Contrôle immuno-virologique du VIH : Facteurs de l'hôte

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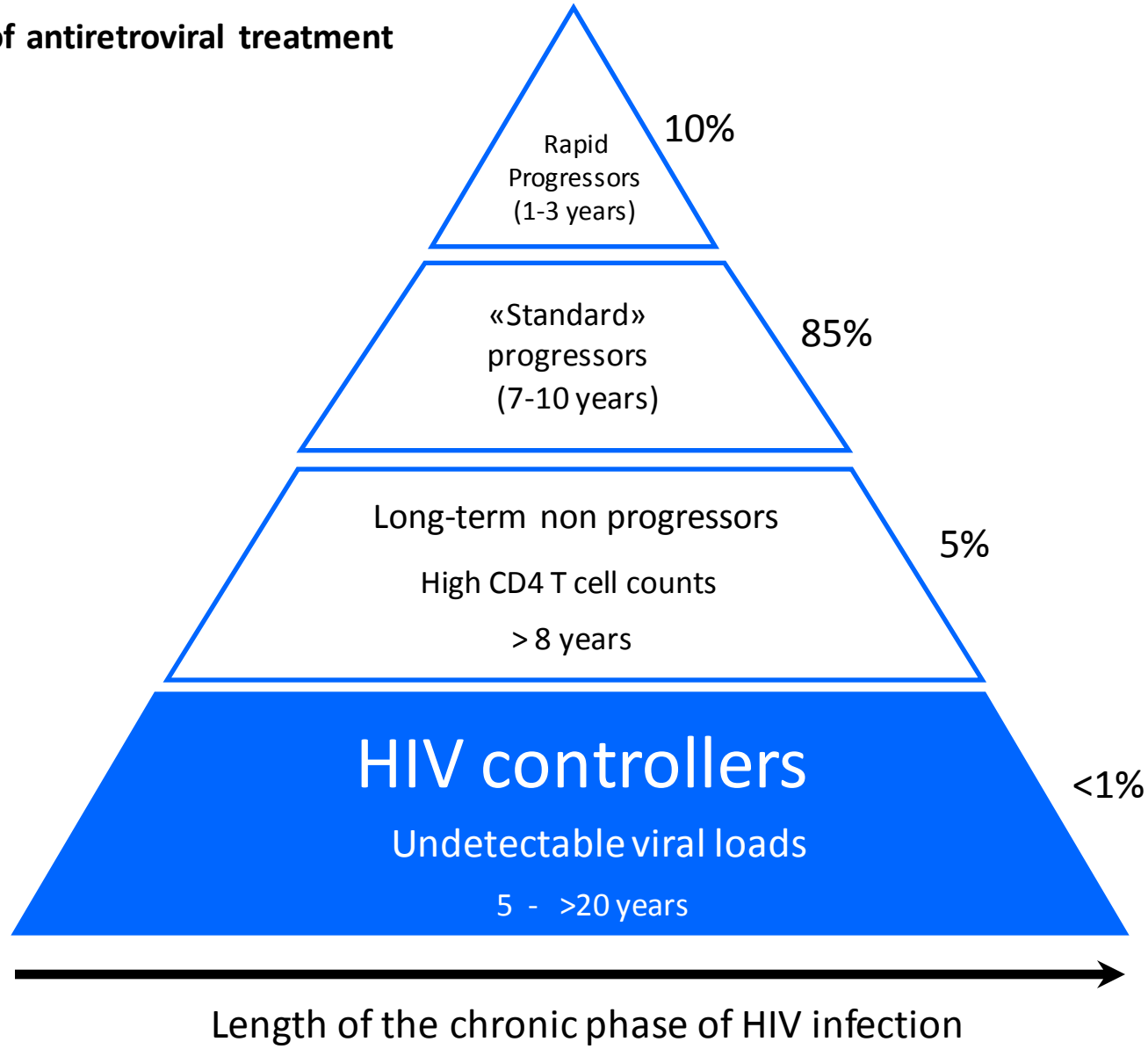
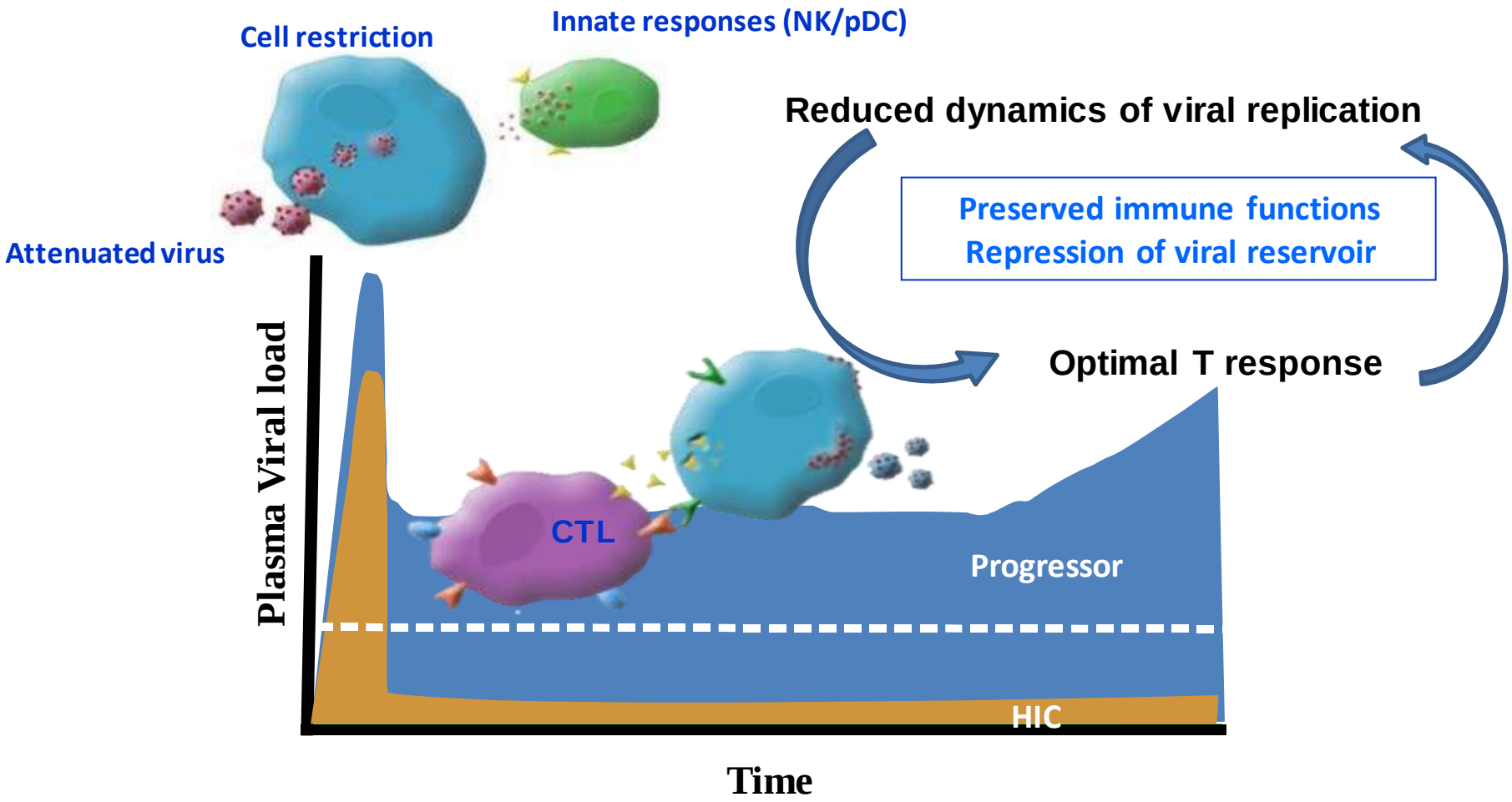
Different profiles of progression to AIDS

