CU-Boulder technology used to identify unexpected bacteria in cystic fibrosis patients

December 3 2007

Molecular technology developed by a University of Colorado at Boulder professor to probe extreme life forms in undersea hydrothermal vents has been used to identify unexpected bacteria strains in the lung fluid of Denver children suffering from cystic fibrosis, findings that may lead to more effective therapies.

Instead of standard culturing techniques, researchers used nucleic acid gene sequencing to rapidly detect, identify and classify pathogens found in the lungs of cystic fibrosis sufferers, said CU-Boulder Professor Norman Pace, who pioneered the method in the 1990s using microbes from Pacific Ocean hydrothermal vents. Pace and his colleagues at CU-Denver's Health Sciences Center and Denver's Children's Hospital identified more than 60 species of bacteria in samples of 28 cystic fibrosis patients in Denver. Thirteen samples contained bacteria that are not routinely assessed by culturing.

The presence of the unexpected bacteria may help explain cases of unidentified lung inflammation and the consequent failure of patients -- primarily children -- to respond to standard treatments, said Pace. "The results show molecular sequencing is a more effective, faster and far less expensive way to assess airway bacteria than routine clinical cultures and better identifies targets for further clinical evaluation," said Pace.

Cystic fibrosis, a life-threatening genetic disease affecting about 30,000 people in the United States, is marked by a build-up of mucus in the lungs and pancreas that can clog organs, according to the Cystic Fibrosis

Foundation. In addition to causing difficulty breathing, the thick mucus acts as a breeding ground for bacteria in the lungs that causes swelling, inflammation and infections that can lead to lung damage. Most deaths from cystic fibrosis are caused by such infections, said Pace.

A paper on the subject was published the week of Dec. 3 in the *Proceedings of the National Academy of Sciences*. Co-authors on the study included Kirk Harris and Mary Ann De Groote of CU-Boulder's MCD biology department, Scott Sagel, Edith Zemanick, Robin Deterding and Frank Acurso of CU-Denver's Health Sciences Center and Robert Kapsner, Churee Penvari and Heidi Kaess of the Mike McMorris Cystic Fibrosis Research and Treatment Center at Denver's Children's Hospital.

About 80 percent of pathogens identified in cystic fibrosis patients using the novel gene sequencing technology belong to three common bacterial groups, including the group that causes strep infections, said Pace. But the remaining 20 percent were from unexpected bacterial strains that would not normally be cultured in cystic fibrosis lab tests.

In one child in the test group, all of the pathogens in the mucus were from a bacterium genus known as "Lysobacter," which is commonly found in soils but not tested for in humans through standard cultures. "In cases like this, doctors could go back and re-test individual children for specific bacterial infections," he said. "This would be another advantage for clinicians using this technology for cystic fibrosis patients."

Pace said the molecular method involves isolating and amplifying bacterial nucleic acid samples from the lung fluids, then sequencing them to census individual pathogens by where they fit on the phylogenetic, or family, tree.

"This is a great example of a successful research collaboration between

campuses in the University of Colorado system," said Pace a member of the National Academy of Sciences and 2001 winner of a $500,000 MacArthur Foundation Fellowship, popularly known as the "genius grant." "My feeling is that those involved in cystic fibrosis research internationally will be very interested in these findings."

Source: University of Colorado at Boulder