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Fields of pharmaceuticals

Two papers in this issue demand the attention of all those interested in developing plant-based pharmaceuticals and vaccines and other therapies to fight infectious diseases. The first demonstrates the successful use of a plant-derived secretory antibody to prevent bacterial infection and the second describes a plant-based oral vaccine. These papers should cause the biomedical research community to take notice because these are not *in vitro* of even pre-clinical tests of principle, but successful human trials that bring affordable, mass produced plant-based immunotherapeutics tantalizingly close.

Over the past ten or twenty years, plant-based medicines have taken a distinctly technological turn. Certainly natural medicines, poultices and oddly smelling infusions, all of which aim to direct an endogenous and often anonymous and assumed plant component to the ailing organ or system, have continued. However, researchers have increasingly worked on extracting, purifying and characterizing plant products for use in mainstream medicine. More recently, and taking advantage of plant engineering technology developed to improve crop yields and disease resistance, the idea of engineering plants to synthesize exogenous products has taken hold. The potential of this technology is very effectively demonstrated in this issue.

Julian Ma and colleagues have already established that plants can be engineered to produce human secretory antibodies. Antibodies are, of course, a front line of defense against pathogens and the idea of mass producing them to treat or prevent infection is not new. This principle of passive immunotherapy was established with the demonstration that topically applied monoclonal antibody directed against the common oral bacterium *Streptococcus mutans* (a major contributor to tooth decay) can prevent it from colonizing the mouth. However, to be successful, very large amounts of antibody have to be delivered to the site of infection and although antibodies can be produced in cell culture or extracted from the milk of transgenic animals, these approaches are unlikely to yield sufficient antibody to support their routine medical use in passive immunotherapy. Plants on the other hand can be cultivated *en masse*.

Now, on page 601 Ma *et al.* show that a monoclonal antibody produced and extracted from genetically engineered tobacco plants can successfully prevent *S. mutans* recolonization of the mouth for at least four months. The practical aspects of their experiment suggest that this approach can be adapted for routine use. The tobacco plants were engineered to assemble a chimeric IgA/IgG secretory antibody. Plants were homogenized—approximately 1 kg of plant material was required to prepare sufficient antibody for one course of treatment—and the purified antibody applied to the teeth of volunteers. All these volunteers had previously harbored oral *S. mutans* but had been treated to remove all traces of the bacteria before application of the antibody. Antibody administered in six doses over an eighteen-day period kept *S. mutans* at bay for four months—the duration of the experiment. Those not receiving antibody showed signs of recolonization by day 21 and complete recolonization by day 88.

The second paper demonstrates important advances not only in the production of immunotherapeutics (in this case a vaccine) but also in the delivery of the vaccine. A globally successful vaccine must not only afford long-term protection but also be delivered easily and cheaply to all those that need it. Often those who need it most are the millions of children in developing countries—countries that cannot support the comparative sophistication of refrigerated vaccine aliquots and needle delivery. Oral vaccines, such as the hugely successful polio vaccine, are the answer. In this respect, Carol Tacket, Charles Arntzen and colleagues present an even more exciting advance, addressing not only the mass production requirements of vaccines but also delivery: Production simply requires growing the plant; delivery is no more demanding than eating it—in this case, a potato.

It was previously known that enterotoxigenic *E.coli* causes diarrhea—a leading cause of death in many developing countries—and that oral immunization with an inactive subunit of the toxic peptide (enterotoxin) results in a protective antibody response. It had also been established that the enterotoxin subunit could be produced in transgenic potatoes and that administration of these potatoes to mice results in partial protection (in the press, *Vaccine*). Here Tacket *et al.* describe a trial involving 11 volunteers that ate either 50 or 100 g of raw, peeled transgenic potato on days 0, 7 and 21 of the study. Ten of these 11 volunteers showed a marked mucosal and systemic antibody response indicative of successful immunization.

We are not likely to be growing vaccines in our vegetable patches for a few years. In the case of Ma *et al.*, an important next step is to address the likely mechanism of the long term protection seen with their passive immunotherapy and to establish just how long this protection lasts. And although Arakawa and Langridge (News & Views; page 550) point out that cooked potatoes retain about half of the enterotoxin immunogen found in the raw vegetable, Tacket *et al.* recognize the limitations of the potato as a delivery vehicle and are working to engineer a banana as a more promising alternative. Nevertheless, these papers are significant advances in plant-based immunotherapeutics, still a relatively small field, and make this area of biomedical research a priority.