Researchers unlock new insights that could help with vaccine development

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Vaccination is the most effective public health measure to prevent infectious diseases. Vaccines can greatly reduce the risk of infection by working with the body's natural defenses to safely develop immunity to

disease. However, the immune system fights infection in many different ways, and in order to be effective, a vaccine must trigger the right type of immune response to recognize and destroy a specific virus, bacteria or parasite.

The majority of vaccines, such as those for polio and measles, stimulate a type of immune response called antibody-mediated immunity. But for some chronic infectious diseases such as tuberculosis and malaria, a different type of immune response, called cell-mediated immunity, is needed. Unfortunately, efforts to create a vaccine that prompts a cell-mediated immune response have had limited success.

Now, researchers at the University of Calgary's Snyder Institute for Chronic Diseases have unlocked new insights that may help in developing this type of vaccine.

"What we already know is vaccination often involves polarizing the immune system towards the type of immune response believed to provide protection to a given infection and away from responses believed to be non-protective," says Dr. Nathan Peters, Ph.D., study lead, associate professor at the University of Calgary's Cumming School of Medicine (CSM) and Faculty of Veterinary Medicine (UCVM).

"Because of this approach, we've been very focused on generating the cell-mediated response that is required to directly fight these chronic infections. What we have realized through our research is that types of immunity that we didn't think were important, or were thought to be non-protective, are actually critical to regulate the protective cell-mediated response to ensure the immune system mounts a balanced defense."

The findings, published in *Cell Host and Microbe*, show that rather than enhancing protection, a highly polarized cell-mediated response that was believed to be protective was, in fact, detrimental.

"By studying the regulation of the body's own immune response to infection, our team has found that excessive polarization can actually backfire," says Dr. Matheus Carneiro, Ph.D., postdoctoral scholar and co-author on the study. "Understanding this drove us to investigate the importance of other aspects of the immune response during these infections. We found these other responses played a big role in regulating excessive inflammation, which, in the absence of regulation, actually facilitated infection."

Peters says this fundamental observation could also help inform vaccine design for infectious diseases such as COVID-19, malaria, tuberculosis and the parasitic disease leishmaniasis.

"These observations provide new insight into the regulation of immunity against infectious diseases and could provide a more holistic framework to design vaccines against those infections that don't have one." he says.

More information: Matheus Batista Carneiro et al, Th1-Th2 Cross-Regulation Controls Early Leishmania Infection in the Skin by Modulating the Size of the Permissive Monocytic Host Cell Reservoir, *Cell Host & Microbe* (2020). DOI: 10.1016/j.chom.2020.03.011

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