Colorectal cancer is the third leading cause of cancer death in the United States and the third most common malignant neoplasm worldwide [1]. Tumorigenesis of colorectal cancer proceeds through a series of genetic alteration including oncogenes such as ras and tumor suppressor genes such as p53 [2]. Colorectal cancer mortality can be drastically reduced by early detection. The common screening tests involve invasive endoscopy examinations, imaging examinations and stool tests [3]. Stool DNA detection represents a promising, non-invasive approach for detecting colorectal cancers in average-risk populations. The method was first proposed in 1991 by Dr. Bert Vogelstein, and the feasibility was proven the next year when his group found the K-ras mutations in the stool of colorectal cancer patients [4]. The commercial diagnostic test using the ras mutations finally reached market in 2003 [5]. In 2004, a group led by Dr. Martin Widschwendter, showed the methylation of a single gene in stool DNA could identify colorectal cancer patients with high sensitivity and specificity [6]. This discovery boosted stool DNA testing for colorectal cancer detection because only around 10% of colorectal cancer are characterized by genetic alterations, but epigenetic mechanisms, such as DNA methylation, occur in most cases [7]. Oncostatin M receptor-β (OSMR), silenced by promoter methylation in colorectal cancer cell lines, is one of the genes frequently methylated in colorectal cancer tissues, but not in normal tissues, and is detectable in stool DNA. Combining with other methylated markers in stool DNA can improve the sensitivity on colorectal cancer screening. Detection and quantification of OSMR promoter methylation in stool DNA is a highly specific diagnostic test for colorectal cancer [8]. Aberrant hypermethylation of DNA can also be detected in the serum of colorectal cancer patients. The methylation of helicase-like transcription factor (HLTF), a potential serum DNA methylation marker, was found to be closely correlated with tumor size and metastatic stage [9]. A recent study showed that the HLTF serum methylation is also associated with an increased risk of disease recurrence, thus it may serve as a predictor of disease recurrence in colorectal cancer [10]. No DNA diagnostic test has yet been widely used for cancer, but these new discoveries may move the field closer to that goal.

Reference


