

Discovery of new signaling intermediates provides clues to novel therapies in pancreatitis

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Signaling initiated by pancreatic digestive enzyme-producing (acinar) cells is essential to development of both pain and inflammation in pancreatitis, according to research published in the inaugural issue of *Cellular and Molecular Gastroenterology and Hepatology*, the new basic science journal of the American Gastroenterological Association.

"A network of intercellular signals involving [pancreatic](#) acinar cells, nerves and immune cells results in progression of pancreatitis," said lead study author Rafiq A. Shahid, MD, from Duke University. "We made an exciting discovery that leukotriene B4 is synthesized and released by acinar cells and, in turn, activates sensory nerves to trigger [pain](#) and [inflammation](#) in [acute pancreatitis](#). If we can develop a treatment that blocks leukotriene B4, we would then be able to limit both pain and inflammation in patients suffering from this disease."

Using a mouse model, researchers explored the previous finding that transient receptor potential vanilloid-1 (TRPV1) receptors on [sensory nerves](#) are involved in development of pain and inflammation in pancreatitis. The activation of TRPV1 receptors plays a vital role in the early stages of development of pancreatitis, so the researchers questioned how these receptors are activated. They found that leukotriene B4 plays a pivotal role in this process.

The results also demonstrate that targeting leukotriene B4 by inhibiting

5-lipoxygenase, which is a key enzyme required for leukotriene B4 synthesis, is beneficial in experimental chronic pancreatitis. This provides an avenue for development and clinical evaluation of 5-lipoxygenase inhibitors for patients with pancreatitis.

"This discovery of previously unknown signaling pathways may lead to new therapeutic opportunities in pancreatitis," said Jerrold Turner, MD, PhD, AGAF, editor-in-chief of *Cellular and Molecular Gastroenterology and Hepatology*. "We are pleased to feature this ground-breaking research in the inaugural issue of the journal."

Pancreatitis is a common disorder that complicates many ailments, including cystic fibrosis and alcoholism. Few therapies exist, and management of the severe pain associated with inflammation is a major obstacle that often requires strong narcotics. However, narcotic use can be dangerous and often adds to the problems of patients with pancreatitis. Learn more about pancreatitis in the AGA patient brochure <http://www.gastro.org/patient-center/digestive-conditions/pancreatitis>.

The authors have no conflicts to disclose.

More information: Shahid, Rafiq A. et al., Acinar Cell Production of Leukotriene B4 Contributes to Development of Neurogenic Pancreatitis in Mice, *Cellular and Molecular Gastroenterology and Hepatology* 2015: 1(1): 75-68, [http://www.cmghjournal.org/article/S2352-345X\(14\)00006-X/abstract](http://www.cmghjournal.org/article/S2352-345X(14)00006-X/abstract)

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