

The Screening Value of MicroRNAs in Colorectal Cancer

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Colorectal cancer is the third most common cancer in men and the second in women; is the second leading cause of death related to the tumoral disease [1, 2]. Early detection of colorectal cancer may lead to a decrease of incidence and mortality, being especially important screening methods in this neoplasia, where symptoms are associated with advanced stages of the disease. Thus, the main goal of colorectal cancer screening is to identify the disease conditions early, when it is easier to treat the tumor. Similarly, monitoring patients who have had colorectal cancer aims to study those patients with a higher risk recurrence.

Both lack of sensitivity and specificity in early stages of colorectal cancer, limited the systematic use of most tumor markers asymptomatic patients. However, it also relies on the assessment of certain tumor markers, quantified in both tumor tissue and peripheral blood [3, 4]. Despite many tumor markers

have been studied in colorectal cancer, only few of them are recommended. The oncological guidelines accept and recommend: 1) The study of fecal occult blood for early diagnosis in people over 50 years. 2) Postoperative CEA levels if the patient is a potential candidate for surgery or chemotherapy of metastatic disease. 3) Microsatellite instability, (MLH1, MSH2, MSH6, PMS2) to identify hereditary nonpolyposis colorectal cancer. 4) The mutation of APC in the diagnosis of FAP [4, 5].

MicroRNAs are short 18–22 nucleotide non-coding RNA sequences that have post-transcriptional activity through binding mRNA; they are involved in regulating gene expression (apoptosis, cell proliferation and differentiation) and have been demonstrated to act as tumour suppressor genes or proto-oncogenes [6]. The recent discovery of the involvement of microRNAs in regulating gene expression through influencing the stability of RNA and the development and progression of tumours has inspired several investigators to evaluate these “antisense molecules” in different body fluids (plasma, serum, stool, urine, tears and saliva).

Fecal markers

Various studies have been focused in the determination of fecal DNA values, quantifying different stool microRNAs. Link et al. found the overexpression of miR-21 and miR-106a in both colorectal neoplastic lesions and adenomas [7]. Kalimutho et al. analysed the promoter hypermethylation of miR-34b/c in

faeces, and they showed that up to 75% of colorectal cancer patients showed hypermethylation of its promoter that correlated with tumor stage, which led them to propose the identification of aberrant methylation in stool as a diagnostic marker [8].

The fecal overexpression of several microRNAs have been determined in colorectal cancer: miR-20a, miR-21, miR-92, miR-96, miR-106a, miR-203 and miR-326 while other microRNAs were underexpressed: miR-16, miR-125b, miR-126, miR-143, miR-144, miR-145, miR-320 and miR-484-5p [9]. Koga et al. Determined a sensitivity of 70% and 46%, and a specificity of 81% y 95% for miR-17-92 and miR-135, respectively [10].

Histological markers

Since Michael et al. Demonstrated a lower expression of miR-143 and miR-145 in colorectal cancer, various studies focused in searching the different microRNAs expression in colorectal cancer.

The overexpression of several microRNAs have been determined in colorectal cancer: miR-15b, miR-17-5p, miR-19a, miR-20, miR-21, miR-29a, miR-31, miR-92, miR-96, miR-135b, miR-148a, miR-181b, miR-182, miR-183, miR-191, miR-200b, miR-200c y miR-212. While other microRNAs were underexpressed: miR-1, miR-9-1, miR-30a-3p, miR-30a-5p, miR-30c, miR-34a, miR-34b, miR-34c, miR-126, miR-129, miR-133a, miR-133b, miR-137, miR-139, miR-143, miR-145, miR-195, miR-342, miR-422a, miR-422b y let-7a-1 [11,12].

Peripheral blood markers

The presence in serum of several microRNAs in different neoplastic diseases has been determined. MicroRNA expression patterns have been compared between tumors in different locations, suggesting the existence of a common microRNA profile in neoplastic disease. Therefore, circulating microRNAs could be used to predict disease progression, but it is still necessary to determine whether the presence of

microRNAs in peripheral blood can determine diagnosis, prognosis, or both. Although several microRNAs have been determined in plasma, microRNAs with high concentrations in colorectal cancer patients are miR-29a, miR-95, miR-135b, miR-221, miR-222 and miR-141; complementary to the CEA test, increased levels of miR-141 have also been associated with liver metastases in patients with colorectal cancer [9,13-18].

There are multiple challenges in the development and implementation of microRNA blood tests as a diagnostic marker of colorectal cancer. Despite the challenges ahead, there are encouraging results in that microRNAs have potential as diagnostic markers for colorectal cancer and other malignancies. Although additional clinical studies are required to substantiate the relationship between microRNAs and colorectal cancer, there is preliminary evidence that microRNAs are related to the diagnosis and prognosis of colorectal cancer. Additionally, it is worthwhile to investigate how microRNAs can most appropriately be used for greater precision in the screening, diagnosis and prognosis of colorectal cancer.

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