Frequencies of CD4+ and CD8+ T cells immune activation are reduced in PLWH after 5 years of antiretroviral therapy

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Background

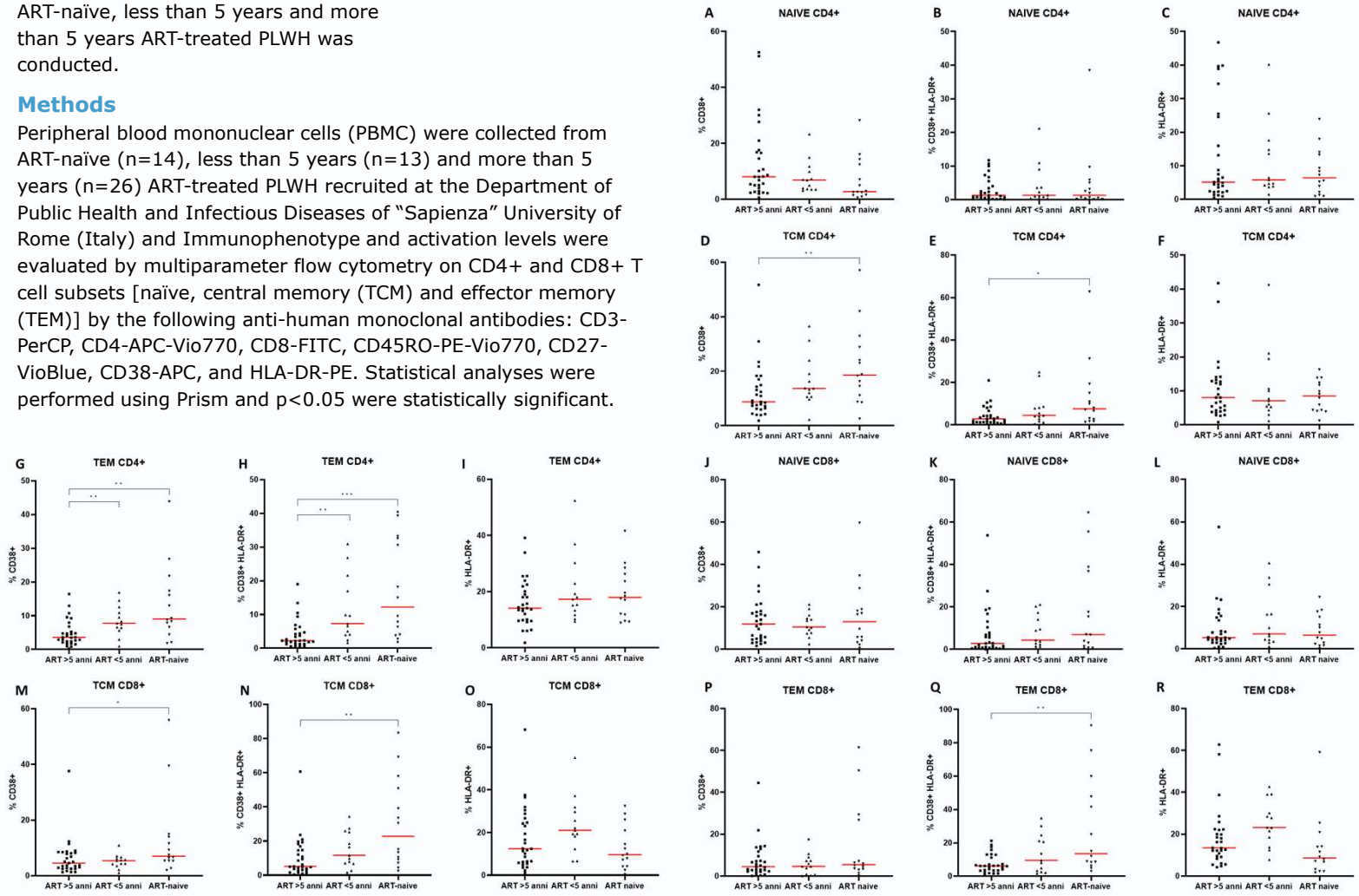
Chronic immune activation represents one of the main determinants of a senescent immune phenotype in people living with HIV-1 (PLWH). To address the effectiveness of antiretroviral therapy (ART) in reducing chronic CD4+ and CD8+ T cells immune activation, an observational study comparing peripheral blood immune activation status between ART-naïve, less than 5 years and more than 5 years ART-treated PLWH was conducted.

Methods

Peripheral blood mononuclear cells (PBMC) were collected from ART-naïve (n=14), less than 5 years (n=13) and more than 5 years (n=26) ART-treated PLWH recruited at the Department of Public Health and Infectious Diseases of "Sapienza" University of Rome (Italy) and Immunophenotype and activation levels were evaluated by multiparameter flow cytometry on CD4+ and CD8+ T cell subsets [naïve, central memory (TCM) and effector memory (TEM)] by the following anti-human monoclonal antibodies: CD3-PerCP, CD4-APC-Vio770, CD8-FITC, CD45RO-PE-Vio770, CD27-VioBlue, CD38-APC, and HLA-DR-PE. Statistical analyses were performed using Prism and $p<0.05$ were statistically significant.

Results

Frequencies of CD4+ naïve and CD8+ naïve T cells expressing CD38, HLA-DR or both markers were similar between the three groups. PLWH treated for more than 5 years exhibited lower frequencies of CD38+ ($p = 0.0074$ and 0.0021) and CD38+ HLA-DR+ CD4+ TCM and TEM cells ($p = 0.0152$ and $p = 0.0002$, respectively), CD38+ CD8+ TCM cells ($p = 0.0358$), CD38+ HLA-DR+ CD8+ TCM and TEM cells ($p = 0.0068$ and $p = 0.0026$, respectively) as compared to ART-naïve PLWH. Moreover, PLWH ART-treated for less than 5 years had increased levels of CD38+ ($p = 0.0058$) and CD38+ HLA-DR+ CD4+ TEM cells ($p = 0.0018$) compared to PLWH treated for more than 5 years. By contrast, no differences in the percentages of the other T cell subsets (HLA-DR+ CD4+ TCM and TEM cells, CD38+ HLA-DR+ and HLA-DR+ CD8+ TCM cells, HLA-DR+ CD8+ TEM cells) were recorded among the three groups.



Immune-activation markers expression by CD4+ and CD8+ cells between more than 5 years, less than 5 years ART-treated and ART-naïve PLWH . Naive CD4+ cells expressing CD38 **(A)**, CD38 and HLA-DR **(B)**, HLA-DR **(C)**; TCM CD4+ cells expressing CD38 **(D)**, CD38 and HLA-DR **(E)**, HLA-DR **(F)**; TEM CD4+ cells expressing CD38 **(G)**, CD38 and HLA-DR **(H)**, HLA-DR **(I)**; naive CD8+ cells expressing CD38 **(J)**, CD38 and HLA-DR **(K)**, HLA-DR **(L)**. TCM CD8+ cells expressing CD38 **(M)**, CD38 and HLA-DR **(N)**, HLA-DR **(O)**; TEM CD8+ cells expressing CD38 **(P)**, CD38 and HLA-DR **(Q)**, HLA-DR **(R)**.

Conclusions

These findings suggest the efficacy of ART in reducing the immune activation levels of TEM CD4+ T cell in both group of treated PLWH, while in TCM CD4+ and TCM and TEM CD8+ the immune activation reduction is observed only after more than 5 years of ART.

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