

Uncovering the evolutionary history of IBD-associated colorectal cancer

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A team of researchers from Queen Mary University of London have reported the genetic events involved in the early development of bowel cancer in patients with inflammatory bowel disease (IBD).

Such knowledge may be able to be exploited to design simple diagnostic tests to stratify patients with IBD at high risk of developing cancer.

IBD more than doubles an individual's lifetime risk of developing [bowel cancer](#), and the risk increases significantly if they have suffered with IBD for a sustained period of time. With this in mind, the study published in Gut performed in collaboration with researchers from St Mark's Hospital and the University of Oxford set out to understand the genetics of how colorectal cancer develops in people with IBD.

Lead researcher Professor Trevor Graham from Barts Cancer Institute at Queen Mary said: "Predicting who with IBD is going to go on to develop [bowel cancer](#) is a big unmet need. If we could do it accurately, it would allow us to target care to those who need it most, and spare low-risk individuals unnecessary worry. Here we have determined which genetic mutations tend to occur early in IBD-associated bowel cancer development. These mutations could form the basis of a simple diagnostic test for predicting who is at high risk."

Establishing a sequence of genetic events

The team looked at the genetic sequences of cancerous and non-cancerous tissue samples collected from patients with IBD-associated colorectal cancer. By comparing the sequences, the researchers were able to establish a timeline of events leading to the development of malignancy.

Notably, the analysis identified some genetic alterations that tended to occur early in the progression to cancer, such as changes to the 'tumour suppressor' protein known as p53. Changes to p53 that result in the alteration or loss of its function usually occur later in the development of bowel cancers that are not associated with IBD, highlighting some genetic differences between [colorectal cancer](#) cases that have developed from IBD and those that have not.

Changes in the number of copies of some chromosomes- the structures that carry our genetic information in the form of genes- were also common in the large majority of IBD-associated bowel cancer samples and accumulated early in their evolutionary timeline.

The team hope that spotting these early genetic changes could be used as indicators to identify which patients with IBD are at immediate risk of bowel cancer, prompting close surveillance of the patient and permitting timely interception with the best treatment options. On the other hand, IBD sufferers not at risk of cancer development could be spared unnecessary worry.

Future directions

First author Dr. Annie Baker from Barts Cancer Institute at Queen Mary said: "In this exciting research we studied how IBD-associated bowel [cancer](#) develops over time, identifying crucial genetic changes that occur either prior to or at the onset of malignancy. Our findings have provided a strong foundation for future work, which will focus on how we can use

this knowledge to improve how doctors assess, monitor and treat IBD [patients](#) in the clinic."

Provided by Queen Mary, University of London

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