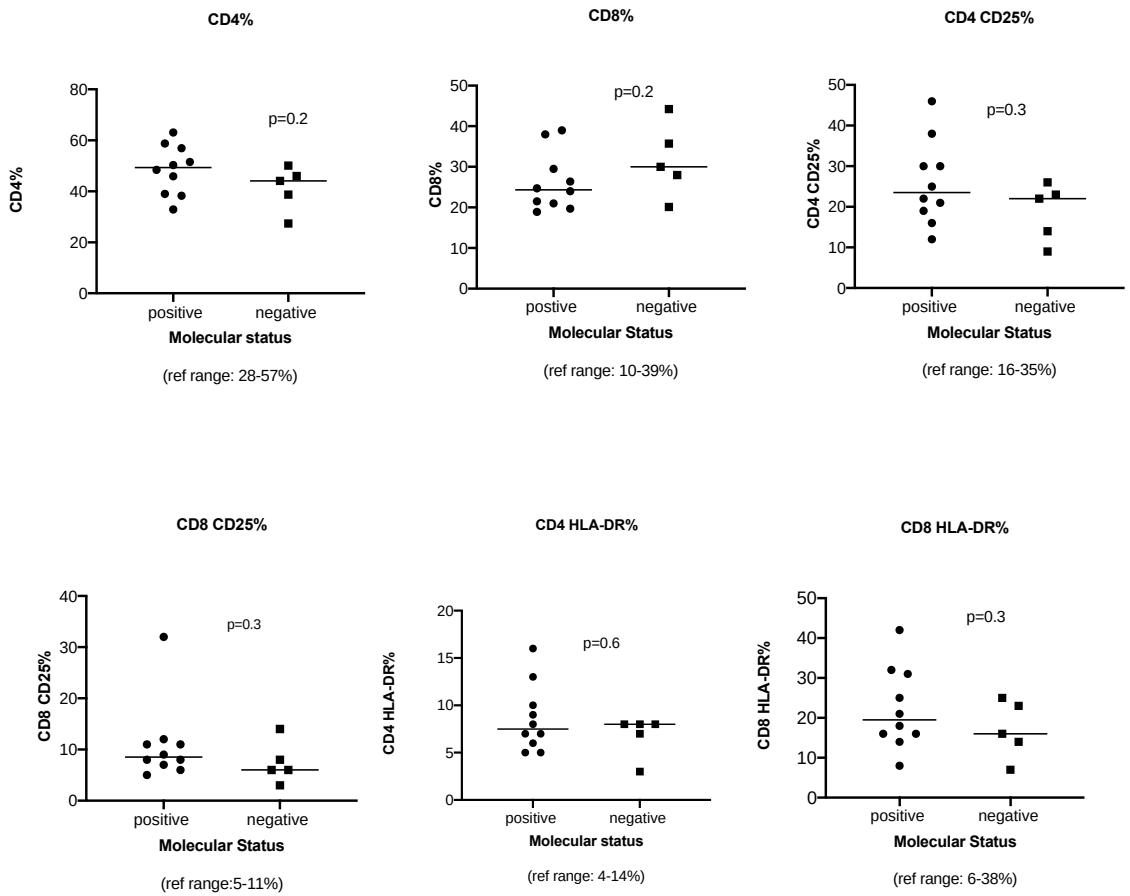
Table 3. Molecular profile of Elite Controllers. 12/17 are molecular positive, 5/17 are molecular negative.

No statistical difference in routine clinical T cell studies between molecular positive and molecular negative EC.

	Median CD4 cells/mL (IQR)	Median CD8cells/mL (IQR)	Median CD4:8 ratio (IQR)
Molecular-Positive EC	1015 (751-1369)	553 (372 -817)	1.9 (1.3-2.5)
Molecular-Negative EC	785 (685-1138)	779 (436 -911)	1.5 (0.8-2.5)

Table 2. Routine T cell results

No difference in T cell activation markers between molecular positive and molecular negative EC.



Figures 2- 7. T cell activation markers

Molecular negative EC have higher frequency of CDT T-cell responses compared with molecular positive EC.

