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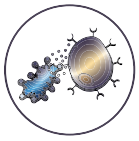

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Editorial

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Is The Time Coming for Plant-Made Vaccines?

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Vaccines have significantly improved human health since their introduction in the last century. They are the most potential weapons to fight the majority of infectious diseases, which are responsible of more than 45% of the total deaths in developing countries [1]. Traditional vaccines are made of a live attenuated or killed pathogen, and either injected or given orally. There are other two categories of vaccines, subunit vaccines and nucleic acid vaccines, being the choice of producing one of them related to factors such as pathogenesis, immunobiology, and epidemiology of the disease [2].

The considerable extension in time of the vaccine production process, its high cost, the stringent conservation conditions required, the need to provide immunization to a high world population with marked differences in packaging, storage, and delivery capacities, and the emerging and re-emerging outbreaks needing a fast response from the pharmaceutical industry have triggered the search for new production platforms of immunogens [3]. As a result, there are numerous reports on the use of yeasts, insect cells, plant cell cultures and transgenic plants for producing recombinant vaccine subunits not only directed to human health but also towards the development of veterinary vaccines [4].

In comparison with the traditional production platforms (microorganisms, animal cell cultures), the plant platform has several characteristic features that had made it a complementary and attractive alternative. Plants could perform post-translational protein modifications and folding typical of eukaryotes with a few differences in glycosylation respect to the animal cell, proteins are not accumulated in inclusion bodies as in bacteria and they do not present biosecurity concerns such as the occurrence of human or animal pathogens, prions, oncogenes or toxins. These advantages have a great influence in the total cost and simplicity of the productive process. As a drawback, there are regulatory concerns regarding GMOs producing biopharmaceuticals that have to be taken into account which are variable according to the legislation of each country. On the other hand, when the plant platform is in a confined placement (e.g.: *in vitro* cultures) the management of the process in controlled conditions (temperature, humidity, photoperiod, sterility) allows the immunogen production in good manufacturing practices and good laboratory practices are a requirement of the pharmaceutical industry. As a consequence, the process would take place in secure facilities operated by trained personnel.

Since 1989, when for the first time it was proposed the use of plants for producing edible vaccines [5], a huge amount of reports has been the proof-of-concept of the platform [6,7]. Those successful expression systems included stable transgenic or transplastomic plants, *in vitro* plant cell cultures, and also the transient expression of the recombinant protein of interest. Some of the efficient models expressed recombinant immunogens against pneumonia and bubonic plague [8], human respiratory syncytial virus [9], non-Hodgkin lymphoma [10], human papillomavirus [11], enteroviruses [12], anthrax [13,14], malaria [15], dengue [16], hepatitis B [17] among others. As for veterinary vaccines, there are promising reports about vaccines against Newcastle disease [18], Bovine diarrhoea viral disease [19], foot and mouth disease [20], and Bovine herpes virus [21].

Nevertheless, when comparing yields of all the available production platforms, plants do not attain yet the high production levels of microorganisms or animal cell cultures [22]. That inconvenience seems partly solved when the expression of the recombinant protein is transiently achieved. On the other hand, plants yield a high amount of available productive biomass hence diminishing the total cost of the productive process. Thus, a considerable effort is being conducted in order to optimize the productivity of the processes in development.

In 2006, the US Department of Agriculture for Veterinary Biologics approved the first vaccine produced in plant cells to protect chickens from the Newcastle Disease Virus (NDV). However, a lot of work has still to be done concerning to dosage, best delivery method and type of immune response elicited for each plant-vaccine system before a plant-made vaccine could be in the market for human use.

The recent news about the FDA approval of the drug Elelyso™ (taliglucerase alfa) is a consequence of development and acceptance of biopharming research which was carried out for more than 20 years. The drug is produced in carrot cells and is used for Enzyme Replacement Therapy (ERT) in patients with Type 1 Gaucher disease.

With many plant-made proteins in the pipeline, and a huge amount of work in the labs, it is expected that in the coming years more recombinant proteins produced in a plant platform will be in the market, and among them, vaccines.

