Rare genetic faults identified in families with bowel cancer

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(Medical Xpress)—Rare DNA faults in two genes have been strongly linked to bowel cancer by Oxford University researchers, who sequenced the genomes of people from families with a strong history of developing the disease.

The researchers sequenced the entire DNA genomes of 20 people from families with a strong history of bowel cancer. Eight of the 20 people had developed bowel cancer, while the rest had a first-degree relative who had developed the disease. The findings are published in the journal *Nature Genetics*.

They found that everyone who had a faulty POLE or POLD1 gene developed bowel cancer or had a precancerous growth in the bowel.

To confirm their findings they then looked for faults in these two genes in almost 4,000 people with bowel cancer, and 6,700 people without the disease.

Neither of the genetic faults was found in people without bowel cancer. However, 12 people with a fault in the POLE gene were found in the bowel cancer group, and one person had a POLD1 gene fault.

The POLD1 fault was also found to increase the risk of getting womb cancer and possibly brain cancer, with seven people in the study being diagnosed with womb cancer and one developing two brain tumours.

Professor Ian Tomlinson, who led the research at the Wellcome Trust Centre for Human Genetics at Oxford University, said: 'These are two rare faults, but if you inherit them your chance of bowel cancer is high. By testing people with a strong family history of the disease for these, we can identify those who are at high risk and try to prevent the disease by using colonoscopy and other methods.'

POLE and POLD1 are genes involved in processes that repair damage to DNA. Without these genes functioning properly, affected individuals can build up damage in their DNA which accumulates and it is thought this may lead to changes that cause bowel cancer.

'This research highlights how much more we still have to find out about the rare gene faults that can increase a person's risk of bowel cancer,' said Dr Julie Sharp, senior science information manager at Cancer Research UK, which part-funded the work.

More information: Palles, C et al Germline mutations in the proof-reading domains of POLE and POLD1 predispose to colorectal adenomas and carcinomas, *Nature Genetics* (2012)

Provided by Oxford University