Library of CRISPR targeting sequences increases power of the gene-editing method

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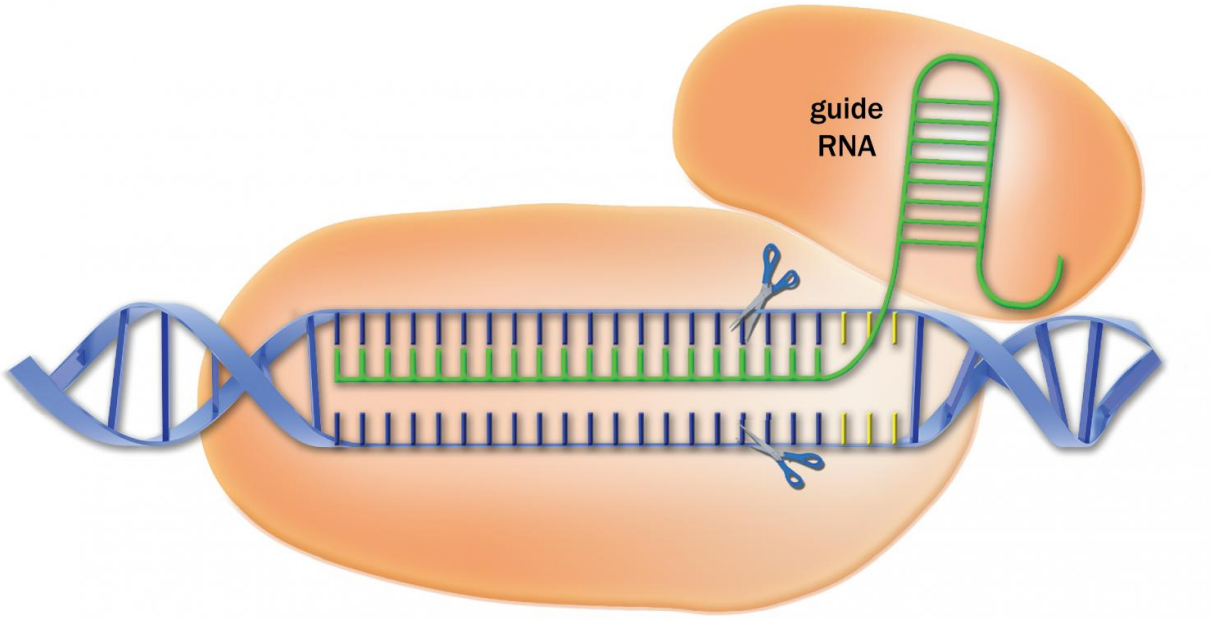

CRISPR-Cas9 is a reprogrammable DNA cutting machine that is being used to edit genomes in many organisms for research purposes. Its primary component, the Cas9 enzyme (orange), cuts genomic DNA (blue). The enzyme is directed to its target--essentially any sequence along the genome--by hitching it to a strand of guide RNA (green) whose sequence is complementary to that of the DNA target. Upon finding and pairing with it, Cas9 snips out the target segment. It can eitherbe deleted or replaced with another DNA sequence (not shown here). A new resource published by Hannon and colleagues provides a library of guide sequences that significantly increases CRISPR's specificity, while limiting off-target effects. The platform also facilitates multiplexing and combinatorial targeting. Credit: Advanced Analytical Technologies

CRISPR, the gene-editing technology that has taken biology by storm, is now more powerful than ever. Scientists have assembled a library of RNA sequences that can be used by researchers to direct the CRISPR-cas9 complex to cut DNA with exquisite, unprecedented precision.

Among other advantages, the new tool greatly increases the likelihood that a CRISPR "cut" (or series of related cuts) will have the functional impact that researchers intend. Disabling or deleting a gene or set of genes is much more certain to succeed fully with the new resource, minimizing the likelihood of "off-target" effects that can diminish the relevance of otherwise carefully planned and executed experiments.

"We've combined a machine learning approach with other strategies to optimize knock-out efficiency," says Professor Greg Hannon of Cancer Research UK Cambridge Institute, who led a team that included Drs. Simon Knott and Nicolas Erard. All three performed some of the research while at Cold Spring Harbor Laboratory (CSHL) prior to Dr. Hannon's move to the UK two years ago. Hannon, who is a CSHL adjunct professor, notes that the CRISPR library also facilitates multiplexing of experiments, as well as combinatorial targeting.

The team's paper introducing the new CRISPR resource appears in *Molecular Cell* July 20th.

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