New genetic markers for ulcerative colitis identified

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An international team led by University of Pittsburgh School of Medicine researchers has identified genetic markers associated with risk for ulcerative colitis. The findings, which appear today as an advance online publication of the journal *Nature Genetics*, bring researchers closer to understanding the biological pathways involved in the disease and may lead to the development of new treatments that specifically target them.

Ulcerative colitis is a chronic, relapsing disorder that causes inflammation and ulceration in the inner lining of the rectum and large intestine. The most common symptoms are diarrhea (oftentimes bloody) and abdominal pain. Ulcerative colitis and Crohn's disease, another chronic gastrointestinal inflammatory disorder, are the two major forms of inflammatory bowel disease (IBD).

"Ulcerative colitis and Crohn's disease are chronic conditions that impact the day-to-day lives of patients," said senior author of the study Richard H. Duerr, M.D., associate professor of medicine and human genetics at the University of Pittsburgh School of Medicine and Graduate School of Public Health. "IBD is most often diagnosed in the teenage years or early adulthood. While patients usually don't die from IBD, affected individuals live with its debilitating symptoms during the most productive years of their lives."

Because IBD tends to run in families, researchers have long thought that genetic factors play a role. Technology developed in recent years has

enabled systematic, genome-wide searches for gene markers associated with common human diseases, and the discovery of more than 30 genetic risk factors for Crohn's disease has been one of the major success stories in this new era of research. While some genetic factors associated with Crohn's disease also predispose individuals to ulcerative colitis, markers specific for ulcerative colitis had yet to be found.

To do so, researchers performed a genome-wide association study of hundreds of thousands of genetic markers using DNA samples from 1,052 individuals with ulcerative colitis and pre-exisiting data from 2,571 controls, all of European ancestry and residing in North America. Several genetic markers on chromosomes 1p36 and 12q15 showed highly significant associations with ulcerative colitis, and the association evidence was replicated in independent European ancestry samples from North America and southern Italy.

Nearby genes implicated as possibly playing a role in ulcerative colitis include the ring finger protein 186 (RNF186), OTU domain containing 3 (OTUD3), and phospholipase A2, group IIE (PLA2G2E) - genes on chromosome 1p36, and the interferon, gamma (IFNG), interleukin 26 (IL26), and interleukin 22 (IL22) genes on chromosome 12q15. RNF186 and OTUD3 are members of gene families involved in protein turnover and diverse cellular processes. PLA2G2E, IFNG, IL26 and IL22 are known to play a role in inflammation and the immune response. The study also found highly suggestive associations between ulcerative colitis and genetic markers on chromosome 7q31 within or near the laminin, beta 1 (LAMB1) gene, which is a member of a gene family known to play a role in intestinal health and disease, and confirmed previously identified associations between ulcerative colitis and genetic variants in the interleukin 23 receptor (IL23R) gene on chromosome 1p31 and the major histocompatibility complex on chromosome 6p21.

"My laboratory is focused on studying the genetic basis for IBD," said

Dr. Duerr. "Through genetic mapping, we and our collaborators are successfully identifying regions of the genome that contain IBD genes. The next steps are to understand the functional significance of IBD-associated genetic variants, and then to develop new treatments that specifically target biological pathways implicated by the genetic discoveries. The overall goal of this work is to improve the lives of the millions of patients worldwide that suffer from IBD."

Source: University of Pittsburgh Schools of the Health Sciences