

# Case report on the effect of antiretroviral treatment on a young man with uncertain HIV diagnosis, immune dysfunction and high expression of HERVs

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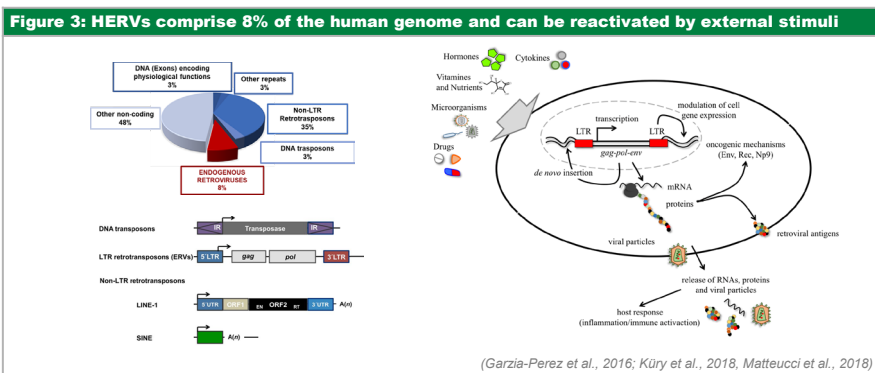
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## Background

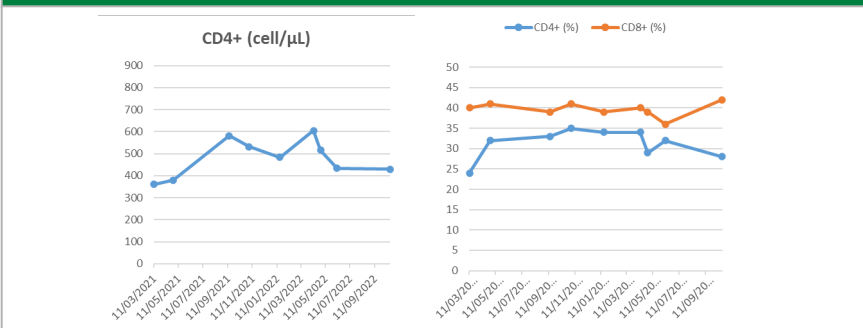
- We describe a clinical case of a 39 years old Italian man, who started to be investigated from 2012 for an uncertain HIV diagnosis, when he began to complain several clinical symptoms.
- Several HIV-1/2 tests, with frequent Ab antigen test positive for one or more viral proteins, never confirmed by immunoblotting and HIV-RNA and HIV-DNA tests were carried out. The first available CD4+ count (May 2013) was 543 cells/ $\mu$ L (35.70%), confirmed later as 526 cells/ $\mu$ L and with a CD4/CD8 of 0.94 (years 2021-2022: **Figure 1 and 2**).
- In April 2021, when he complained of generalized malaise accompanied by night sweats, asthenia and neurological and renal disorders, we carried out ultrasensitive molecular analyses, confirming negative results for HIV-1 RNA, HIV-1 DNA and HIV-2 DNA.
- Together we observed an altered immunophenotype demonstrating a strong immune dysfunction, inverse CD4/CD8 ratio and high exhaustion and senescence markers (**Table 1**).

## Case presentation

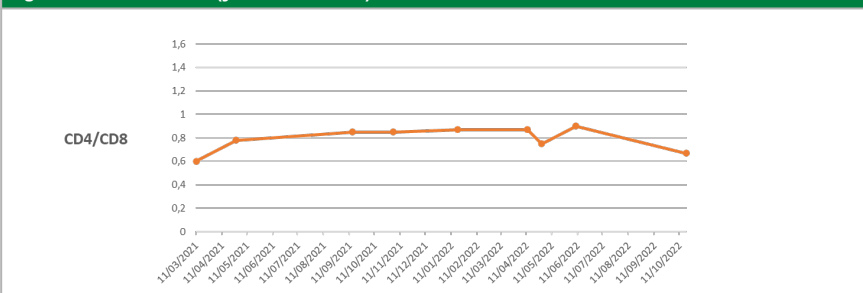
- To formulate a more defined diagnosis, we investigated the expression of human endogenous retroviruses (HERVs), ancestral exogenous retroviral infections that comprise 8% of the human genome. HERVs have been co-opted in physiological roles, but an aberrant expression has been associated to cancer, autoimmunity, neurological disorders, and it has been demonstrated to be activated by infectious agents leading to immunopathology (**Figure 3**).



**Figure 1: Number of CD4 count, CD4+ and CD8+ (%) in years 2021-2022**



**Figure 2: CD4/CD8 ratio (years 2021-2022)**



**Table 1: Values of immunophenotyping and HERVs expression before and during antiretrovirals treatment.**

Immunophenotyping	May 21	T0 (May-23)	T1 (6 month ART Nov-23)	HDs range
CD4%	38	44	46	30-55
CD8%	54	50	50	15-40
CD4/CD8 ratio	0.7	0.8	0.9	>1
CD4+effector memory %		40	48	12-26
CD8+effector memory %		35	35	3-33
CD4+PD1+ %	20	9	23	<9
CD8+PD1+ %	19	20	24	<7
CD8+CD57+ %	30	39	35	<2
CD19+Marginal %		30	30	1-19
Switched B cells %		86	87	21-51
CD169+HLA-DR+ monocytes %		56	11	0.2-1.3
CD169RMF1 (monocytes/lymphocytes MFI ratio)		13	5	<3
HERVs expression	May 21	T0 (May-23)	T1 (6 month ART Nov-23)	HDs range (median IQR)
HERV-K (*)	13.1	7.49	0.16	median 0.002 (IQR 0.000-0.01)
HERV-H (*)	21.8	11.20	0.03	median 0.004 (IQR 0.000-0.07)
HERV-W (*)	0.02	1.86	0.10	median 0.004 (IQR 0.000-0.001)
ENV-HERV-K (lymphocytes) %	60	39	10	median 3.1 (IQR 0.8-9.3)
ENV-HERV-W (lymphocytes) %	0.9	50	27	median 2.9 (IQR 1.2-10.1)

NOTES: healthy donors (HDs); (\*) HERVs mRNA levels as  $2\lambda(-\Delta Ct)$

## References

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## Conclusion

- These results show reduced expression of HERVs after 6 months of antiretroviral treatment, but the persistence of an immune dysfunction. The treatment is still ongoing, and further analysis and clinical investigation may indicate potential benefits and the long-term effects.