Differential upregulation of MR6-Ag/IL-4 receptor complex in breast tumours

I. Mat, D. Melcher and M.A. Ritter
Dept of Immunology, Royal Postgraduate Medical School, Hammersmith Hospital, London, and Dept of Histopathology, Royal Sussex County Hospital, Brighton, UK.

Preliminary studies using monclonal antibody MR6 (which recognises a 200 KD molecule that may be associated with the interleukin 4 receptor, IL-4R, complex) is upregulated in approximately 30% of breast tumours as compared to normal breast epithelium which is either negative or relatively weakly positive. We have now investigated a larger number of breast markers including the epidermal growth factor receptor (EGFR1) and the c-*erb*-B 2 protein. MR6 gave strong labelling of 100% (5/5) of benign proliferations of the breast and 54% (13/24) of grade I and II, lymph node negative tumours. Of grade III lymph node positive tumours, 30% (5/17) were positive, however these showed only weak staining. Two colour immunofluorescence using rabbit anti-keratin antibody and biotinylated MR6 confirmed that greater than 80% of the MR6 positive cells were keratin positive epithelial tumour cells. The c-*erb*-B 2 protein, on the other hand, was not present on benign proliferative tissue but showed strong expression in 40% of grade III lymph node positive tumours. Taken together, these data raise the possibility that the MR6 Ag/IL-4R complex may be involved early in the process of tumourigenesis and suggest that monoclonal antibody MR6 may be a useful addition to the present panel of antibodies used for tumour grading, imaging and perhaps therapy.

Expressions of 1H1, 1C12, 5D4, CA19-9 antigens and feto-acinar pancreatic protein (FAP) in pancreatic cancers, pancreatitis and cancers from tissues surrounding the pancreas

A. Masunaga, T. Ohgida, Y. Fujii, S. Mori and S. Itoyama
Dept of Pathology, Saitama Medical School Medical Centre and Depts of Surgery and Pathology, Institute of Medical Science, University of Tokyo, Japan.

It is important to distinguish pancreatic cancers from cancers of the tissues surrounding the pancreas from therapeutic and prognostic points of view. This study was designed to see whether the various cancers could be distinguished immunohistochemically or not. The Abs used were CA19-9, J-2 (MAb against feto-acinar protein), 5D4, 1C12 and 1H1. The 5D4, 1C12 and 1H1 MAbs were obtained by immunising BALB/c mice with pancreatic cancer cell lines. Immunohistochemistry was performed on 25 formalin-fixed paraffin-embedded tissue sections. It was concluded that 1H1, 1C12 and CA19-9 were useful for immunodiagnosis of pancreatic cancers, 5D4 for duodenal cancers and 1H1 and 1C12 for choleductal carcinomas.

Novel monoclonal antibody for the diagnosis of carcinoma of the oesophagus

P.R. Waingankar and J.S. Nadkarni
Tata Memorial Hospital, Parel, Bombay 400 012, India.

A murine monoclonal antibody (2G3) of IgG1 type was raised against the human oesophageal carcinoma cell line TE-2. Its activity has been evaluated by immunoperoxidase and immunofluorescence on cryostat and paraffin sections of normal tissues, malignant and benign tumours as well as different established cell lines. We found that the antigen recognised by this antibody is expressed mainly by oesophageal carcinoma cells and weakly by some malignant breast cells. We therefore propose to use this novel monoclonal antibody (2G3) for the *in vivo* diagnosis of tumours of oesophagus.

Reactivity of monoclonal antibodies HMFG1 and AUA1 in gastric precancerous lesions and gastric cancer

M. Demonakou, S. Zougri, N. Tanvakis, P. Psaropoulou and D. Skarlos
Sismanoglion General Hospital, Marousi and Agii Anargyri Cancer Hospital, Athens, Greece.

The aim of this study was to evaluate the reactivity of tumour associated epithelium specific AUA1 and HMFG1 Mabs in gastric dysplasia (GD), intestinal metaplasia (IM), and gastric cancer (GC).

Tissues from 70 gastrectomy specimens (25 gastric adenocarcinomas, 9 gastric lymphomas and 36 benign lesions) were stained with HE, PAS/AB PH 2.5, PAS/AB PH1 and the indirect two-stage immunoperoxidase method using Mabs HMFG1 and AUA1 at a concentration of 25 μg/ml with positive and negative controls. IM was diagnosed in 48 specimens (68.5%) and GD in 9 specimens (12%). Twenty-eight cases of IM were of complete (Type 1) and 20 were of incomplete type. HMFG1 reacted with 7.5% of the incomplete IM, with the 91.5% of complete type of IM. The AUA1 pattern of staining in IM was cytoplasmic in the complete type and cytoplasmic and linear at the apical portion of the tall columnar cells in the incomplete form. HMFG1 reacted with the cytoplasm and apical portion of the mucus secreting cells of both complete and incomplete IM. Epithelial dysplasia stained with both Mabs. AUA1 stained 7 out of 9 and HMFG1 stained 8 out of 9 cases. AUA1 reacted with 81% and HMFG1 with 80% of GCs.

We conclude that AUA1 shows positive staining in IM of both complete and incomplete types and HMFG1 is helpful for the detection of the incomplete forms of IM. Finally, both Mabs are positive for GC.

Determination of multidrug resistance *in vivo* by monoclonal antibodies against P-glycoprotein in an MDR-1 transfected melanoma cell line

L. da Cunha, H.J. Haisma, H.M. Pinedo and E. Boven
Dept of Oncology, Free University Hospital, Amsterdam, The Netherlands.

Multidrug resistance (MDR) has recently been recognised in cancer cells and appears to be related with high expression of *p*-glycoprotein (Pgp) in the cell membrane. The MDR phenotype can be determined with monoclonal antibodies (MAbs) against Pgp as shown for cell lines or patients' tumour samples. In order to study the relevance of the MDR phenotype *in vivo* we developed a xenograft model from human melanoma cell line BRO and its MDR-1 transfected subline, BRO mdr1.1. In each passage in nude mice, MDR expression was determined with MAbs (JSB1, MRK16, and C219) directed against different epitopes of Pgp by immunocytochemistry. Simultaneously, *in vitro* cultures of the BRO mdr1.1 cell line without addition of the selective agent (vincristine) were analysed in the same way. A gradual loss of Pgp expression was detected *in vivo*.

	JSB1	MRK16	C219		JSB1	MRK16	C219
BRO mdr1.1	+++	++	+				
mouse p.1	+++	+++	+++	mouse p.4	–	–	–
mouse –.2	+	+	+	mouse p.5	–	–	–

Loss of MDR phenotype was confirmed by the reduction of the resistance factor of vincristine (from 444 to 14) and doxorubicin (from 9 to 2.1). Comparable results were found in cells from *in vitro* culture. RNA blotting has been performed to determine the loss of the MDR gene. We conclude that the decreased staining with the 3 MAbs in subsequent passages of the BRO mdr1.1 model correlates with the loss of Pgp expression and recovery of chemosensitivity.