

Gene associated with reduced mortality from acute lung injury

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Researchers at National Jewish Health and the University of Colorado Denver have discovered a gene that is associated with improved survival among patients with acute lung injury. Acute lung injury (ALI) is often caused by a respiratory infection and results in low oxygen levels in the blood, and fluid in the lungs. It is one of the most vexing problems for intensive care units, afflicting almost 200,000 people in the United States each year, and killing 40 percent of them.

"This discovery could benefit patients in two ways," said James Crapo, MD, senior author and Professor of Medicine at National Jewish Health. "By learning how this specific gene can alter the course of acute lung injury, we can gain insight into the biology of the disease, which could lead to better therapies. It also could become a tool in personalized medicine; by screening for this protective genotype and ones that make a person more susceptible to ALI, we can potentially tailor our treatment individual patients with respiratory infections and ALI to minimize the potential harm."

The researchers looked at the gene for extracellular superoxide dismutase (EC-SOD), a powerful antioxidant that has been associated with reduced lung injury in animal models, and better patient outcomes in chronic obstructive pulmonary disease. After sequencing the EC-SOD gene in 52 randomly selected people, they discovered 28 different places within the gene and its promoter that showed variations. Many of the variations, known as single nucleotide polymorphisms (SNPs) occurred together.

The researchers then looked at the various forms of the EC-SOD gene in two groups of patients with infection-associated ALI. They found that patients with a specific combination of four SNPs, had an 75 percent reduced risk of being on a ventilator as all other ALI patients, and an 85 percent reduced risk of dying.

"This specific set of SNPs, which we call the GCCT haplotype, appears to reduce inflammation in the lung, thereby decreasing the severity of lung injury and ultimately protecting patients from mortality associated with ALI," said John J. Arcaroli, PhD, first author and a post-doctoral fellow at the University of Colorado at Denver. "Although We are not yet sure how these particular SNPs alter the action of the EC-SOD, these findings gives us a good starting point to learn more about possible protective mechanisms in ALI and other lung diseases."

The researchers reported their findings in the January 15, 2009, issue of the *American Journal of Respiratory and Critical Care Medicine*.

Source: National Jewish Medical and Research Center

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