SIV infection may lead to increase in immune-suppressive Treg cells

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Tissue in monkeys infected with a close relative of HIV can ramp up production of a type of T cell that actually weakens the body's attack against the invading virus. The discovery, in lymph nodes draining the intestinal tract, could help explain how the HIV virus evades the body's immune defenses.

If the same pattern is found in people infected with HIV, the finding could lead to a treatment strategy that slows the production of this restraining type of T cell. This would let the immune soldiers go after the virus more aggressively.

The scientists don't know if the simian virus is directly causing the build-up of the inhibitory T cells, called regulatory T cells, but in any case, reducing regulatory T-cell production could boost the body's resistance to the evasive virus.

The research was a collaboration among scientists at the UC Davis School of Medicine, Cincinnati Children's Hospital and the California National Primate Center.

Regulatory T cells, or Tregs, normally tamp down immune-system attacks, presumably to prevent an over-active assault that can cause harmful inflammation or auto-immune disease. The scientists suspect that the high number of Treg cells in the infected primates might prevent their immune systems from mounting a full-on attack against the virus.

The researchers focused on immune cells called dendritic cells that interact with Tregs in preparation for their policing duty. This occurs in lymph nodes throughout the body's lymphatic system -- the part of the circulatory system that also drains many organs of fluids, fatty acids and other substances.

The study found that mature dendritic cells were particularly active in promoting Treg production, and that these promoters were in high concentration in nodes draining the intestine, or mucosa. The intestinal mucosa is the site of early infection and aggressive transmission for both the primate virus and HIV, making it the first line of defense against the invasion.

"The intestinal mucosa contains highly activated 'helper' T-cells that are prime targets for the HIV virus, so it is important to understand how the body fights HIV in this under-studied tissue," said Barbara Shacklett, associate professor of medical microbiology and immunology at the UC Davis School of Medicine.

"We consider the GI tract as a major 'battlefield' between the immune system and HIV. If we can better understand what happens there, we may finally learn how to eradicate the virus," said Shacklett.

Shacklett is a co-author of a paper on the research, entitled "Myeloid dendritic cells isolated from tissues of SIV-infected Rhesus macaques promote the induction of regulatory T cells," published Jan. 28 in the journal *AIDS*. Julia Shaw, a graduate student in Shacklett's lab, co-led the research with Pietro Presicce of the Cincinnati Children's Hospital Research Foundation.

An editorial in the same issue of *AIDS* highlights the new research and related studies that are clarifying the interaction between the simian version of HIV and the Treg cells that can control attacks against them.

Shacklett stressed that Tregs usually increase when the immune system is at risk of over-reacting. Their high numbers lead to a reduced immune attack, although the mechanism is not well understood.

But in persistent infections -- when a strong immune response is called for -- Tregs should decrease in number, taking a "hands-off" approach and freeing the immune army to advance. HIV may sabotage this control by prompting increased Treg production as if the body need not rally its defenses against the virus.

The research draws on earlier research by Shacklett, Shaw and colleagues comparing Treg counts in rectal mucosa of people with high and low HIV viral load. They showed that high viral load was associated with increased frequencies of immunosuppressive Treg in the gastrointestinal mucosa, suggesting these Tregs might be thwarting the body's immune defenses.

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