

Glutathione as an immunoadjuvant

Vishy Venketaraman
Associate Professor

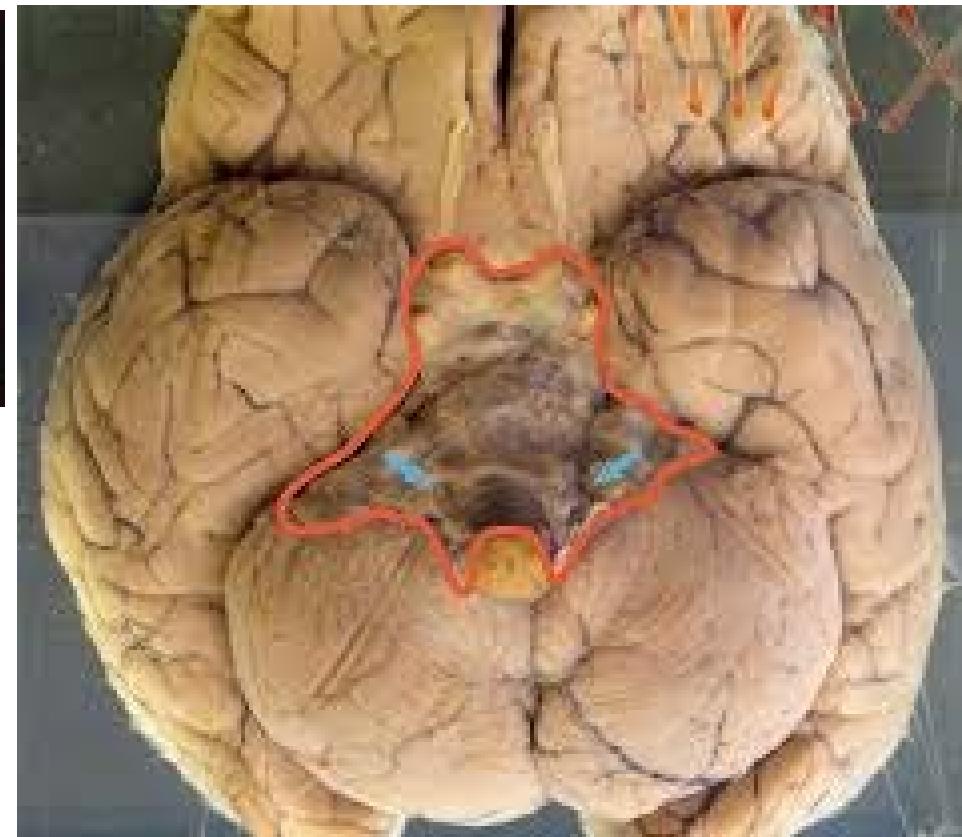
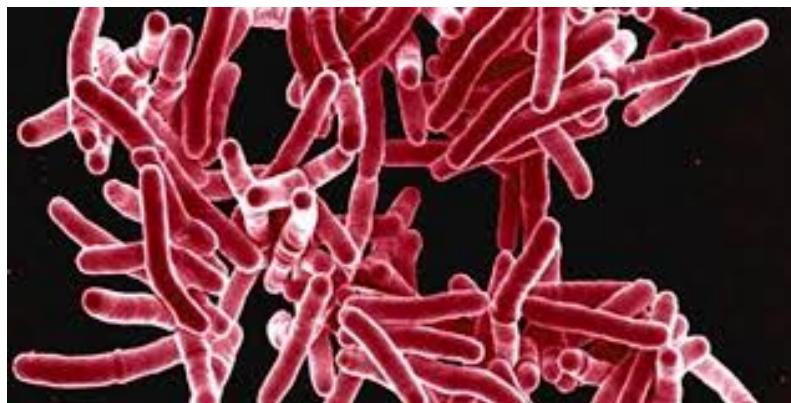


Western University
OF HEALTH SCIENCES

College of Osteopathic Medicine of the Pacific
COMP-Northwest



TB meningitis



GLUTATHIONE

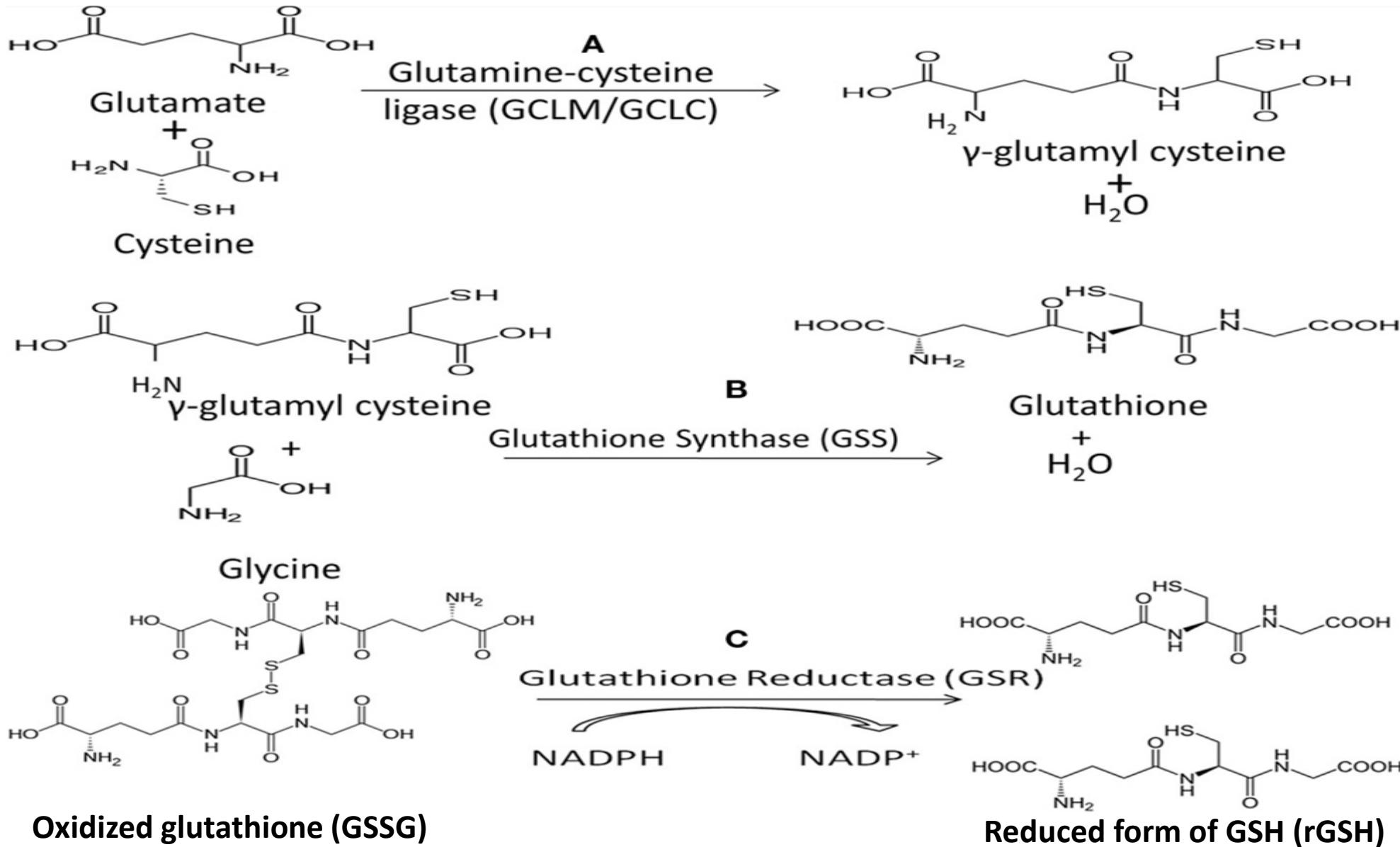


Figure 1A and Table I: Growth of *M. tuberculosis* in the presence and absence of GSH as determined by measuring OD and CFU.

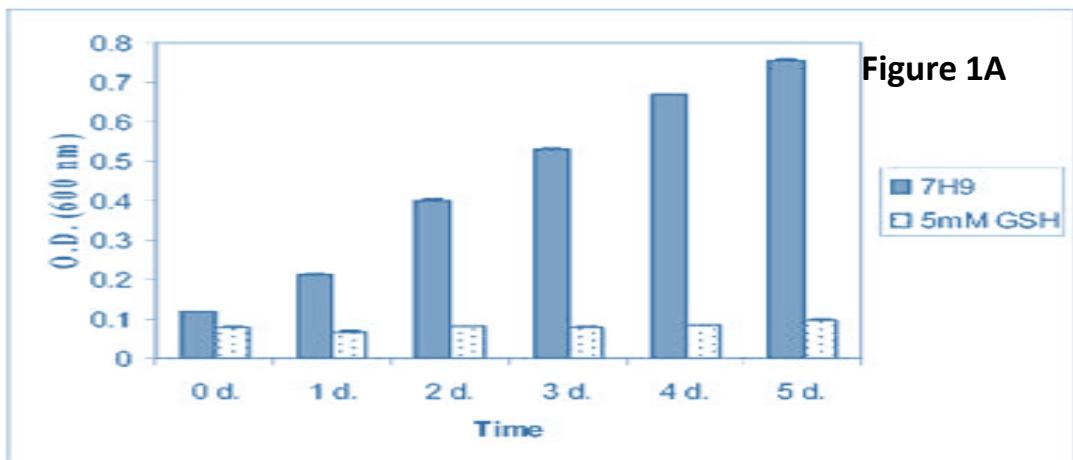
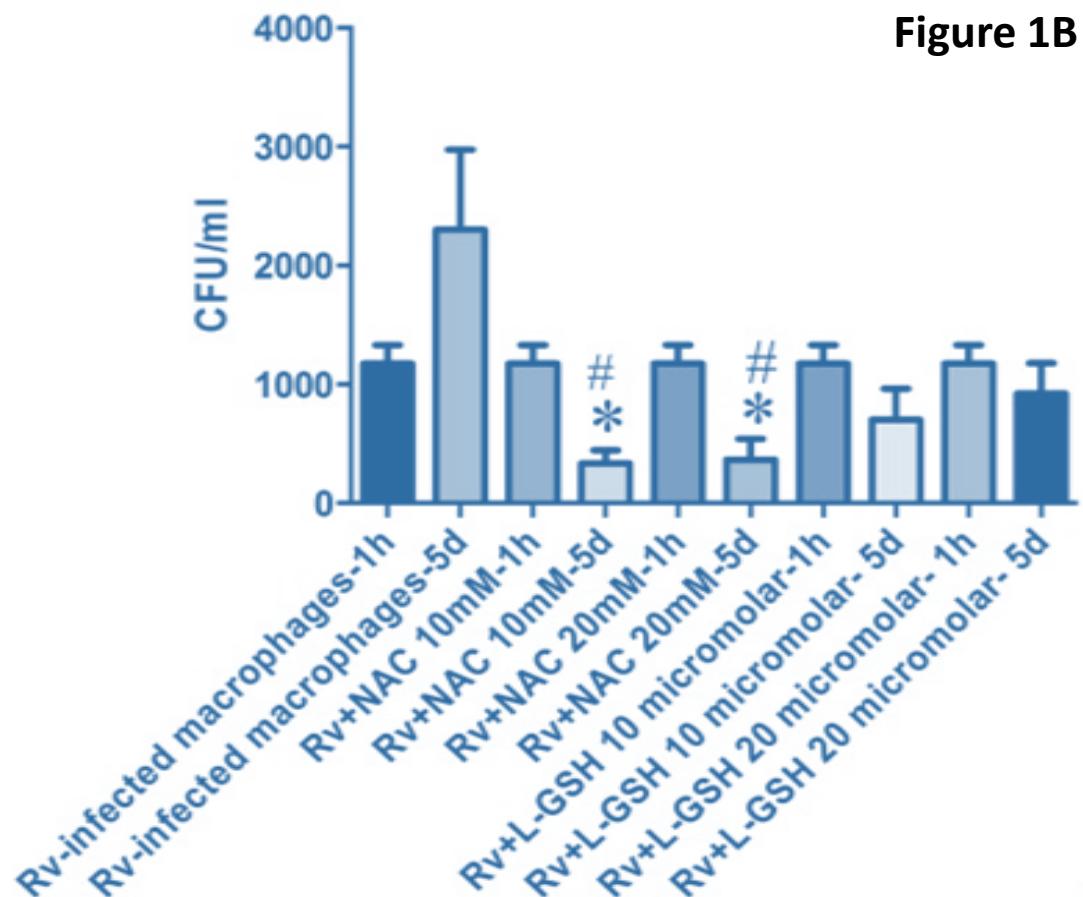


TABLE 1.
Growth of H37Rv in 7 Hg medium

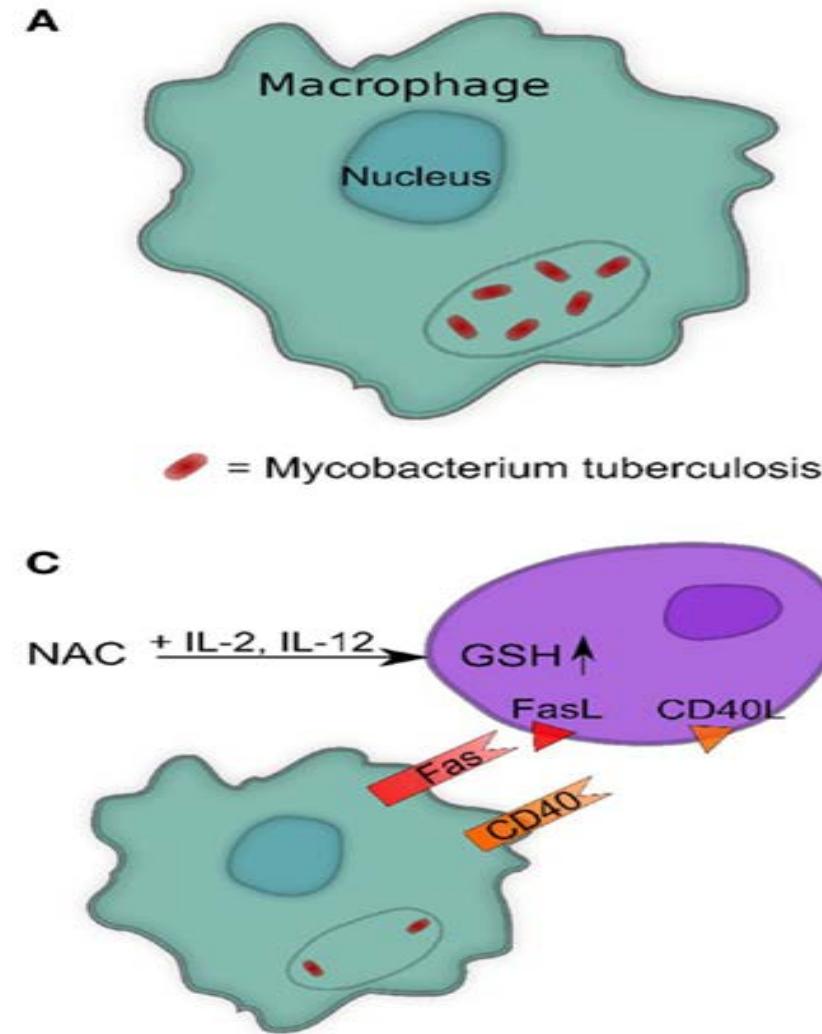
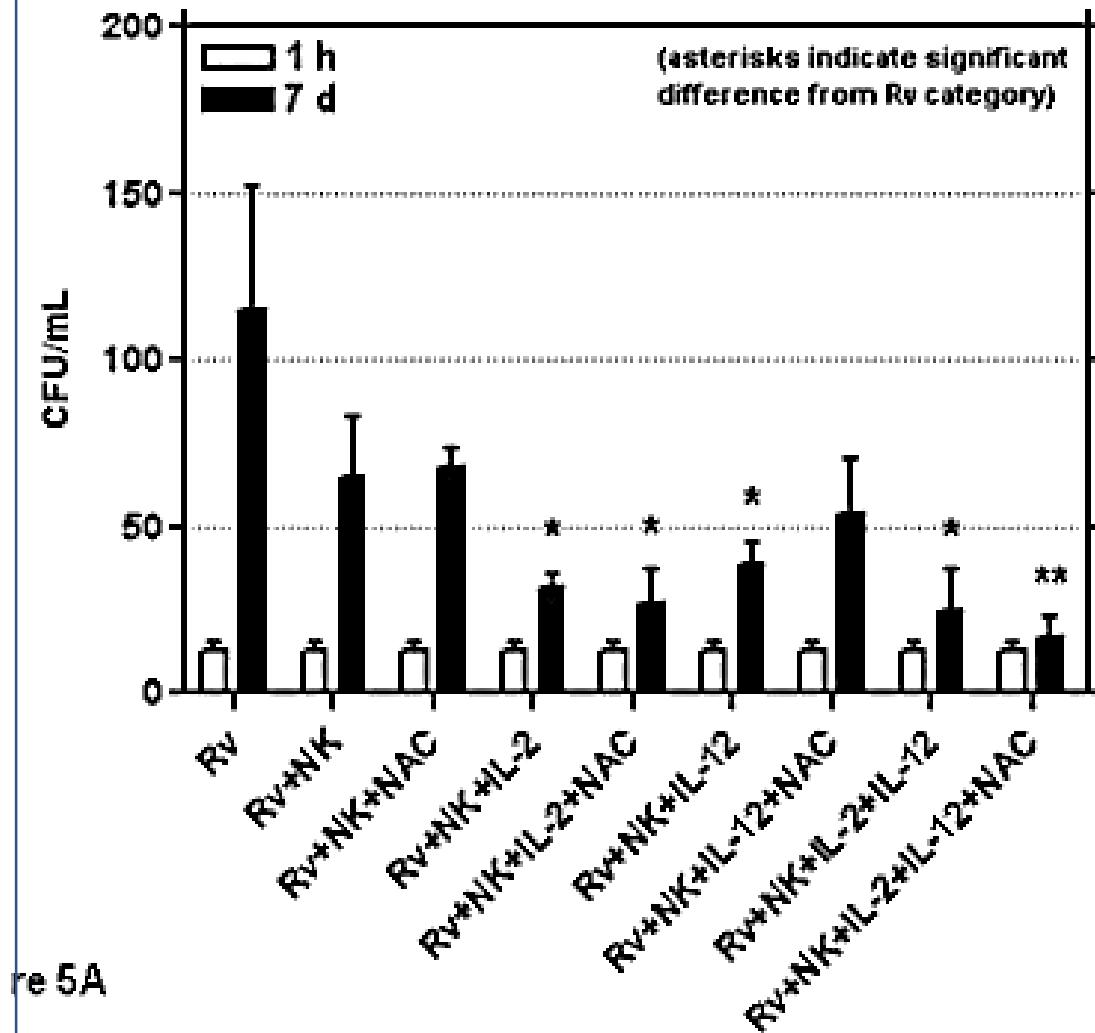
| H37Rv treatment | Mean no. of CFU ^a ± SD on: | | | | | |
|-----------------|---|--|--|--|--|--|
| | Day 0 | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 |
| None | 2.8×10^4 ± 8.81 × 10 ² | 6.4×10^4 ± 4.1 × 10 ³ | 3.3×10^5 ± 1.8 × 10 ⁴ | 7.3×10^5 ± 1.2 × 10 ⁴ | 7.2×10^6 ± 1.6 × 10 ⁵ | 9.8×10^7 ± 2.0 × 10 ⁵ |
| 5 mM GSH | 2.6×10^4 ± 1.2 × 10 ³ | 2.1×10^4 ± 1.0 × 10 ³ | 2.4×10^4 ± 1.0 × 10 ² | 2.4×10^4 ± 1.0 × 10 ² | 2.4×10^4 ± 1.0 × 10 ² | 2.7×10^4 ± 1.0 × 10 ² |



