Advancing gene editing with new CRISPR/Cas9 variant

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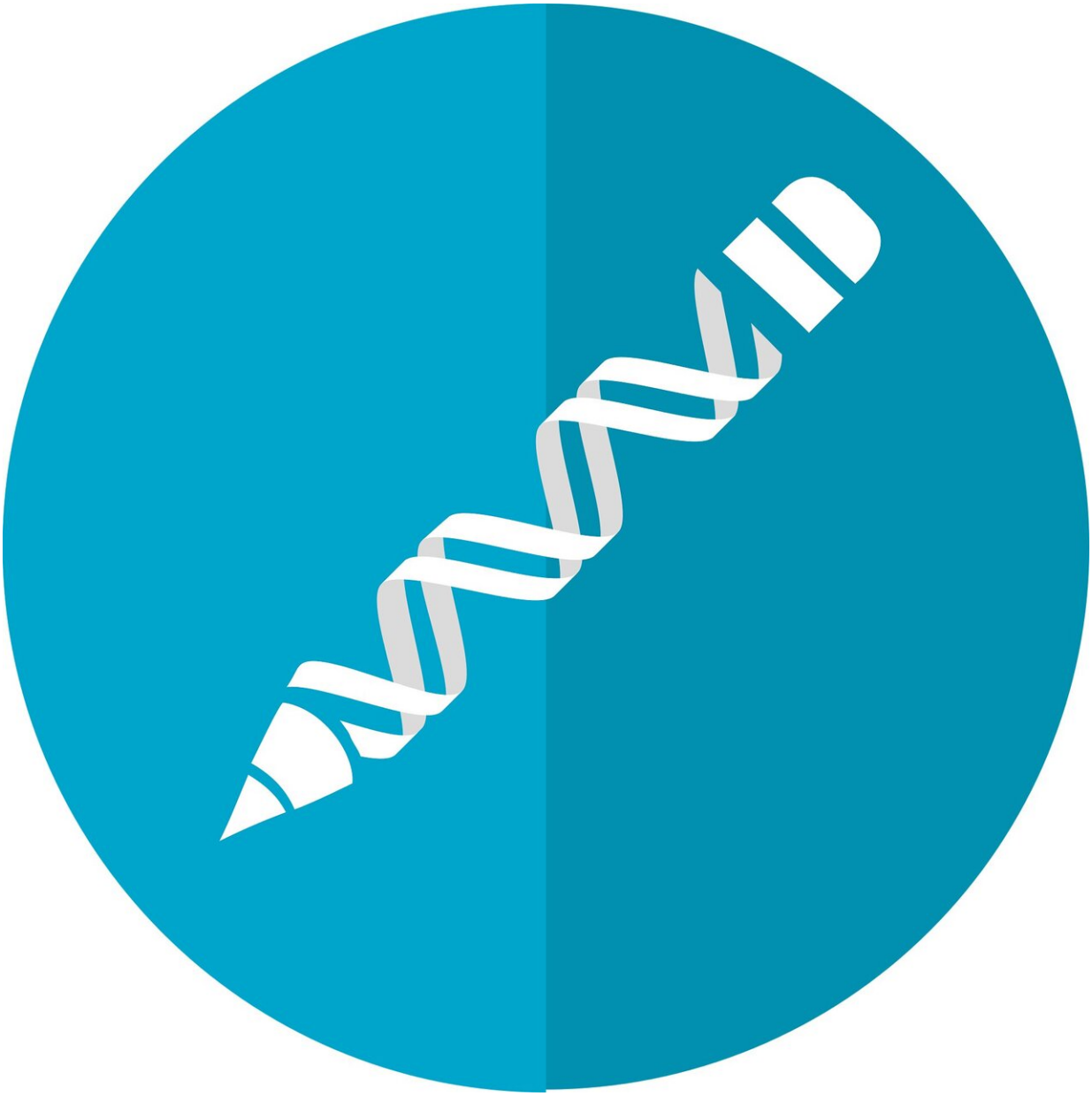

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Using a new variant to repair DNA will improve both safety and effectiveness of the much-touted CRISPR-Cas9 tool in genetic research, Michigan Medicine researchers say.

Those two key problems—safety and efficacy—are what continue to hold CRISPR-Cas9 gene targeting back from its full clinical potential, explains co-senior author Y. Eugene Chen, M.D., Ph.D., a professor of internal medicine, cardiac surgery, physiology, pharmacology and medicinal chemistry, from the Michigan Medicine Frankel Cardiovascular Center.

The new CRISPR-Cas9 variant improves efficiency when inserting a gene or DNA fragment to a precise location in the genome, known as knocking in. It also reduces the rate of unintended insertions or deletions, known as indels, of base pairs that often happen while gene editing.

"We name it meticulous integration Cas9, or miCas9, to reflect its extraordinary capacity to enable maximum integration, yet with minimal indels, as well as to recognize its development at the University of Michigan," write senior authors Chen, Jifeng Zhang and Jie Xu for *Nature*'s "Behind the Paper" series. "It provides a 'one small stone for three birds' tool in gene editing."

The team previously reported Cas9 genome editing in 2014, and reported beneficial effects of a RAD51 agonist, RS-1, in gene editing in 2016.

More information: Linyuan Ma et al, MiCas9 increases large size

gene knock-in rates and reduces undesirable on-target and off-target indel edits, *Nature Communications* (2020). DOI: 10.1038/s41467-020-19842-2

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