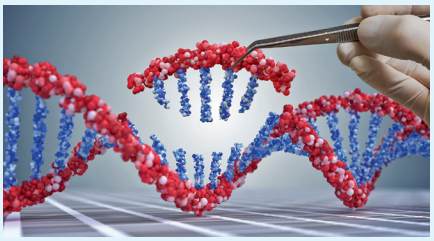
In English

New gene-editing tool could fix genetic defects

A team led by scientists from Harvard University and the Massachusetts Institute of Technology have developed a new gene-editing tool that represents a major advance with respect to the traditional CRISPR method. The researchers used their new technique, dubbed "prime editing," in lab-grown human cells to correct the genetic defects that cause sickle cell disease and Tay-Sachs disease, they report in a study published in Nature.



CRISPR

The gene-editing method CRISPR has transformed biology, giving scientists the ability to modify genes to treat or prevent genetic diseases by correcting dangerous mutations, and to create a host of new genetically modified plants and animals. But the technique, which involves using an enzyme called nuclease that acts as molecular scissors to "cut" DNA, can cause unintended or off-target effects, such as unwanted genetic material being inserted or deleted. This can have negative consequences, including activating genes that cause cancer; most mutations cannot be corrected easily without creating these undesirable genetic by-products.

Base editing

In 2016 a team led by D. Liu developed another method, called base editing, which allows the making of precise edits to single DNA letters without relying on double-stranded breaks. This technique, however, can only be used to fix 4 out of the 12 types of "point" genetic mutations, which include insertions, deletions and combinations of the two. Now Liu, Anzalone and their colleagues have developed a new gene-editing tool that avoids these double-stranded breaks and can correct all 12 types of point mutations.

Prime editing

Prime editors consist of two components, a protein and an RNA molecule. The first is an engineered form of the common CRISPR enzyme Cas9 combined with a second enzyme called reverse transcriptase. The second is an engineered guide RNA, called a pegRNA, which both specifies the target site in the DNA and serves as a template for the desired edit. At the target site, the engineered Cas9 makes a nick in one strand of DNA, and the reverse transcriptase directly copies the pegRNA into a new DNA strand attached at that point, letter by letter. This creates an extra "flap" of DNA with the edited sequence, which is excised by an endonuclease of the cell. The prime editor then cuts the unedited, mismatching strand, prompting the enzymes naturally present in the cell to remake it, thus completing the edit.

(*Adapted from* Scientific American)

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Student worksheet

Comprehension activity

1 Answer the following questions.

- **a.** What is the scope of applicability of genome editing tools?
- **b.** What is the main drawback of CRISPR?
- **c.** Make a list of the steps involved in prime editing.

2 Write a summary of the article (max. 200 characters).

The science in it: explain and justify your answers

3 Has prime editing been applied to human beings yet? Why? What is the state of the art of gene therapy?

4 How many strands of DNA does the Cas9 nuclease in CRISPR cut? How many does the engineered version of it as utilized in prime editing nick? How many instances of DNA pairing does prime editing require to get to completion? As such, which is the most accurate techique?

Go online: find information online and answer the following questions

5 Keep reading the article to complement the list of steps drafted in question 1c with the necessary molecular details.

6 What does the acronym CRISPR-Cas9 stand for? Discover what the original function of these DNA sequences and related enzymes is, and how they have been hijacked to serve human needs.

Glossary

- ***Mutation***: alteration of the nucleotide sequence in the genome.