

CRT Licensing Opportunity



MCM Proteins - Screening Markers for Oral Cancer

- MCM based detection of early stage oral cancer from smears of oral mucosa
- Screening markers for early oral squamous cell carcinoma and dysplasia
- Validated screening marker for the early detection of cancer
- Granted US, EP and JP patent on the target antigen

DIAGNOSTICS | Validation

October 2009

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. 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 a minimally invasive immunocytochemistry approach for the detection of oral squamous cell carcinoma and dysplasia.

Background

Oral squamous cell carcinoma (SCC) is the sixth most common malignancy worldwide, with 75% of cases occurring in the developing world. There is progression through increasing grades of epithelial dysplasia to invasive malignancy. Clinical differentiation of pre-malignant lesions and early SCCs from benign proliferative conditions is difficult due to non-specific clinical appearances. An effective method of early detection of such lesions is therefore urgently required.

Study Data

A study was undertaken to investigate whether SCCs could be distinguished from mild dysplasia and benign keratosis by immunocytochemical analysis of MCM proteins in 101 smears of oral mucosa. Study data demonstrates that 100% of smears of normal mucosa, benign proliferative disease and mild dysplasia contained epithelial cells that were MCM-negative (Figure 1, A). In contrast 97% of SCC samples contained MCM-positive cells (Figure 1, B). Taken together, this data suggests that the values of MCM immunocytochemistry in the analysis of oral smears is consistent to that for other cytological samples, such as smears of the cervix, where detection of MCMs enables dysplastic and malignant cells to be detected with a high degree of sensitivity and specificity.

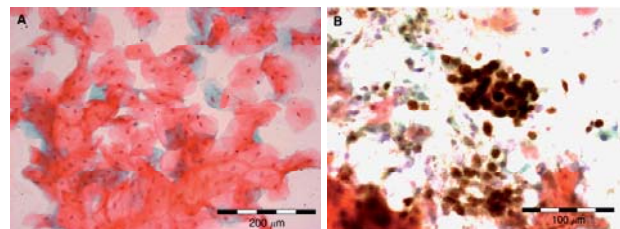


Figure 1: MCM immunocytochemistry in oral smears. Squamous epithelial cells from normal mucosa (A) are negative when stained with antibodies against MCM. In contrast, a cluster of cells from an oral SCC (B) are strongly positive for MCM.

CRT Licensing Opportunity

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 looking for a commercial partner to develop an MCM-based screening test for the detection of early oral squamous cell carcinoma and dysplasia. Granted patents (US, EP and JP) relating to the target antigen and MCM specific antibodies are available for licensing.

References

A minimally invasive immunocytochemical approach to early detection of oral squamous cell carcinoma and dysplasia. Scott, *et al.*, Br. J. Cancer. 2006 **94**: 1170-1175.

Control of DNA replication and its potential clinical exploitation. Gonzalez, *et al.*, Nat. Rev. Can. 2005 **5**: 135-141.

Translational approaches to improving cervical screening. Baldwin, *et al.*, Nat. Rev. Can. 2003 **3**: 217-226

Diagnosis of genito-urinary tract cancer by detection of minichromosome maintenance 5 protein in urine sediments. Stoeber, *et al.*, J. Natl. Cancer Inst. 2002. **94**:1071-1079

Contact: Adrian Ibrahim aibrahim@CancerTechnology.com

Ph: +44 (0)207 269 3640