



## Increasing Colonoscopy Compliance Using a Blood-Based Risk Assessment Test for Colorectal Cancer

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### Abstract

ColonSentry<sup>®</sup> is a minimally invasive, blood-based risk assessment test for colorectal cancer. The test is used to increase patient compliance with colonoscopy. Many physicians have inquired about the incidence of non-malignant lesions found in patients after colonoscopy prompted by an increased risk score on the ColonSentry test. Here we report on the colonoscopy results of five patients with increased ColonSentry risk scores. Of those five patients, three were determined to have polyps, one of which was pre-malignant.

**Key words:** ColonSentry; Colorectal cancer; Biomarkers; Colonoscopy

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### INTRODUCTION

Colorectal cancer is the world's third most common cancer and the fourth most common cause of global cancer death<sup>[1]</sup>. Early detection of colorectal cancer through screening can increase 5-year survival rates to 90%<sup>[2]</sup>. The gold standard for colorectal cancer screening is colonoscopy. However, this procedure is inconvenient and not without risks. Colonoscopy requires bowel preparation, and patients need to take time off work. Minor risks are common; approximately one-third of patients having colonoscopy report minor gastrointestinal symptoms. Rare but serious complications, including bowel perforation, have been estimated to occur approximately 2.8 times per 1000 screening colonoscopy procedures carried out in average-risk populations<sup>[3]</sup>. As a result, many patients are reluctant to undergo colonoscopies, and screening compliance for colorectal cancer is less than for other malignancies such as breast cancer<sup>[1]</sup>.

ColonSentry is a pre-screening blood-based test developed by GeneNews Ltd. The test is convenient and patient friendly, requires no bowel preparation or dietary restrictions and, since it is a simple blood test, carries minimal risks of complications. ColonSentry measures the gene expression profile of 7 genes. Those patients who present with an above-average risk score for colorectal cancer can then be referred for colonoscopy<sup>[4,5]</sup>.

### Materials & Methods

ColonSentry blood samples were collected from patients in Malaysia between 6 June 2011 and 29 August 2013; 250 Malaysian patients had the ColonSentry test.

Samples were collected using PaxGene tubes (PreAnalytix, Hombrechtikon, Switzerland). Whole blood RNA was isolated as described previously<sup>[4]</sup>. Isolated RNA was checked using 2100 Bioanalyzer RNA 6000 Nano Chips (Agilent Technologies, CA). RNA quantity was determined by absorbance at 260nm with a NanoDrop

2000c UV-vis Spectrophotometer (Thermo Scientific, DE).

Quantitative reverse-transcription real-time RT-PCR reaction procedures for the seven gene biomarkers have been described previously<sup>[4]</sup>. Briefly, one microgram of RNA was reverse transcribed into single-stranded complementary DNA (cDNA) using the High Capacity cDNA Reverse Transcription Kit (Applied Biosystems) in 1X RT reaction.

For qPCR, 20 ng cDNA was mixed with Quantitect<sup>®</sup> Probe PCR Master Mix (Qiagen) and Taqman<sup>®</sup> dual-labeled probe and primers corresponding to the gene of interest and reference gene, in a 25 µL reaction volume. PCR amplification was performed using a 7500 Real-Time PCR System (Applied Biosystems).

Sixty-seven patients who had taken the ColonSentry

test were identified as being at or above a 2-fold increased risk for colorectal cancer and were referred for colonoscopy. These patients were asked to provide their colonoscopy results to us if they were going to have a colonoscopy after our ColonSentry test.

## RESULTS

From 6 June 2011 to 29 August 2013, 250 Malaysian patients took a ColonSentry blood test. Sixty-seven of those patients were identified as being at or above a 2-fold increased risk for colorectal cancer and were referred for colonoscopy.

### Patient Follow-Up and Colonoscopy Results

By 01 September 2013, 5 of the patients had submitted their colonoscopy results to us (Table 1).

