THERE'S MORE THAN ONE WAY

by Bernard Dixon

A singular feature of theological literature is its capacity to enshrine profound disagreements about the greatest profundities. While differing opinions over the marginal accoutrements of religious belief are hardly surprising, the same can hardly be said about irresolvable conflict over the central essentials. Particularly dizzying is the disagreement between the proponents of an "immanent" deity and those who argue instead for a "transcendent" god. The former insist that the attributes of the Almighty can be glimpsed in the natural order and through human relationships. Spelling out these things is the *whole point* of their craft. For the latter, on the other hand, the deity is remote, beyond reason, and essentially unknowable. That truth, comprehended only by faith, is *the whole point* of religion.

Far be it from me to venture any opinion whatever on matters of this sort, least of all in an organ of science. I mention such oddities solely because I detect signs of similar conflict within a very different debate—that concerning the release of genetically altered organisms into the environment. There was, indeed, tension at the very inception of this debate: The proposition that we can now contemplate with equanimity the dissemination of engineered microbes into the biosphere follows immediately a decade of reassurance firmly founded on the practicalities and regulations of secure containment. That famous image, the Moon-suited figure spraying ice-minus pseudomonads in a California sunrise, says it all. How can this stuff possibly be safe if they have to dress up like that?

Now biotechnologists are into the question of which arguments should be deployed, and how strongly, in the drive to persuade the public that bacteria, viruses, and plants carrying recombinant DNA may be released for agricultural, medical, and other benefits. Here I sense difficulties—a need to sharpen the reasoning and tidy up the philosophy.

Take pest control, and the incorporation of insecticidal protein genes into valuable crops. On two occasions these past months, I have listened to speakers describing the elegant science that has led to the production of transgenic tobacco and tomato expressing modified *Bacillus thuringiensis* toxin. Such plants display enhanced resistance to lepidopteran pests, and clearly could have a bright future. Moreover, their single limitation—the high degree of specificity between toxin and insect—can be turned to public advantage. Here is a way of fashioning pest resistance which, unlike agrochemical warfare, is capable of being targeted with exquisite accuracy. That element of precision and predictability reduces massively the possible dangers associated with a more indiscriminate approach: there will be no unanticipated deaths among unintended targets. Moreover, BT toxins have been exploited as biological control agents for over 20 years without hazard. It's all very reassuring.

An innocent, primed with these arguments before attending one of the sessions during the Biotech'89 conference and exhibition held in London recently, would have been as discomfitted as I am by the world of theology. For here was Donald Boulter, Head of the Department of Biological Sciences at the University of Durham, England, expressing a very different view. He was proselytising for an alternative strategy—one which, in contrast to BT transgenics, makes plants resistant to a wide variety of would-be attackers. And as for two decades of *B. thuringiensis* experience, there was caution: "little seems to be known about the toxicological significance for mankind of expressing the BT gene in crops."

Boulter's work is every bit as ingenious as that of the BT researchers. It began when he was asked to study the heightened tolerance to the bruchid beetle of a particular line of cowpea, *Vigna unguiculata*, identified at the International Institute for Tropical Agriculture in Nigeria. The biochemical basis of this resistance proved to be elevated levels of a particular trypsin inhibitor. Several such inhibitors have since been discovered, and are thought to work by interfering with the insect's ability to digest protein.

What the Durham researchers have now done, in association with the Cambridge-based Agricultural Genetics Company, is to determine the primary sequence of one of a family of four iso-inhibitors. Using synthetic oligonucleotide probes, they selected a full-length trypsin inhibitor cDNA clone from a cowpea cotyledon cDNA library. The coding sequence for the precursor was placed under control of a strong, constitutive gene promoter and transferred to tobacco by leaf disc transformation using *Agrobacterium tumefaciens*.

Exposed to tobacco budworm, some 20 percent of transformants showed enhanced resistance. The inserted gene was clearly working well in these plants—the inhibitor accumulating to at least 0.5 percent of total soluble protein in young leaves. The resistance is stably inherited in a simple Mendelian pattern, and the plants have proved resistant to an impressive range of insect pests. Very recent work by the Boulter group indicates that the relatively high level of expression required for the inhibitor to be effective carries no significant "yield penalty" for the plants. Although only tobacco has been transformed so far, these are exciting findings.

It's clearly odd, though, for one camp to urge that the *whole point* of biological control is its prudent precision, while another camp pursues the entirely opposite broad spectrum approach. But the Durham team does hold a trump card in the safety stakes. According to a paper reporting their results and due for publication shortly in *Pesticide Science*, one of the authors regularly consumes large quantities of cowpea seeds, containing the inhibitor—and of course its gene. I very much doubt whether Fischoff et al. (*Bio/Technology* **5**:807, Aug. '87) have ingested much *Bacillus thuringiensis*.