In the absence of antiretroviral treatment

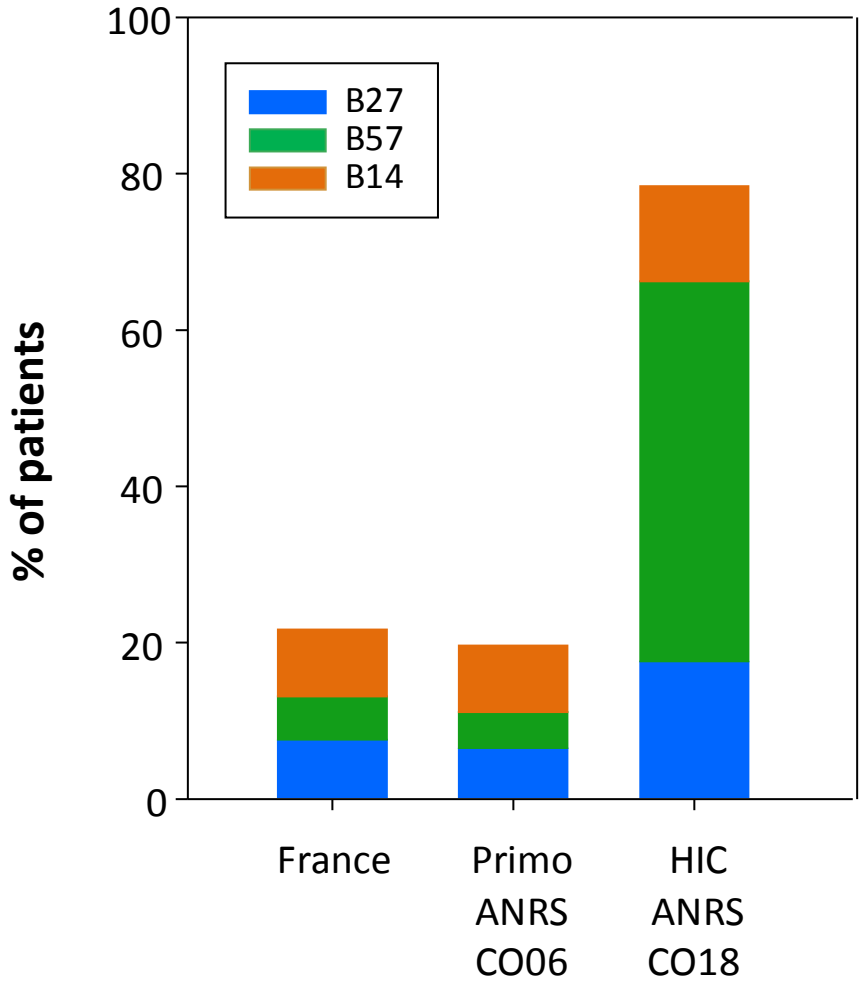


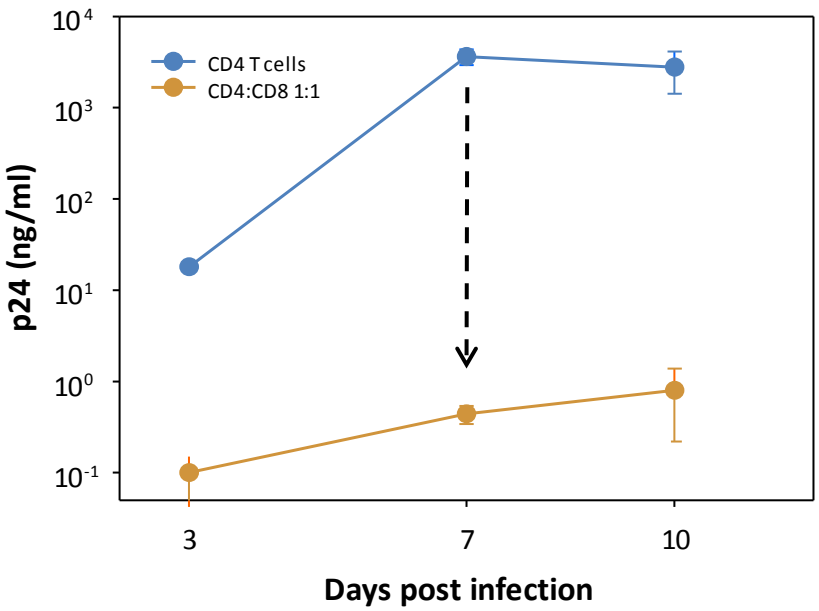
HIV controllers (HIC): infected individuals spontaneously controlling HIV-1 infection



Pancino and Saez-Cirion. Immunological Reviews. 2013

Favorable genetic background and Efficient CD8 T cell responses are associated with control

