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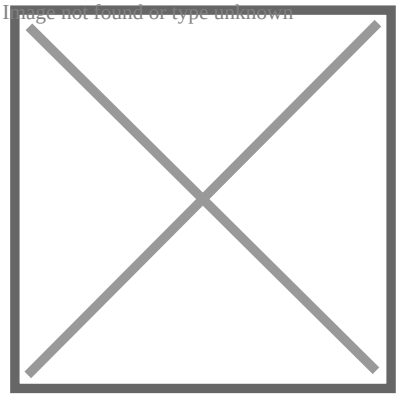

‘CRISPR 2.0’ Used To Change Patient’s DNA For First Time

Description

USA: Transhuman scientists are very clear about hijacking evolution and taking things into their own hands to create humanity 2.0. The first sentence below echoes the the thoughts of former Chief Medical Officer of mRNA Vax maker Moderna: “We are actually hacking the software of life. We think about it as an operating system.” ? TN Editor

Scientists are rewriting the code of life with a new technology that promises to cure inherited diseases by precisely correcting genetic typos. Known as base editing, the technology empowers researchers to pick a single letter amongst the three billion that compose the human genome, erase it, and write a new letter in its place.

Base editing is an updated version of the gene editing tool CRISPR, which has revolutionized life sciences research and is making strides in treating genetic blood and liver diseases. But some scientists think base editing, sometimes billed as CRISPR 2.0, could be safer and more precise than the original. And this summer, the sequel technology is being used in patients for the first time.

On Tuesday, the Boston biotech firm Verve Therapeutics announced that it had edited the DNA of a person with a genetic condition that causes high cholesterol and predisposes them to heart disease. The base editor is designed to tweak a gene in the liver, curtail the accumulation of cholesterol, and hopefully lower the risk of heart attacks.

Base editing is making its way into studies for other conditions as well. Earlier this year, researchers at University College London quietly began a clinical trial using base editors to engineer immune cell therapies for leukemia — likely the first time base editors were used as part of any experimental medicine. And Cambridge firm Beam Therapeutics plans to use base editors to treat people with genetic blood diseases in a trial that will launch later this year. The firm also has early stage programs for cancer, liver disease, immune disorders, and vision loss.

The powerful tool that could make all these treatments possible was first conceived by David Liu at the Broad Institute of MIT and Harvard in 2013, when he realized that CRISPR was not a panacea. CRISPR acts like a pair of molecular scissors that cut specific sequences of DNA. While that’s useful

for turning problematic genes off, it doesn't help to fix them.

"We really need ways to correct genes, not just disrupt them," said Liu. "And that's where base editing comes in."

Liu's base editors are modified versions of CRISPR that act like molecular erasers and pencils, swapping one of the four bases, or letters, of DNA for another. One version, developed by his postdoctoral researcher Alexis Komor in 2016, converts a C into a T. A second base editor, developed by his graduate student Nicole Gaudelli in 2017, changes an A into a G.

These two base editors could correct about 60 percent of all single-letter typos that cause rare genetic diseases, yet that's not what scientists are doing first. The three clinical trials of the technology starting this year will use base editors to intentionally create typos.

The potential power of that strategy is clear in Verve's clinical trial. Scientists have discovered multiple genes that raise cholesterol and increase the risk of heart attacks. People with genetic mutations in one of these genes, called PCSK9, have extremely low levels of LDL cholesterol — often called "bad cholesterol" — and are "remarkably protected against heart attack," Kathiresan said. "Our idea was to develop a gene editing medicine that would mimic the natural situation."

Verve uses base editors to introduce a mutation in the PCSK9 gene of patients with familial hypercholesterolemia. The results in monkeys have been remarkable, lowering levels of LDL cholesterol by about 70 percent after two weeks. The levels remained low for at least two years, Kathiresan said.

"This seems like a bigger effect than I would have predicted," said Dr. Sarah de Ferranti, chief of ambulatory cardiology at Boston Children's Hospital. "Even if it were half as effective, I still think that would be a huge game changer."

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