New research may help patients with intestinal failure, other malabsorptive disorders

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New treatments for intestinal failure and other intestinal absorption disorders are a step closer to the patients who need them after a discovery in Kelly Tappenden's University of Illinois laboratory.

"There are so few therapies for persons with these illnesses, many of them premature babies. Surgery may save a patient's life, but with so much intestine removed, they're unable to digest and absorb nutrients. They have to rely totally on intravenous feeding, which really reduces their quality of life," said Tappenden, a U of I professor of nutrition and gastrointestinal physiology.

Years of research in her lab show that butyrate, a short-chain fatty acid, helps intestine grow and become more functional. "To develop effective treatments, though, we needed to understand why butyrate has this effect. Now we understand the mechanism behind it."

According to Tappenden, butyrate increases the creation of intestinal cells. But, beyond that, it fortifies these new cells, preparing them to be more functional by increasing the transcription of a protein called GLUT2 that plays an important role in intestinal function by transporting sugars into the body.

"It's actually a double hit in terms of benefits. Not only does butyrate cause the intestine to grow in size, but it increases the number of

functional proteins in the cells that are made. Those cells transport more nutrients, thereby reducing the amount of intravenous nutrients needed by these patients," she said.

Knowing how all this works is really important for strategizing and fine-tuning therapies for intestinal absorption disorders, said Tappenden. "Right now, butyrate is not available in the bags of nutrients used for intravenous feeding. But our research tells us that we should at least be encouraging patients to consume more carbohydrates and dietary fiber because intestinal bacteria use these nutrients to make butyrate."

To learn more about butyrate's action at the cellular level, Tappenden isolated human colon cancer cells (Caco2-BBe cells), which behave very much like cells from the small intestine.

"We transfected the promoter portion of the GLUT2 gene in these small intestine-like cells and then exposed them to a variety of short-chain fatty acids—a cocktail of acetate, propionate, and butyrate, as well as each of them individually. Then we watched to see which of them would start manufacturing GLUT2, expecting to see that butyrate alone was responsible," she said.

Sure enough, butyrate alone turned on the promoter responsible for making the GLUT2 intestinal transporter.

"This gives us insight into the cellular mechanisms whereby butyrate could really help people with intestinal failure," she said. "Why? Because it's increasing this important protein that causes the intestine to absorb more nutrients."

The next step is experimenting with administering prebiotics and probiotics to newborn piglets, an excellent model for the human infant because of their similar metabolism and physiology.

The prebiotics contain soluble fiber, the fuel bacteria need to make short-chain fatty acids, such as butyrate. Probiotics contain bacteria that reside in the colon and serve an important role in intestinal function and immunity, she said.

The results of the piglet study should be available this summer.

More information: This study was published in the November/December 2009 issue of the Journal of Parenteral and Enteral Nutrition.

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