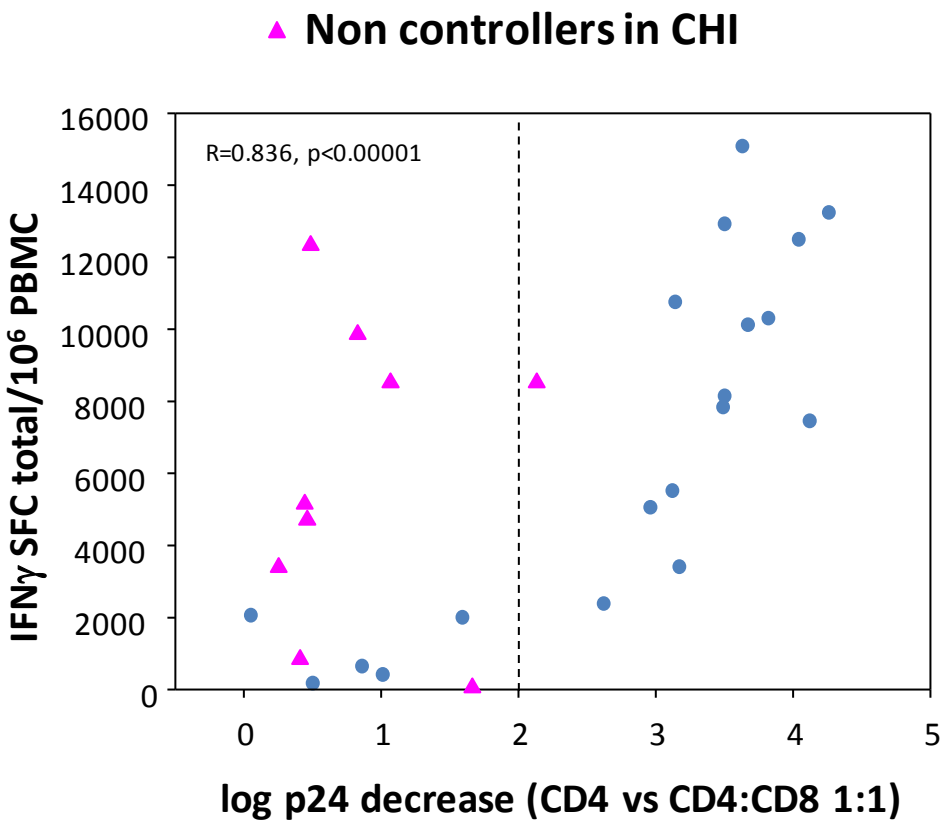




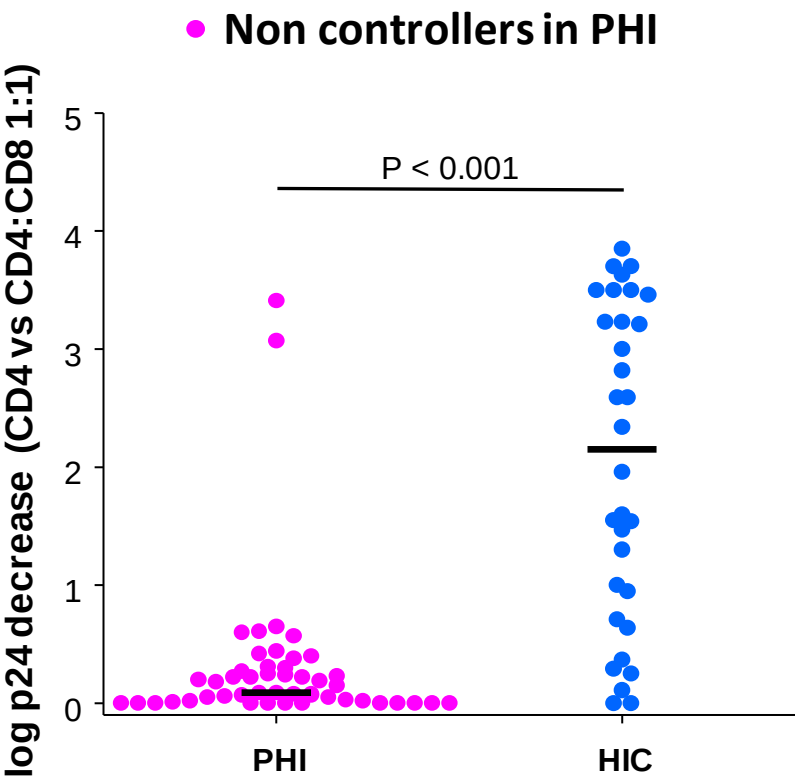
Saez-Cirion et al, PNAS 2007; Nature Protocols 2010

- **Greater and faster upregultaion of cytotoxic mediators**
  Migueles, et al. Immunity 2008; Hersperger, et al. PLoS Pathogens 2010
- **High functional avidity**–Almeida, *et al. JEM 2007*
- **MHC and TCR plasticity**–Chen et al Nat Immunol 2012; Pereyra et al Science 2010; Bailey et al JEM 2006

Strong CD8- T cell capacity to suppress HIV-1 is absent in non controller patients including during PHI



