with the ancient rocks in its centre that date back roughly four billion years, and unstable regions in the east. Compared with the United States, "Canada covers an even wider portion of Earth history that could be investigated", says Andy Frassetto, a seismologist at the Incorporated Research Institutions for Seismology in Washington DC.

EON-ROSE organizers have begun the project with a series of smaller studies, such as Eaton's, while they seek full funding. Another study took place this summer, when researchers from the Geological Survey of Canada and Geoscience BC descended on Mount Meager, which is in southern British Columbia and is Canada's most recently active big volcano. Their goal was to explore whether its volcanic warmth — which heats groundwater up to 240 °C — could be tapped for geothermal energy.

In July, geologists travelled around the mountain in helicopters to install instruments similar to those envisioned for EON-ROSE. The researchers are crunching the preliminary data now, aiming to see where permeable rocks channel Mount Meager's volcanic heat towards the surface. Future studies in other parts of Canada could help geologists to find new sources of geothermal energy — such as in the remote Arctic, where residents often rely on imported diesel, says Stephen Grasby, a geochemist at the Geological Survey of Canada in Calgary who led the work.

Hidden treasure

EON-ROSE also aims to identify mineral deposits by looking for geological structures deep below the surface that might underlie lodes of gold or copper. This approach could make it easier to prospect for minerals in the country's northern reaches, where harsh winters and a shortage of roads make it difficult to explore.

"You could spend forever up there wandering around before you discover anything," says Keith Benn, a mineral-exploration consultant in Port Lambton, Canada. "This is the promise of the EON-ROSE approach — when you look at this expansive territory in northern Canada, we can say, 'we can help you decide where to start'."

Benn is working with mining companies to drum up funding for a pilot EON-ROSE study of the ancient rocks of central Canada.

This focus on energy and mineral exploration goes beyond the purely scientific aims of EarthScope. EON-ROSE organizers hope that a broader focus will help them win funding from industry. "To move forward, we must have practical applications that benefit Canada," says Katherine Boggs, a geologist and project leader at Mount Royal University in Calgary.

Ultimately, the scientists hope to get the bulk of their funding from the federal government — although Canada's general election on 21 October could markedly shift the outlook for science funding.

PRECISE CRISPR TOOL COULD TACKLE HOST OF GENETIC DISEASES

Greater control could allow many more conditions to be treated with gene editing.

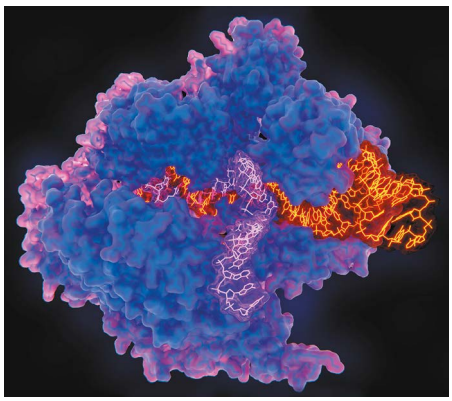
By Heidi Ledford

For all the ease with which the wildly popular CRISPR–Cas9 gene-editing tool alters genomes, it's still somewhat clunky and prone to errors and unintended effects. Now, an alternative offers greater control over genome edits — an advance that could be particularly important for developing gene therapies.

The alternative method, called prime editing, improves researchers' chances of getting only the edits they want, instead of a mix of changes that they can't predict. The tool, described in *Nature* (A. V. Anzalone *et al. Nature* http://doi.org/dczp; 2019) on 21 October, also reduces the 'off-target' effects that are a key challenge for some uses of the standard CRISPR–Cas9 system. That could make prime-editing-based gene therapies safer.

The tool also seems capable of making a wider variety of edits, which might one day allow it to be used to treat the many genetic diseases that have so far stymied gene editors. David Liu, a chemical biologist at the Broad Institute of MIT and Harvard in Cambridge, Massachusetts, and lead author of the study, estimates that prime editing might help researchers tackle nearly 90% of the more than 75,000 disease-associated DNA variants listed in ClinVar, a database developed by the US National Institutes of Health.

