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For Immediate Release

We're taking a closer look at immune 'memory'

Vaccines teach the body to fight disease. We still have a lot to learn about how long that immune "memory" lasts.

The average human has about 1.8 trillion immune cells. These cells patrol the body for bacteria, viruses, cancers, and other threats.

Vaccines enhance this security system by teaching our immune cells to target specific pathogens. According to the World Health Organization, vaccine-induced immunity saves about six lives every minute.

But how long does this protective immune "memory" last?

According to Shane Crotty, Ph.D., Professor and Chief Scientific Officer at La Jolla Institute for Immunology (LJI), we still have much to learn about immune memory.

"There are actually not many studies of human immune memory due to vaccines," says Crotty. "Scientists traditionally don't track immune memory past one year after vaccination—or even six months after vaccination—and that's a bit of a problem."

In a new *Immunity* review, Crotty shares recent advances from the fascinating field of immune memory. His article highlights key steps we might take to develop even more effective, longer-lasting immunity against deadly diseases.

Lessons from COVID-19

The COVID-19 pandemic underscored the need for more research into the fundamental science of immune memory.

As Crotty explains, scientists around the world have found that COVID vaccines can train immune cells to remember the SARS-CoV-2 virus and protect against severe infection for years afterward. "These vaccines are as good, if not better, than your average vaccine at generating immune memory," says Crotty.

And yet scientists face a challenge. The SARS-CoV-2 virus continues to mutate, and people continue to get sick. People also get sick year after year when new strains of influenza or respiratory syncytial virus (RSV) spread through the population.

The continued spread of disease has scientists today taking a closer look at how the immune system builds up immune memory over time.

B cells vs. viruses

The body's B cells are in it for the long haul. These cells are made in the bone marrow, then they travel through the blood to "germinal centers," which are microscopic structures in tissues such as the lymph nodes. Thus begins B cell bootcamp, where the cells learn to target specific pathogens.

Mature B cells are ready to attack. When they meet their pathogen foe, they release a flood of antibodies to neutralize the pathogen before an infection can spread through the body. Once the infection is gone, special "memory" B cells keep patrolling the body for years—even decades.

Vaccines contain molecules that aid in the B cell bootcamp process. B cells respond to vaccine molecules and generate immune memory, just as if the real virus had passed through. Crotty's own work has shown that people who were given smallpox vaccines as children still had memory B cells in their blood over 60 years later.

It turns out COVID vaccines also spark a long-lasting B cell response. "There's been a misunderstanding, where people think the vaccine doesn't generate immune memory for very long," says Crotty. "Actually, the immune memory is there for years after COVID vaccination; the problem is that the virus is changing," says Crotty.

Every new SARS-CoV-2 variant has its own slew of mutations. There was the Delta variant, followed by the Gamma variant, Omicron, Picola, and several other variants that spread around the globe. "This really is a blame-the-virus situation," says Crotty.

How do you teach B cells to fight a virus that is constantly changing?

Crotty says it's important to investigate how our own B cell responses over long periods of time, rather than for only six months or a year after vaccination. As time goes by, scientists could test whether memory B cells are prepared to neutralize new viral variants.

"Then you can do a more rational assessment of how often people should be boosted," says Crotty.

Building better immune memory

Your circulatory system is like a highway. Your blood carries immune cells through the body, delivering them to sites of infection.

Your tissues are more like neighborhoods. Tissues, such as your muscles and lungs, are connected to your circulatory system, but tissues also have their own, local immune cells.

Scientists typically use blood samples to study immune memory. As Crotty points out, blood samples limit us to only observing circulating immune cells. There's a hidden world of memory cells hiding out in our tissues.

Crotty's own laboratory recently pioneered a nasal swabbing technique that allows scientists to sample tissue resident memory cells deep in the nasal passages. These tissues are ground zero when a respiratory virus attacks, and it turns out they are teeming with memory B cells and infection-fighting T cells.

In a 2024 study, led by Crotty and LJI Instructor Sydney Ramirez, MD, Ph.D., researchers showed that nasal swabbing was an effective way to monitor memory B cell and memory T cell populations over time. They could even use this technique to detect changes in tissue-resident memory cells following COVID vaccination or infection.

With this swabbing technique, scientists now have a way to track immune memory in the upper airway. This means they could test more vaccines, such as intranasal vaccines, that are specifically designed to stimulate immune responses in the airways.

Circulating immune cells are good fighters, but tissue resident immune cells may be better first responders, Crotty says. "The vast majority of vaccines only generate immune memory in the blood," says Crotty. "It would be a real innovation for vaccines to work at the site where the infection is going to happen."

Scientists have made major vaccine research breakthroughs since SARS-CoV-2 first emerged. Crotty's review offers a glimpse of how future vaccines might improve health for all.

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