Growth defects in cystic fibrosis may start before birth

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A new study using a pig model of cystic fibrosis (CF) suggests that low levels of a growth promoting hormone at or before birth may contribute to growth defects in patients with CF.

The study, led by University of Iowa researchers and published online the week of Nov. 8 in the Early Edition of the Proceedings of the National Academy of Sciences, could help predict the severity of the disease in patients and may lead to new therapies for growth defects in people with CF.

Growth defects are common in people with CF and have been blamed, in part, on low levels of the growth-promoting hormone called insulin-like growth factor 1 (IGF1). Traditionally, the malnutrition and lung inflammation that accompany CF have been blamed for the decreased levels of IGF1. However, even patients who are relatively healthy often do not reach their full growth potential, and newborns with CF often are smaller at birth than healthy babies.

To investigate the relationship between neonatal IGF1 levels and growth patterns in CF, the research team studied newborn pigs with a CF-causing gene mutation. This animal model, which was generated by the UI researchers and colleagues at the University of Missouri in 2008, has many of the same symptoms and complications that are seen in humans with CF.

"By examining IGF1 at this time point, we eliminated consequences of

lung inflammation, which is absent at birth, and malnutrition, because nutrition in utero is provided by the mother," explained Leah Reznikov, Ph.D., UI postdoctoral fellow in internal medicine and co-first author of the study. "We found that IGF1 levels were significantly reduced at birth in CF newborn pigs."

In addition, the UI researchers found that newborn CF pigs had shorter, smaller bones than pigs without CF suggesting that decreased IGF1 levels are associated with the growth defects, and that IGF1 levels may be reduced even before the pigs are born.

These findings led Reznikov and colleagues, including co-first author Mark Rogan, M.D., a former UI postdoctoral fellow in internal medicine, to examine levels of IGF1 in newborn humans with CF.

By testing blood samples collected through the Iowa Neonatal Metabolic Screening Program and the Iowa Department of Public Health, the researchers found that infants with CF have reduced IGF1 levels compared to healthy infants.

"Collectively, these findings suggest that IGF1 deficits begin very early in the course of CF disease and reductions in IGF1 may, in part, explain growth defects observed at birth in infants with CF," Reznikov said. "The findings also imply that IGF1 may serve as a potential biomarker of the disease and may be useful in prognostication, care and treatment of people with CF."

Patients with CF currently receive replacement pancreatic enzymes and insulin supplementation to counteract effects of CF. One possibility raised by the new findings is that IGF1 supplementation, beginning in infancy, might also be beneficial for growth in patients with CF. However, Reznikov cautioned that more testing is needed before this approach could be tested in humans.

"We would like to increase the sample size in our human studies and examine other parameters to better understand the relationship among CF, IGF1 and growth defects," she said."

If these test results are positive, Reznikov noted that the CF pigs would provide an excellent preclinical system to test whether IGF1 supplementation would be beneficial early in CF.

Provided by University of Iowa