Team investigates chemical modifications to gain deeper insights into genetic regulation mechanisms

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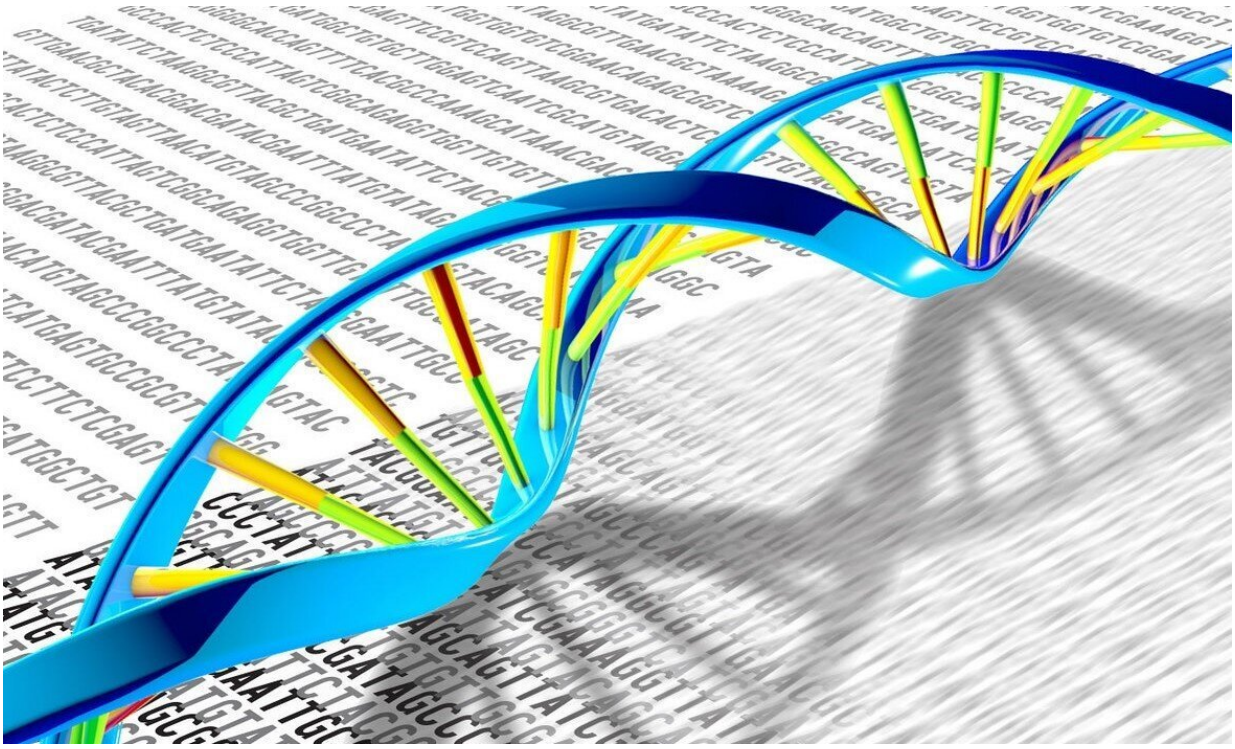

DNA, which has a double-helix structure, can have many genetic mutations and variations. Credit: NIH

University of North Carolina at Chapel Hill researchers have determined whether a specific chemical modification of a protein that packages the

genome called a histone affects gene activity and cell proliferation, according to the paper, "Drosophila melanogaster Set8 and L(3)mbt function in gene expression independently of histone H4 lysine 20 methylation," published in *Genes & Development*.

In their research, the group found that removing the enzymes responsible for adding a specific histone chemical modification or a protein that binds it disrupts gene activity and cell proliferation. However, the disruptions are not directly due to the chemical modification itself, which is the opposite of current models in the field.

"Our study led to a better understanding of genetic regulation mechanisms," said Bob Duronio, co-author and biology professor. "Such understanding provides foundational information that can help when developing new treatments for diseases like cancer that result from defects in the regulation of gene activity and cell proliferation by targeting the pathways and mechanisms of Set8 that are independent of the histone modification."

Initially, the research group wanted to know whether the chemical modification of a particular histone that is added by an enzyme called Set8 is crucial for gene expression and cell growth, as predicted by previous research in the field.

Contrary to earlier predictions, their research showed that Set8 controls gene activity and cell proliferation via a mechanism other than chemically modifying the histone protein. Thus, the fundamental research study has refined the understanding of genetic regulation that is relevant to the understanding of human diseases like cancer.

Unlike previous studies, researchers used a new genetic method developed through a collaborative effort at UNC-Chapel Hill to determine the function of histone modifications independent of enzymes

like Set8.

These research methods can reveal new functions for histone modifying enzymes by shifting the focus from the chemical modification of histones to broader roles of the enzyme, providing new insights into gene regulation mechanisms.

More information: Aaron T. Crain et al, Drosophila melanogaster Set8 and L(3)mbt function in gene expression independently of histone H4 lysine 20 methylation, *Genes & Development* (2024). DOI: 10.1101/gad.351698.124

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