Pigs provide clues on cystic fibrosis lung disease

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Aided by a new experimental model, scientists are a step closer to understanding how cystic fibrosis (CF) causes lung disease in people with the condition. The findings, published online April 28 in the journal *Science Translational Medicine*, could help improve treatments for lung disease, which causes most of the deaths and disability among people with CF.

In particular, the study by a University of Iowa research team and colleagues at University of Missouri appears to answer a long-standing "chicken and egg" question about which comes first in CF lungs -- infection or inflammation.

"Using our model we are beginning to answer that question, and it looks like infection does precede inflammation," said David Stoltz, M.D., Ph.D., UI assistant professor of internal medicine and lead study author. "The importance of that finding is that it could dictate what types of therapy we might use. Knowing that infection is first suggests that if we can prevent or fight infection, then that might delay or prevent the lung disease in people with CF."

For example, the finding would seem to support early and aggressive treatment of lung infections in children with CF, added Stoltz, who also is assistant director of the Adult Cystic Fibrosis Center at UI Hospitals and Clinics.

The new experimental model that Stoltz and his colleagues used were pigs with a CF-causing gene mutation. The team generated the pig model in the hope that it would more closely mimic the human disease than mouse models do.

By studying the CF pigs through their first six months of life, the team has shown that these animals do develop lung disease typical of what is seen in humans, including infection in the lungs, inflammation, and accumulation of mucus in the airways, which is a significant problem for patients with CF.

"This is a really great example where the pig serves as a model for what happens in the human, and the pig reacts to this disease in nearly the same way," said Randall Prather, distinguished professor of reproductive biotechnology at the University of Missouri. "In contrast, when you use mice, they don't get the lung disease that is common in patients with cystic fibrosis."

The team also found that the lungs of newborn CF pigs tended to be infected with more bacteria than lungs of control pigs. Moreover, within a few hours of birth, the CF pigs showed signs that their lungs are less able to get rid of bacteria from their lungs. This problem might represent an initial step in the disease process that results in chronic lung infection in CF.

"Our new model will help us understand the mechanisms of lung disease in humans with CF," Stoltz said. "It also provides a unique opportunity to test different therapies starting at a very early stage of the disease -- much earlier than we can in humans with CF -- and maybe to target preventive therapies that might help delay or even prevent the type of lung disease that affects people with CF."

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