POSTER # 266

Herpesvirus Infections in HIV+ Individuals on ART Are Not Associated with Immune Activation

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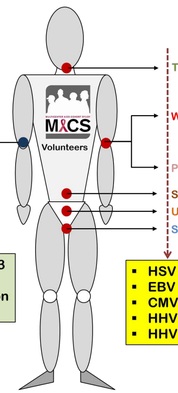
BACKGROUND

- HIV(+) individuals who are virally suppressed on chronic ART continue to be at an increased risk for non-AIDS-associated chronic diseases compared to seronegative individuals.
- This increased risk has been associated with elevated levels of inflammation and immune activation which persist despite effective ART.
- We evaluated whether reactivation of herpesviruses in different body compartments is associated with persistently elevated levels of immune activation and inflammation.
- We enrolled HIV(+) volunteers (N=15) in the Multicenter AIDS Cohort Study who have been virally suppressed on ART and with CD4⁺ T cells ≥500 as well as age-matched controls (N=12).

METHODS & DEMOGRAPHICS

- HIV+
  - On ART; CMV AB+
  - Suppressed for at least 2 years
  - CD4≥500
- Age/risk factor-matched, CMV Ab+ controls

- Median age = 44
- Median CD4 = 803
- Median years infected = 9



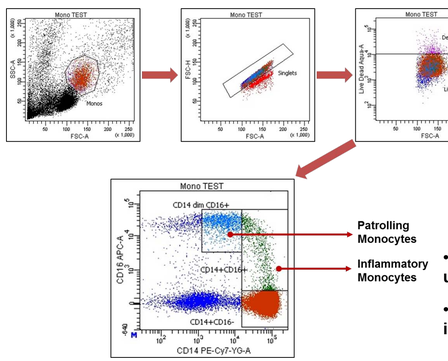
- sCD14/sCD163
- hsCRP & IL-6
- T cell activation
- CD14⁺CD16⁺

- Flow
- ELISA

- HSV 1/2
- EBV
- CMV
- HHV6
- HHV8

- Nucleic acid was isolated from the different specimens using an automated nucleic acid extractor (EasyMag)
- Before isolation, equal amounts of DNA control virus were spiked into each sample.
- Herpesvirus DNA was measured with a high throughput ViiA7 machine in multiplex PCR format
- For each target virus, a virus-specific standard curve series was included in the same run to get accurate viral quantification

INFLAMMATORY/PATROLLING MONOCYTE GATING

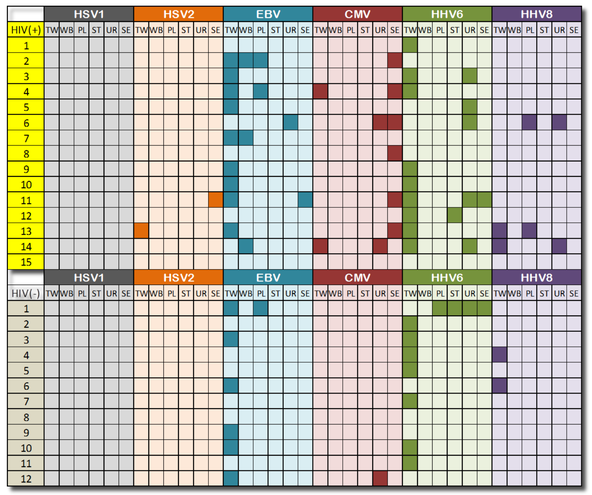


- Inflammatory monocytes (CD14⁺CD16⁺) are reported to have higher expression of pro-inflammatory cytokines.
- Patrolling monocytes (CD14^{dim}CD16⁺) have been shown to recognize viral nucleic acids.

- The monocyte population was gated using forward and side scatter.
- Only live singlets were used in gating inflammatory and patrolling monocytes.

HERPESVIRUS IN DIFFERENT BODY COMPARTMENTS

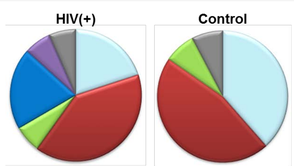
TW – throat wash
WB – whole blood
PL - plasma
ST - stool
UR – urine
SE – semen



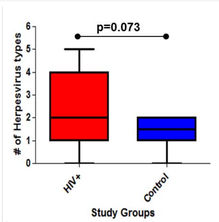
- Herpesviral DNA was detected mostly in throat washings of both HIV(+) and control groups.
- HHV6 and EBV were the most common herpesvirus types detected.
- 40% in the HIV(+) group had herpesvirus reactivation in the blood compared to 8.3% in the control group.
- CMV reactivation was mostly seen in the semen of the HIV(+) group.

