S1mplex: A New Tool for Precision Gene Editing

View U.S. Patent No. 10,907,150 in PDF format.

WARF: P170309US02

Inventors: Krishanu Saha, Jared Carlson-Stevermer, Amr Abdeen, Lucille Kohlenberg

The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in advancing precision gene editing using modular CRISPR ribonucleoprotein complexes.

This highly novel approach has the potential to generate off-the-shelf, preassembled reagents customizable for any patient.

Overview

New tools for human gene editing are rapidly advancing all sectors of biomedicine from basic biology to somatic gene therapy in the clinic. Precise editing of DNA sequences in the human genome can be used to correct mutations or introduce novel genetic functionality for many biomedical purposes. Currently, nonviral delivery of preformed CRISPR ribonucleoproteins (RNPs) is being developed for somatic gene editing applications.

Writing specific DNA sequences into the human genome is challenging with nonviral gene-editing reagents, since most of the edited sequences contain various imprecise insertions or deletions. Faithful writing of DNA – or scarless gene editing – within human cells remains an outstanding challenge, and improved strategies are sought.

The Invention

UW–Madison researchers have developed a modular RNA aptamer-streptavidin strategy, termed S1mplex, to 'sharpen the scalpels' used in genome surgery. In the new approach, CRISPR-Cas9 RNPs are complexed with a nucleic acid donor template, as well as other biotinylated molecules (e.g., quantum dots).

In human pluripotent stem cells, tailored S1mplexes increased the ratio of precisely edited to imprecisely edited alleles up to 18-fold higher than standard gene editing methods, and enriched cell populations containing multiplexed precise edits up to 42-fold.

These advances with versatile, preassembled reagents could greatly reduce the time and cost of *in vitro/ex vivo* gene editing applications in precision medicine and drug discovery, and aid in the development of increased and multiple dosing regimens for somatic gene editing *in vivo*.

Applications

- Potentially include: somatic gene therapy, gene correction for autosomal recessive diseases, CAR T immunotherapies, research tool for human disease modeling, drug discovery and toxicology

Key Benefits

- Advances with the Simplex tool generate new, chemically defined reagents to promote precise editing of the human genome.

Stage of Development

The researchers have found that, using the Simplex approach, precise gene editing is favored at **unprecedented levels** over imprecise editing. Specifically, incorporating diverse new sequences 4-18 nucleotides in length in a scarless and precise manner is up to 4x the levels of imprecise disruption of the target gene sequence without any selection (the current benchmark in the CRISPR-Cas9 field with protein delivery to human cells is approximately 1:1).

Also, they found that enriching for multiplexed, precise gene edits is enabled by the S1mplex approach. Complexed fluorescent labels can be used for the selection of defined sequence edits at two distinct loci, resulting in up to 10 precise edits for every imprecise edit.

Additional Information

For More Information About the Inventors

- Krishanu Saha

Tech Fields

- Drug Delivery : Other drug delivery technologies
- Research Tools : DNA & RNA tools

For current licensing status, please contact Jennifer Gottwald at jennifer@warf.org or 608-960-9854