Key regulator in inflammatory bowel disease identified

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UCD Conway scientists led by Professor Cormac Taylor have pinpointed a key regulator involved in maintaining the functional integrity of the gut lining as part of their reseach into inflammatory bowel disease (IBD). Together with their national and international collaborators, they recently published findings in Gastroenterology that may provide vital information for developing a new therapeutic approach to the treatment of this disease.

The underlying genetic or environmental causes of inflammatory bowel disease remain largely unknown. However, the major problem associated with this chronic condition is that the lining of the gut becomes leaky, allowing material from the lumen of the intestine to pass through this barrier and trigger an inflammatory response.

The intestinal barrier works by maintaining a delicate balance between the proliferation and death of epithelial cells at the surface of the barrier. If the balances tips so that more cells die than grow, as is the case in IBD, the barrier is no longer intact and cannot function properly.

This latest research has shown that in the absence of an oxygen-sensing enzyme, prolyl hydroxylase 1 (PHD1), epithelial cell death is reduced and the intestinal barrier function is enhanced. Therefore, PHD1 may be a useful target for pharmacologic inhibition in IBD.

The team, which also includes scientists from the University of Leuven, Belgium; University of Heidleberg, Germany; University College

London and the Institute of Molecular Medicine, Trinity College Dublin, propose that by delaying or suppressing epithelial cell death, the gut lining would be given time to heal and the integrity of the intestinal barrier could be restored.

Commenting on the research, Professor Taylor said "Inflammatory bowel disease is a condition in need of new and improved therapeutic options. Our current results indicate that targeting the PHD1 enzyme may represent one such approach."

In separate but related research, the Taylor group collaborate with the Irish biopharmaceutical development company, Sigmoid Pharma to facilitate targeted drug delivery to specific areas of the gut as part of a new therapeutic approach to the treatment of IBD. Science Foundation Ireland and the German Research Foundation funded the research by this group.

More information: Loss of prolyl hydroxylase-1 protects against colitis through reduced epithelial cell apoptosis and increased barrier function.
Murtaza M. Tambuwala, Eoin P. Cummins, Colin R. Lenihan, Judith Kiss, Markus Stauch, Carsten C. Scholz, Peter Fraisl, Felix Lasitschka, Martin Mollenhauer, Sean P. Saunders, Patrick H. Maxwell, Peter Carmeliet, Padraic G. Fallon, Martin Schneider, Cormac T. Taylor. Gastroenterology - 02 July 2010 doi: 10.1053/j.gastro.2010.06.068