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# Editing life: A guide to the genetic revolution on our doorstep

A new gene editing technique called CRISPR is revolutionising medicine, and our relationship with our genes. It holds great promise, but also great dangers

THE food on your plate. The pets at your feet. The plants in your garden. The mosquitoes whining in your ear at night. The cells in your body. And perhaps even the brains and bodies of your children. All of these could be transformed by a new gene-editing technique – starting in your lifetime.

Terms like breakthrough and revolutionary are much abused. But when it comes to CRISPR gene editing, they are probably understatements. "The technology is unbelievable," says Kamel Khalili of Temple University in Philadelphia, who thinks it could clear viruses like HIV from the body.

# Major impact

The pace of innovation is breathtaking. Just a few years after its invention, CRISPR gene editing is already having a major impact on biomedical research. It makes it easy to "turn off" genes one at a time, to see what they do. It can introduce specific mutations, to find out why they make cells cancerous or predispose people to diseases. And it can be used to tinker with the genes of plants and animals, to create drought-resistant maize, more muscular police dogs and much more.

In the not too distant future, CRISPR-based research could bring drugs for tackling obesity, more powerful gene therapies and plentiful supplies of transplant organs. "CRISPR is evolving incredibly fast," says Waseem Qasim of University College London, whose team recently used an older form of gene editing to save the life of a baby with leukaemia. "We can't keep up."

Then there is the most controversial application: it could be used to permanently alter the genomes of our descendants, in order to eradicate disease-causing mutations or even to enhance children by adding beneficial gene variants that both their parents lack.

We have been talking about the possibility of genetically engineering humans for decades, says Debra Mathews of the Johns Hopkins Berman Institute of Bioethics in Baltimore. "But we've never had a technology that had a reasonable chance of doing what we want to do without causing harm before."

This so-called germline gene editing hit the headlines in April, when the results of the first attempts to modify human embryos with CRISPR were published by a team in China. Rumours about such attempts had already led to calls for a voluntary ban on editing genes in human embryos. That's one of the issues on the agenda at an international meeting on gene editing hosted by the US National Academy of Sciences this week.

Those in favour of such research say there might be good reasons for allowing germline gene editing, and that it is a powerful tool for understanding human embryonic development, which may reveal why some people are infertile or miscarry, for example.

In the following pages we look at the potential of CRISPR gene editing to transform medicine – and also its dangers.

**Read more:** "CRISPR: The gene-editing revolution on our doorstep"

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*(Image: Stephen Isis/Eyeem/Getty)*

