

Tiny protein variation has huge impact on all animals and plants

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Scientists at Yale and the University of Ottawa have shown how the tiniest biochemical variation in one protein is crucial for the replication and repair of DNA in all plants and animals, they report March 17 in the

journal *Science*.

The findings provide new insight into histones, a highly basic protein that plays a critical role in packaging DNA into chromosomes. For decades, biologists have wondered why one variant of histones, known as H3.1, differs from its otherwise genetically identical twin H3.3 by a [single amino acid](#).

From an evolutionary standpoint, the difference is crucial: the H3.1 variant is found in all [plants](#) and animals, leading scientists to believe that it is somehow involved in genome replication during [cell division](#). Its exact role in this process, however, has remained a mystery.

Using the flowering plant *Arabidopsis thaliana* as a model system, researchers in the lab of Yannick Jacob, assistant professor of molecular, cellular, and [developmental biology](#) at Yale and co-corresponding author of the paper, revealed new insights into the variant's critical role. By manipulating the genome of the plant, they found that the single amino acid change in histone variant H3.1 is crucial in recruiting a specific protein required to repair damaged DNA during replication.

"H3.1 serves as a flag to localize this repair protein at the exact right time and place in the replicating cells," Jacob said. "H3.1 makes sure that the repair pathway is only functional during DNA replication."

When scientists replicated cells without H3.1, Jacob said, they saw "mutations, activation of alternative DNA repair pathways, and many developmental defects."

Understanding the role of H3.1 and its variable amino acid may not only open new therapeutic approaches to human diseases like cancer, Jacob said, but also "demonstrates how the smallest difference in [protein sequence](#) can have such a tremendous functional impact throughout

evolution."

This study was a collaboration between Yale University and a research team at the University of Ottawa. Yale's Yi-Chun Huang is a co-lead author with Ottawa's Hossein Davarinejad. Jean-François Couture of the University of Ottawa is the co-corresponding author on the study.

More information: Hossein Davarinejad et al, The histone H3.1 variant regulates TONSOKU-mediated DNA repair during replication, *Science* (2022). [DOI: 10.1126/science.abm5320](https://doi.org/10.1126/science.abm5320)

Provided by Yale University

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