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COLORECTAL CANCER

Fusobacterium nucleatum found in colon cancer tissue—could an infection cause colorectal cancer?

Two new studies published in *Genome Research* have made tentative steps towards establishing an infectious cause of colorectal cancer (CRC) by finding the periodontal pathogen *Fusobacterium nucleatum* in colon cancer tissue.

Around 18% of cancers worldwide are attributable to a known infectious agent—the unequivocal link between *Helicobacter pylori* and gastric cancer being a prime example. Given the huge numbers of micro-organisms in the colon, investigating the potential infectious agents that cause CRC seems reasonable.

In the first study, Matthew Meyerson and co-workers used next-generation, whole-genome sequencing to characterize the composition of the microbiota of CRC tumors. DNA sequences of *Fusobacterium* species were enriched in CRC tumors compared with control samples; nine CRC samples were initially studied, with an additional 95 CRC tumor samples analyzed to verify results. A number of *Fusobacterium* spp. sequences were discovered in the CRC tumors, with *F. nucleatum* being the most dominant phylotype identified. Finally, using fluorescence *in situ* hybridization, *Fusobacterium* could be detected in histological sections of CRC tumors.

Using a similar genomic approach, Robert Holt and colleagues used shotgun sequencing to mine CRC tumor and control tissue samples for microbial RNA sequences. *F. nucleatum* sequences were over-represented in CRC tumor samples, in both the initial 11 samples analyzed and in the additional 88 specimens tested, and overabundance of *F. nucleatum* sequences in CRC tumors was positively associated with lymph node metastasis. In addition, the researchers cultured an *F. nucleatum* isolate directly from a CRC tumor sample, which *in vitro* studies confirmed to be invasive in human colonic epithelial cells.

"The presence of a specific microbe with a strong preference for tumors was surprising," notes Holt, and both research teams acknowledge that much work is needed to confirm whether *F. nucleatum* truly has a causative role in CRC etiology. "We don't know yet if *Fusobacterium* infection is causing colon cancer, is a consequence of colon cancer, or something in between," warns Meyerson. However, if the causative link is proven, antibiotics and/or vaccines could be future treatment or prevention strategies to combat any infections that might cause CRC.

Katrina Ray

Original articles Kostic, A. *et al.* Genomic analysis identifies association of *Fusobacterium* with colorectal carcinoma. *Genome Res.* doi:10.1101/gr.126573.111 | Castellarin, M. *et al. Fusobacterium nucleatum* infection is prevalent in human colorectal carcinoma. *Genome Res.* doi:10.101101/gr.126516.111

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