

## GM foods - a case for resistance?

Over recent months, the UK Press has become pre-occupied with the perceived problems of 'genetically-modified' (GM) foods. The British public has lived with food scares for more than a decade. The GM food debate is the latest, high profile scare. What, then, are the concerns?

Microbiologically, perhaps the most worrying aspect of GM technology is the incorporation of antibiotic-resistance marker genes into plants that enter the food chain. In the USA, regulators take a relaxed attitude to the presence of resistance genes in food. In the UK, the Advisory Committee on Novel Foods and Processes (ACNFP), in common with a number of other EU Competent Authorities, takes a stricter approach. We consider the presence of a resistance gene in a GM plant must be justified on a case-by-case basis. A recent consultation exercise conducted by the USA Food and Drug Administration (1) shows that the problem is now being more widely debated. The ACNFP have responded, voicing concerns about the use of markers that have the potential to impact on human health (2).

It is reasonable to question why antibiotic resistance genes are present in GM plants. To engineer 'desirable' traits into plants, gene cassettes are assembled, in which groups of genes, necessary to confer the trait on a plant, are linked together. Geneticists use antibiotic resistance markers to select for genetic events. Cloning vectors, used to assemble gene cassettes, exploit resistance genes. These may be incorporated into the GM plants. For GM plants where a direct selection may be applied, the resistance genes do not play a role in the plant and need not be incorporated. An example is plants that are resistant to herbicides. Only GM plants will be able to grow following herbicide treatment.

Other cases are more complex. Where there is no direct selection for a rare GM transformation event, then antibiotic resistance markers are exploited. For example, to engineer fruit with delayed softening, altering the properties of enzymes responsible for softening will achieve this. The gene encoding the modified enzyme is linked with a gene conferring kanamycin resistance on the plant. Treating plant cells with this antibiotic will kill those cells that have not acquired the resistance gene and its linked genetic material, in this case the gene encoding the modified enzyme. Alternative markers are being developed.

The safety assessment of GM plants is rigorously regulated in Europe, both by a directive controlling the deliberate release of GM plants into the environment and the novel foods regulation. Plants that are being considered for market approval were engineered several years ago and the problem of antibiotic resistance markers in GM plants will persist for some time.

Kanamycin is an old and very toxic antibiotic. There are safer alternatives and it is unlikely ever to have a significant use in human or veterinary medicine. Other markers are more difficult to justify; for example the *bla*<sub>TEM</sub> gene, conferring resistance to ampicillin and found in many bacterial cloning vectors. This gene has shown a remarkable capacity to mutate, both to increase its spectrum of activity and to resist inhibitors (3). Its presence in plants allows it the opportunity to mutate.

The safety evaluation of GM foods includes an assessment of the risk of transferring resistance genes to the gut flora of humans or animals. Bacteria in this environment have generally been regarded as being unlikely to take up and express foreign DNA. This may no longer be a safe assumption (4). Other microbes are much better at genetic transformation. These include pathogens in the respiratory tract that may express DNA from the dust generated during processing GM plants (5,6,7). If they acquire resistance genes from GM plants, treating their infections would become more difficult. In conclusion, however, remember that resistance is as old as antibiotic therapy (8,9). Although GM plants may pose a small risk that bacteria acquire resistance genes, the most significant threat to antibiotic therapy comes from the inappropriate use of antibiotics in human medicine. Antibiotics are one of the greatest triumphs of this century. It would be a tragedy if we threw away this gift as we approach the millennium. We must all share responsibility to ensure that this does not happen.

## References

- (1) Details of the FDA consultation exercise can be found at <http://vm.cfsan.fda.gov/~dms/opa-armg.html> accessed on July 6, 1999
- (2) 1998 ACNFP Annual Report, Ministry of Agriculture Fisheries and Food, London
- (3) Bush, K. & Jacoby, G. (1997) Nomenclature of TEM beta-lactamases. ***Journal of Antimicrobial Chemotherapy*** **39**,1-3 (For on-line information on mutations of the *bla*<sub>TEM</sub> gene consult <http://www.lahey.org/studies/webt.htm>)
- (4) Mercer, D.K. Scott, K.P. Bruce-Johnson, W.A. Glover, L.A. & Flint, H.J. (1999) Fate of free DNA and transformation of the oral bacterium *Streptococcus gordonii* DL1 by plasmid DNA in human saliva. ***Applied & Environmental Microbiology*** **65**, 6-10
- (5) Bovre, K. & Hagen, N. (1981). The family Neisseriaceae: Rod shaped species of the genera *Moraxella*, *Acinetobacter*, *Kingella*, and *Neisseria*, and the *Branhamella* group of cocci. In ***The Prokaryotes: a handbook on habits, isolation and identification of bacteria. Volume II*** pp1506-1529. Edited by Starr, M.P., Stolp, H., Truper, H.G., Balows, A. & Schlegel, H.G. Springer Verlag, Berlin
- (6) Percival, A., Corkill, J.E., Arya, O.P, *et al.* (1976) Penicillinase-producing gonococci in Liverpool. ***Lancet*** **ii**, 1379
- (7) Phillips, I. (1976) Beta-lactamase producing penicillin-resistant gonococcus. ***Lancet*** **ii**, 656-657
- (8) Chain, E., Florey, H.W., Gardner, A.D., Heatley, N.G., Jennings, M.A., Orr-Ewing, J. & Sanders, A.G. (1940) Penicillin as a therapeutic agent ***Lancet*** **ii**, 226-228

- (9) Abraham, E.P. & Chain, E. (1940) An enzyme from bacteria able to destroy penicillin *Nature* **146**, 837