Research links 29 genome regions with common form of inflammatory bowel disease

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An international team of researchers has made new links between 29 regions of the genome and ulcerative colitis – a common form of inflammatory bowel disease (IBD). The new findings increase the total number of genome regions known to be associated with inflammatory bowel disease to 99.

The results point to several biological processes, including the way that our bodies maintain the lining of the intestinal wall, which are likely to play an important role in the development of ulcerative colitis.

The causes of inflammatory bowel disease are not fully understood, although it is thought that patients with inflammatory bowel disease have an overactive immune response against typical gut contents. Together, ulcerative colitis and Crohn's disease – the two primary causes of inflammatory bowel disease – affect one in 250 people in Europe, North America and Australasia.

Unlike Crohn's disease, which can impair any part of the human digestive tract, ulcerative colitis is restricted to the large bowel. Up to 20 per cent of ulcerative colitis patients will require surgery to remove the entire large bowel.

"The outcomes and quality of life for patients with ulcerative colitis can be bleak", says Dr. John Rioux, from the Montreal Heart Institute and the Université de Montréal, senior author on the paper, and co-chair of the International IBD Genetics Consortium. "To understand the genetic

causes of the disease, we carried out the largest study of the disease to date – taking a magnifying glass to over one million sites in the genomes of more than 26,000 people."

"Ultimately, we hope that unmasking the genetic processes that give rise to the disease will minimise the need for surgical outcomes, by opening the door for new therapies that can stop the disease in its tracks."

"With one in 160 Canadians living with either Crohn's disease or ulcerative colitis, we have among the highest rates of IBD in the world," says Dr. Kevin Glasgow, Chief Executive Officer of the Crohn's and Colitis Foundation of Canada. "Given the often limited treatment options and quality of life for patients with ulcerative colitis, the Canadian IBD community welcomes this research breakthrough and looks forward to its therapeutic application."

The team carried out a genome-wide scan to look for changes in the genetic code common to patients with ulcerative colitis. They did this by looking at genetic data from more than 32,000 apparently healthy people, and more than 16,000 people suffering from ulcerative colitis.

Using the technique, the team homed in on 29 new regions that are associated with the disease – bringing the total number for ulcerative colitis to 47 and the total for inflammatory bowel disease to 99.

Like signposts, these regions pointed the researchers towards several genes that might play an important role in ulcerative colitis.

"The genomic regions we have identified give us an insight into the biology underlying ulcerative colitis," says Dr. Carl Anderson, from the Wellcome Trust Sanger Institute and first author on the paper. "These important initial discoveries are the building blocks on which we can begin to derive better IBD treatments, though much further work is

needed before these become a clinical reality. "

"To give us a better understanding of IBD biology, we compared the results of this ulcerative colitis study to those of a similar study we recently completed looking at Crohn's disease, and the results were very informative."

The team found significant overlap between the genetic regions associated with each disease, with at least 19 of the total 47 ulcerative colitis regions also associated with Crohn's disease.

The researchers show that many of the overlapping regions include genes involved in expanding and maintaining a group of T-cells involved in our immune response. The finding supports the idea that the way our immune system responds to the natural bacteria found in the gut could be an important part of the disease profile of inflammatory bowel disease.

The researchers suggest that the candidate genes – including several key members of the 'IL23 pathway' – could provide good targets for researchers developing therapeutic interventions against the disease.

As well as finding genes that point towards a shared biology – the researchers also found evidence of genetic events that might be unique to ulcerative colitis.

"For many patients, ulcerative colitis means a lifetime of bloody diarrhoea and stomach pains," says Dr. John Rioux. "The disease can be very severe in some patients resulting in life-threatening inflammation of the large bowel, and there is an increased risk of developing bowel cancer. This is a really unpleasant and intrusive illness that typically affects young adults, and for which we presently have no known cure. "

"We have some good medical therapies, but for many patients these are either not effective or poorly tolerated. We therefore have an urgent unmet therapeutic need and it is my great hope that we can translate our really exciting genetic findings into effective new therapies in the next five to ten years, " said Dr. John Rioux.

The new findings open the door for further research to explore the candidate genes identified and their possible role in the development of the ulcerative colitis and inflammatory bowel disease.

Inflammatory bowel disease is a term used to describe conditions that are characterised by inflammation of the gastrointestinal tract. The term IBD is used predominantly to describe two diseases: Crohn's disease and ulcerative colitis. In Crohn's disease, the inflammation can affect any part of the digestive tract. In ulcerative colitis, the inflammation affects only the colon. Together, ulcerative colitis and Crohn's disease affect one in 250 people in Europe, North America and Australasia. Inflammatory bowel disease should not be mistaken for irritable bowel syndrome – a separate disease which can present some similar symptoms.

More information: Anderson C A et al. (2011) Meta-analysis identifies 29 additional ulcerative colitis risk loci, increasing the number of confirmed associations to 47. Nature Genetics. Published online before print at doi:10.1038/ng.764

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