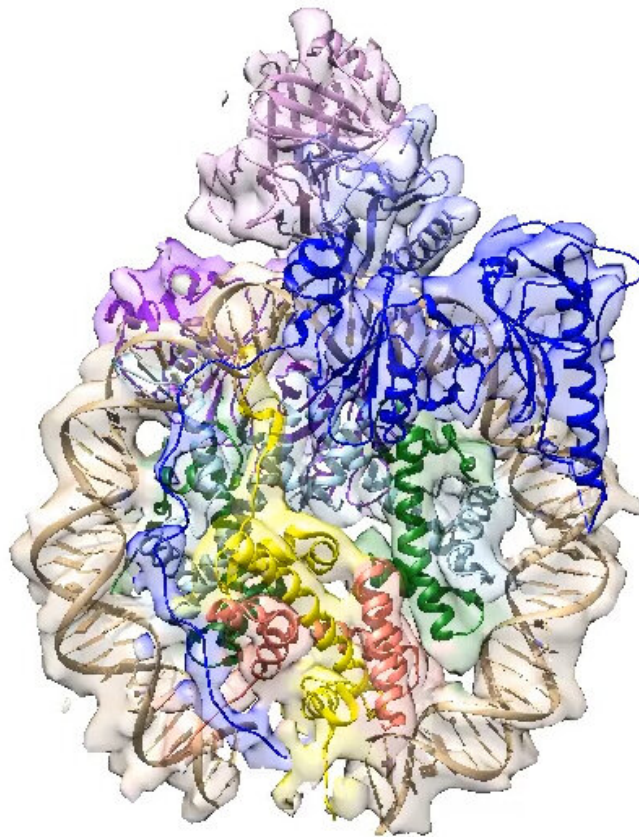


# Scientists now know what DNA's chaperone looks like

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A visualization of the FACT protein. Credit: Liu et al. 2019

It's long been known that the proteins that package DNA, like students at

a high school dance, require a chaperone. But what exactly that guardian looks and acts like has been a mystery—until now.

A team of researchers at the University of Colorado Boulder has cracked the puzzle of the Facilitates Chromatin Transcription (FACT) [protein structure](#). This [protein](#) is partly responsible for making sure everything goes smoothly and no improper interactions take place when DNA temporarily sheds and replaces its guardian proteins, or histones.

These findings, which are the result of a project five years in the making at CU Boulder and out today in the journal *Nature*, will have ripple effects for not only our understanding of the genome and [gene transcription](#), but for our understanding of cancer and the development of anti-cancer drugs.

"This is just the start for this protein. It's not the end," said Yang Liu, a research associate in the Department of Biochemistry at CU Boulder and one of the study's lead authors.

Ever since its discovery in 1998, the FACT protein has been of great interest for those who study DNA, largely because of the possibilities it presents. But, despite decades of effort, many of the central questions of how the protein works remain unanswered.

The FACT protein is an essential type of histone chaperone. These guardian proteins escort other proteins during the deconstruction and reconstruction of nucleosomes, or the structural unit responsible for organizing and packaging DNA. This happens during gene transcription (the step where DNA is copied into RNA), DNA replication (where the entire genome is replicated faithfully) and DNA damage repair (which is essential to prevent disease such as cancer).

However, with no clear structure for the protein available, scientists have

been less than clear as to how exactly it does both: How does one protein both destroy and maintain?

This new research sheds light on both.

"For a long time, people have been trying to find the mechanism behind how [this protein] helps transcription," said Keda Zhou, a research associate in biochemistry at CU Boulder and the other lead author for the paper. "People have been working on different aspects of this protein, so we're really happy that we're the first to see it in action. It's really exciting."

The research team, aided by two other labs also led by women also managed to finally solve the puzzle by isolating the FACT protein and, through a combination of hard-work, ingenuity and tenacity, map it out and catch it in the act of both destroying and maintaining the nucleosome.

What they found is that FACT resembles the saddle and fork of a unicycle, made up of multiple domains that straddle the nucleosome 'wheel' of the unicycle. Up until that point, researchers were seeing only one domain at a time, causing confusion and contradictory results.

And yet, it appears that none of those differing findings are wrong.

Liu and Zhou's work "really put everything together. And it seems like everybody's right, which is just really cool," said Karolin Luger, the endowed chair of biochemistry at CU Boulder, a Howard Hughes Medical Institute Investigator and the study's senior author.

This discovery is only the beginning for this protein, both for Luger's lab and the broader medical community.

"There are lots of unknowns," said Zhou. "But this is a starting point."

**More information:** FACT caught in the act of manipulating the nucleosome, *Nature* (2019). DOI: [10.1038/s41586-019-1820-0](https://doi.org/10.1038/s41586-019-1820-0) , [nature.com/articles/s41586-019-1820-0](https://www.nature.com/articles/s41586-019-1820-0)

Provided by University of Colorado at Boulder

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