

Joel Hochman, Executive Director of the National Foundation for the Treatment of Pain (<http://www.paincare.org>), has a physician's perspective of what effect such a drug might have on what he calls 'the shameful blight' of the current under-treatment of pain. 'It holds the promise of providing a means of blocking pain peripherally, with no impact on cognitive function,' he said. 'Such a medication would eliminate 'opiophobia' and should make every physician willing to treat pain.'

After taking out a full patent on the drug [3], Livett and his team are seeking a commercial partner to take the compound into human trials and develop it into a therapeutic option for sufferers of chronic pain. Given that the acceleration of recovery in injured nerves is a unique property not previously documented for other analgesics, and given that the experiments have been repeated several times, Khalil commented, 'We are extremely confident.'

References

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Edible vaccines against human papilloma virus

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Mice can develop an immune response against human papilloma virus (HPV), the cause of cervical cancer, if they eat potatoes containing a vaccine directed against the disease. A research team has created it for those to whom the vaccine matters urgently – women in developing countries, where 80% of deaths from cervical cancer occur.

'The beauty of an oral vaccine is that you don't need a needle,' said Robert Rose, Assistant Professor of Medicine, Microbiology and Immunology at the University of Rochester Medical Center (<http://www.rochester.edu>), who presented the findings. 'In most cases you don't even need a doctor.'

HPV

Human papilloma virus is one of the most common sexually transmitted diseases, and the cause of virtually all cases of cervical cancer. Not all types of HPV cause pre-cancerous changes, but certain strains of the virus incorporate themselves into cell nuclei and cause the

cell to divide abnormally. Screening can detect cervical cancer, and vaccines are in development, but at present, preventive measures such as safe sex and limiting the numbers of sexual partners are the only sure ways to avoid infection.

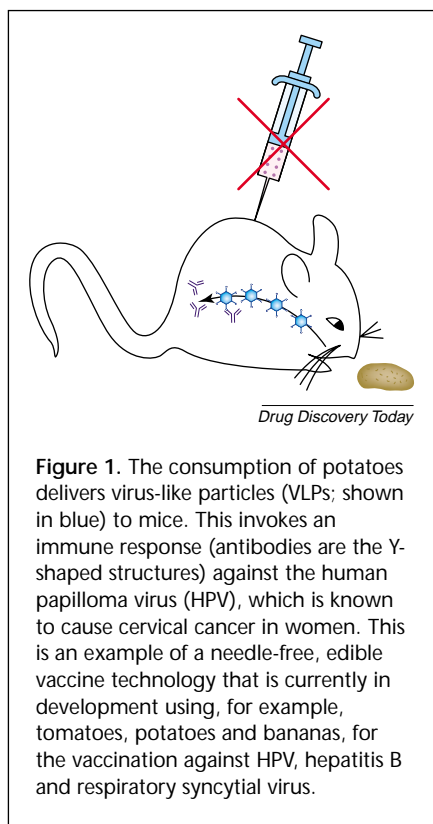
The prospect of delivering vaccines by transgenic fruits or vegetables in developing countries is a 'very attractive' way to prevent cancer in large numbers of women at low cost, commented Martin Bachmann, Executive Vice President and Chief Scientific Officer at Cytos Biotechnology (<http://www.cytos.com>), because powerful diagnostic tools are largely missing in these areas. Introducing novel vaccines to developing countries is a major problem, he observed, largely because of the cost and distribution problems. 'Since raw potatoes may not be particularly delicious to eat, it remains to be seen whether this particular choice of vegetable turns out to be optimal,' he added. 'On the other hand, who would not want to prevent his sexual diseases with a beer and chips?'

VLP technology

The researchers in Rochester began studying HPV in the 1980s, but the latest developments are a collaboration between scientists at Rochester and others at Cornell University (<http://www.cornell.edu>) and Tulane University Health Sciences Center (<http://www.tulane.edu/hsc.cfm>). Rose presented the latest results at the recent fifth annual *Conference on Vaccine Research* in Baltimore, MD, USA [1].

In the early 1990s, the Rochester team isolated the gene sequence of the HPV protein envelope [2], and created virus-like particles (VLPs) that are non-infectious but resemble viral particles. Immunization with VLPs, they found, could induce potentially protective immunity against infection [3]. Oral vaccinations in mice induced serum IgA and IgG antibodies against VLP that efficiently neutralized HPV (type 11) virions *in vitro* [4,5].

In 1997, the group began a VLP vaccination study in human volunteers [6]. The subjects tolerated the vaccine well,



they found, and it induced high levels of binding and neutralizing antibodies. The VLP technology using an injectable form of the vaccine against HPV is currently in Phase II trials; Rose expects that Phase III trials will soon follow at GlaxoSmithKline (<http://corp.gsk.com>).

Recent results

However, of the 230,000 or so women who die of cervical cancer every year, about 80% of them are in developing countries, where annual checkups are almost non-existent and injections are expensive and difficult to deliver. Enter the potato, into which the team inserted VLP-encoding DNA; they later found VLP expressed in the leaves and potatoes themselves.

In preclinical studies, they fed mice the transgenic potato, containing 5 µg doses of VLP, each week for four weeks, followed by a booster after a further two weeks with an otherwise sub-immunogenic oral dose of purified VLPs. Those mice that ate HPV transgenic

potatoes in combination with adjuvant had increased levels of antibodies against HPV (Fig. 1).

Recent results also show that VLPs are immunogenic when co-administered with transdermal patches containing of *Escherichia coli* LT(R192G), a heat-labile enterotoxin (developed by John Clements at Tulane) which contains a mutation that prevents activation and toxicity, producing a non-specific adjuvant [7]. These mice had higher titers of serum antibody to VLP than animals immunized with VLPs alone.

Yes, we do need bananas!

Potatoes are only one, and perhaps not the best, choice of a whole edible cornucopia being considered as vehicles for vaccines: other researchers have garnished bananas, tomatoes, apples, soybeans, corn, and other edibles with vaccines against hepatitis B, respiratory syncytial virus, even tooth decay. Hugh Mason and Charles Arntzen at Cornell University's Boyce Thompson Institute for Plant Biology (<http://www.bti.cornell.edu>) and Arizona State University (<http://www.asu.edu>) are at the forefront of this research [8]. Their own food of choice is the banana, which is 'universally accepted, tasty, and can be eaten uncooked,' said Rose. Eating the edible vehicle raw prevents denaturation of the antigen.

'The [banana] crop could be grown locally in the developing world, where huge numbers of people are at risk from HPV,' he added. To date, three clinical trials of transgenic edible vaccines have been published [reviewed in 8], involving bacterial and viral diarrhoea and hepatitis B.

This technology would also avoid the risk of HIV or hepatitis B infection which accompanies needle vaccination in developing countries. However, the public might be suspect genetically modified foods, Rose observed, and they would have to be strictly contained, and propagated in settings where vaccine dosage levels could be controlled.

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