Researchers suggest boosting body's natural flu killers

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A known difficulty in fighting influenza (flu) is the ability of the flu viruses to mutate and thus evade various medications that were previously found to be effective. Researchers at the Hebrew University of Jerusalem have shown recently that another, more promising, approach is to focus on improving drugs that boost the body's natural flu killer system.

Emergence of new influenza strains, such as the recent avian influenza (H5N1) and swine influenza (H1N1 2009), can lead to the emergence of severe pandemics that pose a major threat to the entire world population. Recently, the concern regarding the emergence of such a pandemic arose when a new and deadly avian influenza strain (H7N9) was discovered in China, causing the death of six people in only one month.

The body's immune system can fight influenza infection. Natural killer (NK) cells, which are an essential component of this system, can recognize and eliminate influenza-virus-infected cells and inhibit the spread of the virus in the respiratory system.

But, as Ph.D. student Yotam Bar-On and Ofer Mandelboim, the Dr. Edward Crown Professor of General and Tumor Immunology at the Institute for Medical Research Israel Canada (IMRIC) of the Hebrew University Faculty of Medicine, have revealed in a paper published in *Cell Reports*, the influenza virus is able to escape from the NK cells activity, allowing it to spread in the respiratory system.

They show that this is accomplished by the influenza virus utilizing the enzymatic activity of the neuraminidase protein to neutralize the NK cells' receptors that are responsible for detecting the influenza-virus-infected cells. This, in effect, neutralizes the NK cells' ability to accomplish their designated flu-killing duty.

With the aid of the neuraminidase protein, the influenza virus is free to exit from the infected cell, enabling it to infect new neighbor cells and spread in the respiratory system. Anti-flu drugs were developed to inhibit this spread of the virus by inhibiting the neuraminidase enzymatic activity. But, as with other, earlier anti-influenza drugs, the flu viruses are able to gain the upper hand. The extensive use of neuraminidase inhibitors has caused the emergence of new, drug-resistant influenza strains.

For example, during the spread of the swine influenza pandemic in 2009, the Health Protection Agency in the UK reported that 99% of the viruses analyzed were resistant to these inhibitors. It was shown that the virus was able to change the neuraminidase structure so the drug can no longer bind this protein, and therefore the desired inhibitory effect is lost.

But, despite this, Bar-On and Mandelboim have shown that this type of widely used drug has the effect of boosting the activity of the NK cells, enabling them to better eliminate the influenza virus. They stress, therefore, that efforts should be focused on developing effective new drugs that would maintain and enhance this NK cell activity, thereby leading to more effective elimination of the influenza virus and better recovery from flu infection without the susceptibly to the changes in the neuraminidase protein structure currently brought about by mutating flu viruses.

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