Venketaraman *et al*; Infect Immun 2005

Lagman *et al*; PLoS One 2015

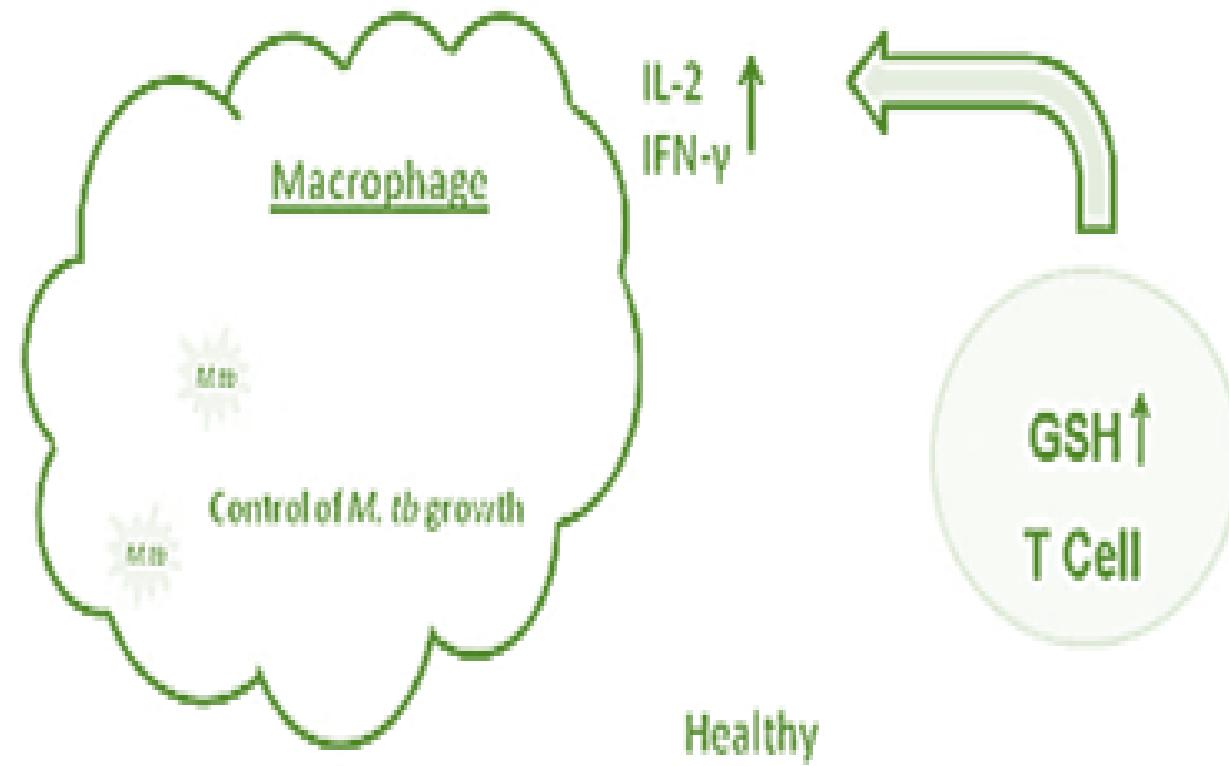
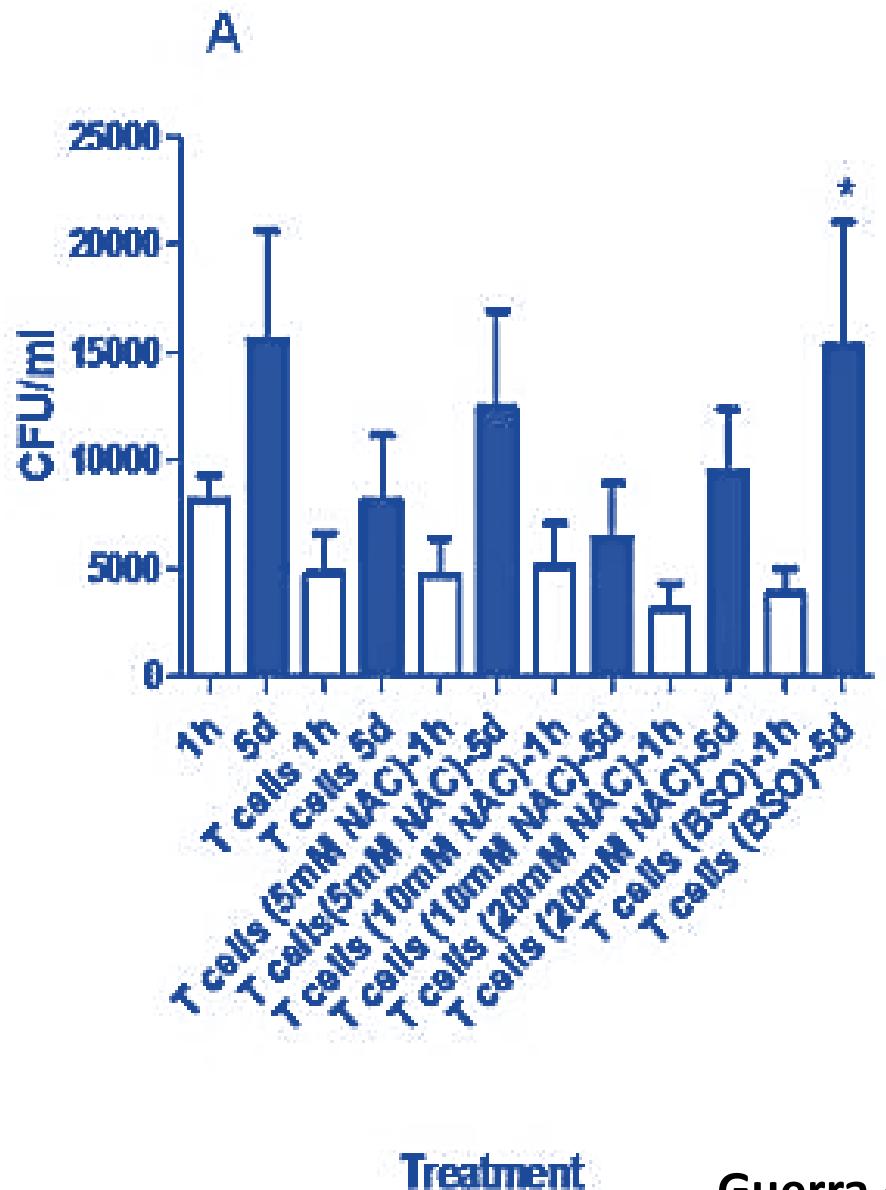
Survival of H37Rv inside monocytes co-cultured with NK cells.



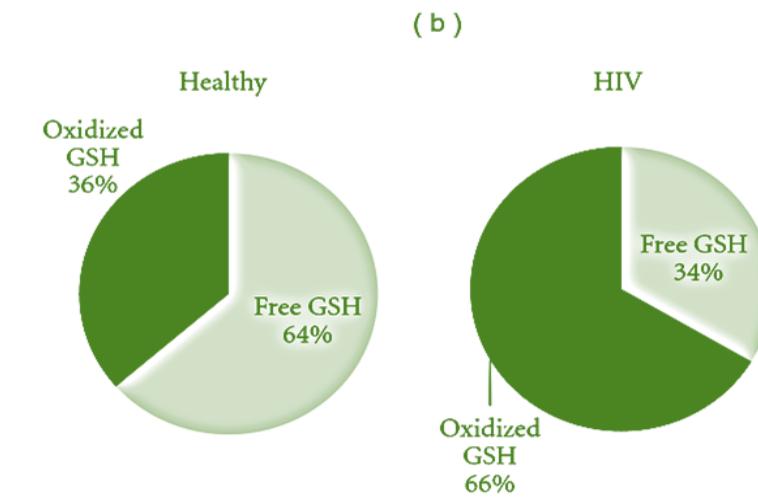
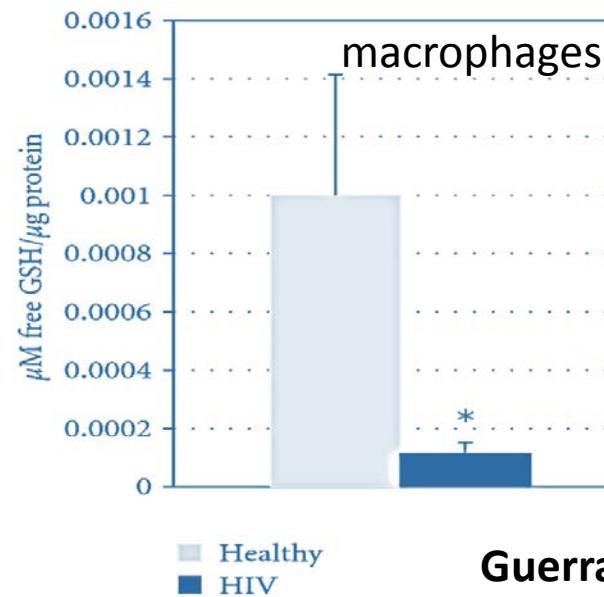
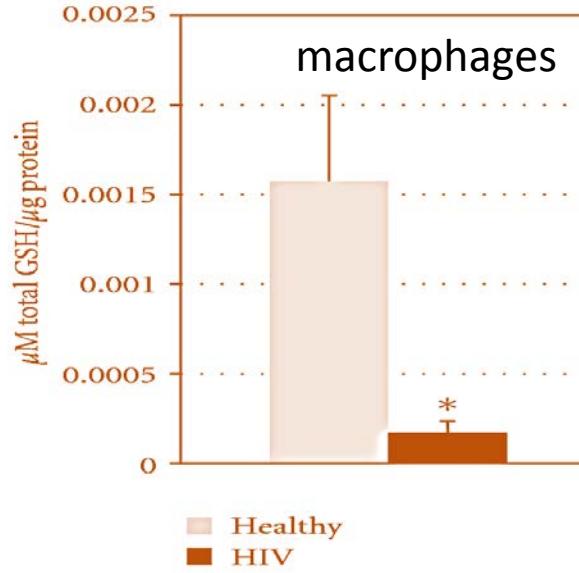
Millman *et al*; J Interferon Cytokine Res 2008

Allen *et al*; Front Immunol. 2015

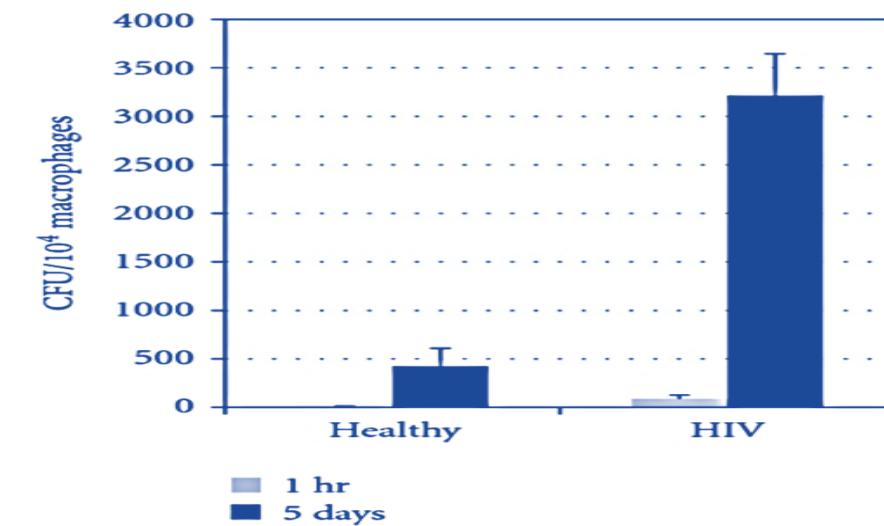
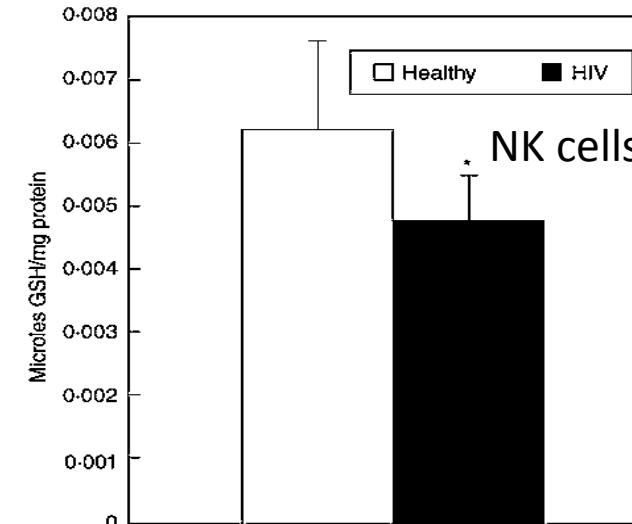
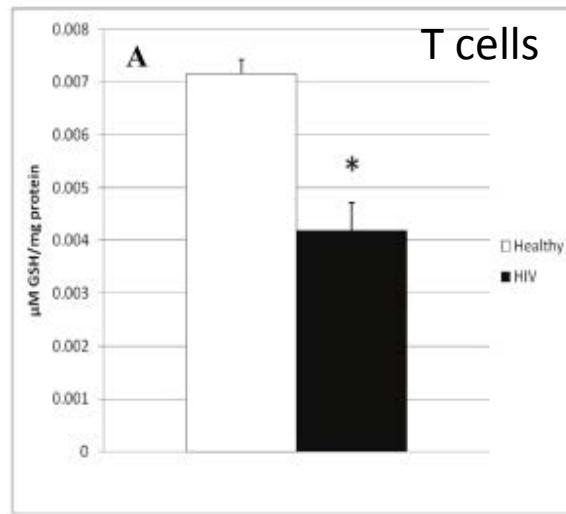
Survival of H37Rv inside monocytes co-cultured with T cells.



