

CRT Licensing Opportunity



MCM Proteins - Diagnostic Markers for Lung Cancer

- Diagnostic test based on MCM detection in sputum
- Combined chest X-ray and MCM testing provides rapid and cost effective first line diagnosis
- Simplified approach removes requirement for highly skilled histopathologist
- Marker qualification through assessment of a cohort of 597 symptomatic patients

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 histopathologist, 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 a negative diagnosis.

The sputum MCM immunocytochemistry test, in combination with chest x-ray, offers a rapid and cost effective approach for the diagnosis of lung cancer. Second line more invasive tests could be utilised only for MCM positive patients, which would lower the number of patients to be tested. 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, in combination with chest X-ray for lung cancer detection, 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.

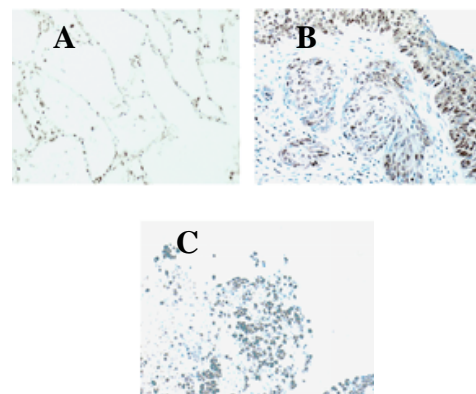


Figure 1: Expression of MCM in the lung. (A) A normal lung parenchyma with MCM expression in ~15% of alveolar pneumocytes. (B) SCC of lung with severely dysplastic overlying epithelium showing MCM expression in ~90% of nuclei. (C) Small cell carcinoma of lung showing expression of MCM in 90% of nuclei.

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The accuracy of the combined MCM/x-ray test is equivalent to the current standard diagnostic approach of sputum cytology and chest x-ray, but offers the added advantages of time and cost efficiency, as it removes the requirement for a highly skilled histopathologist at initial diagnosis. Positive MCM staining is a clear indication of the presence of cancer cells, hence the test is less subjective in its interpretation and may be suitable for automated image analysis.

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 a multiple-territory portfolio of granted patents (W01999/021014) 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

- Scarpini, *et al.* Improved screening for anal neoplasia by immunocytochemical detection of minichromosome maintenance proteins. *Cancer Epidemiol Biomarkers Prev.* 2008 17(10):2855-64 [PMID:18843031].
- Scott, *et al.* A minimally invasive immunocytochemical approach to early detection of oral squamous cell carcinoma and dysplasia. *Br J Cancer.* 2006 94(8):1170-5 [PMID: 16622441].
- Baldwin, *et al.* Translational approaches to improving cervical screening. *Nat. Rev. Canc.* 2003 3: 217-226 [PMID: 12612656].
- Stoeber, *et al.* Diagnosis of genitor-urinary tract cancer by detection of minichromosome maintenance 5 protein in urine sediments. *J. Natl. Cancer Inst.* 2002 94: 1071-1079 [PMID: 12122098].
- Freeman, *et al.* Minichromosome maintenance proteins as biological markers of dysplasia and malignancy. *Clin. Can. Res.* 1999 5: 2121-2132 [PMID: 10473096].

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