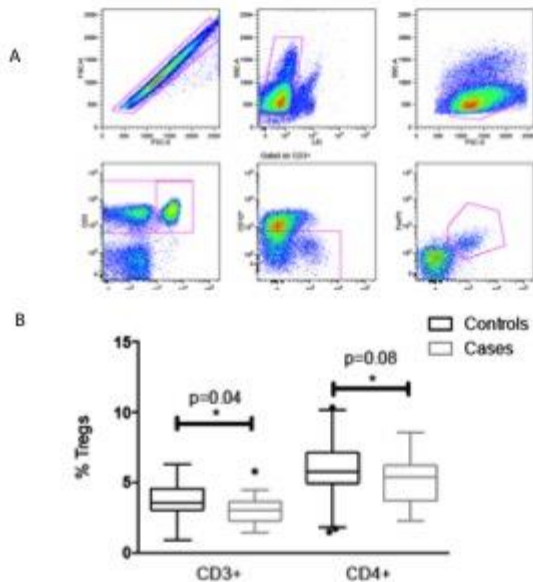


# Some rest is good

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A) Gating scheme used to identify regulatory T cells (Tregs) and B frequencies of Tregs in controls and cases as percentages of total CD3+ or CD4+ T cells.

*Image provided by Dr. Laura Pattacini.*

More than thirty years into the HIV epidemic, we still do not know which kind of immunity can protect us from infection. The research is complicated by the fact that HIV infects CD4+ T cells, dendritic cells and macrophages, which are all part of the immune system, and is more likely to replicate in activated cells. Therefore, a vaccine that activates this part of the immune system might inadvertently increase the possibility of a productive infection. On the other hand, its lack of induction affects other compartments of the immune system, such as B and CD8+ T cell. How to solve this puzzle? Some individuals are exposed to HIV yet do not acquire the virus, defying the odds; therefore, looking at their immune asset may help identifying correlates of protection from infection.

Starting from this idea, a team of researchers at Fred Hutch and University of Washington compared the immune responses of two groups of subjects, both highly exposed to HIV as a result of being in a relationship with an HIV-infected partner. One group included subjects that remained seronegative in the course of the study, while the other included only those that later seroconverted (although all samples were obtained before seroconversion). The groups were comparable for demographic characteristics as well as for their HIV exposure level, estimated by a score calculation based on an algorithm that takes into account several variables such as viral loads of the HIV-infected partner

and frequency of unprotected sex (the algorithm was developed at the University of Washington and details can be found in Kahle E et al, *Journal of acquired immune deficiency syndromes* 2013).

This collection of samples represents a unique opportunity to investigate factors that influence seroconversion in HIV exposed individuals. Two main hypotheses have been formulated to explain HIV 'resistance': one is defined the immune quiescence hypothesis, which assumes that a state of general low immune activation prevents HIV infection by limiting the numbers of possible target cells, the second hypothesis supports a role for HIV-specific CD4+ and CD8+ T cell responses in protection from HIV.

A study from Dr. Laura Pattacini and co-investigators (Vaccine and Infectious Disease Division), published in the *Journal of Acquired Immune Deficiency Syndromes*, reports that samples from individuals who did not acquire HIV were characterized by higher frequency of regulatory T cells (Tregs). Tregs play a fundamental role in controlling activation of several types of immune cells, in order to terminate the immune response after an infection is cleared as well as to avoid autoimmunity. On the other hand, no differences were found in HIV-specific immune responses detected by cytokine secretion upon in vitro stimulation with HIV-peptide pools. These findings, especially the increased frequency of Tregs in non-seroconverters support the immune quiescence hypothesis.

The results open a path for further studies: "We plan to continue our investigations to identify novel mechanisms of protection from HIV-1 infection in HIV-1 exposed seronegative individuals, though we will next turn our focus to investigating the genital mucosal tissues, as a critically relevant tissue site for protection for individuals exposed to HIV-1 via the sexual route" said Dr. Jennifer Lund, principal investigator and coordinator of the project. Science Spotlight will surely follow-up with her in the future to report what happens at the sites of HIV infection.

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[Pattacini L, Baeten JM, Thomas KK, Fluharty TR, Murnane PM, Donnell D, Bukusi E, Ronald A, Mugo N, Lingappa JR, Celum C, McElrath MJ, Lund JM.](#) 2015. Regulatory T-cell activity but not conventional HIV-specific T-cell responses are associated with protection from HIV-1 infection. *Journal of acquired immune deficiency syndromes*. doi: 10.1097/QAI.0000000000000919. [Epub ahead of print]