And the specificity of the changes that prime editing is capable of could make it easier for researchers to develop models of disease, or to study specific gene functions, says Liu.



JUAN GAERTNER/SPL

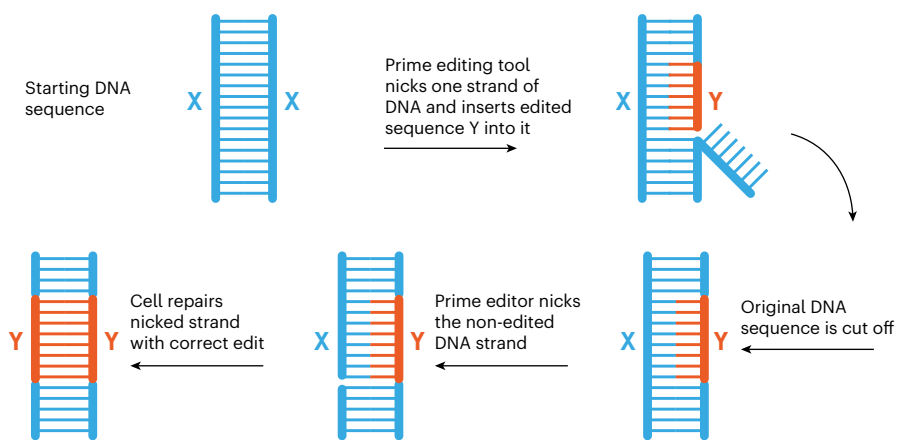
A new gene-editing tool offers more control than CRISPR–Cas9 (pictured).

"It's early days, but the initial results look fantastic," says Brittany Adamson, who studies DNA repair and gene editing at Princeton University in New Jersey. "You're going to see a lot of people using it."

Prime editing might not be able to make the very big DNA insertions or deletions that CRISPR–Cas9 is capable of — so it's unlikely to completely replace the well-established editing tool, says molecular biologist Erik Sontheimer at the University of Massachusetts Medical School in Worcester. That's because for prime editing, the change that a researcher wants

PRECISION EDITOR

Prime editing reduces the number of unintended changes to a genome by inserting the edits researchers want to make into the DNA itself. This contrasts with CRISPR–Cas9, which relies on the cell's repair system to make the changes.



to make is encoded on a strand of RNA. The longer that strand gets, the more likely it is to be damaged by enzymes in the cell.

"Different flavours of genome-editing platforms are still going to be needed for different types of edits," says Sontheimer.

But prime editing seems to be more precise and versatile than other CRISPR alternatives. Those include modified versions of CRISPR–Cas9 that enable researchers to swap out one DNA letter for another, and older tools such as zinc-finger nucleases, which are difficult to tailor to each desired edit.

Freedom through control

CRISPR–Cas9 and prime editing both work by cutting DNA at a specific point in the genome. CRISPR–Cas9 breaks both strands of DNA at once and then relies on the cell's own repair system to patch the cuts and make the edits. But that repair system is unreliable and can insert or delete DNA letters at the points where the genome was cut. This can lead to an uncontrollable mixture of edits that vary between cells.

Even when researchers include a template to guide the edits, the DNA repair system in most cells is much more likely to make those small, random insertions or deletions than to add a specific sequence to the genome. That makes it difficult for researchers to use CRISPR–Cas9 to overwrite a piece of DNA with a sequence of their choosing.

Prime editing bypasses these problems (see 'Precision editor'). It, too, uses Cas9 to recognize specific DNA sequences, but the prime editor's Cas9 enzyme is modified to nick only one DNA strand. Then, a second enzyme called reverse transcriptase, guided by a strand of RNA, makes the edits at the site of the cut.

The prime-editing enzymes don't have to break both DNA strands at the same time to make changes, freeing researchers from relying on the cell's genome repair system — which they can't control — to make the edits that they want. This means that prime editing could enable the development of treatments for genetic diseases caused by mutations that aren't easily addressed by existing gene-editing tools.

