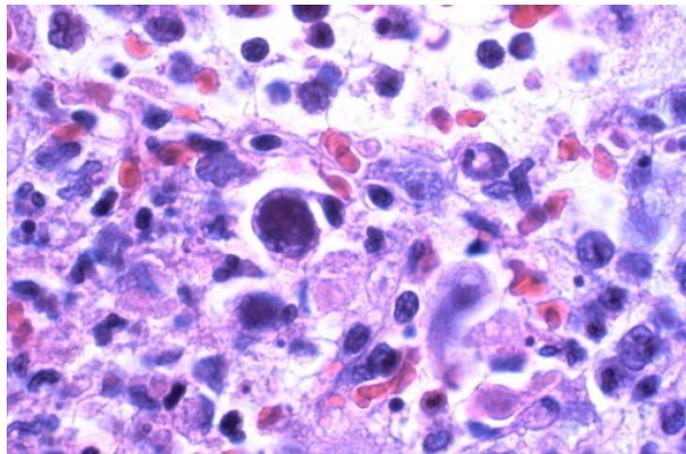


# SCIENTIFIC AMERICAN

## Your Immune System Is Made, Not Born

New research dispels the belief that the strength of the body's defense system is genetically programmed

By [Esther Landhuis](#) on January 29, 2015



Some people seem better than others at fighting the flu, and you might suspect they were born that way. A new study of twins, however, suggests otherwise.

In one of the most comprehensive analyses of immune function performed to date, researchers analyzed blood samples from 105 sets of healthy twins. They measured immune cell populations and their chemical messengers—204 parameters in all—before and after participants received a flu shot. Differences in three fourths of these parameters depended less on genetics than on environmental factors, such as diet and prior infections. Genetics had almost no effect on how well individuals responded to the flu vaccine, judged by antibodies produced against the injected material. And among identical twin siblings, who have the same genome, immune system features differed more strikingly within older twin pairs than in younger sets. The findings, published January 15 in *Cell*, argue that life habits and experiences shape our body's defenses more than the DNA passed down from our parents.

Although prior twin studies had hinted that nonheritable factors contribute to some autoimmune disorders, such as multiple sclerosis, the recent analysis was one of the first to quantify genetic and environmental effects on the general immune system. “We were surprised by the degree

of environmental influence on so many components,” says Mark Davis of Stanford University School of Medicine, senior author on the new study. One finding was particularly striking. A single environmental factor—a past infection with common cytomegalovirus—affected 58 percent of the tested parameters. Whereas the results don’t show whether these changes produce an overall stronger or weaker immune response, they do indicate “cytomegalovirus has a really profound effect,” Davis says. The Epstein–Barr virus, another microbe that frequently infects people, had no such effect.

Cytomegalovirus’s profound influence on the immune system is, perhaps, not so shocking. In order to survive, viruses must hijack a person’s host cells to churn out more viral particles. “They have to get past physical and innate barriers—it is tough to succeed,” says Peter Barry, a biologist who studies cytomegalovirus at the University of California, Davis. “The fact that a virus is still around means it is really good at what it does.” Indeed, cytomegalovirus has learned to set up shop almost anywhere in the human body. Yet although more than three of five adults have been infected with the microbe, most would not know it. That is because roughly one tenth of a person’s circulating T cells are specific for cytomegalovirus. “It takes a ridiculously large chunk of our immune repertoire to keep this virus in check,” Barry says. Scientists are uncertain as to why the Epstein-Barr virus, which also infects most people and lingers in the body, doesn’t trigger a big ongoing immune response like cytomegalovirus does. It could be that the Epstein-Barr virus primarily infects B cells whereas cytomegalovirus can hide in a variety of cell types. Davis says his team is taking a closer look at Epstein-Barr virus’ effects on the twins’ immune parameters and plans to report the findings soon. Some researchers think the cytomegalovirus findings could explain why the elderly tend to respond poorly to the flu vaccine. T cells develop in the thymus, but this gland shrinks with age, slowing production of new T cells and leaving us stuck with the ones in circulation. As we get older, a growing proportion of that T-cell pool is used up on cytomegalovirus, with fewer cells available to fight seasonal infections. In the Stanford study, the heightened divergence of immune parameters in older twin pairs lends credence to this theory, Barry says.

But there is also evidence to suggest cytomegalovirus could have benefits. Research in mice shows that cytomegalovirus-infected animals do better at fighting off bacterial pathogens. And in a study of monkeys, researchers discovered that a cytomegalovirus-based vaccine protected 50 percent of animals from infection by simian immunodeficiency virus.

Based on the new study, it is hard to say if being infected with cytomegalovirus is good or bad for the immune system. Ultimately, it is going to depend on the individual, notes Chris Benedict, an immunologist

at the La Jolla Institute for Allergy and Immunology in California. Infectious diseases and autoimmune disorders are two of our biggest killers. “It’s always a balancing act,” Benedict adds. “The immune system has to respond well to infections but not so robustly that it causes autoimmunity.” For someone with an underactive immune system, cytomegalovirus might rev things up just enough to fend off a harmful pathogen. But if a person’s immune cells hover on the verge of hyperactivity, cytomegalovirus could push the system into danger. Seeing this microbe singlehandedly shift such a wide range of immune parameters calls for caution in interpreting personal DNA tests that claim to predict one’s risk of a host of diseases from Alzheimer’s to cancer. “Clearly some types of mutations are bad news but sequencing your genome is not going to tell you everything about your health,” Davis says. “There’s a whole dialogue that goes on between your genome and the environment.”

He considers the new findings a key step toward his eventual goal of capturing that cross talk with a benchmark assay that measures the health of a person’s immune defenses at the systems level. “We’ve been working on pieces of the immune system for a long time. But we don’t understand too much about how the whole system fits together,” Davis says. “We now have the tools to begin doing that.”