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The colon is defended from bacteria by a self-sacrificing sentinel cell

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A lone Sentinel cell monitors and coordinates the defense of the entrance to the colon's most sensitive parts. The Sentinel cell detects nearby bacteria and signals to a line of defensive cells to send out a cascade of mucus to push away the invaders. As a final self-sacrificing action the cell commits suicide and ejects itself into the intestinal lumen.

Researchers at the Sahlgrenska Academy, University of Gothenburg, have discovered a new group of cells that can wash away the bacteria that have penetrated through the protective mucus barrier. The discovery, published in the journal *Science*, may be important in understanding how inflammatory bowel disease, e.g. ulcerative colitis, occurs.

The human colon is protected by a mucus layer that prevents bacteria from coming in direct contact with the tissue, which would otherwise cause inflammation. The protective mucus layer is made up of proteins (mucins) produced and secreted by so-called goblet cells. The research team in Gothenburg has previously shown the presence of a mucus layer as the colon's first line of defense, and the same group now shows that there is also a subset of goblet cells, which form a second line of defense against bacteria that made it through the mucus layer. The discovery is published in the leading international journal Science.

In the colon there are depressions (called crypts) at the bottoms of which are stem cells which constantly produce new intestinal cells. At the entrance of these crypts, a special type of defensive cell has now been

discovered.

"These cells are like sentinels guarding the entrance to the crypt. As soon as they discover traces of bacteria in the crypt opening, it starts a chain reaction ending up in a violent mucus explosion that washes away the bacteria", says George Birchenough, a postdoctoral researcher at the Sahlgrenska Academy, University of Gothenburg.

Flushing away bacteria is a suicide mission for the Sentinel.

"When the Sentinel goblet cell is emptied it pushes itself out as a catapult. If this does not prevent the bacterial attack and this continues there are no new sentinels to send forward, thus leaving the crypt open for bacteria invasion and the potential onset of inflammatory bowel disease such as ulcerative colitis", says Professor Gunnar C. Hansson at the Sahlgrenska Academy, who together with Malin Johansson leads research into mucus and mucins at University of Gothenburg.

George Birchenough, a researcher in the group, did most of the work at the microscope, where he analyzed mouse tissue. Through the microscope, he has been recording in real time how the newly discovered cell type triggers the rapid chain reaction that creates the cascade of mucus that washes away bacteria. The group has identified and compiled the mechanisms underlying the chain reaction, and has already begun the next step in the process to establish the role of these cells in disease and to confirm their presence in the human gut.

"It is rare to discover a new type of cell with a previously unknown function, and it is particularly pleasing that all the work done here in Gothenburg by our research group", says Gunnar C. Hansson.

The research group in Gothenburg was the first to discover that the mucus layer in the gut acts as a barrier that separates the intestinal bacteria from the intestinal surface. This discovery has completely changed our understanding of mucosal biology and created a whole new area of research that has since been followed by a series of revolutionary discoveries about how the mucus layer is created, maintained, moves and can be damaged. This has great significance for understanding how our intestinal bacteria interact with us. The researchers are aiming toward new ways to treat a range of intestinal diseases such as ulcerative colitis.

More information: G. M. H. Birchenough et al, A sentinel goblet cell guards the colonic crypt by triggering Nlrp6-dependent Muc2 secretion, *Science* (2016). DOI: 10.1126/science.aaf7419

Provided by University of Gothenburg