**Table 1**  
**Colonoscopy and ColonSentry<sup>®</sup> Test Results for the Five Patients Who Have Submitted Their Colonoscopy Results**

Patient ID	Gender	Age	ColonSentry <sup>®</sup> risk score	Colonoscopy & pathology results
GND100343	M	73	+ 7.7X	Two sessile polyps not sent to pathology
GND100345	F	64	> + 10.0X	Normal colonoscopy
GND100053	F	53	+ 8.4X	Benign hyperplastic polyp
GND100055	M	56	+ 7.7X	Normal colonoscopy
GND100220	M	42	+ 4.2X	Four polyps: 1 moderately atypical tubular adenoma 3 benign polyps

## Discussion

Of the 67 high risk patients referred for colonoscopy, 5 patients submitted their colonoscopy results to us for analysis. Sixty-two patients did not submit their results

(if any) to us. Of the 5 patients, 3 were found to have polyps, including 1 patient who had a premalignant, moderately atypical tubular adenoma (Figure 1).

内視鏡診断: (1)終末部回腸リンパ濾胞過形成  
(2)多発性大腸ポリープ  
(3)内痔核



生検: 結腸の一部を採取すること  
ポリペクトミー、EMR、EPMR: 腫瘍全体を切除すること

病理検査 No. 12-46225

病理診断: 1: 良性リンパ濾胞性過形成、2: 管状腺腫、3, 4: Group 1 (過形成性ポリープ)

所見:

1: 回腸粘膜です。腺上皮には、atypismなし。間質では、濾胞様のリンパ球の集簇をみる。浸潤するリンパ球には、atypismなし。  
2: 粘膜内に、中等度異型をもった管状腺腫(低異型度腺腫)の増殖をみる。断端不明。  
3, 4: 過形成性ポリープです。

悪性所見なし  悪性所見あり  要再検査  要観察

### Colonoscopy Result

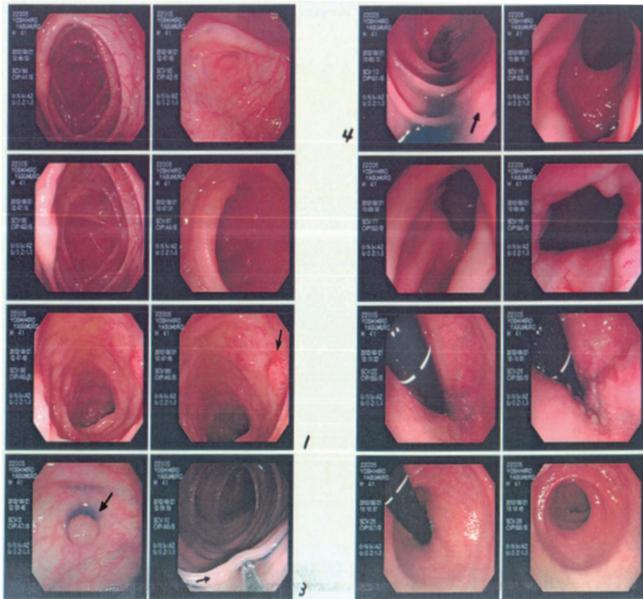
4 non-malignant polyps found.

### Pathology Diagnosis

**Polyp 1.** Extensive formation of benign lymphoid follicles.

**Polyp 2.** Tubular adenoma.

**Polyps 3 and 4.** Group-1 extensive formation of polyps.



**Figure 1**  
**Patient GND100220: Colonoscopy report and images**

These findings indicate that the ColonSentry test can predict the presence of non-malignant colorectal lesions as well as the presence of colorectal cancer. Currently, only a few results have been made available to us, as only five patients have given us their colonoscopy results. The remaining 62 patients with an increased-risk score have not provided us with their colonoscopy results. As more increased-risk patients submit their colonoscopy results to us, we expect to extend these preliminary findings.

In a previous paper published in 2010 we identified the 7-gene biomarker panel, which forms the basis of the ColonSentry test, and we discuss these genes in that report (4). These biomarkers are probably not conventional cancer biomarkers but rather are subtle, systemic alterations in blood gene expression in response to disease.

## CONCLUSION

Based on the above preliminary findings, the ColonSentry test may be able to predict the presence of polyps, including pre-malignant polyps. This should provide a

## Pathology Observation

**Polyp 1.** Mucous of ileum. No atypism in glandular epithelium. At mesenchyma, assembly of lymphoid follicles-like cells. Infiltrated lymph showed no atypism.

**Polyp 2.** In the mucous, proliferation of moderate atypical tubular adenoma (pre-malignant polyp) could be observed.

**Polyps 3 and 4.** Extensive formation of polyps.

further impetus for patients with an elevated risk score on the ColonSentry test to proceed to colonoscopy.

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