HIV-1 specific CD8 T-cells were measured with an ELISPOT assay which detects IFN-γ produced in response to immunodominant HIV peptide pool consisting of gag, env, nef and vif peptides.

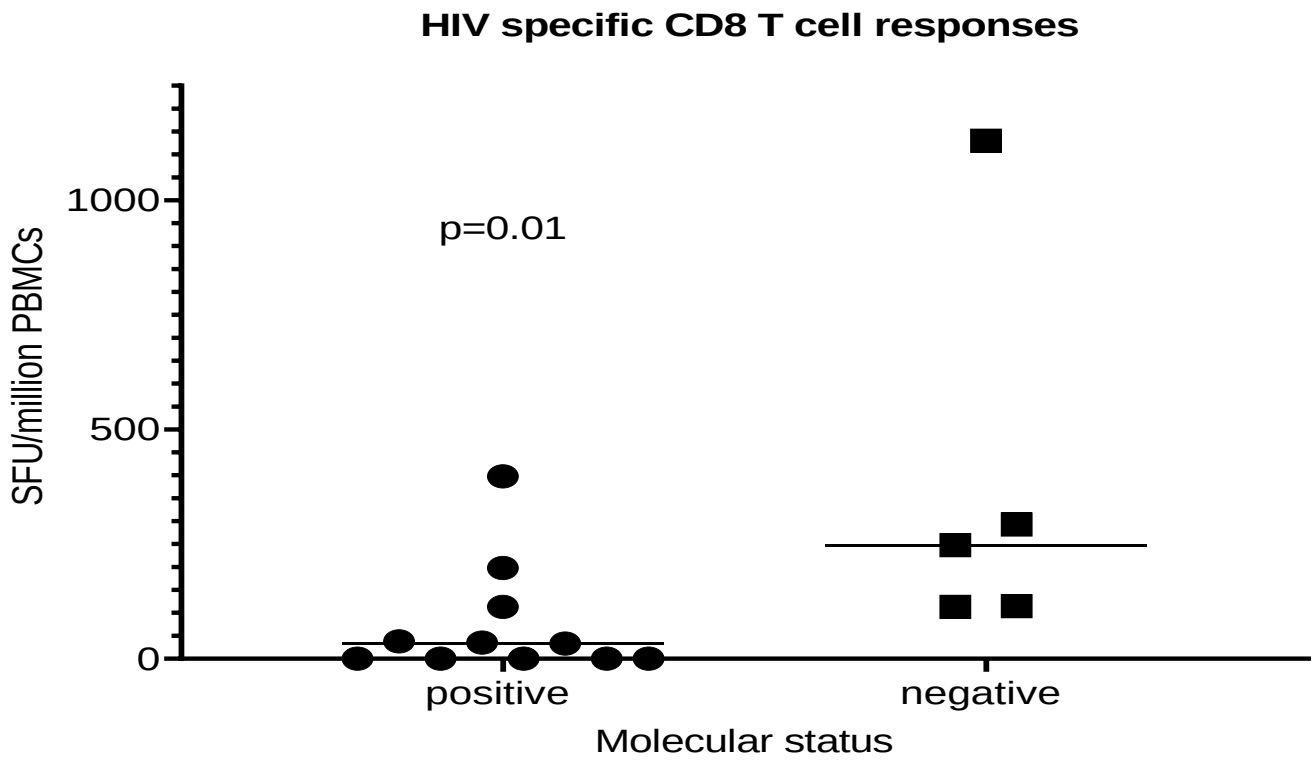
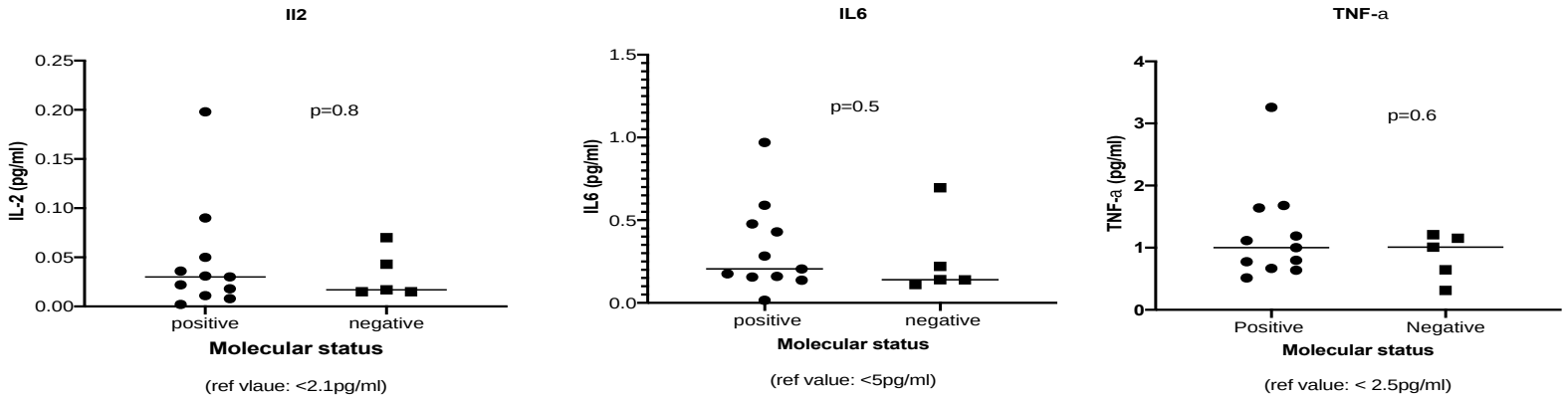
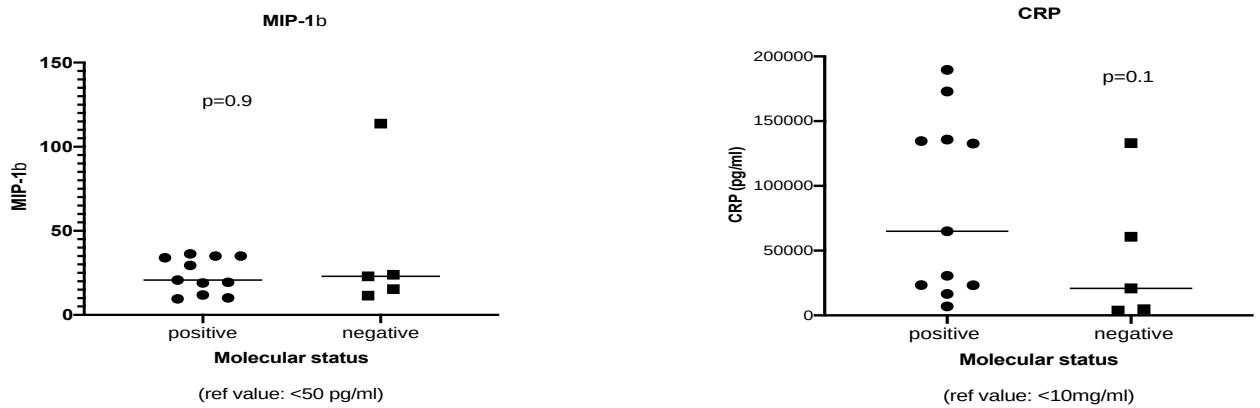


Figure 8. The frequency of HIV specific CD8 responses was significantly higher(p=0.01) in the molecular negative EC (median=248 SFU/106 PBMCs), IQR=115-293 than molecular positive (median =33 SFU/106 PBMCs) IQR= 0-75.

No difference in plasma cytokines between molecular positive and molecular negative EC.





CONCLUSIONS

- We have described the molecular, serological and immunological characteristics of a small but long-standing HIV+ EC cohort (median time from diagnosis 8 years).
- In this cohort, the EC can be further categorised as molecular positive and molecular negative.
- The higher frequency of HIV specific CD8 responses observed can suggest that this may be important in the level of control
- In this cohort, irrespective of molecular status of EC, there is no evidence of increased T-cell activation or inflammation.
- Further studies are essential to determine the role of lifelong ART in such EC.

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QUESTIONS?

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