Plantibodies

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Introduction

Antibodies are bioactive molecules and because of their binding properties have varied applications which range from medical diagnosis to therapy, the sensitive detection and removal of environmental contaminants, control of pathogens and industrial purification processes.¹

In 1964 the generic term 'immunoglobulin' was internationally accepted by WHO for proteins of animal origin endowed with known antibody activity and for certain other proteins related to them by chemical structure. Immunoglobulins are synthesized by plasma cells and to some extent by lymphocytes. Immunoglobulins are glycoproteins, each molecule consisting of two pairs of polypeptide chains of different sizes. The smaller chains are light (L) chains (mol.wt-25,000) and larger chains are

ABSTRACT:

Antibodies play an important role in host immune response to pathogens. Hence the recombinant antibodies are used for various purposes ranging from diagnosis to prevention of disease in the form of vaccines. For this purpose of vaccines are traditionally produced in animals and administered to humans and now antibody production in plants has acquired significance as an emerging system for the production of many recombinant proteins that can be used for therapeutic purpose.

Key words: Antibody, Disease Prevention, Vaccines.

heavy (H) chains (mol.wt-50,000). Simplest antibody molecule has a 'Y' shape and consists of two H chains and two L chains.²

These antibodies are part of animal immune systems while plantibody is an antibody produced by genetically modified crops and are produced in plants by transforming them with antibody genes from animals.³ A transgenic plant contains a gene or genes that have been artificially inserted.

The concept of using plants for recombinant antibodies (plantibodies) production (Figure 1) was first reported in 1983.⁴ This combination of antibody and plant engineering, two rapidly advancing technologies, has resulted in the expression of a diversity of molecular forms in different plant species.⁵

Immunization:

Active immunization is the resistance developed in an individual as a result of an antigenic stimulus which is otherwise known as adaptive immunity. Passive immunity is the resistance transmitted to recipient in readymade form i.e., preformed antibodies are administered. There is no antigenic stimulus and recipient's immune system has no active role. The immunity is transient usually lasting only for days or weeks only till the passively transmitted antibodies are metabolized and eliminated. The main advantage of passive immunization is it acts immediately and can be employed in conditions requiring instant immunity.¹ Plantibodies confers passive immunity in an individual and can be used in the form of vaccines.

Transgenic plants expressing antigens are used as an inexpensive oral-vaccine production and delivery system so immunization is possible through consumption of an "edible vaccine" to provide passive immunization and disease prevention.⁶ Genetically engineered plants and plant viruses are also used to produce vaccines against several human diseases for life threatening infections such as diphtheria, cholera and AIDS.⁷

Disadvantages of conventional culture systems:

For mammalian cell cultures:

- The high set-up and running costs,
- The limited opportunities for scale-up and
- The potential contamination of purified recombinant antibodies with human pathogens.

Bacterial fermentation systems:

- The yields of such products in bacteria are generally low because the proteins do not fold properly.⁸

The advantages of plants:

- The low production costs- requiring only traditional cultivation practices and labor.
- Large scale processing possible.
- Scale-up is rapid and efficient, requiring only the cultivation of additional land.
- Unlike transgenic animals, there is no need to maintain a founder herd, because transgenic plant lines can be stored as seed.
- Minimal risks of contamination with human pathogens.⁹
- The ability to introduce new or multiple transgenes by sexual crossing of plants.
- The avoidance of ethical problems associated with transgenic animals.

- Production size is flexible and easily adjustable to the needs of changing markets.
- The general eukaryotic protein synthesis pathway is conserved between plants and animals, so plants can efficiently fold and assemble full-size serum immunoglobulins and secretory IgA.^{10, 11}

Disadvantages:

- Allergic reactions to plant protein glycans and other plant antigens.
- Plant and product contamination by mycotoxins, pesticides, herbicides and endogenous metabolites.
- Regulatory uncertainty, particularly for proteins requiring approval for human drug use.¹²

Studies using mice administered recombinant IgG isolated from plants showed that there were some differences in the glycan groups present on the recombinant antibody but neither the antibody nor the glycans were immunogenic.¹³

Choice of species:

A large number of different crops can be used to produce antibodies including tobacco (*Nicotiana tabacum* and *N. benthamiana*), cereals (rice, wheat, maize), legumes (pea, soybean, alfalfa) and fruit and root crops (tomato, potato).¹⁴

Many factors should be considered before choosing the crop variety. Leafy crops like tobacco generally have the greatest biomass yields per hectare, because they can be cropped several times a year. Tomatoes also have high biomass yield, but production costs are increased.

Antibodies expressed in potato tubers and cereal grains are stable at room temperature for months or even years without loss of stability, while tobacco leaves must be dried or frozen prior to transport or storage to maintain the activity of recombinant proteins. However, extraction of proteins from seeds is more expensive than from watery tissue, such as tomatoes.

