NEWS

UT scientists tinker with gene-mapping device to make DNA editing safe

By **Marty Toohey**
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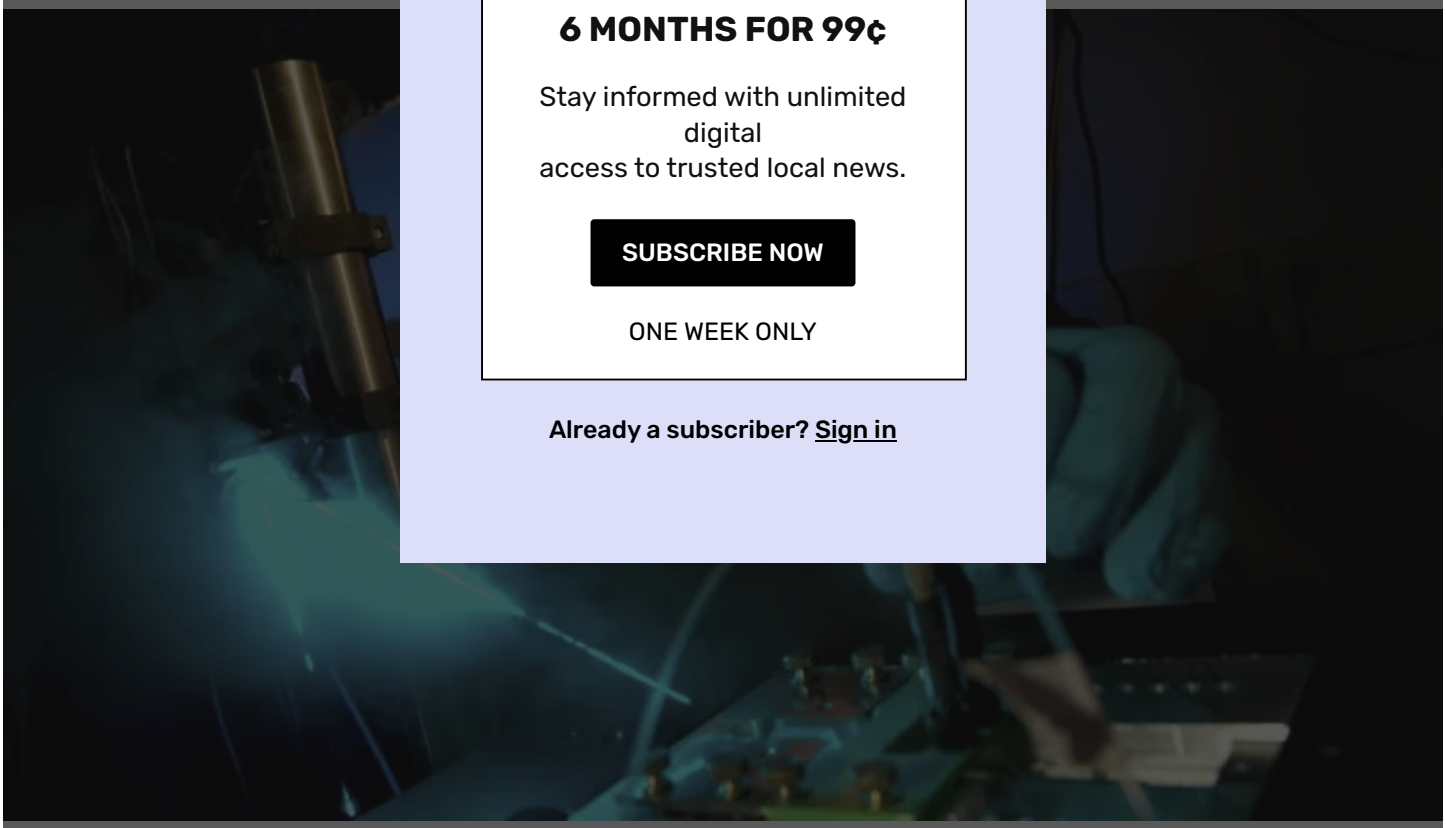
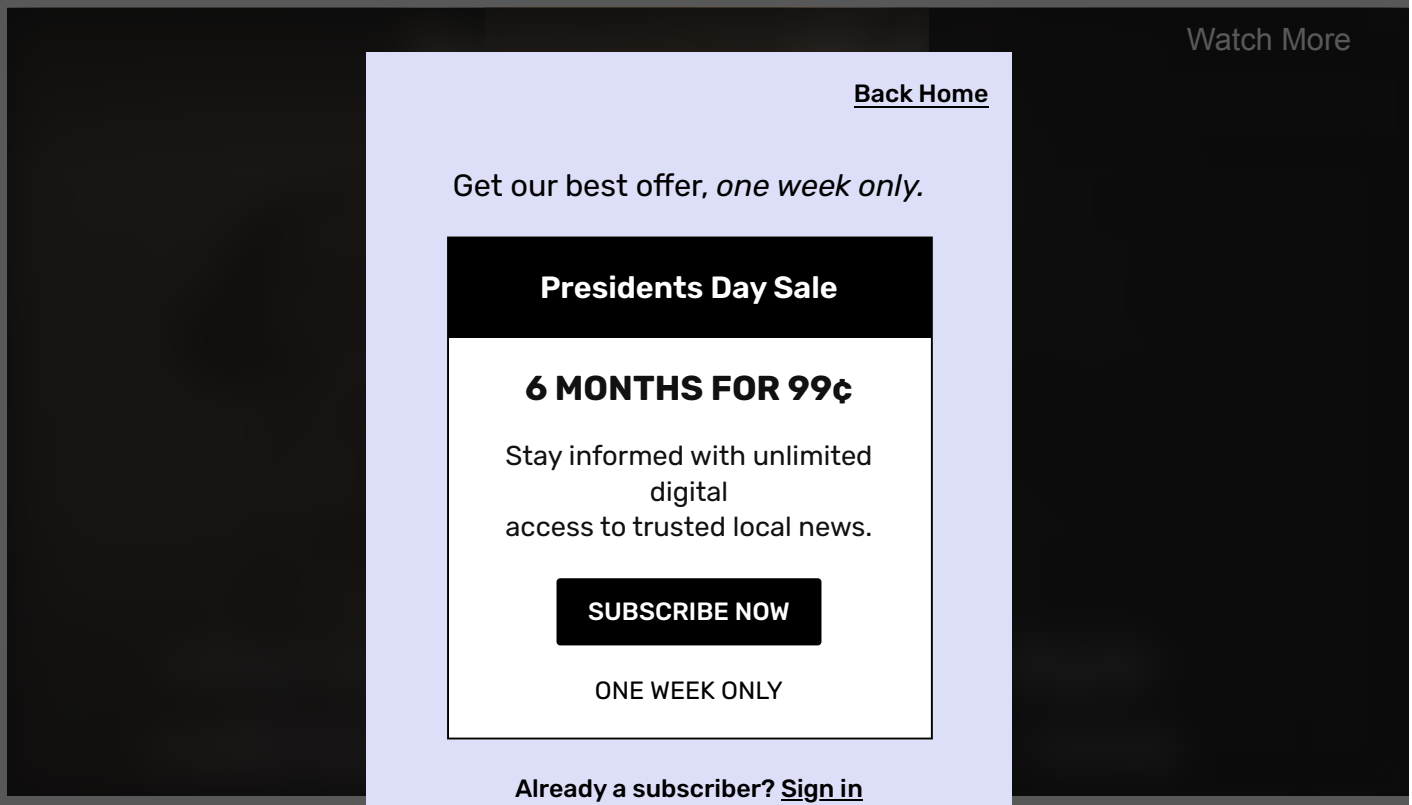


