

COLORECTAL/ANORECTAL FREE PAPERS

OC-004

CIRCULATING TUMOUR MARKERS CAN DEFINE PATIENTS WITH NORMAL COLONS, BENIGN POLYPS AND CANCERS

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Introduction Colorectal cancer is the second highest cause of death from cancer in the UK. Early diagnosis represents the best opportunity for cure, but early colorectal cancer is often asymptomatic.

Current screening programmes already reduce mortality and the incidence of cancer, but rely on faecal occult blood testing which has limited sensitivity, as well as acceptability to patients and health care providers.

A diagnostic blood test may offer improved patient compliance and outcome, representing a desirable target.

Methods In this study, we optimized a series of promising diagnostic markers utilizing circulating free DNA (cfDNA), with a preparation method allowing small DNA fragments to be purified.

cfDNA was isolated from samples obtained from 85 patients, including 35 patients without endoscopic abnormality, a group of 26 patients with large benign colorectal adenomas, and 24 patients with colorectal carcinomas.

In each case, real time quantitative polymerase chain reaction (RT-PCR) was performed for Line 1 79 bp, Line 1 300 bp, Alu 115 bp, Alu 247 bp and mitochondrial primers. In addition, carcino-embryonic antigen was measured by ELISA. Each marker was analysed between normal, polyp and cancer populations using Mann–Whitney U tests and ROC curves. The best performing were analyzed in combination by logistic regression. A Bonferroni correction was applied.

Results The average age of the normal population was 54.1 years, the polyp population 70.2 years and the cancer population 71.5 years. The mean polyp size was 54.3 mm (5–200 mm).

Table 1 OC-004 Circulating DNA levels by pathology (normal, polyp, cancer descending order).

Mitochondrial DNA ng/ml plasma	Line 1 79 / Line 1 300 ratio	Alu115 / 247 ratio	Line 1 300 ng/ml plasma	Alu247 ng/ml plasma
0.90	6.67	10.01	1.54	2.86
2.68	7.76	11.89	3.25	5.56
4.05	9.11	14.02	3.56	7.51

Table 2 OC-004 Receiver operating curve (ROC) values for the DNA markers (below) .

Polyps vs normal	0.596	0.756	0.743	0.512	0.511	0.691	0.731	0.797
Cancer vs normal	0.574	0.757	0.675	0.759	0.772	0.594	0.716	0.863
Polyps and cancer vs normal	0.586	0.756	0.713	0.624	0.629	0.647	0.724	0.810

The total DNA in ng/ml plasma was 7.96 in the normal group, 15.04 in the polyp group and 30.09 in the cancer group.

Analysing total DNA, mitochondrial DNA and Alu 247 bp fragment DNA levels, there were highly significant differences between the polyp and cancer group versus the normal group ($p = 0.001$).

Conclusion The best three marker DNA model was able to discriminate the normal population from populations with adenoma and carcinoma with a ROC curve of 0.810.

Addition of CEA increased the ROC to 0.855 and the combination had a positive predictive value of 81.1% for polyps and cancer.

Circulating DNA markers in combination with other markers offer the prospect of a simple blood test to screen for colorectal cancers and polyps.

Competing interests None.

Keywords cancer, colorectal, DNA, plasma.