Distinct Plasma Protein Changes Precede Loss of Spontaneous HIV Control

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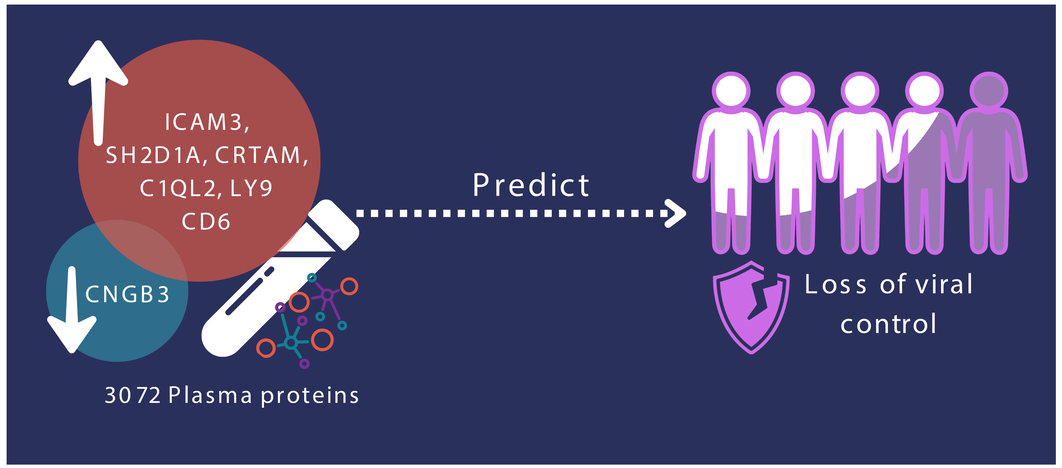
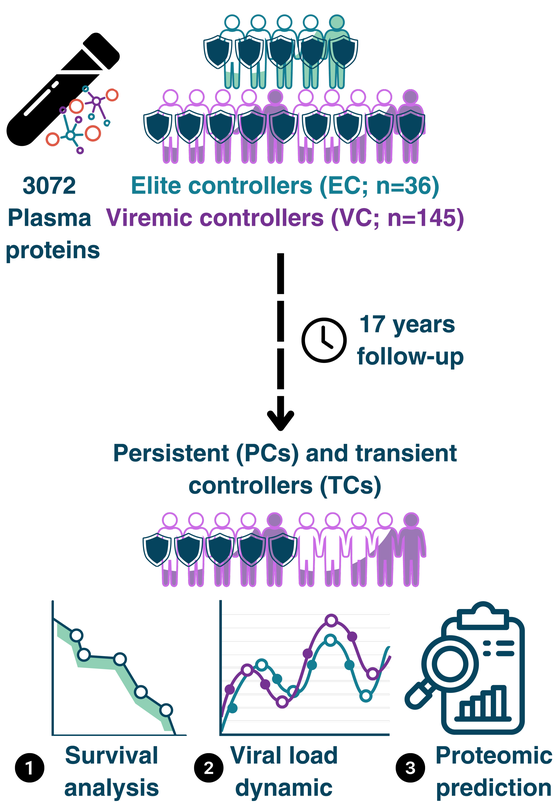
BACKGROUND

Understanding antiretroviral therapy (ART)-independent control of HIV is of paramount importance and central for HIV cure. Spontaneous HIV controllers are divided into elite controllers (EC; VL<50 c/ml) and viremic controllers (VC; VL<10.000 c/ml). Some lose viral control (transient controllers, TCs; VL>10.000 c/ml), while others are persistent (PCs).



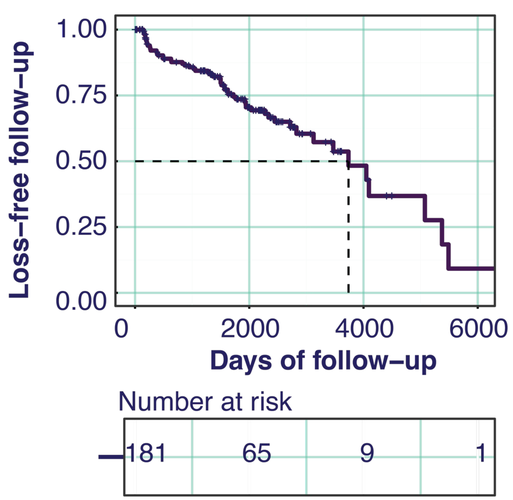
METHODS

The Dutch National ATHENA cohort



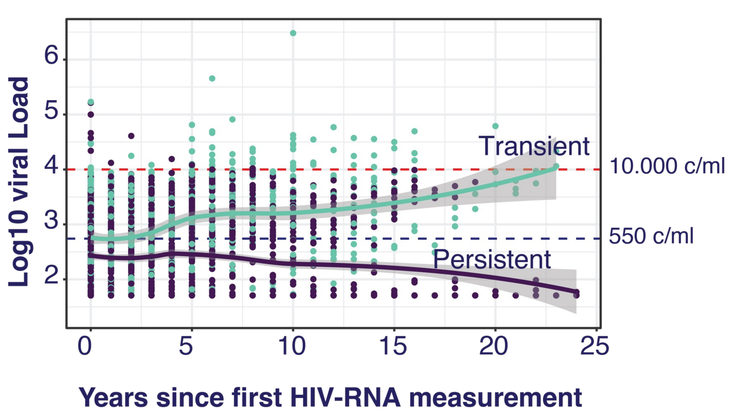
RESULTS

Survival analysis

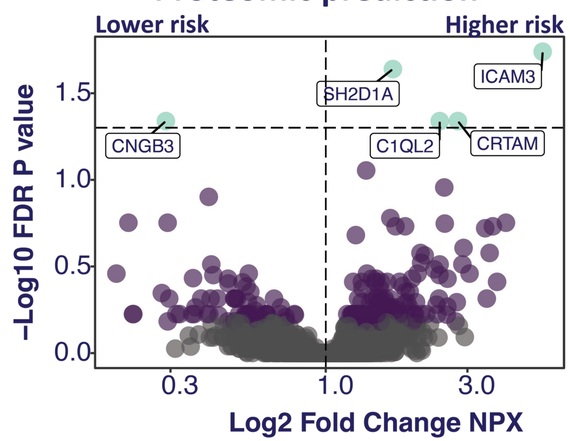


- Loss of controller status occurred in 31% (56/181) of HIV controllers, mainly in VC, after median of 10 years since HIV diagnosis.

Viral load dynamic



Proteomic prediction



- Over time, TCs exhibited an annual increase in VL by 1371 c/mL, whereas PCs exhibited a more stable VL.
- Dysregulation of 5 out of 3072 plasma proteins was observed over a median period of 4.2 years before loss of HIV control. Additionally, using an alternative definition of loss of viral control (either a 1000 c/ml increase in moving median viral load or viral load exceeding 10,000 c/ml), ICAM3, CRTAM, CD6, and LY9 were identified as associated with a higher risk of loss of viral control.

CONCLUSIONS

- Several years before loss of spontaneous viral control, TCs exhibited the upregulation of plasma proteins with known immune and cellular functions
- Our findings advance our understanding of ART-independent control mechanisms, underscoring the prospect of identifying early biomarkers for impending loss of HIV control.

ADDITIONAL KEY INFORMATION

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