

## Armed for bioterror

By: Ean Higgins

Advances in genetic engineering have raised concerns among security agencies about the prospect of terrorists creating a new superbug and unleashing it against perceived enemies. Ean Higgins reports

THE idea of the experiment was to make female mice less fertile in order to help curb mouse plagues, which often cost the Australian farm sector dearly. Canberra immunologists Ron Jackson and Ian Ramshaw injected 10 mice with a mousepox virus that had been modified with a gene producing interleukin-4, a natural chemical secreted by the immune system.

The modification could, it was thought, trick the mice's immune systems into rendering their eggs infertile.

The type of mouse, called Black 6, was known to be naturally resistant to the effects of mousepox. So if they were infected with the modified mousepox, the idea went, they would remain healthy to scurry around, spreading the virus along with the infertility gene to other mice.

What happened six days later left Jackson and Ramshaw stunned. One mouse was dead, with its tissues swollen up -- a classic case of mousepox -- and several others looked the worse for wear. Before long, the other mice died.

Jackson and Ramshaw realised they had managed by accident to create a supervirus. The IL-4 modification had undermined the production of the mice's defence cells, leaving them more exposed to diseases they should normally be able to cope with. Just to be sure,

Jackson and Ramshaw vaccinated another group of mice against mousepox, then injected them with the modified virus. Even then, 60 per cent of the mice died.

Jackson and Ramshaw held off for two years before publishing their results, and when they did, it caused alarm all the way to America's CIA.

The implication was that diseases could, potentially, be made far more deadly through genetic engineering, and existing vaccines rendered less effective. Further advances in genetic engineering have left US security services even more worried.

A CIA report released in November last year warns that advances in biotechnology have greatly increased the potential danger of biological warfare.

“The effects of some of these engineered biological agents could be worse than any disease known to man,” the CIA says. “The same science that may cure some of our worst diseases could be used to create the world's most frightening weapons.”

The CIA highlighted Jackson and Ramshaw's work, saying a similar technique could be used to increase the lethality of diseases.

After the September 11 attacks in 2001, the White House budgeted nearly \$US6billion to counter the threat of bioterrorism. But even this huge effort is now regarded as insufficient.

The US -- considered to be the No.1 target of a bioterror threat -- is not even close to adequate levels of preparedness for a bioterror attack, according to a recent report from the congressional General Accounting Office.

In response, President George W. Bush a few weeks ago signed a series of measures designed to improve US defences against bioterrorism, including a new national centre to assess threats.

This week in San Francisco, at the world's biggest biotechnology conference, BIO 2004, companies and researchers showcased new measures designed to fight bioterrorism. Among them was the Australian firm Anadis, which is promoting the world's first anti-anthrax spray.

Anthrax has been used in terror attacks: a sect in Japan pumped it into a factory in Tokyo, and after September 11 spores were mailed to US congressmen, costing lives among mail workers.

What is particularly worrying security and health authorities is that the scientific advances in genetic engineering are moving at such a pace that if the technology falls into the wrong hands, the danger and severity of an attack could rise exponentially.

Some diseases, such as anthrax, for example, are not normally contagious. However, if through genetic engineering a non-contagious disease could be made to spread from one human to another, it would be a vastly more dangerous weapon.

The scientific community has shown astounding ability in recent years to manipulate diseases -- including recreating polio. Stephen Prowse, the chief executive officer of the Australian Biosecurity Co-operative Research Centre, says the new capabilities reflect advances in dissecting the genetic make-up of an entire virus.

Theoretically, it would be possible to take DNA from one virus and combine it with another to achieve the desired effect.

“You could, for example, modify a bird flu to make it more infectious among humans. Just chop up the bird flu and chop up conventional human flu, and make a recombinant,” says Prowse.

He adds, however, that such an experiment would be much more difficult than it sounds, requiring a fair bit of sophisticated technology.

But Ramshaw sees this sort of bioterrorism as "a likely scenario". Ramshaw, who is head of vaccine immunology at the Australian National University, points to smallpox, one of the greatest fears among the security establishment.

