Opening up new pathways for treating inflammatory bowel diseases

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Credit: AI-generated image (disclaimer)

Inflammatory bowel disease (IBD) is a chronic condition affecting 1 in 250 people in Europe. Current treatment is ineffective for many. However, a team of European scientists has increased understanding of the causes of IBD, opening the way for the development of new treatments.

The term IBD refers primarily to two diseases: Crohn's disease and ulcerative colitis. Both involve inflammation of the gastrointestinal tract, but there are important differences between the two. Ulcerative colitis affects only the colon, and can be cured only by its complete removal. Crohn's disease can affect the entire digestive system, and is currently incurable.

Sufferers of both diseases are likely to experience abdominal pain, diarrhoea, rectal bleeding, anaemia and weight loss; and symptoms usually come and go.

IBD is usually treated with immune-suppression drugs that reduce inflammation and painful symptoms. But drugs only cause symptomatic relief, are not effective for everyone, and can lead to long-term side effects.

Until now, little has been known about the exact causes of the conditions, although it is widely believed that they occurs when microbes within the intestine trigger an immune response in individuals predisposed to IBD.

The EU-funded project IPODD ('IBD: proteases offer new targets for drug discovery') looked into the role of specific enzymes - matrix metalloproteases (MMPs) - during the final steps in the chain of events that lead to IBD.

MMPs break down other proteins, such as those found in the space around cells, clearing the way for inflammatory cells to target tissue. MMPs are controlled by TIMPs - tissue inhibitors of metalloproteases. When there is an imbalance between MMPs and TIMPs, tissue damage and chronic inflammation follow.

The IPODD team compared the expression of MMPs in chronically

inflamed and healthy gut and were able to identify enzymes that could be targets for TIMPs or drugs.

Another key finding was the discovery that the proteases (enzymes that break down proteins and peptides) associated with inflammation sometimes originate from gut bacteria. This new insight into the causes of IBD is likely to lead to research into the various inhibitors and agonists of bacterial proteases in the gut, and screening for compounds that may be used in drugs to treat IBD.

IPODD was the first research project to focus specifically on the role of MMPs in IBD. This was made possible thanks to the multidisciplinary nature of the team - it included experts in immunology, microbiology, probiotics, neuro-gastroenterology, genetics and drug development from six EU countries plus New Zealand. The team was coordinated by the University of Sheffield in the UK.

The team received almost EUR 3 million in EU funding under the health programme of the Seventh Framework Programme for Research and Technological Development (FP7). They completed their work in May 2011.

More information: IPODD project factsheet
cordis.europa.eu/projects/rcn/88203_en.html

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