Scientists uncover changes in proteins that regulate 'gut leakiness' and identify a link with common digestive diseases

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Scientists at Trinity College Dublin have made an important advance in understanding the biological factors that keep the lining of the gut wall intact. Associate Professor, Maria O'Sullivan at Trinity's School of Medicine and St James's Hospital and colleagues, showed that changes in specific proteins may contribute to a 'leaky-gut' wall which may have important implications for common chronic digestive diseases such as irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD).

This work, conducted and first authored by Ewa Wilcz-Villega, was published by the leading US journal, the *American Journal of Gastroenterology*.

"We are familiar with a leaky pipe but when the gastrointestinal tract is not functioning properly it may also become 'leaky' allowing inappropriate access of substances from inside the gut (e.g. digested products, bacteria) to leak through the gut lining and into the body, which in turn triggers inflammatory and immune responses. This 'leaky gut' or 'intestinal' permeability' is a feature of a number of inflammatory related gastrointestinal diseases, including inflammatory bowel disease and irritable bowel syndrome," comments Associate Professor O'Sullivan.

The team's research showed that a protein, which helps cement cells in the lining of the gut together, was lower in the intestine of people with

irritable bowel syndrome, suggesting a leakier gut. People with lower levels of this protein experienced more severe abdominal symptoms, including pain. Other experiments demonstrated that a mediator released from immune cells (namely mast cells) was capable of decreasing this protein. This key protein is called JAM-A (Junctional Adhesion Molecule A) and this is the first reporting of alternations in JAM-A protein in the gastrointestinal tract in IBS. These novel findings may ultimately lead to better therapeutic targets for IBS and other inflammatory diseases.

Provided by Trinity College Dublin