In principle, it should be almost impossible for terrorists to get their hands on the virus. The disease was eradicated in 1980 and stocks are kept safely hidden away at two locations, one in the US and the other in Russia.

However, diseases normally associated with animals could be used instead. Although not as infectious as smallpox, monkey pox is lethal and transmissible to humans. Ramshaw says it has a genetic make-up similar to human smallpox, and could possibly be adjusted to become a highly contagious disease.

Monkey pox would be "generally available", Ramshaw says, as would camel pox, which is "all over the place in the Middle East" and has 99 per cent of the same genetic make-up as human smallpox.

Through genetic engineering processes, it might be possible to recreate smallpox itself or a new "designer" disease.

Former Iraqi leader Saddam Hussein's regime was known to be conducting experiments with camel pox, which some intelligence analysts believed were aimed at doing just that. "The technology is such that you are going to be able to do lots more things than have been done in the past," Ramshaw says.

The number of people familiar with the technology is spreading -- there are about four or five institutions in Australia capable of such research, Ramshaw says, and dozens elsewhere around the world.

Another factor in the equation is the scenario of "suicide bioterrorism", which the federal

Government has conceded it has considered as a possible threat. In this case terrorists would not need a crop-duster or aerosol spray to spread a transmissible disease, but inject themselves with the virus and then spread it through direct contact.

In the US, the threat of suicide bioterrorism has been explored by the Centre for Deterrence of Biowarfare and Bioterrorism at the University of Louisville in Kentucky, which has trained more than 4000 health and security professionals in how to cope with a bioterrorism attack.

Its co-director, Richard Clover, says the centre has, in particular, looked at the possibility of smallpox with a three-day window in which a self-infected terrorist could spread the disease.

However it is transmitted, the likelihood of bioterrorism remains a matter of debate among the intelligence community.

According to the Australian National University's head of terrorism studies Clive Williams, groups such as al-Qa'ida are more likely to choose traditional technology such as bombings aimed at specific targets.

The greater risk, he says, is more likely to come from "religious sects who have scientists among their membership" or even "a scientist who has gone a bit potty". Williams says the point, however, is that if one of the bioterrorism scenarios did come true, it could be far more disastrous than anything al-Qa'ida has done so far. The Spanish flu epidemic in 1918-19 killed at least 20 million people.

"The consequences are very high, even though the likelihood is very low," Williams says.

In Australia, the Government has considered the threat serious enough to

have imported 50,000 vials of smallpox vaccine, which can be diluted to treat up to 250,000 people as a preventative or curative measure.

A plan has been developed requiring hospitals and doctors to report immediately any symptoms in patients for six diseases suspected of bioterrorist potential: smallpox, anthrax, tularemia, botulism, plague, and viral haemorrhagic fevers such as ebola. The Department of Health would then assess the probability that the cases constituted a terrorist attack in co-operation with security agencies.

The paradox, as posed by the CIA, is that experimentation with diseases through genetic modification -- usually in a bid to find cures -- is creating the knowledge that terrorists could employ.

However, Singapore-based terrorism expert Rohan Gunaratna says there is no choice but to advance such research, and authorities might have to help fund it where required. ``The governments must continue to stay one step ahead of the terrorists," he says.

## WORST SCENARIOS

### MAKING A KILLER POX

1. Take an animal pox, such as monkey pox, which has a genetic code similar to human smallpox and can affect humans and occasionally be fatal.
2. Genetically modify the monkey pox virus to increase its lethality, possibly by adjusting the immunity gene.
3. The result is a new human superpox for which existing smallpox vaccines may be less effective.

### MAKING A KILLER FLU

1. Dissect the genetic code of the avian flu virus, which is highly contagious and lethal among birds and transmissible from birds to humans, but not from human to human.
2. Take sections of the genetic code of a common human flu virus that is contagious among humans and splice it with the avian flu virus.

3. Recombine the DNA. The result is a new human superbug that is as lethal as the avian flu and as contagious as human flu.

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Caption: Accidental discovery: Ramshaw was stunned when a genetic experiment to render female mice infertile created a killer super-virus Picture: Mark Graham

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