Previously, researchers, including Liu, thought that they would need to develop gene-editing tools specific to each category of change they wanted to make in a genome: insertions, deletions or DNA letter substitutions. And the options were limited when it came to making precise substitutions.

An older technique, called base editing, which is comparable in precision to prime editing, chemically converts one DNA letter directly into another — changing a T to an A or a G to a C — without breaking both DNA strands. That's something CRISPR–Cas9 can't do. Developed by Liu, base editing could be useful for correcting genetic diseases caused by single-letter mutations, including the most common form of sickle-cell anaemia.

But base editing can't help with genetic disorders caused by multi-letter mutations such as Tay–Sachs disease, a usually fatal illness typically caused by the insertion of four DNA letters into the *HEXA* gene. So Liu and his colleagues set out to create a precise gene-editing tool that gave researchers the flexibility and control to make multiple types of edits without having to create bespoke systems.

"It's fantastic," says Sontheimer. "The breadth of the mutations that can be introduced is one of the biggest advances. That's huge."

Liu's team, and others, will now need to carefully evaluate how well the system works in a variety of cells and organisms. "This first study is just the beginning — rather than the end — of a long-standing aspiration in the life sciences to be able to make any DNA change at any position in an organism," says Liu.

RUSSIAN SCIENTIST EDITS HUMAN EGGS IN EFFORT TO ALTER DEAFNESS GENE

Denis Rebrikov says he does not plan to implant gene-edited embryos until he gets regulatory approval.

By David Cyranoski

Russian biologist Denis Rebrikov has started editing genes in human eggs with the goal of repairing a mutation that can cause deafness. The news, detailed in an e-mail he sent to *Nature* on 17 October, is the latest chapter in a saga that kicked off in June, when Rebrikov revealed his controversial intention to create gene-edited babies resistant to HIV using the popular CRISPR tool. So far, only one person has claimed to have created a baby from a gene-edited embryo — the Chinese scientist He Jiankui, in November 2018.

Rebrikov's e-mail (see Q&A on page 466) follows a September report in the Russian magazine *N+1,* in which he said a couple who both have a genetic mutation that impairs their hearing had started procedures to collect eggs that would be used in an attempt to create a gene-edited baby. The eggs that Rebrikov has edited so far are from women without the genetic mutation. He says the goal of those experiments is to learn how to allow couples with the mutation to have a child with unaffected hearing.

He also wants to better understand potentially harmful 'off-target' mutations, which are a known challenge of using the CRISPR–Cas9 system to edit embryos.

Rebrikov says he does not plan to use the tool to create such a baby yet — and that his previously reported plan to apply this month for permission to implant gene-edited embryos in women has been pushed back.

Instead, he says, he will soon publish the results of his egg experiments, which also involved testing CRISPR's ability to repair the gene linked to deafness, called *GJB2*, in body cells taken from people with the mutation. People with two mutated copies of *GJB2* cannot hear well without interventions such as hearing aids or cochlear implants. Rebrikov says that these results will lay the groundwork for implanting an edited embryo.

Rebrikov adds that he has permission from a local review board to do his research, but that this does not allow transfer of gene-edited eggs into the womb and subsequent pregnancy.

Apart from the couple who agreed to start undergoing egg collection, he is in discussion with four other couples in which both would-be parents have two mutated *GJB2* genes, he says.

Rebrikov also provided further information about the couple who agreed to the procedures. In September, *N+1* reported that the couple hadn't signed a consent form and had backed away from the idea of creating a gene-edited child, citing personal reasons.

"I will definitely not transfer an edited embryo without the permission of the regulator."

But Rebrikov now says that this is only a temporary hurdle. He notes that the woman who donated the eggs has taken a one-month pause while she gets a cochlear implant.

Rebrikov also emphasized that he will not move forwards without approval from the Ministry of Health of the Russian Federation. "I will definitely not transfer an edited embryo without the permission of the regulator."

That might not come any time soon. Earlier this month, the ministry released a statement saying that production of gene-edited babies is