Medical Xpress

Gene chips accurately detect pneumonia in ICU patients on ventilators

November 17 2008

Even seasoned doctors have a difficult time diagnosing pneumonia in hospitalized patients breathing with the assistance of a ventilator. That's because a patient's underlying illness often skews laboratory test results and masks pneumonia's symptoms.

Now, researchers at Washington University School of Medicine in St. Louis report they have validated the use of gene chip technology to rapidly and accurately detect pneumonia associated with ventilator use in hospitalized patients. While more testing is needed among larger patient groups, their work suggests gene chips may lead to early, more accurate diagnosis and treatment of ventilator-associated pneumonia, one of the most common and deadly hospital-acquired infections in the United States.

The research will be presented by J. Perren Cobb, M.D., director of Washington University's Center for Critical Illness and Health Engineering on Monday, Nov. 17 at the sixth annual Symposium on the Functional Genomics of Critical Illness and Injury. The symposium is a prelude to the Inaugural Meeting of the U.S. Critical Illness and Injury Trials Group, led by Cobb, on Nov. 18 and 19. Both meetings are at the National Institutes of Health in Bethesda, Maryland.

"This is an important step towards validation of a specific molecular test for diagnosing infection - particularly pneumonia - and predicting patients' recovery," says Cobb. "If we could determine which patients are destined to develop pneumonia based on early changes in the activity

of genes that regulate immune response, we could give them antibiotics sooner, with the hope that we could prevent or curtail the infection."

Cobb and his team first analyzed patterns of expression in more than 8,000 genes in a small patient cohort at Barnes-Jewish Hospital, where Cobb specializes in the care of critical illness and injury. The researchers used the gene chips to study gene expression patterns in infection-fighting white blood cells obtained from blood samples drawn every 48 hours. The team found changes in the activity of 85 genes could pinpoint the early activation of the immune system in response to pneumonia, typically several days before clinical symptoms developed. By adding computational tools to their genomic analysis, the researchers also showed they could objectively monitor patients' recovery by graphing changes over time, using a tool they developed called a "riboleukogram."

The researchers then evaluated the 85-gene riboleukogram in 158 ICU patients on ventilators as part of a large-scale collaborative research program funded by the National Institute of General Medical Sciences. The technology accurately identified the 52 patients who developed pneumonia in the days following the insertion of their breathing tubes.

The riboleukograms looked similar in all patients in the first several days after the breathing tubes had been inserted. But between days 4-7, the expression of the 85 genes was significantly altered in the patients who had developed pneumonia vs. those who had not. The modified gene expression occurred some 24 to 72 hours before clinical symptoms of pneumonia were detected by physicians in the ICU.

"This suggest that we could start patients on antibiotics sooner, say at the first change in these genomic vital signs, which could significantly improve their ability to recover from pneumonia," Cobb says.

Interestingly, the researchers noted that as the health of the patients with

pneumonia improved, alterations in the expression of the 85 genes diminished, indicated they had returned to a healthy state. Thus, Cobb and colleagues suggest that riboleukogram technology can be used to quantify immune health and disease, acting as an EKG for the immune system.

Source: Washington University School of Medicine