Short Communication

Prolonged localisation of a monoclonal antibody against CEA in a human colon tumour xenograft

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Tumour localisation with polyclonal antibodies directed against CEA, in xenografts of human colon carcinomas, was first demonstrated by Primus et al. (1973) and Goldenberg et al. (1974) using organ counting and photoscanning techniques. More recently studies demonstrating successful localisation (Colcher et al., 1983; Herlyn et al., 1983 and Pimm & Baldwin, 1984) and immuno-radiotherapy (Zalcberg, 1984) in the human tumour xenograft using monoclonal antibodies against various tumour markers have been reported. In most studies the paired labelling technique of Pressman et al. (1957) has been adopted enabling the dynamics of distribution and clearance of specific anti-tumour antibodies to be compared with normal immunoglobulin. The xenograft model is particularly useful for providing a measure of the potential of the antibody for both diagnostic imaging of tumours and for therapy since it indicates the amount of specific antibody retained by tumour and its residence time. This helps to define its effective half-life and dosimetry for optimal therapeutic administration.

In the present work, described here in preliminary form, we have used the paired distribution method to evaluate a monoclonal antibody (1H12) which is directed against CEA. This IgG-1 antibody has been chosen for its high specificity for CEA and lack of cross-reactivity with human granulocytes and red cells. In this respect it is similar to the monoclonal antibody (MAb 35) described by Buchegger et al. (1983) which is effective in the localisation of colo-rectal tumours.

1H12 was purified from mouse ascites fluid, in yields of 800–1000 μg ml⁻¹, by affinity chromatography on CEA-Sepharose. After radio-iodination by the chloramine T method, to a specific activity of 6 μCi μg⁻¹, 1H12 was shown to bind to MAWI colon tumour cells (see below) by solid phase assay and to purified CEA by double antibody radio-immunoassay and SDS-polyacrylamide electro-

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Our studies have also shown that 1H12 may remain in the tumour at maximal levels at least up to 12 days after injection (Figure 2). During this period a gradual increase in the uptake of antibody by tumour was noted reaching 6.3% of the injected dose at day 9 and falling off slightly by day 12. This latent accumulation may be the result of the continued excretion or re-expression of CEA at the tumour cell surface which has been reported to take place every 6 h (Rosenthal et al., 1980). It would however be expected to be limited by the reduced levels of 1H12 in the blood (Figure 2).

Prolonged retention of a radiolabelled anti-tumour antibody is important since it increases the effective half-life and radiation dose received by individual tumour cells. The results reported here suggest that 1H12 is a strong candidate for therapy trials. Prolonged retention of an antibody in tumour appears not to adversely affect its clearance from normal organs. This is seen with 1H12 where the tumour:blood ratio rose steadily from 0.04:1 at 1 h to over 3:1 at 12 days (Figure 3).

Our results are similar to those reported by Colcher et al. (1984) for an unrelated antibody which remained in tumour up to 19 days after
injection. This contrasts with previous reports using monoclonal antibodies to various tumour markers where optimal tumour localisation was between 3 and 7 days (Mach et al., 1974; Hedin et al., 1982; Buchegger et al., 1983; Herlyn et al., 1983 and Zalzberg et al., 1983).

In conclusion these studies have provided new information concerning the dynamics of distribution for a monoclonal anti-CEA antibody from 1 h to 12 days. It will be important to study the effect of escalating and sequential doses in relation to therapy and the results here should facilitate the design and interpretation of such experiments.

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