A vaccine candidate that supports immunity where it matters most

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Credit: National Cancer Institute

Almost all infections make us sick by getting past our first line of defense - the sticky mucous surfaces that line our mouths, our eyes, our lungs and our guts. Once through, it's up to the immune cells that reside in our bodies to fight the disease. Now researchers have found that one virus activates the immune system to continually feed sentinel cells into the mucous membranes where they could offer better and more

immediate protection at the front lines, preventing disease before it occurs. The work was published online October 29th, in the journal *Cell Reports*.

"If you could get immune cells into those first-line tissues, like the lungs, or the mouth, then you might be able to prevent the disease developing, and a lot of current research suggests that you should improve how quickly the immune system responds," says senior author Christopher Snyder, Ph.D., an Assistant Professor in the Department of Microbiology and Immunology at Thomas Jefferson University. "Our work shows that cytomegalovirus activates the immune system to do just that, explaining why this virus might make for an excellent delivery system for vaccines against a number of pathogens including HIV or tuberculosis."

To develop vaccines, researchers often use viruses that are relatively harmless to humans but have useful immune properties, loaded with pieces of more dangerous viruses like HIV or tuberculosis. Cytomegalovirus (CMV) is a herpesvirus, belonging to the same genus as viruses that cause chicken pox and mononucleosis. Most people in the world have been infected and most remain infected with CMV, despite rarely experiencing symptoms. Because a CMV infection is always there, the human immune system remains active against it, producing large numbers of memory T cells, a type of cell responsible for long-lasting immunity. "This so called 'memory inflation' is a property that vaccine researchers find very appealing," says Dr. Snyder.

In this research, Dr. Snyder together with first author Corinne Smith, a graduate student in Dr. Snyder's lab and others, showed that in mice, these "inflated" circulating memory T cells against CMV also feed the mucosal tissues that act as a first barrier to most pathogens. Previously, researchers had assumed that some memory T cells made it to mucosal tissues after most infections, but it was unclear how long they would last

once there, and whether they played much of a role in protecting against subsequent infections. "We think that CMV helps maintain active cells in the mucous tissue because it's an ever-present infection that the immune system is constantly reacting to at a low level," says Dr. Snyder.

"There is still a lot we don't know about the immune cells that reside in mucosal tissues, and how they interact with the rest of the immune system," says Smith. "But if we could bolster the numbers of immune cells in the first-line barrier tissues to fight against some of the most dangerous infections, we may be able to develop vaccines that offer patients better protection."

Because of its unique properties, the authors are also interested in developing CMV into a vaccine against cancer.

More information: C.J. Smith, et al., "Murine CMV infection induces the continuous production of mucosal resident T cells," *Cell Reports*, 2015.

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