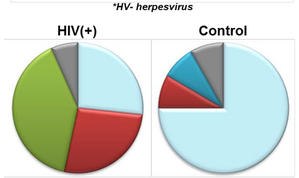
HERPESVIRUS REACTIVATION IN HIV(+) AND CONTROLS

- 14/15 HIV(+) and 11/12 controls showed evidence of herpesvirus reactivation in at least one body compartment.
- HIV(+) subjects tended to have more types of herpesvirus that reactivated compared to controls (p=0.073) with up to 5 types of herpesviruses reactivating in different compartments while on suppressive ART.
- HIV(+) subjects reactivated in more body compartments (median=2) than controls (p=0.037)

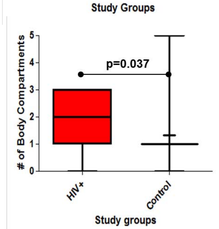


*HV- herpesvirus





*BC – body compartment



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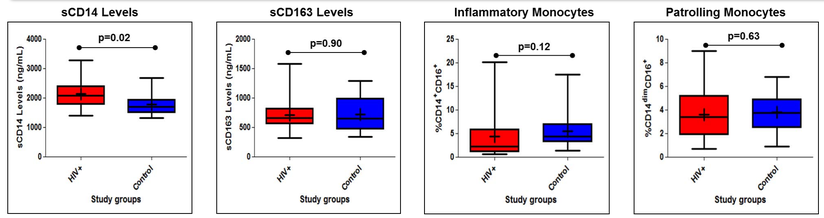
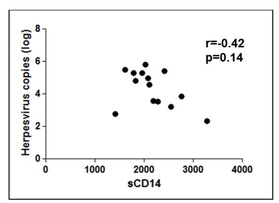
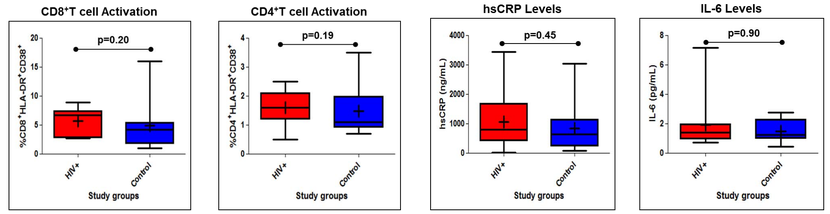
INNATE IMMUNE ACTIVATION

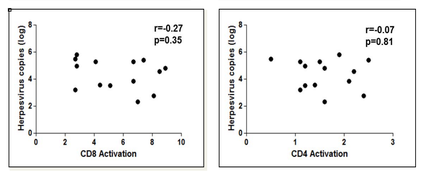




- Despite virologic suppression and immune reconstitution, levels of sCD14, a marker of monocyte activation, were still elevated in the HIV(+) group.
- Levels of macrophage activation (sCD163) as well as the frequencies of inflammatory and patrolling monocytes are similar between the two groups.
- Levels of sCD14 did not correlate with the number of viral copies of reactivating herpesviruses.
- The frequency of circulating inflammatory monocytes correlated with the number herpesvirus copies reactivating in the blood. (r=0.6; p=0.02)

T CELL ACTIVATION AND SYSTEMIC INFLAMMATION





- Levels of T cell activation as well as the levels of inflammatory markers, hsCRP and IL-6, were comparable between the two groups.
- CD8⁺ and CD4⁺ T cell activation as well as the levels of hsCRP and IL-6 did not correlate with the number of viral copes or reactivating herpesviruses.

CONCLUSIONS

- Despite virologic suppression and immune reconstitution on ART, HIV(+) individuals have more herpesvirus reactivating in different body compartments.
- Monocyte activation, as measured by sCD14, remains elevated in HIV(+) individuals on effective ART.
- However, viral reactivation, in terms of viral copies, number of herpesvirus types, or number of body compartments where the herpesviruses reactivated, did not correlate with levels of sCD14, T cell activation, and soluble inflammatory biomarkers.