Science pic: Stains and scars [1]

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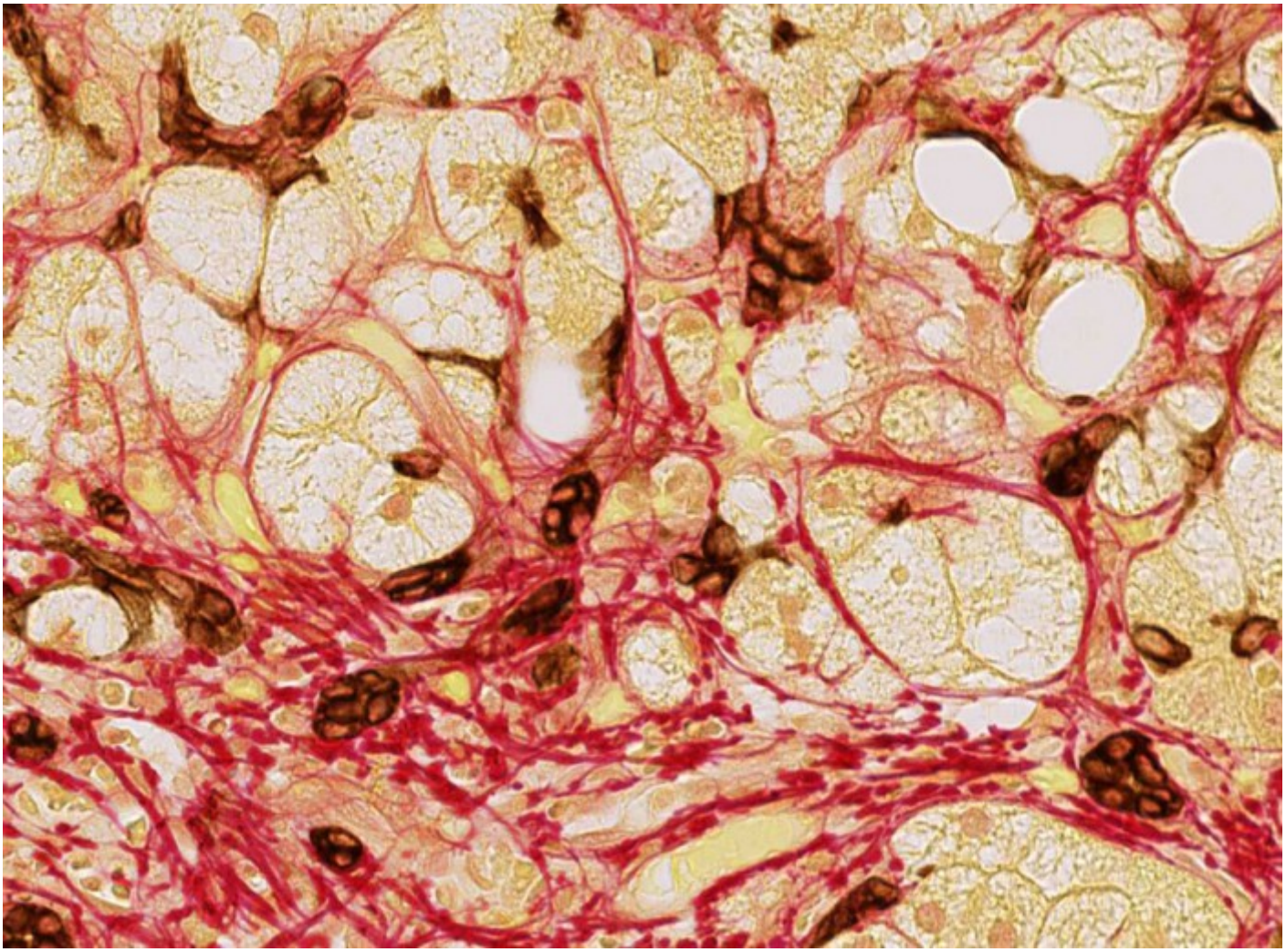

Image: Chandra Saravanan/Novartis

Small changes in tissue structure can have dramatic consequences. Especially in the liver. This sample from a patient diagnosed with cirrhosis is a case in point. It's riddled with collagen fibers (red) that interfere with essential functions of the liver.

But the fibers didn't form overnight. They grew gradually over time, and researchers at the Novartis Institutes for BioMedical Research (NIBR) are exploring the molecular and cellular events that triggered their growth.

"If we understand the molecular and cellular events that lead to fiber formation, then we might be able to design novel treatments to aid patients with a variety of liver diseases," says Keith

Mansfield in Preclinical Safety at NIBR.

A healthy liver accomplishes many tasks—it stores excess nutrients, rids the body of harmful substances in the bloodstream, and more. Patients with diseases such as hepatitis, alcoholism and diabetes can develop cirrhosis of the liver. In all cases, cirrhosis is characterized by collagen fiber formation, which leads to scarring. A scarred liver struggles to keep up and eventually fails.

While many groups have focused on understanding the diseases that lead to liver scarring, few have explored the mechanisms of cirrhosis itself.

NIBR researchers suspect that bile duct epithelial cells are involved. The liver produces a yellow liquid called bile to help the body digest food. Bile duct epithelial cells serve as conduits that transport this fluid to the small intestine. And they're abnormally abundant near collagen fibers in cirrhotic liver tissue.

Researchers in NIBR's Preclinical Safety group investigate bile duct epithelial cell patterns by applying histological stains to thin sections of human liver samples. In the image above, collagen fibers were stained with a chemical called picrosirius red. A yellow counterstain provides a visual contrast that highlights the cellular details. On the same piece of tissue, an antibody-immune-detection method was used to locate the bile duct epithelial cells and color them brown.

"Understanding the spatial relationship between the bile duct epithelial cells and collagen production is an important first step in determining the cellular events that lead to fiber formation," says Chandra Saravanan, a pathologist in Preclinical Safety.

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