Immune response to seasonal coronaviruses may offer protection against COVID-19

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A research group led by Shin-ichiro Fujii of the RIKEN Center for Integrative Medical Sciences have found that individuals with a certain HLA type may be able to mount a killer T cell response to COVID-19, thanks to the T cells responding to a portion of the virus's spike protein that is also present in seasonal coronaviruses that cause the common

cold. This work, published in *Communications Biology*, could help explain the different responses between populations, and could potentially be used as a way to develop a new type of vaccine against the disease.

Up until now, most of researchers have focused on the antibody response to the virus, which prevents initial infection. However, once the virus infects cells, to eliminate viruses quickly, effector lymphocytes—NK cells or memory T cells—become critical. Based on the consideration that NK cell response should be relatively similar across people, they decided to focus on memory killer T cells, which lead an attack against viruses that they "remember."

The authors chose to look at individuals with HLA type A24, a type that is relatively common in Japanese and some populations in other countries including several Asian countries. According to Fujii, this choice was made because it was easy to find individuals with this HLA type, as others are much less common, and also because they felt it might offer insights into why some populations in Asia have appeared to be less susceptible to the infections.

The group began by using in silico analysis to look for parts of the SARS-CoV-2 spike protein that can bind highly with HLA-A24. As a result, they identified six potential epitopes—sequences of amino acids that immune cells respond to. They then looked at the reaction of peripheral immune cells in people with the HLA-A24 type who had not been infected with SARS-CoV-2, to see whether they had memory killer T cells that would respond to antigens from the virus. In fact, around 80 percent of uninfected healthy donors with the A24 type HLA did show a reaction for a single peptide—a sequence they called the QYI epitope—which they identified. Finally, they found that QYI-specific memory killer T cells from donors with the A24 serotype showed cross-reactivity against the relevant epitopes, which are relatively conserved

from human coronaviruses including seasonal coronaviruses.

The group then looked at the response in patients with blood cancers, who are known to be particularly susceptible to serious COVID-19. The response was much smaller than those from non-exposed healthy individuals. Importantly, however, the group discovered that even in patients with blood cancers, there is a "hotspot," located in the spike protein of the virus—a sequence of 27 amino acids around the QYI epitope—and that T cells responding to this can still mount a vigorous immune response. For the hotspot, 100 percent of healthy people and 65 percent of blood cancer patients responded. According to Fujii, "This leads to the hope of developing vaccines that could boost the immune response even in immunocompromised patients.

The real goal of this work, says Fujii, is not to find differences between population but rather to find ways to prevent people from dying of the disease. "The real hope," he says, "is that we will be able to develop vaccines that can stimulate a strongly targeted reaction by T cells against the infection. We have demonstrated that this could be possible in this particular HLA group, but now need to look at other types."

More information: Kanako Shimizu et al, Identification of TCR repertoires in functionally competent cytotoxic T cells cross-reactive to SARS-CoV-2, *Communications Biology* (2021). DOI: 10.1038/s42003-021-02885-6

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