RNA Interference

TO THE EDITOR: The article on RNA interference by Kitabwalla and Ruprecht (Oct. 24 issue) is most timely in view of the excitement produced by the recent demonstration that small interfering RNAs (siRNAs) have important functions in RNA cleavage involved in host defense against viruses and in the destruction of deleterious messenger RNAs of other kinds. However, I believe the authors err in describing Dicer as an RNA-dependent RNA polymerase limited to plants and drosophila (in the legend to Fig. 1 in their article). Dicer was initially described as the endogenous ribonuclease that generates siRNAs from longer double-stranded RNAs and appears to be essential to the process of RNA interference in all cases in which siRNA is not supplied exogenously. What may be limited to lower organisms is, rather, the RNA-dependent DNA polymerase capable of spreading the RNA interference phenomenon systemically.1

Peter T. Rowley, M.D.
University of Rochester School of Medicine
Rochester, NY 14642
peter_rowley@urmc.rochester.edu


THE AUTHORS REPLY: We thank Dr. Rowley for his comment and wish to clarify certain points. The field of RNA interference is moving rapidly. Since we submitted our article, Dicer, an endonuclease that cleaves long double-stranded RNA molecules into fragments of 21 to 23 base pairs, has been cloned from complementary DNA libraries of human testis and HeLa cells.2,3 This recombinant human protein was overexpressed in insect cells, purified, and found to cleave double-stranded RNA in cell-free systems into characteristic short fragments.2,3 Thus, Dicer activity has now been found not only in plants and drosophila but in mammalian cells as well, even though enzymes from mammalian organisms appear to differ in their ATP requirements from those of lower organisms.2,3 What seems to be restricted to plants and drosophila is an amplification loop carried out by Dicer in concert with an RNA-dependent RNA polymerase that generates more siRNA molecules for repeated rounds of targeted gene silencing. There is no evidence of involvement of any “RNA-dependent DNA polymerase,” as Dr. Rowley suggests, in the phenomenon of RNA interference.

Moiz Kitabwalla, Ph.D.
Ruth M. Ruprecht, M.D., Ph.D.
Dana–Farber Cancer Institute
Boston, MA 02115
ruth_ruprecht@dfci.harvard.edu


Spinal Cord Disease in West Nile Virus Infection

TO THE EDITOR: Recent letters to the Journal from Leis et al.1 and Glass et al.2 (Oct. 17 issue) as well as reports by others3 have described a poliomyelitis-like syndrome occurring in patients with West Nile virus infection. In these patients, acute flaccid paralysis developed that was suggestive of involvement of anterior horn cells of the spinal cord, but the histopathology of the spinal cord was not described.

We report the histopathological findings from the spinal cord of an 81-year-old man with West Nile virus infection (positive serologic tests for IgM) who presented with a four-day history of fever accompanied by nausea, vomiting, and ataxia. Analysis of the cerebrospinal fluid showed a white-cell count of 1444 per cubic millimeter, with 85 percent neutrophils. Acute flaccid paralysis developed, and the patient died 11 days after presentation. Magnetic resonance imaging showed marked abnormal enhancement of the cauda equina.

At autopsy, mild cerebral edema was present, with evidence of meningoencephalitis. There was variable involvement of the spinal cord, with the lumbar cord being most affected. There was focal