Plantibodies,providing an end to the quest for a safe immunotherapeutic approach for the treatment of cancer

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*Abstract:*A plantibody is an antibody produced by plant that has been genetically engineered with animal DNA. Transgenic plants offer an attractive method for large scale production of antibodies for immunotherapy. These antibodies have no risk of transmitting diseases to humans because they are produced without the need of the antigen or infectious microorganisms. Plantibodies can be made at an affordable cost and easier manufacturing due to the availability and relatively easy manipulation of genetic information in crops.Thus plants offer several advantages as an mAb(monoclonal antibody) production system such as the lack of pathogen, relatively low-cost manufacturing, and ease of production scale-up. Commercial use is not yet legalized, but clinical trials are underway to implement the use of plantibodies for humans as injections. They have kindled the hope for an affordable treatment of diseases such as cancer and diabetes.

Plantibody Production:

There are several methods which are used for the production of plantibodies.

1.Conventional method, which uses transformation and transient expression vector to introduce new genes into a host cell.

2. Plant tissue culture , the most economic and time-saving method for production of antibodies from plants.

3. An experiment on tobacco plant established its breeding and sexual crossing as a method for production of plantibody.

4.Some researches suggest use of transgenic seeds in place of green plant tissue as plants cannot store antibodies for an extended period of time because they contain a high level of proteases which can degrade them(1).

Plantibodies and cancer:

Several works have shown that soybeans, tobacco, potatoes, corn, alfalfa and similar crops are promising alternative for the production of recombinant therapeutic proteins(2,3,4) Antibodies against ovarian, testicular and colon cancer as well as melanoma, B-cell lymphoma and human have already been expressed in transgenic tobacco(5).

The use of mAbs in diagnosis and treatment of various carcinomas has increased in recent years. mAbs against tumor-associated antigens have proven effective in cancer treatment,especially in conjunction with classical chemotherapy and radiotherapy(6,7).By binding to antigen expressed on the surface of cancer cells, mAbs trigger antibody-dependent cell-mediated cytotoxicity(ADCC),which kills abnormal cells(8-10). ADCC requires the presence of tumor cells overexpressing the tumor–associated antigen,efficient binding of the mAbs to this antigen, and effector cells,e.g.,macrophages that recognize mAbs through their Fc receptors(11).

Non-Hodgkin lymphomas (NHLs) represent a serious threat, and some 70 thousands new cases have been diagnosed in USA in 2014, only (12). The majority of NHLs express the leucocyte antigen CD20, an integral transmembrane glycoprotein of 33– 37 kDa, that represents a preferential target for immuno-therapy (13). The mouse/human chimeric anti-CD20 antibody Rituximab (C2B8) is the first antibody-based drug approved for the treatment of patients with recurrent B-cell lymphomas (14). Nevertheless, only about 48% of patients treated with Rituximab respond to the therapy, with< 10% showing a complete remission of the tumour (15). For this reason, there was a need to develop novel antibodies or antibody formats with improved efficacy against B-cell lymphomas (16,17). In recent years, recombinant antibody–cytokine fusion proteins (immunocytokines, ICs) have shown a significantly enhanced efficacy against some types of cancers (18,19).In particular, a dimeric bivalent antibody format based on a scFv-Fc fused to IL-2 (2B8-Fc-hIL2) has been successfully produced in *N. benthamiana* plants by agroinfiltration. The purified, plant-produced 2B8-Fc-hIL2 revealed a CD20 binding activity comparable to that of Rituximab and a full biological activity as confirmed by cell proliferation and ADCC assay(20).

Animal and clinical studies with plant-produced single-chain variable fragment lymphoma vaccines have demonstrated specific immunogenicity and safety. Vaccine antigen consists of a protein containing the patient's tumor-specific sequence, the Id, intended to induce a specific immunological response leading to complete molecular remission and long-term disease-free survival.Antibodies are raised against this antigen in plants which can be used as vaccines. This manufacturing process is reliable and robust, the manufacturing time from biopsy to vaccine is <12 weeks and the expression and purification of antigens require only 2 weeks. The process is also broadly applicable for manufacturing monoclonal antibodies in plants, providing 50- to 1000-fold higher yields than alternative plant expression methods(21).

Six plant-derived antibodies have been developed as human therapeutics, two of which have reached phase II clinical trials. One of these is a full-length IgG specific for EpCAM (a marker of colorectal cancer) developed as the drug Avicidin by NeoRx and Monsanto(22).

Thus I can conclude that plantibodies can be the safest immunotherapeutic approach for both the treatment of cancer as well as for developing vaccines in near future.

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