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Commentary

Novel Method for Screening Colorectal Neoplasm

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Colorectal cancer (CRC) is one of the leading causes of cancer death worldwide with the majority of cases having no previous family history. The most effective way to reduce mortality is to detect precancerous adenoma in an early stage. Several screening methods are now available; however as each modality has its limitation there is no superb strategy so far to conquer cancer death with colorectal cancer (Winawer et al., 1997). Fecal occult blood testing (FOBT) is the most widely employed screening tools, but sensitivity varies from 30% to 90% and depends on whether the specimens are rehydrated or not. The value of colonoscopy in screening can be appreciated, but it is costly and invasive. Moreover its effectiveness also depends on the endoscopist's skill. Computed tomographic colonoscopy (CTC) may another modality and rapidly evolving, but there are no controlled trials of screening CTC (Johnson et al., 2008). The risk of cumulative radiation exposure is also unknown. A special adaptation of capsule endoscopy has been developed to obtain images of the colon using tiny video cameras embedded in the two ends of an ingested capsule; however several studies have found a relatively low sensitivity for polyp detection (Rokkas et al., 2010). Current serum markers are not sufficiently sensitive or specific to be used for screening.

The advent of 16S rRNA-based analyses has allowed investigation of the human colonic microbiota at the level of phylotypes and bacterial species (Shen et al., 2010). The rationale of this method applying for the colorectal cancer screening is intriguing. In the colon, trillions of commensal bacteria, termed the microbiota, are in close proximity to a single layer of epithelial cells. Evidence from animal and human studies suggests that intestinal commensal bacteria are not innocent bystanders but rather active participants in health. They contribute to the regulation of cell proliferation, differentiation and gene expression in host epithelial cells (Sanapareddy et al., 2012).

Goedert et al. reported a very interesting research to address a new way of screening colorectal neoplasm (Goedert et al., 2015). They have created a cancer screening project in Shanghai area with combined methods of fecal immunohistochemical test (FIT), colonofiber and microbiota analysis. After informed consent was provided by 95 consecutive FIT positive patients, 61 patients had successful fecal microbiota profiling and colonoscopy. They confirmed 24 completely normal patients, 20 colorectal adenoma (CRA), 2 colorectal carcinoma and 15 with other conditions. Through the meticulous statistical analysis, they found that most of the compositional difference between CRA and normals reflected relative abundance of *Proteobacteria* taxa ($p = 0.04$) and, to a lesser extent, rare candidate division TM7 taxa ($p = 0.04$). Median relative abundance of *Proteobacteria* taxa was 3-fold higher in CRA than in normals ($p = 0.03$). They developed and applied a rank-based distance metric to quantify and test for differences in composition (beta diversity). This method originated with the Wilcoxon rank-sum test, with which CRA associations were observed across most of 18 detected phyla. They suggest that this method is feasible and effective.

Recently, many efforts have been made to unveil the contribution of intestinal microbiota to gut diseases, employing culture-independent techniques (Goedert et al., 2015; McCoy et al., 2013). In contrast to gastric cancer, where just one bacteria (*Helicobacter pylori*) has been associated as to the disease, no single bacterial species has been identified as a risk factor for CRC. But current studies accumulate many interesting data from Bench to Bedside in terms of microbiota contribution to colorectal neoplasm (Dennis et al., 2013).

In general, the cancer screening test needs several important points. It must be convenient to patients, and have good sensitivity and specificity with relative low cost. In terms of cost, such new technique as 16S rRNA-based analyses is still expensive. Therefore researchers have to take the balance between patient's welfare and national economy. Less expensive analyses such as fecal pH or organic acids including short chain fatty acid (SCFA) may become a candidate of screening for colorectal cancer (Ohigashi et al., 2013). Changes of these factors affect microbial community, and promote carcinogenesis either directly or indirectly.

While the causes of colorectal cancer are not fully known, it is becoming increasingly clear that the gut microbiota provide an important contribution (Arthur et al., 2012). To identify the composition of bacterial communities in the colon is an important step in our understanding of their role in the large bowel cancer and development of effective prognostic, preventative or therapeutic strategies. In more diverse populations fecal microbiota analysis might be employed to improve for colorectal adenoma and ultimately reduce mortality from CRC.

Disclosure

The author declared no conflicts of interest.

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