Factors associated with the loss of elite HIV control after more than 20 years from diagnosis.

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Moral-Turón C[1], Gasca-Capote C[1], Casado C [2], Antequera M[1], Rafii-Idrissi Behnnia M[1], Vidal F[4,5], Olalla J[6], Sandonis V[2], Peraire J[4,5], Rull A[4,5], Valenzuela-Fernandez A[3], Lopez-Cortes LF[1], Blanco J[5,7,8, 9], Pernas M[2], Ruiz-Mateos E1[1]

[1] Institute of Biomedicine of Seville (IBiS), Virgen del Rocio University Hospital, Spanish National Research Council (CSIC), University of Seville, Clinical Unit of Infectious Diseases, Microbiology and Parasitology, Seville, Spain. [2] Molecular Virology Unit, Retrovirus Reference and Research Laboratory. National Centre of Microbiology, Carlos III Health Institute, Majadahonda, Spain, [3] Cellular and Viral Immunology Laboratory, Pharmacology Unit, Department of Medicine, Faculty of Health Sciences of the University of La Laguna, Ofra Campus, Tenerife, Spain, [4] Joan XXIII University Hospital of Tarragona, IISPV, University of Rovira i Virgili, Tarragona, Spain, [5] CIBERINFEC, Institute of Health Carlos III (ISCIII), Madrid, Spain, [6] Internal Medicine Department, [6] Costa Del Sol Hospital, Marbella, Spain, [7] IrsiCaixa, Badalona, Spain, [8] Germans Trias i Pujol Research Institute (IGTP), Badalona, Spain, [9] University of Vic-Central University of Catalonia (UVic-UCC), Vic, Spain.

BACKGROUND

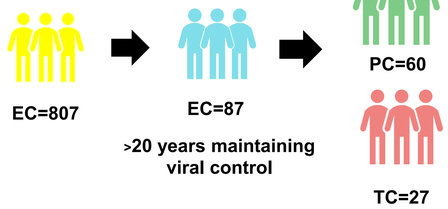
Persistent or exceptional elite controllers (PC) show undetectable HIV-1-RNA levels in plasma by commercially available techniques in the absence of antiretroviral treatment (ART) for more than 20 years and no clinical progression. However, anecdotal cases of loss of virological control are being reported in these individuals. At a population level, the factors associated with this loss of elite status are unknown.

OBJECTIVE

Analyzed clinical, epidemiological, and immunogenetic factors associated with the loss of elite control status after more than 20 years of follow-up from the HIV Controller Spanish cohort (ECRIS).

METHODS

From the HIV Controller Spanish cohort (ECRIS) (n=807), elite controllers who had virological control below the limits of detection for more than 20 years were selected.



We analyzed clinical, epidemiological, and immunogenetic factors associated with the loss of elite control status after more than 20 years of follow-up using binary logistic and Cox regression models

RESULTS

Table 1. Characteristics of elite persistent controllers (>20 years) from the ECRIS cohort.

Variable	Value
Total participants	87
Sex	39,1% (women) 60,9% (men)
ADVP transmission	83,90%
Age of diagnosis [IQR]	24 [21-29]
Nadir CD4+ T cell count (cell/ul) [IQR]	459 [350-675]
Participants with HLA typing	61
Protective HLA-B14, HLA-B27 or HLA B57	57,10%
Participants who lost elite control after >20 years (TC)	27 (31%)
Participants who mantain elite control after >20 years (TC)	60 (69%)

The absence of protective HLA-B alleles is associated with the loss of elite controller status after more than 20 years of follow-up.

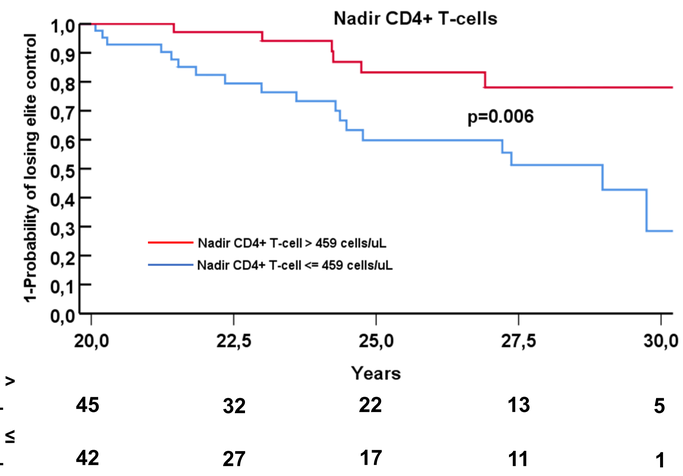


Figure 1. Kaplan–Meier curves showing the probability of losing elite control after 20 years of follow-up, stratified by nadir CD4+ T-cell count (>459 vs. ≤459 cells/µL). In univariate analysis, no differences were found between groups in sex, age, transmission route, or calendar year of diagnosis, whereas nadir CD4+ T-cell counts differed significantly (516 [397–718] in persistent controllers vs. 363 [270–601] in transient controllers, p = 0.006).

