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Research Protocol

Fecal MicroRNA's: A Promising Tool for Colorectal Cancer Screening

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Abstract

Introduction: Screening guidelines for the prevention and early detection of colo-rectal cancer (CRC) have evolved with a significant decrease in the prevalence and mortality in CRC. In the Western countries < 65% of the eligible population is up-to-date with screening, while nearly 28% has never been screened.

Aims and Methods: MicroRNAs (miRNAs) are short, endogenous, noncoding RNAs that regulate gene expression affecting various processes including angiogenesis and metastasis. There has been great interest in looking at the expression of various miRNAs for detection of CRC. Our preliminary study to detect aberrantly expressed miRNA in stools was conducted in the past two years and 48 patients were taken into consideration: 20 CRC and 28 advanced adenomas (AD). Mi-RNA test in stools (Quiagen tests) was performed in all 48 patients and compared to a control group of 20 patients. Patients with CRC had a significantly higher stool miR-21 level ($p < 0.01$) and miR-92a level ($p < 0.0001$) compared to controls.

Results: Mi-RNA test showed a 73% sensitivity (14 patients) in CRC and 58% (16 patients) in AD. 79% and 75% specificity was observed for CRC and AD.

Conclusion: While colonoscopy is still the dominant screening test, there is considerable interest in the development of accurate noninvasive screening markers with notable improvements in stool-based tests and mi RNA in particular which provides viable non-invasive options for average risk persons. Mi RNA would offer advantages over colonoscopy, including ease of completion, low cost, and low risk. Ongoing research of miRNA will quantify its uptake, adherence, cost-effectiveness, and appropriateness of the testing interval.

Keywords: *Fecal MicroRNA's; Colorectal Cancer Screening; Colonoscopy; Colo-Rectal Cancer (CRC)*

Introduction

Genes expressions in human body are regulated by Mi-Rna's which appears like a long set of nucletides (22^{nt}).

SY Lee and K Kang discovered in 1993 that Micro Rna are copious in plants as well as in animals [1-5].

Micro Rna's are genes able to regulate target mRNA by binding complementary sequences in the 'so called' 3' UTRs (untraslated regions). They are a new class of gene regulators controlling and biding partially complementary sequences in 3'untranslated regions (UTRs) in target mRNAs.

Micro RNAs can regulate several processes by overregulating or inhibiting target genes. Various studies indicates that the genome in human subjects may contain up to 1000 miRNAs.

Several studies have demonstrated that miRNAs genes, which have been calculated in around 3 - 5% of the whole workforce of genetic material, are able to regulate essential biological processes such cell proliferation, apoptosis, stress resistance and, above all, neoplastic growth.

Micro RNAs, well regulated during growth of normal tissues are misregulated in tumors.

They may determine tumour suppression in normal tissue and cell overgrowth in cancer.

Several studies have demonstrated that:

- Micro RNAs are misregulated in almost all human tumors
- MicroRNAs work as tumour suppressor genes or as oncogenes if misregulated
- Micro RNAs have a cell specificity
- Micro RNAs have great resistance to RNAase degradation and appear as valuable molecular markers.

Medical literature show a clear interference of Micro Rna in carcinogenesis and neoplastic growth in CRC. Micro RNAs have been indicated as good markers for early diagnosis of CRC as well as treatment and recurrence of the specific pathology.

In colorectal cancer a link between miRNAs altered funtions and carcinogenesis has been demonstrated. A reduction of prevalence and mortality of CRC are the results of better screening guidelines in the detection of the disease. Nearly 65% of the general population has been totally or partially screened in the developped countries versus 35% of total lack of screening.

Following the guidelines recently presented by several gastroenterological association early detection and prevention of colorectal cancer may significantly decrease the prevalence and the mortality of this pathology.

In Europe and the USA screening tests for CRC are performed in more than 65% of the population. A value between 28 and 35% of the population has never been screened according to the statistics of different countries.