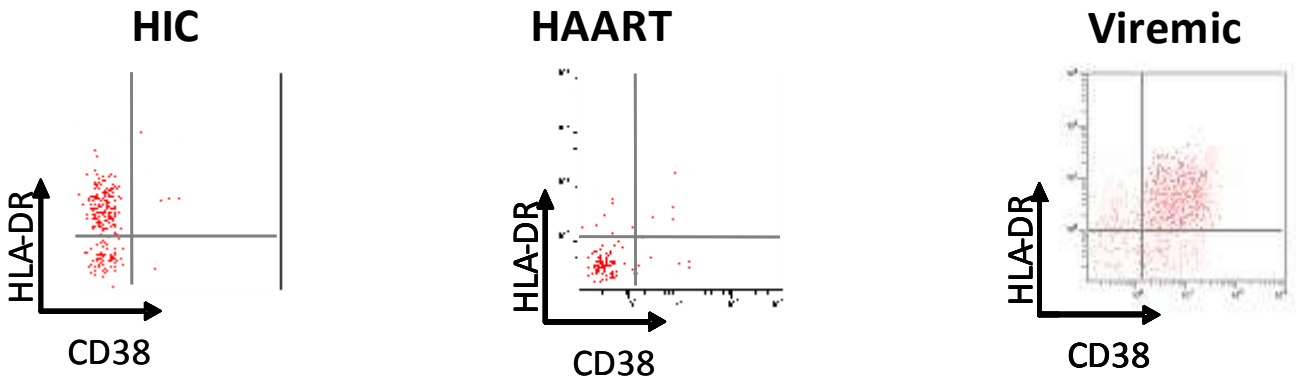
Saez-Cirion et al, JI 2009



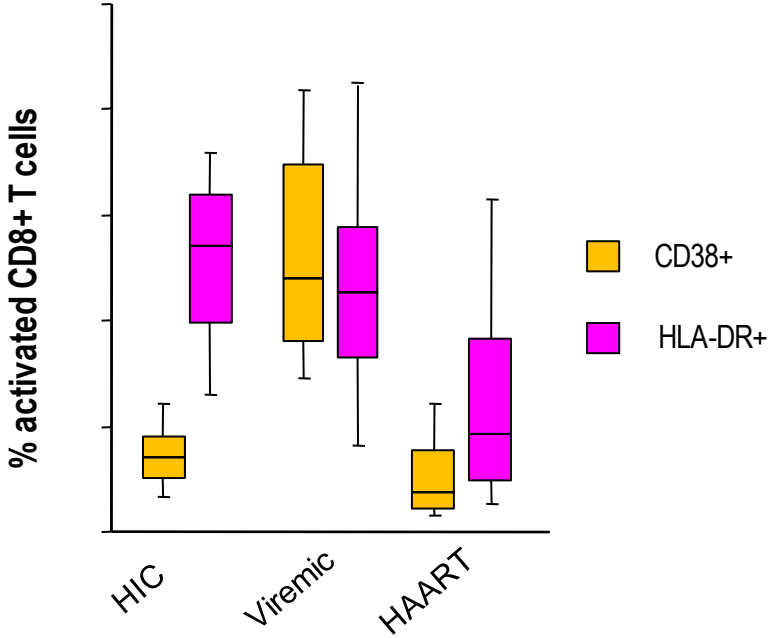
Lecuroux et al PLoS One, 2013

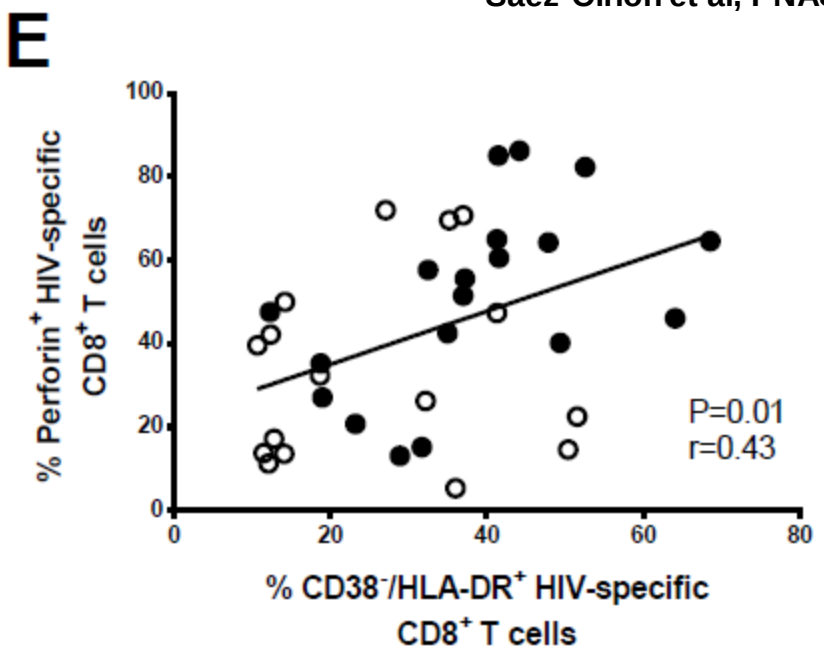
The superior HIV-suppressive capacity of CD8+ T-cells from HIC is likely related to intrinsic characteristics of their cells

HIV-specific CD8 T cell from HIV controllers have an unusual activation phenotype



