Review Article

Plantibodies: paving novel avenues for immunotherapy

Abstract

Plantibodies are derived from transgenic plants through genetic engineering technology. This review article emphasizes the significance of plant derived antibodies, various methods for production of transgenic crops, potential application and limitations.

Keywords: plantibodies, transgenic, vaccines

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Introduction

Infectious disease accounts for approximately 25% of all deaths worldwide, 63% of death in children and 45% of the death has been reported from developing countries. Vaccination is one of the effective means in preventing infectious diseases. World Health Organization states that 30million children born every year are deprived of immunization by the modern standards available in the country. The above scenario alerts the need for large scale production of vaccines against infectious diseases so as to increase the global immunization compliance. Strategies for implementation of novel routes for immunization and the production of edible vaccines are the areas of future research work.[1] The concept of green revolution originated in 1960s in response to the prodigious transfer of technology coordinated through agricultural agencies[2] The utilization of transgenic (genetically modified) plants for the expression of therapeutic recombinant proteins is gaining wide acceptance in the scientific community[3] Plantibody is an antibody produced by the genetically modified plants[4] Transgenic plants are the ones, whose DNA is modified by means of genetic engineering technology.[5] The original description of antibodies derived from plants demonstrated the principle of co- expression of two recombinant gene products in plants that were correctly folded and assembled in to a molecule that was functionally identical to its mammalian counterpart.[3] Transgenic plant as expression vectors can revolutionize the large scale production of vaccines, therapeutic and diagnostic recombinant proteins.

Transgenic plants

The genetically modified transgenic crop contains genes that have been artificially inserted. The inserted gene sequence is known as transgene that comes from an unrelated plant or from a different species. The advantage of transgenic crops include improved shelf life, higher yield, improved quality, pest resistance, resistance to a variety of biotic and abiotic stresses.[5] Transgenic crops can be cultivated in mass and various parts of the plant (leaf, seed, fruit) can serve as vehicle for the large scale production of biomedical products for global health.[6]

Plant derived recombinant antibodies

Antibodies are complex glycoprotein that can recognize and bind to target antigens with great specificity. This specific binding capacity allows antibodies to be utilized in the field of diagnosis, prevention and treatment of various diseases.[7–10] Antibodies and their derivatives represent the most important group of biotechnology derived products currently in clinical trials.[11] Plants can express and assemble full length heavy chains with light chains extremely efficiently, to form whole antibody. There is significant similarity between the mechanism of folding and assembling of antibodies in plants and animals; hence plant based expression system are efficient in producing full length immunoglobulin. Research work proves that same glycosylation sites were utilized in both the plant and animal based expression systems, but when compared to murine antibody glycans on the plant antibody were more heterogeneous. The difference in the glycosylation pattern of plantibodies does not have any impact on the binding of antigen or its specificity.[11] In 1990 the first recombinant plant derived pharmaceutical protein-human serum albumin was produced from transgenic tobacco (Nicotiana tabacum) and potato plants. The first scientific journal describing plant derived vaccines was published in 1992.[12]

Advantages of transgenic plants over animals

Production of recombinant proteins in plants and their administration provides an added margin of safety when compared to that produced from transgenic animals.[6] The salient feature of plantibodies is that transgenic crop is free of contamination with mammalian pathogens thus reducing the screening costs for viruses & bacterial toxins.[5] Relative ease of genetic manipulation and reduced economical constraints offer added advantage over transgenic animals. Plants might also provide an ideal vehicle for oral delivery of vaccine antigens owing to the presence of thick cell wall composed of cellulose and sugars that may provide protection against degradation by the gastrointestinal tract.[2]

Methods of production of transgenic plant

Transgenic crops are composed of genes that are derived from species within the same kingdom (plant to plant) or between kingdoms (bacteria to plant). Inserted DNA is slightly modified for efficient expression within the host. The target for new transgenic DNA is the nucleus of the plant cell. Transgenic crops can be generated by the biolistic method (paticle gun method) or by Agro bacterium tumefaciens mediated transformation method. In the gene gun method (Micro Projectile Bombardment) DNA is bound to tiny particles of gold or tungsten which is subsequently shot in to plant tissue under high pressure using gun. Agrobacterium method makes use of soil dwelling bacteria-Agro bacterium tumefaciens. It has the ability to infect plant cells with a piece of its DNA that is integrated in to a plant chromosome, through a tumor inducing plasmid that can control the plant's cellular machinery.[5]

Sources of transgenic crops

Many recombinant proteins have been expressed in several important agronomic species of plants which includes tobacco, corn, tomato, potato, banana, alfalfa, canola, spinach, maize, lettuce etc.[12]

Techniques for purification of Plantibody

i. Filtration

ii. Immunofluorescence

iii. Chromatography

iv. Diafiltration

v. Polymer fusion[4]

Evaluation techniques for plantibody

i. Radioimmunoassay

ii. ELISA & western blot analysis

iii. Immunofluorescence[4]

Applications of plantibody

The achievements of plant derived vaccines and sera can be classsified under two categories

i. Vaccines and antibodies for infectious diseases

ii. Vaccines and antibodies for cancer

List of infectious diseases includes Respiratory Synctial Virus (RSV), HIV, anthrax, diphtheria, SARS and small pox virus.[6] Hepatitis B surface antigen (HBsAg), rabies virus glycoprotein E coli heat labile enterotoxin, Norwalk viral capsid protein are the medically important antigens expressed in the transgenic plants. Plant derived vaccines offers the advantage of convenient storage, elimination of health professionals for their delivery and the use of renewable resources for large scale production.[2]

CaroRx (Dental caries vaccine)

Plant derived antibody that is currently in Phase II clinical trial is a chimericsecretoryIg A/G from the Guy's hospital London was produced from transgenic tobacco plant. The antibody is specific for the major adhesins of streptococcus mutans which are responsible for dental caries. Topical application following oral prophylaxis helps to prevent recolonization by streptococcus mutans and leads to the replacement with harmless endogenous flora.[7]

Monoclonal antibodies

T84.66 is a monoclonal antibody that can recognize carcinoembryonic antigen which is a tumor associated glycoprotein. This antigen is widely used as a tumor markerfoecolorectal carcinoma, breast carcinoma and pancreatic carcinoma. This antibody was produced from transgenic tobacco by agro infiltration.[6]

Immunotherapy

Plantibodies may also be used as topical immunotherapeutic agents. Various cytokines, growth factors, hormones, recombinant enzymes made from transgenic plants are under different phases of clinical trial.[12] Plantibodies reactive with epidermal growth factor were recently licensed to treat epithelial cancers. In the near future these antibodies may emerge as therapeutic tool in the treatment of oral cancer

Limitations

i. Plant derived recombinant proteins or antibodies possess increased risk of immunogenicity or allergenicity.[11]

ii. Transgenic plant and product contamination by mycotoxins, pesticides, herbicides and endogenous metabolites.

iii. Regulatory issues, particularly for therapeutic proteins requiring approval for human use.[5]

Conclusion

Plant biotechnology is a fascinating arena for future research works and molecular farming can even challenge the established production technologies for large scale production of vaccines.Plantibodies serves as an alternative production system for meeting the demand of vaccine production and can be used for global health.

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Conflict of interest

The author declares no conflict of interest.

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