MedicalXpress

Major immune system branch has hidden ability to learn

January 26 2009

Half of the immune system has a hidden talent, researchers at Washington University School of Medicine in St. Louis have discovered.

They found the innate immune system, long recognized as a specialist in rapidly and aggressively combating invaders, has cells that can learn from experience and fight better when called into battle a second time. Scientists previously thought any such ability was limited to the immune system's other major branch, the adaptive immune system.

The finding, published online this week in the *Proceedings of the National Academy of Sciences*, will help scientists better understand the immune system and seek new ways to modulate its responsiveness. Low immune responsiveness like that found in some genetic disorders and conditions like AIDS can leave the body dangerously vulnerable to infection; but too much can put it at risk of autoimmune conditions such as rheumatoid arthritis.

Vaccines take advantage of a property researchers call "immune memory," which is found in adaptive immune cells that can learn to recognize a particular invader and more quickly and forcefully attack the invader if it returns. By exposing the immune system to a weakened or dead version of a pathogen such as measles, a vaccine stimulates the body so that it can much more effectively respond to naturally occurring infections of the same or similar agents.

The new ability scientists identified has a similar result — cells that can

fight back more effectively after an initial stimulation - but the cells are not adaptive immune cells. They are the innate immune system's natural killer cells, which can switch between an active infection-fighting state and a dormant resting state.

"We're calling this new property 'memory-like,'" says senior author Wayne M. Yokoyama, M.D., the Sam J. and Audrey Loew Levin Professor of Medicine. "Natural killer cells can't specialize in recognition of a particular pathogen, but we found that once they've been activated, they can respond more easily and effectively to the next call for activation."

Previous efforts to learn what happens to natural killer cells after activation were hampered by the fact that the cells do not return to a resting state in cell cultures. This shortens their already brief life spans, which are measured in weeks.

To overcome this, lead author Megan A. Cooper, M.D., Ph.D., a postdoctoral fellow in pediatric rheumatology, activated mouse natural killer cells in culture, stained them with a fluorescent green dye and injected them back into the mice.

Scientists tracked the cells and re-extracted them one to three weeks later. They found the cells had returned to their resting state, but could be reactivated more easily and responded more vigorously to activation. Improved responses included increased cell replication and production of interferon gamma, a compound that has anti-pathogen activities and helps spread the immune response by activating additional immune cells. This appeared to be true of both the original cells and their descendants, identifiable by reduced levels of green dye.

Cooper notes that in newborns and young infants the adaptive immune system is largely unavailable. She speculates that it may one day be

possible to help the body defend itself during this period by finding a way to prime this memory-like mechanism in natural killer cells.

"Other innate immune cells may also have similar properties," Yokoyama says. "It should be possible to therapeutically exploit these memory-like properties to make more effective immune cells."

Cooper and Yokoyama, who is a Howard Hughes Medical Institute investigator, plan to further study how natural killer cells acquire their "memories."

Reference: Cooper MA, Elliott JM, Keyel PA, Yang L, Carrero JA, Yokoyama WM. Cytokine-induced memory-like natural killer cells. *Proceedings of the National Academy of Sciences*, online week of January 26, 2009.

Source: Washington University School of Medicine