

Article published in Food Ethics, Autumn '08, pp. 2-4 (www.foodethicscouncil.org).

This much we know...

The science: we have more answers but not enough

Dr Peter Lund is Senior Lecturer in molecular genetics, cell biology and biotechnology in the School of Biosciences, University of Birmingham, and member of the government's Advisory Committee on Novel Foods and Processes.

p.a.lund@bham.ac.uk

The front cover of the international science journal Nature on 24th April shows two rows of papaya, one genetically modified to resist papaya ringspot virus, the other not. The non-resistant variety bears a few solitary fruit and appears ravaged by the virus, whereas the GM plants are far healthier, with large clusters of fruit on each plant.

GM varieties now account for over half the commercial papaya planting on Hawaii, and pictures of this type are part of the stock-in-trade of the agbiotech industry. The big news reported in Nature¹ was the complete sequence of the genome of the transgenic papaya – the first of any commercial GM crop – and the paper reporting this sequence concludes that this “should ... serve to lower regulatory barriers currently in place in some countries”.

Robin McKie, writing enthusiastically in the Observer², says “as Nature's cover shows, the technology seems ripe to help feed a planet whose population will rise from 6.5 billion people, many of them already hungry, to around nine billion by 2040”. But a quick trawl of the web reveals many concerns about this apparent success story – reports of contamination of non-GM plants, questions about the evolution of viruses which may become able to grow on the GM variety, and issues about losses of market share for exporters.

Anyone familiar with the GM debate of the last few years, and the controversies surrounding it, will be tempted to shrug their shoulders and ask what is new. Then, as now, examples of what appeared to be dramatic successes in the development of novel crops were followed by counter-arguments about loss of yield, risks of gene flow to non-transgenic varieties, the effects on the economics of farming, and the short-term nature of GM solutions. So as the potential of GM to help address the growing food problems in the world is revived as a political talking point what, if anything, has changed in recent years, as the GM debate has partly receded into the background?

From a scientific perspective, the most dramatic change is unquestionably the growth in the ability of scientists to analyze the different species concerned at the genetic level. The Nature paper reporting the complete DNA sequence of GM papaya is only one of numerous papers to come tumbling out of laboratories around the world as the costs of sequencing fall and the rates of data generation improve. On the day of writing (14th July) the GOLD (genomes online³) database reports nearly 4,000 genome projects, some complete, some in progress.

Costs have fallen from millions to thousands of dollars per genome, and the time taken to determine a whole genome sequence from years to weeks or even days. Sequencing a whole plant genome is still a serious undertaking, but well within reach of a competent scientific consortium.

On the back of this technical revolution comes a host of other methods which enable scientists to gather large scale data about organisms in ways that were barely thought of ten years ago. One of these is metabolomics: the ability to identify and measure most of the different small chemical constituents (metabolites) present in a given species, tissue, or crop. Another is proteomics, which does the same thing for all detectable proteins.

This at least has allowed one of the controversies about GM to be addressed: that of “substantial equivalence”. This term was initially introduced as a regulatory definition, not a scientific one, and

given the high degree of variability in the composition of non-GM crops, it is a notoriously hard concept to pin down with any rigour. However, published data comparing GM and non-GM varieties of potato shows that using the most precise technical and analytical tools currently available for metabolic and proteomic analysis, the only statistically significant differences seen between them are those anticipated from the particular genetic modification made: unintended consequences of the genetic manipulation are not seen^{4,5}. Whether this is generally true for all GM crops can only be judged on a case-by-case basis, but at least the methods are now available to do such assessments.

However, the indisputable success of technical progress in describing what a GM crop actually is at the genetic level can translate into misplaced over-enthusiasm for the technology as a whole: the high-powered microscope of molecular biology is not the best tool to assess the performance of GM crops in the field, or to pursue concerns about safety to human health or the environment. What indicators are there that would enable us to judge whether the world-wide GM experiment is a success story, a dismal failure, or somewhere in between?

