# THE IMPACT OF CART ON THE INTRACELLULAR ANTIOXIDANT CAPACITY IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF PEOPLE LIVING WITH HIV

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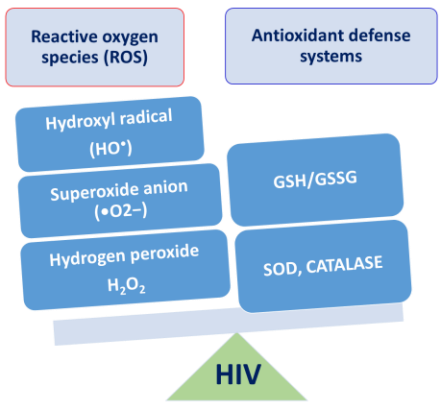
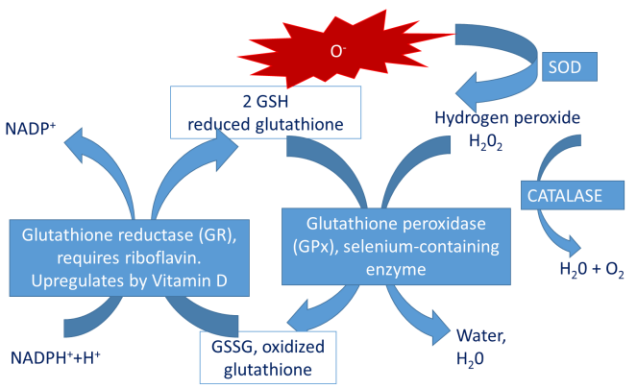
## BACKGROUND:

A number of recent data reveal that continuous oxidative stress increases the rate of comorbidities in people living with HIV regardless of successful cART and sustained HIV viral suppression.




**AIM: To evaluate the antioxidant capacity in peripheral blood mononuclear cells (PBMCs) from people living with HIV on cART using the glutathione/glutathione disulfide (GSH/GSSG) ratio, intracellular catalase and superoxide dismutase (SOD) levels.**




## MATERIALS AND METHODS:

Peripheral blood samples were obtained from HIV-positive individuals on long-term cART, with persistently suppressed HIV viral load and recovered CD4 absolute count (AC), (A, n=29), untreated HIV+ individuals (B, n=11) and gender- and age-matched HIV- volunteers (C, n=28) after informed consent. The absolute count (AC) of CD4+ and CD8+ T cells were determined by flow cytometry. PBMCs were isolated by density gradient separation, and cell lysates were prepared at 1x10^6 PBMCs in 200 µl PBS by sonication. Concentrations of GSH and GSSG [nmol/mg], SOD and catalase [U/l] were determined by spectrophotometry.

**RESULTS:** CD4 AC in group A and C was similar in contrast with group B (773 and 931 vs. 241, p<0.0001) in contrast to CD4/CD8 ratio **(Fig. 1A,B)**. Intracellular GSH was lower in group B as compared to A and C though without statistical significance (12.4 vs. 16.3 and 17.3, p>0.05). Noteworthy, GSSG levels remained significantly higher in both HIV+ groups (8.45 and 16.4 vs. 3.54 for controls, p<0.01) **(Fig. 2A,B)**, in direct correlation with CD8AC (R=0.40, p<0.05) **(Fig. 3B)**. In our hands, cART seemed to restore GSH/GSSG ratio, which was significantly decreased only in group B (mean 2.8 vs. 4.9 and 5.5 for A and C, p<0.05) **(Fig. 3A)**. The mean intracellular catalase and SOD concentrations were lower in controls as compared to groups A and B (36.5 vs. 41.0 and 40.5, p>0.001 and 18.9 vs. 32.5 and 47.8, p>0.01, respectively) **(Fig. 4A,B)**.

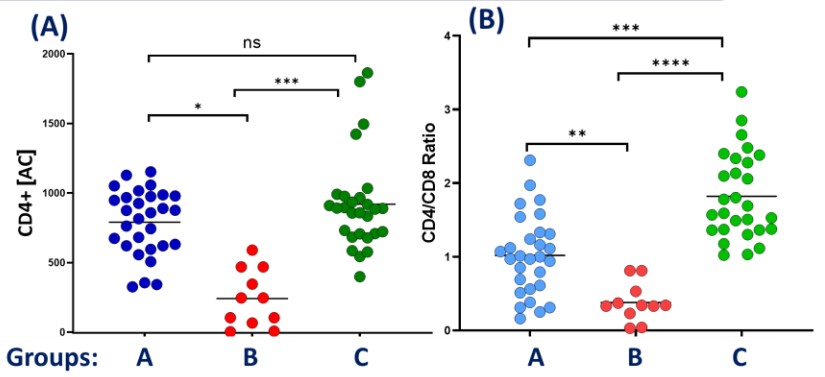



Figure 1. (A): Absolute count of CD4+ cells and CD4/CD8 ratio (B) in HIV+ individuals on continuous cART with suppressed viral load (group A), HIV+ cART-naive people with detectable VL (group B) and HIV-negative volunteers (group C)

