Using bone marrow stem cells to treat critically ill patients on verge of respiratory failure

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Researchers are reporting this week new study results they say provide further evidence of the therapeutic potential of stem cells derived from bone marrow for patients suffering from acute lung injury, one of the most common causes of respiratory failure in intensive care units.

Led by Drs. Michael A. Matthay and Jae W. Lee at the Cardiovascular Research Institute of the University of California, San Francisco, the team writes in a *Journal of Biological Chemistry* "Paper of the Week" that its experiments have revealed how a type of bone marrow stem cell bolsters damaged lung cells.

"We found that these stem cells secreted a significant quantity of a protein that restored the barrier that keeps fluid and other elements out of the lungs," said Lee, an associate professor of anesthesia at UCSF. "We're optimistic about the promise that future clinical trials may hold."

Scientists for decades have harnessed the natural regenerative properties of bone marrow to treat patients with blood-related diseases. And, of late, investigations into the potential of using bone marrow stem cells to treat damaged tissues have intensified.

There are two types of stem cells in bone marrow. One kind, hematopoietic stem cells, is tasked with producing red and white blood cells, depending upon the immune system's needs. The other,

mesenchymal stem cells, is the focus of Matthay and Lee's work. While mesenchymal stem cells also support the production of blood cells, scientists today are quite interested in their ability to differentiate into cells that, when mature, develop into tissues throughout the body.

"Within the past several years, there has been an increased interest in understanding the biology of stem cells for clinical use as cell-based therapies," Lee said.

Acute lung injury is brought on by a number of conditions, such as pneumonia and sepsis, also known as blood poisoning. In some cases, acute lung injury develops into a more serious condition, known as acute respiratory distress syndrome, and results in insufficient oxygenation of blood and eventual organ failure.

Buried in the depths of healthy lung tissue, tiny groups of cells called alveoli stretch open to accommodate oxygen with each breath and then remove carbon dioxide during exhalation. Each alveolus is lined with a layer of epithelial cells that serve as a critical barrier -- keeping certain substances in and certain substances out -- so that the gas balance inside is appropriately maintained.

In contrast, inflammation due to injury or infection can make the border of epithelial cells become more porous than it should be. The increased permeability allows an often-deadly mix of substances, such as fluid and cells, to seep into and accumulate in the alveoli.

Despite extensive research on acute lung injury and acute respiratory distress syndrome, the mortality rate for patients remains high -- at about 40 percent, Lee said, and pharmacological therapies that reduce the severity of lung injury in experimental studies have not yet translated into effective clinical treatment options.

"Current treatments are primarily supportive care, and, therefore, innovative therapies are needed," explained co-author Arne P. Neyrinck.

The team decided to re-create the unhealthy lung conditions in the lab -- by culturing human alveolar cells and then chemically causing inflammation -- and to observe how the presence of bone marrow stem cells would change things.

"We then introduced mesenchymal stem cells without direct cell contact, and they churned out a lot of protein, called angiopoietin-1, which prevented the increase in lung epithelial permeability after the inflammatory injury," said Xiaohui Fang, the first author of the manuscript.

The authors say the findings are the first to demonstrate how mesenchymal stem cells revive the epithelial border of the alveoli, and they hope clinical trials will prove the therapy is a viable one for preventing respiratory failure in critically ill patients.

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