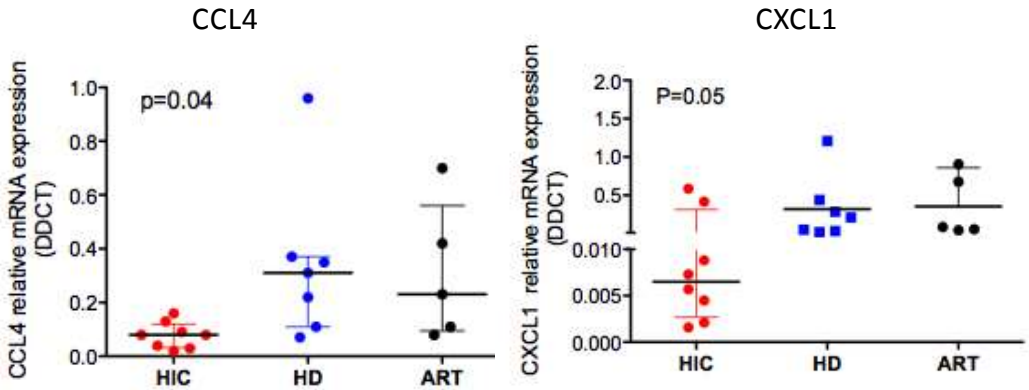
Saez-Cirion et al, PNAS 2007



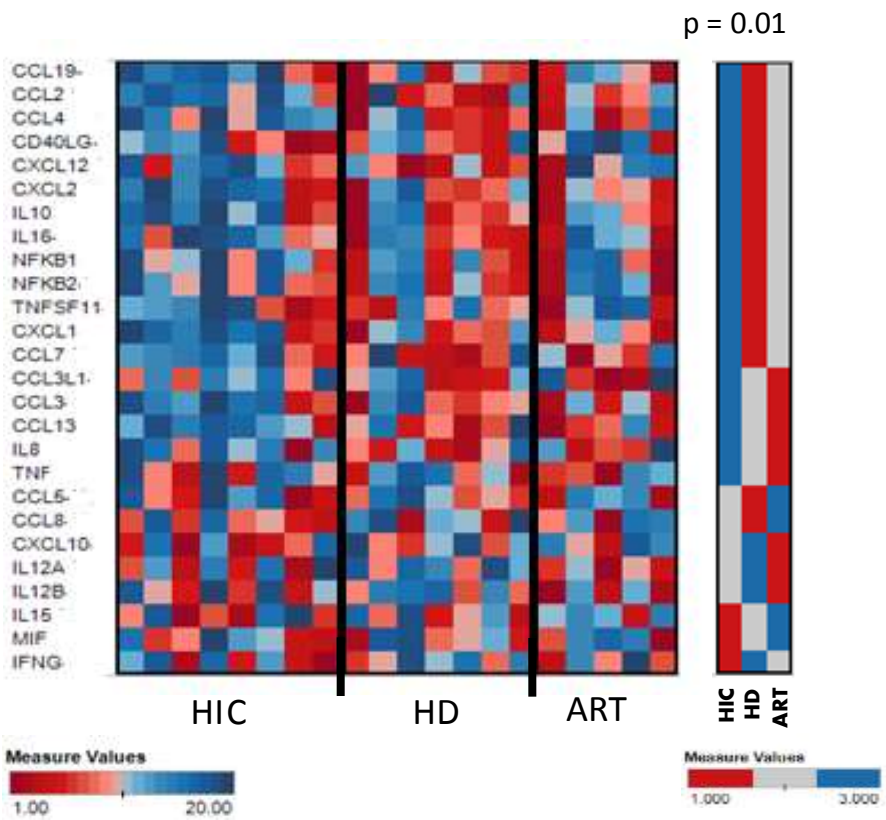


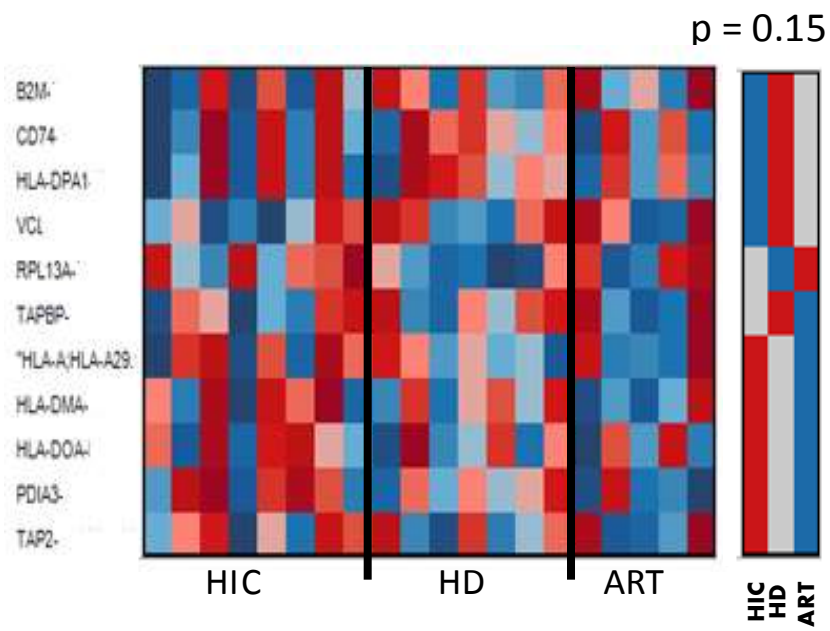
Hua et al, submitted

mDC from HIC have a non inflammatory profile

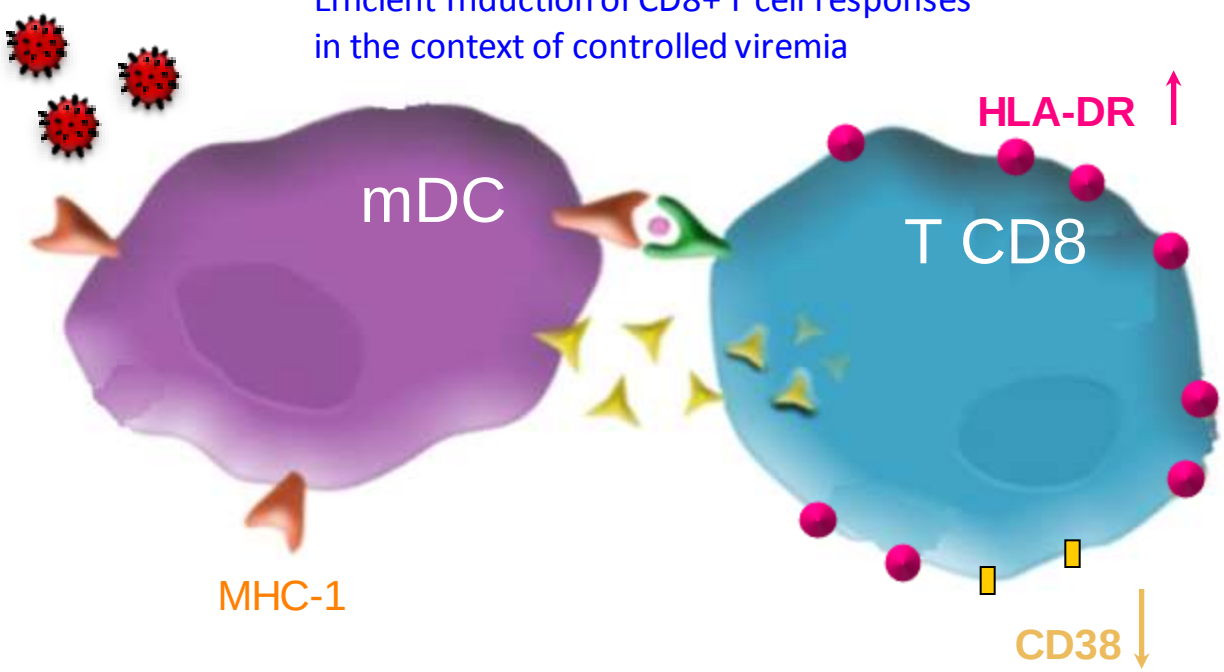


No alteration in genes necessary for induction of CD8+ T cell response





Efficient Induction of CD8+ T cell responses
in the context of controlled viremia



non inflammatory profile → Limit generalized immune activation

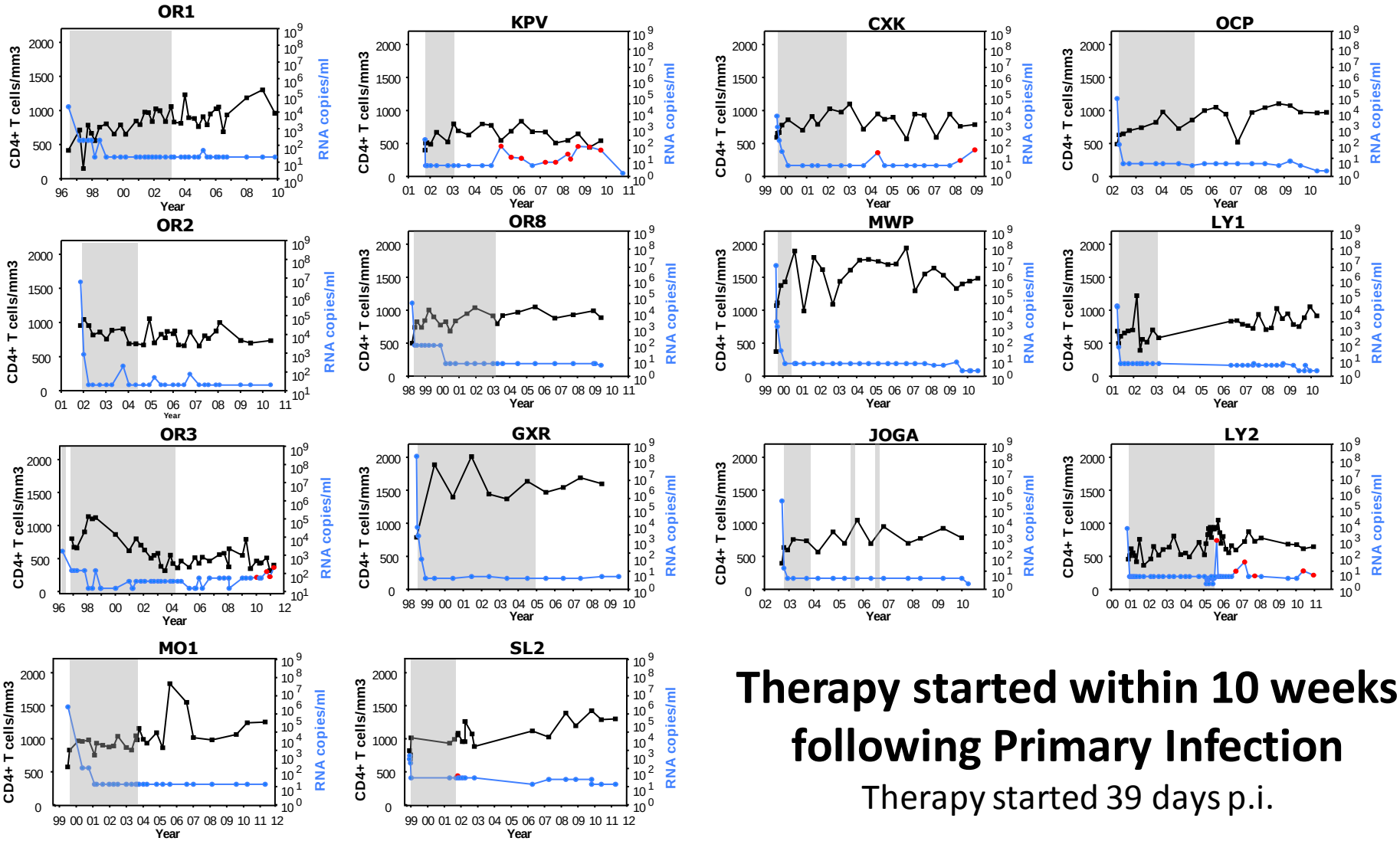
Is it possible to induce a HIV controller-like status?