In terms of adoption by farmers, GM appears to be ahead in the argument. The most recent USDA report⁶ shows that GM soybeans in the USA make up 90% of the crop, and cotton and corn varieties engineered to be resistant to herbicides or to insect attack all make up greater than 50% of the USA's acreage. The world-wide acreage of cultivated GM crops has increased at least 50 fold since 1995, and although the USA leads the charge, many countries are close behind, notably China, India, and Brazil⁷. In the USA at least, this increased adoption is driven by the farmers' expectation of improved yield, or at least greater profits. Are these being realized?

A report from the Soil Association⁸ suggested not, although several of the papers and reports cited in this study are quoted selectively or out of context, and do indeed provide what appears to be robust evidence of increased yields or higher profits, at least in the short term^{6,9}. One thing that has not changed in the GM debate, however, is the difficulty in obtaining reliable data from an unbiased source, and given the enormous complexity of the issues involved, it is probably still too early to state whether GM crops represent, overall, a net long term economic benefit for farmers who plant them.

Environmental issues have always been a key component of the GM debate, with one focus being the issue of gene flow from GM to non-GM crops. It is now accepted that measurable gene flow between closely related species occurs at a low level all the time¹⁰ and is not something which is new to GM. The apparent discovery in 2001 of GM material in landraces of maize in Mexico¹¹ has not been supported by subsequent studies¹², but such gene flow can indisputably occur and a small number of cases have been reported where a transgene has been found in a near relative, presumably due to adventitious cross-pollination¹³.

Whether or not the novel gene will become established in the plant over the long term (through the process known technically as introgression) remains unclear, but the potential is certainly there.

Recent studies under controlled field conditions have shown that transgenes can persist through several generations when transferred into weedy relatives, even in the absence of selection, although this causes reduced fertility in the plant¹⁴. A clear consequence of introgression of a herbicide resistance gene would be that weeds related to the crop would not be controllable by use of the herbicide.

There are potential methods available to prevent or minimize the unwanted spread of genes from GM plants to their near relatives, collectively known as GURTs (or genetic use restriction technologies). Many of these are unpopular as they are seen as giving undue power to seed retailers, an example being the infamous "terminator" technology, which renders plants unable to produce seed. These technologies often illustrate the point, made over and over again in the GM debate, that it is not the ingenuity or even the utility of a technology that drives its usage and

Article published in Food Ethics, Autumn '08, pp. 2-4 (www.foodethicscouncil.org).

ultimately its acceptance, but its place and potential impact in the complex network of biological, economic, and social interactions that make up agricultural in the broadest sense.

What of the health concerns about GM food? The Pusztai affair served as both a catalyst and focal point for much of the controversy about GM food¹⁵, and several years on it is perhaps surprising there have still been few feeding trials reported in the scientific literature. In part, this may be because scientists can see little point for doing such studies and publishing them, given that nearly all published data show no effects of a GM diet, and given also the high level of compositional equivalence between GM foods and their immediate biological parents referred to above.

Regulatory bodies such as the Advisory Committee on Novel Foods and Processes see the results of large numbers of animal studies, which in my experience have never reported any significant ill effects, but these are generally neither peer-reviewed by independent professional toxicologists nor published in the scientific literature; moreover, they are often conducted by the very companies who are applying for permission to market the foods that they are testing.

A series of claims about major negative effects of GM soya on rat health have been made by Russian scientist Irina Yermakova, which have received some press and internet attention, but her data are yet to be subjected to any kind of peer review, and concerns have been expressed about how her studies were done¹⁶. Overall, little work has been done over the last few years looking at the effects on animal health of GM food consumption, and in the work that has been done and properly reviewed, effects are generally not seen. An exception is in a series of studies undertaken in Italy and Mexico on the effects of GM soya on mice, which do show evidence of subtle histological differences in some tissues of animals fed on diets which contain either GM or non-GM soy^{17, 18}. These studies are interesting and it is to be hoped that they will be repeated and extended, but it is not yet clear whether the variations seen are more significant than those which would be seen between animals fed on differing non-GM diets.