Stephen Jones, a molecular biology postdoctoral fellow, demonstrates the CHAMP, a device created for scientists to more safely use a new kind of gene editing technique called CRISPR, in the laboratory of Ilya Finkelstein at UT on Friday. JAY JANNER / AMERICAN-STATESMAN

Austin American-Statesman

Ilya Finkelstein chuckles when recounting the origins of the project that landed the University of Texas scientist and his colleagues in the prestigious academic journal Cell.



According to a peer-re ntists to more safely use a new kind of gene editing technique called CRISPR — a technology that has embroiled much of the scientific world in seemingly fantastic debates, such as whether creating mushrooms that don't brown in supermarkets could lead to people creating new animals or ordering babies with designer DNA.

Thanks to CRISPR, the debates are no longer abstract arguments inspired by science-fiction films. Th the shelves of stores. Chinese scientists in 20 g CRISPR to manipulate human em ay many scientists feared it would. Only tw implications of CRISPR only marginall s are using the technology on human rnering international headlines earlier this m

Finkelstein and his coll basically makes CRISPR less likely to sc to their paper. They say their work could en diabetes while significantly reducing t

The breakthrough was ke the setup for a joke about a mismatched set of people walking into a bar — a mechanical engineer, a mathematician, a biochemist and an astrophysicist. And it started with a humble plea:

“Does anyone want to earn a Ph.D. digging through the garbage?”

‘Make this safer’

Finkelstein began mak fessor in the Department of Molecu o is dedicated to studying the how the h d been looking for an opportunity to work wi

The technology — wh interspaced short palindromic repeats” — g experiments on yogurt cultures. They f that fight viruses quite effectively. Other lly came CRISPR, which exploits the syst es. It allows researchers to use proteins to cut out selected segments of DNA and, if needed, insert new ones.

