Scottish Government Health Directorates Chief Scientist Office

CHIEF SCIENTIST OFFICE

FOCUS ON RESEARCH

Characterisation of genetic and epigenetic alterations in the VMP1/miR21 region in Crohn's disease – implications for pathogenesis and translation to clinical application (ETM/395)

Researchers
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Aim

Inflammatory bowel disease (IBD) is thought to be caused by a combination of environmental factors, such as diet and smoking, and mutations in genes.
We originally identified changes in methylation (which are chemical marks on the genes) at the VMP1/miR21locus in patients with IBD. In this project we set out to look at the VMP1 gene in more detail, to sequence it to look for new mutations in patients, to look at the methylation marks on the gene in patients and healthy people, and to see if we could use these methylation marks as a clinical tool to help identify people with IBD more quickly. VMP1 is involved in the way the cells recycle components (a process known as autophagy) and we investigated this using cultured cells in the laboratory. We also looked at whether we could identify people with IBD using only the methylation marks on a set of genes.

Project Outline/Methodology

We sequenced DNA from 300 individuals, people with IBD and healthy people to act as controls. This allowed us to examine the DNA sequence in a region around one end of the VMP1, we also looked at the methylation marks on the DNA in some of the same individuals. We obtained serum samples from the same people and measured the amounts of the VMP1 protein in the serum. We tried to see if the amounts of VMP1 protein was related to the amount of a small molecule known as miR21 in the serum as it was thought that miR21 may control the amount of VMP1 in a cell. Using cells grown in the lab we looked at whether this small molecule, miR21, could control the cell recycling process (autophagy).

Key Results

By sequencing part of the VMP1 gene in both patients with IBD and healthy people we showed that there were no new mutations in this gene and that therefore the gene is highly conserved. This may indicate that it is essential and that any new mutations in this region of this gene would be harmful.

Our most interesting finding was that by looking at methylation at a number of different genes in the cell we were able to distinguish between people with IBD and those without. Using as few as 2 or 3 methylation sites (places where we know there may be a chemical added to the gene) we could say with high accuracy who had IBD and who didn't. This could be very useful for doctors as sometimes it can be difficult to tell IBD from other intestinal problems without expensive and invasive tests.

Conclusions

IBD can be distinguished from other intestinal conditions by the chemical marks on DNA, this may lead to the development of a diagnostic test which could help clinicians come to a diagnosis.

What does this study add to the field?

It tells us that there is a particular chemical signature associated with IBD which we may be able to use to help diagnosis.
Identification of more of the genes involved in developing IBD may lead scientists to develop new targets for therapy.

Implications for Practice or Policy

It may be possible to develop the methylation differences as a test that clinicians could use.

Where to next?

Work will continue in the lab to confirm and extend these findings. We are currently looking at markers which will predict disease progression and allow targeted use of therapies to the patients where they will be most effective.

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