RNA 'heroes' can disarm bad-actor proteins in leukemia: study

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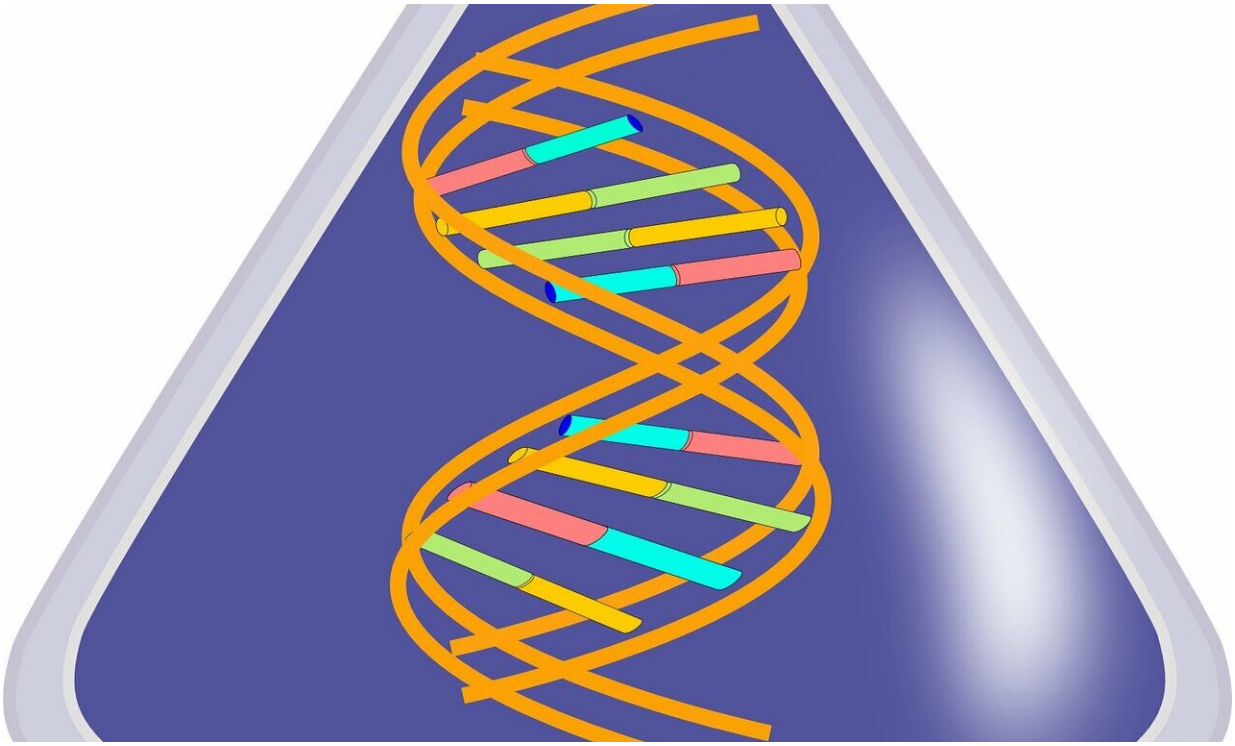

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Scientists at The University of Texas Health Science Center at San Antonio (UT Health San Antonio) believe it may be possible to prevent DNA changes driven by two proteins highly active in leukemia and other cancers. They reported a new mechanistic target for drug development Jan. 21 in the journal *eLife*.

The proteins, called METTL-3 and METTL-14, can alter the chemical structure of DNA—the molecular vault in cells that stores a person's genetic information. This is a new understanding, said article senior author Yogesh Gupta, Ph.D., assistant professor of biochemistry at UT Health San Antonio's Greehey Children's Cancer Research Institute. For 27 years since the discovery of METTL-3 and -14, scientists believed that the proteins could only alter a separate molecule called RNA, but not DNA, he said.

RNA molecules, which float inside cells either reading out DNA instructions to make proteins or influencing this process indirectly, can form different shapes such as hairpins. Dr. Gupta, lead author; Shan Qi, a Ph.D. student in the Gupta lab; and the team observed that RNA of a certain structure like a hairpin can act as a glue that binds to METTL-3 and -14, preventing it from changing DNA's chemical structure.

"It is a desirable therapeutic target," Dr. Gupta said. "By uncovering the DNA-altering function of METTL-3 and -14 and learning that it can be regulated by certain RNAs, we provided information that will help in drug discovery research."

"Our next step is to understand DNA, RNA and METTL-3 and -14 interaction so that we can identify the areas on the proteins for the purpose of drug development," he said.

More information: Shan Qi et al, RNA binding to human METTL3-METTL14 restricts N6-deoxyadenosine methylation of DNA in vitro, *eLife* (2022). DOI: 10.7554/eLife.67150

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