

Researchers discover a genetic defect linked to pediatric liver disease

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Researchers from the University of Colorado Anschutz Medical Campus, in collaboration with several other institutions, have discovered a genetic defect linked to Biliary atresia (BA), the most common pediatric cause of end-stage liver disease, and the leading indication for liver transplantation in children.

Their findings were published January in the journal *Hepatology*.

"We don't know the cause of Biliary atresia, which interferes with our ability to treat affected children," said study co-author Ronald Sokol, MD, a pediatric gastroenterologist and hepatologist at Children's Hospital Colorado and Director of the Colorado Clinical and Translational Sciences Institute (CCTSI) at CU Anschutz.

By identifying a genetic mutation linked to the disease, Sokol, along with researchers from Emory University, University of Utah, Children's Hospital of Philadelphia, Washington University at St. Louis, and others, may finally determine the cause of this devastating condition. The group used next-generation gene sequencing to discover that a [genetic defect](#) of the gene PKD1L1 was linked to BA in a subset of patients.

Some children with BA also have splenic abnormalities and cardiac malformations called [biliary atresia](#) splenic malformation syndrome or BASM. Researchers hypothesized that the genetic factors causing an asymmetric position of organs in the body could also cause the development of BA in BASM patients, and that the genes involved could be discovered using whole exome sequencing.

So they sequenced DNA specimens from 67 subjects with BASM, including 58 patient-parent trios. Researchers looked at 2,016 genes—a subset of the full genome—that were associated with proteins that were candidates to cause a disease like BA. The study found five patients who had two copies of mutations in the gene PKD1L1 and three additional patients who had one mutation in the gene.

"The importance of this is that researchers have never identified a gene, when mutated, that causes BA," Sokol said. "This is the first time it has been found."

The CCTSI's Pediatric Clinical and Translational Research Center played a key role in the study. The patients who were participants came from a liver disease research network, which Dr. Sokol chairs, the Childhood Liver Disease Research Network (ChiLDReN). This network has been funded by the NIH for 15 years and includes 14 centers across the nation, Canada and the UK.

The gene that was identified may be the first of other genes to be found to be linked with BASM or BA. Understanding what causes BA is a breakthrough that could lead to new therapeutic approaches that would ultimately avoid [liver transplantation](#).

In the first analysis of the data, researchers looked at more than 2,000 genes. Now that they have the data from the whole exome sequencing, researchers can go back and analyze the other 18,000 [genes](#) for other genetic causes of BA.

"What we learn about what causes the disease could translate into new therapeutic targets and strategies," Sokol said.

Provided by CU Anschutz Medical Campus

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