'Chromosomal catastrophes' in colorectal cancer

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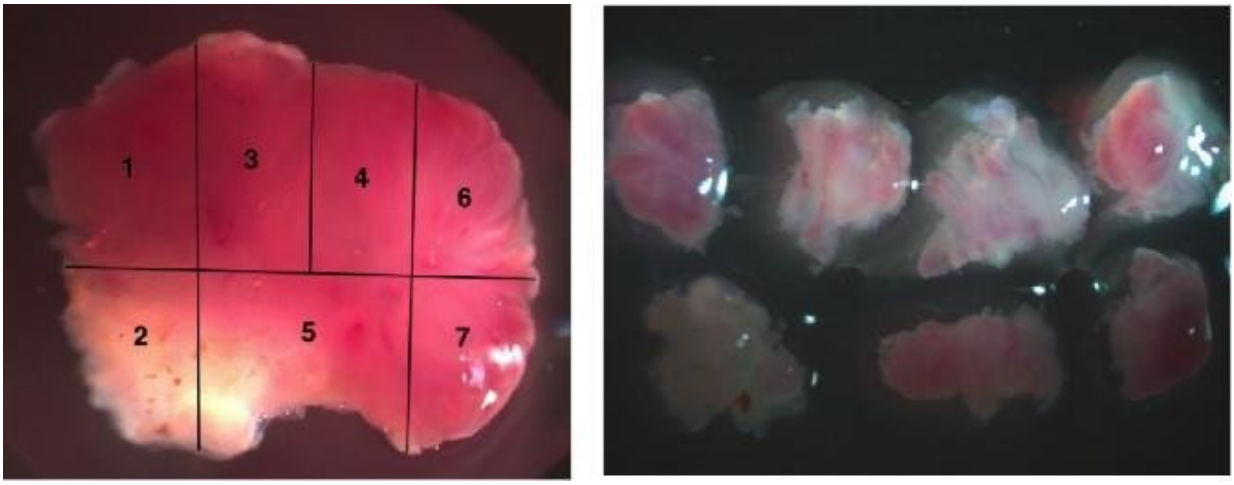


Credit: Queen Mary University of London

"Chromosomal catastrophes" have been found to occur along the evolutionary timeline of colorectal cancer development, according to new research led by Queen Mary University of London.

The findings are published in *Nature Ecology & Evolution*.

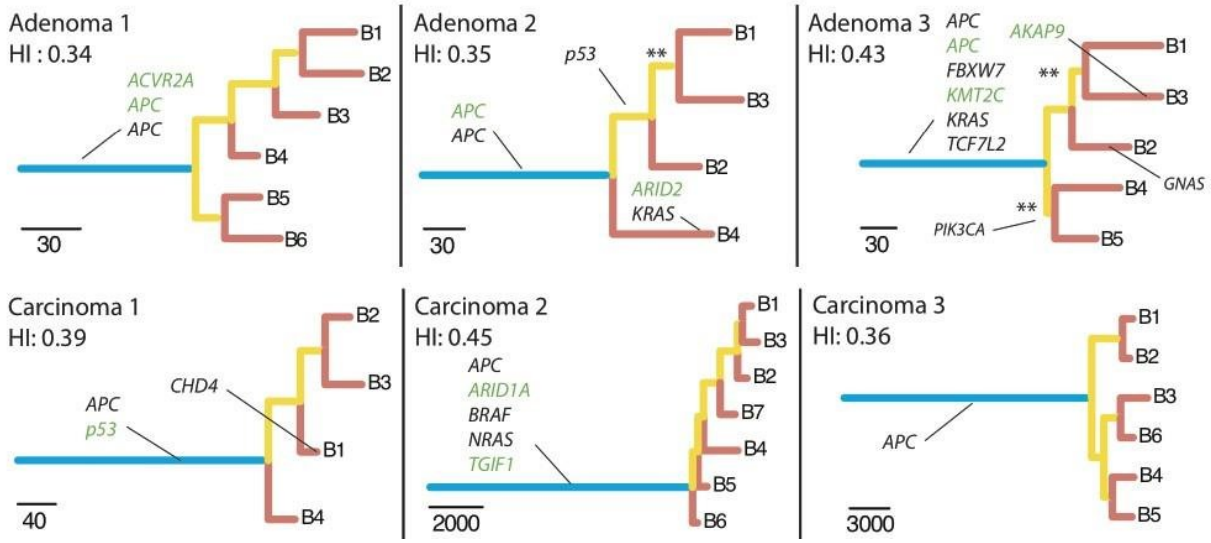
Lead author Dr. William Cross from Queen Mary University of London said: "Our results change the way in which we understand how bowel cancers develop. Although the classical model of colorectal cancer development appears correct in some cases, our results suggest that we

