Flu-induced stress response is critical for resistance to secondary infection

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A new study reveals how infection with the influenza virus impacts the way that the immune system responds to subsequent infections. The research, published by Cell Press in the February 18th issue of the journal *Cell Host and Microbe,* provides a new understanding of the physiological and pathological consequences of the flu.

Much of what is known about how the immune system protects against infection comes from studies examining exposure to a single pathogen. However, in the natural environment, organisms are commonly exposed to multiple infectious agents at the same time, so it is important to determine how the host's response to one pathogen alters its response to another. This is particularly relevant for infection with influenza because it is often accompanied by secondary bacterial infections that are more lethal that the initial viral infection.

"Several studies have demonstrated that infection with influenza virus can result in a suppression of the immune system," explains senior study author, Dr. Ruslan Medzhitov from the Department of Immunology at the Yale University School of Medicine. "However, these studies focused primarily on the local effects of influenza at the site of infection. The effect of influenza virus infection on the systemic immune response is less well understood."

Dr. Medzhitov's group examined the effects of influenza virus lung infection on the subsequent systemic response to bacterial infection using a well characterized mouse model of bacterial infection. Infection

with influenza resulted in a profound suppression of the systemic antibacterial immune response. Somewhat surprisingly, the researchers discovered that the influenza-associated immunosuppression was due to an increased production of glucocorticoids (GC). GCs are produced in response to stress and are known to play a key role in regulating inflammation.

The researchers went on to show that the virus-induced GC production was necessary to control inflammation. Importantly, although mice without GCs were better able to suppress the secondary bacterial infection and had a relatively normal response to infection with a single pathogen, the lack of GC production in the co-infected mice caused a lethal excessive inflammatory response.

The authors proposed that lung damage caused by infection with influenza triggered the stress response and GC production. "We have delineated a mechanism by which infection with influenza virus, through the induction of GC, leads to suppression of the systemic immune response to a secondary bacterial infection," says Dr. Medzhitov. "However, we also found that the induction of GC is critical for survival of co-infection."

More information: Jamieson et al.: “Influenza Virus-Induced Glucocorticoids Compromise Innate Host Defense against a Secondary Bacterial Infection.” Publishing in Cell Host & Microbe 7, 103-114, February 18, 2010. DOI 10.1016/j.chom.2010.01.010

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