

compared to older patients. There were two patients with post-polypectomy bleeding. One occurred during the endoscopy and was successfully treated endoscopically and the other was an early post polypectomy haemorrhage managed conservatively. Neither of the patients required transfusion. There were no cases of perforation or post-polypectomy syndrome.

Summary The diagnostic yield of colonoscopy as part of the National Bowel Cancer Screening Program remains high with an adenoma detection rate of 34%.

Application of numerical ecology methods to microarray data reveals obscured patterns in the mucosa-associated microbial community of the human colorectum

D AGUIRRE DE CARCER,¹ PÓ CUÍV,¹ T WANG,^{1,2} T REVERTER,¹ D WORTHLEY,³ V WHITEHALL,³ ES KLAASSENS,¹ S KANG,¹ S DENMAN,¹ G YOUNG,⁴ B LEGGETT,³ C MCSWEENEY,¹ M MORRISON^{1,5}

¹CSIRO Preventative Health National Research Flagship, ²Shanghai Jiaotong University, China, ³Royal Brisbane and Women's Hospital Research Foundation and Queensland Institute of Medical Research, ⁴Flinders University, ⁵The Ohio State University, USA

The mucosa-associated microbial community of the human colorectum has been implicated in the pathogenesis of several diseases. Previous studies have largely employed methodologies that failed to reveal patterns generally obscured by inter-subject variability. To overcome this problem we describe the use of numerical ecology methods to analyse data produced using a gut microbe-specific phylogenetic microarray.

DNA samples were prepared from biopsy tissue collected from the caecum, transverse, sigmoid and rectum of 10 patients following normal colonoscopy (5 males and 5 females, mean age 56 years). Fluorescently labeled cRNA was prepared for each sample and hybridized to a DNA microarray consisting of 766 unique probes for gut bacteria. We then used analysis with respect to instrumental variables applied to correspondence analysis, which is a method often employed in numerical ecology; but only recently applied to microarray data. This type of analysis allows for the "subtraction" of effects (e.g. subject), which then allows the remaining effects to be effectively compared in a statistically valid fashion.

Consistent with previous studies, the diversity profiles generated possessed a marked inter-subject variability. However, we were also able to identify significant differences in the profiles on the basis of sex. *Streptococcus* and *Ruminococcus* genera were more abundant in females; and males possessed a greater abundance of *Bacteroides* and *Faecalibacterium*. Furthermore, when the subject effect was subtracted, we observed for the first time evidence of a longitudinal gradient for specific microbes with respect to biopsy site.

The application of numerical ecology methods to the analysis of data generated with a phylogenetic microarray has proven to be a powerful new methodology in the study of the mucosa-associated microbial community of the human colorectum.

Biological function of the mutated in colorectal cancer (MCC) gene

N SIGGLEKOW, L PANGON, EA MUSGROVE, M KOHONEN-CORISH

Cancer Research Program, Garvan Institute of Medical Research, Sydney

The 'mutated in colorectal cancer' (MCC) gene was discovered in 1991 leading to the identification of the closely linked adenomatous polyposis

coli (APC) gene, but is only rarely mutated in colon cancer. Few studies initially addressed its significance, but MCC was recently identified as a 'driver' of colon carcinogenesis alongside APC (1), and an MCC methylation defect was detected in up to 50% of colon cancers, which causes silencing of gene expression (2). We now investigate the role of MCC in cell cycle regulation.

HCT-15 colon cancer cells were transfected with the complete MCC coding sequence or an empty vector control. Cells were counted daily for 7 days and analysed for the distribution of cell cycle phases using flow cytometry. Potential phosphosites were identified in the MCC protein by immunoprecipitation of endogenous MCC from SW480 and HCT116 cell lines, using nano-ESI-LC-MS/MS mass spectrometry.

MCC-null HCT-15 cells re-expressing wild type MCC exhibited a marked decrease in cell proliferation compared to control cells. More specifically, MCC re-expression resulted in a decrease of the S phase population, with a concurrent increase in the G1 and G2/M cell cycle population. These data indicate that MCC may induce partial blocks during the G1/S and G2/M phase transitions of the cell cycle. We also analysed endogenous immunoprecipitated MCC from HCT116 and SW480 cell lines and identified two phosphorylated amino acids (Serine 293 and Serine 294), located in a highly conserved region of the protein, a cyclin dependent kinase (CDK) phosphorylation consensus site (SSPGR).

We conclude that MCC has a function in regulating the cell cycle. Identification of phosphorylated Ser293/294 residues in a conserved CDK substrate motif suggests that MCC itself is regulated by a CDK. When MCC expression is lost in colon cancer, this novel function as a cell cycle regulator is also lost. This is consistent with a role as a tumour suppressor. Our data provide a potential cellular mechanism whereby an MCC defect promotes colon cancer.

References

1. Starr et al. 2009. A transposon-based genetic screen in mice identifies genes altered in colorectal cancer. *Science* 323:1747.
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Can bowel symptoms be used to identify patients with colorectal cancer?

BA ADELSTEIN,¹ L IRWIG,¹ P MACASKILL,¹ RM TURNER,¹ S CHAN,¹ PH KATELARIS²

¹Screening and Test Evaluation Program, School of Public Health, University of Sydney, NSW, Australia, ²Concord Repatriation General Hospital, University of Sydney, NSW, Australia

Introduction Many bodies advise that people with bowel symptoms should have a colonoscopy to detect colorectal cancer. However, the evidence base for these recommendations is weak. Our aim was to determine which bowel symptoms predict cancer on colonoscopy.

Methods A validated, structured self-administered questionnaire was completed by patients who subsequently had colonoscopy. Information was collected on symptoms, demographics and medical history. Multiple logistic regression modelling was used to identify predictors of colorectal cancer. An ROC curve was estimated for each model.

Results Cancer was found in 159 patients and no cancer or adenoma in 7,577 patients. The only bowel symptoms that predicted cancer were rectal bleeding, change in bowel habit and rectal mucus. Prediction was strongest in patients who had symptoms at least weekly and commencing within the previous 12 months; abdominal pain was predictive only in such patients. The odds ratios never exceeded 4.27. Less frequent symptoms, or those of shorter duration, were not predictive; and neither were urgency,