Nature Publication on Loops, Flags and Tension in DNA

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Two protein complexes carry the major responsibility for the spatial organisation of chromosomes in our cell nuclei. DNA tension plays a surprising role in this. Together with Austrian colleagues, nanoscientist Cees Dekker and his PhD candidate Roman Barth of the Kavli Institute of Nanoscience at TU Delft now publish how they have visualised this in detail in Nature on April 19.

#1 Cohesin loops DNA

It has been known for more than a century that the long DNA strands in cell nuclei are neatly folded into the characteristic shape of chromosomes, resembling bottlebrushes , in preparation for cell division. And also between divisions, chromosomes are organised into loops that are important for regulating the processing genetic information. In 2018, Dekker and his group were the first to visualise how SMC protein complexes such as condensin and cohesin extrude loops in DNA.

#2 CTCF flags have a direction and determine where a loop begins and ends…

The DNA-binding protein CTCF was found to play a key role in the positioning of loops along the genome. Dekker: “If you think of DNA as a rope, onto which CTCF flags are pinned at two points, cohesin makes the loops from one flag to the other, but only if the CTCF is oriented correctly. Only one side of the CTCF protein is able to interact with cohesin. Then again, it doesn’t always do this, because we thought CTCF would also fail frequently. But now we have measured it. The interaction between the two proteins turns out to be much more subtle than we predicted.”

That CTCF and cohesin work together to establish loop boundaries has become basic knowledge in the field, says PhD candidate Roman Barth: “In every conference presentation I attended in the past year, the basic premise was that the cohesin complex extrudes loops

between correctly oriented CTCF molecules. But nobody had ever seen in detail how that happens. We have now been able to visualise the essence of this."

#3: … And DNA tension plays a surprising role in this

Colleagues in Jan-Michael Peters' group at the Institute of Molecular Pathology in Vienna succeeded in making the proteins available in pure form. The two ends of a DNA molecule were attached to a surface; the DNA and proteins were stained with a fluorescent dye. The researchers then made an unusual discovery, Dekker explains. "In the data, Roman discovered that it made a difference whether the DNA strand was very loose or under tension. Without tension, cohesin often ignored the CTCF flag, even if correctly oriented, but when the DNA was under more tension, the CTCF acted as a perfect barrier. So, under the influence of DNA tension, CTCF becomes like a smart traffic light, allowing cohesin to pass or not, depending on the local traffic situation."

When cohesin collides with a CTCF protein, it can stop or continue. The researchers saw that it can also turn around, or even dissolve altogether. How and why this happens are the next questions Dekker hopes to answer.

Read the original article on Delft University of Technology.