## Gene editing decoded

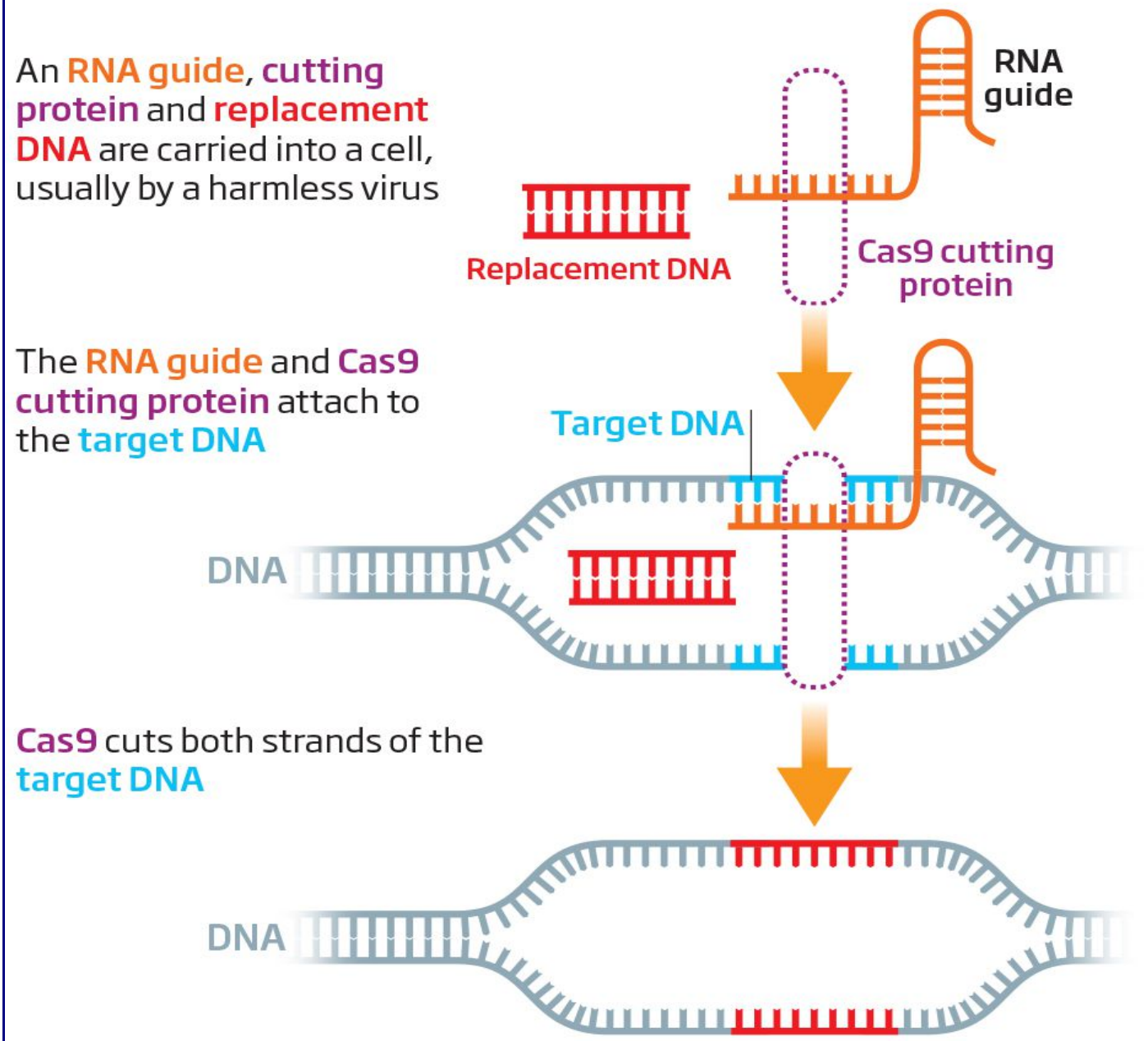
**Germline editing** Altering the genes of sperm and egg cells, or early embryos, so that changes are passed to subsequent generations

**Somatic cells** All cells in the body except sperm and eggs. Changes to these cells are not passed on to offspring

**CRISPR** Gene-editing technique derived from a mechanism that bacteria use to fight off viruses. Cheaper, faster and more precise than earlier methods

# Cut and paste

CRISPR allows one or more genes to be edited far more precisely than ever before




**Gene drive** Gene-editing technique that allows traits to spread faster through a population than they would normally

**PGD (preimplantation genetic diagnosis)** Screening embryos fertilised through IVF for genetic diseases before they are implanted in a woman's uterus

### How do CRISPR gene splicers work?

The first forms of genetic engineering involved adding extra bits of DNA to the genomes of plants and animals, with no control over where they ended up. One method involved shooting bullets coated with DNA at cells.

Gene editing, in contrast, adds DNA to precise spots in a genome, or alters a specific sequence, so is far superior. While a few methods of gene editing had been developed, until the advent of CRISPR, it was usually slow, difficult and very expensive.

CRISPR targets a particular DNA sequence using a piece of RNA that's complementary to that DNA. Linked to it is a protein derived from bacteria, called Cas9. The RNA finds the right bit of DNA and binds to it, then Cas9 cuts it (see diagram above). The cell's repair mechanisms will re-join the two pieces, but in the process the DNA sequence gets slightly altered. This is how genes can be disabled.

## Donor DNA

If, however, donor DNA with ends that match the DNA on either side of the cut segment is added to cells too, the cell thinks it is a fragment of broken DNA and will splice it into the genome exactly where the cut was made – adding DNA to a precise spot.

The Cas9 protein can also be modified so that instead of cutting DNA, it controls the activity of the local gene or genes – boosting or blocking their activity.

The effects of this will be short-lived: things return to normal once the Cas9 protein breaks down.

But it may be possible to produce longer-term changes in gene expression through epigenome editing, which alters gene switches, rather than genes themselves. This could one day help treat the wide range of disorders thought to involve epigenetic changes, including addiction and depression.

By **Michael le Page**

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