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Extraordinary immune cells may hold the key to managing HIV

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People who manage to control HIV on their own are providing scientists with valuable information about how the immune system eliminates virus-infected cells. A new study, published in the December 4th issue of *Immunity*, a Cell Press publication, identifies specific characteristics of the immune cells that successfully destroy HIV-infected cells and may drive strategies for developing the next generation of HIV vaccines and therapies.

Long-term nonprogressors (LTNPs) or elite controllers are rare individuals who are able to contain HIV for many years without any type of antiretroviral therapy. "Direct and indirect lines of evidence in humans and animal models suggest that virus-specific immune cells, called CD8+ T cells, mediate this control. However, the mechanisms by which this occurs remain unknown," says senior study author Dr. Mark Connors from the National Institute of Allergy and Infectious Disease in Bethesda, Maryland.

Using sophisticated new tools that can precisely measure the killing capacity of HIV-specific CD8+ T cells on a per-cell basis, Dr. Connors and colleagues compared how cells from LTNPs and progressors battle HIV by destroying infected cells. The CD8+ T cells of LTNPs efficiently eliminated infected cells by successfully loading granules with the proteins necessary for poking holes in the membranes of target cells and subsequently delivering a death-inducing molecule called granzyme B to cells infected with HIV.

In contrast, the CD8+ T cells of progressors lysed HIV-infected cells poorly. The researchers went on to show that CD8+ T cells of progressors were deficient in their ability to load lytic granules and deliver cytotoxic proteins to target cells. Elimination of infected cells readily distinguished LTNPs from progressors and was not restored in patients on antiretroviral therapy. However, the diminished abilities of the HIV-specific CD8+ T cells of progressors were reversible after treatment with phorbol ester and calcium ionophore, suggesting that these cells may retain the capacity to perform at the level seen in LTNPs.

Taken together, these findings demonstrate that LTNPs exhibit a superior ability to kill HIV-infected cells. "This capacity of CD8+ T cells is the function that is the best correlate of immunologic control we have observed thus far," says Dr. Stephen Migueles, the lead author of the study. He went on to say, "It will be very important for us to determine whether this is also predictive of immunologic control in vaccines. Clear correlates of immunologic control of HIV in chronic infection or vaccines have been sought for many years. If this function is also predictive of control in vaccines, this could be an extremely important milestone for HIV vaccine research."

Source: Cell Press