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Cystic Fibrosis Research News

Title:
Club cell secretory protein and lung function in children with cystic fibrosis

Lay Title:
Club cell secretory protein is reduced in children with cystic fibrosis who have severe lung disease

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What was your research question?
Club cell secretory protein (CC16) is a protein that is produced in the airways and has important protective effects against lung infections and inflammation. Levels of CC16 can be easily measured in blood. We sought to determine whether severity of lung disease (i.e., lower lung function) in children with cystic fibrosis is associated with blood levels of CC16 and/or genetic variants near the CC16 gene.

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Why is this important?

Deficits in the levels of the CC16 protein may help to explain why some people with cystic fibrosis have more severe lung disease than others. Similarly, people with cystic fibrosis who carry specific genetic variants near the CC16 gene may be more susceptible to develop severe lung disease. If these theories are true, CC16 could be used to predict ahead of time what children with cystic fibrosis will develop severe lung disease. In addition, novel therapies aimed at increasing CC16 could be tested in patients with cystic fibrosis to prevent severe lung disease.

What did you do?

We measured levels of CC16 in blood from 260 children with cystic fibrosis who had the worst and the best levels of lung function (LOW and HIGH lung function groups, respectively). We also measured genetic variants close to the CC16 gene and tested whether these variants were associated with worsening of lung function in children with cystic fibrosis.

What did you find?

We found that children with cystic fibrosis and LOW lung function had remarkably lower levels of CC16 in their blood than did children with cystic fibrosis and HIGH lung function. We also found that a CC16 genetic variant called rs3741240A was strongly associated with lower levels of CC16 in blood. Children with cystic fibrosis who carried the rs3741240A variant had faster worsening of their lung function between ages 7-16 years than those who did not carry that variant.

What does this mean and reasons for caution?

These results indicate that deficits in CC16 may increase the risk for severe lung disease in patients with cystic fibrosis. However, caution should be used because our data cannot prove whether CC16 deficits cause lung disease, or whether, instead, lung disease causes CC16 deficits. Also, our study included only a very specific group of children with cystic fibrosis: non-Hispanic white participants with no previous infections by the germ *Pseudomonas aeruginosa*.

What's next?

Future studies should address the following three questions: (1) Can we use CC16 levels in blood to predict ahead of time what children with cystic fibrosis will go on to develop severe lung disease as adults? (2) Can the association of rs3741240A with severe lung disease be replicated in larger and more diverse populations of people with cystic fibrosis? (3) Can we

use therapies aimed at increasing CC16 to prevent or delay the development of severe lung disease in people with cystic fibrosis?

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