Unfortunately, the provision and regulation of genetic enhancement technology will not be easy. Unlike healthcare, there are almost no limits to genetic enhancements. There can always be greater resistance to diseases, greater longevity, greater physical prowess and greater mental capacity. Furthermore, the innate desire to advantage one's children is so powerful that affluent citizens may buy reprogenetics elsewhere even if their society bans or limits its use—just as Europeans now travel to the USA to purchase human eggs from selected donors.

The use of genetic enhancement could greatly increase the gap between the 'haves' and the 'have-nots' in the world. A gap between classes within societies may emerge initially. But when the cost of reprogenetics drops, as the costs of computers and telecommunications did, it could become affordable to the majority in Western and other industrialised countries. Ultimately, type II genetic enhancements will become feasible too, and then there really will be no limitations. When this happens, the economic and social advantages that wealthy countries maintain could be expanded into a genetic advantage. And the gap between wealthy and poor nations could widen further with each generation until all common heritage disappears. A severed humanity might be the ultimate legacy of unfettered global capitalism.

When genetic enhancements become affordable, the genetic gap between wealthy and poor nations could widen further with each generation. A severed humanity might be the ultimate legacy of unfettered global capitalism

The only alternative seems remote today and it may never be viable: a single world state in which all children are provided with the same genetic enhancements and the same opportunities for health, happiness, and success. But politics are far more difficult to predict than science.

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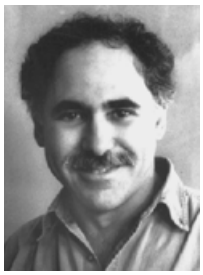

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Vaccine cornucopia

Transgenic vaccines in plants: new hope for global vaccination? • *by Giovanni Levi*

Infectious diseases are still the major threat to life for children and young adults in the third world, causing more than 13 million deaths a year. According to the World Health Organisation, diarrhoeal diseases—such as cholera, dysentery and typhoid fever—alone claim nearly two million lives a year among children under five. Antibiotics to combat these infections exist, but their improper use has largely contributed to the gradual erosion of their efficacy, due to the development of resistance. As David L. Heymann, Executive Director for Communicable Diseases at the WHO pointed out to the US House of Representatives, 'We may only have a decade or two to make optimal use of the medicines presently available', (Heymann, 2000). Also, the price of some antibiotics is still prohibitively expensive for many people in the poorest parts of the world.

If existing treatments fail or are inaccessible, prevention and vaccination become an alternative. It is, therefore, critically important to rapidly develop new strategies of global vaccination. By eradicating smallpox, the WHO has already proven that such a goal can be reached and is now planning to take on polio.

An ideal vaccine for a global vaccination programme should be safe, easy and cheap to produce, temperature stable, and easy to deliver and administer. Effective vaccines against numerous diseases exist, but often do not fulfil all of these demands. A promising alternative could be vaccine production in transgenic plants. European, American and Chinese scientists recently explored the potentials and limits of this technology at a meeting in Erice, Italy, organised by the World Federation of Scientists (http://www.federationofscientists.org/) in collaboration with the European Biotechnology Node for Interaction with China (http://www.ebnic.org/).

Vaccine production in transgenic plants would have several major advantages compared with present technologies. First of all, the cost of production could be reduced by up to three orders of magnitude. For a large-scale production of tomato-based edible vaccines, the cost could be less than one US¢ per dose.

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Proteins stored in plant cells would be stabilised against temperature changes, making it possible to overcome the need for cold storage. Furthermore, the administration of plant-derived edible vaccines would not require the use of disposable needles or specialised medical personnel. And when presented as a banana, a vaccine will find a better welcome from children than a syringe. The low costs of production and distribution would allow poor countries to design their own programmes of vaccination without depending on external financial aid. Eating a fruit, vegetable or a plant-derived product is not in conflict with most cultural habits, and would make plant-based vaccines more generally acceptable. Last but not least, plant-derived vaccines would be free from animal pathogens, such as prion proteins, that might contaminate vaccine preparations derived from animal products.

