Patients with high potassium cysts exhibit increased expression of 323/A3 monoclonal antibody

S.P. Courtney, B.J. Harrison, S. Williams and R.E. Mansel
University of Wales College of Medicine, Cardiff, UK.

High potassium breast cysts have been suggested as markers of patients at increased risk of developing breast cancer. The monoclonal antibody (MAb) 323/A3 exhibits enhanced expression in the cytoplasm of aprocrine metaplasia when a patient is known to have breast carcinoma. The aim of this study was to determine whether these markers of risk identified similar groups of patients. 10 patients were studied who had breast biopsies taken and in whom cyst aspiration had been performed. The cysts were grouped according to high potassium (K+) or low K+. Staining of the breast tissue sections was carried out with 322/A3 using avidin-biotin horseradish peroxidase complex (ABC Vectastain Reagent, Vector Labs) with diaminobenzidine as the chromogen. Staining was noted in the cytoplasm of ducto-lobular tissue, basal membrane and cytoplasm of apocrine metaplasia. The cytoplasm of ducto-lobular tissue stained whether low K+ (4 cases) or high K+ (6 cases) as did the basal membrane of apocrine metaplasia. The cytoplasm of apocrine metaplasia did not stain in the low K+ cyst patients but 5 out of 6 stained in the high K+ patients. This difference was statistically significant using Fisher's exact test ($P = 0.046$). These results suggest that increased cellular activity is responsible for the production of high K+ cysts and may indicate a field change phenomenon.

The effect of tamoxifen on the expression of 24K monoclonal antibody

S.P. Courtney, A. Baildon, R.E Mansel and A. Howell
Dept of Surgery, University of Wales College of Medicine, Cardiff and Dept of Medical Oncology, Christie Hospital, Manchester, UK.

Monoclonal antibody (MAb) 24K identifies an oestrogen regulated protein. It has been used to examine the expression of oestrogen receptors in breast and uterus. The effect of tamoxifen on the expression of 24K MAb before and after treatment has been correlated with clinical response to tamoxifen in breast carcinoma tissue. Nineteen patients who had biopsies in breast cancer tissue before and after treatment with tamoxifen were studied. Immunohistochemical (IHC) staining was carried out using avidin-biotin horse radish peroxidase complex (ABC Vectastain, Vector Labs). The cytoplasmic staining patterns were recorded as no stain, weak, or strong and clinical response as progressive disease (9 patients), static disease (4), partial response (5) or complete response (1). There was no overall change in staining pre- and post-treatment and no correlation between responders and non-responders (Table 1).

Table 1.

	Strong stain		Weak stain		No stain	
	Before	After	Before	After	Before	After
Progressive disease	2	1	3	6	4	2
Static disease	1	1	2	1	1	2
Partial response	1	2	1	0	3	3
Complete response	–	–	–	–	1	1

We conclude that 24K MAb is not suitable as a biological marker to predict response to tamoxifen.

Polylysine guided delivery of radionuclides to C6 glioblastomas in rats

S. Kornguth, A. Kyritsis, S. Lohmiller, H.I.Robbins, J. Cohen, R.J. Nickles and P. Turski
University of Wisconsin, Madison, Wisconsin 53706, USA.

Polylysine-DTPA-Gd was shown by us to have utility in the MR imaging *in vivo* of C6 glioblastomas in rats. Polylysine (PL) has several advantages over antibodies as a guiding molecule for the delivery of imaging and radiotherapeutic agents: (a) PL is chemically homogeneous and the size of the polymer may be controlled, (b) the PL can enter the C6 tumour without permeabilising the BBB, (c) the addition of one DTPA per 10 lysyl residues does not diminish tumour binding properties and (d) the PL is not immunogenic. This report describes the organ and tumour distribution of PL-DTPA nuclides in rats with the C6 tumour, as a function of nuclide (^{153}Gd or ^{89}Zr), time after injection of the nuclide (24–72 h), route of delivery (intra-aortic vs. intravenous). The kidneys had the highest concentration of PL-DTPA-nuclide followed by the liver and spleen. PET showed that the major radioactivity is in the kidney and spleen. Following intraaortic administration, there was a 4–6 fold higher concentration of PL-DTPA nuclide in the tumour portion of brain than in control contralateral brain. T1 weighted MR images of the tumour revealed a high signal intensity at the tumour margin after treatment with 1 μg of Polylysine-DTPA-Gd. The tumour margin was validated on tissue sections that were stained with thionine. PL is a useful carrier of imaging and radiotherapeutic agents to malignant brain tumours.

Monoclonal antibody uptake and distribution in a subcutaneous xenograft following intratumour injection

G. Rowlinson-Busza, A. Bamias, T. Krausz and A.A. Epenetos
Imperial Cancer Research Fund and Royal Postgraduate Medical School, Hammersmith Hospital, London, UK.

Nude mice bearing subcutaneous xenografts of the human colon adenocarcinoma HT29 were given intratumour injections of a mixture of ^{125}I-labelled specific antibody (AUA1) and ^{131}I-labelled control antibody (HMFG1), or with the labels reversed. After dissection at 1 h and 4 h post-injection, both specific and control antibodies had tumour activity of 47–63% of the injected dose (% id). By 24 h, the tumour contained 43% id of AUA1 which persisted at around this level for 5 days after administration and remained at nearly 20% id at 18 days. In contrast, the HMFG1 level was 23% id at 24 h, which continued to fall and was less than 5% id at 7 days. Normal organ levels were less than 2% id/g for both antibodies, with HMFG1 being higher at all times than AUA1, resulting in specificity indices greater than 20 by 5 days. Autoradiography of tumours removed 2 h post-injection of ^{125}I-labelled AUA1 or HMFG1 showed high levels of antibody at the injection site. At 48 h and 7 days post-injection, the specific antibody was bound to the surface of tumour cells in islands remote from the injection site, whereas the control antibody was found only in stroma and blood vessels or as diffuse non-specific uptake.

These data indicate that intratumoral injection of radiolabelled monoclonal antibodies may achieve high radiation doses in accessible tumours without systemic irradiation.