Putting the Moves on Plant Viruses

The biotech industry aims to use plant viral "movement proteins" in the design of new gene-transfer systems

ESPECIALLY IN HIGH FLU SEASON, THE VIruses that specialize in animals like us seem to have it easy compared to their cousins who specialize in infecting plants. Flu and cold viruses clearly have no trouble spreading through the cells lining the nose and throat, creating their own brand of misery. But for your average plant virus, every target cell is encased in tough cellulose walls. So how have plant viruses solved their problem? They make special "movement proteins" that serve as molecular tugboats, easing the spread of viral particles from cell to cell.

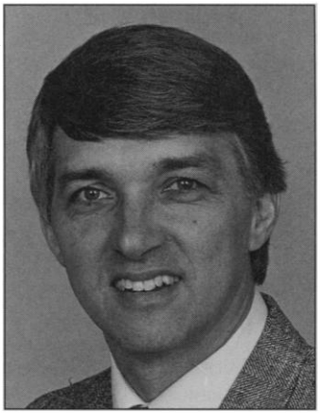
This isn't news to plant virologists who have studied movement proteins for about 10 years, but recent work in several labs has suggested that the proteins may be just as valuable to the biotech industry as they are to plant viruses. Researchers are using them to design novel viral vectors that can easily put new genes into plants, where they will be expressed at high levels, thereby turning the plants into factories for making pharmaceutical proteins and industrial enzymes. A demonstration project completed last summer in which scientists at Biosource Genetics Corporation of Vacaville, California, and the University of California, Riverside, produced the protein tricosanthin, an experimental AIDS drug, in field tobacco, has already shown that the approach works.

The plant virus vectors might also be useful in agriculture for genetically engineering new strains of crop plants. In particular, they might be valuable for the cereals, which are hard to genetically engineer by current methods. And the work might even allow the viral proteins to be turned against the viruses, by aiding in the development of virus-resistant plants.

Interest is now running high. About a dozen industrial and academic groups in the United States and Europe are working on the proteins. And the European Economic Community has announced plans for a consortium, including labs in the United Kingdom, France, and Spain, that will be putting about $1 million into movement protein research.

If all this plant research flowers, it will confirm the prescience of early workers in the field, starting with Joseph Atabekov, a plant virologist at Moscow State University who suggested in the late 1970s that special molecules are needed for plant viruses to spread throughout infected plants. But it wasn't until the early 1980s that researchers began to get an idea about what the special molecules might be from work on tobacco mosaic virus (TMV). The genome of TMV, which is the best characterized plant virus, encodes only four known proteins. And in 1982, Milton Zaitlin of Cornell University used a mutant TMV strain that can infect plants systemically at low temperatures, but not at high ones, to produce evidence pointing to one in particular, known as the "30-kilodalton protein," as the movement protein.

Another milestone came in 1987, when Roger Beachy's group, then at Washington University in St. Louis, demonstrated in living plants that the protein is indeed needed for TMV transport. They did this by introducing the gene for the protein into the plants and showing that a mutant TMV strain that is normally unable to spread could then move through the plants.



Plant tinkerer. *Scripps Institute's Roger Beachy.*

More recently, researchers have been focusing on finding out how movement proteins work. In 1989, for example, Beachy, who is now at the Scripps Research Institute in La Jolla, California, and William Lucas of the University of California, Davis, showed that the TMV movement protein accumulates in the plasmodesmata, thin strands of cytoplasm that extend from plant cells through the cell wall, forming narrow bridges between cells. Just how the movement protein facilitates transport of TMV through the plasmodesmata is unclear, however.

But much of the recent research has been aimed at putting the movement proteins to work in the biotech industry. When the Biosource Genetics-Riverside group decided to use TMV to make tricosanthin in tobacco plants, for example, they were careful to ensure that the gene for the movement protein remained intact. That enabled the virus to spread swiftly throughout the plants and commandeer the plants' own protein-synthesizing machinery to make tricosanthin. "If you don't have movement protein, you won't get the high levels of protein expression needed for commercial production," says company vice president Laurence Grill.

Although Grill declines to reveal how much tricosanthin the infected plants produced, he says that an acre of them would be more valuable than an acre of ordinary smoking tobacco. He also notes that TMV is not a serious pathogen. At most it reduces tobacco production by 10%—the tricosanthin-producing plants appeared green and healthy—and the small yield reduction is not important when the goal is to make valuable pharmaceutical or industrial proteins. Nor did the company have any problems getting the necessary regulatory approvals for a field trial of the infected plants.

Movement proteins may also be used to widen the host range of TMV so that it can infect monocot plants, such as cereals, as well as dicots, such as tobacco. In the past year, Beachy and Curtis Holt, also of Scripps, have put the gene encoding the movement protein of a monocot virus into the TMV genome, giving it the ability to infect orchids, which are monocots. And Beachy predicts that a year or two of tinkering with the modified TMV will enable the researchers to use it to put new genes into more economically important monocots, including cereals. This work is currently limited to the lab, but when the time comes for field trials it's a fair bet that a genetic manipulation that widens the range of a virus will be subjected to greater regulatory attention than the Biosource Genetics vector.

While much of the applied work has been devoted to using movement proteins to enhance viral spread in plants, it might also be possible to use them to develop virus-resistant plants. That might be done, Beachy says, by creating plants carrying a mutant movement protein that can find its way to the plasmodesmata and block the function of the normal movement proteins produced by invading viruses. In as yet unpublished work, the Scripps group has identified a mutant movement protein that may do the trick. Thus movement protein research might offer another weapon that can protect plants against disease as well as provide new methods of producing proteins for agriculture, medicine, and industry.

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