Low Tryptophan Catabolism Marks Immune Preservation in HIV+ Viremic Non-Progressors

0246

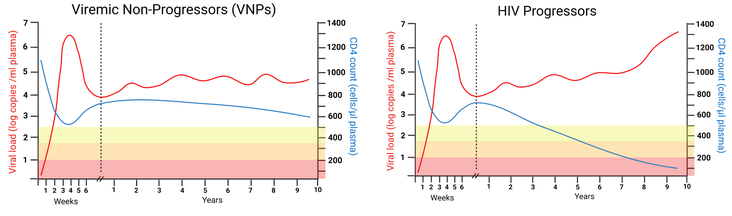
Ángel Bayón-Gil[1], Aaron Goldman[2], Judith Dalmau[1], Kai Ying Hong[2], Jane Koshy[2], Leila Giron[2], Mohamed Abdel-Mohsen[2], Javier Martínez-Picado[1,3,4,5], Maria C Puertas[1,4]

[1]IrsiCaixa AIDS Research Institute, Badalona, Spain, [2]The Wistar Institute, Philadelphia, PA, US, [3]University of Vic-Central University of Catalonia (UVic-UCC), Vic, Spain, [4]CIBERINFEC, Madrid, Spain, [5]Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain

Contact author: abayon@irsicaixa.es; mcpuertas@irsicaixa.es.

BACKGROUND

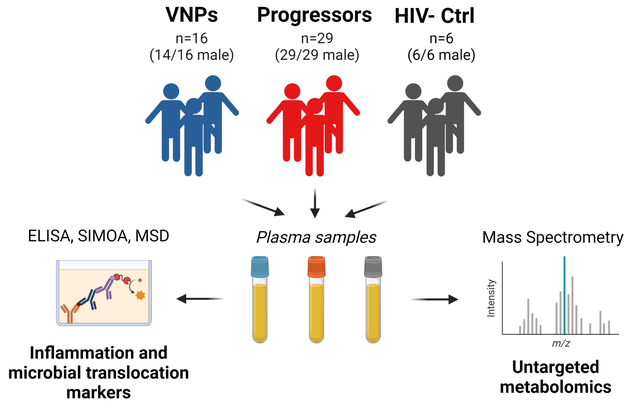
Viremic Non-Progressors (VNPs) maintain high CD4⁺ T cell counts despite high HIV viremia in the absence of antiretroviral treatment (ART), resembling non-pathogenic SIV infection in natural hosts.



We have previously shown that VNPs express lower levels of Interferon (IFN)-stimulated genes than HIV Progressors across multiple immune cells. Elevated **IFN responses** can alter **host metabolism** to impact immune homeostasis. We aim to explore the potential links between IFN responses, host metabolic alterations, and immune status in VNPs.

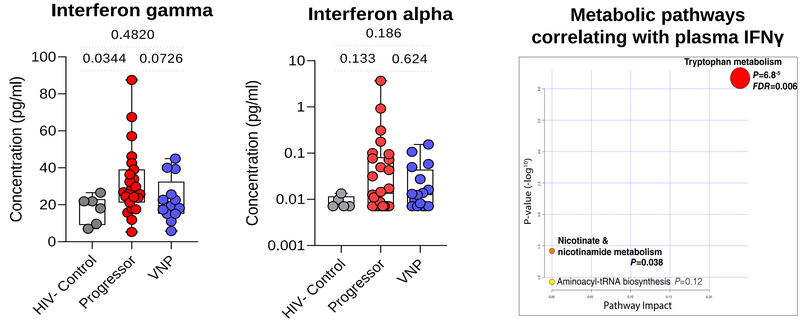
METHODS

We retrospectively selected plasma samples from 16 ART-naive **VNPs** and 29 ART-naive HIV **Progressors** with similar viral load (VL; median log VL>4) but different CD4 decay rates (median annual CD4 loss <10% and >10%, respectively). Plasma samples from six **HIV-1 seronegative** individuals (HIV- Ctrl) were included as a reference.