Assay of GSH in macrophages, T cells and NK cells lysates from healthy and HIV-infected subjects



Guerra et al; Clin Dev Immunol 2012

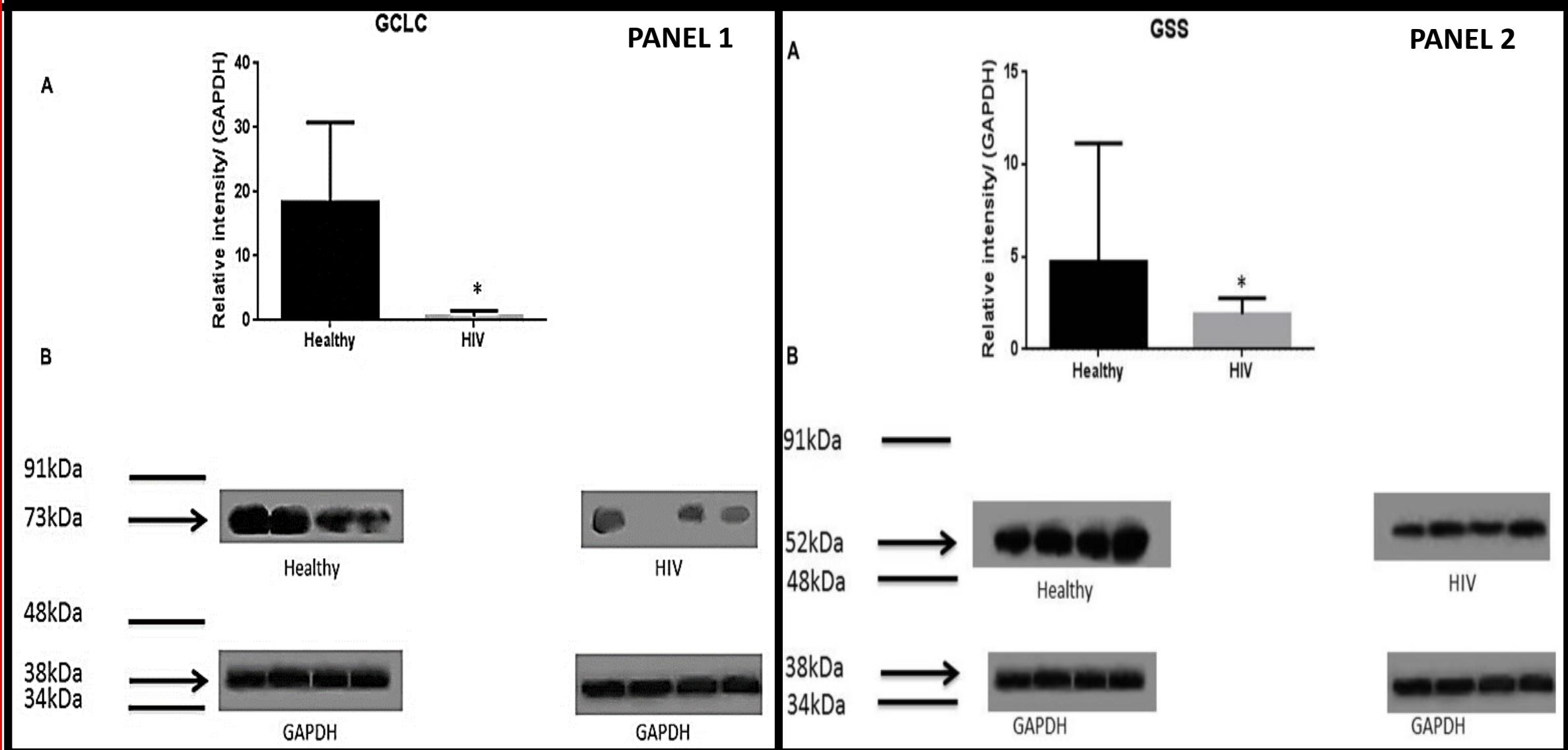


Guerra et al; PLoS One 2011

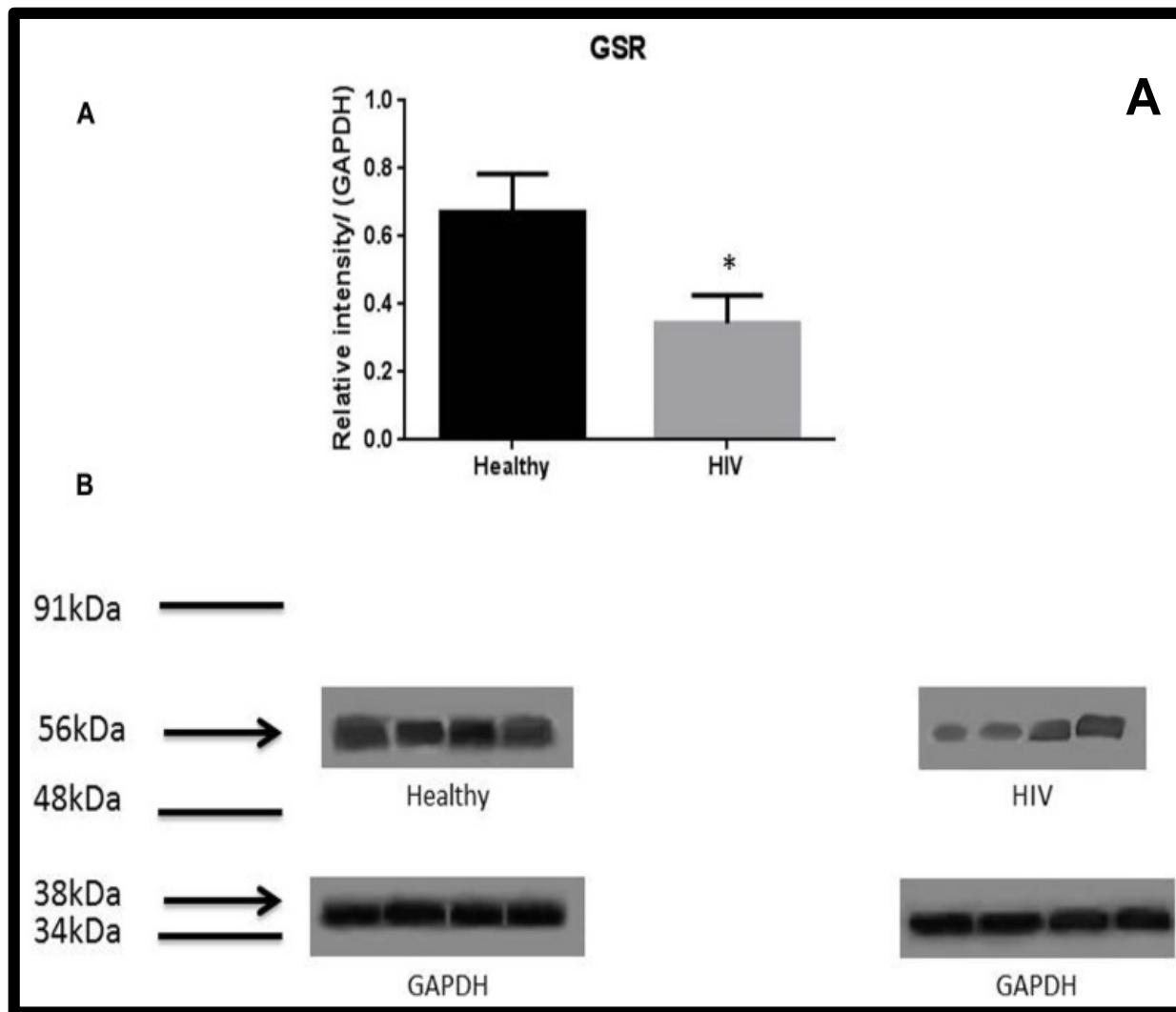
Guerra et al; Clin Exp Immunol 2012

Guerra et al; Clin Dev Immunol 2012

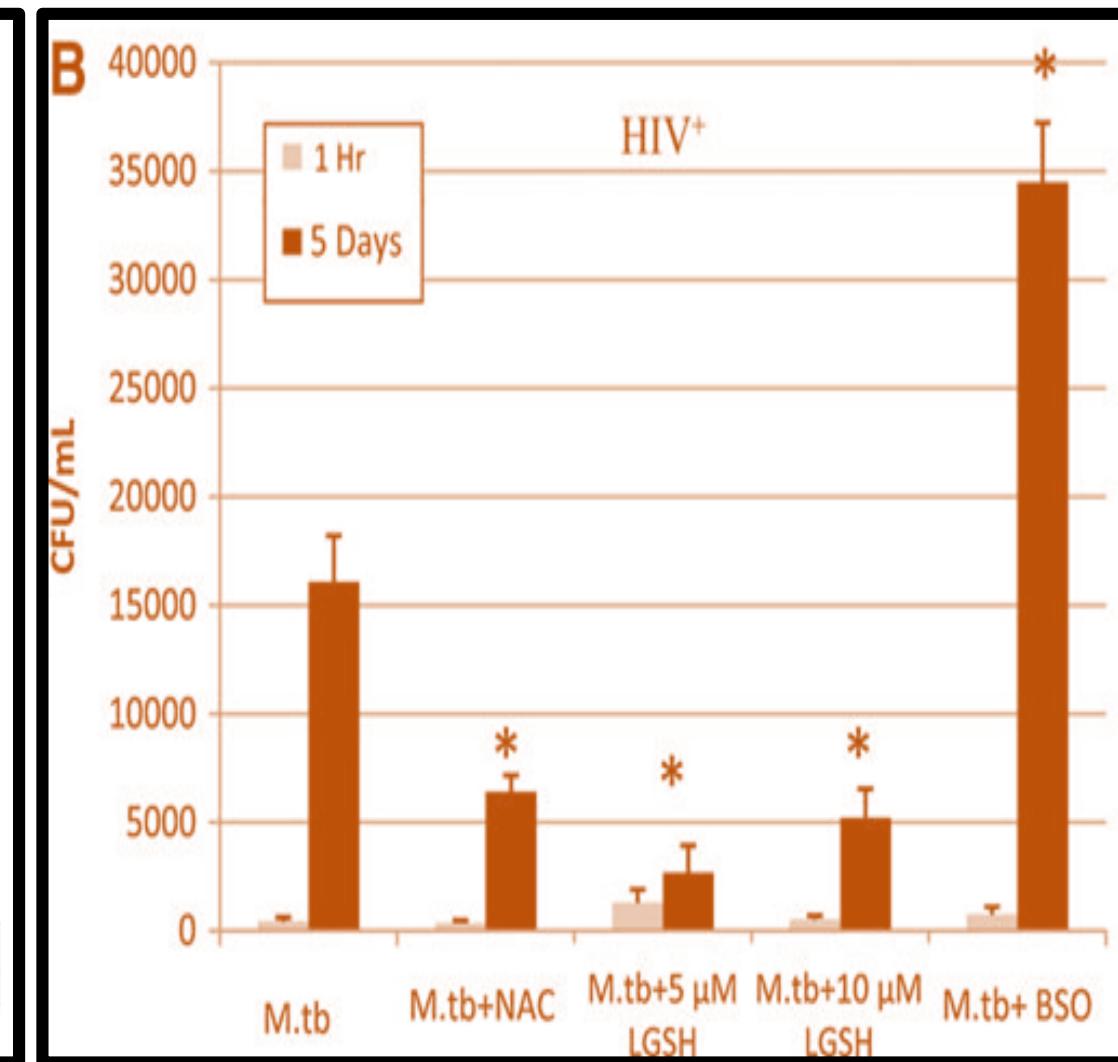
Quantifying GCLC (Panel 1) and GSS (Panel 2) enzyme levels in Healthy and HIV-infected subjects.



Quantifying the levels of GSR (Panel A) and *Mtb* survival (Panel B) in HIV-positive subjects.

