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DOMESTICATION

Sweet! A naturally transgenic crop

One of the world's most important staple crops, the sweet potato, is a naturally transgenic plant that was genetically modified thousands of years ago by a soil bacterium. This surprising discovery may influence the public view of GM crops.

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Strains of bacteria from the genus *Agrobacterium* have a well-characterized and widely utilized capacity to introduce DNA into plant cells[1]. The transferred DNA (T-DNA) is specified by short left and right border sequences, and is delivered from the bacterium into plant cells by a mechanism that evolved from bacterial conjugation[2]. Essentially, the bacteria have sex with the plant. The bacteria-derived genes perturb plant hormonal balances causing tumour-like galls, and also modify plant metabolism to support bacterial growth, by forcing the plant to produce sugar–amino acid conjugates called opines that can only be used as nutrients by agrobacteria. Previously, using less-refined methods, some evidence was found for *Agrobacterium*-derived sequences inherited in the germ lines of *Nicotiana glauca* and *Linaria vulgaris* species, so heritable genetic modification of plants without human intervention is not new[3,4]. But these plants are not important food crops. Now, Kyndt *et al.*[5] report in *Proceedings of the National Academy of Sciences USA* that during or prior to domestication, *Agrobacterium*-derived T-DNA became incorporated into the genome of one of the world's staple crops, the hexaploid sweet potato (*Ipomoea batatas*).

From small RNA sequencing of cultivar Huachano, and assembly of these into longer fragments, homology was detected to several known *Agrobacterium* T-DNA genes. Sequencing of flanking regions revealed that Huachano carries two surprisingly unmodified T-DNAs, one (IbT-DNA1) with at least four intact *Agrobacterium* genes, and another (IbT-DNA2) containing five. Moreover, IbT-DNA1 is inserted into the intron of a plant F-box gene, possibly disrupting its expression. The F-box family contains hundreds of genes, some of which are involved in central signalling pathways such as phytohormone responses. The genes inside the T-DNA region are expressed at low but detectable levels. The IbT-DNA1 domain, but not IbT-DNA2, was ubiquitously found in the genomes of 291 tested hexaploid sweet potato cultivars, and not found in wild relatives. In another cultivar, Xu781, the T-DNA1 sequence has itself received an insertion of a plant retrotransposon, and the T-DNA at this locus maintains a more complex inverted repeat structure.

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The bacterium that provided the T-DNAs is probably *Agrobacterium rhizogenes,* a strain that induces hairy root proliferation instead of crown galls. It contains two transferable T-DNA regions: TR-DNA corresponds to IbT-DNA1 (harbouring the auxin biosynthesis genes *iaaH* and *iaaM*) and TL-DNA (harbouring the various *Rol* genes) to IbT-DNA2. Unlike the T-DNA1 domain, IbT-DNA2 was only found in 42 out of 204 tested hexaploid cultivars, 2 of 9 tetraploid relatives and a single diploid, among 217 genotypes investigated. At some point in the past, perhaps around domestication, thousands of years ago in Latin America, it is possible that an *Agrobacterium* infection resulted in a sweet potato clone that possessed an interesting trait, which was selected by humans, and somatically propagated as a tuber or root, and subsequently by sexual reproduction.

In one sense, this is nothing new. Horizontal gene transfer is well known to provide an evolutionarily significant source of genetic diversity. It occurs rarely, but its results are widespread. For example, nematodes that colonize plant roots carry bacteria-derived genes for cell wall degrading enzymes that help them to exploit plants[6]. Analysis of multiple genomes revealed that scores of genes from bacteria have transferred into the hereditary material of humans and other animals[7].

Many interesting questions remain. Can the T-DNA delivery event be dated? The bacterial genes are expressed, but are they still functional, and could they complement mutated *Agrobacterium* strains? Can the process be repeated by infecting a wild-relative non-T-DNA-containing Ipomoea genotype with *A. rhizogenes*? Most importantly, do the *Agrobacterium* genes on the T-DNAs confer an agronomically useful trait or phenotype, perhaps in storage root yield, shape, taste or nutritional composition, which might have been selected by early plant domesticators? Could sugar-based agrocinopines or other opines contribute to the taste of sweet potato? Some plant biologists have facetiously suggested that scientists should use CRISPR–Cas9 editing methods to engineer a 'non-transgenic' sweet potato derivative in which T-DNA1 and T-DNA2 have been deleted, in order to render sweet potato acceptable to organic consumers. This experiment would have the added benefit of enabling tests of whether the T-DNAs confer a useful phenotype.

Where does this leave those anxious about GM crops? Hopefully, less anxious. GM proponents have long referred to *Agrobacterium* as nature's natural genetic engineer. No clearer example can be imagined for the safety of the *Agrobacterium*-mediated DNA transfer process than the fact that all cultivated sweet potato genotypes carry an ancient GM event, and that the results of that event have been eaten with impunity for centuries by millions of people. Surely, the time has come for those opposed to GM to desist from criticizing the method of making GM crops, and confine their criticisms to the purposes for which the method is used. While some criticize use of GM to confer glyphosate herbicide tolerance to facilitate weed control, their arguments mostly pertain to the properties (and the vendor) of the herbicide, rather than the GM method itself. Such discussions rarely compare glyphosate with the herbicides it replaced, but rather with some utopian world in which weeds can be controlled without herbicides. Regardless, new genome editing methods that evade GM regulation are already delivering herbicide tolerance[8].

Plant scientists must always be prepared to debate the purposes, economic mechanisms and actors that deliver GM crops, and also the broader question of how to achieve sustainable and productive agriculture. However, Kyndt and colleagues[5], by showing that we have been eating the products of genetic engineering for millenia, demonstrate that there is no longer (if there ever was) any rationale for intense safety scrutiny for every crop line that has arisen from use of GM methods. ❐

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