Genetic Engineers Build a Better Tomato

Green, flavorless, and rock hard, the store-bought tomato is perhaps the cruelest invention of American agriculture. Now hope is in sight for a tomato that tastes

THE DEMISE OF THE EDIBLE TOMATO is one of the great tragedies of American agriculture. Now Calgene Inc., a biotech company in Davis, California, and a research team at the University of Nottingham have taken what could be the first step toward putting flavorful tomatoes back on supermarket shelves with the creation of a genetically engineered tomato that softens more slowly.

What makes most store-bought tomatoes so pale, mealy, and generally flavorless is that they are picked green, refrigerated, and then gassed with ethylene to bring on the red color. Vine-ripened tomatoes are considered too soft for shipping.

Because these genetically engineered tomatoes won't soften and bruise so quickly, they could be left to ripen on the vine, allowing the full flavor to mature, and could then be shipped without refrigeration, predicts Robert Goodman, Calgene's executive vice president for research.

The benefits should also extend to processing, a key interest of Campbell's Soup Company, which supported the Calgene research. The genetically engineered tomatoes could probably be processed at lower temperatures, speculates Goodman, which would mean a higher proportion of solids to liquid in canned tomatoes. The upshot, says Goodman, is that "the sauce would stick to your spaghetti." All this remains to be proved, however. At this stage Calgene has an engineered tomato growing in the greenhouse that seems to have a longer shelf life, but it is not clear how it stacks up in terms of flavor, texture, and firmness.

What the two research groups have done is to turn down production of a key enzyme, polygalacturonase, that is responsible for fruit softening. The enzyme, which is switched on only when the fruit begins to ripen, breaks down cell walls. The English study, led by Donald Grierson of Nottingham and performed in cooperation with ICI Seeds, was published in the 25 August *Nature*. Calgene's work, which is headed by William Hiatt, will be published soon in the *Proceedings of the National Academy of Sciences*.

This work represents one of the early successes with "antisense" RNA technology now being tried in a number of labs. It involves putting a gene into a cell backwards—in the reverse orientation—which then somehow regulates gene expression.

An antisense mechanism operates naturally in bacteria to control gene expression, and for the past few years investigators have been trying to adapt this approach for engineering eukaryotic cells. Success in plants is brand new. Just a few months ago Alexander van der Krol and his colleagues at the Free University in Amsterdam used antisense RNA, for the first time, to turn off an endogenous plant gene—the gene that gives petunia and tobacco flowers their color.

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Tomatoes. *By putting a gene in backwards, two groups have engineered what could be a tomato that tastes like a tomato.*

To create their new tomatoes, both groups took a similar tack: they first cloned the softening gene—or more specifically, its complementary DNA—and then hooked it up, backwards, to a regulatory sequence that would ensure that, once the antisense gene was back in the plant, it would be switched on continuously. Both used a plasmid vector, the Ti plasmid, to carry the antisense gene back into the plant chromosome. Thus, the transgenic tomato has two versions of the gene: the normal one and the antisense, or reverse gene.

Once inside the chromosome, the antisense gene starts making antisense RNA, or backwards RNA, which is complementary to the messenger RNA made by the normal gene. Although the exact mechanism is not clear, it is thought that when the unaltered gene starts pumping out its normal RNA, the antisense RNA binds to it and inactivates it, thus blocking formation of the enzyme. At any rate, it works: in both experiments, expression of the softening gene is turned down about 90%. What's more, the trait is stably inherited.

The antisense technique could have wide applications in plant biotechnology, say the Calgene researchers, who envision other bruise-free fruit and perhaps decaffeinated coffee beans. Calgene has applied for a patent on the technique in the United States and abroad. Grierson's group has also applied for a European patent.

The next step, for both groups, is to figure out exactly what how much the softening process has been retarded and to otherwise characterize the new, transgenic tomato. A key question, says Calgene's Hiatt, is whether fiddling with that one gene has caused any undesirable and unexpected changes in fruit quality.

Calgene will begin field tests in Mexico this fall. Product evaluation should be complete in about 2 years. By that time, the regulatory situation in the United States might be clear as well. Calgene, along with several other plant biotech and food-processing companies, is already working with the Food and Drug Administration to figure out just how to handle transgenic crops.

Grierson's group in England is not planning field tests or marketing at this stage. Instead, they are concentrating on basic studies of the engineered tomato and on figuring out exactly how the antisense gene works—a key step if this approach is to be used to engineer other crops.

■ LESLIE ROBERTS