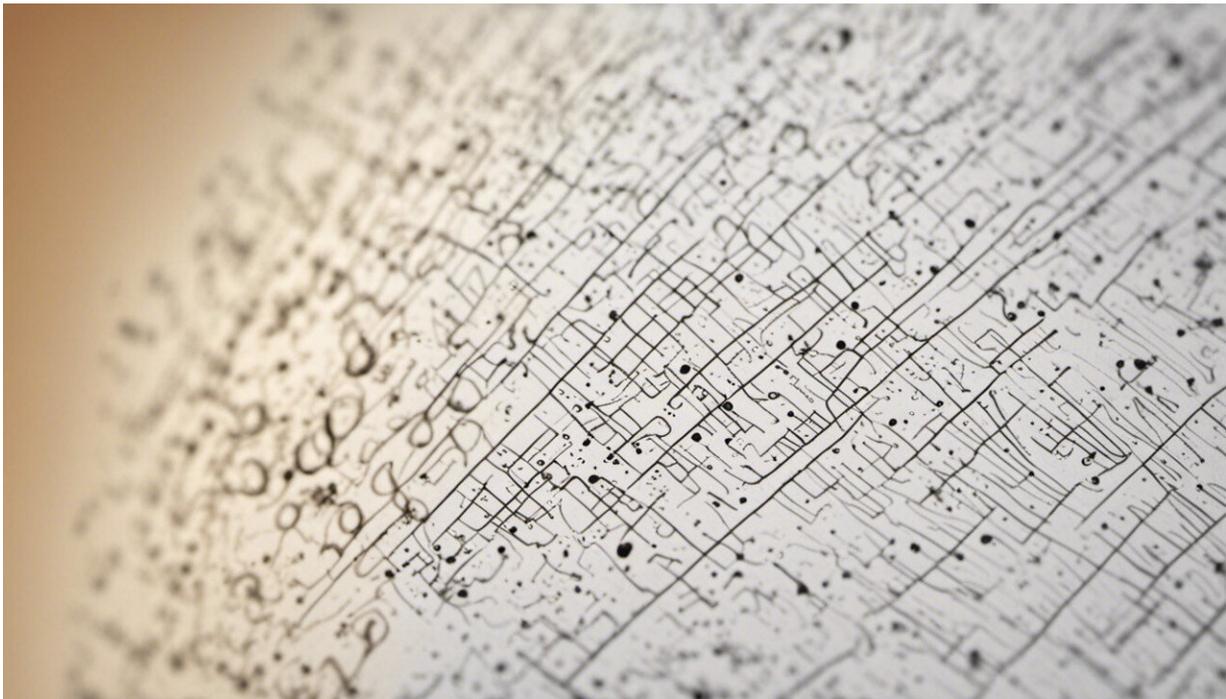


# Bioengineers develop tool for reprogramming genetic code

January 27 2015, by Bjorn Carey

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Credit: AI-generated image ([disclaimer](#))

Biology relies upon the precise activation of specific genes to work properly. If that sequence gets out of whack, or one gene turns on only partially, the outcome can often lead to a disease.

Now, bioengineers at Stanford and other universities have developed a

sort of programmable genetic code that allows them to preferentially activate or deactivate genes in living cells. The work is published in the current issue of *Cell*, and could help usher in a new generation of gene therapies.

The technique is an adaptation of CRISPR, itself a relatively new genetic tool that makes use of a natural defense mechanism that bacteria evolved over millions of years to slice up infectious virus DNA.

Standard CRISPR consists of two components: a short RNA that matches a particular spot in the genome, and a protein called Cas9 that snips the DNA in that location. For the purposes of gene editing, scientists can control where the protein snips the genome, insert a new gene into the cut and patch it back together.

Inserting new [genetic code](#), however, is just one way to influence how the genome is expressed. Another involves telling the cell how much or how little to activate a particular gene, thus controlling how much protein a cell produces from that gene and altering its behavior.

It's this action that Lei Stanley Qi, an assistant professor of bioengineering and of chemical and systems biology at Stanford, and his colleagues aim to manipulate.

## **Influencing the genome**

In the new work, the researchers describe how they have designed the CRISPR molecule to include a second piece of information on the RNA, instructing the molecule to either increase (upregulate) or decrease (downregulate) a target gene's activity, or turn it on/off entirely.

Additionally, they designed it so that it could affect two different genes at once. In a cell, the order or degree in which [multiple genes](#) are

activated can produce different metabolic products.

"It's like driving a car. You control the wheel to control direction, and the engine to control the speed, and how you balance the two determines how the car moves," Qi said. "We can do the same thing in the cell by up- or downregulating genes, and produce different outcomes."

As a proof of principle, the scientists used the technique to take control of a yeast metabolic pathway, turning genes on and off in various orders to produce four different end products. They then tested it on two mammalian genes that are important in cell mobility, and were able to control the cell's direction and how fast it moved.

## Future therapies

The ability to control genes is an attractive approach in designing genetic therapies for complex diseases that involve multiple genes, Qi said, and the new system may overcome several of the challenges of existing experimental therapies.

"Our technique allows us to directly control multiple specific [genes](#) and pathways in the genome without expressing new transgenes or uncontrolled behaviors, such as producing too much of a protein, or doing so in the wrong cells," Qi said. "We could eventually synthesize tens of thousands of RNA molecules to control the genome over a whole organism."

Next, Qi plans to test the technique in mice and refine the delivery method. Currently the scientists use a virus to insert the molecule into a cell, but he would eventually like to simply inject the molecules into an organism's blood.

"That is what is so exciting about working at Stanford, because the

School of Medicine's immunology group is just around the corner, and working with them will help us address how to do this without triggering an immune response," said Qi, who is a member of the interdisciplinary Stanford ChEM-H institute. "I'm optimistic because everything about this system comes naturally from [cells](#), and should be compatible with any organism."

Provided by Stanford University

Citation: Bioengineers develop tool for reprogramming genetic code (2015, January 27) retrieved 26 April 2024 from

<https://phys.org/news/2015-01-bioengineers-tool-reprogramming-genetic-code.html>

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