Research on plant-based vaccines has already left the experimental stage. Most of the technical difficulties—the generation of appropriate vectors and transduction protocols—in the production of vaccines in bananas, tomatoes, carrots and even seaweed have already been solved. The US Food and Drug Administration has approved three human trials of transgenic plants containing subunit vaccines (Walmsley and Arntzen, 2000). The first phase I/II human clinical trial for a plant-derived transgenic antigen was performed in 1997 and proved that the B subunit of *Escherichia coli* heat-labile toxin, delivered in edible potato samples, was capable of inducing an immune response in humans (Tacket *et al.*, 1998). More human phase I/II trials using orally delivered potato-derived hepatitis B surface antigen as a booster for the commercial hepatitis B vaccine are currently in progress. Results from trials using a potato-derived Norwalk virus-like particle as a vaccine against viral diarrhoea have just been published (Tacket *et al.*, 2000). In China, researchers have initiated the production of transgenic plant vaccines against cholera and other severe infectious disorders (including vaccines for veterinarian use).

Although these first clinical trials have shown that edible plant vaccines can induce a modest degree of antibody-based immune response (Tacket *et al.*, 1998, 2000), their capacity to protect against disease still remains unproven. It is important to expand our knowledge of mucosal immunity before plant-based vaccines can be licensed and implemented for wide use to avoid potential problems such as the induction of oral tolerance instead of an immune response. In part, these will be product-specific questions and will relate to the type of protection needed for different diseases.

While regulations for the production of active compounds in plants are being developed in the USA, it appears urgent that similar actions are also taken in the EU. Although several European laboratories are involved in transgenic plant vaccine research, difficulties come from national and regional regulations that do not yet discriminate between transgenic plants as sources of food and as therapeutic agents.


Marietta Schupp

Transgenic plant products could be delivered in their native form or could be the starting material for the production of processed edible vaccines. These could be administered as dried formulations, such as capsules, a powder to add to milk or other liquids, or as a pasteurised purée. But regardless of their form, plant-based vaccines will have to be considered as pharmaceutical products and handled according to the same regulations as any other drug. Appropriate measures, such as the use of seedless or male-sterile varieties and growing in closed green houses, are being planned to prevent mixing of these transgenic plants with the wild-type population.

International agencies are now introducing the concept of plant-based vaccine production to developing countries and are helping to build up 'in country' capacity for vaccine manufacture. Obviously, the transfer of this technology to third-world countries will have to go hand in hand with the development of appropriate training and monitoring programmes to ensure that plant vaccines are used properly. Furthermore, international organisations involved in large-scale vaccination programmes must be prepared to give guidance and assistance for the implementation of this technology. They should also anticipate and prevent abuses, such as the vaccination of populations without informed consent or even military applications. These actions are broadly needed, of course, and are not specific to plant-based vaccines.

A further aspect of the problem is that all infectious diseases currently targeted by edible plant vaccines are transmitted through water and food. The major health problems in less developed countries derive from poor nutrition, and inadequate water supply and sanitation. The result is a high level of diseases, such as hookworm, hepatitis, cholera and chronic dysentery. Although plant-based vaccines can effectively target these ailments, vaccination is only a limited biological and technological solution to a social problem. Even if edible vaccines can help to reduce child mortality in developing countries, they should not be considered a panacea. Investment in vaccines will only succeed if at the same time there is a long-term commitment to promote other components of health care and the general development of the country.

Most scientific and technical problems for vaccine production in transgenic plants have been solved and the first clinical trials to test its safety and efficacy are

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under way. It is reasonable to predict that it will not be long before we can test its efficacy in large-scale immunisation tests. It is now 135 years since Louis Pasteur's first vaccination. Will his initial vision of an infection-free world ripen to completion thanks to a transgenic banana?

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Bahar, Inet (TK-Istanbul)
Bartek, Jiri (DK-Copenhagen)
Bartels, Dorothea (D-Bonn)
Becker, Peter (D-Munich)
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Noegel, Angelika A. (D-Koeln)
Pages, Montserrat (E-Barcelona)
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Peñalva, Miguel A. (E-Madrid)
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Pugsley, Anthony (F-Paris)
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Wilkinson, David (UK-London)
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