Edible vaccines: Go green with molecular farming

Researchers today are in the quest of developing genetically altered plants that could provide protection to infectious diseases. Plant products acting as vaccines would be inexpensive to produce and thus can easily be made available in developing countries. Transgenic plants that express foreign proteins of industrial or pharmaceutical value, represent an economical alternative to fermentation-based production systems[1]. Specific vaccines have been produced in plants as a result of the transient or stable expression of foreign genes[2]. In many countries supported by the World Health Organization (WHO), children receive vaccines against a few preventable diseases. All other vaccines for preventable diseases (like hepatitis-B) which are not included in the Universal Immunization Programme (UIP), are to be purchased locally. The prices of hepatitis-B/DTP combination vaccines vary from Rs 255 to 50 per dose, depending on the manufacturing company[3]. Further, there is no objective justification for WHO's policy support to universal hepatitis-B vaccination in India. The cost of these vaccines is one of the factors preventing the use of vaccination by common man, leaving thousands of children at risk to preventable diseases. The principal costs of most marketable vaccines are in production, packaging and delivery. Vaccines gain further expenses related to the use and disposal of needles and syringes, trained personnel to administer injections, and refrigeration required during shipping and storage. These economic factors prevent widespread vaccination of livestock, poultry and swine against avoidable diseases. Advances in molecular biology of diseases have identified many candidate proteins or peptides that may function as effective subunit vaccines. For some vaccine antigens, transgenic plants may provide an ideal expression system in which transgenic plant material can be fed directly to people as their oral dose of recombinant vaccine. Plants under investigation include banana, potato, lettuce, tobacco, wheat, soybean, rice, spinach, corn, legumes, tomato and *Arabidopsis*[4]. These plants could be used to fight diseases like cholera, measles, hepatitis-B, Norwalk virus, rabies virus and enterotoxigenic *Escherichia coli*[5].

Edible plant vaccines are effective as delivery vehicles for inducing oral immunization. This is because adjuvant for immune response is not necessary, production cost is low, excellent safety and extraction and purification are not required. In addition, there is convenience and safe in storage and transport of vaccines, ease of mass production system by breeding compared to an animal system, reduced need for medical personnel and sterile injection conditions and reduced dependence on foreign supply.

Charles J. Arntzen (Biodesign Institute, Arizona State University) is a pioneer in edible vaccines. The hepatitis-B surface antigen (HBsAg) and Norwalk virus capsid protein (NVCP) expression cassettes were expressed as virus-like proteins (VLP) and their expression profiling was done using plant binary expression vectors pHB117, pMHB, pNV3M110 and pNVT110 in transgenic potato[6]. Banana and potato expressing a transgene for antigen (HbsAg or NVCP), grown commercially in fields, cost less for a single dose compared to vaccines under UIP or hepatitis-B/DTP combination vaccines. As regards the criticism that transgenic crops (generated through nuclear genome transformation) pose many threats including harmful side effects and genetic pollution through inter-generic gene transfer, the chloroplast transformation system has many attractive advantages over nuclear transformation. The plastids of higher plants are genetically semi-autonomous: they have their own genome, transcription and translation machinery. Chloroplast genes are inherited maternally, so gene pollution caused by transgene escape through pollen can be controlled and also the development of weeds resistant to toxin (herbicide) can be reduced[7].

Still some significant challenges need to be overcome before vaccine crops become a boom in reality. However, while access to healthcare remains limited in much of the world and the scientific community is struggling with complex diseases such as HIV and malaria, plant-derived vaccines represent an alluring prospect. The economic and technical payback offered by plant-derived vaccines compared to combination vaccines makes them ideal substitutes for conventional vaccines. Our understanding of the mechanisms of protein targetting and storage will further improve this technology. Above all, social acceptance of this technology in the developing countries will govern commercial achievability of this technology.

1. Ma, J. K.-C., *Nature Biotechnol.*, 2000, **18**, 1141–1142.
2. Giddings, G., Allison, G., Brooks, D. and Carter, A., *Nature Biotechnol.*, 2000, **18**, 1151–1155.
3. Madhavi, Y., *Curr. Sci.*, 2006, **90**, 1465–1469.
4. Tripurani, S. K., Reddy, N. S. and Rao, K. R. S. S., *Afr. J. Biotechnol.*, 2003, **2**, 679–683.
5. Daniell, H., Streatfield, S. J. and Wycoff, K., *Trends Plant Sci.*, 2001, **6**, 219–226.
6. Huang, Z., Elkin, G., Maloney, B. J., Beuhner, N., Arntzen, C. J., Thanavala, Y. and Mason, H. S., *Vaccine*, 2005, **23**, 1851–1858.
7. Daniell, H., Chebolu, S., Kumar, S., Singleton, M. and Falconer, R., *Vaccine*, 2005, **23**, 1779–1783.

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