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Scientists reactivate immune cells exhausted by chronic HIV

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Scientists at the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, have demonstrated why certain immune cells chronically exposed to HIV shut down, and how they can be reactivated.

Healthy B cells have a balanced mix of surface proteins that the immune system can use, like the gas pedal and brake of a car, either to activate the cell or to damp down its activity. However, in people with long-term HIV infection who have not begun antiretroviral therapy, their B cells—responsible for producing anti-HIV antibodies—display a surplus of inhibitory receptors, the surface proteins used to apply the brakes on a B cell. Scientists from the NIAID Laboratory of Immunoregulation led by Lela Kardava, Ph.D., Susan Moir, Ph.D., and Anthony S. Fauci, M.D., NIAID Director and Chief of the laboratory, wanted to know if this phenomenon can help explain why B cells become "exhausted" and essentially shut down in people who are HIV-infected but treatment-naive.

To test their hypothesis, the scientists used molecules called small interfering RNAs (siRNAs), which acted at the genetic level to prevent exhausted B cells from replenishing inhibitory receptors. After treatment with siRNAs, the exhausted cells responded more normally to conditions that typically would spur a B cell into action, such as the presence of a virus, demonstrating that the excess of inhibitory receptors may explain why exhausted B cells are so unresponsive.

Because B cells generally are difficult to manipulate, the new siRNA-based approach may hold promise for scientists seeking to develop therapies to improve the human antibody response against HIV and other pathogens by altering the expression of specific B-cell genes.

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