Researchers identify variations in four genes associated with an increased risk of colorectal cancer

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An international research team co-led by cancer prevention researcher Ulrike "Riki" Peters, Ph.D., M.P.H., and biostatistician Hsu Li, Ph.D., at Fred Hutchinson Cancer Research Center has identified variations in four genes that are linked to an increased risk of colorectal cancer. Peters and colleagues from 40 institutes throughout the world published their findings online ahead of the April print issue of *Gastroenterology*.

Peters and colleagues for the past four years have been studying the genes linked to colorectal cancer through the Genetics and Epidemiology of Colorectal Cancer Consortium, a collaboration involving researchers from North America, Australia and Europe who have pooled data from approximately 40,000 study participants, about half of whom have colorectal cancer. Fred Hutch houses GECCO's coordinating center and Peters is its principal investigator.

The genomewide-association study was conducted in two phases. The first involved rapidly scanning complete sets of blood DNA from 12,696 people with colorectal cancer or a precancerous condition called adenoma. This data was then compared to the same set of variants from 15,113 healthy controls of European descent.

Of 2.7 million genetic variants identified, the 10 most statistically significant mutations associated with colorectal cancer were then further analyzed in a follow-up genomewide-association study of 3,056 colorectal cancers or adenomas and colon-tissue samples from 6,658 healthy controls of European and Asian descent.

The research team uncovered mutations in the following genes – all genetic variants that previously had not been associated with colorectal cancer:

- NABP – a gene involved in DNA repair
- LAMC1 – the second gene in the laminin gene family found to be associated with colorectal cancer
- CCND2 – a gene involved in cell-cycle control, which is a key control mechanism to prevent cancer development
- TBX3 – a gene transcription factor that targets a known colorectal cancer pathway

If a person carries one or two copies of any of these genetic variants, their risk of colorectal cancer is increased by 10 percent to 40 percent compared to a person who does not harbor such DNA genetic variants, Peters said.

"These findings could potentially lead to new drug targets and, in combination with previously identified genetic and environmental risk factors, identify subgroups of the population that can benefit most from colorectal-cancer screening and could be targeted for early or more frequent endoscopy, a very effective screening tool for colorectal cancer," said Peters, a member of the Public Health Sciences Division at Fred Hutch.

More information: "Identification of Genetic Susceptibility Loci for Colorectal Tumors in a Genome-wide Meta-analysis," *Gastroenterology*, 2013.

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