Study reveals flu-fighting role for well-known immune component

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University of Georgia scientists have discovered a new flu-fighting role for a well-known component of the immune system. Kimberly Klonowski, assistant professor of cellular biology in the UGA Franklin College of Arts and Sciences, and her colleagues found that administering a cell-signaling protein known as IL-15 to mice infected with influenza reduces their peak viral load by nearly three times.

"We gave the IL-15 intranasally and found that it enhanced the movement of the immune system's natural killer cells and CD8 T cells into the lung airways," said Klonowski, whose findings were recently published in the journal PLoS ONE. "As a result, the animals that received it cleared the virus faster than the control group."

Klonowski cautioned that the protein is only effective against influenza for a defined period of time immediately following infection, which would make its use as a flu treatment difficult to implement. She added that IL-15 has been tested as a vaccine-booster, or adjuvant, in other viral diseases such as HIV, monkey pox and hepatitis B ; understanding its mechanism of action is essential to maximizing its effectiveness in these contexts.

IL-15 was discovered nearly 20 years ago and is part of a group of immune system proteins known as interleukins. Klonowski noted until recently, however, its primary role was thought to be the maintenance of immune memory cells. Yet Klonowski and her colleagues found that concentrations of the protein surge in the respiratory tract in response to influenza infections, which led them to hypothesize that it also might play a role in controlling the virus.

The scientists devised a series of experiments in mice to discern the role of IL-15 in the immune response. It turns out that IL-15 is one of the body's critical first responders during influenza infection.

First, the scientists blocked the action of IL-15 in mice infected with influenza and found that the number of natural killer cells was reduced 20-fold at the site of infection in comparison with the control group, which received a placebo. Next, scientists administered IL-15 into the airways of mice infected with influenza and found that these mice had three times more natural killer cells than the control group. In addition, their peak viral load decreased by nearly three times.

Klonowski said that despite what their name might suggest, natural killer cells really aren't the most effective components of the immune system. They do indeed kill infected cells, but not in numbers great enough to completely eradicate infection. CD8 T cells that arrive later in the immune response are the ones that clear the infection, riding in like a cavalry to save the day. Klonowski's study suggests that CD8 T cells require the initial presence of natural killer cells, which send some still-unknown signal that subsequently attracts CD8 T cells to the infection site. Her study found that without the presence of IL-15 and the natural killer cells it recruits, the cavalry never makes it to the site of the battle in the respiratory tract.

The researchers are now working to identify the molecular signals that the natural killer cells send with the ultimate goal of directing CD8 T cells more rapidly and precisely to the site of infection. "Even though this paper deals with natural killer cells, we are still really focused on the CD8 T cells, because they're the cell population that is required for complete viral clearance," she said.

More information:
www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0037539

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