

# CRT Licensing Opportunity



## MCM Proteins - Screening Markers for Colorectal Cancer

- Markers for the early detection of colorectal cancer in faeces
- MCM based immunocytochemistry identifies cancer colonocytes isolated from faeces
- MCM marker over expressed in colonic adenocarcinomas
- Validated screening marker for early detection of cancer

DIAGNOSTICS | Validation

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## Introduction

MCM or minichromosome maintenance family proteins are essential for the initiation of DNA replication. They are present throughout the cell cycle but are down-regulated following cell cycle exit and differentiation. Research in the laboratories of Professor Ron Laskey and Dr Nick Coleman (The Hutchison/MRC Research Centre, Cambridge) has demonstrated that antibodies against MCMs enable ready identification of malignant and pre-malignant cells undergoing continuous proliferation. This has prompted a clinical application in cancer screening approaches that rely on the detection of malignant or pre-malignant cells exfoliated from surface epithelia. Work undertaken in Dr Coleman's laboratory has led to the analysis of MCM proteins as novel screening markers for the early detection of colorectal cancer in stool samples.

## Background

Colorectal cancer is the third most common form of cancer, and accounts for the greatest proportion of deaths in the Western world. Colorectal cancer screening includes faecal occult blood testing and flexible sigmoidoscopy, but better tests are needed if accuracy, safety, affordability and compliance rates are to improve. In normal large bowel mucosa, members of the MCM family are confined to the proliferative compartment in the basal third of the crypts (Figure 1, A). By contrast MCMs are expressed throughout the epithelium, including in surface colonocytes when colonic adenomas or adenocarcinomas are present (Figure 1, B).

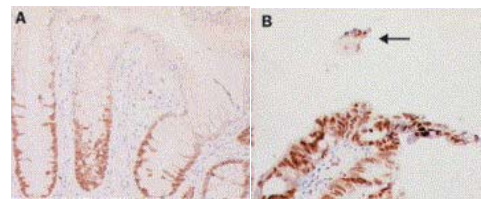


Figure 1: MCM expression in colonocytes shown by immunoperoxidase stain. (A) MCM expression in healthy colonic crypts. (B) MCM expression in colonic adenocarcinoma.

## Study Data

Retrieval of colonocytes from faeces has been used to distinguish between normal and neoplastic cells by immunocytochemistry for MCM proteins. MCM expression in colonocytes from faeces of 40 patients with symptomatic colorectal cancer and 25 healthy controls demonstrate 100% specificity and 92.5% sensitivity for the detection of colorectal cancer. No expression of MCM protein was detected in colonocytes retrieved from stool of healthy volunteers (Figure 2, C), while cells retrieved from stool of patients with adenocarcinoma of sigmoid colon express MCM protein (Figure 2, D). Optimisation of colonocyte isolation from stool samples has recently been completed.

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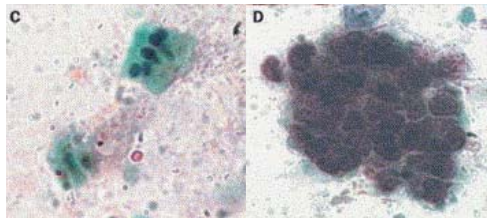


Figure 2: MCM expression in colonocytes shown by immunoperoxidase stain. (C) No expression in colonocytes from healthy volunteer. (D) Cells retrieved from stool of patient with adenocarcinoma.

## Commercial Opportunity

Diagnostic products based on antibodies targeting MCM proteins are currently being developed with commercial partners for cervical (late stage) and bladder cancer. CRT are now looking for a commercial partner to develop an MCM-based test for the detection of early stage colorectal cancer in stool samples. Such a test may be used clinically as a secondary investigation following faecal occult blood testing, in order to increase overall specificity. Granted patents (US, EP and JP) relating to the target antigen and MCM specific antibodies are available for licensing.

## References

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