Slowing down immune system's 'brakes' may improve HIV vaccines

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Like a skittish driver slamming the brakes, a special class of T cells may be limiting the effectiveness of therapeutic vaccines for HIV by slowing the immune system response too soon, report University of Pittsburgh health science researchers in the current issue of *PLoS ONE*.

Their study, the first to look at the role of regulatory T cells in therapeutic HIV vaccines, may help researchers improve the efficacy of such vaccines by devising methods to circumvent the braking mechanism of these cells.

Regulatory T cells (Treg) are critical because they prevent the immune system from turning against itself by suppressing the immune response. Without the braking action of Treg, autoimmune disease could flourish. But what if these cells are shutting down the immune response before a therapeutic vaccine has had a chance to bolster immunity against HIV?

Pitt researchers sought to answer this question as follow-up to a clinical trial of a therapeutic dendritic cell-based HIV vaccine they developed to activate the CD8, or killer T cell, response. First reported in 2008, their findings indicated only limited success of the vaccine in the 17 patients enrolled in the trial. For the current study, the researchers went back to the freezer, removed Treg from the patients' blood cell samples and found it was masking a two-fold increase in immune response to HIV induced by the vaccine.

"When we removed Treg from blood cells, we found a much stronger

immune response to the vaccine, giving us insight into how we can develop more effective HIV vaccines," said Charles R. Rinaldo, Jr., Ph.D., professor and chairman, Department of Infectious Diseases and Microbiology, Pitt's Graduate School of Public Health and the study's senior author. "Treg normally shuts down CD8 responses once the infection has been controlled, but in this case it appears to be putting on the brakes early and possibly limiting the vaccine's ability to do its job effectively."

One theory is that HIV-infection drives up Treg, which in turn shuts down the HIV-1- specific CD8 T cell response, he said.

"We know how to treat HIV, but are still learning how to use immunotherapy strategies to completely flush it out of the body," added Bernard J.C. Macatangay, M.D., assistant director, University of Pittsburgh Immunology Specialty Laboratory and the study's lead author. "Our findings show Treg plays an important role, but we need to figure out how to maintain the right balance by getting around these cells without blocking them completely."

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