Monoclonal antibodies show promise as effective HIV therapy

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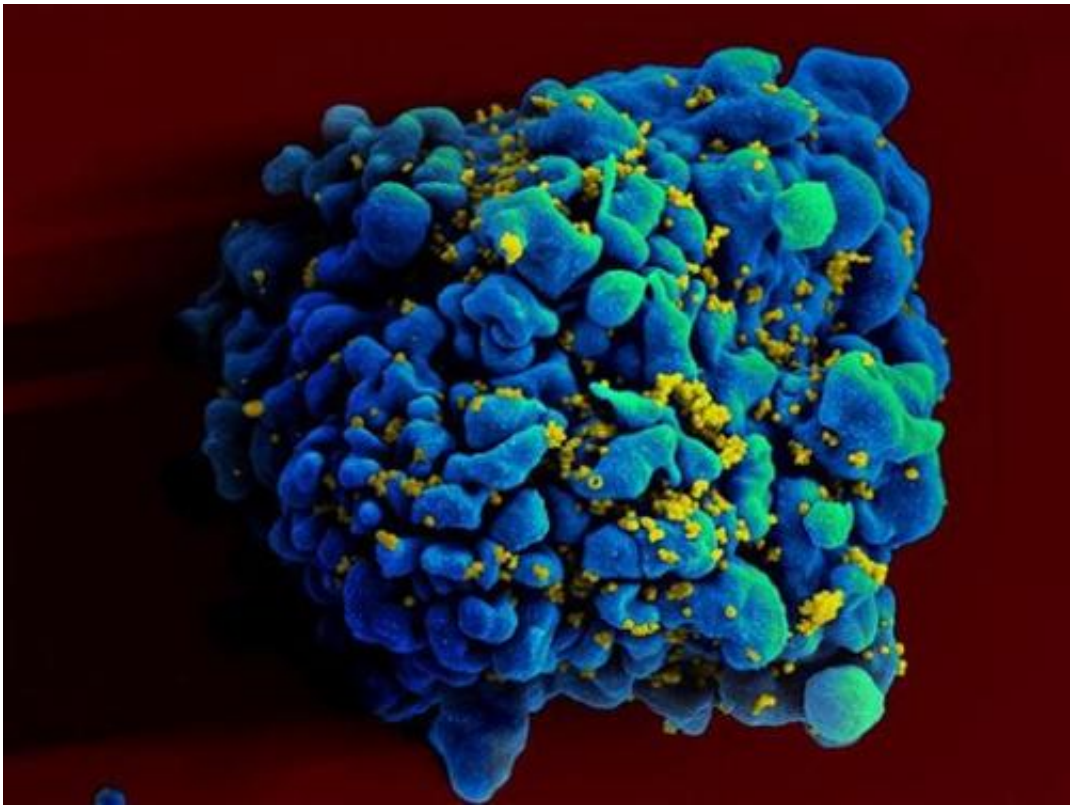

This April 12, 2011 electron microscope image made available by the National Institute of Allergy and Infectious Diseases shows an H9 T cell, colored in blue, infected with the human immunodeficiency virus (HIV), yellow. Doctors may one day be able to control a patient's HIV infection in a new way: injecting swarms of germ-fighting antibodies, two new studies suggest. Reports by Dr. Dan Barouch of Harvard and the Beth Israel Deaconess Medical Center in Boston and the National Institutes of Health were published Wednesday, Oct. 30, 2013 in the journal *Nature*.

A research team led by investigators at Beth Israel Deaconess Medical Center (BIDMC) has demonstrated that a group of recently discovered antibodies may be a highly effective therapy for the treatment of HIV. Published on-line today in the journal *Nature*, the findings encourage the development of these monoclonal antibodies as a novel therapy in humans.

"Our data demonstrate, for the first time, profound therapeutic efficacy of broad and potent HIV-specific monoclonal antibodies in rhesus monkeys chronically infected with a highly pathogenic simian-human immunodeficiency virus," said the study's lead author Dan H. Barouch, MD, PhD, Director of the Center for Virology and Vaccine Research at BIDMC, Director of the Vaccine Program at the Ragon Institute of MGH, MIT, and Harvard, and Professor of Medicine at Harvard Medical School. Simian-human immunodeficiency virus is a monkey version of HIV.

Antibodies work through a mechanism that is distinct from that of traditional antiretroviral therapies, which are the standard treatment for HIV. "Antibodies directly target free virus as well as virally infected cells, whereas existing antiretroviral drugs only inhibit the replicating virus," explains Barouch. "Antibodies may, therefore, offer a unique therapeutic strategy that could potentially be combined with antiretroviral drugs."Although highly effective in the majority of patients, current antiretroviral therapies are limited by toxicities and resistance, and are unable to cure HIV infection.

Barouch and his colleagues administered a cocktail of HIV-specific monoclonal antibodies or single monoclonal antibodies into rhesus monkeys chronically infected with simian-human immunodeficiency virus.

"The antibody treatments resulted in a rapid and precipitous decline of

virus in both blood and tissues of the infected monkeys," notes Barouch. Following a single antibody infusion, viral loads dropped sharply to undetectable levels in three to seven days, and cell-associated virus levels were also reduced in the blood, lymph nodes and the gut. Moreover, antibody infusions significantly boosted the monkeys' own immune responses against the virus, which appeared to have long-term benefit.

"In most cases, the virus rebounded when antibody titers declined after a median of 56 days, but, remarkably, the subset of animals with the lowest starting levels of virus maintained undetectable viral loads for the duration of the study, in the absence of further antibody infusions," adds Barouch.

"These data strongly encourage the development of monoclonal antibodies as a novel therapy for HIV in humans," he notes. "Monoclonal antibodies in conjunction with antiretroviral drugs can be explored for treatment intensification, pre- and post-exposure prophylaxis, and virus eradication strategies for HIV in humans."

More information: dx.doi.org/10.1038/nature12744 and dx.doi.org/10.1038/nature12746

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