Abnormal cellular process implicated in gut inflammation and onset of inflammatory bowel disease

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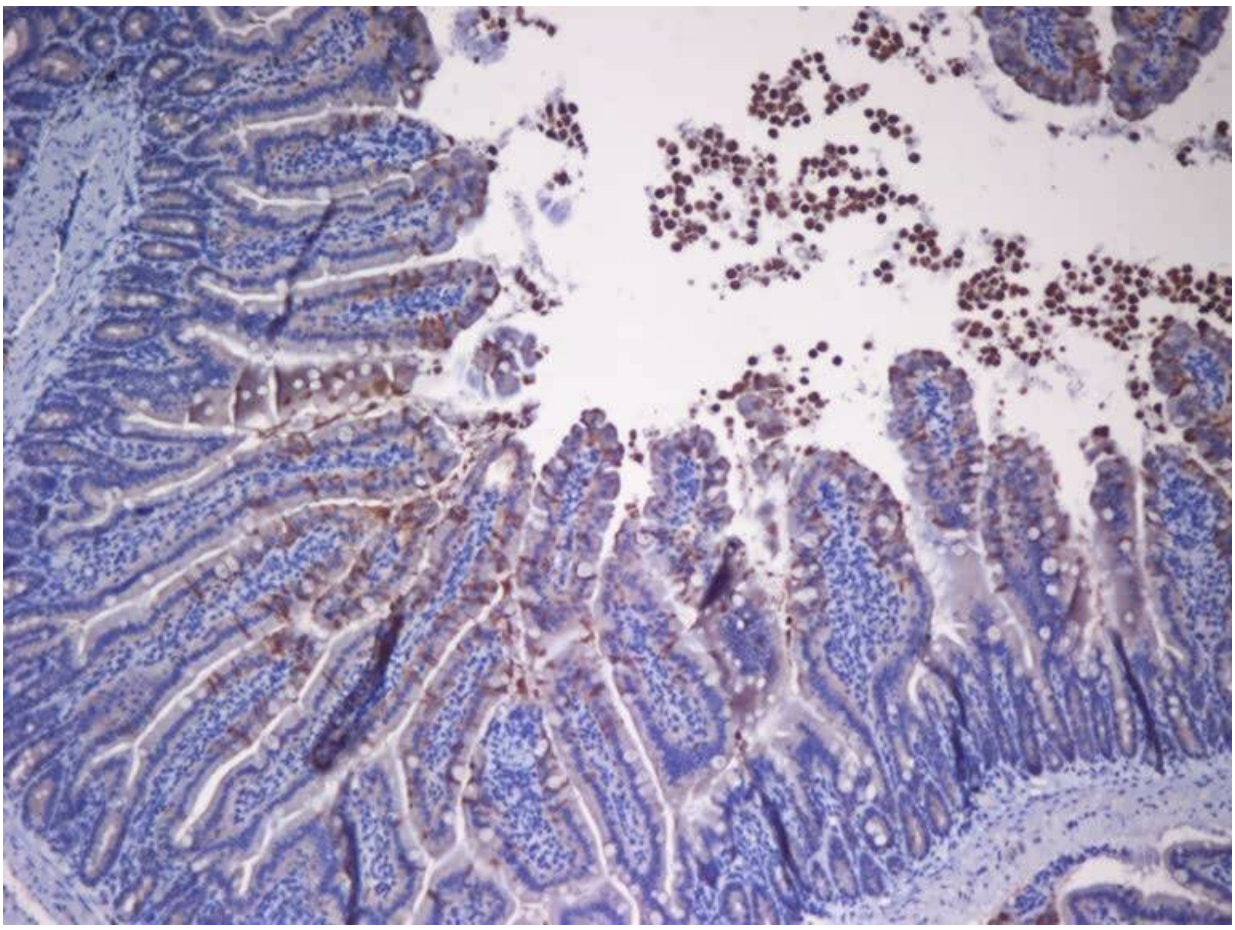

Characteristic folds and projections (villi) of the intestinal lining. Cells undergoing apoptosis (dying and detaching) in response to inflammation are stained brown. Credit: Quadram Institute

Elevated levels of the key cellular process of apoptosis have been implicated in intestinal inflammation and inflammatory bowel disease (IBD) in a new study from the Quadram Institute.

IBD is a long-term, painful and debilitating condition characterised by inflammation in the gut. Over 300,000 people in the UK suffer from IBD, and there is currently no cure. Symptoms can be treated to varying degrees of success with drugs, dietary changes or surgery, but more effective therapies are needed to reduce IBD's impact.

The lining of the gut allows absorption of nutrients but prevents harmful microbes and other gut contents from getting across. This lining is made up of a single layer of specialised cells, and undergoes continual renewal or 'turnover', with new cells constantly being generated and lost. Maintaining the normal functioning and renewal of the barrier is tightly regulated and critical to maintaining good health.

A collaboration of scientists from the Quadram Institute, the University of East Anglia and the University of Oxford have been focusing on how breakdown the renewal of the gut lining is related to IBD. A new study from the team, published in the journal *Cell Death & Disease*, has combined cell tracing analysis in mouse models with mathematical modelling to better understand epithelial cell processes during health and inflammation. The study was funded the Biotechnology and Biological Sciences Research Council (BBSRC) and the Engineering and Physical Sciences Research Council (EPSRC).

Under conditions of chronic, ongoing inflammation, the normal renewal of the gut lining was impaired, with an increase in controlled cell death, known as apoptosis, and slower turnover of the lining. The researchers believe that these results give an indication of the early events in the epithelium preceding the onset of IBD.

What they now want to unpick is how these changes lead either to recovery, or to the further destabilisation of the epithelium and the onset of IBD. There is a growing body of evidence implicating the microbiota in the process of driving IBD development. Combining observational approaches with mathematical modelling will be valuable in unravelling the complex interactions between epithelial cells, the immune system and microbes. With that detailed information it will be possible to identify new targets or strategies on which new therapies to treat or prevent IBD can be based.

More information: Aimée Parker et al. Elevated apoptosis impairs epithelial cell turnover and shortens villi in TNF-driven intestinal inflammation, *Cell Death & Disease* (2019). DOI: 10.1038/s41419-018-1275-5

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