AGRICULTURAL GENETICS COMPANY

TRYPSIN INHIBITOR CONFERS PEST RESISTANCE

Comparison of bud worm damage to tobacco plants without (*Left*) and with (*Right*) the gene for the cowpea's trypsin inhibitor.

LONDON—In the latest insult to the innocent, if not harmless, tobacco plant, British plant scientists funded by Agricultural Genetics Company (AGC, Cambridge, U.K.) have endowed it with a gene from the cowpea. The gene encodes a protein that is a natural inhibitor of insect trypsin (a digestive enzyme), so the engineered tobacco plants are relatively pest resistant.

This approach, while similar in concept to the introduction of the gene for *Bacillus thuringiensis* toxin into plants, has the advantage of producing a much broader spectrum of resistance, according to AGC's director of research and development, Paul Boseley.

The inhibitor itself was isolated by Donald Boulter and his team at the University of Durham from a variety of cowpea (the name AGC prefers to the more common American name, black-eyed pea) bred by the International Institute for Tropical Agriculture in Nigeria to combat the problem of stored beans being attacked by beetles. After the inhibitor had been identified two years ago, AGC agreed to fund the cloning of its gene and attempts to express it in tobacco. The company holds patents on the gene and its use; Durham will benefit through a royalty agreement.

Much of the research was carried out by Vaughan Hilder, a company employee attached to Durham. But the transformation work was performed at the Agricultural and Food Research Council's Plant Breeding Institute (Cambridge, U.K.), using one of its agrobacterial Ti plasmid vectors, in which the inhibitor gene is placed under the control of a constitutive cauliflower mosaic virus promoter.

It will be five years before resistant plants are available commercially, guesses Boseley. At present, the gene exists only in immature tobacco plants, and there is no proof—although every expectation—that it will be stably inheritable. Nor is it yet certain that the inhibitor expressed in plants has as broad an action against insects as it does when added directly to their feed. Lack of transformed plants has so far limited tests to the bud- and army worm. Both fail to grow and eventually die when fed on the plants.

One problem that would no doubt have to be faced were food crops to contain the gene is whether the insect trypsin inhibitor has any inhibitory action on human trypsin. Boulter says that in Africa cowpeas are sometimes eaten raw without apparent harm, and that rat feeding experiments have not shown the inhibitor to be harmful either.

For the commercial success of the project, AGC is banking on the adaptability of the technology to major monocotyledenous crops; the rice cut worm, the corn ear worm, and the boll weevil are among the pests that are sensitive to the trypsin inhibitor, at least when it is fed to them. Prospective commercial partners in rice, corn, and maize will need to be able to offer seed marketing facilities, since AGC has none. The company's main hope in that direction lies in the U.K. government's long-promised sale of the National Seed Development Organization together with a part of the Plant Breeding Institute. This overdue sale offer, however, could be delayed indefinitely by an early general election. For such a purchase, Agricultural Genetics Company would need to raise additional funds; its initial capitalization, completed in 1984, was for $24 million.

Meanwhile, the company has moved a step closer to an involvement in plant breeding as a result of its recent negotiations with the Agricultural and Food Research Council. Set up in 1983 with first rights on discoveries emerging from the council's plant biotechnology program, AGC has now secured an extension of that agreement until 1993 and has gained the right to breed plants that result from the research, although not to the exclusion of other U.K. plant breeders. **—Peter Newmark**

ASM MEETING

BLUEPRINT FOR PROTEIN DESIGN

ATLANTA—The subtitular question before an overflow session here on "The Second Half of the Genetic Code" was "Is Molecular Genetics Ready for Protein Structure Technology?" The answer, it seems, is "almost."

The seminar at the American Society for Microbiology's 87th annual meeting was sponsored by the National Institutes of Health's Microbial Genetics Study Section—in response, said convenor Gerald Liddel of NIH, to a spate of proposals for experiments in site-directed mutagenesis which would, the proposers all assure NIH, elucidate the principles of protein folding and clarify the relationship between function and primary structure.

In closing the seminar, Charles Yanofsky (Stanford University, Stanford, CA) offered a highly schematic analysis that attributed the current advances in protein engineering to nine technologies:

- new cloning techniques, especially those of cloning full-length cDNA;
- rapid methods for DNA sequencing;
- better algorithms for deducing protein sequences from DNA sequences;
- the emergence of protein sequence data bases which rapidly identify proteins of similar primary structure, and suggest where to look for similarities of function;
- improved understanding of prokaryotic and eukaryotic gene regulation and expression;
- advances in chemical, enzymatic, and synthetic techniques for *in vitro* mutagenesis;
- improvements in X-ray crystallography, including better strategies for