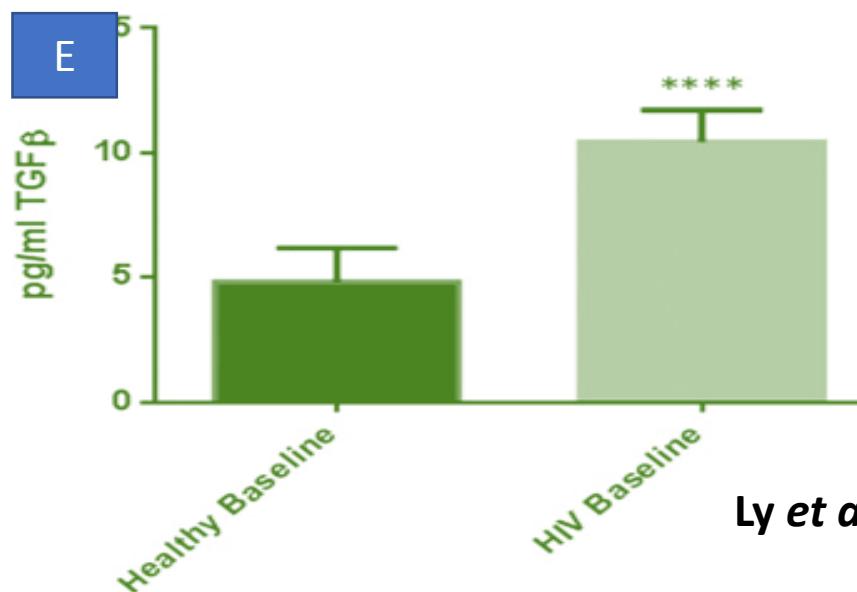
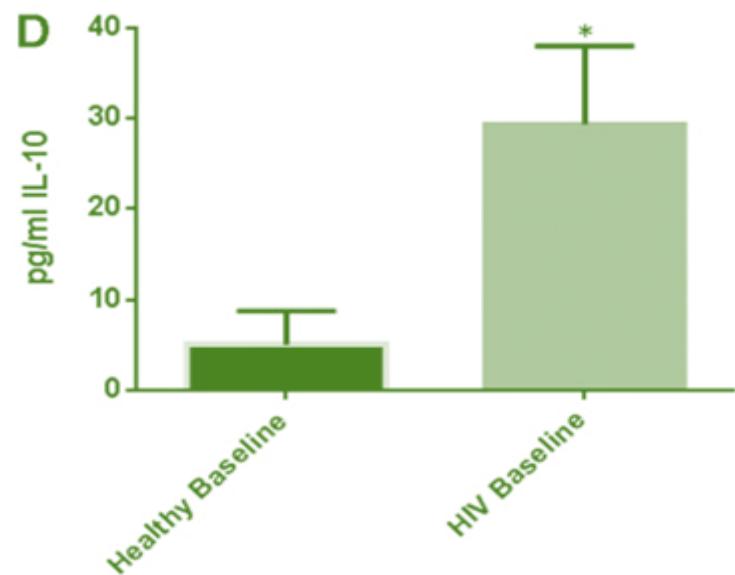
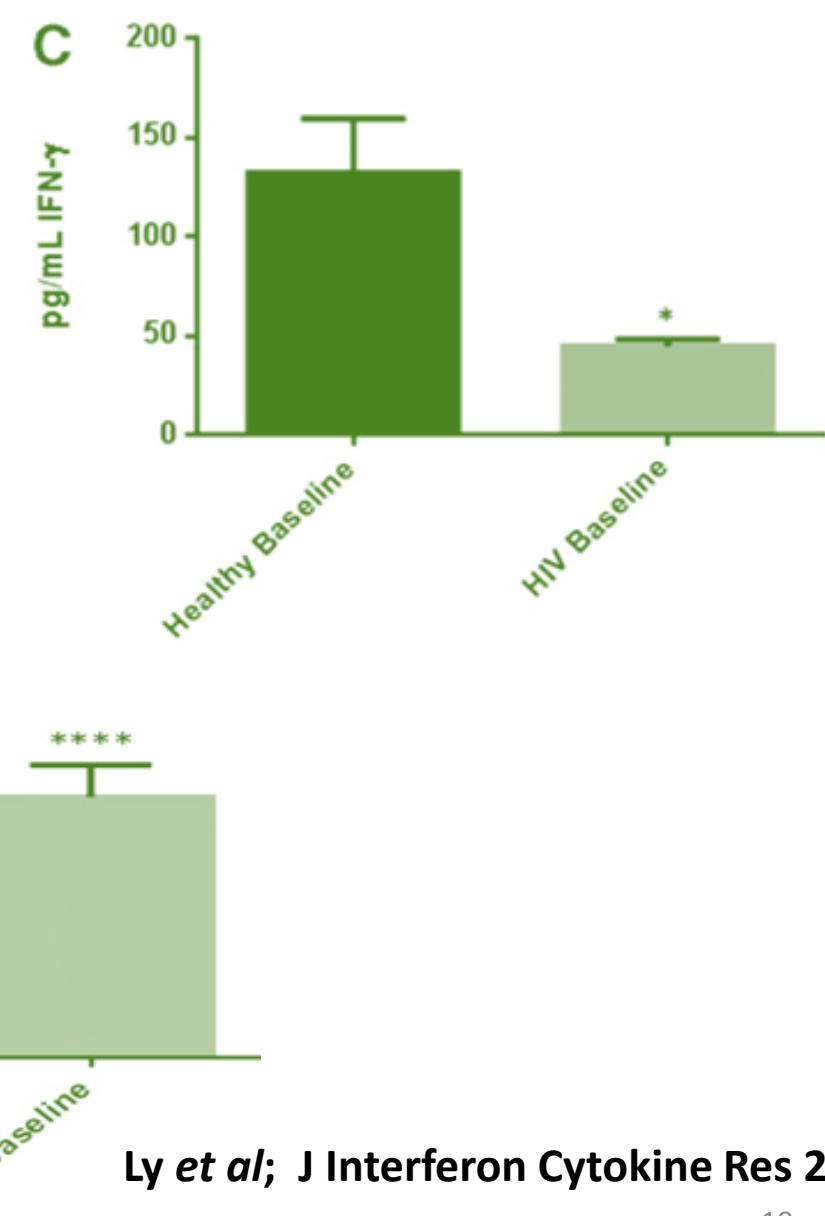
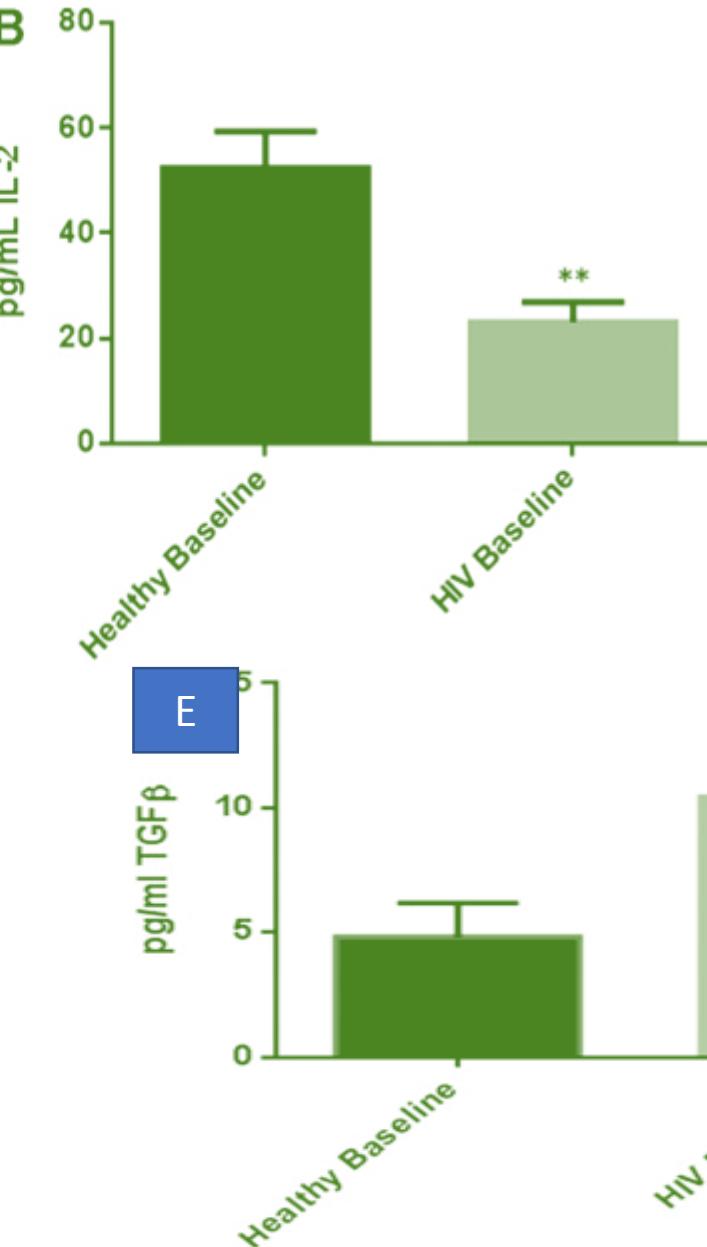
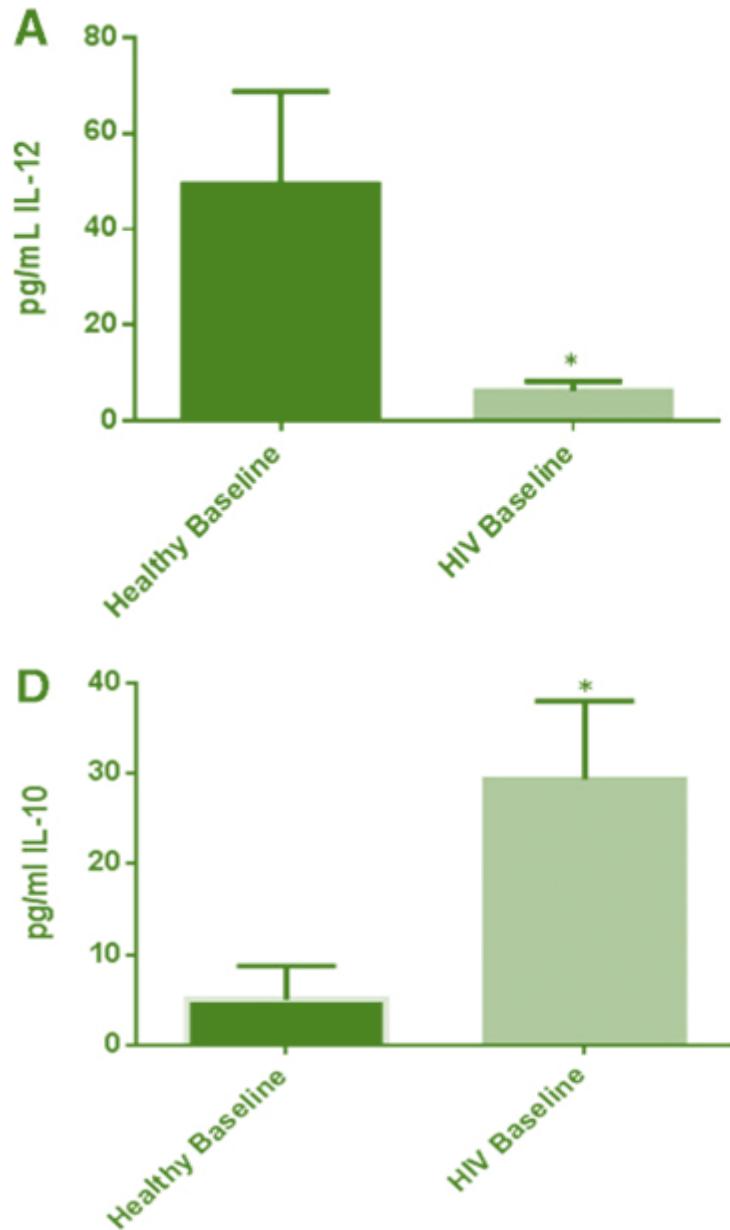


Morris *et al*; Frontiers Pharmacol 2014

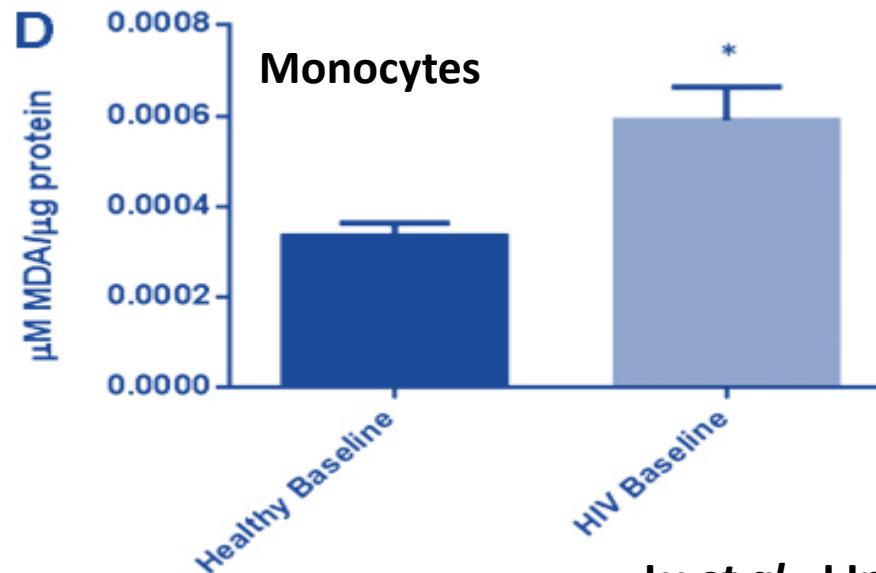
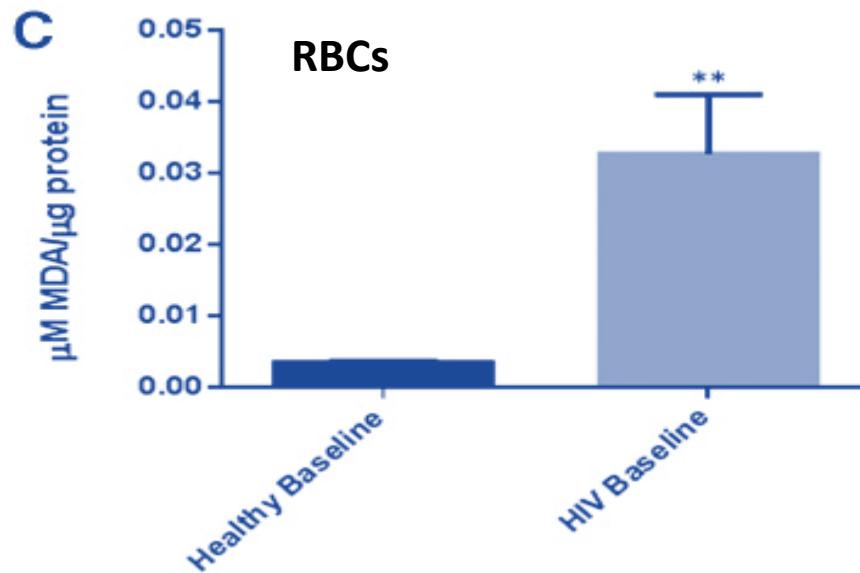
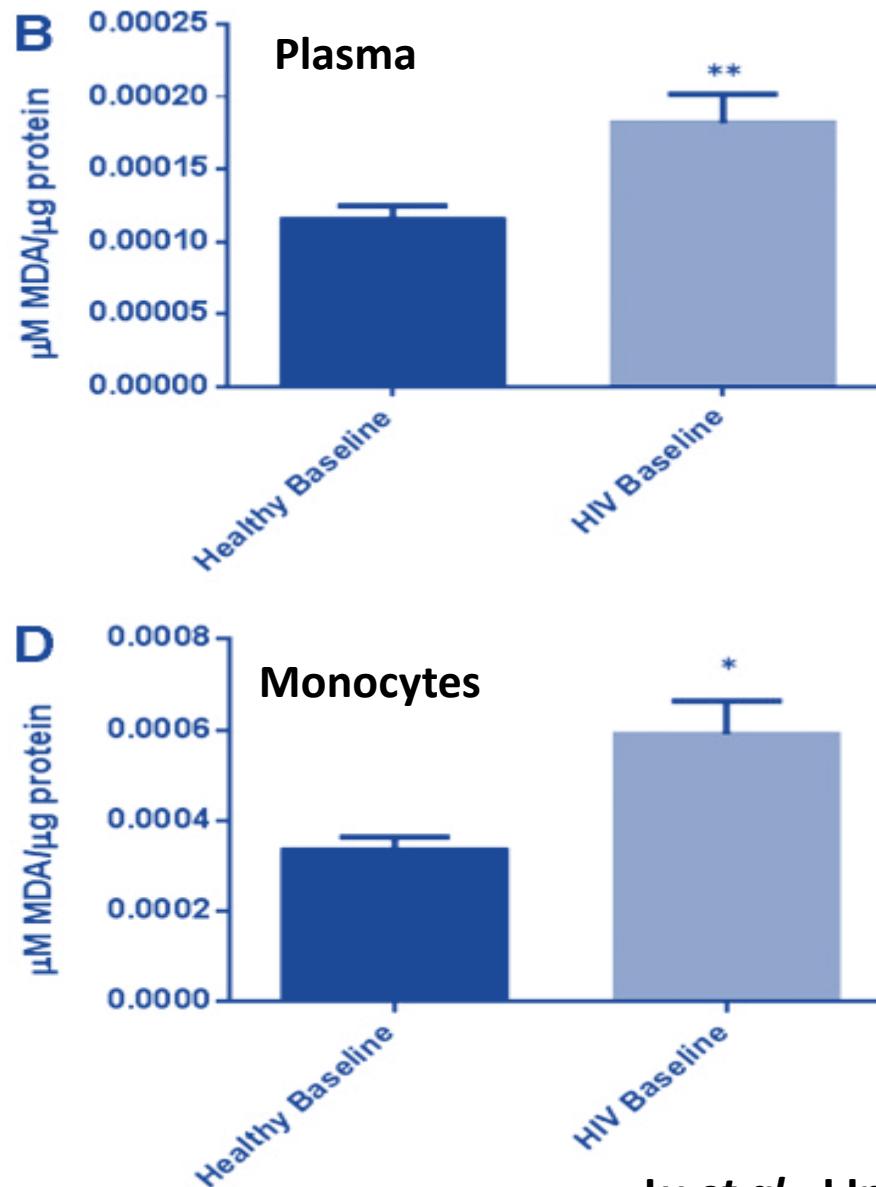
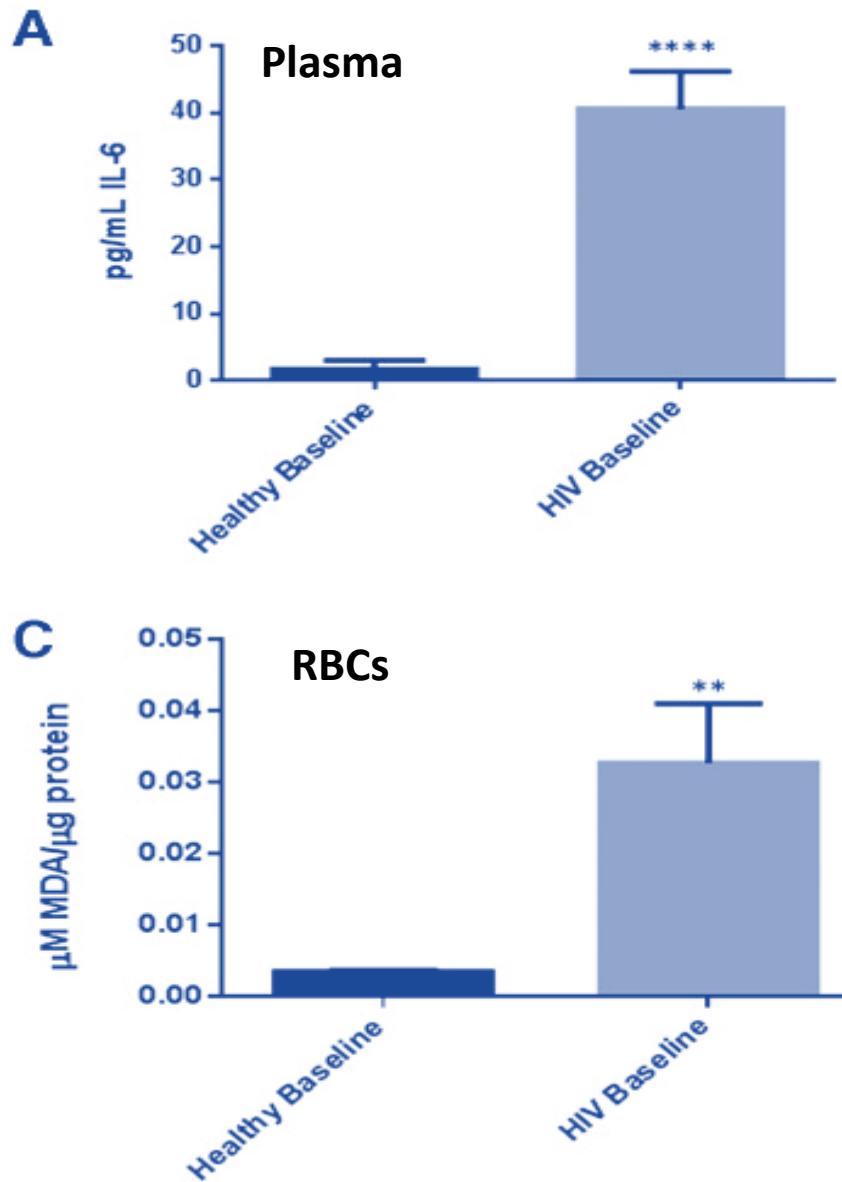


