MedicalXpress

Poorly understood cell plays role in immunity against the flu

March 22 2010

A new understanding of a certain cell in the immune system may help guide scientists in creating better flu vaccines, report researchers from the Program in Cellular and Molecular Medicine and the Immune Disease Institute at Children's Hospital Boston (PCMM/IDI). Reporting online March 21 in *Nature Immunology*, they show, for the first time, that white blood cells known as resident dendritic cells (DCs) capture flu viruses and show them to B-lymphocytes, another white blood cell that recognizes germs and launches an antibody attack. Harnessing this previously unknown function could help activate the immune system more effectively against the flu virus.

"The government is putting a lot of money into vaccine development," says senior investigator Michael Carroll, PhD, director of the immunology graduate program at PCMM/IDI. "A lot of people are thinking about how to target vaccines, and this kind of information will tell us what cell type we would want to target."

Carroll's lab, in collaboration with Shannon Turley of the Department of Cancer Immunology and AIDS at Dana Farber Cancer Institute and Department of Pathology, Harvard Medical School, closely examined what happens when a flu vaccine is injected into mice, a good model for human vaccination. They focused specifically on what happens in the lymph node, where germs and vaccine antigens are filtered.

"We're trying to break down this black box that we know as the lymph node, and identify the different cells that are there, how they interact

with each other and what the general rules are," Carroll says. "Then, you can begin to manipulate it to improve vaccines and immune responses."

When it comes to building permanent immunity, B-lymphocytes are the key players because they can remember specific germs and mount a rapid antibody attack. One way B-lymphocytes first encounter germs in the lymph nodes is through the help of macrophages, white blood cells that trap germs and "show" them to B-lymphocytes. For this reason, some researchers believe macrophages to be a prime target in developing a vaccine. Carroll's lab designed their experiment to test this concept for the flu virus - and got surprising results.

Working with a mouse model of influenza vaccination, the lab attached fluorescent labels to an inactivated strain of human H1N1 virus, allowing the inactivated flu virus to be tracked in the body. Imaging showed that macrophages trapped the virus in the lymph nodes and prevented most of it from entering the circulation. However, the macrophages did not bring the virus to B-lymphocytes, contrary to what was predicted. Instead, experiments which eliminated the macrophages from the mouse models showed that it was actually the resident DCs in the lymph nodes that were bringing the flu virus to the B-lymphocytes, thus inducing the B-lymphocytes to launch an antibody attack.

To confirm this observation, the researchers injected the mice with an agent to block a specific receptor on the surface of the resident DCs. With this receptor blocked, the B-lymphocytes never sprang into action. When it comes to the flu virus, these results suggest that any targeted vaccine must aim for resident DCs and not macrophages.

"This is the first clear definition of what the resident DCs are doing," Carroll says. The study adds to a growing body of research centered on DCs, which studies continue to show to play a role in stimulating other cells in the immune system.

Targeting influenza vaccines to DCs could make them more effective, Carroll believes. One hypothetical way of doing this would be to attach the virus to an antibody that would home in on the DC cell surface receptor. This method would require further research to confirm the antibody could actually bind to the DC receptor.

In the future, Carroll's lab would like to define a similar immune system pathway for Streptococcus pneumoniae, a bacterium that can cause diseases such as pneumonia, meningitis and middle ear infections.

More information: Santiago F. Gonzalez, Veronika Lukacs-Kornek, Michael P. Kuligowski, Lisa A. Pitcher, Søren E. Degn, Young-A Kim, Mary Cloninger, Luisa Martinez-Pomares, Siamon Gordon, Shannon J. Turley & Michael C. Carroll. "Capture of influenza by medullary dendritic cells via SIGN-R1 is essential for humoral immunity in draining lymph nodes." *Nature Immunology* March 21 (advanced online publication).

Provided by Children's Hospital Boston