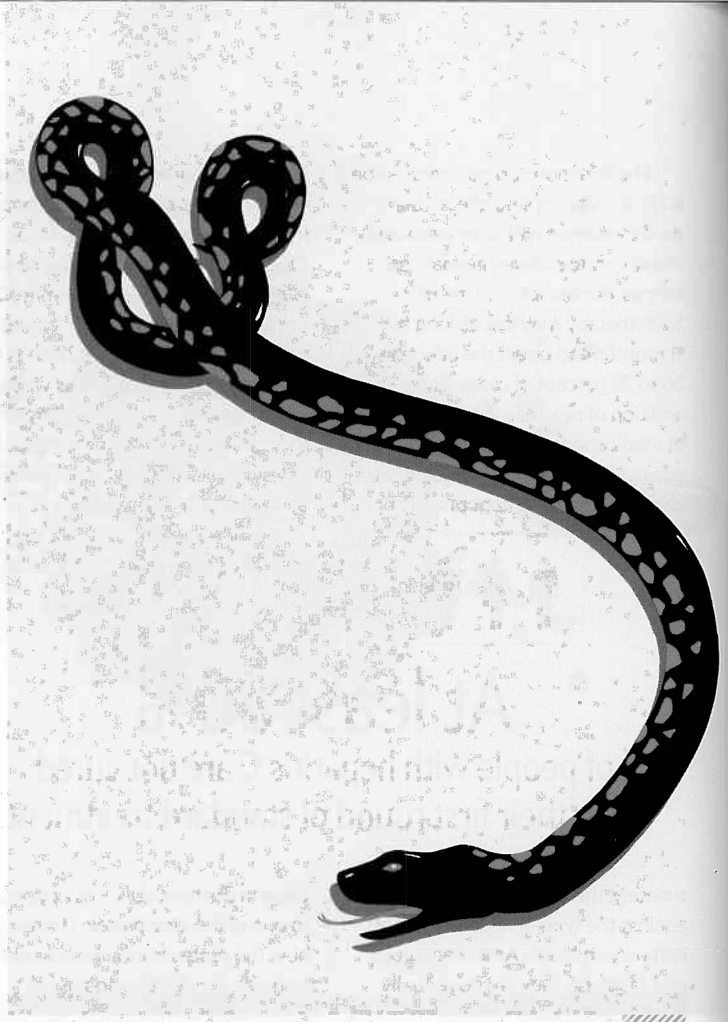
DEFEATING NATURE'S TERRORISTS

An RNA-based treatment may stop the Ebola virus in its tracks

By Ferris Jabr



At first, people infected with the Ebola virus appear to have the flu—fever, chills, muscle aches. Then the bleeding begins. As the virus hijacks cells throughout the body to make copies of itself, it overwhelms and damages the liver, lungs, spleen and blood vessels. Within days organs begin to fail and many patients fall into a coma. Some outbreaks, primarily in Central and West Africa, have killed up to 90 percent of infected individuals.

That terrifying prognosis may be about to change. Using so-called small interfering RNA, or siRNA, Thomas W. Geisbert, now at the University of Texas Medical Branch at Galveston, and his many collaborators have devised a highly promising treatment that has saved the lives of six monkeys infected with the virus. As reported this past January, the treatment has also passed its first safety test in an uninfected human volunteer. One of Geisbert's collaborators, Ian Maclachlan of Burnaby, British Columbia–based Tekmira Pharmaceuticals, and his team have received a $140-million grant from the U.S. Department of Defense to develop the therapy further.

Working together, the scientists engineered an siRNA to prevent the Ebola virus from making a particular protein, without which it cannot replicate itself. "If you knock out that one, in theory you knock out everything," Geisbert says. The researchers also designed another siRNA to thwart manufacture of a second protein that the virus uses to weaken an infected individual's immune system. There is no danger of the siRNAs interfering with typical cellular duties because the targeted viral proteins do not exist in the cells of humans or other mammals.

Maclachlan and his colleagues encapsulated the lab-made siRNAs in little bubbles of fat that cells would readily transport across their membranes. Then they injected the preparation into several rhesus macaques, which had been infected with Ebola virus less than an hour earlier. In one study, two of three monkeys given a total of four doses of the treatment in the first week after exposure survived. In a second study designed to test the effectiveness of a higher dose, all four monkeys that received seven siRNA injections lived. Tests revealed that the treated monkeys had far fewer virus molecules in their blood than is typical for an infected animal. The macaques tolerated the siRNA injections well, and those that survived were still healthy 30 days later.

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The study was a "milestone," says Gary Kobinger of the University of Manitoba, who is working on a different Ebola treatment based on antibodies. He believes Geisbert and his team "are leading the effort toward clinical development."

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