

Antibodies from unconventional B cells less likely to neutralize HIV, study finds

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Antibodies derived from a type of immune cell found in unusually high numbers in HIV-infected individuals with chronically uncontrolled virus levels are less effective at neutralizing HIV than antibodies derived from a different type of immune cell more common in people without HIV, scientists report. The findings help explain why people infected with HIV cannot sufficiently clear the virus with effective antibodies. The study was supported by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health.

NIAID scientists and researchers at Yale University and University of Maryland drew these conclusions by studying blood samples from 25 donors with chronic HIV infection. The donors were not taking antiretroviral drugs to suppress the level of HIV in their blood, or viral load, at the time of the study. Like many individuals with persistent levels of HIV, the donors' blood samples had abnormally high numbers of immune cells called tissue-like memory (TLM) B cells, compared with resting memory (RM) B cells, which account for the majority of memory B cells in people without HIV.

To better understand how this abnormal distribution of B cell types in people with uncontrolled HIV affected their immune response to the virus, researchers compared HIV-specific antibodies derived from both TLM and RM B cells. Generally, as B cells divide in response to a pathogen like HIV, genes that produce infection-fighting antibodies mutate, and descendant cells producing the most effective antibodies predominate. Despite the fact that TLM B cells generally divided more frequently than their RM counterparts, researchers found that the antibodies derived from TLM B cells showed genetic evidence of fewer adaptive mutations than those derived from RM B cells. In turn, these antibodies were less likely to effectively neutralize HIV than those derived from RM B cells. The RM B cells, in contrast, showed evidence of generating

antibodies with more helpful mutations.

The researchers believe this difference in B cell distribution among those with uncontrolled HIV adds to a list of reasons most people do not make effective antibodies against the virus.

More information: Eric Meffre et al. Maturational characteristics of HIV-specific antibodies in viremic individuals, *JCI Insight* (2016). [DOI: 10.1172/jci.insight.84610](https://doi.org/10.1172/jci.insight.84610)

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