MedicalXpress

Protein controlling gut's protective force field identified

September 25 2014

Scientists have identified a protein in the human intestine that helps to protect against attack from opportunistic bacteria that strike when our defences are down. The protein receptor is activated during illness, producing a force field on the gut's surface made of a sugary substance that encourages the growth of protective bacteria.

Scientists deleted the IL-22RA1 gene that produces the receptor protein from the mouse genome. In the absence of this gene, which is associated with inflammatory bowel disease (IBD) in humans, the mice were found to be more susceptible to over-colonisation by harmful *Enterococcus faecalis* bacteria.

"The gut prevents over-colonisation by fuelling the growth of bacteria that will restore balance," explains Tu Anh Pham, first author from the Wellcome Trust Sanger Institute. "We confirmed this by treating the mouse models with the intestinal coating produced in wild-type mice and found that many of them regained their former equilibrium."

Investigating the mechanism further in the lab, researchers found that the protective force field works by inducing fucosylation, where a sugar-like substance is produced that coats the surface of the epithelial cells of the intestine, creating a healthy microbiota in which a whole host of protective bacteria will thrive.

Using organoids, an emerging research tool that enables scientists to grow small intestinal tissue clusters using cells from the original tissue

and stem cells, researchers were able to take a closer look at epithelial cells in which IL-22RA1 receptors were working correctly.

Researchers sequenced the organoid RNA, the molecules that regulate gene expression in these cells, to identify the series of pathways affected by the activation of the IL-22RA1 receptor. Many of the pathways identified have previously been linked to autoimmune diseases such as IBD. In addition, Fut2, the gene involved in the related process of fucolysation, has known links to Crohn's disease.

"In this research we've used the Sanger Institute's expertise in mouse genetics to look at the microbiota in the context of a whole system and in extraordinary detail on a cellular level using organoids," says Dr Trevor Lawley, senior author from the Sanger Institute. "Both perspectives are indispensable in our work to understand the complex interplay between the host and the unique mixture of bacteria each one of us harbours."

Now that researchers have a better understanding of the host's genetics, they can begin to identify the protective bacterial groups that proliferate when the IL-22RA1 receptor is activated. It is hoped that these bacterial species could be used therapeutically.

"We might, in the future, be able to harness what we know about this receptor and the bacteria it promotes to protect vulnerable patients," says Professor Arthur Kaser, Consultant Physician in the Department of Gastroenterology at Addenbrookes Hospital, Cambridge. "If we can replenish their microbiota and help them produce the correct environment in their gut, we will be able to give them the strength they need to battle infection."

Provided by Wellcome Trust Sanger Institute