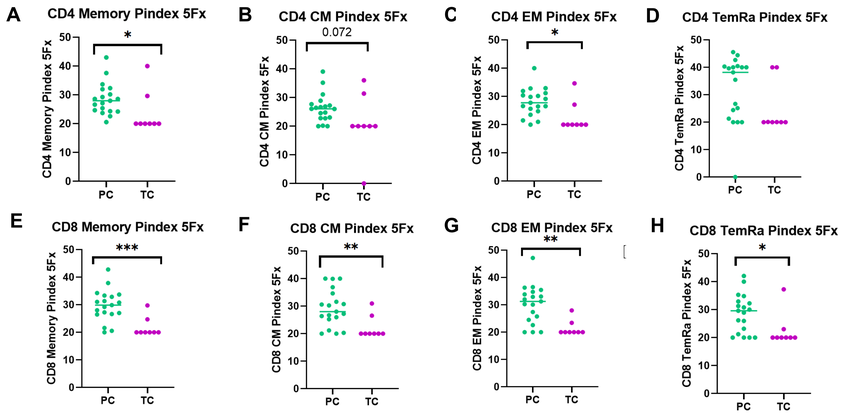
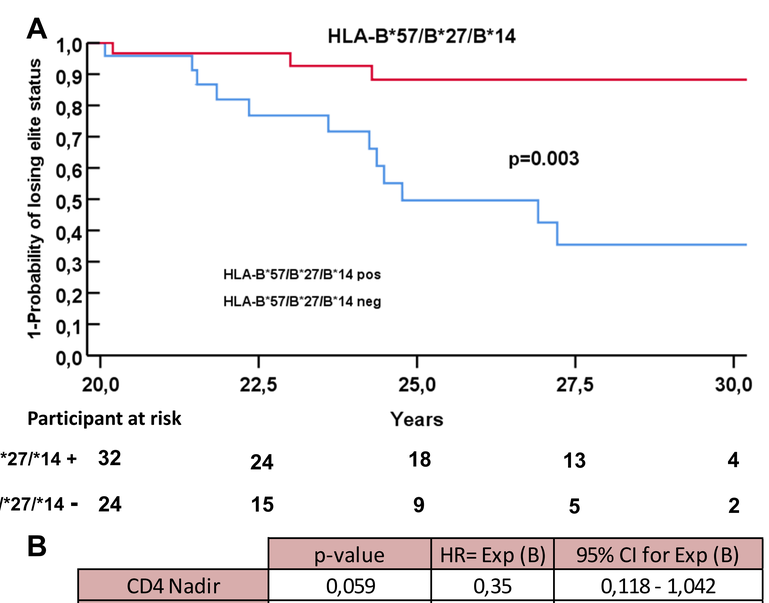


Figure 3 Gag-specific CD4+ and CD8+ T-cell polyfunctionality (IFNγ, TNF-α, IL-2, CD107a and Perforin). PC showed higher Gag-specific T-cell polyfunctionality than TC in A-D) Total memory, central memory (CM), effector memory (EF) and terminally differentiated (TemRA) CD4+ T-cells and in E-F) Total memory, central memory (CM), effector memory (EF) and terminally differentiated (TemRA) CD8+ T-cells.



B

	p-value	HR= Exp (B)	95% CI for Exp (B)
CD4 Nadir	0,059	0,35	0,118 - 1,042
HLA B27_14_57	0,005	0,191	0,06 - 0,608

Figure 2. A) Kaplan–Meier curves showing the probability of losing elite control after 20 years of follow-up, stratified by the presence of protective HLA-B14, HLA-B27, or HLA-B57 alleles. In univariate analysis, the presence of protective alleles was markedly more frequent in persistent controllers compared with transient controllers (74% vs. 22%, p = 0.001). After 25 years of follow-up, 91% of individuals carrying protective HLA-B14/B27/B*57 alleles still maintained elite control, whereas in those lacking these alleles, 58% of participants had already lost control.
B) In the Cox regression model, only the presence of protective alleles was independently associated with the absence of loss of control after 20 years of follow-up (p; Exp (B) [confidence interval [Exp (b)]; p=0.005; 0.191 [0.06-0.608]).

CONCLUSIONS

- Loss of control in controllers with more than 20 years of follow-up is relatively common and is primarily associated with the absence of protective HLA-B alleles.
- T-cell responses or innate immune factors may play a key role in sustaining exceptional long-term control

PLAIN LANGUAGE SUMMARY

PC can naturally suppress HIV to undetectable levels for decades without therapy, a phenomenon often linked to the presence of certain protective host genetic factors.

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Contact: cmoral-ibis@us.es
eruizmateos-ibis@us.es