TARGETED INFLAMMATORY PLASMA PROTEOMICS SHOWS UPREGULATION OF DISTINCT PATHWAYS

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BACKGROUND

• Despite long-term suppressive antiretroviral therapy (ART), people living with HIV (PLHIV) display persistent inflammation leading to non-AIDS-related comorbidities.

• To increase our understanding of the underlying mechanisms, we compared plasma inflammatory protein concentration between PLHIV using long-term suppressive ART and healthy controls (HC) and correlated these with markers of inflammation.

METHODS

Discovery cohort (192 PLHIV & 416 HC) Validation cohort (649 PLHIV & 98 HC)

Targeted proteomics 92 inflammatory proteins by Olink®
Plasma inflammatory markers (n=16) by ELISA
White blood cells population by flow cytometry
PLHIV (n=192) were followed-up for 5 years for clinical events

RESULTS

Compared to healthy controls, PLHIV exhibited a distinct and upregulated inflammatory protein (n=29; Figure 1A), consisting of mucosal defense chemokines, CCR5 and CXCR3 ligands, and growth factors (Figure 1B). Unsupervised clustering of plasma inflammatory proteins clearly differentiated PLHIV with high levels of inflammation (n=65) from those with low inflammation (n=123) (Figure 2A).

During five years follow-up, PLHIV in the high inflammation group were at higher risk to develop malignancies (13.8% vs 4%; relative risk 3.4; 95% confidence interval 1.2 to 9.8) and showed a trend for cardiovascular disease events (12.3% vs 7.3%) compared to PLHIV with low inflammation (Figure 2B).

ADDITIONAL FINDINGS

• Differentially expressed proteins correlated strongly with plasma inflammatory markers in PLHIV using long-term suppressive ART.

• Malignancy development associated with higher TNFRSF14 and FGF-23 protein expression, while higher QSM, CCL19, SLAMF1 and HGF associated with cardiovascular disease events.

CONCLUSIONS

• Distinct inflammatory proteins and pathways may serve as potential biomarkers and therapeutic targets in PLHIV on long-term ART.

• Clinicians should be aware that PLHIV with a high inflammation endotype are at increased risk to develop malignancies and cardiovascular diseases.

CONTACT INFORMATION

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