Design for controllability

Hirokazu Tsukaya

Efforts to design genetically modified (GM) crops have focused on minimizing the amount of foreign DNA present in the genome. One reason for this development is to address consumer concerns about unforeseeable effects of either the transgenes or the technology used to introduce them into plant genomes. The latter risk has not been completely assessed, but the former can be dealt with both by minimizing the amount of the foreign DNA inserted and by taking precautionary steps in the selection and adaptation of the transgene itself. In fact, first-generation GM crops contain many unnecessary DNA sequences, such as antibiotic-resistance genes and T-DNA border sequences.

These efforts, however, are not only in response to consumer concerns; they will also be helpful to GM engineers. To make maize tolerant to high sodium concentrations, for example, it only requires the introduction of a salt-tolerance gene. Other DNA sequences, such as antibiotic-resistance genes, are only needed to select transgenic cells. Afterwards, they become unnecessary at best and detrimental at worst, as they preclude the use of the same antibiotic to select for the introduction of further foreign DNA sequences. New methods are already being used to transfer transgenes and cisgenes, and to introduce specific mutations that do not require any marker genes [1]. Along with these efforts, discussions have begun about establishing a precise definition of GM [2,3]. The main argument is that if the plant does not contain any transgenes, it is not subject to GM regulation [3,4].

But are these new endeavours sufficient to prevent potential harm to humans or the environment? The accident at the nuclear reactor in Fukushima, Japan, in March 2011, demonstrated that a disastrous event can overcome even supposedly safe design—the power plant was not built to withstand the double impact of an earthquake and a tsunami. Thus, rather than simply minimizing risk, we need to develop an emergency control that can shut down everything if the system gets out of control. In the case of GM organisms, no matter how they have been created, we need to be able to trace every individual plant and control its biological activity.

In short, we need a tag that identifies a GM crop as such. It is usually possible to identify a GM plant or plant product by using PCR-based analysis to detect the transgene or selection markers. However, new techniques that enable site-specific mutagenesis or the introduction of cisgenes without selection markers would generate 'stealth' GM products that are unidentifiable. Furthermore, private companies do not necessarily share information about the nature of the transgene, the selection markers and the exact technique used to generate a certain plant line, which would also make detection impossible. Thus, an easily identifiable tag would help to identify GM crops no matter how and where they have been created.

This should be a germination control or 'terminator' gene, such as that developed by Monsanto under the moniker 'genetic use restriction technology' (GURT), but which was abandoned for commercial use after severe protests [5,6]. One variety of GURT would make the viability of the transgene dependent on treatment with a specific chemical; it would be easy to design GM plants based on GURT that would stop the production of viable seeds if not regularly treated with the activator compound. As transgenic plants with the terminator gene would not grow without the reagent, the escaping of transgenes into the wild would be highly unlikely. If a particular GM line were found to be harmful to human health or the environment after release, the only necessary action to eliminate them would be to withhold treatment.

Natural organisms cannot be controlled as easily. Invasive species, such as *Caulerpa taxifolia*, have disastrous effects on the ecosystems into which they are introduced, and human efforts to keep them under control have largely failed. Thus, the most important aspect of artificial products is that they must be controllable. The nuclear disasters at Fukushima and Chernobyl happened because humans lost control over the reactors. As with reactors, GM crops are artificial constructs over which we must maintain control.

Thus, the international community, including plant breeding companies, should discuss the possibility of tagging all GM crops with the terminator system. As the tag and the introduced gene must be inseparable, GM engineers must insert any designed transgene with a terminator tag in tandem. Such GM organisms could then be considered as the 'same in kind' as non-GM plants with a similar phenotype after appropriate risk and safety assessment. Of course, possibilities other than the terminator system should be investigated; however, at the moment it is the best option. If the idea of a general tag for all GM plants were accepted, researchers could then improve the tag to make it more compact and safer than Monsanto's terminator technology and give us even stricter control over GM organisms. The terminator is not a terminus, but a start.

CONFLICT OF INTEREST

The author declares that he has no conflict of interest.

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Hirokazu Tsukaya is at the Graduate School of Science, The University of Tokyo, Japan and Councillor for the National Committee for Plant Biology, Science Council of Japan.
E-mail: tsukaya@nibb.ac.jp

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