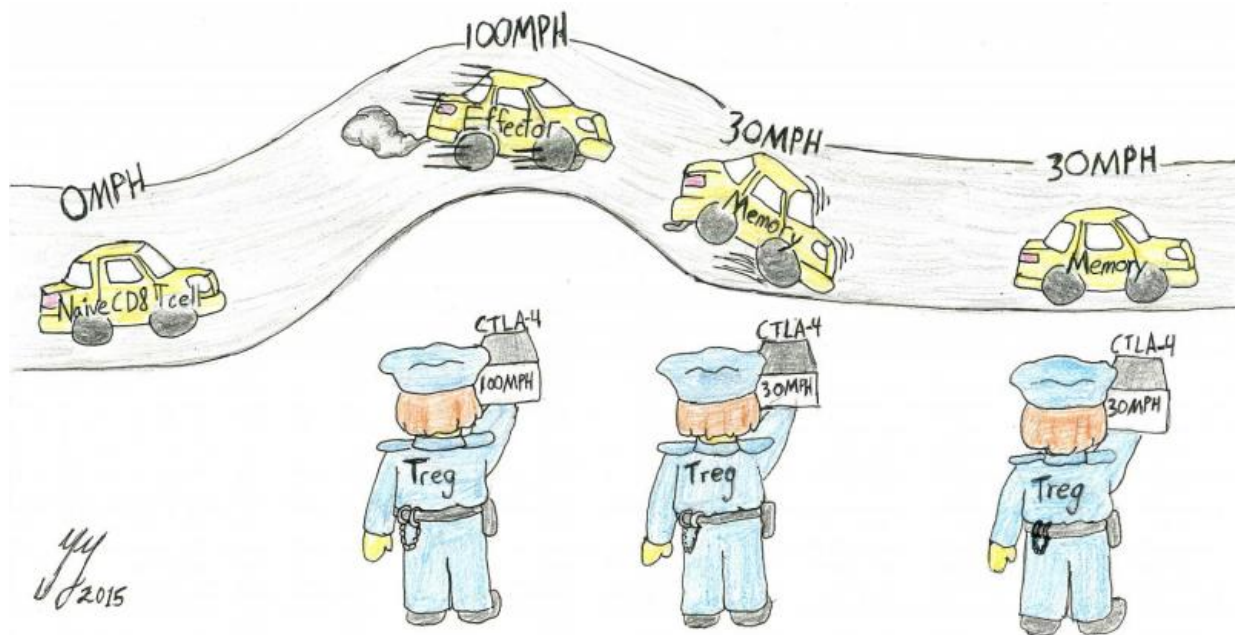


Returning killer T cells back to barracks could improve vaccines

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Regulatory T cells police the immune system, making sure that killer T cells coming back from battling pathogens transition into a resting state, but still prepared to fight if the pathogen returns. The researchers say these findings are important for the development of more effective, faster-acting vaccines. Credit: Surojit Sarkar, Vandana Kalia, Yevgeniy Yuzefpolskiy

Just as militaries need to have trained, experienced soldiers ready for future wars, making sure that the immune system has enough battle-ready T cells on hand is important for fast-acting, more effective

vaccines, according to Penn State researchers.

In a study of [immune response](#) in mice, the researchers found that regulatory T [cells](#)—Tregs—are critical for the [immune system](#)'s ability to remember and fight off future pathogen attacks. T cells, which are specialized types of [white blood cells](#), play important roles in the immune system and [immunological memory](#).

"Immunological [memory](#) is the capability of your immune system to remember the diseases and pathogens it fought off in the past, and the generation of long-lived immunological memory is the basis of effective vaccination," said Surojit Sarkar, assistant professor of immunology in veterinary and biomedical sciences.

Sarkar likens the immune system, which is made up of many different cells, to an army that battles pathogens and diseases that are invading the body. Initially T cells are called up to attack the pathogens, but these cells, called naïve T cells, have no experience or immediate defenses against the invader. As the T cells increase in number and generate defenses to take on the threat, they become effector—or killer—T cells.

Once the battle is over, though, the immune system retains some killer T cells that have encountered the pathogen as memory T cells, Sarkar said.

"Once the T cells clear the pathogen, just like in warfare, you do not leave your weapons drawn, you holster them," said Sarkar. "In the case of the immune system, those charged killer T cells also downregulate their killer machinery."

The researchers found that the regulatory T cells, another type of T cell commonly known for their role in preventing the immune system from attacking the body's own cells and tissues—autoimmunity—suppressed the killer T cells through a protein on their surface—cytotoxic T-

lymphocyte associated protein-4.

"I like to think of Tregs as the police of our immune system—their job is to keep other [immune cells](#) in check, said Vandana Kalia, assistant professor of immunology in veterinary and biomedical sciences, who worked with Sarkar on the study. "In the case of memory T cells, Tregs serve to keep their killer functions in check and help maintain them in a quiescent, yet ready to kill, state."

She added that the CTLA-4, expressed at high levels on Tregs, applies the brakes on these activated killer T cells to slow them down.

According to the researchers, who report their findings in today's (June 16) issue of *Immunity*, the study could have a far-reaching impact on immunity to a wide array of infectious diseases and even cancer vaccines and tumor immunity.

The researchers suggest that accelerating T cell memory following an immunization could lead to vaccines that become effective more quickly. For example, health care workers who are preparing to go to the field to fight an epidemic might only need to wait days, rather than weeks, for their vaccinations to become effective.

The findings could also help guide the development of future vaccines.

"What our study is doing is looking at the basic concepts of how [the immune system](#)'s memory develops and such fundamental information is critical for advancing our current vaccine development efforts," said Kalia.

Although the last few decades have established the importance of immunological memory in vaccination, the basic idea has been known for centuries, said Sarkar.

"The Greek historian Thucydides observed that people who had been exposed to the plague once—and survived it—felt more comfortable helping other plague victims because they knew that they would not be attacked fatally again," said Sarkar.

Provided by Pennsylvania State University

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