Scottish Government Health Directorates Chief Scientist Office

CHIEF SCIENTIST OFFICE

FOCUS ON RESEARCH

Investigation of vimentin as a regulator of NOD2 responsiveness to adherent-invasive E. coli in the pathogenesis of Crohn's disease (ETM/137)

Researchers
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Aim
We identified vimentin as a potentially important protein in the development of Crohn's disease (CD) and we wished to investigate it's role further. Our aim was to look at vimentin expression in healthy controls and CD patients and to investigate the importance of the interaction between vimentin and two more important CD protein, NOD2 and ATG16L1. When these proteins stop working properly it affects the way the cell recycles old components, a process known as autophagy, and this is thought to be part of the reason that CD starts.

Project Outline/Methodology
In previous work we identified vimentin as a protein that interacts with NOD2. We obtained blood and biopsy samples from patients attenting clinics at the Western General Hospital, and blood from healthy controls working at the hospital. We were able to look at the amounts of vimentin in the different cells using various standard lab techniques. We also developed a method for measuring vimentin in serum as commercially available kits were not suitable for our work. We used other standard lab techniques to look at recycling (autophagy) in these cells, to see if cells from patients had different levels of recycling from healthy controls.

Key Results
We have shown that levels of the vimentin protein are similar in the blood and from gut biopsies from both CD patients and healthy controls, so CD patients don't seem to have unusual amounts of vimentin. We did this using several different methods so that we could be sure of our results. We showed that vimentin did not appear to be expressed in specialised cells that express NOD2 (called Paneth cells). Using one method (immunohistochemistry) we couldn't see any NOD2 in cells other than the paneth cells, when we looked at samples from healthy people, but in CD patients we could see NOD2 in other cells. This could mean that the two proteins are not normally expressed together, but that they are in some patients and this could help cause CD.

We have shown that the three CD-associated proteins, vimentin, NOD2 and ATG16L1, form a complex together and this complex is altered in response to proteins that are contained in the cell walls of bacteria.

Lysosomes are "bubbles" in cells which move various components around the cell. We have shown that vimentin can affect the distribution of lysosymes in the cell. The presence of vimentin causes these bubbles to accumulate in certain places in the cell.

The levels of autophagy appear similar in controls and CD patients;

Conclusions
NOD2 appears to be differently expressed in some patients although levels of vimentin seem to be similar.

What does this study add to the field?
We have shown that the three proteins form a complex together and that therefore they probably all influence recycling in the cells, possibly contributing to the development of CD.

Implications for Practice or Policy
Possible new tests.

Where to next?
Further studies to confirm and extend findings.

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