Farnesoid-X receptor (FXR) knockout (KO) mice are protected from acute inflammatory injury in dithizone (DI)/Klebsiella and cecal ligation puncture models of injury. A: standard injury grading of each of the controls. B: Arrowhead, villus injury; arrow, basement membrane separation, both of which are absent in FXR KO. Credit: American Journal of Physiology-Gastrointestinal and Liver Physiology (2024). DOI: 10.1152/ajpgi.00063.2024
Removing a nuclear bile acid receptor that regulates glucose and lipid stability from the intestine blocks gut inflammation in mice, according to researchers at Children's Hospital Los Angeles. Their findings are published in the *American Journal of Physiology-Gastrointestinal and Liver Physiology*.

The farnesoid (FXR) bile acid receptor plays a significant role in gut inflammation. This is the first documented case of FXR deletion protecting the intestinal barrier in multiple models of acute intestinal inflammation.

Failure of the intestinal barrier has long been associated with body-wide infection (sepsis) that originates in the gut. Intestinal barrier protection is due to lowered inflammatory cells and maintenance of tight junctions linking the intestinal lining. When these cells do not stick together, intestinal contents leak into the abdominal cavity and other areas of the body, resulting in disease.

Gut inflammation can cause a number of health conditions, including ulcerative colitis and Crohn's disease. The effects are wide-ranging and include:

- Stomach pain
- Diarrhea
- Weight loss
- Anemia
- Loss of appetite

In this study, physiologists measured the amount of inflammation in the intestine after FXR was removed. Then, they used advanced microscopy to see the molecules that link epithelial cells and observe how a lack of FXR affects the intestinal barrier in the presence of disease. The lack of this receptor kept the gut barrier intact and prevented the animals from
"Inflammatory diseases of the intestine are a hallmark of many pathologies, including inflammatory bowel disease and gut-origin sepsis," said Christopher Gayer, MD, Ph.D., the study's lead author and chief of pediatric surgery at Children's Hospital Los Angeles. "The purpose of this research is to better understand the role of FXR within the intestinal epithelium which could help control and manipulate inflammation."