Occult CMV replication is a persistent driver of effector T cell expansion in PWH on effective ART

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BACKGROUND

CMV infection is a driver of immune activation and senescence, with greater impact in the setting of HIV-1 co-infection, where it contributes to CD8⁺ T cell expansion and low CD4/CD8 T cell ratios. CMV replication occurs primarily in people living with HIV-1 (PLWH) with low blood CD4⁺ T cell counts, but occult CMV replication may persist in some tissues due to incomplete CD4⁺ T cell reconstitution on antiretroviral therapy (ART), particularly in the gut, dissociated from restored blood CD4⁺ T cell counts. This occult CMV replication may drive CMV-specific antibodies and effector T cells even in PLWH on successful ART.

METHODS

In a sub-study of ANRS EP61 GALT, 15 PLWH who were also CMV seropositive (CMV+), 15 controls without HIV but CMV+, 12 PLWH without CMV (CMV-) and 12 double-negative controls were included for FACS immunophenotyping of circulating T cells. CMV viremia was assessed by PCR. Anti-CMV IgG titers were measured as a marker of immune stimulation by CMV.

RESULTS

CMV viremia was negative in all CMV+ subjects.

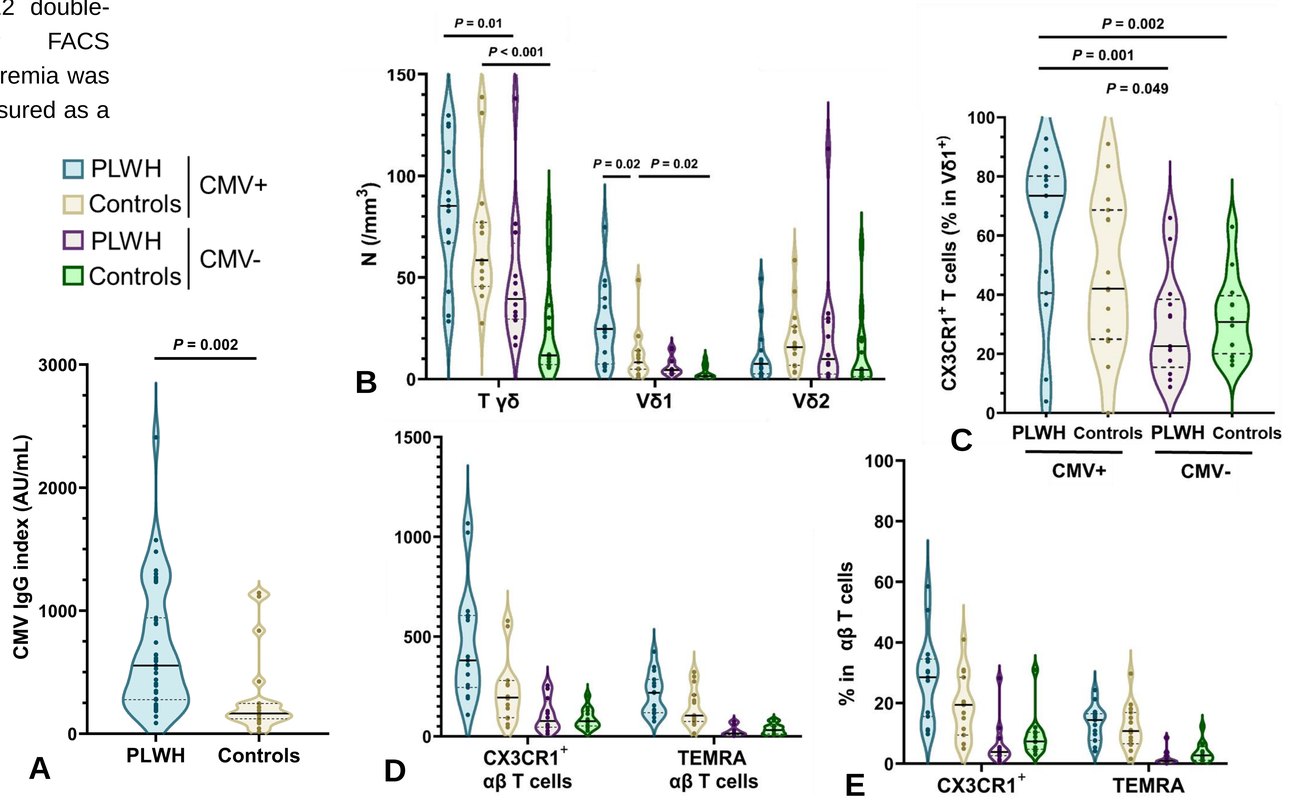
Figures.

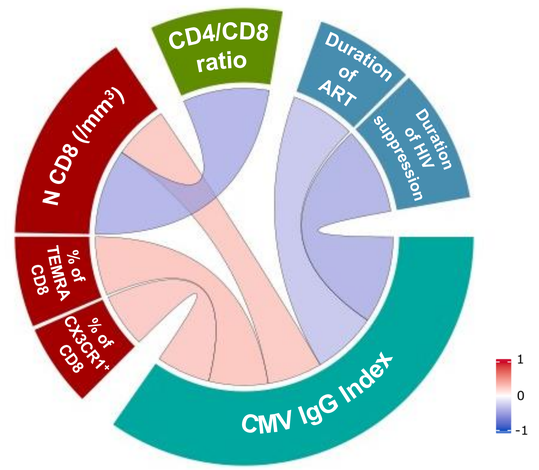
(A) CMV+ PLWH had significantly higher anti-CMV IgG titers than CMV+ HIV-negative controls

(B and C) Effectors CX3CR1⁺ Vδ$_1$ T cells subset expansion among circulating non conventional γδ T cells during HIV-1 infection under ART according to CMV serological status

(D and E) CX3CR1⁺ and TEMRA subsets expansion among circulating CD3⁺ αβ T cells according to serological status

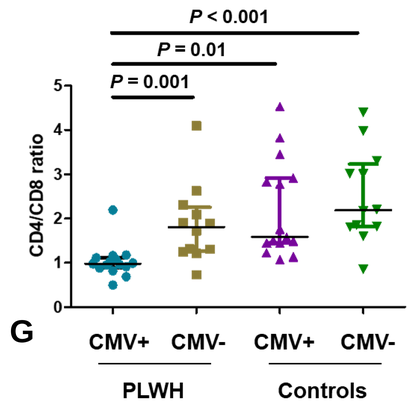
In PLWH on effective ART, even with restored CD4⁺ T cell counts and undetectable CMV DNA in the blood, **occult CMV replication** is associated with expansion of **CX3CR1⁺ CD8** and **Vδ$_1$** T cells, which correlates with anti-CMV IgG levels





(F) Associations between CMV IgG index, CD8 T cells and time on ART in PLWH (n = 42). Color scale indicates Spearman's correlation coefficient.

(G) CD4/CD8 ratio according to HIV-1 and CMV status



CONCLUSIONS

Occult CMV replication during HIV-1 infection is involved in the expansion of several circulating T cell populations, particularly Vδ1 T cells, even in PLWH on effective ART with restored circulating CD4 T cell counts and undetectable CMV DNA in their blood. CX3CR1 expression on T cells is associated with CMV status and is likely driven by occult CMV replication. CMV IgG titers may be used as a surrogate for occult CMV replication.

ADDITIONAL KEY INFORMATION

Contact delobel.p@chu-toulouse.fr

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