The Use of Antibiotic Resistance Markers to Develop Biotech Crops

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Scientists use “antibiotic resistance markers” as a tool for recognizing when they have successfully introduced a new gene into a plant cell. Some people have questioned whether cells containing these markers could be transferred to bacteria in people or animals, making antibiotic medicines less effective. Extensive research has concluded that the use of antibiotic resistance markers is safe.

Plant biotechnology works by inserting genes that convey advantageous characteristics into plant cells. When a gene is delivered to plant cells, only an extremely small percentage of cells incorporate the gene into their DNA. In order to identify which cells have incorporated the gene or genes of interest, researchers in the laboratory deliver selectable or screenable “markers” that are coupled with the advantageous gene. Cells that contain these markers can be easily identified in the whole population of cells to which the DNA was delivered. Therefore, by selecting those cells that express the marker gene, researchers are able to identify those few cells that have incorporated the gene of interest into their DNA.

ANTIBIOTIC RESISTANCE MARKERS

One useful form of marker is a gene that confers resistance to antibiotics. These genes are called “antibiotic resistance markers.” Scientists generally expose the plant cells to the specific antibiotic to which the antibiotic resistance gene confers resistance. Because only cells that contain the antibiotic resistance gene can survive, scientists can be sure that some of those surviving plant cells also contain the advantageous gene. This is the only time plant cells are exposed to the specific antibiotic, and this only occurs in the laboratory. Plants derived from these cells neither contain, nor produce, antibiotics.

Antibiotic resistance markers are useful tools in plant biotechnology. They have been used to produce many beneficial pharmaceutical and plant products.

QUESTIONS ABOUT POSSIBLE ANTIBIOTIC RESISTANCE

Some people have asked whether antibiotic-resistance genes could be inadvertently transferred from the plant cells to bacteria in the guts of animals and humans, making the bacteria resistant to antibiotics and thus rendering some antibiotics less useful for treating bacterial diseases. This question has been the subject of extensive scientific and regulatory review around the world, with the consistent conclusion that antibiotic-resistance markers are unlikely to be transferred from the cells of biotech plants to bacteria. An additional conclusion is that even if the markers were transferred, they would be of little relevance to human health and safety. (European Commission, 1996; FDA, 1994; FDA, 1998).

Internationally recognized scientific bodies that have reviewed the use of antibiotic resistance markers include the Organization for Economic Cooperation and Development and the United Nations World Health Organization and Food and Agricultural Organization, as well as regulatory agencies in various countries (Argentina, Canada, Japan, US, and Europe). These agencies have consistently concluded that these genes have never been shown to be transferred from crops derived through biotechnology to bacteria in nature.

BARRIERS TO THE TRANSFER OF ANTIBIOTIC RESISTANT GENES

Several natural barriers make it very unlikely that a transfer of an antibiotic-resistant gene would occur. For example, the DNA contained in food — including the antibiotic-resistance gene — is broken down in the human gut during the digestive process. The digestive system is well adapted to destroy DNA in general. DNA constitutes a source of energy and building materials in our diet, and our digestive tract is very efficient in breaking down DNA into its component parts. Even before the advent of foods derived through biotechnology, humans and animals have been exposed to bacteria that contain antibiotic resistance genes. In fact, the antibiotic resistance genes used in plant biotechnology were obtained from naturally occurring bacteria from human and animal guts or the environment. Even if such a transfer could occur, organizations that have reviewed the use of antibiotic resistance genes have concluded that there would be no significant impact, since these markers already exist commonly in

bacteria in the gut and in soils.

In addition, precautions are taken when choosing genes to be used as antibiotic resistance markers in the development of biotechnology crops. For example:

1) The genes chosen confer resistance to a narrow range of specific antibiotics that are no longer important for medical or veterinary treatment. The most widely used antibiotic resistance marker, nptII, confers resistance to the antibiotics kanamycin and neomycin. These compounds are no longer used to any significant extent in medical applications because they have severe side effects and many bacteria are already resistant to them.

2) Genes are chosen that occur frequently in natural microbial populations to which people are already exposed. It is common to find bacterial strains in the human gut and in soil that are resistant to these antibiotics.

Based on all of these factors, the current use of antibiotic resistance marker genes is considered safe. These genes are unlikely to be transferred to bacteria. Even if they were, the genes chosen are already widespread in nature and would not impact the use of antibiotics in medical or veterinary applications. The biotechnology industry continues to expand the scope of safe and effective tools that scientists can use to develop crops derived through biotechnology, including exploring options for markers that do not use antibiotic resistance genes.

REFERENCES AND FURTHER INFORMATION

U.S. Food and Drug Administration. 1994. Secondary Direct Food Additives Permitted in Food for Human Consumption; Food Additives Permitted in Feed and Drinking Water of Animals; Aminoglycoside 3'-phosphotransferase II. Federal Register 59:26700-26711.

U.S. Food and Drug Administration. 1998. Guidance for Industry: Use of Antibiotic Resistance Marker Genes in Transgenic Plants. Pp. 28.
For more information visit http://vm.cfsan.fda.gov/~dms/opa-armg.html.

ACNFP (Advisory Committee on Novel Foods and Processes). 1996. Report on the use of antibiotic resistance markers in genetically modified food organisms. Clarification of Principles for Decision Making. ACNFP, London.

Nielson, K.M., Bones, A. M., Smalla, K., and van Elsas, J. D. 1998. Horizontal gene transfer from transgenic plants to terrestrial bacteria - a rare event? FEMS Microbiology Reviews 22:79-103.

Prins, T. W., and Zadoks, J. C. 1994. Horizontal gene transfer in plants, a biohazard? Outcome of a literature review. Euphytica 76:1094-1098.

Schlüter, K., Futterer, J., and Potrykus, I. 1995. "Horizontal " gene transfer from a transgenic potato line to a bacterial pathogen (Erwinia chrysanthemum) occurs - if at all - at an extremely low frequency. Bio/Technology 13:1094-1098.

European Commission Scientific Committee on Animal Nutrition. 1996. Opinion on Bt corn CG 176.
For more information visit http://europa.eu.int/comm/dg24/health/sc/scp.

European Commission. 1996. Opinion of the Scientific Committee on Plants on the genetically modified cotton line, insect-tolerant.
For more information visit http://europa.eu.int/comm/dg24/health/sc/scp/out18_en.html.