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Scientists uncover liver's role in preventing dissemination of lung infection

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Researchers at Boston University School of Medicine (BUSM) have discovered the regulation and functional significance of the acute phase response during a lung infection. The findings, which will be published in the May edition of the *Journal of Clinical Investigation*, demonstrate that the liver responds in order to increase defenses in the blood that prevent localized infections from spreading throughout the body.

The study was led by Joseph P. Mizgerd, Sc.D., professor of medicine, microbiology and biochemistry at BUSM, and Lee J. Quinton, PhD, assistant professor of medicine and pathology at BUSM.

The acute-phase response is an innate immune response where dozens of blood proteins change in concentration due to physiological stresses such as infection, inflammation and injury. The change in concentrations of these proteins, such as C-reactive protein, can be measured in the blood and can indicate risk or progression of disease.

"While the acute-phase response was discovered in 1930, the mechanism and meaning behind the changes in certain blood protein concentrations are not well understood," said Mizgerd, who also is the director of the Pulmonary Center at BUSM.

In this study, the researchers mutated two transcription factor genes, STAT3 and RelA, in liver cells. These cells, called hepatocytes, generate the blood proteins that change during an acute-phase response. Prior to infection, these mutations had no measurable effects. In response to

pneumonia, which normally triggers the acute phase response, these mutations completely prevented such changes in the blood proteins. Thus, the acute-phase response was specifically inhibited.

The inability of the blood protein concentration levels to change led to those bacteria escaping from the lungs into the blood, which were then attacked ineffectively by the immune cells trying to destroy them. This exacerbated the infection, allowing it to spread to the blood and other organs.

"For the first time, we have shown the acute-phase response that occurs as a result of a lung infection triggers the liver to mount bloodstream defenses, preventing the infection from spreading throughout the body," said Mizgerd.

Provided by Boston University Medical Center