Revamped CRISPR could be more accurate and effective against human diseases, including sickle cell anemia

CRISPR is not perfect. Base editors (think of them as gene-editing pencils) can rewrite individual DNA letters. They home in on specific areas of DNA and swap out certain bases — A, C, T, or G — for others. But after the swap, base editors—like the cytosine base editor that converts C•G to T•A — perform unwanted off-target edits. Until now, even the best CRISPR tool, SpCas9, could only bind to about one in 16 locations along DNA, leaving many genetic mutations out of reach.

Now, in two papers published in Nature Biotechnology, researchers at Harvard University, the Broad Institute, and the Howard Hughes Medical Institute have invented new CRISPR tools that address both issues. The first paper describes newly designed cytosine base editors that reduce an elusive type of off-target editing by 10- to 100-fold, making new variants that are especially promising for treating human disease. The second describes a new generation of all-star CRISPR-Cas9 proteins the team evolved that are capable of targeting a much larger fraction of pathogenic mutations, including the one responsible for sickle cell anemia, which was prohibitively difficult to access with previous CRISPR methods.

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