Regulatory T cells harbor HIV/SIV virus during antiviral drug treatment

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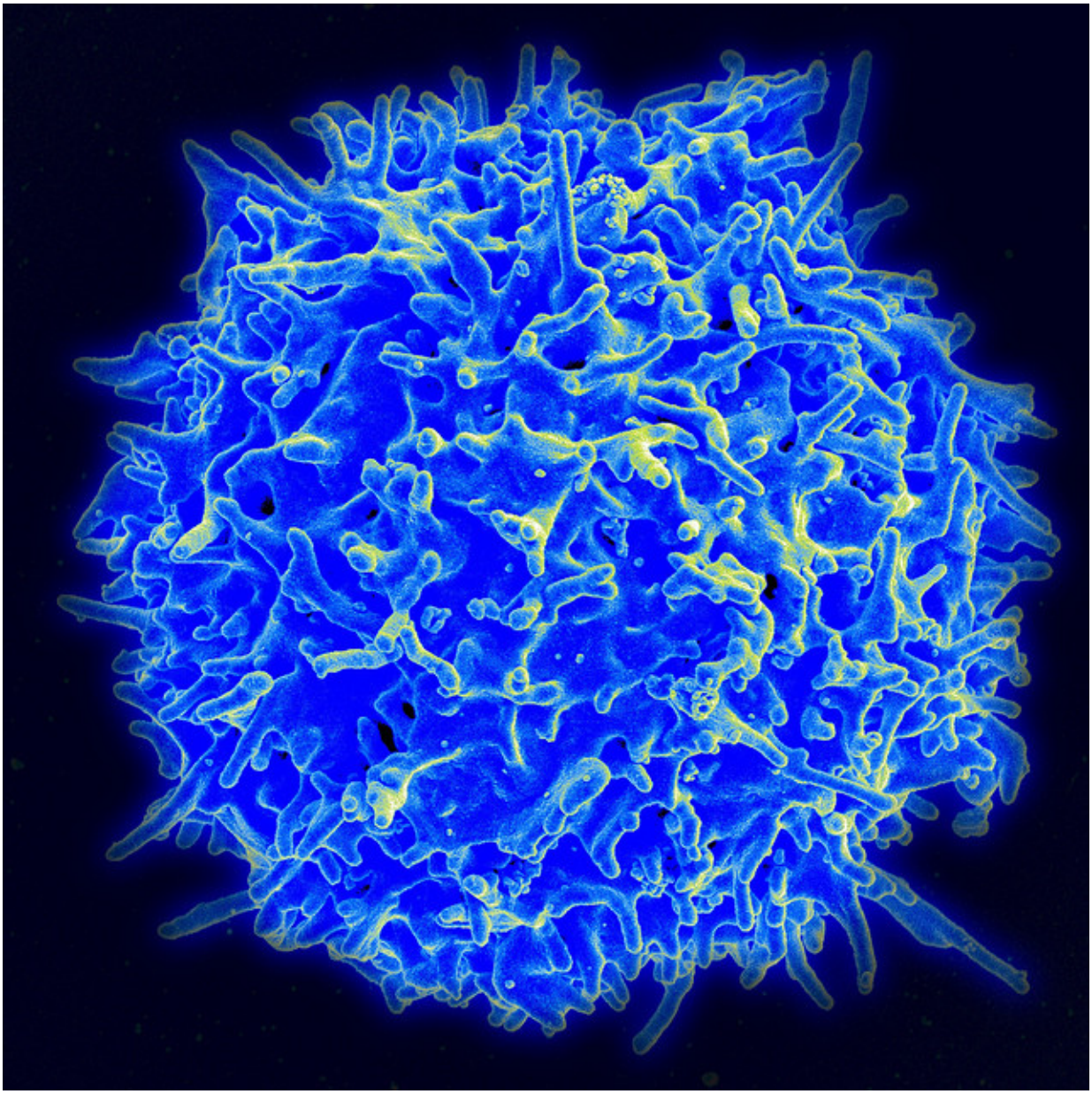

Scanning electron micrograph of a human T lymphocyte (also called a T cell) from the immune system of a healthy donor. Credit: NIAID

Scientists at Yerkes National Primate Research Center, Emory University have identified an additional part of the HIV reservoir, immune cells that survive and harbor the virus despite long-term treatment with antiviral drugs.

Their findings are scheduled for publication in *Immunity*.

The cells display a molecule called CTLA4, the target of an FDA-approved cancer immunotherapy drug, ipilimumab. This information should help those trying to eradicate HIV from the body.

Researchers led by Mirko Paiardini, PhD, infected macaques with HIV's relative SIV and treated them with standard antiviral drugs similar to what humans receive for HIV. At the time of analysis, almost all the animals (8 out of 9) showed undetectable SIV in their blood. The team probed for CD4+ memory T cells, which are known to shelter persistent virus.

"We found that a certain group of memory CD4+ T cells displaying CTLA4, but not another co-inhibitor receptor called PD1, harbor viral DNA at higher frequencies than other groups of memory CD4+ T cells," says Paiardini, associate professor of pathology and laboratory medicine. "These cells can be found in multiple tissues, such as lymph node, spleen, gut and bone marrow, and contain replication-competent and infectious virus."

The Yerkes team worked with researchers at NCI/Leidos Frederick led by Jacob Estes, PhD, using a technique called "DNAscope", to visualize

latently infected cells in lymph nodes. Previous research had shown that HIV-infected cells persist in regions of the lymph nodes called B cell follicles. The newly identified group of infected cells is found outside the B cell follicles.

Working in close collaboration with Rafick Sekaly, PhD, at Case Western Reserve University, the research team also showed that the CTLA4-positive PD1-negative cells have the characteristics of regulatory T cells, whose job is to put a brake on the immune system and prevent it from getting too excited.

"It provides a strong rationale for targeting these cells," Paiardini says. "Depleting latently infected T-regs can not only reduce the reservoir, but also induce a stronger antiviral immune response."

The researchers also worked with Vincent Marconi, MD, a physician treating HIV in Atlanta, to confirm that similar cells were present in human lymph nodes. The human samples came from six HIV-positive individuals who had been on antiviral drugs for an average of three years.

Based on the team's findings, CTLA-4 should be considered as an additional target when designing immunotherapies aimed at purging the viral reservoir, Paiardini says.

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