CRISPR is fast enough that experiments that used to take months or years can be finished in days, accelerating the pace of scientific advancement. The technique has spread so quickly that no one at the University of Texas is sure how many of its scientists are using CRISPR in their experiments.

Scientists are still dete ules interact with various types of DNA. R molecules? Do they sometimes confuse on one instead of the other? How do you tes

Finkelstein is among th nique can do for humanity by, for instan s that the technology is nowhere near ready modifying the DNA of each cell in an adult, a ryos.

“That said, no one is lis esman. “So why not try to make this safer?”

‘I love gadgets’

The idea started with an expensive DNA sequencer that researchers on the floor above Finkelstein's lab have been using to analyze peoples' genes. The DNA is loaded onto special slides before being placed in the machine, which uses a chemical process to analyze the DNA. O — complete with the DNA. Finkelstein saw ch to test CRISPR.

The problem: Finkelste joining the project.

"I guess the moral of th telling people they will be digging through tra ss or naïve to know what they're doing," he

Wry observations asid goes beyond evolution. Finkelstein notes that p ke green corn — something that would

“Essentially, we’re short-circuiting evolution. Now we can do things evolution can never do,” Finkelstein said. “We’re at the ‘Gattaca’ moment,” he added, referencing the 1997 sc-fi film about genetic manipulation, “I really think that.”

As Finkelstein was looking for people to help make the “moment” safer, Cagri Savran happened to be looking for a project on which to work.

Savran is a professor c g at Purdue University. His lab makes medical blood impurities. He had collaborated with nd, when the opportunity for a sabb ded Savran to spend it in Austin.

Savran wanted to brar partnering with people who practice “f nt bring over one of his projects from Purdu ss the hallway and introduced him to Fink an could build a machine to conduct ex in had noticed were sitting in a trash bin or

Savran agreed. He was not aware that the project had a shortage of scientists.

“I’m an engineer,” he told the Statesman. “I love gadgets, finding gadgets and tearing them apart and putting them together, even if I have to pull parts out of the trash.”

‘You can’t have it leaking’

The team working on t hree people are listed as lead authors on the eam members say the project worked largely ts, mentalities and approaches. Finkelstei or, said his contribution boiled dov alk to one another, and two, to keep the li

The fundamental challenge the team faced: compiling the mind-boggling amount of data needed to really know if CRISPR can be trusted to accomplish what its proponents say it can. To that end, Savran built a machine mounted on a high-resolution microscope. To use it, scientists load the slides created by DNA sequencer

and then squirt them with a solution that includes CRISPR proteins. The contraption then tracks the various proteins and their interactions with various sections of DNA.

It essentially performs many mini-experiments at once.

The machine's design and software are open source. That means that, in theory, anyone with the funds can build one and run it. Savran said his challenges included making the machine simple enough that any biology student could use it, sturdy enough that no one would break it, and reliable enough that "you don't have it leaking all over a really

Other challenges called … an cells are mostly empty space, with the … that mapping them is akin to mapping the co… ress, a UT astrophysicist who has … "computational biology." Press and his … what was happening on the slides — a syste… eaches of the universe.

The UT team hopes the work will form the basis for all sorts of CRISPR tests around the world.

‘Nothing is perfect’

This is where the ethics debate meets the realities of human progress.

In a study published earlier this month in the journal Nature, scientists explained how they successfully edited genes in human embryos to repair a common serious mutation that causes fatal heart conditions. As a New York Times article noted, “The research marks a major milestone and, while a long way from clinical use, it raises the prospect that gene editing may one day protect babies from a variety of hereditary conditions.”

The article added: “The an genetic engineering, once feared and unthinkable, and is sure to renew ethical concerns that some might try to design babies with certain traits, like greater intelligence or athleticism.”

The UT researchers envision their work being used to help prevent or cure sickness — tailoring individual gene therapies for people, as opposed to tailoring new kinds of people. The hypothetical question du jour at UT asks: What if scientists can discover

whether a particular CRISPR protein will cure a case of diabetes but also cause cancer?

Finkelstein argues that if they can, they should — even if they cannot make the technology perfect.

“Whenever you look at this precision cutting, you always worry about cutting in the wrong place,” Finkelstein said. “Nothing is going to be perfect. The question is whether we we can live with the risk.”

Savran uses a more Au

“One thing I had to get used to was the traffic in the Austin area,” he said. “I had to take extra care to drive as safely as possible. Even then there was risk. But the benefit, at least for me, was worth the risk.”

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