The presence of toxic metabolites such as alkaloids in tobacco presents a disadvantage, so edible plants lacking such compounds would be preferred expression hosts. Since most pharmaceutical antibodies will be produced by industry, the costs of production and processing in different crops will have to be evaluated very carefully.⁹

Therapeutic applications

Six plant-derived antibodies have been developed as human therapeutics, two of which have reached phase II clinical trials. One of these is a

Figure 1: Plantibody Production

Figure 2: Caro Rx™

full-length IgG specific for EpCAM (a marker of colorectal cancer) developed as the drug Avicidin by NeoRx and Monsanto. The five remaining antibodies are CaroRx, scFvT84.66, Anti-HSV, 38C13 and PIPP (antiHCG).^[12]

CaroRx

The other plant-derived antibody currently in phase II clinical trials is CaroRx, a chimeric secretory IgA/G produced in transgenic tobacco plants. The antibody is specific for the major adhesin of *Streptococcus mutans*, the organism responsible for dental caries in humans. Topical application following elimination of bacteria from the mouth helps to prevent recolonization by *S. mutans* and leads to the replacement of this pathogenic organism with harmless endogenous flora (Figure 2).

In a preliminary study of Caro Rx™, anti-*S. mutans* antibodies were orally administered to 84

human subjects. Upon the application of SA I/II, monoclonal antibodies prevented the colonization of artificially and naturally implanted *S. mutans*. In addition, protection from recolonization (with just 3 weeks of application) lasted for two years.¹⁵

Since IgG and secretory IgA may play a role in preventing bacterial adhesion to salivary glycoproteins or mucosal receptors, passive immunization and vaccine development against periodontal diseases has been attempted because of the success of passive immunization against *S. mutans*.¹⁶

Conclusion

The advances like plantibodies owing to their advantages are considered as breakthrough in techniques of molecular biology and may offer potential benefits for other fields like medicine in near future.

References

1. Stoger E, Sack M, Fischer R, Christou P. Plantibodies: applications, advantages and bottlenecks. *Curr Opin Biotechnol* 2002; **13**:161-166.
2. Ananthanarayan R and Paniker J: Antibodies-Immunoglobulins. Text book of Microbiology, 8th edition: 2009, Orient longman, 95-101.
3. Jain P, Pandey P, Jain D, Dwivedi P. Plantibody: An overview. *Asian journal of Pharmacy and Life Science* 2011; **1**(1): 87-94.
4. Hiatt A, Cafferkey R, Bowdish K: Production of antibodies in transgenic plants. *Nature* 1989; **342**:76-78.
5. Fischer R, Emans N. Molecular farming of pharmaceutical proteins. *Transgenic Res* 2000; **9**:279-299.
6. Kusnadi AR, Nikolov ZL, Howard JA. Production of recombinant proteins in transgenic plants: practical considerations. *Biotech Bioeng* 1997; **56**:473-484.
7. Moffat AS. Exploring transgenic plants as a new vaccine source. *Science* 1995; **268**:658-660.
8. Chadd HE, Chamow SM. Therapeutic antibody expression technology. *Curr Opin Biotechnol* 2001; **12**(2):188-194.
9. Fischer R, Twyman RM, Schillberg S. Production of antibodies in plants and their use for global health. *Vaccine* 2003; **21**:820-825.
10. Hiatt A, Cafferkey R, Van Dolleweerd C, Drake PM, Ma J. A murine monoclonal antibody produced in transgenic plants with plant-specific glycans is not immunogenic in mice. *Transgenic Res* 2000; **9**(3):187-194.
11. Ma JK, Hiatt A, Hein M, Vine ND, Wang F, Stabila P et al. Generation and assembly of secretory antibodies in plants. *Science* 1995; **268**(5211):716-719.
12. Doran P.M. Foreign protein production in plant tissue cultures; *Curr Opin Biotechnol* 1999; **11**: 199-204.
13. Chargelegue D, Vine N, Van Dolleweerd C, Drake PM, Ma J. A murine monoclonal antibody produced in transgenic plants with plant-specific glycans is not immunogenic in mice. *Transgenic Res* 2000; **9**(3):187-194.
14. Schillberg S, Emans N, Fischer R. Antibody molecular farming in plants and plant cells. *Phytochem Rev* 2002; **1**(1):45-54.
15. Larrick J.W., L. Yu, J. Chen, et al. Production of antibodies in transgenic plants; *Research in Immunology* 1998; **149**(6): 603-608.
16. Malhotra R, Kapoor A, Grover V, Tuli AK. Periodontal vaccine. *Indian J Dent Res* 2011; **22**:698-705.