need to rethink certain aspects of it."

Prof Trevor Graham from Queen Mary University of London said: "Bowel cancer is one of the most common cancers in the UK. Our study gives more insight into how bowel cancer develops, and provides a foundation that we can build upon to develop tools to predict who is at risk of developing the disease."

As tumours grow, different cells acquire various genetic changes that allow them to adapt to their environment. The cells that acquire changes that confer the best chance of survival and growth within the environment are favoured, and so increase in number. This is the basis of cancer evolution. In this way, numerous populations of cells with different genetic codes build up, creating tumours that are highly genetically diverse or heterogeneous.

Understanding how cancers develop and change over time is a big challenge. For obvious reasons, scientists can't simply sit and watch a cancer growing in a person. The researchers from Queen Mary's Barts Cancer Institute were part of a collaborative team that set out to identify when particular genetic changes arise during bowel cancer development.



Credit: Queen Mary University of London

By comparing the genetics of benign and cancerous bowel tumours, the international team—led by Prof Trevor Graham (Queen Mary University of London) and Prof Ian Tomlinson (University of Oxford and the University of Birmingham) - revealed that the benign growths were more heterogeneous than the cancerous tumours.

In addition, the team identified some other striking differences between the genetic makeups of the two tumour types. Unlike the benign samples, the cancerous tumours appeared to have largely rearranged chromosomes (structures that carry our genetic information in the form of genes), with sections of the genetic code being lost or gained.

Using mathematical modelling, the researchers were able to determine when these rearrngements occurred in the timeline of cancer development. Surprisingly, they found that the majority of the genetic alterations occurred very close together in time, possibly even in a single incident referred to by the researchers as a 'chromosomal catastrophe." This event appeared to be associated with the transition from benign to cancerous tumours.

On the National Health Service, bowel cancer screening is offered to individuals aged 55 and over. When pre-cancerous growths are found within the bowel, they are removed during endoscopy; however a risk of cancer development still exists in some cases. Currently, there is no way of determining which individuals are likely to develop cancer in the future.

With a growing understanding of the genetic events that result in the evolution of malignancy, the team hypothesise that by examining the pre-cancerous tissue removed from a patient, it may be possible to identify genetic features associated with the progression towards cancer. Patients at high risk of developing cancer can then be monitored accordingly.

The research, supported by Cancer Research UK, The Wellcome Trust, Bowel and Cancer Research, NIHR Oxford Biomedical Research Centre, and other funders, has provided insights into the evolutionary timeline of cancer progression and the team hope that the findings may aid in the identification of individuals at high risk of developing cancer.

To build upon the findings of the current research, the team endeavour to identify the cause of the chromosomal catastrophes. Knowing the cause of these vast genetic rearrangements may provide a means of predicting cancer risk and, if this event could be prevented, may provide an avenue that could be exploited for the development of novel cancer therapies.

More information: The evolutionary landscape of colorectal tumorigenesis, *Nature Ecology & Evolution* (2018). DOI: 10.1038/s41559-018-0642-z

Provided by Queen Mary, University of London