

Antibody directed enzyme prodrug therapy - making a complex system work in practice. Richard Begent, Royal Free & University College Medical School, London, UK

In antibody directed enzyme prodrug therapy (ADEPT) and antitumour antibody linked to an enzyme is given intravenously. It localises to deposits of cancer and clears from normal tissues. A prodrug is then given which is activated selectively in the tumour by the antibody-targeted enzyme. The system has exceptional selectivity and potential for high potency because each enzyme molecule can activate many molecules of prodrug. Several enzyme prodrug combinations have been investigated and activity shown in tumour model systems. Clinical trials with antibody to CEA, carboxypeptidase G2 enzyme and mustard prodrugs have shown evidence of tumour response. The system is complex and it is desirable to study the mechanism of action in experimental models and clinical trials so that the principles can be validated and the treatment optimised. Data have been produced on the function of antibody-enzyme molecules, of prodrug and of their biodistribution and function which confirm that ADEPT is a viable approach to therapy in man. These studies have also led to development of the therapy with improved therapeutic results.