

Lay Summary-David Qualtrough  
*The role of Fascin in IBD-related cancer risk*

Background

Both ulcerative colitis (UC) and Crohn's colitis patients have an increased risk of developing colorectal cancer (CRC), the second biggest cancer killer in the United Kingdom, in fact 15% of all deaths in patients with inflammatory bowel disease (IBD) are attributed to CRC. The risk of cancer in IBD increases with early age of diagnosis, longer duration of symptoms, and the severity of inflammation and dysplasia.

The precise mechanism by which long-term inflammation of the intestinal epithelium (lining) leads to cancer is poorly understood. Dysplasia of the gut epithelium is common in patients with longstanding IBD and is thought to be a pre-malignant condition. The factors governing whether this abnormal growth progresses to form a tumour are unclear, and this highlights the need for predictive markers for malignant progression in the clinical management of IBD.

We have been studying the role of the Fascin protein in the initiation and development of sporadic and familial colorectal cancers. Fascin is not expressed in the normal colorectal epithelium, but is highly expressed in cancer. Laboratory studies using cultured cells have shown that Fascin is able to promote cell growth, decrease normal cell-cell contacts, and promote cell motility and invasion. Each of these cellular processes is altered in the transformation of a normal cell into a cancer cell and allows the cancer to invade surrounding tissues and spread throughout the body to form secondary tumours (metastases). These data suggest that expression of Fascin promotes progression to malignancy in colorectal tumours.

Hypothesis

The expression of Fascin could act as a predictive marker for the progression of IBD-associated dysplasia to cancer.

Aims

We propose to undertake a pilot study to determine whether Fascin is expressed in IBD and also IBD-associated dysplasia and cancers. We will determine the distribution of Fascin in representative tissue samples and find the point during the progression of non-dysplastic IBD through dysplasia to cancer, at which Fascin expression is switched on. This will allow us to show whether Fascin expression could be used as a predictive marker in the progression of IBD to cancer allowing earlier identification of patients at high risk of developing malignant disease. The results of this study will lead us to move on to the longer term aim of dissecting the mechanisms which regulate Fascin expression in IBD, and how this is influenced by current anti-inflammatory therapeutic strategies.

Methodology

We will use well-established immunohistochemical techniques, protocols and antisera to determine the expression of Fascin in resected tissue from patients with IBD and IBD-related cancer with appropriate controls.

Ethical approval for this study has already been obtained.