Researchers discover how cells recognize viral toxin

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New research from McMaster University has identified how specific proteins on the surface of cells, known as class A scavenger receptors, bind to double-stranded RNA and bring it into the cell, jumpstarting the immune response to a virus. Photo by Evah Smit.

(PhysOrg.com) -- For many years it's been known that the fever, achiness and other symptoms you feel during the flu are triggered by a viral molecule that travels through the body acting like a toxin.

But what scientists haven't understood is how this molecule - known as double-stranded RNA - is recognized and taken up by cells.

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bind to double-stranded RNA and bring it into the cell, jumpstarting the immune response to a virus.

This finding, published in the March 26 issue of the journal PLoS Pathogens, could lead to the development of new antiviral therapies.

"Since the 1950s and '60s, it's been known that double-stranded RNA is a viral toxin," said Karen Mossman, an associate professor in the Department of Pathology and Molecular Medicine in the Michael G. DeGroote School of Medicine. "But what we haven't known is how cells recognize double-stranded RNA outside of the cell. We know how they respond to it. We know they take it up. But we've never appreciated how that happens."

Mossman, an investigator with the Michael G. DeGroote Institute for Infectious Disease Research at McMaster University, led a research team to investigate the "gatekeeper" function of scavenger receptors in both human and mouse cells. Until now, it was thought that the role of scavenger receptors was limited to the removal of foreign substances and waste materials from the body.

The researchers examined the five members of the class A scavenger receptor family and discovered that they all had overlapping functions in mediating the response of a cell to double-stranded RNA. They also found that no matter what type of cell they looked at - including those not thought to express scavenger receptors - all had at least two or three scavenger receptor family members.

"We found that they are ubiquitously expressed," Mossman said. "But that make sense to us because nearly every cell type responds to double-stranded RNA."

Previously, scavenger receptors were thought to be found only on white

blood cells, or macrophages, and a small population of other blood cells. The McMaster research has shown that scavenger receptors are also expressed on fibroblast cells, which play an important role in healing wounds and maintaining the structural framework of tissue.

By identifying these receptors, the researchers have uncovered an ideal target for antiviral drug therapies which could potentially decrease the side effects associated with viral infections.

"Now that we know what to manipulate, we can start looking at how we can manipulate it to be beneficial during a viral infection," Mossman said. "Since all viruses make double-stranded RNA, targeting these receptors should be effective against many different viral infections including influenza and other pandemic viruses."

The research was supported with funds from the National Institutes of Health (NIH) and the Canadian Institutes of Health Research (CIHR).

"Since double-stranded RNA is produced by many different viruses, Dr. Mossman's findings may have a significant impact on the treatment of a wide variety of infections," said Dr. Marc Ouellette, scientific director of the Institute of Infection and Immunity at the Canadian Institutes of Health Research. "Understanding the mechanism employed by viruses to infect surrounding cells is important if we are to develop more effective antiviral therapies, and prevent the spread of viral infections to a wider population."

More information: Paper: www.plospathogens.org/article/ … journal.ppat.1000829

Provided by McMaster University