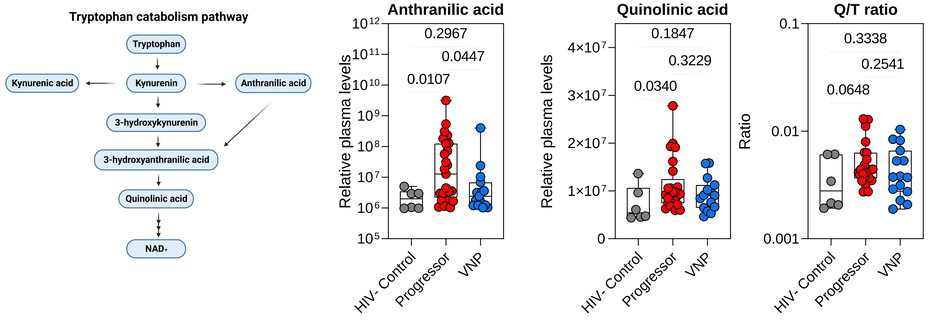


RESULTS

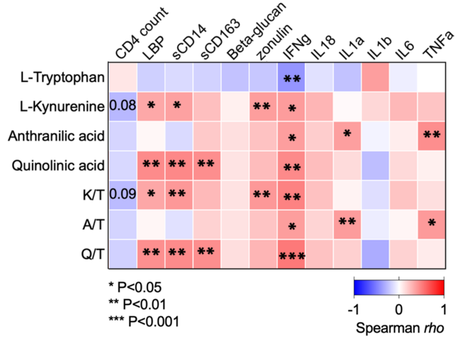
Plasma levels of the proinflammatory type II IFN (**IFNγ**) were similar in VNPs and HIV- controls, but increased in Progressors. However, no difference in the levels of the antiviral type I IFN (**IFNα**) was observed among the three groups. Levels of plasma IFNγ were strongly associated with an upregulation of **tryptophan (Trp) catabolism** and nicotinamide metabolism pathways.



Levels of metabolites within the Trp catabolism pathway with established immunomodulatory roles were increased in Progressors, but not in VNPs, compared to HIV- controls.

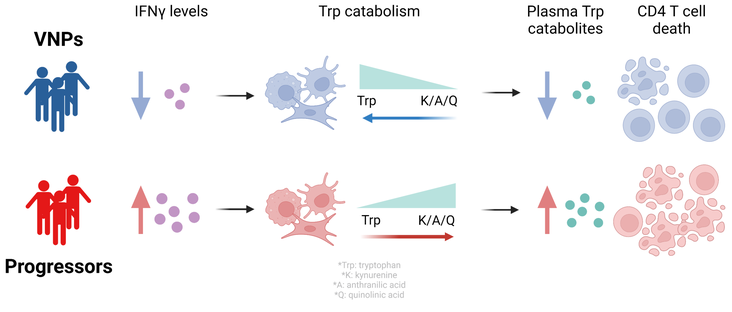


Finally, high Trp catabolism correlated with high levels of proinflammatory cytokines and low CD4 counts**.**



CONCLUSIONS

Increased Trp catabolism, as observed in HIV Progressors, is known to restrain CD4 T cell function and decrease T cell survival. Conversely, we have found that unaltered Trp metabolic profile was linked to immune preservation in VNPs.



Unraveling the mechanistic links between Trp catabolism pathway and the phenotype of VNPs may guide the development of novel therapeutic strategies to maintain immune homeostasis during HIV infection. Trp metabolites might also serve as biomarkers of immune preservation in HIV infection.

Unaltered **tryptophan** (Trp) metabolic profile with low levels of Trp catabolites is associated with **immune preservation** despite high HIV replication in **Viremic Non-Progressors**.

IrsiCaixa Institut de Recerca de la Sida · The Wistar Institute · ciberinfec · Gobierno de España · Ministerio de Universidades