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Antibody-Linked Cytotoxic Agents in the Treatment of Cancer: Current Status and Future Prospects

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Abstract

Antibodies against tumor cell surface antigens have been used as selective carriers of anticancer drugs, which themselves lack selectivity. Although such antibodies have been demonstrated in tumor hosts, xenogeneic antitumor sera should provide larger yields of better-defined antitumor antibodies for therapeutic purposes. This review examined factors that influence the immune response to tumor-associated transplantation antigens (TATA) and the methods for rendering tumor cells more immunogenic.

Consideration was also given to techniques for elimination of irrelevant immunoglobulin molecules. These could involve purification of both antitumor sera and TATA fractions for immunization, as well as tailoring of the immunization protocol. Various toxic agents that have been linked to antitumor globulins with retention of agent and antibody activity were tabulated: alkylating drugs, antibiotics, antimetabolites, cell surface agents, protein synthesis inhibitors, and unconventional anticancer agents that selectively convert nontoxic arsenicals or halides into cytotoxic derivatives. The methods by which effective conjugates can be produced and their possible mode of action were described for the different types of agents. Several problems inherent in this modality of tumor therapy include: 1) the necessity of binding therapeutically effective amounts of antitumor agent, 2) ensuring of delivery of drug in active form to target sites, 3) avoidance of host reactions to foreign proteins, and 4) possible emergence of resistant tumor cell populations. Antibody-linked cytotoxic agents may find their greatest use in the eradication of small numbers of circulating tumor cells and micrometastases remaining after removal of primary tumors.

Topic: antibiotics, excretory function, alkylating agents, immune response, antineoplastic agents, arsenicals, cancer, cytotoxin, antibodies, neoplasm, surface antigens, antimetabolites, globulins, histocompatibility antigens, immunization, protein synthesis inhibitors, toxins, immunoglobulins, antibodies, neoplasms, tumor cells, avoidance behavior, serum, micrometastasis, circulating tumor cells, molecule, host (organism)

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