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PERSISTENT IMMUNE ACTIVATION IN HIV-1 TREATED SUBJECTS COMPARED WITH NON-HIV CONTROLS

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BACKGROUND

Low-grade inflammation predict non-AIDS events in people living with HIV.

We compared the inflammatory profile of HIV-infected participants on long-term antiretroviral therapy (ART) to two HIV-uninfected groups, with distinct health behaviors.

METHODS

Design: a cohort-nested cross-sectional study

Study participants:

- **108 men and 42 women from the ANRS Primo cohort** (national, prospective, multicenter cohort of individuals diagnosed in acute or early HIV infection), treated >3 years with sustained HIV RNA < 50 copies/mL

- **100 men and 41 women from the ANRS Cohvac cohort** (cohort of volunteers who participated in HIV preventive vaccine trials implemented between 1992 and 2007)

- **102 men from the ANRS Ipergay trial** (preexposure prophylaxis trial, among men who have sex with men a high risk for HIV infection)

HIV negative controls were matched 1:1 with Primo subjects for sex and age by 5-year strata of age.

Measures:

Plasma levels of ten soluble biomarkers, including non-specific markers of inflammation (us-CRP, IL-6, TNF-α, sTNFRII), markers associated with monocyte activation (sCD14, sCD163, CXCL10), epithelial dysfunction (I-FABP, IL-17) and fibrosis (hyaluronic acid).

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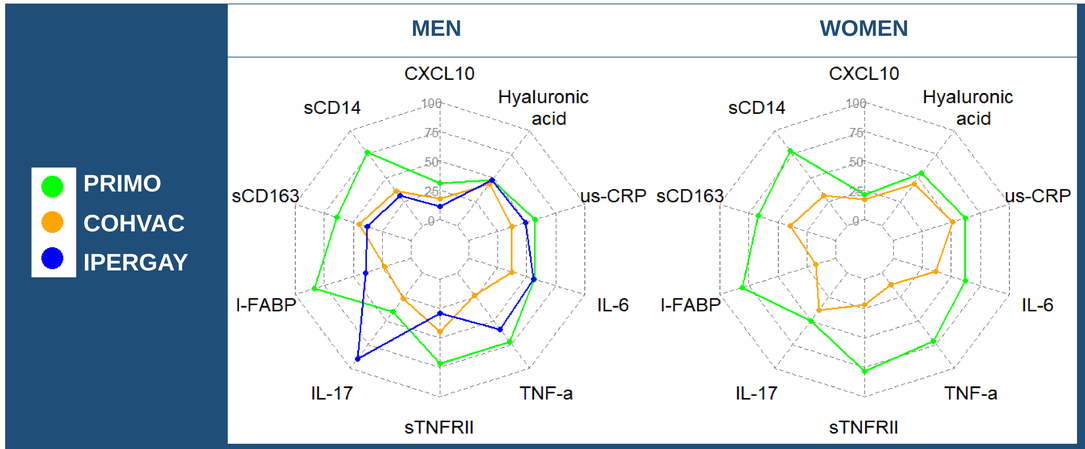


Figure 1. Comparison of inflammatory profiles as shown by radar chart

Each axis displays the proportion from 0 to 100% of high producers for a given biomarker, i.e. the proportion of individuals who had a level greater than the median level of the three groups combined.

After adjusting for age, smoking, alcohol use, and body mass index, both PRIMO men and women had higher levels of sCD14, sCD163, sTNFRII and I-FABP than their IPERGAY and COHVAC counterparts.

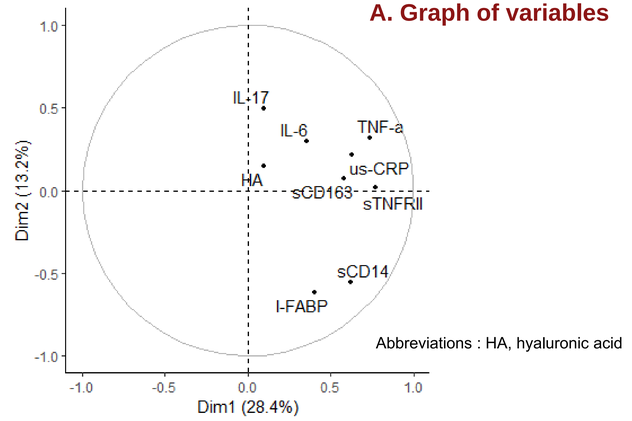
RESULTS

Table 1. Characteristics of study participants

Variables	Primo, n= 150		Cohvac, n=141		Ipergay, n=102		P-value
Age, years	47	(41, 53)	49	(44, 55)	47	(41, 51)	
Women	28.0	(42)	19.1	(41)	0	(0)	
Overweight or obesity	23.3	(35)	nd	nd	28.4	(29)	0.98
Current smoker	50.0	(75)	12.9	(18)	42.2	(43)	< .0001
Alcohol consumption	71.3	(107)	23.4	(33)	75.5	(77)	< .0001
Cumulative treatment duration, months	73	(60, 94)					
CD4 T-cell count, cells/µL	733	(598, 896)					
CD4:CD8 ratio	1.2	(0.9, 1.7)					
Ultrasensitive HIV RNA level							
Detectable	36.0	(54)					
Detection threshold, copies/mL	3	(2, 3)					
Detectable samples, copies/mL	11	(4, 34)					
Total HIV DNA levels, $\log_{10}$ copies/10^6 PBMCs	2.54	(2.04, 2.88)					

Data are presented as the median (interquartile range) or percentage (No.).
Abbreviations. nd, not documented; PBMCs, peripheral blood mononuclear cells

A. Graph of variables



Abbreviations : HA, hyaluronic acid

B. Graph of individuals

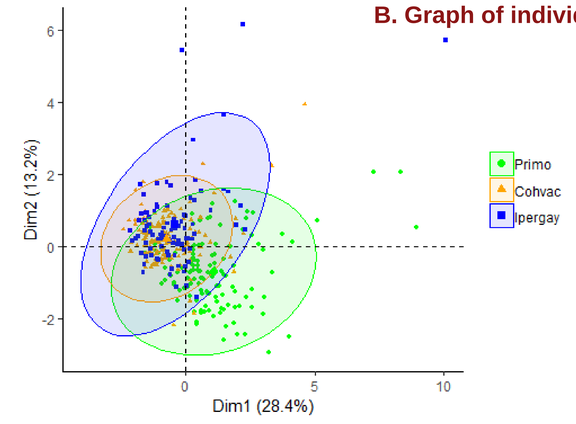


Figure 2. Principal components (PC) analysis

A. Graph of variables. The first PC was mainly defined by sTNFRII, us-CRP, TNF-α and sCD163. The second PC was mainly defined by IL-17 and I-FABP. Soluble CD14 contributed to both components.

B. Graph of individuals. The ellipse of the Primo participants partly overlapped with those of the Cohvac and Ipergay groups: one-third of the Primo participants had an inflammatory profile similar to that of the majority of controls, while the remaining two-thirds showed increased inflammatory levels, especially of sTNFRII, sCD14, sCD163 and I-FABP.

CONCLUSIONS

After a median of 6 years on suppressive ART, HIV-infected participants maintained high levels of monocyte activation and gut epithelial activity.