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Plantipharma Technology: Production of Antibodies, Anti-HIV, Anti-Ebola Virus, Anti-End-Stage Metastatic Melanoma and Other Recombinant Biotech Drugs in Crops

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Biopharmaceuticals are proteins that are produced in different living expression systems through genetic engineering, and used for therapeutic, disease diagnosis or as food supplements.

Biopharmaceuticals have been mostly produced in genetically engineered Escherichia coli (E. coli) microbe, with recombinant human insulin being the first to receive Food and Drug Administration (FDA) approval for its clinical use [1].

Plantipharma is biopharmaceuticals that are produced in plant expression system through plant genetic engineering. When a plantipharma product is produced in plants as an antibody, such antibody is called plantibody [2].

To date, over two dozens of monoclonal antibody-based therapeutics have been approved by the FDA for clinical use and many more are in the pipeline for FDA approval. Due to the effectiveness of the technology to treat diseases and their use to diagnose diseases, the monoclonal antibody technology has been growing at a swift, and their revenues are expected to rise steadily due to their great potentials. For example, the revenues of the six top therapeutic monoclonal antibodies rose from $6.4 billion in 2004 to $11.7 billion in 2006 [3].

It is believed (Matakas et al. [4]) that it is more economical to produce biopharmaceuticals in plants than in *E. coli* because plants use the freely available energy of sun, do not require costly bioreactors for downstream processing, and do not require chemical engineering or fermentation expertise as plants can be easily grown in the fields by farmers. Furthermore, certain biopharmaceuticals cannot be produced in *E. coli* due to their anti-microbial activities [5]. However, their productions are safe to the host plant as its expression system.

A few examples of plantipharma that have been produced to date include human serum albumin, hepatitis B vaccine, anti-diarrhea vaccine, anti- Norwalk virus vaccine, anti-rabies vaccine, anti- pancreatitis, anti- influenza vaccine, anti-cystic fibrosis, non-Hodgkin's lymphoma, anti- pancreatitis, lactoferrin as an anti gastrointestinal infection, anti-malaria artemisinin, cyanoverin-N anti-HIV, interleukin-2 (IL-2) anti-melanoma, human saliva secretory protease inhibitor (SLPI) as anti-HIV drug, and plantbodies.

Certain other Plantipharma proteins have been produced in rice, maize, sunflower, lettuce, alfalfa, chicory plants, banana, and potato. However, tobacco is considered an ideal plant expression system for these proteins because tobacco plants have abundant vegetative biomass, it is easy to grow tobacco in the fields, it has short growing season, and due to its scale up as each tobacco plan can produce hundreds of thousands of viable seeds.

The author's research team recently produced the recombinant human IL-2 (rhIL-2) protein in tobacco leaves, purified the rhIL-2, compared the biological activity of the plant-produced rhIL-2 with that of commercially available *E. coli* produced rhIL-2 on murine splenic CD4+ T-cells, and found the plant produced IrhL-2 to be as effective as that of its *E. coli* produced version. The rh IL-2 is already an FDA-approved immunotherapeutic treatment for end-stage metastatic melanoma and renal cell cancer [4].

Most recently, the author's research team also produced the recombinant human saliva secretory leukocyte protease inhibitor (rhSLPI) in tobacco leaves, purified the rhSLPI and confirmed its biological activities against the serine protease α-chymotrypsin. The human saliva SLPI is well known for its anti-HIV activities. In fact, the reason that HIV in not transmitted through saliva in healthy and young is known to be because human saliva contains SLPI i.e. an anti-viral protein [6]. When produced in large-scale from plants, human SLPI also has potentials to be used as a wound-healing and as a .anti-inflammatory biotech drug [5].

Very recently, three major monoclonal antibodies were produced in tobacco leaves and used as a mixed cocktail serum against the causal protein of Ebola. Also recently, a human Ebola vaccine was produced in tobacco leaves, purified and tested against non-human primates in the form of intravenous immunoglobulin therapy. This vaccine was found 100% effective against non-human primates [7]. This plantipharma vaccine is expected to become soon available for FDA approval for clinical testing. While the human Ebola vaccine triggers the immune system to preventative, but timely (2-3 weeks) produce antibody against the disease, the anti-Ebola mixed cocktail serum can play an immediate immune response treatment as a bio-therapeutic approach for patients who has already been infected with the virus. Therefore, both the mixed cocktail antibody serum and the vaccines are important to be used in the present Ebola epidemic situation.

