Cellular pathway discovered that may re-energize immune cells to eliminate HIV

January 12 2016, by Tina Shelton

Researchers at the University of Hawai'i (UH) and Oregon Health Sciences University (OHSU) have revealed a novel new immune pathway that can be targeted to increase the immune system's ability to eliminate HIV, the virus that can lead to AIDS.

The research team led by Lishomwa Ndhlovu, MD, PhD, at the UH John A. Burns School of Medicine (JABSOM) Hawai‘i Center for AIDS, and Jonah Sacha, PhD, from OSHU, identified a novel negative checkpoint receptor on T cells, TIGIT, which may be responsible for making immune cells dysfunctional and unable to control or eliminate the HIV virus.

The discovery, published in the January 2016 issue of the scientific journal *PLoS Pathogens*, will give new directions to vaccines and therapies that will potentially reverse these exhausted cells and allow them to control HIV-1 replication, but also serve in "Shock and Kill" HIV curative strategies.

Background

When a person becomes infected with HIV, starting combination antiretroviral drug treatment will, in most cases, successfully suppress HIV in the blood. However, the treatment is powerless to clear infection and restore full health. Furthermore, if people with HIV stop taking antiretroviral drugs, they experience a rapid, aggressive rebound of the

virus in the blood. This indicates that HIV has found a way to hide and establish a "dormant reservoir," but more importantly, evade elimination by the immune system.

In the absence of treatment, HIV infection is brought partially under control by the infected person's immune system, specifically by an immune system cell called a CD8+ Killer T cell. The response of these CD8+ T cells and HIV during the early stages of infection is crucial and will determine how the disease will progress. Over time, however, the immune damage mediated by HIV infection will affect the function of the CD8+ T cells, even if with the addition of antiretroviral drugs.

These immune cells are key players in eliminating HIV infected reservoir cells. One proposed strategy to eradicate HIV being considered is the "Shock and Kill" approach, first to "Shock" the infected cells with agents that will awaken the dormant virus and then allow the immune system to "Kill" the reactivated virus. A major obstacle with this approach has been that although CD8+ Killer T cells can recognize HIV-1 infected cells, these T cells are unable to eliminate the reactivated HIV viral reservoir.

"A preponderance of emerging evidence indicates that the functions of the HIV-specific CD8+ Killer T cells are severely compromised and enters a state of 'exhaustion,' rendering the cells less effective at eliminating HIV infected cells," said Glen Chew, a PhD candidate in Immunology at JABSOM and lead author of the study.

According to the World Health Organization (WHO), since the beginning of the epidemic, almost 78 million people have been infected with the HIV virus and about 39 million people have died of HIV. Globally, approximately 35 million people were living with HIV at the end of 2013 and an estimated 0.8% of adults aged 15–49 years worldwide are living with HIV. There is no approved vaccine or curative

treatment.

Currently an estimated 2,900 people in the Hawaiian islands are living with HIV/AIDS, with many others unaware of their HIV status. The Hawai‘i Center for AIDS has launched a fundraising campaign, "Hawai‘i to Zero" (H20) Initiative, to raise additional resources in its mission to discover a cure for HIV.

More information: Learn more about the H20 initiative at: hawaii2zero.jabsom.hawaii.edu/

Glen M. Chew et al. TIGIT Marks Exhausted T Cells, Correlates with Disease Progression, and Serves as a Target for Immune Restoration in HIV and SIV Infection, *PLOS Pathogens* (2016). DOI: 10.1371/journal.ppat.1005349

Provided by University of Hawaii at Manoa