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Lax laws, virus DNA and potential for terror

· Loopholes mean anyone can order gene sequences
· Scientists back voluntary regulation as first step

- James Randerson, science correspondent
- The Guardian, Wednesday 14 June 2006
- Article history

The smallpox virus last wreaked havoc on the human population in 1977 before a World Health Organisation programme eradicated it from the planet. It now exists only in government laboratories in the US and Russia.

But ordering part of this long-dead pathogen's DNA proved easier than anyone dared imagine. All it took was an invented company name, a mobile phone number, a free email address and a house in north London to receive the order by post.

What the investigation makes clear is that anyone, without any attempt to prove they are part of a legitimate research organisation, can order DNA sequences from any potential pathogen without fear of extensive questioning. In our case, VH Bio Ltd did not realise it was supplying part of the smallpox genome, but many scientists argue that it is the responsibility of companies selling custom-made pieces of DNA to check their orders for potentially dangerous sequences.

Without modifications which meant the strand ordered by the Guardian could never form part of a functional gene, it would probably have fallen under the Anti-Terrorism, Crime and Security Act 2001. This lists so-called Schedule 5 pathogens and toxins including smallpox virus, ebola virus and the plague bacterium. These, along with any DNA "associated with the pathogenicity of the micro-organism" are illegal to keep or use without first notifying the authorities.

In November, New Scientist magazine surveyed 12 gene synthesis companies in North America and Europe. Only five said they always screened their orders for suspect sequences and three said they never did. These were all doing relatively large-scale synthesis, providing sequences a few hundred letters long, but there are many more companies like VH Bio Ltd which make so-called oligonucleotides, sequences around 100 letters or smaller.

Of three UK-based sequencing companies other than VH Bio Ltd canvassed by the Guardian, one did not screen customers or sequences, one carried out checks on customers only and a third checked customers and had carried out a pilot study on screening DNA orders but is not currently doing so. Screening shorter sequences is

more difficult because a chance match to a suspect piece of DNA is more likely. "Because they are short, sequence screening can pick those up, but the false positive rate is high," said Robert Jones at Craic Computing in Seattle, which produces software to screen sequence orders against a database of DNA from nasty pathogens.

The Guardian's investigation has sparked calls for DNA synthesis companies to be better regulated.

Edward Hammond, a biological weapons expert with the Sunshine Project, an NGO that campaigns against the development of biological weapons, said: "The most worrisome thing ... is that [the field of synthetic biology] is going to enable people to create potentially very dangerous diseases that don't otherwise exist or to recreate ones that have been wiped off the face of the earth."

The emerging science of synthetic biology holds great potential for medicine and other fields. There are, for example, research projects to develop synthetic bacteria that seek and invade tumour cells and yeast cells that produce a malaria drug.

Eckard Wimmer at the State University of New York in Stony Brook said the 2002 experiment to make polio virus from scratch by stitching together short strands of DNA was fairly easy. "We did it as a wake-up call," he said. "It's surprising to me after all these discussions for at least four years, no more urgent recommendation has gone out to these companies saying that if you don't [carry out more rigorous checks] you may be in trouble," he said.

At a synthetic biology conference in Berkeley, California, last month delegates discussed how to minimise misuse of the technology. Delegates are currently consulting on four "resolutions", which include an effort to develop improved and freely available software tools to screen DNA orders for potentially dangerous sequences and a pledge to "encourage individuals and organisations to avoid patronising companies that do not systematically check their DNA synthesis orders".

But synthetic biologists have defended their efforts to regulate the field. "If scientists are willing to get the ball rolling when few others are acting, then they should be encouraged," said George Church, a leading synthetic biologist at Harvard. He argued that voluntary regulation would would be quicker than legislation and would not preclude new laws.

FAQ Viruses

How big is the genome of a virus?

Virus genomes - the sum total of their DNA - range from around 3,000 DNA letters long to more than a million. The polio virus genome has 7,741 letters, influenza virus has 13,500 letters, ebola has 19,000 and smallpox has 185,000.

How easy is it to 'glue' strands of DNA together?

This is relatively simple and getting easier all the time. A basic university laboratory would have the capability.

Which viruses have been manufactured from scratch?

Eckard Wimmer at the State University of New York showed in 2002 that it was possible to make polio virus from scratch by making its genome from short lengths of DNA. He said he did this as a "wake up call" to warn that the World Health Organisation's polio eradication effort could be thwarted by terrorists. Other viruses that have subsequently been built from scratch include the 1918 influenza strain.

How do you recreate a virus?

Prof Wimmer's team used the DNA sequence of polio available on the web as a template for hundreds of short strands of DNA each around 70 letters long. The team assembled these in order to recreate the full genome sequence and used this as a template for a mirror image sequence in DNA's chemical cousin RNA - the genetic material used by polio virus. The team then added these RNA strands to human cells which took up the sequence and manufactured copies of the virus.