Morris *et al*; J Interferon Cytokine Res 2013

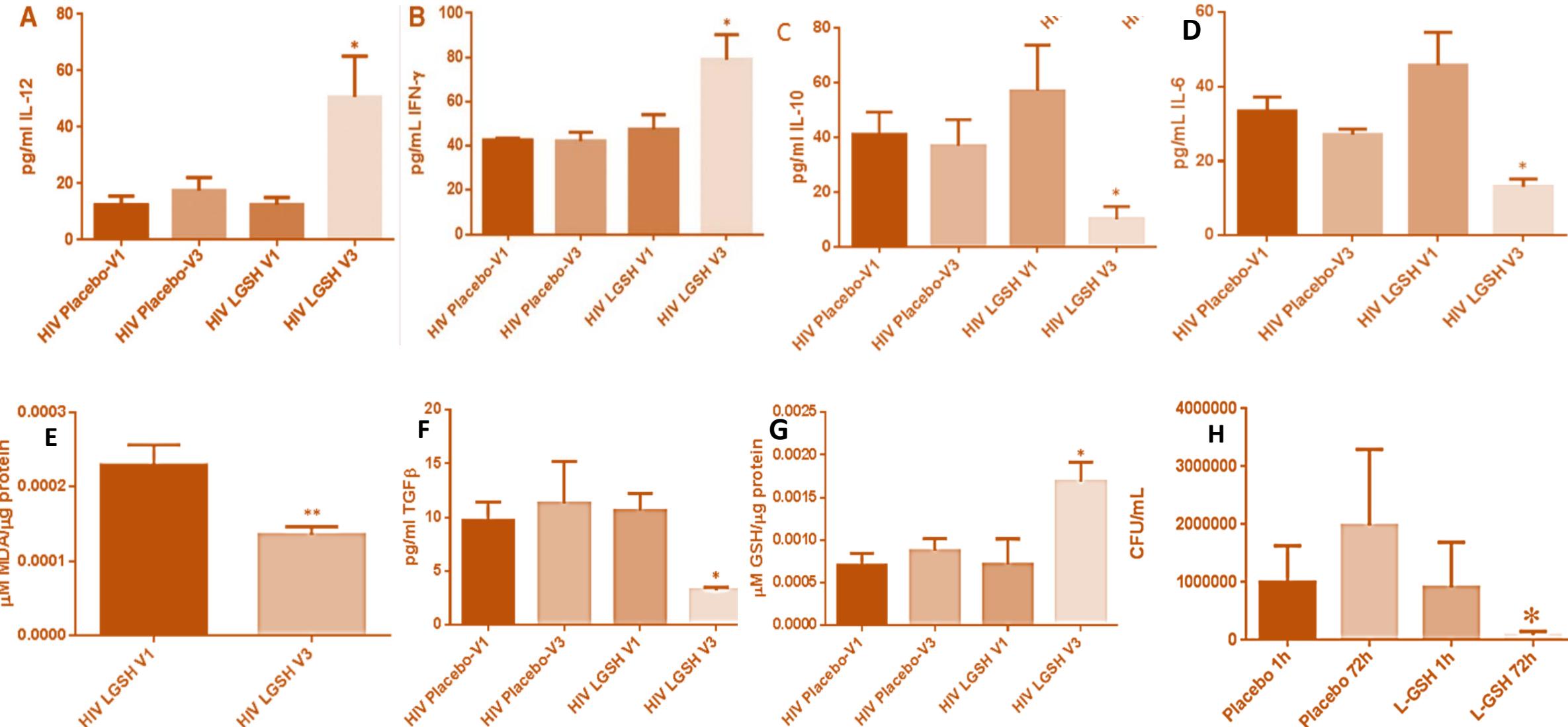
Assay of IL-12, IL-2, IFN- γ , IL-10 and TGF- β in plasma samples from healthy and HIV positive individuals.



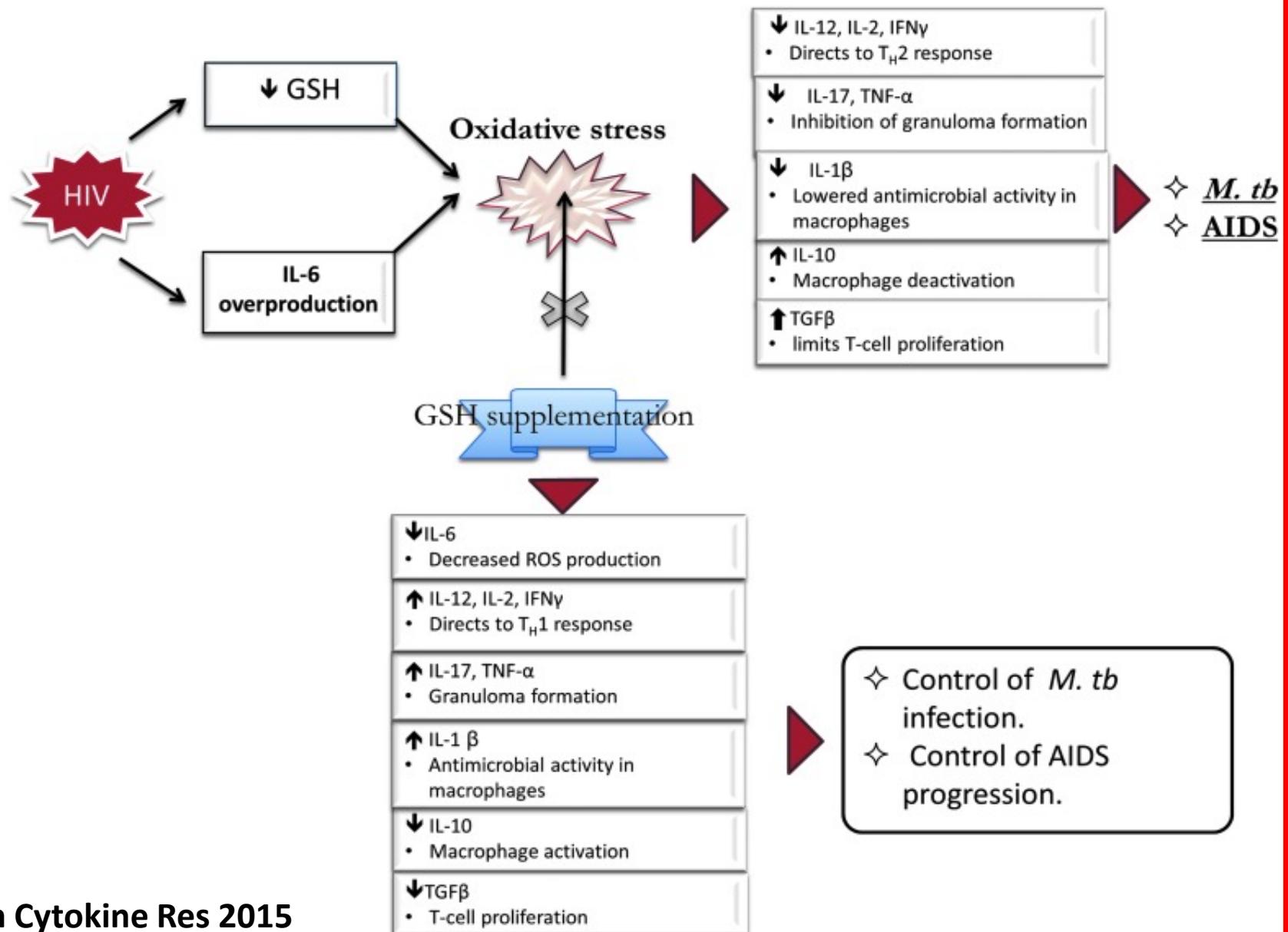
Baseline comparison of the interleukin-6 (IL-6) and reactive oxygen species (ROS) markers between healthy volunteers and HIV-positive individuals.



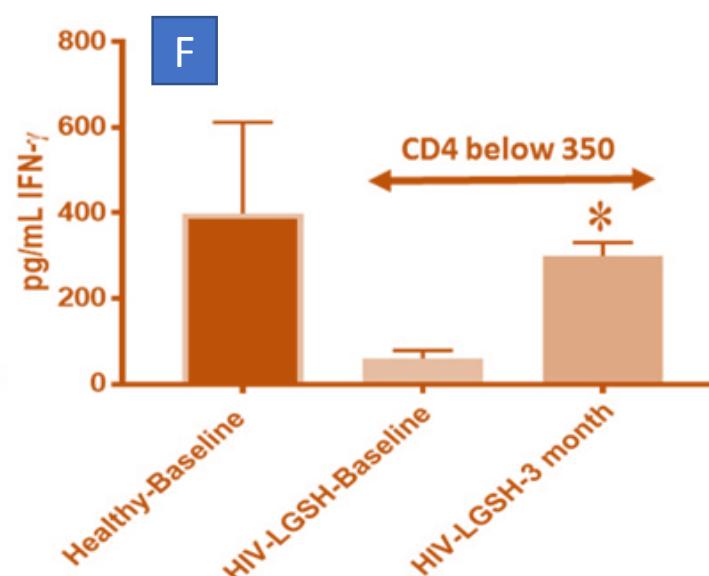
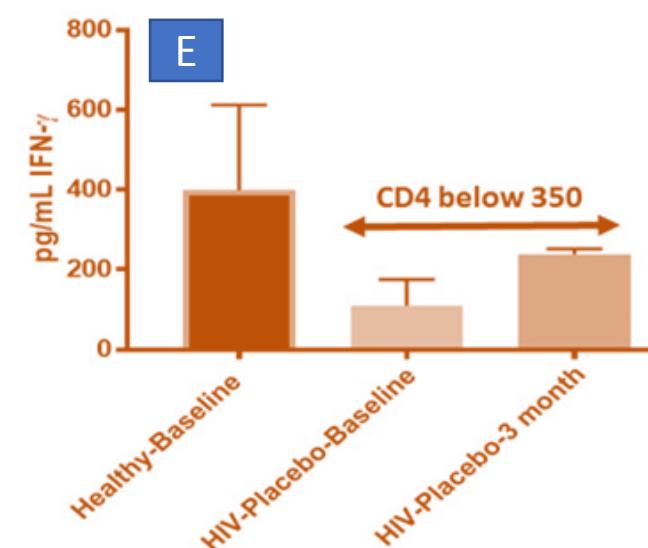
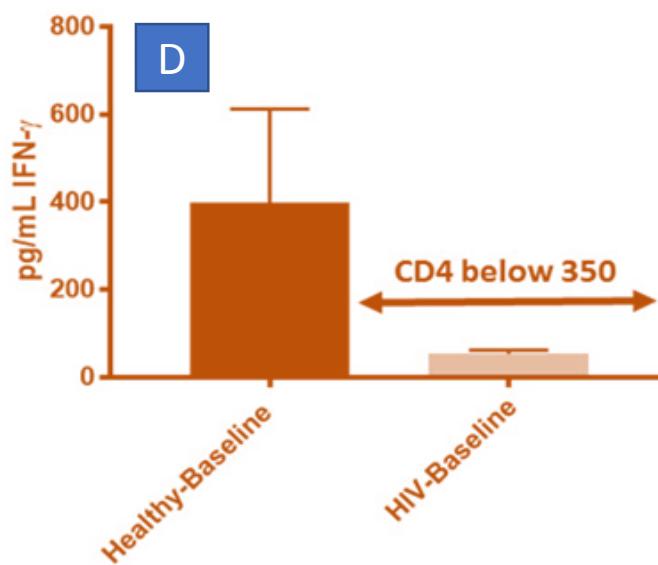
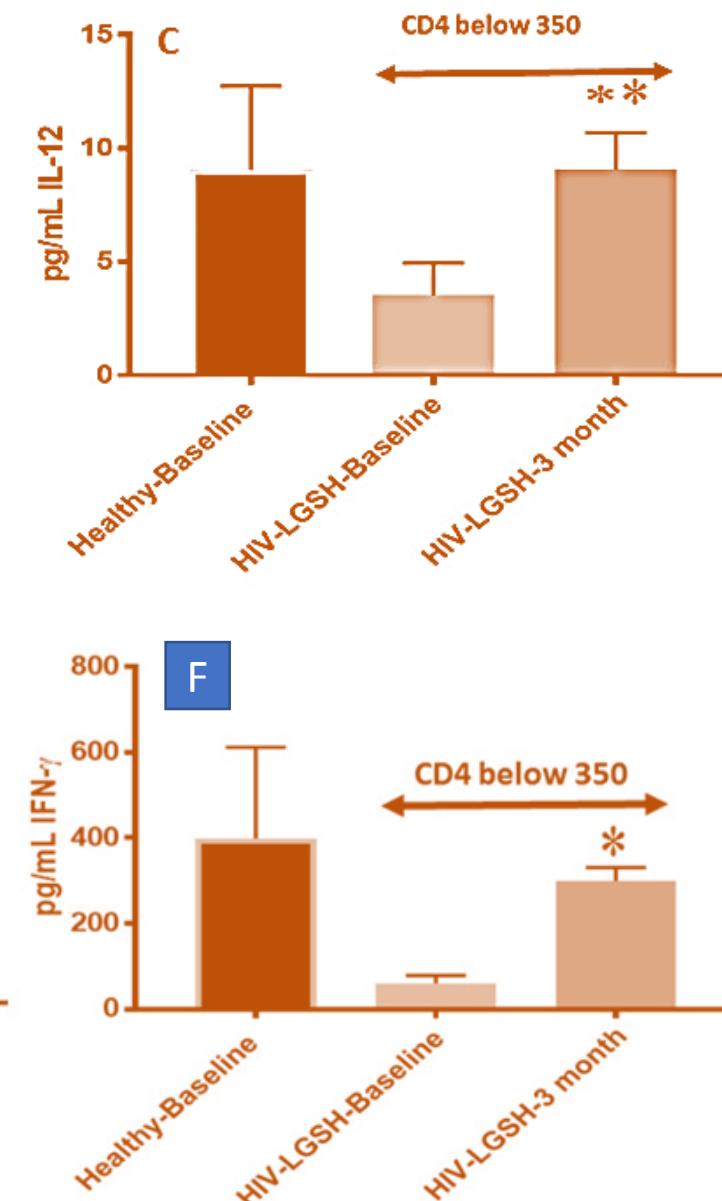
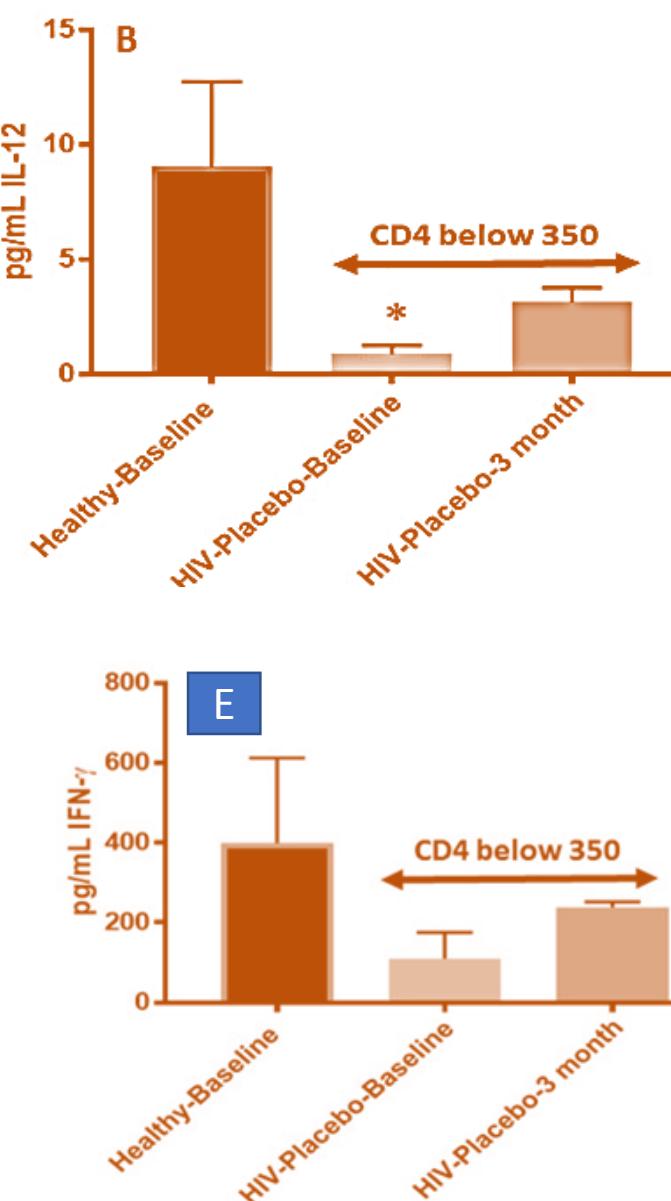
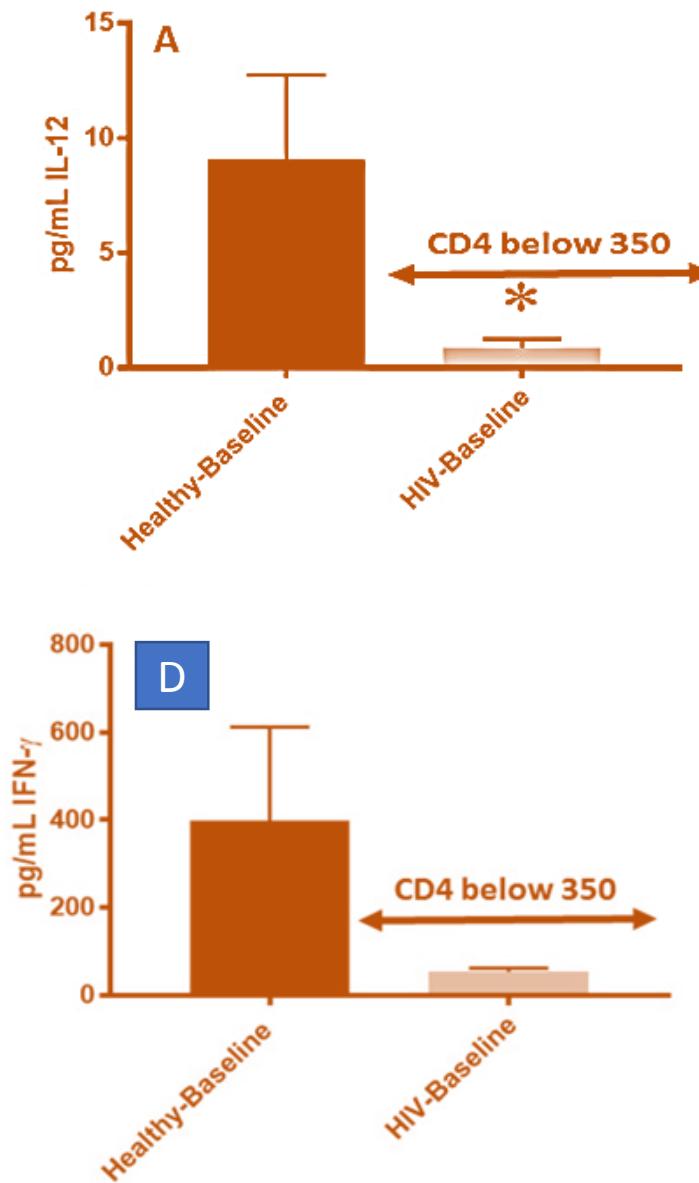
Changes in the levels of plasma cytokines (IL-12, IFN- γ , IL-10, IL-6 and TGF- β), free radicals, GSH, and *Mtb* survival in HIV positive subjects at pre- and post-GSH supplementation.