anRS

VISCONTI Study

Virological and Immunological Studies in CONtrollers after Treatment Interruption

ANRS VISCONTI : Post-Treatment Controllers (PTC)



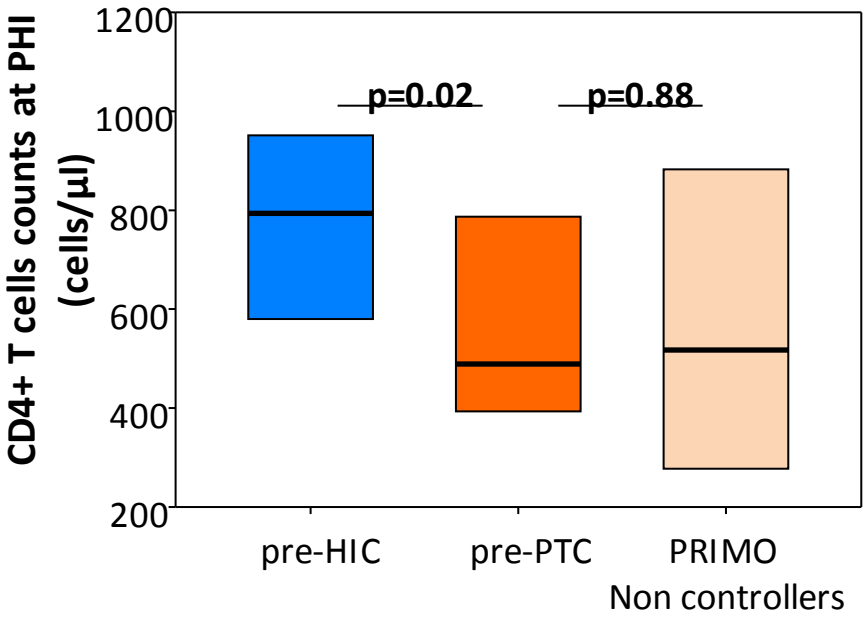
Therapy started within 10 weeks following Primary Infection

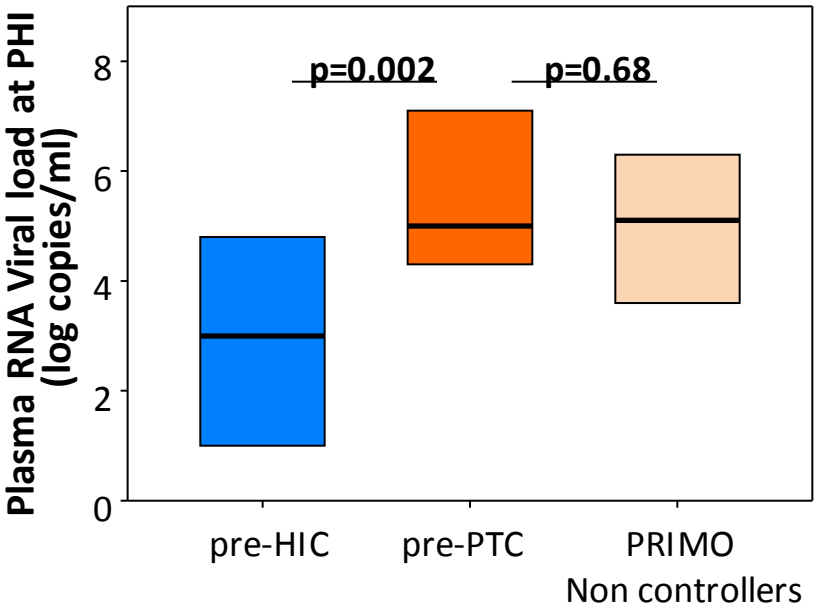
Therapy started 39 days p.i.

3 years on therapy followed by 7.5 years of control off therapy

Saez-Cirion et al PLoS Path 2013

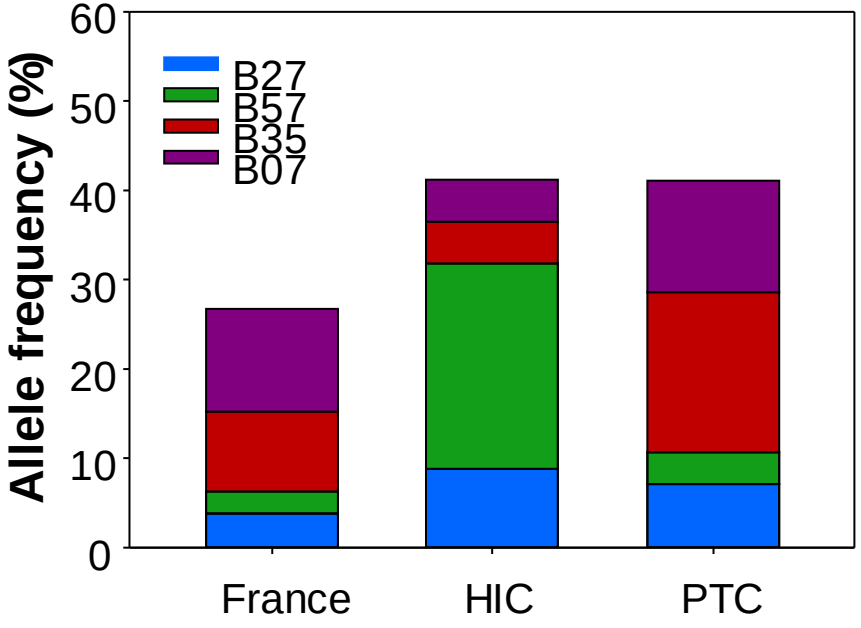
Post-treatment controllers have a tougher primary infection than HIV controllers

