Using light to speed up CRISPR-Cas9 gene editing

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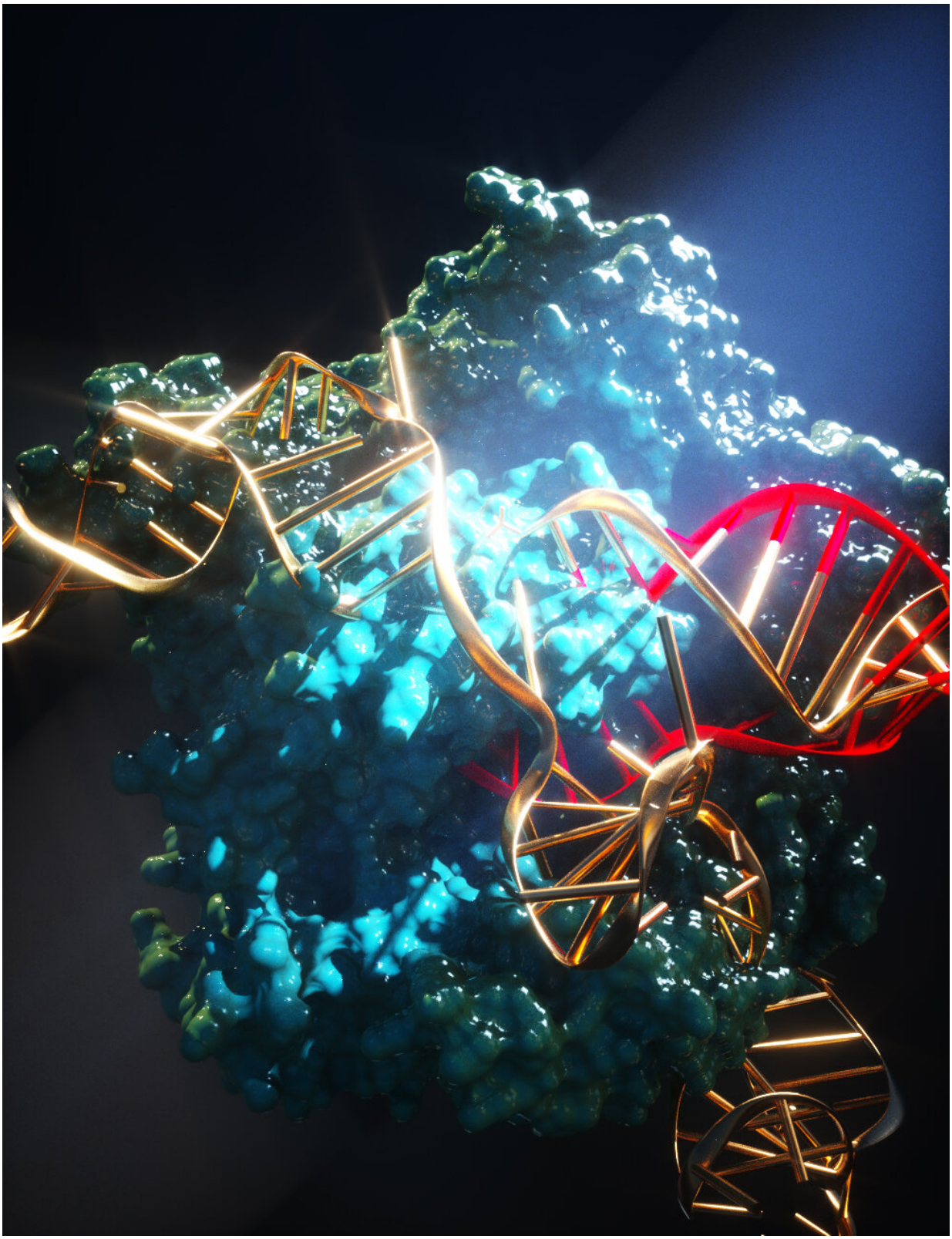

Very fast CRISPR activated by light. Credit: Ella Marushchenko

A team of researchers at Johns Hopkins University has developed a way to speed up the CRISPR-Cas9 gene-editing process by using light-sensitive nucleotides. In their paper published in the journal *Science*, the group describes their process and its precision. Darpan Medhi and Maria Jasin with the Memorial Sloan Kettering Cancer Center have published a Perspective piece in the same journal issue outlining the evolution of CRISPR-Cas9 gene editing and giving an overview of the work done by the team in Baltimore.

With CRISPR-Cas9 gene editing, the enzyme Cas9 is used as scissors to cut strands of DNA at specific spots for editing. A guide RNA molecule is used during editing to help the Cas9 enzyme bind to the DNA at the desired strand spot. Currently, this part of the process takes several hours to complete. In this new effort, the researchers have reduced the time to mere seconds.

The work involved altering some of the guide RNA sequencing by adding light-sensitive nucleotides. Doing so prevented the guide from doing its job until light was applied. And once that light was applied, the binding took place within a matter of seconds. The researchers call it a "caged approach," because the guide is restrained until directed to carry out its job. They have named it very fast CRISPR (vfCRISPR).

The researchers note that holding back the editing process and then activating it so quickly on-demand opens up the possibility of studying the process in more detail. They further state that the procedure also improves precision to the degree that it allows for a single allele to be edited at a time. That may allow researchers to create heterozygous mutations to study complex traits in new ways. Medhi and Jasin describe the work by the team as moving CRISPR-Cas9 from a blunt instrument to a precise tool. They further suggest that vfCRISPR is likely to be a

transformative advance because it will allow a better understanding of the kinetics involved in the cellular response to double-strand breaks during editing.

More information: Yang Liu et al. Very fast CRISPR on demand, *Science* (2020). DOI: 10.1126/science.aay8204