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Killer virus

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A virus that kills every one of its victims, by wiping out part of their immune system, has been accidentally created by an Australian research team. The virus, a modified mousepox, does not affect humans, but it is closely related to smallpox, raising fears that the technology could be used in biowarfare.

The discovery highlights a growing problem. How do you stop terrorists taking legitimate research and adapting it for their own nefarious purposes?

The Australian researchers had no intention of producing a killer virus. They were merely trying to make a mouse contraceptive vaccine for pest control. "But it's a good way to show how to alter smallpox to make it more virulent," says Ken Alibek, former second-in-command of the civilian branch of the Soviet germ-warfare programme.

Ron Jackson of CSIRO's wildlife division and Ian Ramshaw at the Australian National University, both in Canberra, inserted into a mousepox virus a gene that creates large amounts of interleukin 4. IL-4 is a molecule that occurs naturally in the body. As part of a study aimed at creating a contraceptive vaccine, they were trying to stimulate antibodies against mouse eggs, which would make the animals infertile. The mousepox virus was merely a vehicle for transporting the egg proteins into mice to trigger an antibody response. The researchers added the gene for IL-4 to boost antibody production. The surprise was that it totally suppressed the "cell-mediated response"--the arm of the immune system that combats viral infection.

Mousepox normally causes only mild symptoms in the type of mice used in the study, but with the IL-4 gene added it wiped out all the animals in nine days. "It would be safe to assume that if some idiot did put human IL-4 into human smallpox they'd increase the lethality quite dramatically," says Jackson. "Seeing the consequences of what happened in the mice, I wouldn't be the one who'd want to do the experiment."

To make matters worse, the engineered virus also appears unnaturally resistant to attempts to vaccinate the mice. A vaccine that would normally protect mouse strains that are susceptible to the virus only worked in half the mice exposed to the killer version. "It's surprising how very, very bad the virus is," says Ann Hill, a vaccine researcher from Oregon Health Sciences University in Portland. If bioterrorists created a human version of the virus, vaccination programmes would be of limited use.

Alibek, who now works on developing novel treatments for anthrax for the defence contractor Hadron in Virginia, says this highlights the drawback of working on vaccines against bioweapons rather than treatments. "I'd say any vaccine could be overcome by one or another genetically engineered virus or bacterium," he says.

Is it possible that research into new vaccines against cancer and other diseases could inadvertently create lethal human viruses? Many of the most promising modern vaccines depend on viruses to transport genes into the body, and contain genes that directly alter the immune response. But researchers have not been too concerned because the evidence until now suggested that changes in the genetic make-up of viruses invariably makes them less virulent, not more. One way to reduce the risk, says Gary Nabel of the National Institutes of Health, is to use only viruses that cannot replicate. "There are some replication-competent [viral vaccines] around, but there is increasing concern about



How to kill a mouse

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their use," he says.

Defence experts are also worried about preserving the freedom to publish medical findings while trying to stop the information falling into the wrong hands. According to D. A. Henderson, a former US presidential adviser, and director of the Center for Civilian Biodefense Studies at Johns Hopkins University in Baltimore, what are effectively blueprints for making microorganisms more harmful regularly appear in unclassified journals. "I can't for the life of me figure out how we are going to deal with this," he says.

The Australian researchers consulted their country's Department of Defence before submitting the work for publication, and only decided to go ahead after considerable thought. A report will appear in a February issue of the *Journal of Virology*. "We wanted to warn the general population that this potentially dangerous technology is available," says Jackson. "We wanted to make it clear to the scientific community that they should be careful, that it is not too difficult to create severe organisms."



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