Medical Xpress

Boosting immunity in older adults: Study unmasks new infection-fighting T cells

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In the autumn years of life, the immune system also begins to "retire" and becomes less effective at fighting infection. University of Arizona Health Sciences researchers have made a discovery that may help measure immune system status, risk of infection and response to vaccination. Credit: University of Arizona Health Sciences

Sixty-five is the age when many people retire, kick back and take it easy. And so it often is with the human immune system.

After years of fending off influenza and other infectious diseases, the immune system gradually starts to lose its oomph for fighting infection. As a result, viruses, bacteria and other microbial intruders are a common killer of adults 65 and older.

New findings from a study led by the University of Arizona Health Sciences Department of Immunobiology show it may not have to be that way.

The study examined blood samples from 92 volunteers, age 21 to 97. Researchers focused on a subset of T cells - white blood cells that fight infection and decrease in number as adults age - specifically, T cells labeled "naïve" because they have not yet been exposed to a virus or other infection.

"When there is an infection, like an influenza virus, for example, a small cohort of these naive T cells - only those that have special molecules on their surface that will bind to fragments of the influenza - are deployed in a very targeted manner," said Janko Nikolich-Žugich, MD, PhD, head of the Department of Immunobiology and Elizabeth Bowman Professor of Medical Research at the UA College of Medicine - Tucson, and the study's principal investigator.

These deployed naive T cells then become effector T cells, he said. Unlike the naive cells, which cannot harm the virus, effector cells are "armed" and able to clear the virus using antiviral molecules they now make. "Once they have done away with the infection, most of the effector T cells will die, but a substantial number will survive and become 'memory' cells,' which will remember and fight off an infection, if and when it recurs," Dr. Nikolich-Žugich said.

The breakthrough came when the researchers, focusing on navie T cells, discovered that when stimulated with pieces of virus, a portion of the cells began making interferon-gamma, a powerful anti-viral molecule.

They found that among these naive cells - which now looked functionally more like memory cells - many were marked to attack cytomegalovirus (CMV), a type of herpes virus that infects most people and is carried for life without harm, kept in check by a highly functioning immune system, but devastating to those with suppressed immune systems, including older adults.

These naive T cells are "a new 'flavor' of naive cells that are not completely naive," Dr. Nikolich-Žugich said. "So our new discovery is that there is more diversity than we realized within the naïve cells, and that some already have committed to dealing with CMV and other really persistent infections, and others are really, truly naive."

Dr. Nikolich-Žugich and his colleagues have named the "new flavor" of T cells "T memory cells with naive phenotype."

One next step, Dr. Nikolich-Žugich said, is to count the number of these cells in an individual's blood sample, which may indicate the fitness of that person's immune system.

Another step will be to vaccinate some of the people in the study cohort and monitor these special T memory cells before and after vaccination, to test whether it can predict responses to vaccination. In addition to influenza vaccine - which confers more protection on younger adults than older adults - Dr. Nikolich-Žugich would like to try a vaccine given to prevent Japanese Encephalitis Virus - a cousin of West Nile Virus, which belongs to the same group as the Zika and Dengue viruses.

"Giving a vaccine that most people have not been given in their lifetimes

will give us a better idea of how fit is their immune system," he said.

"The biggest challenge for us going forward is to measure the status of the immune system, including these new cells, and actually show, in an average person, if you are below a certain level of a T cell population, or a certain cytokine or a certain antibody, what is your risk of infection or poor response to vaccination. And if you are at risk, how can we work to help you and your immune system."

Also co-director of the UA Center on Aging and a member of the UA BIO5 Institute, Dr. Nikolich-Žugich has focused nearly 20 years of his career on how aging affects the immune system and what can be done to better protect older adults from infectious disease.

"Older adults are by far the largest group of people who are vulnerable to infections, because of their weakened immune systems," he said. Some are more vulnerable than others, and not everyone is susceptible to the same extent.

"The challenge for us is to figure out who is, and to what extent, and what we can do to help."

The study, "Human memory T cells with a naive phenotype accumulate with aging and respond to persistent viruses," was published June 6 online before print in *Nature Immunology*.

More information: Vesna Pulko et al, Human memory T cells with a naive phenotype accumulate with aging and respond to persistent viruses, *Nature Immunology* (2016). DOI: 10.1038/ni.3483

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