Researchers discover way to halt lung inflammation in animal models

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(PhysOrg.com) -- Acute inflammation of the lung is a poorly recognized human disease that develops in surprising and unexpected ways. The acute lung injury (ALI) or adult respiratory distress syndrome (ARDS) is a vital new concern for soldiers, but it can develop in anyone during a systemic infection, after severe trauma, as a result of bone fracture, following severe burns and in many other ways as well-- the initial cause may have nothing apparent to do with the lung itself. However, an answer to halting lung inflammation may have been discovered, thanks to a University of Colorado School of Medicine researcher and his team.

Recent studies show that between 60,000 and 100,000 people die each year in the United States from ALI/ARDS, more than twice as many fatalities as those from breast cancer. Recognition that the disease represents an uncontrolled inflammation of the lung has led to some important developments for treatment but even today mortality hovers around 60 percent for those people in whom the disease was identified early enough to initiate treatment.

In a study titled Xanthine Oxidoreductase Promotes the Inflammatory State of Mononuclear Phagocytes through Effects on Chemokine Expression, Peroxisome Proliferator-activated Receptor-γ Sumoylation, and HIF-1α publishing today in *The Journal of Biological Chemistry*, researchers use animal models of ALI/ARDS to show that the aggressive inflammatory state of specific immune cells can be switched off to control the runaway inflammation.

“We now know that cells of the so called innate immune system, neutrophils and macrophages, are involved in causing lung injury that can result in lung failure and death,” said Richard Wright, PhD, associate professor at the University of Colorado School of Medicine and lead study researcher. “While these cells are very important for our natural ability to fight off infection, the circumstances that lead to ALI/ARDS can overwhelm this beneficial role. Study of the neutrophils and macrophages that are responsible for ALI/ARDS has led to important ideas which offer hope for new concepts and options for treatment. For example, it is now known that the macrophage itself can exist in both an aggressive inflammatory state and in a more reparative state that can even help the lung to heal.”

The researchers now have several drugs that work to achieve the same effect. Ideally, the researchers would like to see that by switching the state of the macrophages to the more reparative state, the ongoing inflammation will be stopped and the capacity of the lung to repair itself will improve.

“This could provide us with a vital new approach to treating this still devastating disease and reduce the persistent mortality of ALI/ARDS,” said Wright.

"The results from this study clearly show how an essential enzyme involved in a vital metabolic pathway in our body can control the inflammatory state of key immune cells responsible for acute inflammatory diseases,” said Mehdi Fini, MD, a research instructor at the University of Colorado School of Medicine and one of the authors of the paper. “The data from this study will also help us understand and dissect the molecular pathway involved in differential behavior of these cells in the pathogenesis of other diseases of the lung including chronic obstructive pulmonary disease (COPD), lung fibrosis and lung cancer.”

Other University of Colorado School of Medicine researchers who collaborated on the study include Jenifer Monks, PhD, and Sean Colgan, PhD.

Provided by University of Colorado Denver