European Cystic Fibrosis Society

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Title:

Meconium Ileus due to GUCY2C gene mutations in 3 unrelated South Indian families

Lay Title:

Bowel blockage in new-born babies from meconium ileus can occur because of a rare gene mutation we have found in South Indian families.

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What was your research question?

It is well known that the most common underlying cause of meconium ileus is cystic fibrosis but there are some new-born babies who have this complication with no obvious underlying cause. We have carried out whole exome gene sequencing (DNA sequencing) to look for other gene defects that can cause this complication.

Why is this important?

It is important to try and diagnose all possible causes of meconium ileus. If there is an alternative genetic cause of this problem there will be a significant risk of it recurring in subsequent pregnancies.

What did you do?

We carried out whole exome sequencing in three children with meconium ileus having excluded cystic fibrosis as the cause of their bowel blockage. We particularly focused on the sequence of a gene called GUCY2C. This gene codes for a protein called guanylate cyclase 2C which is expressed in cells lining the intestines. The protein has an important role in activating the chloride channel that is defective in people with cystic fibrosis.

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What did you find?

The three babies with meconium ileus that we investigated all had two copies of variants in the GUCY2C gene that were likely to result in an inability to make the protein needed to activate the cystic fibrosis chloride channel in gut cells.

What does this mean and reasons for caution?

These three unrelated cases add to those described in just three other families described so far in case reported from other parts of the world. As yet we do not know the extent to which defects in the GUCY2C gene might be responsible for more cases, but we hope this publication will draw further attention to the possibility of this gene defect in babies with meconium ileus who do not have cystic fibrosis.

What's next?

We suggest that gene sequencing tests, paying particular attention to variations in the GUCY2C gene, should be considered in all non-cystic fibrosis cases of meconium ileus. Long term follow up of identified cases will help to find out if there are any other problems which occur in children with this type of gene defect.

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