Where does this leave us? A problem in the GM debate is that while it often becomes polarized around particular issues which are amenable to quantitative testing, it is driven by deeper ideals and beliefs which are not. Thus although in the main the scientific evidence on the health effects and environmental impacts of GM foods gives rise to no obvious concerns, it fails to address the intuitive dislike of these foods which is expressed by many people.

This dislike may result from socio-political concerns that are raised by GM around (for example) ownership, intellectual property, corporatism, and the appropriateness of technological solutions to what are often human problems. It may arise simply from a feeling of intrinsic wrongness about the crossing of species barriers that GM food unquestionably entails.

The legitimacy of adoption of GM in the UK and Europe should certainly not depend solely on the scientific criteria – though these perhaps need to inform the future debate more than they have done in the past – but also on a host of wider human and social questions that science cannot address. At this most important level, the debate remains as complex, and as unresolved, as ever.

Endnotes

1. Ming R *et al.* (2008) The draft genome of the transgenic tropical fruit tree papaya (*Carica papaya* Linnaeus). *Nature* 452: 991-6
2. <http://www.guardian.co.uk/commentisfree/2008/apr/27/gmcrops.food>
3. www.genomesonline.org
4. Catchpole *et al.* (2005) Hierarchical metabolomics demonstrates substantial compositional similarity between genetically modified and conventional potato crops *Proc Natl Acad Sci USA* 102: 14458-14462

Article published in Food Ethics, Autumn '08, pp. 2-4 (www.foodethicscouncil.org).

5. Lehesranta et al. (2005) Comparison of tuber proteomes of potato varieties, landraces, and genetically modified lines. *Plant Physiol.* 138: 1690-1699
6. <http://www.ers.usda.gov/publications/eib11/eib11.pdf>
7. http://en.wikipedia.org/wiki/Genetically_modified_food
8. http://www.organicconsumers.org/articles/article_11493.cfm 10
9. Qaim M and Zilberman D (2003) Yield Effects of Genetically Modified Crops in Developing Countries. *Science* 299: 900 - 902
10. Ellstrand NC *et al.* (1999) Gene flow and introgression from domesticated plants into their wild relatives, *Annu. Rev. Ecol. Syst.* **30** 539–563
11. Quist D and Chapella IH Transgenic DNA introgressed into traditional maize landraces in Oaxaca, Mexico. *Nature* **414**, 541-543
12. Ortiz-García S *et al.* (2005) Absence of detectable transgenes in local landraces of maize in [Oaxaca, Mexico](#) (2003–2004), *PNAS* 102: 12338-12343
13. Warwick, S.I. *et al.* (2003) Hybridisation between transgenic *Brassica napus* L. and its wild relatives : *Brassica rapa* L., *Raphanus raphanistrum* L., *Sinapis arvensis* L., and *Erucastrum gallicum* (Willd.) O.E. Schulz. *Theoretical and Applied Genetics* 107: 528-539.
14. Warwick S.I. *et al.* (2008) Do escaped transgenes persist in nature? The case of an herbicide resistance transgene in a weedy *Brassica rapa* population. *Mol Ecol.* 17:1387-95.
15. http://en.wikipedia.org/wiki/%C3%81rp%C3%A1d_Pusztai
16. <http://www.acnfp.gov.uk/acnfpapers/gmissues/acnfpogmsoya>
17. Malatesta M *et al.* (2002) Ultrastructural morphometrical and immunocytochemical analyses of hepatocyte nuclei from mice fed on genetically modified soybean. *Cell Struct Funct.* 27 :173-80.
18. Magaña-Gómez JA *et al.* (2008) Pancreatic response of rats fed genetically modified soybean. *J Appl Toxicol.* 28 :217-26.