The Plantipharma system has multiple number of advantages over the *E. coli* expression system, and has recently became the ideal platform for production of recombinant biopharmaceuticals [8,9]. As per Matakas et al. [4], the advantages of plant expression system over the *E. coli* system include: (1) the fact that plants use freely available energy of sun while E. coli growth require chemical energy inputs; (2) Plant scale-ups are easy and almost unlimited, especially in case of tobacco as one tobacco plant can produce hundreds of thousands of seeds; (3) Plants can be grown in the field with minimum "hands-on care" with minimum needs for personnel training as compared to large-scale

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growing of *E. coli*; (4) plants seeds require less processing, storage, and distribution; (5) plants used as Plantipharma have abundant vegetative biomass production; and most importantly (6) plants have a more conserved molecular machinery that usually leads a better folding of complex and multi-component proteins such as antibodies human and animal proteins similar to the protein processing in animals, including humans [10].

Genetically modified plants have been far more accepted by public, and their approval for field production have been less stringent in the United States than in European countries. In the US, the United States Department of Agriculture-Animal and Plant Inspection Services (USDA-APHIS) oversees the regulations for the field testing of genetically modified plants, and FDA issues permits for the clinical applications/treatments of plantipharma biotech drugd.

In the European countries, a program called Pharma-Planta, funded by the European Commission communicates with agencies associated with the development of regulations for genetically modified plants including plantipharma. The Pharma-Planta develops, oversees and monitors specific guidelines for the production of plantipharma productions. It also develops robust risk assessments and risk-management practices to assure the health and environmental impact of the genetically modified plants on human health, ecosystem and the environment [11].

Considering the high costs of *E. coli* produced biotech drugs including monoclonal antibodies, plantipharma can become an economically preferred technology, and also a an ideal humanitarian way of producing vaccines and biotherapeutics in developing nations as developing country farmers already know how to grow and harvest crops in the fields, and purification and downstream processing of plant produced proteins are not difficult.

Among crops, tobacco is considered to be the best plant expression system for production of plantipharma products. It is expected that revenues produced from tobacco leaf produced biopharmaceuticals to become higher than revenues produced from cigarettes manufacturing [4]. Therefore, the author expects quick advancement in plantipharmas technology, especially when tobacco is used as the plant expression system host.

References

1. (1982) Human insulin receives FDA approval. FDA Drug Bull 12:18-19.
2. Goodsell DS (2001) The Molecular Perspective: Antibodies. The Oncologist 6: 547-548.
3. Dimitrov DS, JD Marks (2009) Therapeutic antibodies: current state and future trends--is a paradigm change coming soon?. Methods Mol Biol 525: 1-27.
4. Makatas JD, Balan V, Carson IV WF, Gao D, Brandizzi F, et al. (2012) Plant-produced recombinant human interleukin-2 and its activity against splenic CD4+T-cells. Intl J Life Sci Biotechnol & Pharma Res 2: 193-203.
5. Park SH, Crockett E, Mei C, Nguyen T, Fotoh H, et al. (2014) Production of Biologically Active Recombinant 1 Human Secretory Leukocyte Protease Inhibitor in Plants. European Journal of Biomedical and Pharmaceutical Sci. In press.
6. Shugars DC (1999) Endogenous Mucosal Antiviral Factors of the Oral Cavity. The Journal of Infectious Diseases. Suppl 3: S431-435.
7. Qiu X, Wong G, Audet J, Bello A, Fernando L, et al. (2014) Reversion of advanced Ebola virus disease in nonhuman primates with ZMapp. Nature 514: 47-53.
8. Obembe OO, Popoola JO, Leelavathi S, Reddy SV (2011) Advances in Plant Molecular Farming. Biotechnology Advances 29: 210-222.
9. Sirko A, Vaněk T, Góra-Sochacka A, Redkiewicz P (2011) Recombinant Cytokines from Plants. International Journal of Molecular Sciences 12: 3536-3552.
10. Hein MB, Tang Y, McLeod DA, Janda KD, Hiatt A (1991) Evaluation of Immunoglobulins from Plant Cells. Biotechnology Progress 7: 455-461.
11. Sparrow P, Irwin JA, Dale PJ, Twyman RM, JK Ma (2007) Pharma-Planta: Road testing the developing regulatory guidelines for plant-made pharmaceuticals. Transgenic Research 16: 147-161.

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