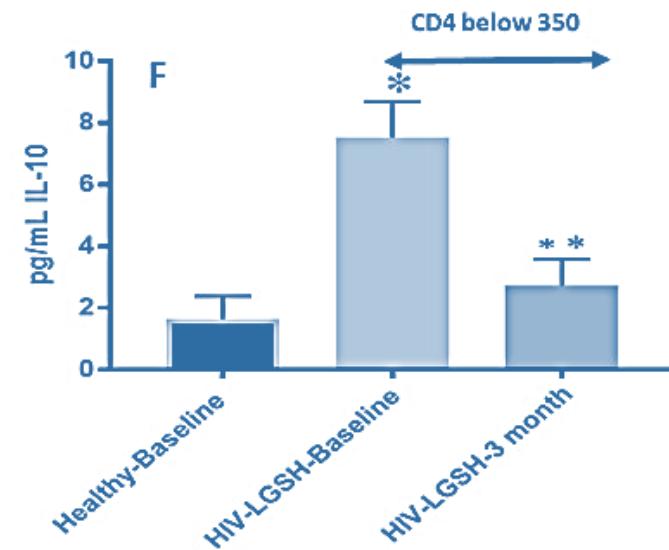
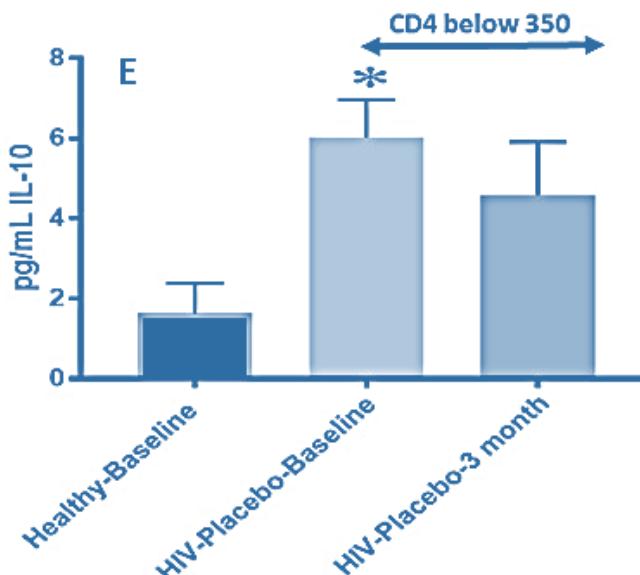
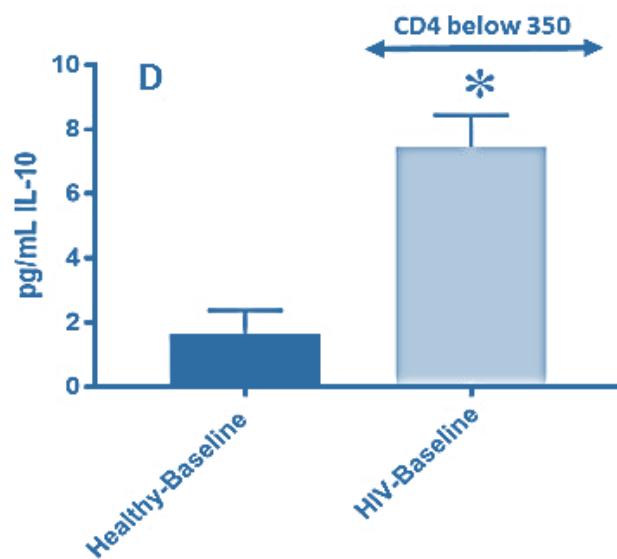
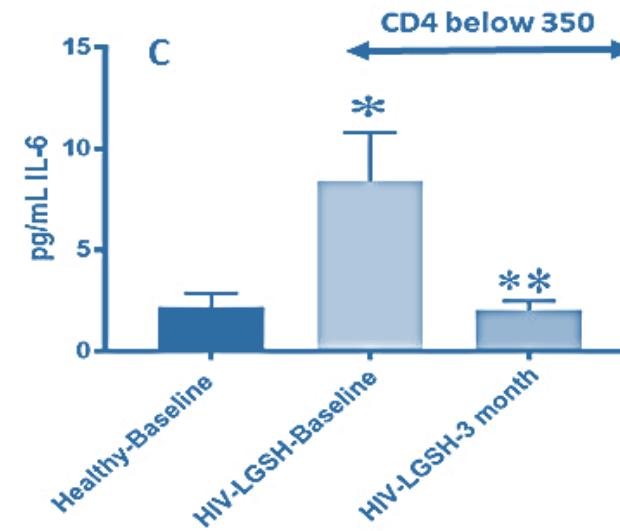
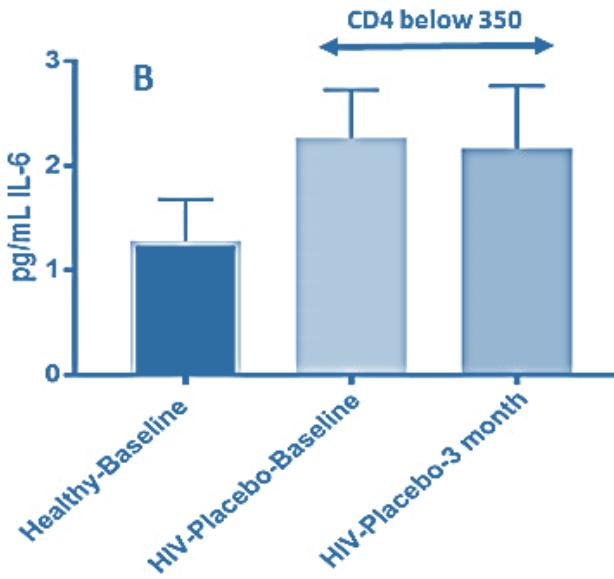
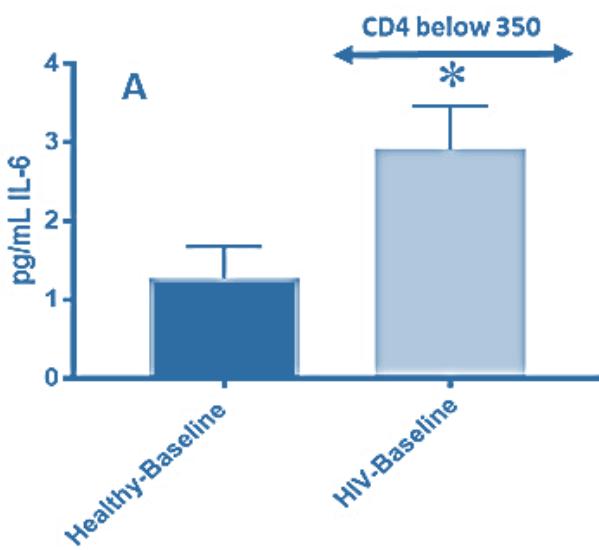
Cycle of HIV induced oxidative stress



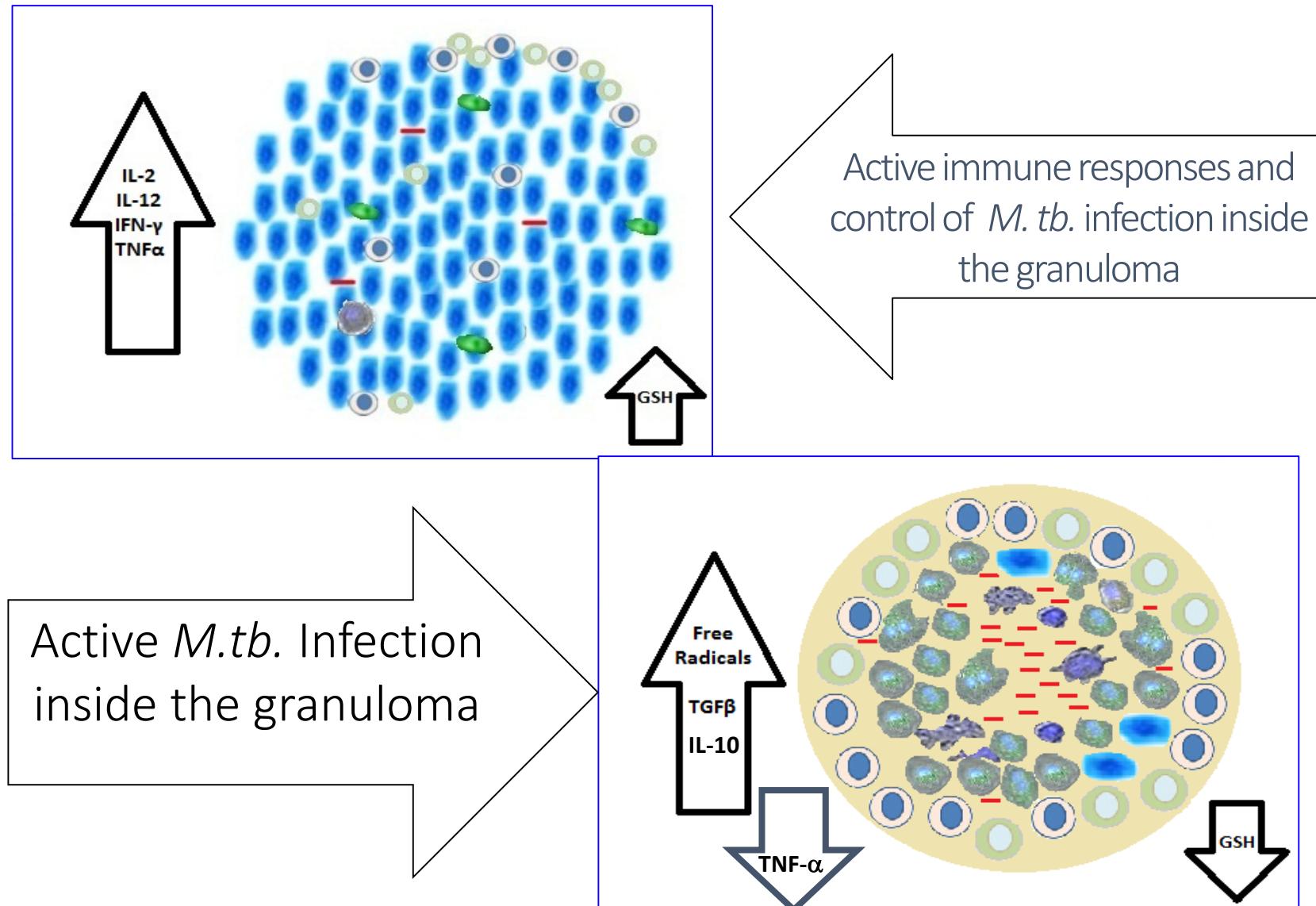
Second clinical trial in HIV positive subjects with low CD4 T cell counts



Second clinical trial in HIV positive subjects with low CD4 T cell counts

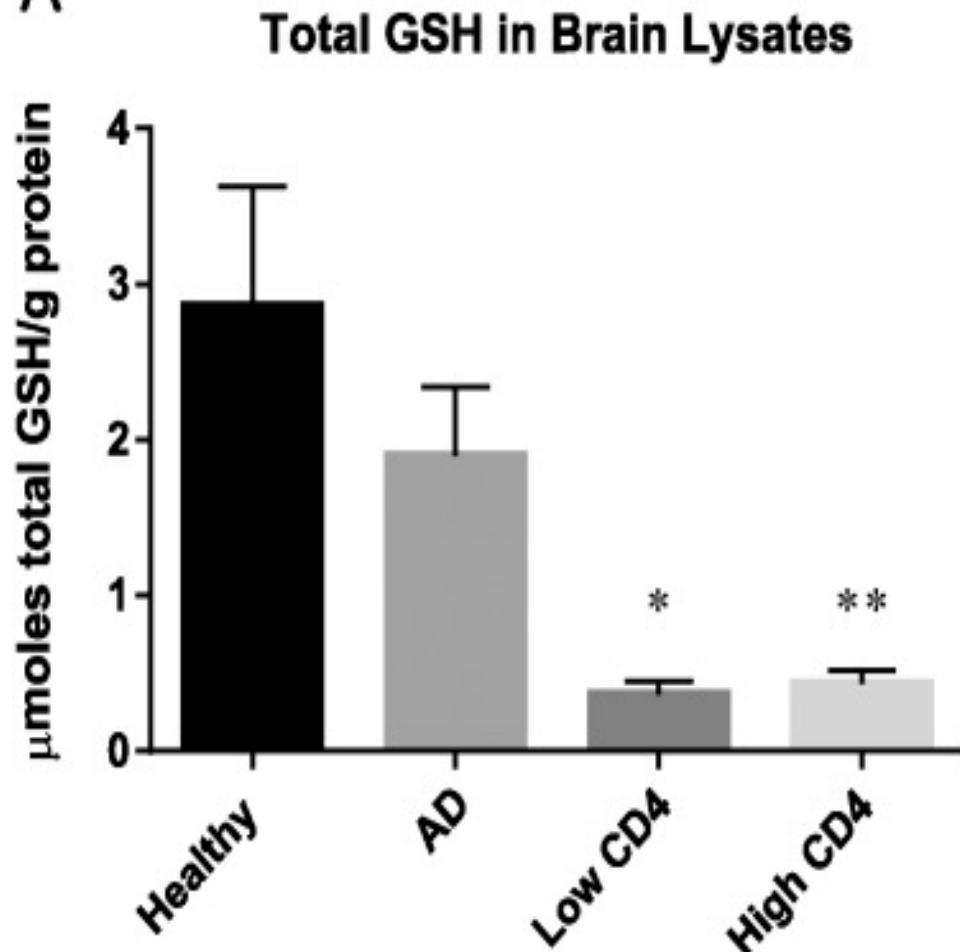


Summary of our clinical trial findings:

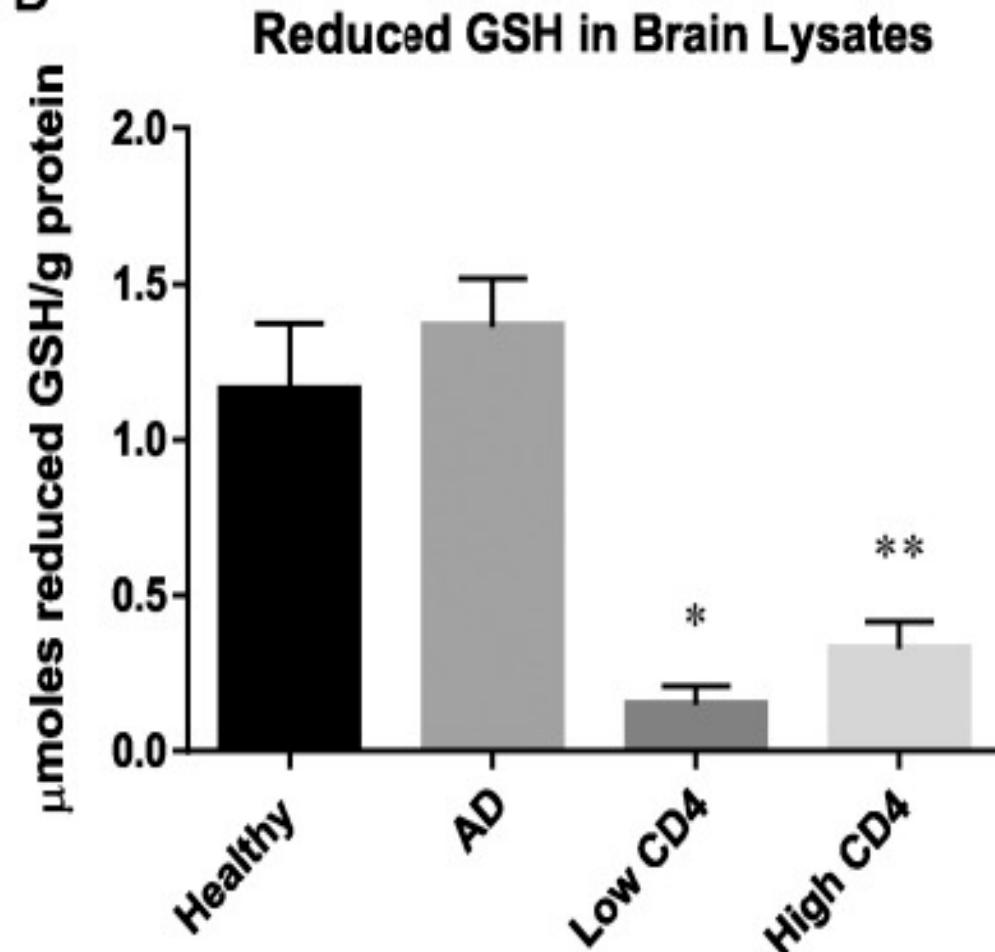


Assay of total GSH and rGSH in brain lysates from healthy, AD, and HIV-1 positive subjects.

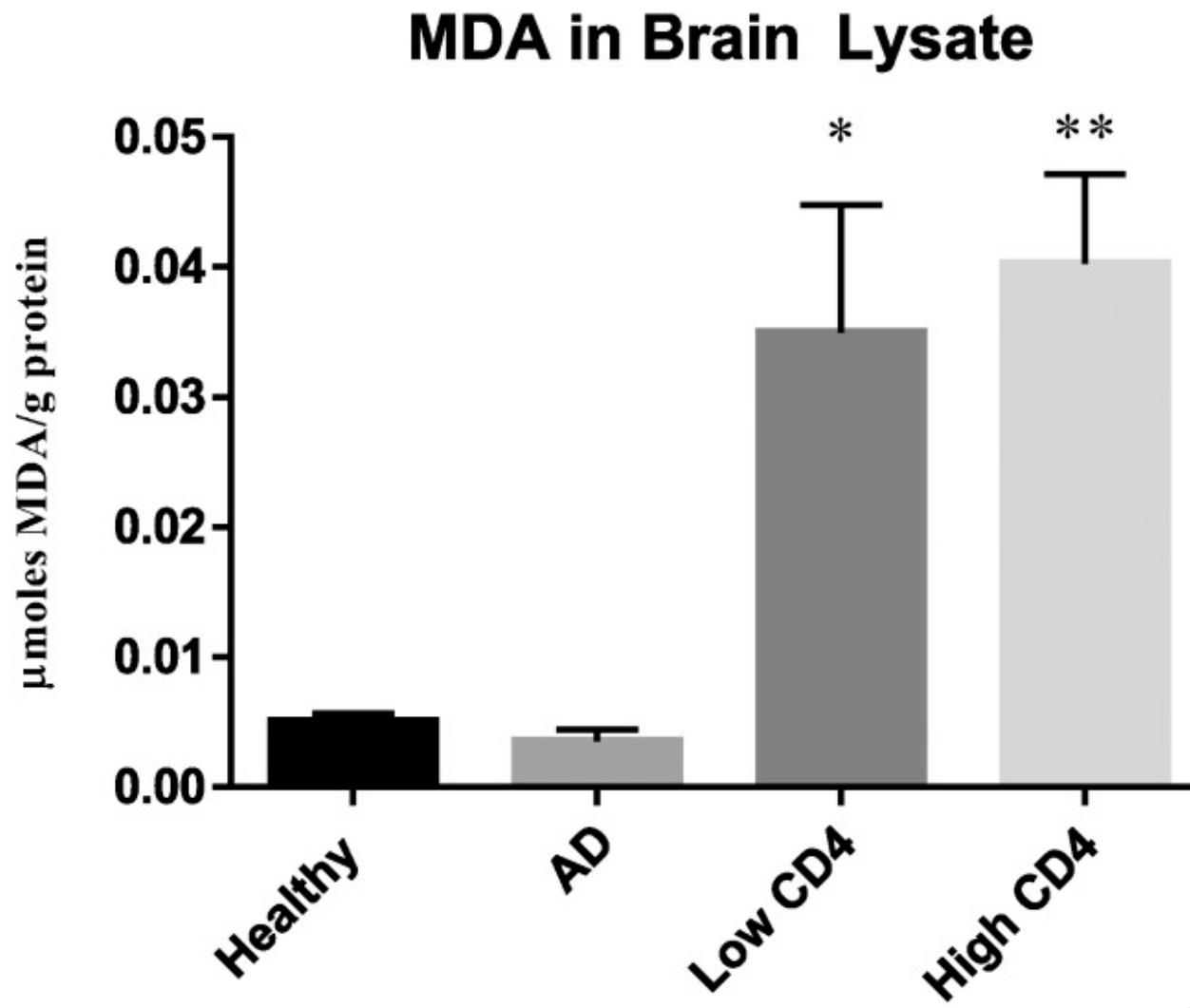
A



B

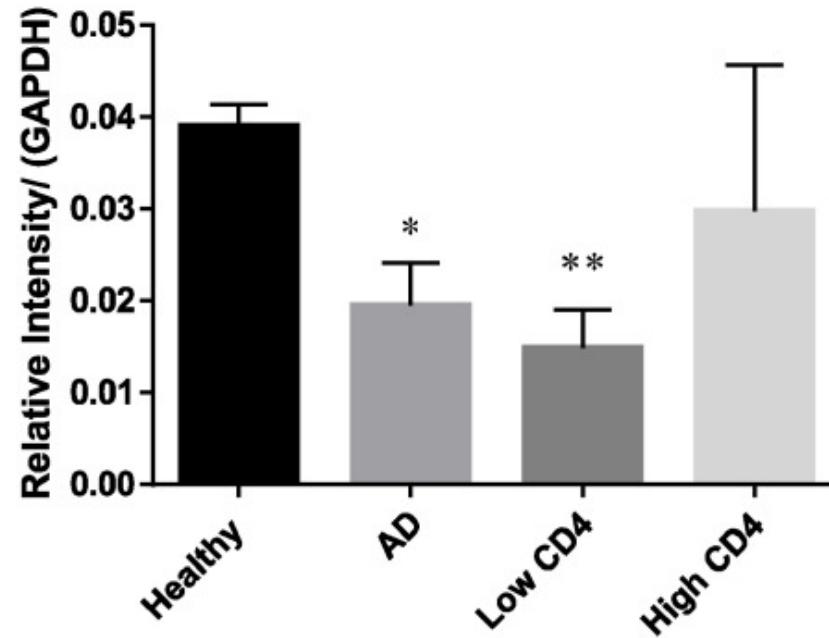


Assay of MDA in brain tissues from healthy, AD, and HIV-1-positive subjects.

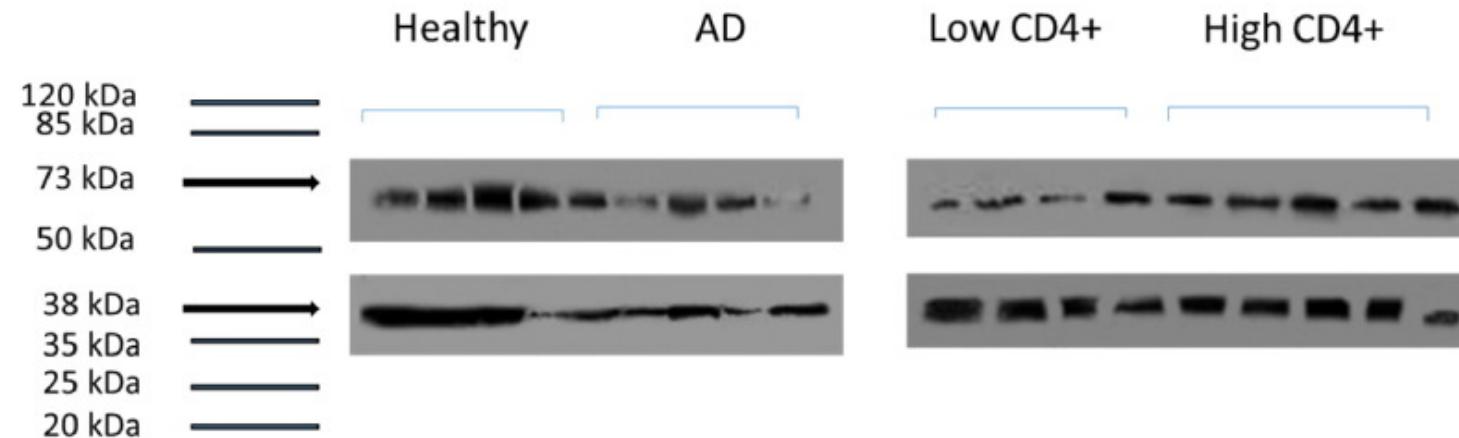


Western blot analysis of a GSH *de novo* synthesis enzyme, GCLC, in brain tissue from healthy subjects

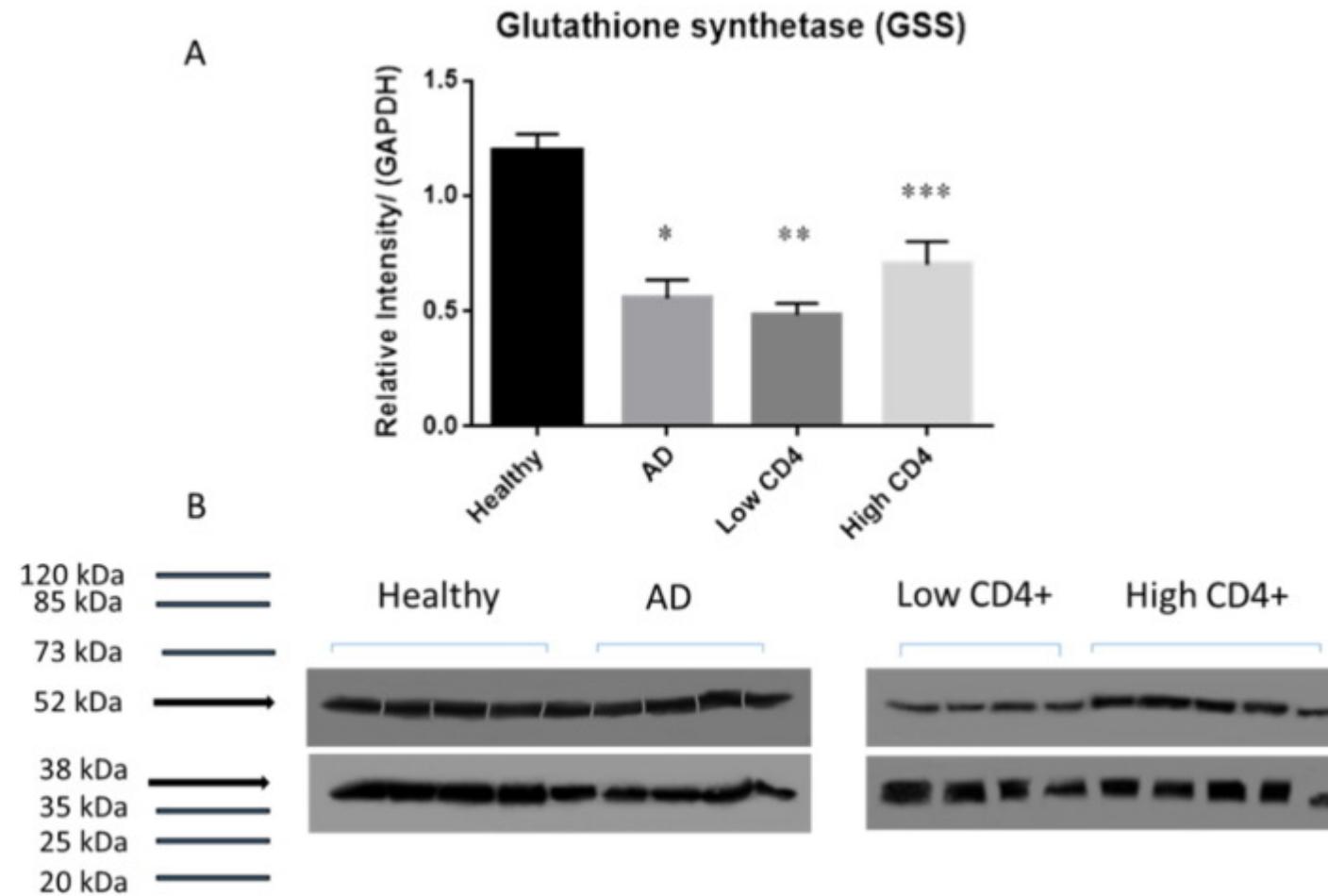
A Glutamate-cysteine ligase catalytic subunit (GCLC)