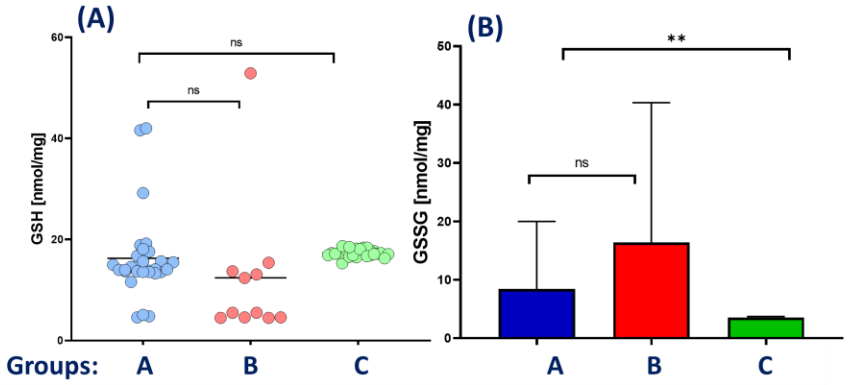



Figure 2.(A): GSH and GSSG (B) concentration in group A, group B and group C, unpaired ANOVA, p<0.01

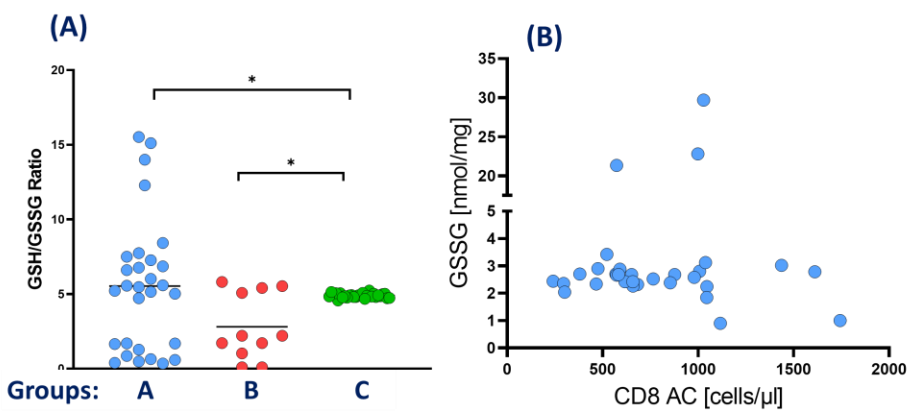



Figure 3.(A) GSH/GSSG ratio and correlation (B) between CD8 +T AC and GSSG ratio in HIV+ individuals.

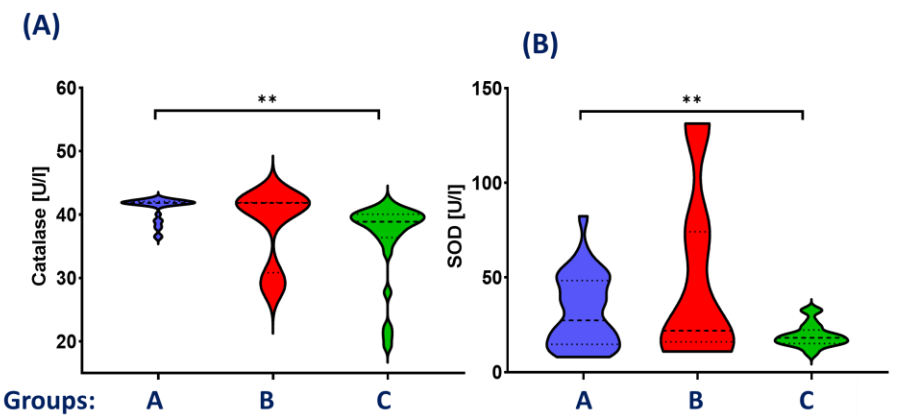



Figure 4.(A): Catalase and SOD (B) levels in group A, group B and group C unpaired ANOVA, p<0.01

**CONCLUSIONS:** In spite of restored GSH/GSSG balance, the persisting high GSSG levels in the settings of long-term cART indicate possible disturbances in Glutathione reductase activity in PBMCs of HIV-positive individuals. Affected cellular redox status, in line with increased Catalase and SOD levels may signal immune activation in the settings of undetectable HIV viral load and changes in share of lymphocyte subpopulations. These results reevaluate oxidative stress in the settings of long-term cART monitoring.

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