Cytokine controls immune cells that trigger inflammatory bowel disease, study finds

18 April 2017

Dr. Tim Denning, associate professor in the Institute for Biomedical Sciences at Georgia State University. Credit: Georgia State University

A certain cytokine, or small protein that helps cells communicate during immune responses, can control whether immune cells promote or suppress inflammatory bowel disease, a finding that could lead to new treatments, according to a study led by Georgia State University.

Inflammatory bowel disease, chronic inflammation of all or part of the digestive tract, affects about 1.5 million Americans. The two main types, Crohn's disease and ulcerative colitis, develop from uncontrolled inflammation in the intestine, which can lead to severe diarrhea, pain, fatigue, weight loss and even death.

Researchers from Georgia State, Emory University and University of Michigan found the cytokine IL-36? controls whether T cells, which play an active role in immune responses, become aggressive or suppressive. They discovered IL-36? promoted the development of a specific type of T helper cell, Th9, which is associated with several diseases, including asthma, cancer and inflammatory bowel disease. The findings are published in the journal *Mucosal Immunology*.

"We were very intrigued whether the cytokine we were studying, IL-36?, could be promoting intestinal inflammation through the development of these Th9 cells, and that's in fact what we found," said Dr. Tim Denning, lead author and associate professor in the Institute for Biomedical Sciences at Georgia State. "When we were discovering this, we also found it simultaneously inhibits a suppressive population of T cells termed regulatory T cells or Tregs, which are known to suppress inflammatory bowel disease."

"Our conclusions were that IL-36? plays a critical role in driving the differentiation of pro-inflammatory Th9 cells and inhibiting the development of the suppressive Tregs. We think this can have major implications in the treatment of human inflammatory bowel disease, particularly ulcerative colitis, which has been shown to be associated with Th9 cells."

In a previous study, the researchers identified the cytokine IL-36? as being highly expressed in the inflamed intestine of mice and humans. They found IL-36? played a dual function, driving some of the pro-inflammatory process that aided in wound healing in inflammatory bowel disease.

The current study investigated the pro-inflammatory function of IL-36? in mice to determine how IL-36?

functions in human inflammatory bowel disease. The researchers performed in vitro and in vivo experiments in mice.

In the future, the researchers will investigate how to block the ability of IL-36? to bind to its receptor.

"If we can block the interaction of this cytokine with its receptor, we may be able to inhibit all of this cascade that we have defined and potentially develop a therapeutic for patients with inflammatory bowel disease, particularly ulcerative colitis," Denning said.

More information: A Harusato et al. IL-36? signaling controls the induced regulatory T cell–Th9 cell balance via NF?B activation and STAT transcription factors, *Mucosal Immunology* (2017). DOI: 10.1038/mi.2017.21

Provided by Georgia State University