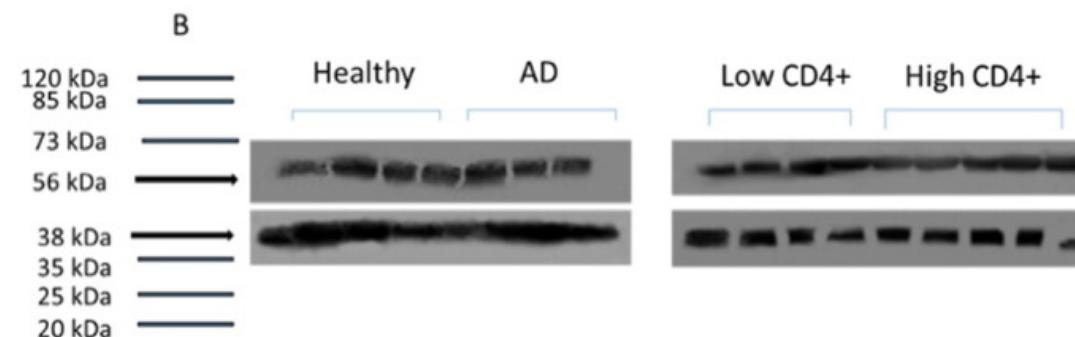
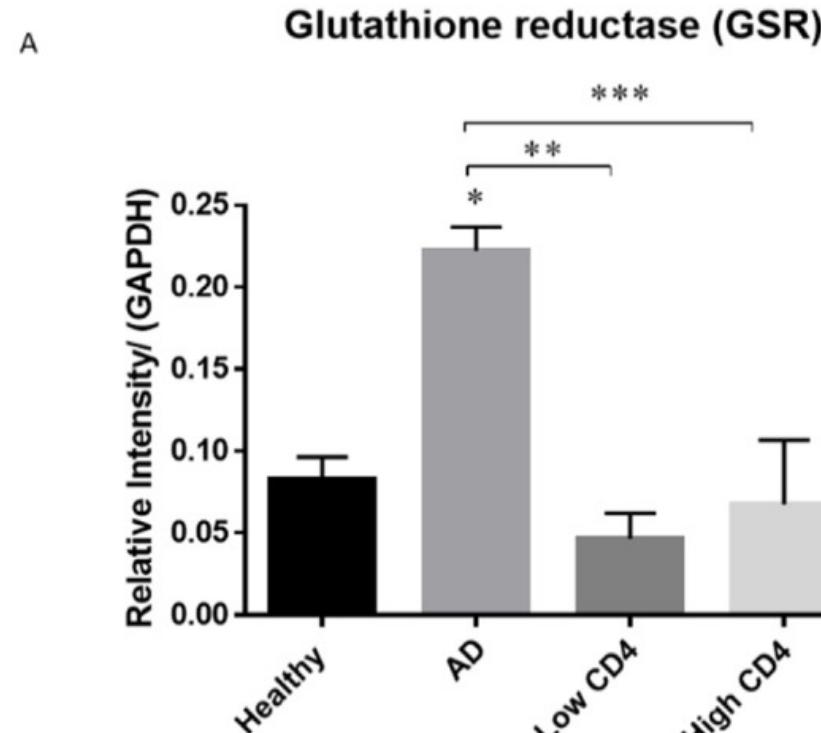
B



Western blot analysis of GSS, a GSH *de novo* synthesis enzyme in brain tissues derived from healthy, AD and HIV-1-positive subjects



Western blot analysis of a recycling enzyme, GSR, in brain lysates from healthy, AD and HIV-1-positive subjects

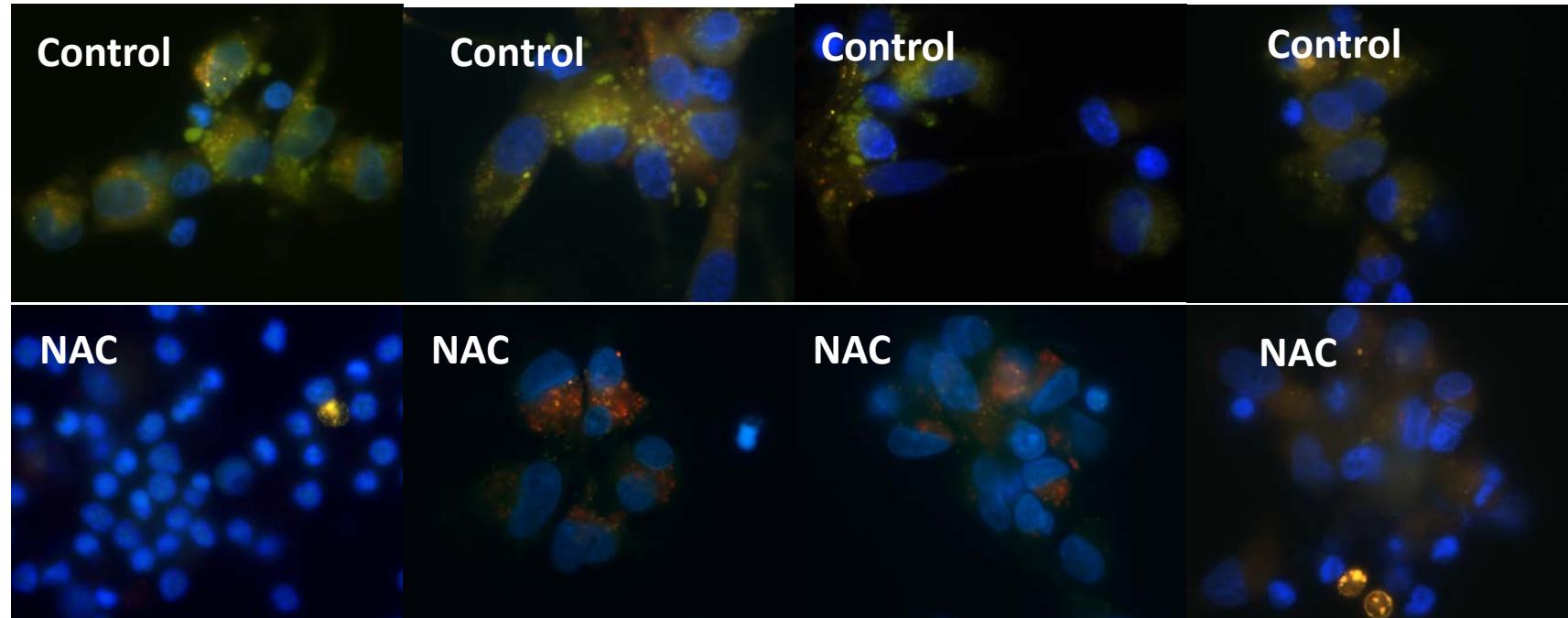
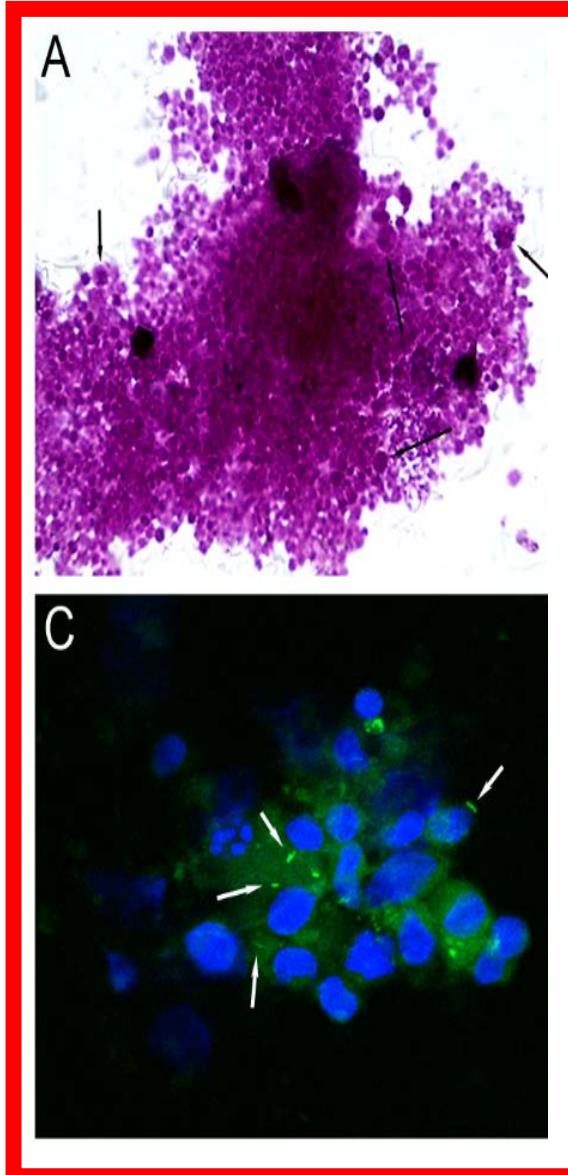


Other related studies

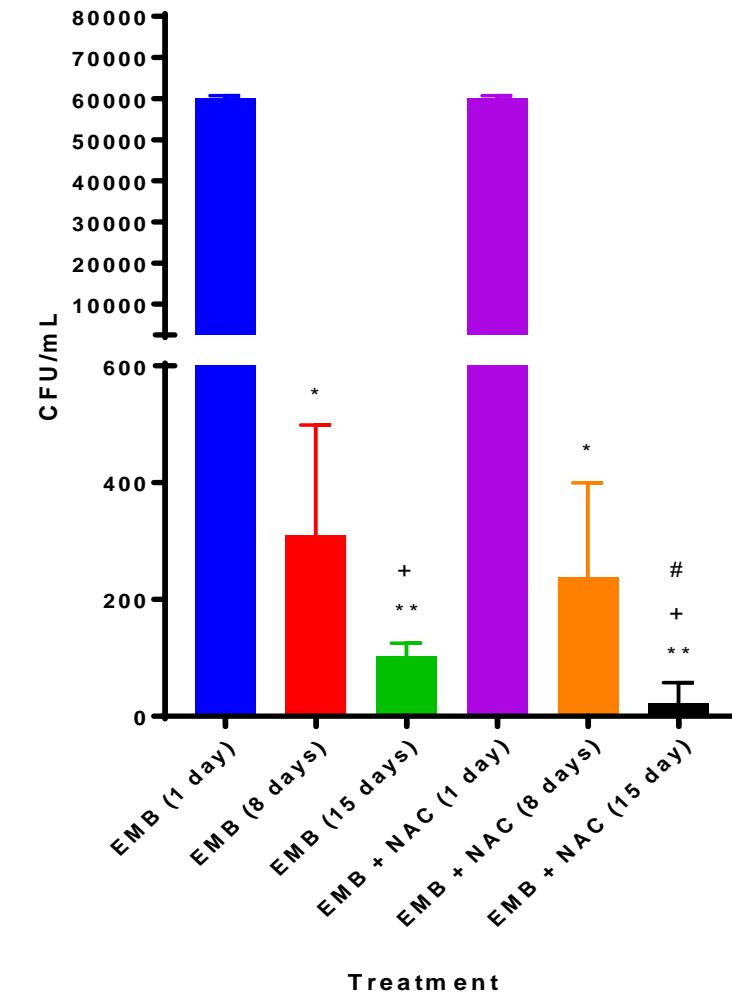
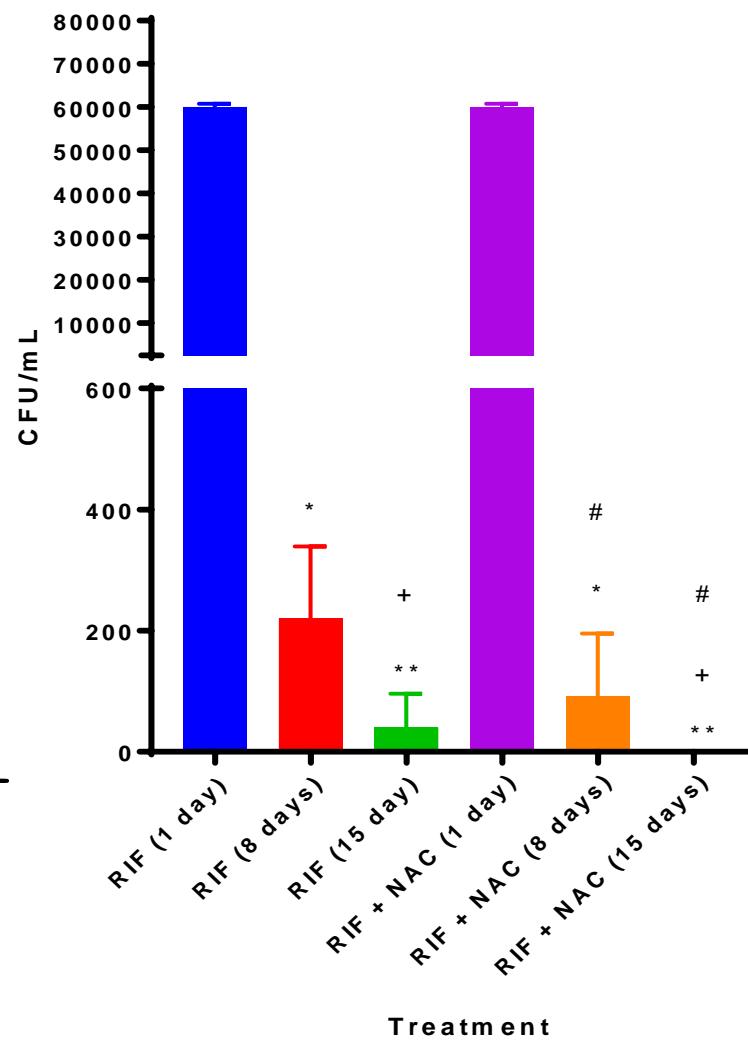
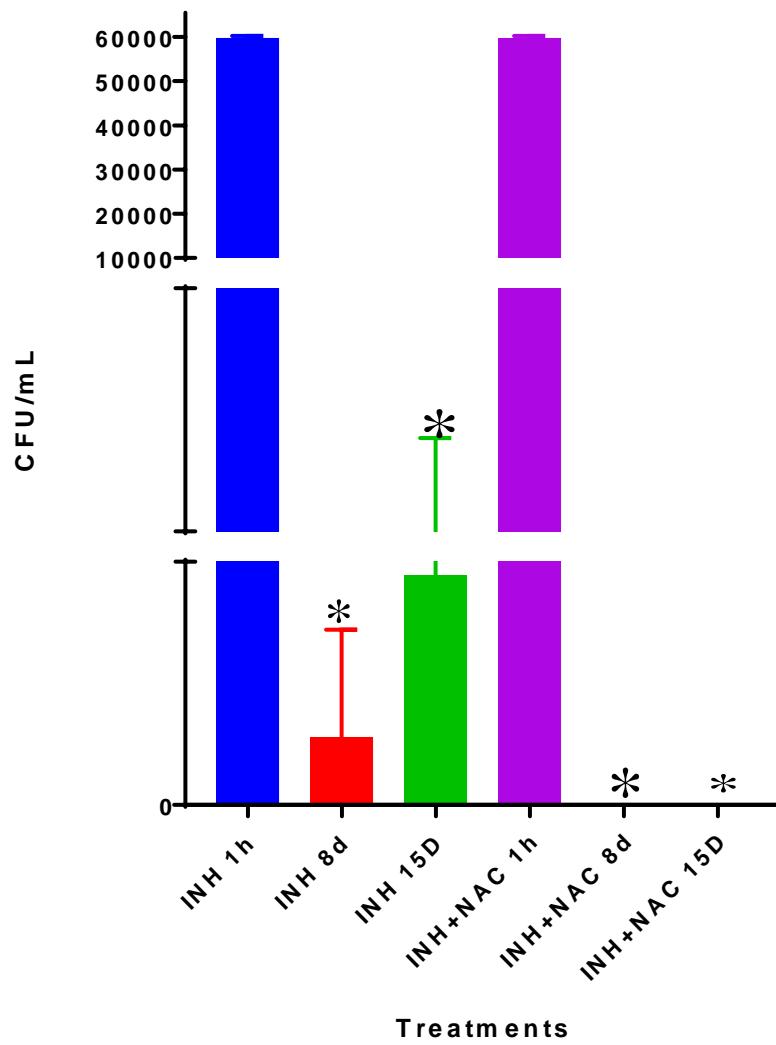
[N-acetyl-cysteine exhibits potent anti-mycobacterial activity in addition to its known anti-oxidative functions.](#) Amaral EP, Conceição EL, Costa DL, Rocha MS, Marinho JM, Cordeiro-Santos M, D'Império-Lima MR, Barbosa T, Sher A, **Andrade BB**. BMC Microbiol. 2016 Oct 28;16(1):251.
PMID: 27793104

Clinical trial in TB patients. Aurum Institute

Effects of NAC in granulomatous responses against *Mtb* infection



Synergistic effects of antibiotics+GSH in improving granulomatous responses against *Mtb* infection



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- *Your Energy Systems (2009-2016)*
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