# Biologist believes an intestinal cell type may be source of inflammatory bowel disease

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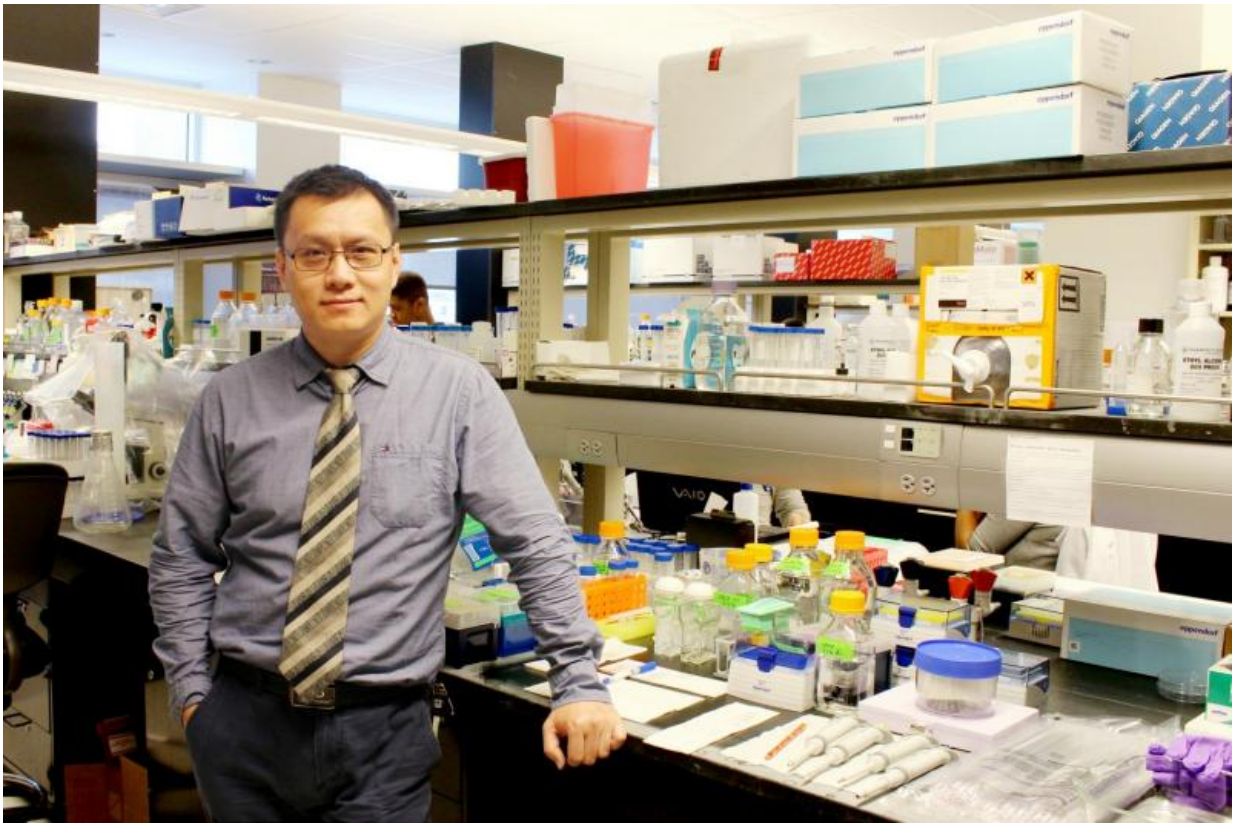

Biologist Nan Gao Gao leads a research team that is looking into whether a special intestinal cell type might be at the root of IBD – and if so, whether altering the cell's behavior could eliminate the disease. Credit: Nora Luongo

With all that we humans put in our mouths, one of our digestive systems'

most important jobs is self-preservation – keeping the linings of the intestines and other vital organs from breaking down under the strain they endure. In more than 16 million Americans according to the National Institutes of Health, that process has failed, creating a serious ailment called inflammatory bowel disease, or IBD.

"People with that disease can suffer from abdominal pain and cramping," says Nan Gao, an assistant professor of biology at Rutgers University-Newark (RU-N). "It has a great effect on people's lives because there is no clear treatment for it," he adds. "We also believe it can lead to colon cancer."

Gao leads a research team that is looking into whether a special intestinal cell type might be at the root of IBD – and if so, whether altering the cell's behavior could eliminate the disease. The Paneth cell, first discovered in the late 19th century, is nearly unique among cells because it plays a dual role. It is part of the thin mucosal layer that lines the intestinal wall, but it also has an immune function – emitting special compounds called anti-microbial peptides that can destroy bacteria that live in the gut.

When it works normally, Gao believes, the Paneth cell acts as a forward defense for the intestinal wall – protecting thicker layers of the wall that lie beneath the lining against invasion by the bacteria. It's all an elegant balance, he says, between the work of bacteria that aid digestion and the preservation of the intestine. But if Paneth cell activity is weak or nonexistent – possibly because of gene mutations – those bacteria might pierce the intestinal wall's lining and start degrading its main structure. That in turn can trigger the body's immune system to fight back – by rushing its most powerful weaponry to the scene of the breach.

In many people, the immune response is measured and appropriate, and beneficial. But for some people – again because of possible gene

mutations – the attack is too powerful, triggering harmful inflammation. Much as the "autoimmune" disease type 1 diabetes attacks the pancreas, or rheumatoid arthritis degrades joints, in IBD the patient's own immune system destroys the tissue of the intestine.

It is a chain reaction so destructive that Gao wants to get to the bottom of what the Paneth cell does by exploring the cell's function in the lab – and that requires a research team that can examine the problem with a wide range of expertise. RU-N has funded the creation of such a team, providing $80,000 to Gao through one of six Initiative for Multidisciplinary Research Team (IMRT) awards it granted to members of its faculty in 2015.

Gao's group includes faculty members associated with other areas of Rutgers, including Rutgers New Jersey Medical School and the university's Graduate Programs in Molecular Biosciences.

One of those scientists is George Yap, associate professor of medicine at the medical school and a member of its Center for Immunity and Inflammation. Yap, an expert in immunology, brings a research interest in toxoplasmosis, a potentially deadly disease caused by a parasite that enters the body when people eat raw meat or inhale infected cat litter. "The portal of entry of the parasite is the intestine, so the Paneth cell might also be involved in resisting the parasite," says Yap, who adds that because Gao has genetically designed a model of the Paneth cell that is well suited to lab experimentation, "we can really see what is going on."

Gao and Yap add that the benefits of the work might go even farther – such as improving knowledge about gastrointestinal distress that many cancer patients suffer when they undergo radiation treatment and chemotherapy. They also might gain new insight into hospital-acquired infection, for which cancer patients are also at heightened risk. One day, according to Gao, if the work goes well, it could even lead to new gene

therapies – designed to help patients by fine-tuning the Paneth cell's function.

Gao says whatever scientific progress the team makes is only possible because of the wide range of expertise that RU-N's IMRT award has permitted him to bring together. "This multidisciplinary approach makes us capable of answering some really deep questions."

Provided by Rutgers University