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Commentary

Faecal microbiota transplantation, a promising way to treat colorectal cancer

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Colorectal cancer is the fourth most common morbidity worldwide and the second most common among women [1]. This disease is caused by both genetic and environmental factors, such as high-fat diet and disrupted gut microbiota [2]. Despite great advances in cancer treatment options, drug resistance and insensitivity to treatment in patients with colorectal cancer necessitate the development of effective therapeutic alternatives. In addition, an increasing number of studies have shown that the gut microbiota plays a key role in the incidence and progression of colorectal cancer.

In *EBioMedicine*, Li and colleagues [3] showed that faecal microbiota transplantation (FMT) with faeces of patients with colorectal cancer accelerates the progression of adenoma to adenocarcinoma could cause chronic inflammation and disturb the ecological balance of the mice's gut microbiota. This study is of great importance because, although a previous study [4] showed that gavage of faecal samples from patients with colorectal cancer promoted the intestinal carcinogenesis in both germ-free and control mice, the effect of gut microbiota on $Apc^{min/+}$ mice had not been investigated. Furthermore, given the fact that adenomas with epithelial dysplasia are often considered as a benign precursor of neoplasms [5], it is necessary to explore the factors influencing the progression of adenoma to adenocarcinoma.

The gut microbiota can digest complex dietary residues that are resistant to digestion by enteric enzymes. This process can not only provide energy for the microbiota but also result in the release of short-chain fatty acids (SCFAs), including butyrate, which could be used for metabolic needs by the colonocytes, maintain mucosal integrity, and suppress inflammation and carcinogenesis [6]. Analysing the faecal supernatant of patients with colorectal cancer, Li and colleagues [3] found that the relative abundance of *Roseburia* spp and *Clostridium* spp was lower than that in the faecal supernatant of healthy patients, consistent with Wang and colleagues' findings [7], whereas the relative abundance of *Akkermansia* spp and *Ruminococcus* spp was higher, consistent with Weir and colleagues' results [8]. Similarly, the number of pathogenic bacteria increased after FMT, whereas the number of bacteria secreting SCFAs (such as *Ruminococcus* spp, *Roseburia* spp, and *Clostridium* cluster XlVa spp) and the production of SCFAs in the caecum decreased, which could be one of the reasons for the destruction of intestinal mucosal barrier and the occurrence of chronic inflammation in $Apc^{min/+}$ mice after transplantation.

To further understand the molecular mechanisms induced by FMT, Li and colleagues [3] conducted further tests and showed that the gut microbiota from patients with colorectal cancer could activate the Wnt signaling pathway. This pathway is classified into canonical (β-catenin dependent) and non-canonical (β-catenin independent) [9]. Consistent with Li and colleagues' results [3], Jiang and colleagues [10] also showed that the canonical Wnt pathway played an essential role in different stages of tumour development.

The study from Li and colleagues provides direct evidence that gut microbiota from patients with colorectal cancer can increase tumour proliferation, which is of great relevance and far-reaching influence for future studies of colorectal cancer. However, outstanding questions require further investigations. For example, the gut microbiota from the faeces of patients with colorectal cancer could be further sub-classified and analysed to assess the role played by each microbial strain and its metabolites in promoting the progression of adenoma to adenocarcinoma. From a clinical point of view, although the translational from *in vitro* testing to clinical use may take some time, Li and colleagues' finding

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[3] suggest that targeted treatment of the gut microbiota could be a promising strategy for patients with colorectal cancer.

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