THE UNIVERSITY of EDINBURGH

News Release

Issued: 14 May 2017

Gene study points towards new therapies for bowel diseases

A key gene that helps to explain an underlying cause of incurable bowel disorders such as Crohn's disease has been identified by scientists.

Blocking the gene harms vital parts of the cell and leads to bowel disease, while targeting these vital cell parts with drugs can reverse damage, the study shows.

The findings aid understanding of the cause of these lifelong conditions and could lead to new treatments, scientists say.

Inflammatory Bowel Disease – or IBD – includes Crohn's Disease and Ulcerative Colitis and affects around 300,000 people in the UK. The causes of these disorders are unknown and there is currently no cure.

The gene – known as MDR1 – governs an important extractor system for toxins in the gut, removing damaging substances from intestinal cells.

A research team – led by the University of Edinburgh – showed that MDR1 function was lower in colonic biopsies from people with inflamed IBD compared with those without inflammation.

To demonstrate how MDR1 dysfunction leads to bowel damage, the scientists then showed that mice lacking MDR1 had faulty mitochondria – parts of the cell often referred to as 'batteries'. These play a vital role in energy generation and cell health.

This mitochondrial dysfunction resulted in colitis – inflammation in the inner lining of the bowel that is a defining feature of IBD.

Scientists further implicated the role of mitochondria by linking IBD to a large number of genes involved in regulating these cell batteries. The researchers analysed genetic data from 90,000 people – 40,000 of whom had IBD.

The study also showed that a drug called Mitoquinone – which protects the mitochondria against toxins – can reduce colitis and promote bowel recovery in the mice lacking MDR1, which scientists say is a significant step forward.

Lead author Dr Gwo-Tzer Ho, Honorary Consultant Gastroenterologist at the University of Edinburgh's MRC Centre for Inflammation Research, said: "IBD has a serious impact on quality of life, with 6,000 new cases diagnosed per year in the UK. We have shown that MDR1 and mitochondrial function are important jigsaw pieces in the complex causes of IBD.

"Our studies highlight the importance of shielding the mitochondria from damage. This will open new approaches to drug targets that focus on the mitochondria to better design treatments for patients."

The research – carried out in collaboration with researchers at the University of Bristol and in the USA and Japan – was funded by the Medical Research Council and Crohn's and Colitis UK. It is published in the journal *Mucosal Immunology*.

For further information, please contact:
Kate McAllister, Press & PR Office, tel 0131 650 6357, email Kate.McAllister@ed.ac.uk