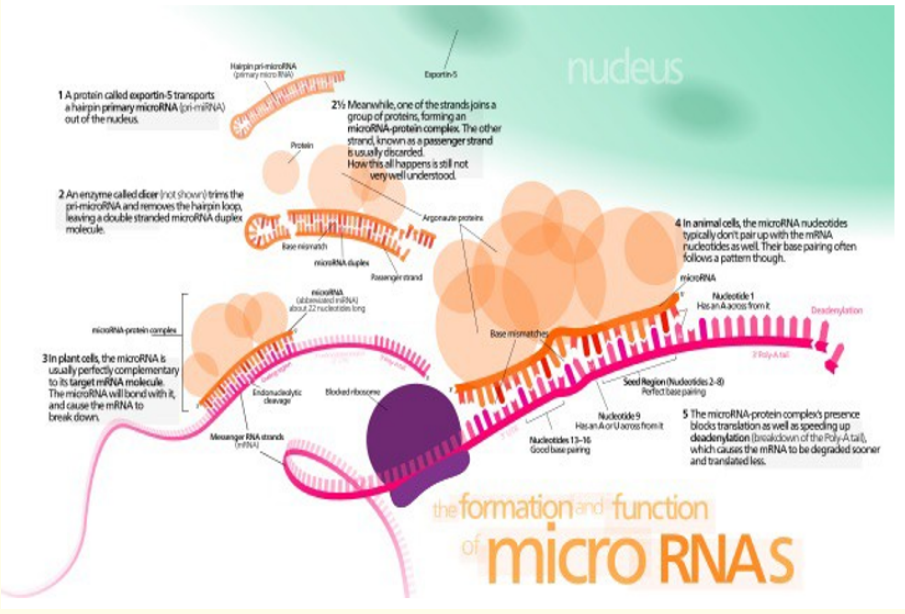

Figure 1:*Formation of MiRna.*

Methods

Angiogenesis and metastatic disease in CRC are regulated by gene expression controlled by MicroRNAs. Recently interaction between MicraRNAs and detection of CRC has become a subject of great interest. Our preliminary study to detect aberrantly expressed miRNA in stools was conducted in the past two years.

48 patients were taken into consideration.

20 CRC and 28 advanced adenomas (AD).

48 patients were submitted to MiRna test in sample stools (Quigen tests) and compared to a control group of 20 patients.

Molecular markers in stool samples are a potential strategy for colorectal cancer (CRC) screening.

Mi-RNA levels in CRC tissues and stool samples were detected by PCR (quantitative reverse transcription).

Noncoding RNAs (ncRNAs) are small 22nt filament of RNA which are able to control gene expression determining several, different processes that include metastasis formation and angiogenesis. An intensive interest by the scientific community has been placed in the detection of CRC through various miRNA expressions. Following the interest in this new tool (aberrant mi RNA) as an instrument to determine CRC and AD in aberrant mi RNA in stools, we selected 48 patients (20 CRC and 28 AD) to be tested. All 48 patients were tested for aberrant miRNA using Quigen test and compared with a group of 20 normal patients considered as a control group. In our study Levels of miRNA 21 and miRna 92 were significantly higher than in the control group ($p < 0.01$).

Results

In our studies patients with CRC had a significantly higher stool miR-21 level ($p < 0.01$) and miR-92a level ($p < 0.01$) compared to controls. Mi-RNA test showed a 73% sensitivity (14 patients) in CRC and 58% (16 patients) in AD.

79% and 75% specificity was observed for CRC and AD respectively.

Our study demonstrated that stool-based miRNA were stable with highly reproducible detection. The expression of miR-21 and miR-92a was significantly higher in CRC tissues compared with their adjacent normal tissues ($p < 0.0001$).

Stool miR-92a, but not miR-21, was significantly higher in patients with polyps than in controls ($p < 0.0001$).

In our study 435 copies/ng of stool RNA was taken into consideration as a cut-off value.

in our study we found a positivity of 73% (14 cases) in colorectal cancer and a positivity of 58% (16 patients) in advanced adenomas. In our study we also found a specificity of 79% in colorectal cancer and 75% in advanced adenomas.

In our study we compared colonoscopy vs other screening tests and we found that colonoscopy is still the leading screening test. A growing interest and consideration to non invasive screening markers are recently being developed in particular after notable improvement in stool-base tests like miRNA. This option will represent a viable non-invasive option for average risk patients.

The miRNA option is easy to complete, not expensive and with no risk compared to the ongoing colonoscopy.

We need further studies in order to quantify the validity of test and the cost-advantage together with efficacy of this test versus a colonoscopy.

