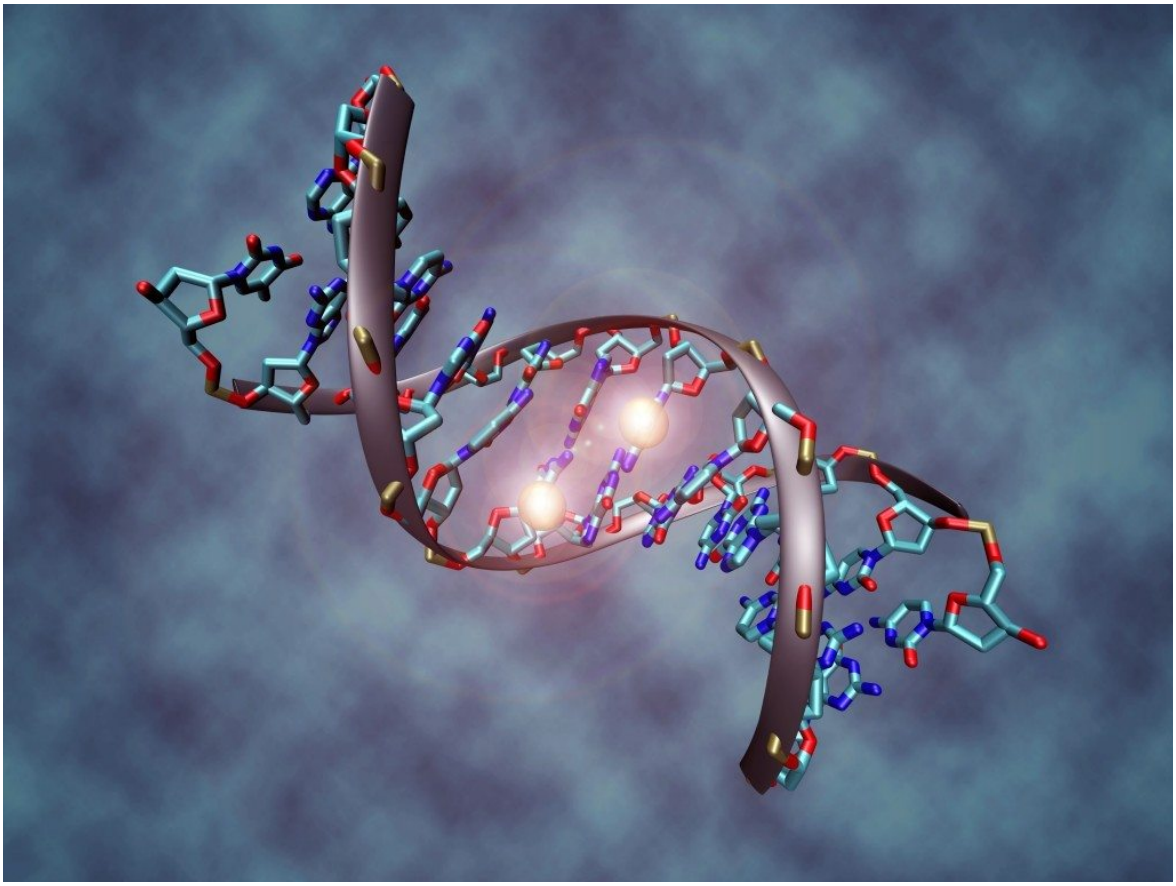

CRISPR DNA Editing Tool Gets Major Upgrade

Technocrat and Transhuman geneticists are salivating to get their hands on this revolutionary technology that will give them total and direct control over the human genome and other DNA-based life forms. TN Editor

A new form of the genome-editing tool CRISPR-Cas9 appears to significantly expand the range of diseases that could be treated with the technology, by enabling scientists to precisely change any of DNA's four "letters" into any other and insert or delete any stretch of DNA — all more efficiently and precisely than previous versions of CRISPR. Crucially, scientists reported on Monday, it accomplishes all that without making genome-scrambling cuts in the double helix, as classic CRISPR and many of its offshoots do.

News about this “prime editing” began circulating among CRISPR-ites this month, when the inventors unveiled it at a meeting at Cold Spring Harbor Laboratory. Since then, “the excitement has been palpable,” said genetic engineer Fyodor Urnov of the University of California, Berkeley, who was not involved in the research.

“I can’t overstate the significance of this,” he said, likening the creation of ever-more kinds of genome-editing technologies to the creation of superheroes with different powers: “This could be quite a useful Avenger for the genome-editing community, especially in translating basic research to the clinic” to cure diseases ranging from sickle cell to cystic fibrosis.

Prime editing’s inventors, led by David Liu of the Broad Institute of MIT and Harvard and postdoctoral fellow Dr. Andrew Anzalone, say it has the potential to correct 89% of known disease-causing genetic variations in DNA, from the single-letter misspelling that causes sickle cell to the superfluous four letters that cause Tay-Sachs disease. All told, they report making 175 edits in human and mouse cells.

“There are more than 75,000 DNA changes associated with genetic diseases,” Liu told reporters ahead of the online publication in Nature describing prime editors. “Collectively, they cover all of these.”

Prime editing improves on CRISPR-Cas9 (and all of the tweaks researchers have made to it in the last seven years) in several crucial ways, Liu said. It can change any of DNA’s four nucleotides, or “letters” — denoted A, T, C, and G — into any other, a total of 12 possibilities.

One of Liu’s earlier CRISPR inventions, called base editing, can make only four of those changes: C-to-T, T-to-C, A-to-G, and G-to-A. It cannot, for instance, correct the sickle-cell-causing mutation in the hemoglobin gene, which requires changing a T to an A at a precise spot.

“Prime editing,” Urnov said, “is excellent for the repair of [such] point mutations,” which are the cause of some 7,000 inherited genetic diseases.

Unlike other forms of CRISPR, prime editors easily make those repairs in

non-dividing cells such as neurons and muscle cells, which genome-editing researchers are eyeing as targets for treating diseases ranging from Duchenne muscular dystrophy to Rett syndrome.

In addition to changing one nucleotide to another, prime editors can remove a precise number of nucleotides from a precise spot in the genome. For instance, the Broad scientists removed (from human cells growing in lab dishes) the four nucleotides in the gene HEXA that cause Tay-Sachs disease. Elsewhere, they were able to remove as many as 80.

“It looks like prime editing will offer some new capabilities to the genome editing community,” said biochemist Benjamin Kleinstiver of Massachusetts General Hospital, whose research centers on turning genome editing into “molecular medicine.”

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