



Possibilities for Significantly Reducing Various Diseases by Edible Vaccines

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DESCRIPTION

In particular in developing countries, edible vaccines provide exciting possibilities for dramatically reducing a number of diseases like measles, hepatitis B, cholera, diarrhoea, etc. To improve the effectiveness and applicability of this new vaccination technology, however, a number of technical and regulatory obstacles must be overcome.

Malaria

Humans are affected with malaria through the bite of an infected mosquito. It continues to be one of the leading global causes of illness and mortality in people. The WHO estimates that there are more than 225 million cases of malaria worldwide, with 781,000 deaths. Merozoite Surface Protein (MSP) 4, MSP 5 from *Plasmodium falciparum*, and MSP 4/5 from *P. yoelli* are the three antigens currently being researched for the creation of a plant-based malaria vaccine. Recombinant MSP 4, MSP 4/5, and MSP 1 co-administered orally to mice together with CTB as a mucosal adjuvant have been shown by Wang to generate antibody responses that are effective against blood stage parasites.

Measles

Measles is an infection of the respiratory system caused by a virus. In an experiment, it was possible to achieve MV-H (Measles Virus Haemagglutinin from Edmonston strain) antibody titers in mice given tobacco, and secretory IgA was discovered in their excretions. Parenteral and subsequent oral MV-H boosters combined with a prime boost method could result in titers 20 times higher than those needed for human protection. These titers were much higher than they would have been with either immunization given alone. Atypical measles, which can occasionally occur with the existing vaccine, is not caused by the MV-H edible vaccine. Therefore, it might work better to completely eradicate it. Similar experiments in monkeys have been spurred by the results in mice. In addition, measles-

resistant transgenic lettuce, rice, and baby food are being created. 35 g-50 g of MV-H lettuce is sufficient when given with CTB (adjuvant); but, if given alone, a higher dose would be needed.

Hepatitis B

The Hepatitis B virus causes Hepatitis B, a potentially fatal liver infection. The virus is one of the most prevalent human pathogens, with estimates of 400 million infections worldwide. Positive results from the first human trials of a potato-based Hepatitis B vaccine have been published. Any effort to lessen the spread of the Hepatitis B virus requires access to substantial amounts of the vaccine HBsAg because immunization is the only known way to avoid the disease. One potato could contain the required amount of HBsAg for one dosage. Specific antibody concentrations were much higher than the 10 mIU/mL protective limit in humans. The pCMV-S plasmid encoding the HBsAg subtype ayw displayed higher expression in roots than in leaf tissue of the transgenic potato after being cloned into CaMV. Additionally, it was discovered that the transgenic potato's roots expressed the antigen greater than its leaf tissues. Transgenic potatoes do not, however, express enough HBsAg to be used as an oral vaccination. More research is being done to raise the level of HBsAg using various promoters, such as the patatin promoter, and transcription-regulating elements.

Cholera

The small intestine gets infected with cholera, which results in profuse amounts of watery diarrhea. In the underdeveloped world, it contributes to up to 10 million annual fatalities, mostly in children. Studies supported by the WHO have shown the potential for an effective cholera vaccine that also offers cross protection against enterotoxigenic *E. coli*. Plants were modified with the gene encoding the B component of the *E. coli* heat-labile enterotoxin to overcome this limitation (LT-B). When mice were given transgenic potatoes expressing LT-B, serum and secretory antibodies were shown to be induced; these antibodies were

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protective in an *in vitro* bacterial toxin assay. The edible vaccine has already received its first "proof of concept."

Diabetes

India is not an exception to the global rise in diabetes prevalence. Diabetes affects more than 100 million people globally. Juvenile-onset diabetes, commonly known as type I diabetes or Insulin-Dependent Diabetes Mellitus (IDDM), typically affects children and young people and makes up 5%-10% of all cases of diabetes that are officially diagnosed in North America.

Diabetes can be averted in mice by feeding them plants that have been genetically modified to generate a protein associated to the disease, according to research by Ma and Hein at the University of Western Ontario. The concept is based on "oral tolerance," in which the autoimmune system is gradually turned off by instructing the body to tolerate "antigenic proteins." When administered to mice, the pancreatic protein Glutamic Acid Decarboxylase-67 (GAD67), which is connected to the start of IDDM, is known to prevent diabetes. The Canadian team created transgenic potato and tobacco plants that carried the GAD67 gene, fed the plants to non-obese diabetic mice, and the mice spontaneously developed insulin-dependent diabetes. The findings were intriguing while 70% of untreated mice acquired

diabetes; just 20% of pre-diabetic animals fed transgenic plants did so. Additionally, the treated mice displayed elevated levels of IG1, a cytokine-associated antibody that inhibits unfavorable immunological reactions. In order to prevent diabetes in an animal model, it appears that the antigen generated by plants maintains immunogenicity.

HIV

A retrovirus called the Human Immunodeficiency Virus (HIV) causes Acquired Immuno-Deficiency Syndrome (AIDS), a disorder in which the immune system gradually fails, allowing malignancies and life-threatening opportunistic infections to proliferate. First attempts at splicing HIV protein into CPMV for an edible vaccine have been successful. Two HIV protein genes were successfully injected into tomato plants using a needle together with CaMV as a promoter. Polymerase Chain Reaction (PCR) was used to show that the expressed protein was present in many plant tissues, including the mature fruit and second-generation plants. Recently, the Tat protein expression cloned into TMV was effectively inoculated into spinach. Tat antigen was shown to be present in up to 300 g-500 g of spinach leaf tissue per gram. The antibody titers in mice that were fed this spinach and then given DNA injections were greater than those in the controls, peaking at 4 weeks after vaccination.