In the scientific world detection of colorectal cancer through mi RNA has recently become an important tool.

In the past two years a study was performed to find a method to detect aberrant miRNA.

Following the interest in this new tool (aberrant mi RNA) as an instrument to determine CRC and AD in aberrant mi RNA in stools, we selected 48 patients (20 CRC and 28 AD) to be tested.

All 48 patients were tested for aberrant miRNA using Quigen test and compared with a group of 20 normal patients considered as a control group.

A new set of molecular markers are being tested as a potential inexpensive tool to screen colorectal cancers and advanced adenomas. A quantitative reverse transcription (PCR) was used to detect miRNA levels in colorectal cancers and advanced adenomas. Colorectal cancers were compared with controls and levels of miRNA 21 and miRNA a92 were found higher in CRC and AD. in our study we found a positivity of 73% (14 cases) in colorectal cancer and a positivity of 58% (16 patients) in advanced adenomas. In our study we also found a specificity of 79% in colorectal cancer and 75% in advanced adenomas. In our study miRNA in feces were stable and the detection quite easy. miRNA21 and miRNA 92a were found at higher level both in CRC and AD compared to control patients.

miRNA 92a were more elevated than the control group but miRNA 21 showed levels no different from control group.

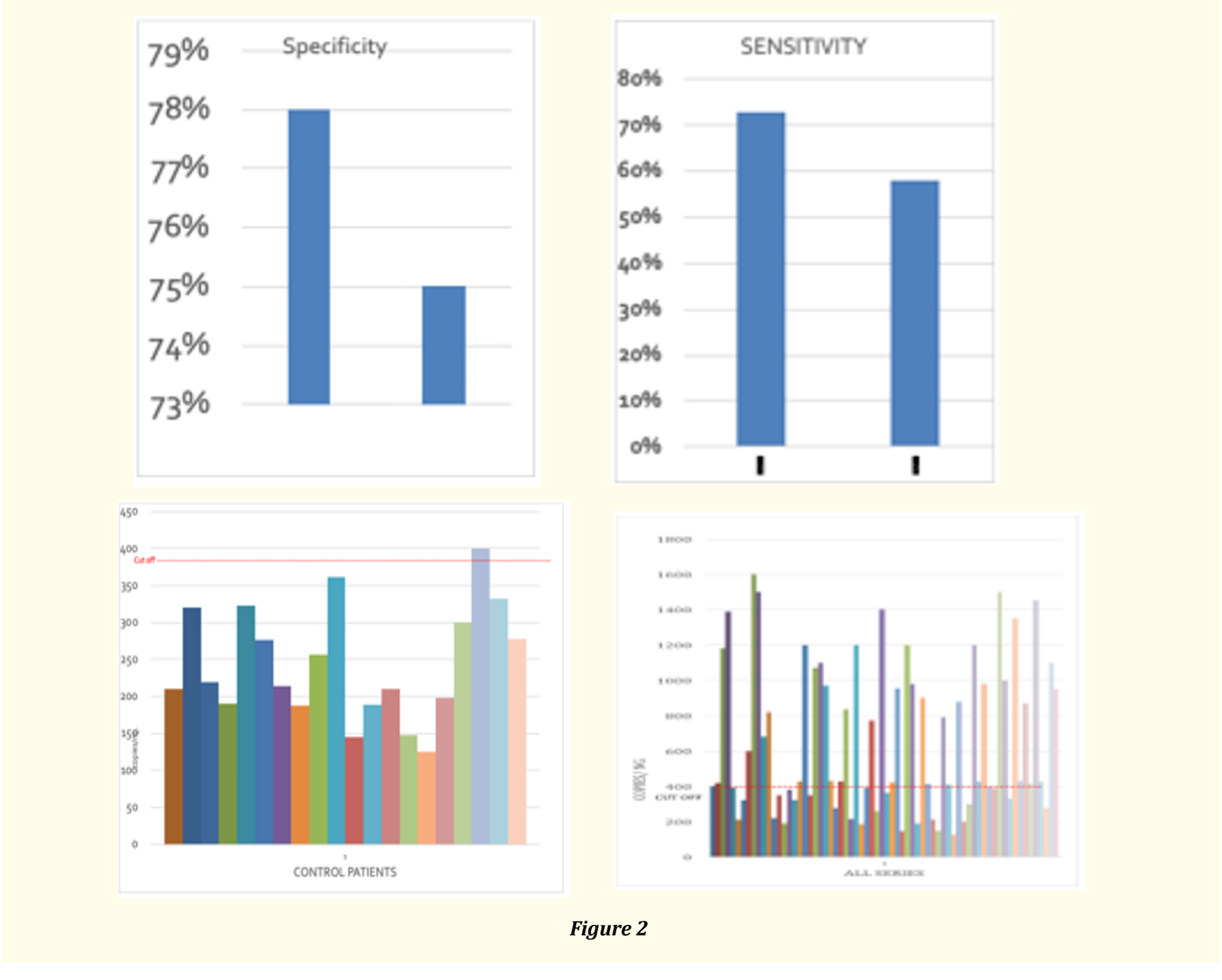

Figure 2

Conclusion

Methods in use for cancer diagnosis at this time don't have enough sensitivity and specificity to help the diagnosis of CRC in early stages.