References

1. Arntzen C, Plotkin S, Dodet B (2005) Plant-derived vaccines and antibodies: potential and limitations. Vaccine 23: 1753-1756.
2. Ellis RW (2001) Technologies for the design, discovery, formulation and administration of vaccines. Vaccine19: 2681-2687.
3. Smith J, Lipstich M, Almond JW (2011) Vaccine production, distribution, access, and uptake. Lancet 378: 428-438.
4. Xu J, Dolan MC, Medrano G, Cramer CL, Weathers PJ (2012). Green factory: Plants as bioproduction platforms for recombinant proteins. Biotechnol Adv 30: 1171-1184.
5. Mason HS, Lam DM, Arntzen CJ (1992) Expression of hepatitis B surface antigen in transgenic plants. Proc Natl Acad Sci U S A 89: 11745-11749.
6. Rybicki EP (2010) Plant-made vaccines for humans and animals. Plant Biotechnol J 8: 620-637.
7. Haq TA, Mason HS, Clements JD, Arntzen CJ (1995) Oral immunization with a recombinant bacterial antigen produced in transgenic plants. Science 268: 714-716.

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8. Alvarez ML, Pinyerd HL, Crisantes JD, Rigano MM, Pinkhasov J, et al. (2006) Plant-made subunit vaccine against pneumonic and bubonic plague is orally immunogenic in mice. Vaccine 24: 2477-2490.

9. Belanger H, Fleysh N, Cox S, Bartman G, Deka D, et al. (2000) Human respiratory syncytial virus vaccine antigen produced in plants. FASEB J 14: 2323-2328.

10. Buonaguro F, Butler-Ransohoff J (2010) PharmaPlant: the new frontier in vaccines. Annals of Oncology 21: 2420-2427.

11. Giorgi C, Franconi R, Rybicki EP (2010) Human papillomavirus vaccines in plants. Expert Rev Vaccines 9: 913-924.

12. Chen HF, Chang MH, Chiang BL, Jeng ST (2006) Oral immunization of mice using transgenic tomato fruit expressing VP1 protein from enterovirus 71. Vaccine 24: 2944-2951.

13. Brodzik R, Bandurska K, Deka D, Golovkin M, Koprowski H (2005) Advances in alfalfa mosaic virus-mediated expression of anthrax antigen in planta. Biochem Biophys Res Commun 338: 717-722.

14. Chichester JA, Musiychuk K, de la Rosa P, Horsey A, Stevenson N, et al. (2007) Immunogenicity of a subunit vaccine against Bacillus anthracis. Vaccine 25: 3111-3114.

15. Chowhdury K, Bagasra O (2007) An edible vaccine for malaria using transgenic tomatoes of varying sizes, shapes and colors to carry different antigens. Med Hypotheses 68: 22-30.

16. Coller BA, Clements DE, Bett AJ, Sagar SL, Ter Meulen JH (2011) The development of recombinant subunit envelop-based vaccines to protect against dengue virus induced disease. Vaccine 29: 7267-7275.

17. Guan ZJ, Guo B, Huo YL, Guan ZP, Wei YH (2010) Overview of expression of hepatitis B surface antigen in transgenic plants. Vaccine 28: 7351-7362.

18. Berinstein A, Vazquez-Rovere C, Asurmendi S, Gomez E, Zanetti F, et al. (2005) Mucosal and systemic immunization elicited by Newcastle disease virus (NDV) transgenic plants as antigens. Vaccine 23: 5583-5589.

19. Nelson G, Marconi P, Periolo O, La Torre J, Alvarez MA (2012) Immunocompetent truncated E2 glycoprotein of bovine viral diarrhea virus (BVDV) expressed in Nicotiana tabacum plants: a candidate antigen for new generation of veterinary vaccines. Vaccine 30: 4499-4504.

20. Dus Santos MJ, Carrillo C, Ardila F, Ríos RD, Franzone P (2005) Development of transgenic alfalfa plants containing the foot and mouth disease virus structural polyprotein gene P1 and its utilization as an experimental immunogen. Vaccine 23: 1838-1843.

21. Pérez Filgueira DM, Zamorano PI, Domínguez MG, Taboga O, Del Médico Zajac MP, et al. (2003) Bovine herpes virus gD protein produced in plants using a recombinant tobacco mosaic virus (TMV) vector possesses authentic antigenicity. Vaccine 21: 4201-4209.

22. Fischer R, Schillberg S, Hellwing S, Twyman RM, Drossard J (2012) GMP issues for recombinant plant-derived pharmaceutical proteins. Biotechnol Adv 30: 434-439.

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