Breakthrough in understanding life-threatening childhood liver disease

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Researchers at the University of Colorado School of Medicine and The Children's Hospital have taken a big step toward understanding what causes one of the most serious liver diseases in infants.

The disease is called biliary atresia, It blocks the bile ducts in young infants, through which bile, crucial for digestion, flows to the small intestine. The disease is rare – it strikes in about one in 10,000 births. But it's life-threatening.

"It is fatal if not treated quickly," says Cara Mack, MD, who led the CU research.

Surgical removal of the blocked main bile duct can buy time but ultimately the treatment in the majority of cases is a liver transplant during infancy or childhood, a procedure that is both complicated and expensive.

Until now, doctors weren't sure what caused biliary atresia, which is important to know in order to develop better treatments. The CU researchers propose that an infection late in the third trimester of pregnancy or soon after birth initiates the bile duct injury.

The body fights off the infection and infants initially show no signs of a problem. But then, Mack says, the body continues to battle as if the infection still was active. The body, however, is attacking itself -- the bile ducts specifically -- not the infection. This is called an autoimmune

process.

Why? Mack's research in a mouse model of the disease suggests that it may be that the bile ducts have been changed and the body's protective system senses that. Or it may be that the bile ducts give off a protein that is similar to proteins produced by the infection, launching the body's defenses into action. In these investigations, Mack and colleagues identified an immune system compound, anti-enolase antibody, that reacts to both virus and bile duct proteins. This antibody may contribute to the bile duct injury in biliary atresia.

"After a viral infection has resolved," Mack says, "the body's immune defenses turn on the bile ducts and cause continued damage."

That leads to scarring of the bile ducts, eventually blocking them so that "bile is not able to flow from the bile ducts into the intestines," says Mack, an associate professor in pediatrics with CU, who practices at The Children's Hospital in Aurora.

The discovery, published recently in the journal *Gastroenterology*, isn't a cure. But it is a big step, "pointing the way to new diagnostic tests and, eventually, to improved treatment options for this devastating disease," Mack says.

Provided by University of Colorado Denver