

Scientists link immune system's natural killer cells to infant liver disease

July 22 2009



Pranavkumar Shivakumar, Ph.D., (standing), and Jorge Bezerra, M.D., of Cincinnati Children's Hospital Medical Center, analyze a bile duct tissue sample from a 7-day-old mouse. Their study in the *Journal of Clinical Investigation* links an over-reactive response by natural killer cells in the immune system to the onset of biliary atresia in infants, a disease in which blocked bile ducts can cause severe liver damage and death. Credit: Cincinnati Children's Hospital Medical Center

Scientists have linked an overactive response by one of the immune system's key weapons against infection - natural killer, or NK, cells - to the onset of biliary atresia in infants, a disease where blocked bile ducts can cause severe liver damage and death.

Researchers at Cincinnati Children's Hospital Medical Center also report that blocking a gene that helps NK cells attack [bile duct](#) tissues lessens

damage and may be a way to treat the most common cause of chronically progressive [liver disease](#) in [children](#). The study, to be published in the Aug. 3 [Journal of Clinical Investigation](#), is posted online on the journal's website.

"Our findings underscore the developing immune system's role in causing injury to bile ducts soon after birth, and they have implications for developing new therapies to block the disease by targeting certain cells or pro-inflammatory circuits," said Jorge A. Bezerra, M.D., the study's senior investigator and research director of the Division of Gastroenterology, [Hepatology](#) and Nutrition at Cincinnati Children's.

"The next steps for translating these findings into clinical application would include pre-clinical trials of biologics to halt disease progression by blocking the Nkg2d receptor and depleting NK cells at the time biliary atresia is diagnosed," he added.

Very little is known about the cause of biliary atresia, although it has been traced to the immune system responding to an infection in the liver and bile ducts. Surface tissues inside the bile ducts are damaged, which in turn allows [inflammatory cells](#) to block the duct and the ongoing accumulation of fibrotic tissue. Biliary atresia affects about one in every 15,000 babies.

The current frontline treatment is surgery to remove and replace obstructed bile ducts with sections of the child's intestine. Without surgery, bile cannot enter the intestines to aid digestion, and instead backs up into and damages the liver. Corrective surgery is successful 65 to 85 percent of the time and is not considered a cure, although it can allow babies to have several years of fairly good health. In more severe cases, children may require a liver transplant.

To better understand the disease's apparent link to the developing and

still immature infant immune system, researchers in this study analyzed the livers of infants diagnosed with biliary atresia. They discovered elevated populations of NK cells in the bile ducts. The NK cells over-expressed genes involved in creating substances that are cytotoxic, or toxic to living cells. This finding led the research team to experiment with a mouse model of biliary atresia.

In the mouse experiments, the scientists used a rotavirus infection to induce biliary atresia in newborn mice. Similar to what was observed in diseased human infant livers, the researchers found that active NK cells were the most abundant cells populating the mouse livers and bile ducts at the time of obstruction. Furthermore, they discovered that NK cells rely on the receptor gene, *Nkg2d*, to make contact with and attack bile duct surface cells by attaching to the *Nk2d* protein, which resides on the membranes of bile duct cells. Once that contact is established, NK cells break down the membranes of bile duct surface cells, leading to tissue damage.

When researchers blocked the *Nkg2d* receptor and depleted the number of NK cells, it prevented damage to bile duct surface tissues, even with the presence of rotavirus infection. The continuity of the mouse pup bile ducts was maintained, bile was able to flow from the liver to the intestines, and the animals grew well into adulthood without liver-related symptoms.

Source: Cincinnati Children's Hospital Medical Center ([news](#) : [web](#))

Citation: Scientists link immune system's natural killer cells to infant liver disease (2009, July 22) retrieved 5 February 2024 from <https://medicalxpress.com/news/2009-07-scientists-link-immune-natural-killer.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.