AIDS
2022 Oct 1;36(12):1617-1628. doi: 10.1097/QAD.0000000000003301. Epub 2022 Jun 22.

No evidence that circulating HIV-specific immune responses contribute to persistent inflammation and immune activation in persons on long-term ART

Adam R Ward[1,2,3], Allison S Thomas[4], Eva M Stevenson[1], Szu-Han Huang[1,2], Sheila M Keating[5,6], Rajesh T Gandhi[7], Deborah K McMahon[8], Ronald J Bosch[9], Bernard J Macatangay[8], Joshua C Cyktor[8], Joseph J Eron[10], John W Mellors[8], R Brad Jones[1,2]; ACTG A5321 Team
Affiliations expand

- PMID: 35730388
- PMCID: PMC9444951 (available on 2023-10-01)
- DOI: 10.1097/QAD.0000000000003301

Abstract

Objective: People with HIV (PWH) have persistently elevated levels of inflammation and immune activation despite suppressive antiretroviral therapy (ART), with specific biomarkers showing associations with non-AIDS-defining morbidities and mortality. We investigated the potential role of the HIV-specific adaptive immune response, which also persists under ART, in driving levels of these clinically relevant biomarkers.

Design: Cohort-based study.

Methods: HIV-specific IFN-γ-producing T-cell responses and antibody concentrations were measured in blood at study entry in the ACTG A5321 cohort, following a median of 7 years of suppressive ART. HIV persistence measures including cell-associated (CA)-DNA, CA-RNA, and plasma HIV RNA (single-copy assay) were also assessed at study entry. Plasma inflammatory biomarkers and T-cell activation and cycling were measured at a pre-ART time point and at study entry.

Results: Neither the magnitudes of HIV-specific T-cell responses nor HIV antibody levels were correlated with levels of the inflammatory or immune activation biomarkers, including hs-CRP, IL-6, neopterin, sCD14, sCD163, TNF-α, %CD38 + HLA-DR + CD8 + and CD4 + cells, and %Ki67 + CD8 + and CD4 + cells - including after adjustment for pre-ART biomarker level. Plasma HIV RNA levels were modestly correlated with CD8 + T-cell activation (r = 0.25, P = 0.027), but other HIV persistence parameters were not associated with these

biomarkers. In mediation analysis, relationships between HIV persistence parameters and inflammatory biomarkers were not influenced by either HIV-specific T-cell responses or antibody levels.

Conclusion: Adaptive HIV-specific immune responses do not appear to contribute to the elevated inflammatory and immune activation profile in persons on long-term ART.