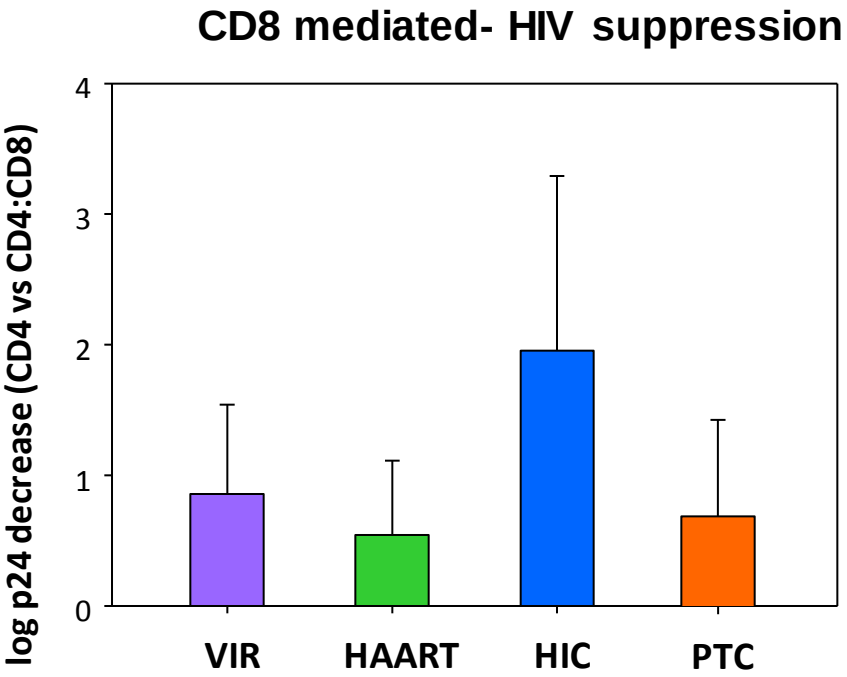




Saez-Cirion et al PLoS Path 2013

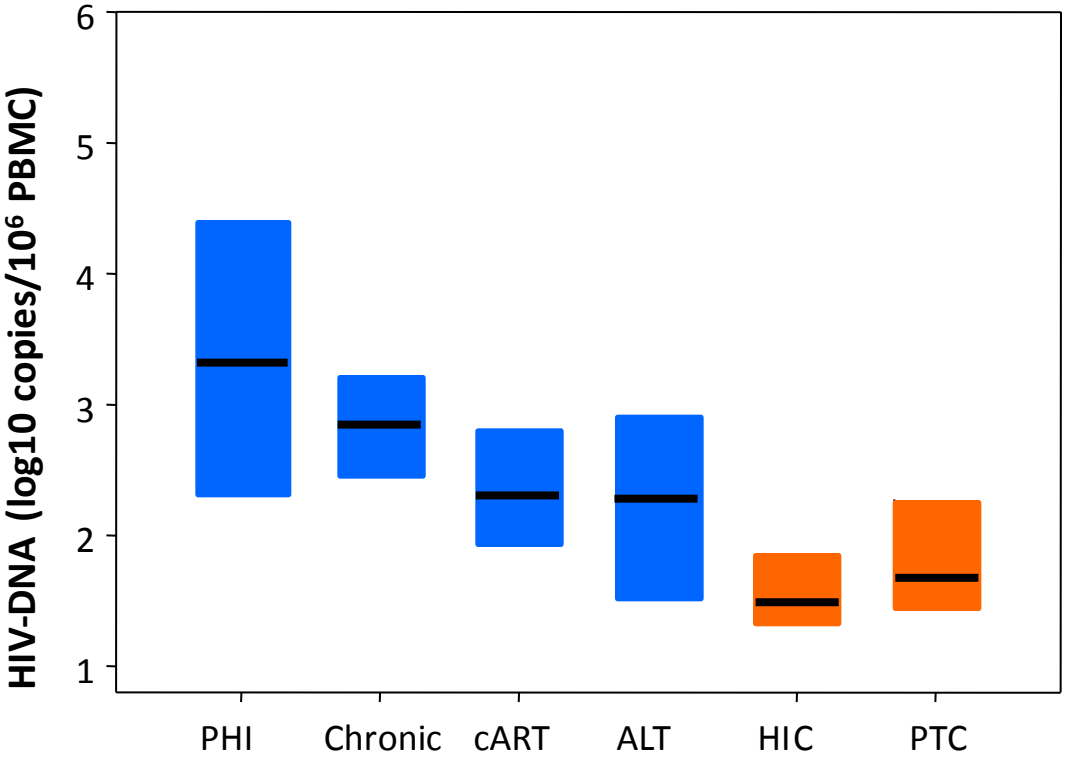
Post-treatment controllers don't have a favorable MHC background

