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Scientists use gene editing to correct mutation in cystic fibrosis

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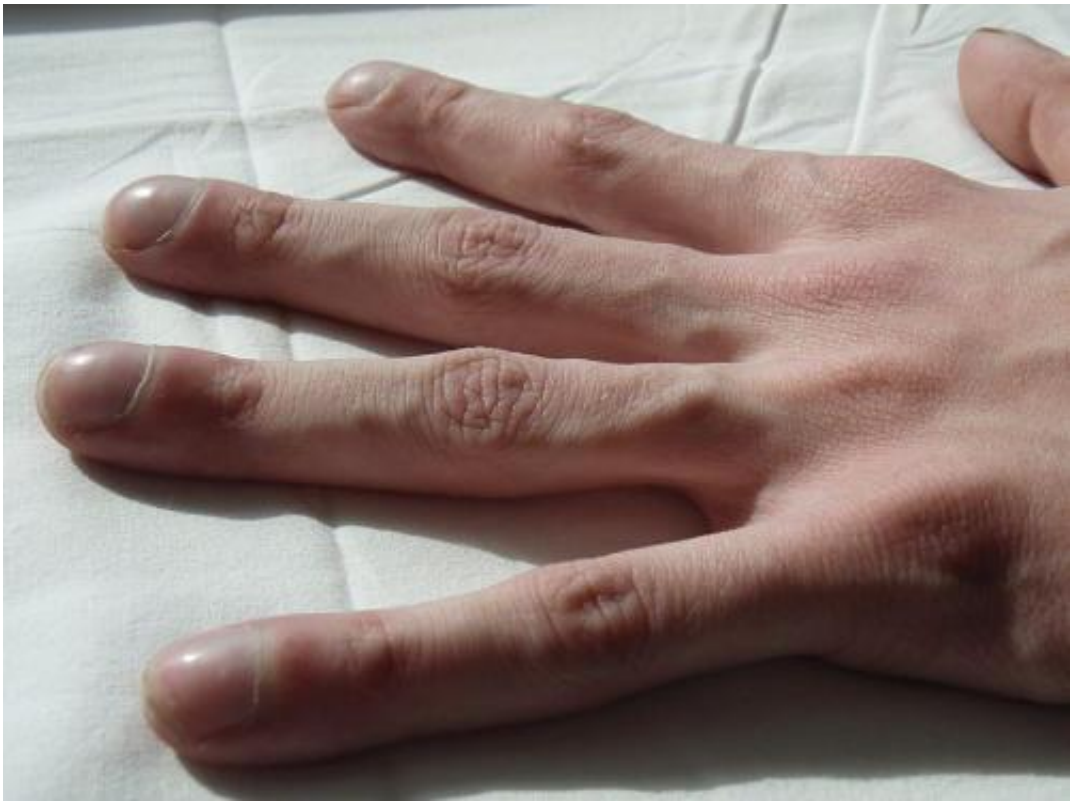

"Clubbing" of the fingers is a classic features of Cystic Fibrosis, although not present in many patients. Credit: Jerry Nick, M.D./ Wikipedia

Yale researchers successfully corrected the most common mutation in the gene that causes cystic fibrosis, a lethal genetic disorder.

The study was published April 27 in *Nature Communications*.

Cystic fibrosis is an inherited, life-threatening disorder that damages the lungs and digestive system. It is most commonly caused by a mutation in the cystic fibrosis gene known as F508del. The disorder has no cure, and treatment typically consists of symptom management. Previous attempts to treat the disease through gene therapy have been unsuccessful.

To correct the mutation, a multidisciplinary team of Yale researchers developed a novel approach. Led by Dr. Peter Glazer, chair of therapeutic radiology, Dr. Mark Saltzman, chair of biomedical engineering, and Dr. Marie Egan, professor of pediatrics and of cellular and molecular physiology, the collaborative team used synthetic molecules similar to DNA—called peptide nucleic acids, or PNAs—as well as donor DNA, to edit the genetic defect.

"What the PNA does is clamp to the DNA close to the mutation, triggering DNA repair and recombination pathways in cells," Egan explained.

The researchers also developed a method of delivering the PNA/DNA via microscopic nanoparticles. These tiny particles, which are billionths of a meter in diameter, are specifically designed to penetrate targeted cells.

In both human airway cells and mouse nasal cells, the researchers observed corrections in the targeted genes. "The percentage of cells in humans and in mice that we were able to edit was higher than has been previously reported in gene editing technology," said Egan. They also observed that the therapy had minimal off target, or unintended, effects on treated cells.

While the study findings are significant, much more research is needed to refine the genetic engineering strategy, said Egan. "This is step one in a long process. The technology could be used as a way to fix the basic

genetic defect in cystic fibrosis."

More information: *Nature Communications*, nature.com/articles/doi:10.1038/ncomms7952

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