

Scientists 'grow' a virus for first time

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Disturbing test shows terrorists could do it, too

Gareth Cook, Boston Globe Friday, July 12, 2002

Scientists financed by the Pentagon announced Thursday that they have synthesized a virus from scratch for the first time, raising the possibility that terrorists could create biological killers once thought beyond their reach.

A team of State University of New York researchers was able to build a polio virus relying only on a listing of its genetic sequence, information that is publicly available.

The genetic codes for many dangerous pathogens, including smallpox and Ebola, are freely accessible on the Web. The team relied on technology that is generally available in molecular biology labs around the world.

Dr. Eckard Wimmer, professor of molecular genetics and microbiology at SUNY- Stony Brook and leader of the project, said they made the virus to send a warning that terrorists might be able to make biological weapons even when they could not obtain a natural virus.

"You no longer need the real thing in order to make the virus and propagate it," Wimmer said.

"This should really raise some red flags," said Barry R. Bloom, dean of Harvard's School of Public Health.

This paper "means that more complicated viruses can be created -- and that it is also possible to create viruses that do not exist in the wild."

PENTAGON PROVIDED FUNDS

The work, published in today's issue of the journal *Science* and posted on the magazine's Web site Thursday, was underwritten by the Pentagon's Defense Advanced Research Projects Agency as part of a program to develop biowarfare countermeasures.

It does not represent a major technical advance -- biologists have long suspected the work could be done. But it does mark a broader milestone in science: It is the closest researchers have come to synthesizing life from simple chemical building blocks. Viruses occupy a biological gray zone, between living and nonliving.

The work also adds to a roiling scientific debate over what kind of information -- from genetic sequences of diseases to potentially dangerous chemical recipes -- should be freely published in a world fearful of terrorism.

"This work should never have been done, funded or published," said J. Craig Venter, director of the Center for the Advancement of Genomics. "Somehow the whole system broke down here."

But Wimmer said publishing the work would not give any new help to bioterrorists, because the team used methods and information that are already known. The work, he said, was intended to serve as a warning of what is now possible.

"What can be done will be done," Wimmer said. "If it is not done by sensible scientists, then it will be done by terrorists."

The Defense Advanced Research Projects Agency said it had provided about \$300,000 over the past three years for the work. "Understanding the process of viral DNA production is key to identifying new ways to kill viruses and understand how viruses could change and escape from vaccines," the agency said in a statement.

Experts agree that the research -- or the synthesis of any pathogen -- does not violate the 1972 treaty banning germ weapons, which gives wide latitude to all kinds of defensive research.

POLIO UNLIKELY FOR BIOTERROR

Polio is one of the simplest viruses to make because its genetic sequence is relatively short, but scientists said it is likely that more complex viruses could eventually be built. Polio would be an unlikely choice for bioterrorists because so much of the population is already vaccinated, and other pathogens are more devastating.

But the work complicates the global effort to eradicate polio, a disease that has been abolished from the industrialized world but is still active in parts of Asia and especially Africa. In the past, health officials dreamed of a world in which the polio virus had been completely wiped out, but the concept of "eradication" loses its meaning if the virus can be re-created at will.

"We have been focusing on eliminating natural transmission," said James LeDuc, director of the Division of Viral and Rickettsial Diseases at the federal Centers for Disease Control in Atlanta. "There is no strategy for preventing chemists from making it in a lab."

Dr. Steven Block, a Stanford University expert on the applications of biotechnology to biowarfare, called the work on the polio virus a stunt. "This is not the route to new kinds of terrific genetically engineered bioterror," he said.

Even if people were not vaccinated, he said, polio would not make a good bioweapon because it is not as infectious and lethal as many other pathogens. In most cases, Block said, it would be far easier to obtain a natural virus than to try to build one from scratch.

The one exception, he said, is smallpox, because the world's two known remaining stocks of the virus are closely guarded. But smallpox would be nearly impossible to synthesize from scratch using the same technique, he said.

THREE-YEAR PROCESS

Making the polio took three years, although Wimmer said it could probably now be done in six months. His collaborators were Dr. Aniko V. Paul, another professor in his department, and Dr. Jeronimo Cello, a postdoctoral researcher.

The polio virus genome is tiny, consisting of 7,500 chemical units, or bases, of RNA. The human genome, by contrast, has more than 3 billion units.

Still, even assembling a genome of 7,500 units is tedious. The machines, which usually make DNA rather than RNA, can reliably make only 50 to 100 bases in a stretch. So the Stony Brook scientists ordered numerous 60-base stretches from a company that sells mail-order DNA for as little as 40 cents a base. The

stretches were then painstakingly strung together.

The DNA was then converted into RNA using a commercially available enzyme. The next step would be to put the RNA into cells to churn out new viruses.

But Wimmer put the RNA instead into a mixture of proteins taken from cells, a technique he developed in 1991. That allows him to claim that the virus was manufactured without the use of any living cells.

The New York Times contributed to this report.

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