

# CRT Licensing Opportunity



## MCM Proteins - Diagnostic Markers for Lung Cancer

- Rapid, high throughput diagnostic test based on MCM detection in sputum
- Combined chest X-ray and MCM testing provides improved first line diagnosis
- Marker qualification through assessment a cohort of 597 symptomatic patients
- Simplified approach removes requirement for highly skilled cytopathologist at initial diagnosis

DIAGNOSTICS | Validation

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### Opportunity

Over 1.3 million people worldwide are diagnosed with lung cancer each year and over a million die. Routine testing of symptomatic patients at presentation includes cytology of the sputum and chest X-ray, with suspicious cases progressing to spiral CT scans, bronchoscopy and finally histological analysis of tumour sections. Analysis of sputum cytology using conventional morphological criteria needs to be performed by a highly skilled cytopathologist, making this a time consuming and costly diagnostic approach. Moreover, despite the sensitivity of imaging modalities such as X-ray and CT scans, the specificity of these tests is poor with an estimated 98% of suspicious areas seen on CT scans turning out to be benign. This can result in patients undergoing further unnecessary, costly and potentially harmful invasive procedures in order to confirm the absence of lung cancer.

The sputum MCM immunocytochemistry test offers a rapid high-throughput, and cost effective approach for detection of lung cancer. MCM staining of sputum in combination with chest X-ray could be employed for lung cancer diagnosis, with second line more invasive tests utilised only for MCM positive patients. The combined test could also support a screening programme for early detection of lung cancer in non-symptomatic high risk individuals, leading to a reduction in the number of lung cancer patients diagnosed at a late stage.

### Biomarker Qualification

Immunohistochemistry studies on squamous cell carcinoma (SCC) and small cell lung cancer samples have previously shown that MCM expression is upregulated relative to normal lung parenchyma (Figure 1). The value of MCM immunocytochemistry of sputum for lung cancer detection, in combination with chest X-ray, has been explored in a study of 597 symptomatic patients presenting at Aberdeen hospital. The performance of the MCM test was assessed by comparison with the "gold standard" of clinical diagnosis founded on histopathology.

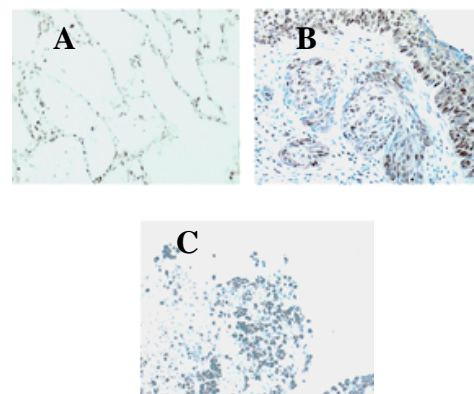


Figure 1: Expression of MCM in the lung. (A) A normal lung parenchyma with MCM expression in ~15% of alveolar pneumocytes. (B) SCC of lung with severely dysplastic overlying epithelium showing MCM expression in ~90% of nuclei. (C) Small cell carcinoma of lung showing expression of MCM in 90% of nuclei

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In the cohort of 597 patients, sputum MCM testing was used in combination with chest X-ray. The combined test has a specificity of 78%, with improved sensitivity (71%) and negative predictive value (NPV) (85%) over using each test alone. High specificity and NPV values mean that a high proportion of patients with a negative test do not have cancer and can avoid unnecessary further testing. The data demonstrate that combining sputum MCM testing with chest X-ray would be a reliable diagnostic test for lung cancer.

## Background

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 identification of malignant and pre-malignant cells in a variety of samples, including cervical smears, sputum and urine. The groups have been instrumental in progressing the clinical development of MCMs in a variety of cancer screening approaches. Diagnostic products based on antibodies targeting MCM proteins are currently in development for cervical and bladder cancer.

## Commercial Opportunity

CRT is looking for a commercial partner to develop a MCM sputum-based test for the detection of lung cancer under a licence to granted patents (US7459157, EP1025444 and JP3774196) relating to the target antigen and MCM specific antibodies.

## Cancer Research Technology

CRT is an oncology focused development and commercialisation company. The MCM test for lung cancer is one of a robust pipeline of projects currently available from CRT for licensing and co-development.

## References

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