Immune responses provide clues for HIV vaccine development

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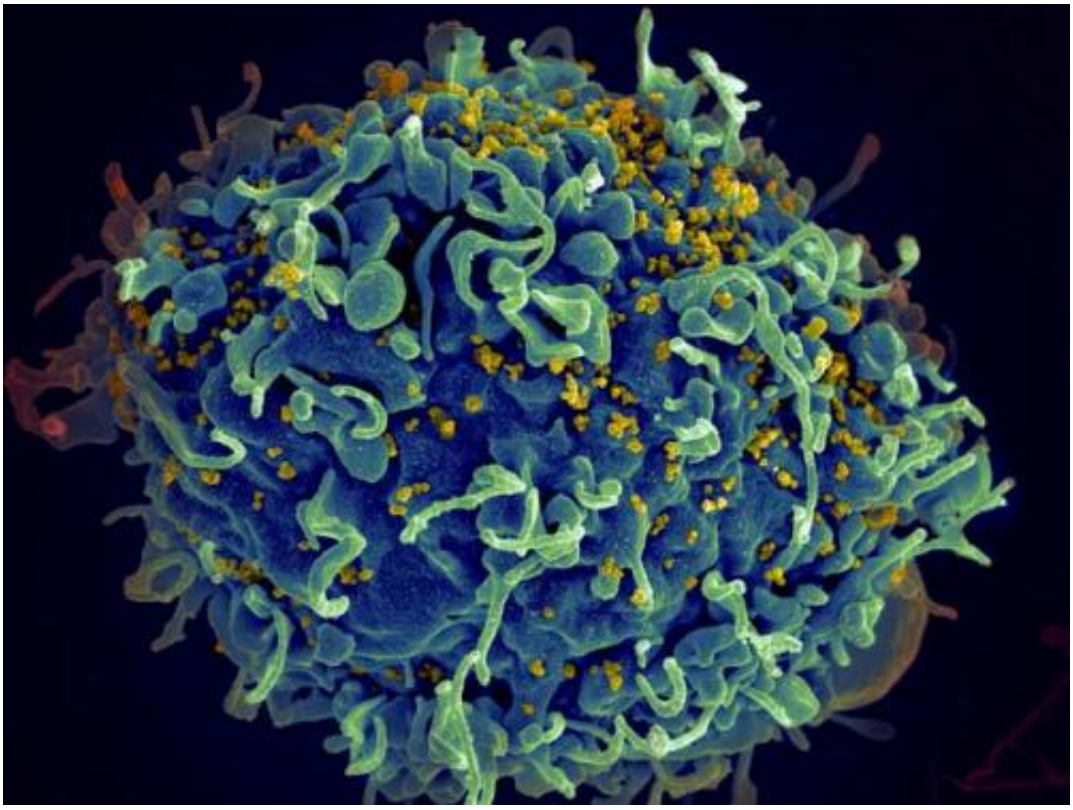

HIV, the AIDS virus (yellow), infecting a human immune cell. Credit: Seth Pincus, Elizabeth Fischer and Austin Athman, National Institute of Allergy and Infectious Diseases, National Institutes of Health.

Recent research has yielded new information about immune responses associated with—and potentially responsible for—protection from HIV infection, providing leads for new strategies to develop an HIV vaccine.

Results from the RV144 trial, reported in 2009, provided the first signal of HIV vaccine efficacy: a 31 percent reduction in HIV infection among vaccinees. Since then, an international research consortium has been searching for molecular clues to explain why the vaccine showed this modest protective effect.

A new review outlines findings that hint at the types of immune responses a preventive HIV vaccine may need to induce. The article was co-authored by leaders in HIV vaccinology, including Anthony S. Fauci, M.D., director of the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, and lead author Lawrence Corey, M.D., of the Fred Hutchinson Cancer Research Center.

Analyses of RV144 volunteers revealed that particular vaccine-induced immune responses, including production of certain antiviral antibodies and CD4+ T cell responses to HIV's outer shell, or envelope, correlate with reduced HIV infection. Many RV144 vaccinees produced antibodies in the immunoglobulin G (IgG) family that bind to sites within part of the HIV envelope called V1V2. These antibodies were linked to protection against acquiring HIV. However, high levels of a different type of envelope-binding antibody belonging to the IgA family were associated with a lack of protection against HIV infection. Evidence suggests that IgA may block the protective action of IgG. Recently, monkey studies testing vaccine regimens different from those in RV144 have supported the notion that enhancing protective antibody activity may increase vaccine efficacy.

Guided by findings from human and monkey studies, researchers are working to improve upon the efficacy of the RV144 vaccine regimen. They are investigating strategies to increase the magnitude and durability of vaccine-induced immune responses associated with protection from HIV infection, as well as developing vaccines to elicit production of

antibodies that are broadly neutralizing against a variety of HIV strains. As development of an effective HIV vaccine continues, efforts stemming from the modest success of the RV144 trial have "produced a momentum and series of immune targets that will hopefully lead to an effective global vaccine effort," the authors conclude.

More information: L Corey et al. Immune correlates of vaccine protection against HIV-1 acquisition. *Science Translational Medicine* DOI: 10.1126/scitranslmed.aac7732 (2015).

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