

Genome editing: Is it a national security threat?

The exponentiating capabilities and applications of CRISPR genome editing make for a strange dichotomy. On one hand, earlier this year, the director of U.S. national intelligence, James Clapper, [named genome editing as a potential weapon of mass destruction \(WMD\)](#), alongside things like North Korean nuclear weapons, Russian cruise missiles with new capabilities, and undeclared chemical weapons in Syria. In the [annual worldwide threat assessment report](#) the concern reads like this:

Research in genome editing conducted by countries with different regulatory or ethical standards than those of Western countries probably increases the risk of the creation of potentially harmful biological agents or products. Given the broad distribution, low cost, and accelerated pace of development of this dual-use technology, its deliberate or unintentional misuse might lead to far-reaching economic and national security implications.

On the other hand, you can purchase a do-it-yourself CRISPR kit for \$100 or so. Some CRISPR kits actually are [designed for elementary school](#) children, and that's not something that we can ever expect of nuclear materials or nerve gas. What's happening? Is genome editing really so powerful that it could do major damage, either accidentally, or through foul play? Or is the government merely being prudently cautious, making a profound statement to promote discussion about what the appropriate regulations should be?

CRISPR as a biotech sea change

Genome editing means making changes in selected nucleotide sequences of an organism's DNA analogous to making changes in selected letters or words of written text of a book. Researchers have been able to do this [since the early 1990s](#), using engineered nucleases, proteins able to make double stranded cuts in DNA. Early genome editing was very difficult and expensive, however, because the nucleases had to be custom-made for each editing task. Think of it as having to make a computer specifically to edit a particular sentence in a book, then having to design new computer hardware to do something else to a different sentence. Early genome editing systems have included zinc finger nucleases (ZFNs) and transcription activator-like effector nucleases (TALENs). ZFNs and TALENs are still used for specialized applications, but 2012 marks the advent of programmable nuclease systems. In other words, novel genome editing tasks can be achieved with what amounts to a routine software upgrade.

CRISPR sequences were discovered as components of an adaptive immune system in prokaryotic organisms—Bacteria and Archaea. They are associated with sequences coding for nucleases called Cas proteins; these work together in complex ways to cut up DNA from viruses that otherwise would kill the prokaryote. Most prokaryotes have many different Cas proteins, but a bacterial species called *Streptococcus pyogenes* uses just one type of Cas, called Cas9, to do all the jobs for which other species require many different types of Cas.

Rather than having a built-in capability to recognize, and attach to, the sequence of DNA that needs to be

cut, Cas proteins work in concert with special RNA molecules. When it comes to Cas9 of *S. pyogenes*, it uses two different RNA strands. One RNA strand acts like glue to attach the Cas9 protein to the target DNA, so it can cut. The other RNA strand is like a sensor that finds sequence on the DNA where the cut needs to be made. The Researchers realized that Cas9 could be adapted for cutting any genes inside any organism, plus, to keep things really simple they combined the two strands of RNA into one.

As a result, if you want to knock out any gene in any organism, you just buy a CRISPR kit containing Cas9, which will operate as a DNA scissors wherever it is led. And, you order the RNA that binds the Cas9 and also has a sequence corresponding to the DNA sequence that you want to edit. To do something completely different, you only need to change the RNA sequence—the software—while using the same Cas9 system—the hardware. Whereas the the older genome editing technologies require specialized labs and teams of highly trained people, CRISPR editing can be done in your kitchen, or in your garden. Or it could be done as a science fair project, by say a 4th grader who might want to knock out a certain gene in a certain flower and see what that does to the petals.

By adding multiple RNA sequences, CRISPR-Cas9 also can be use to knock out many genes at once, plus you can DNA sequences to be inserted to replace the sequences that your remove; in other words you can paste as well as cut.

Can you build a pathogen using CRISPR?

This possibility may be what underlies the growing concern that genome editing could be used in bioterrorism. That is reason for biologists to convene and determine clearly what an unsuspecting person, or someone with nasty plans, could do with a do-it-yourself CRISPR kit. But for someone without expertise, the answer to the question of whether you could build pathogen—for instance convert a common, harmless bacterium into anthrax, or build a smallpox virus from scratch—it's probably that it's extremely unlikely. Putting a whole bunch of genes together in a specific way is a long way from knocking out one specific gene. This is not something that a take-home kit could do, but the rationale for a national security concern may be this: just as the capabilities of your smartphone can be boosted with novel software, so could any biological system. While a child cannot get an app that downloads another app onto her phone that could harm the world, a hacker could make his own app, or modify a purchased app and do harm.

What are the potential worst-case consequences of a potential biological hacker not merely using the kit biological software to flip a few genes, but to modify the software itself? This alarmist-sounding view may be speculative, but it's the role of national security organizations to consider and prepare for worst-case scenarios, and this may be the motivation for Clapper's report.

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