they don't work against type B strains, which account for about 30% of infections. And flu strains that are resistant to both drugs already have cropped up, says Ruben.

He and others caution that strains resistant to neuraminidase inhibitors also could arise if the drugs came into wide use. "If they were available over the counter year in and year out, that would [foster] the resistant strains," says Ruben. Gilead's Kim counters that the resistant strains are less likely to appear with the new antivirals because their target, neuraminidase's docking site, is virtually identical among different flu strains. To become resistant to the drugs, the virus would have to acquire genetic mutations that affect the docking site—changes that would be more likely to cripple the mutated strain than to give it a selective advantage. But Ruben points out that Glaxo researchers have already shown in the lab that flu viruses can develop resistance to their compound. "Resistance will be an issue, but nobody knows yet how important an issue it will be," says Alan Kendal, an epidemiologist and flu expert at the Emory School of Public Health in Atlanta.

Even if resistance doesn't develop, Kendal worries that the new drugs could end up boosting the overall number of flu sufferers by discouraging people from getting vaccinated prior to the flu season. Many of those infected might be able to limit the severity of their illness by taking antiviral compounds, but most would pass along the virus to other people before they experienced symptoms and took an antiviral. For that reason, he predicts, even if a magic bullet for the flu does make it to market, public health officials are likely to keep their focus on prevention.

–Robert F. Service

PLANT RESEARCH

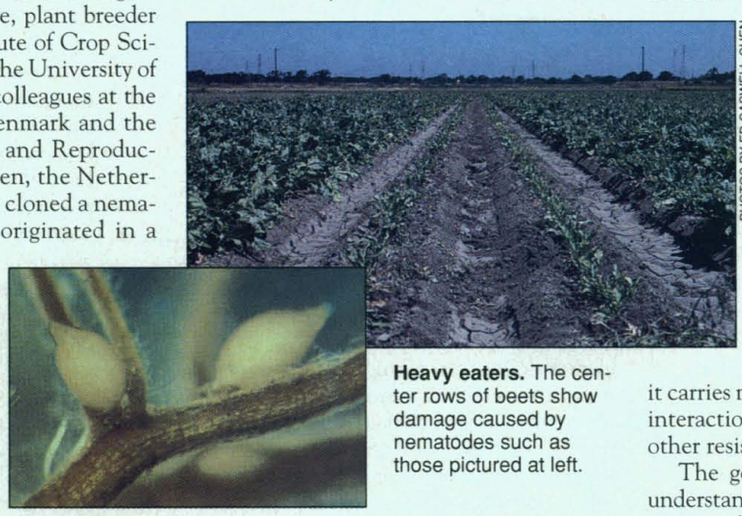
First Nematode-Resistance Gene Found

Nematodes are hearty eaters. Although barely visible to the human eye, these voracious threadworms annually destroy about $100 billion in crops worldwide. Some have a particular taste for sugar beets, while others also enjoy munching on a wide variety of other crops, including oilseed rape and cauliflower. And because classical plant breeding has so far failed to produce commercial crop varieties that resist the onslaught, protection relies largely on toxic chemical pesticides or crop rotation. But that could soon change.

On page 832 of this issue, plant breeder Christian Jung of the Institute of Crop Science and Plant Breeding at the University of Kiel, in Germany, and his colleagues at the University of Aarhus in Denmark and the Center for Plant Breeding and Reproductive Research in Wageningen, the Netherlands, report that they have cloned a nematode-resistance gene that originated in a wild beet plant. In the past 2 to 3 years, researchers have identified more than a dozen genes that make plants resistant to pathogens, including bacteria, viruses, and fungi (*Science*, 23 September 1994, p. 1804). But the new gene, called *Hs1*$^{pro\text{-}1}$, is the first one for resistance to an animal pest. The work "rounds out description of the range of plant genes that confer resistance to disease," says Purdue University plant biologist Gregory Martin.

The sequence of the protein encoded by the new gene provides a few clues to its function: Like the proteins made by other resistance genes, it may detect chemical signals made by the pest and then trigger an as-yet-unknown defensive reaction. But even before the resistance mechanism is known, says Jung, the gene might be engineered into major commercial crops, such as oilseed rape, to create resistant varieties.

In hunting down the gene over the last 8 years, the team transformed adversity into opportunity. Plant breeders have long tried to capitalize on the natural nematode resistance of plants such as wild beets by breeding them with susceptible crops such as the sugar beet, but the hybrids only had partial resistance and were unsuitable for commercial use. Out of that failure, however, came a clue to the location of the resistance gene. Jung's team and the Netherlands team found that some of the hybrids carried the nematode-resistance gene from wild beet on a tiny chromosomal translocation formed by two chromosomes breaking and joining abnormally. This was "a very, very fortunate find," says nematologist Valerie Williamson of the University of California, Davis, as it allowed researchers to focus their gene hunt on a small bit of the wild-beet genome that carried the breakpoint.



PHOTOS BY ED CASWELL-CHEN

Heavy eaters. The center rows of beets show damage caused by nematodes such as those pictured at left.

That lucky break, together with a particular marker sequence that was always inherited with nematode resistance, ultimately helped Jung and his colleagues home in on a candidate gene. They only found the suspect DNA in resistant plants, for example, and the predicted sequence of the protein it encoded revealed some motifs, such as repeated sequences rich in the amino acid leucine, previously found in other resistance genes. The team eventually confirmed its finding by transferring the gene into susceptible beet roots in culture and showing that the transformed roots resisted damage by nematodes.

The researchers found that nematodes trying to feed on the resistant roots were thwarted when their feeding structures degenerated. What causes that degeneration is unclear, but the products of other resistance genes have turned out to be receptors located in the plant cell membrane that set off a defensive reaction when tweaked by some product made by the pathogen. Similarly, the researchers suggest, the Hs1$^{pro\text{-}1}$ protein may serve as a membrane receptor for compounds injected into root cells by the nematode's piercing mouthpart. They note that the protein's overall structure suggests it resides in the membrane, and that the leucine-rich repeats it carries may be involved in protein-protein interactions between host and pathogen in other resistance proteins.

The goal now, besides getting a better understanding of the resistance mechanism, is to use the gene to create new lines of resistant sugar beets and other crops. Jung cautions that that may not be easy, mainly because it may be difficult to regenerate whole plants from the cells used for the gene transfers. "Sugar beet is a notoriously recalcitrant variety," he notes. Also, there are various strains of nematodes, and a gene that offers resistance to one may not work against others. Still, Jung has organized a large team of plant biologists to work on the problem and expects to tame nematodes' appetite: "We hope to have disease-resistant plants in the lab by the end of the year."

–Anne Simon Moffat