# Researchers show that four-stranded DNA is formed and unfolded

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Nasim Sabouri, Department of Medical Biochemistry and Biophysics, Umeå University. Credit: Photo: Markus Marcetic © Knut och Alice Wallenbergs Stiftelse/Kungl. Vetenskapsakademien

Researchers at Umeå University in Sweden have discovered that specific DNA sequences that are rich in the DNA building block guanine in the yeast species, *Schizosaccharomyces pombe*, can form four-stranded

DNA. In a study published today in the journal *Nucleic Acids Research*, the researchers also show that the motor protein Pfh1 can unfold these DNA structures and thus contribute to maintaining an intact genome.

DNA molecules are known for their spiral shape, with two strands wrapping around each other. But DNA can also appear in other configurations. One of these forms consists of a guanine-rich four-stranded DNA, a so-called G4 structure. Guanine is one of DNA's four building blocks. A number of earlier studies of different organisms have indicated that G4 structures are formed in the genome and fulfil important biological functions such as controlling gene expression.

"By using different biochemical and biophysical methods, we show that specific DNA sequences from the Schizosaccharomyces pombe's ribosomal and telomeric DNA regions have a strong tendency to form G4 structures," says Nasim Sabouri, Assistant Professor at the Department of Medical Biochemistry and Biophysics, and one of the researchers in the study.

G4 structures can present a threat if they exist continuously in the genome. Helicases are a type of specialized motor protein with the ability to unfold different kinds of DNA. Until now, there were very few studies about G4 structures in Schizosaccharomyces pombe, also known as fission yeast. It was also not known which protein is responsible for the unfolding of the G4 structures.

"Our cell biological analysis show that a helicase, called Pfh1, binds to specific guanine-rich DNA sequences in the yeast cell. We also show in biochemical experiments that Pfh1 has the ability to unfold G4 structures. An efficient unfolding of these structures is necessary in order to secure the integrity of the genome during DNA replication," says Nasim Sabouri.

Research on G4 structures is at its early stage. But researchers believe that G4 structures can inhibit certain processes in the cells, including DNA replication, and have tied them to the development of cancer and neurodegenerative diseases in humans. It is clear that the formation and elimination of G4 structures must be well-balanced to satisfy the cell's needs and ensure its integrity.

"An interesting research area is the development of molecules with the specific ability to bind to and stabilize G4 structures. This could potentially be used to turn off the expression of certain genes that are involved in tumour formations. We are hopeful that our advancements in understanding of G4 structures could eventually facilitate the development of new drug treatments for cancer. This is something we would like to focus more on," says Nasim Sabouri.

**More information:** *Nucleic Acids Research*, G-rich telomeric and ribosomal DNA sequences from the fission yeast genome form stable G-quadruplex DNA structures in vitro and are unwound by the Pfh1 DNA helicase. Authors: Marcus Wallgren, Jani Basha Mohammad, Kok-Phen Yan, Parham Pourbozorgi-Langroudi, Mahsa Ebrahimi and Nasim Sabouri. DOI: 10.1093/nar/gkw349

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