Several aspects of miRNAs including their capability of interference with multiple targets and pathways make them essential in clinical diagnosis.

Endoscopy is still the leading test for CRC but a considerable improvement in a new noninvasive screening markers together with reliable refinement in stool-based tests like mi-RNA must be put in place to reduce the risk of the average patient.

Improving the quality of genetic test as Mi-RNA will offer advantages over endoscopic procedures. In particular implementation of non invasive procedures, low cost, and no risk factors needs to be considered. New reserch on miRNA will make clear the possibility of its market diffusion, efficiency, cost-effectiveness, and time-interval of the tests.

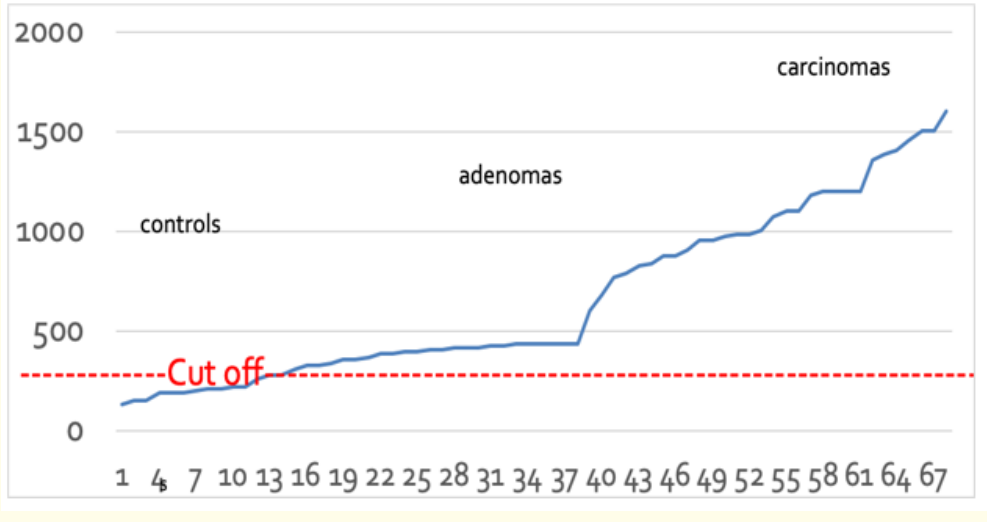

Figure 3

Bibliography

1. To Yau., *et al.* "MicroRNA-221 and microRNA-18a identification in stool as potential biomarkers for the non-invasive diagnosis of colorectal carcinoma". *British Journal of Cancer* 11.9 (2014): 1765-1771.

2. Brandon T Dickinson., *et al.* "Molecular markers for colorectal cancer screening". *Gut* 64.9 (2015): 1485-1494.

3. Brandon T Dickinson., *et al.* "Evidence-based Guidelines for Precision Risk Stratification-Based Screening (PRSBS) for Colorectal Cancer". *Cancer* 4.3 (2013): 172-192.

4. Tung On Yau., *et al.* "Faecal microRNAs as a non-invasive tool in the diagnosis of colonic adenomas and colorectal cancer: A meta-analysis". (2019).

5. Bing Chen., *et al*. "Emerging microRNA biomarkers for colorectal cancer diagnosis and prognosis" (2019).

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