Editorial

Subviral Pathogens: Viroids and Prions

T. O. DIENER
Plant Virology Laboratory, ARS, USDA, Beltsville, MD

Until about 12 years ago, it was generally believed that all infectious diseases of plants and animals are caused either by microorganisms (bacteria, fungi, etc.) or by viruses. Since then, disease-causing agents smaller and less complex than viruses have come to light. First, in 1971 the potato spindle tuber disease was shown to be caused by small, unencapsidated molecules of autonomously replicating RNA. Today, about a dozen diseases of higher plants are known to be caused by similar subviral agents for which the term *viroid* has been adopted. Second, the agent of a neurological disease of sheep and goats, scrapie, which has long been known to possess unusual properties, has recently been shown to contain an essential protein and is therefore fundamentally distinct from viroids. The scrapie agent appears to be even smaller than viroids. For this and similar pathogens, the term *prion* has been proposed.

The smallest known viruses capable of independent replication contain genomes of a size corresponding to a molecular weight of about 1 million; it therefore appeared reasonable to assume that this size represents the minimal amount of genetic information required for a virus to code for virus-specified products and to subjugate the host cell's metabolism. Indeed, viruses with smaller genomes, although known, are not capable of independent replication but require certain functions provided by a helper virus present in the same cell. In the absence of helper virus, no replication of these "defective" or "satellite" viruses takes place.

Viroids, on the other hand, introduce into their host cells a far smaller amount of genetic information than do viruses, yet their replication does not require the assistance of detectable helper viruses. Because of this, the discovery of viroids came as a surprise and was greeted, initially, with considerable skepticism. Fortunately, evidence for the correctness of the viroid concept soon became indisputable, and today several viroids are among the small number of pathogens whose molecular structures are completely known.

Three viroid groups can be distinguished on the basis of nucleotide sequence homologies: 1) the potato spindle tuber viroid (PSTV) group, to which also belong the citrus exocortis, chrysanthemum stunt, tomato planta macho, and tomato apical stunt viroids; 2) the coconut cadang-cadang viroid; and 3) the avocado sunblotch viroid.

In contrast to our extensive knowledge of viroid structure, functional aspects of viroid-host relationships are still largely unknown. Consensus exists, however, that viroids 1) are not translated into viroid-specified polypeptides, 2) are replicated by host enzymes from RNA templates, and 3) are replicated by a rolling circle-type mechanism with the circular viroid serving as a template, resulting in the synthesis of oligomeric strands of the viroid and its complement.

The most serious agricultural problem known to be caused by a viroid is the coconut cadang-cadang disease, which has killed millions of palm trees. Most other viroid-incited diseases of crop plants either cause relatively little damage or can be kept under control by sanitary measures. Modern rapid, sensitive, and specific diagnostic methods that make use of recombinant DNA technology and solid-state nucleic acid hybridization are beginning to be implemented and will further lessen the danger of large-scale losses caused by known viroids.

Viroids, however, pose another threat to agriculture. All known viroid diseases of crop plants appear to be of recent origin (20th century), and some evidence suggests that these diseases originated by chance transfer of viroids from reservoirs in wild plants in which, because of lack of symptoms, the viroid had remained unnoticed. Likely, such transfers have occurred throughout history, but only modern agricultural practices, such as widespread monoculture, enabled the viroids to maintain themselves in the crop plants. Support for this theory of disease origin has come from the isolation of a viroid, different in its nucleotide sequence from any previously known viroid, from many healthy looking specimens of an ornamental plant that is widely sold at commercial nurseries in the United States. This plant, *Columnea erythrophae*, an epiphyte from the tropical rain forests of Costa Rica, is commonly grown in hanging baskets close to windows. In potato, the *Columnea* viroid causes a disease resembling spindle tuber disease but more severe. The *Columnea* viroid thus provides a scenario whereby a new disease could suddenly appear seemingly out of nowhere, because no suspicion would fall on the symptomless *Columnea* plant from which the potato disease would have originated.

Furthermore, the tomato planta macho viroid, which is the cause of a new and destructive tomato disease in Mexico, occurs naturally and harmlessly in several species of wild plants in the geographic area where the disease had first been noticed. These observations suggest that knowledge of the nature and extent of viroid reservoirs in wild plants is essential if one wishes to prevent the sudden appearance of new and possibly catastrophic crop diseases in the future. In this endeavor also, nucleic acid hybridization tests will be invaluable.

What about prions? So far, these have been identified only in animals, but no compelling reasons exist why similar pathogens could not occur also in plants. Thus, I believe plant pathologists should be aware of their existence and characteristics.

Today, prion research is at the stage that viroid research was in about 1970. As was the case then with the potato spindle tuber agent, properties of the scrapie agent have to be deduced indirectly by virtue of its biological activity, because it cannot yet be recognized as a physical entity. Molecular biologists, particularly, are not too comfortable with such an approach, so it is not surprising that recent results with the scrapie agent are not universally accepted. It must be remembered, however, that the essential physical/chemical properties of the viroid were established long before it could be recognized as a physical entity.

The recent work with the scrapie agent clearly shows it is fundamentally dissimilar to both viruses and viroids. The scrapie agent is resistant to inactivation by most procedures that modify or hydrolyze nucleic acids, but requires a protein for expression of its infectivity. Whether or not, despite the agent's resistance to nucleases, a small nucleic acid is also required or whether the protein constitutes the complete agent remains to be determined. Needless to say, should the latter possibility be correct, prions would conflict with commonly held beliefs of molecular biology even more fundamentally than did viroids.