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Scientists identify 'decoy' molecule that could help sharply reduce risk of flu death

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The flu virus can be lethal. But what is often just as dangerous is the body's own reaction to the invader. This immune response consists of an inflammatory attack, meant to kill the virus. But if it gets too aggressive, this counterattack can end up harming the body's own tissues, causing damage that can lead to death.

Now, a University of Maryland School of Medicine (UM SOM) researcher has for the first time uncovered new details about how this response plays out. Furthermore, he has identified a "decoy" molecule that can rein in this runaway inflammatory response. The results are published in the latest issue of the journal *Cell Reports*.

"We think this molecule has real potential as a strategy to protect patients from the body's tendency to respond too strongly to some viruses," said the researcher, Vladimir Y. Toshchakov, Ph.D., assistant professor in the UM SOM department of microbiology and immunology.

A key player in the response to flu is a group of molecules known as toll-like receptors (TLRs), which trigger the inflammatory response to the virus. When this response spirals out of control it can very often be deadly. Many researchers have been looking for ways to dial this down.

Toshchakov focused on a molecule called 2R9, which can block signals from the toll-like receptors. 2R9 is known as a "decoy" molecule because it finds its way into the sequence of signals, and so hinders the signals, stopping the communication that leads to the inflammation.

In experiments on mice that were especially vulnerable to flu, he found that 2R9 had a powerful effect. In the group treated with the molecule, only 22 percent died; by comparison, in the group that did not receive 2R9, around 90 percent died.

Toshchakov notes that 2R9 did not completely block the body's response to the flu virus. This is crucial: a balance is necessary. If the body doesn't mount any attack on the virus, the virus will proliferate, causing harm and perhaps death. But too much response is also harmful. 2R9 seems to modulate the response safely in the middle of these extremes.

He also looked at how 2R9 interacted with human cells; it seemed to have a similar affect as in mice. This indicates that using it makes sense to continue testing the molecule as a potential human treatment.

"Eventually, we want to see whether this compound, and this pathway, can help treat people with the flu," says Toshchakov.

Even without a larger outbreak, such as the 1918 Swine Flu epidemic that killed 18 million people worldwide, flu remains a serious public health threat. Every year, the illness kills between 22,000 and 28,000 Americans, according to the Center for Disease Control and Prevention.

"Dr. Toshchakov's work is an exciting move forward in the fight against flu," said Dean E. Albert Reece, M.D., Ph.D., MBA, who is also the vice president for medical affairs, University of Maryland, and the John Z. and Akiko K. Bowers distinguished professor and dean of the School of Medicine. "This defines bench-to-bedside: Starting with basic scientific questions, he and his colleagues have identified a promising candidate that could in the future have real clinical use."

Provided by University of Maryland