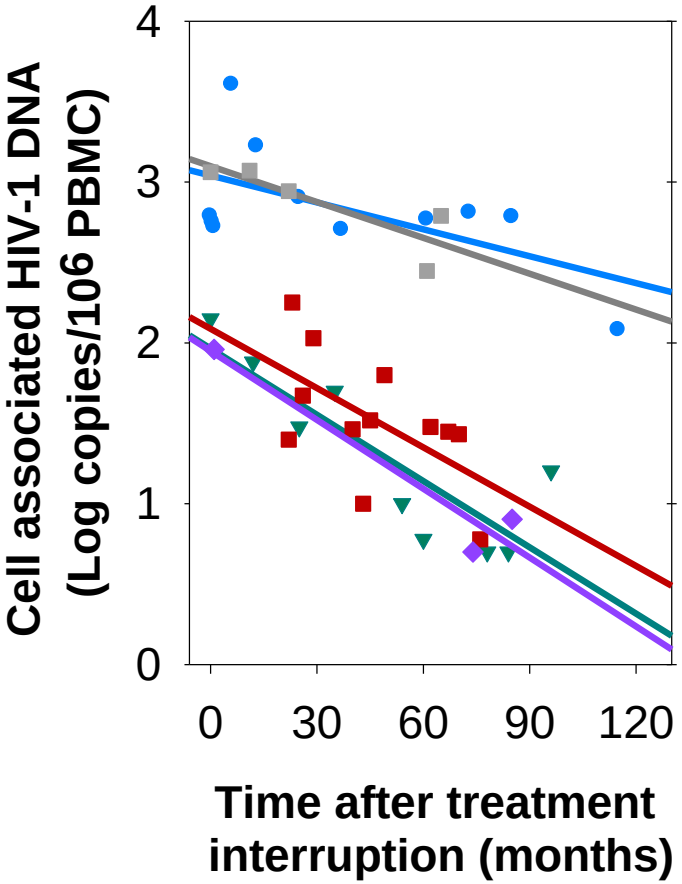




Saez-Cirion et al PLoS Path 2013

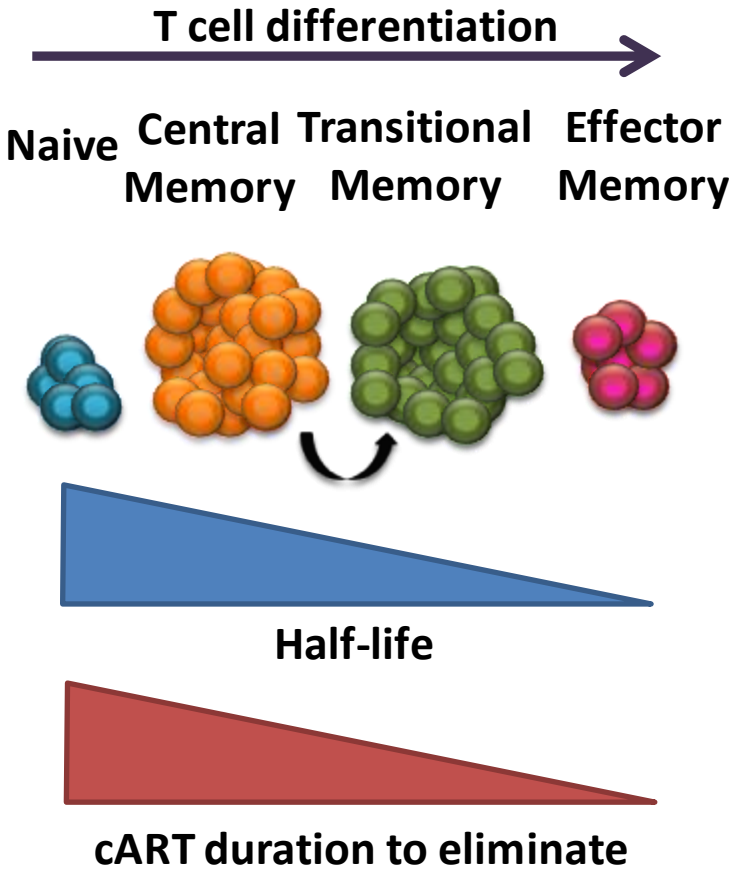
Post-treatment controllers have low levels of HIV-1 DNA in PBMC, which further decreased after treatment interruption in some cases

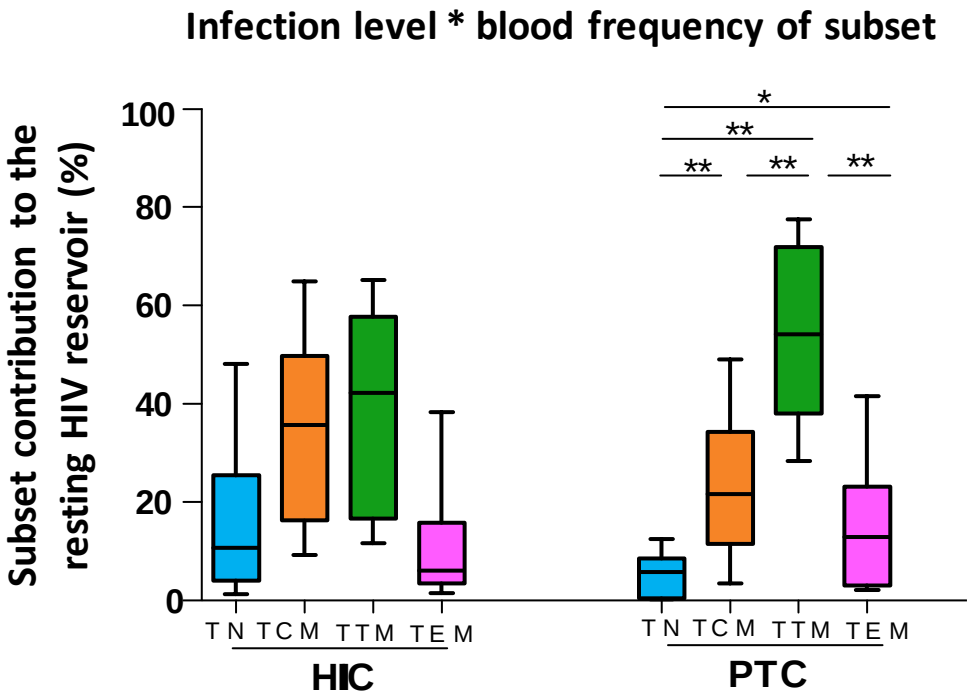




Saez-Cirion et al PLoS Path 2013

Skewed CD4 subsets distribution in PTC impacts the subsets contribution to the HIV reservoir



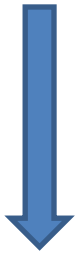


- A contribution to the HIV reservoir:
- Major for TTM subset
- Low for the TN and TCM subsets

Saez-Cirion et al PLoS Path 2013

EARLY TREATMENT

Limiting the establishment of the viral reservoir
Limiting viral diversity
Reducing immune activation
Preserving and cooperating with immune responses



Limiting the dynamics of viral replication in acute infection may be crucial for spontaneous control of infection

HIV controllers (HIC)

Asymptomatic primary infection, **low viral loads** and **high CD4** T cell counts in PHI

80% HIC carry one **protective HLA**-class I allele

Generally **strong HIV-specific T cell** responses with strong capacity to eliminate infected cells

Abnormal **high** levels of **T cell activation**

Estimated **frequency: 0.5%** of HIV infected patients

Post-Treatment Controllers (PTC)

Symptomatic primary infection, **high viral loads** and **low CD4** T cell counts in PHI

57% PTC carry one **HLA**-class I allele associated with **high viral loads**

Generally very **weak HIV-specific T cell** responses with poor capacity to eliminate infected cells

Low levels of **T cell activation**

Estimated **frequency: 5-15%** of HIV infected patients interrupting a >12 months-length treatment initiated in primary infection

Acknowledgements

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ANRS CO18 "HIV controllers"

ANRS CO15 "ALT"

FHDH "French Hospital Database on HIV"

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OBJECTIVES

- **To build an international cohort of Post Treatment Controllers in order to :**
  - Uncover mechanisms underlying viral control, i.e. HIV remission
  - Identify predictive markers associated with viral control after treatment interruption
- **Main Outcome:**

  To identify patients in whom HAART could be safely interrupted

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