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Scientists track the influence of a cancer inhibitor on a single DNA molecule

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Researchers in Delft University of Technology's Kavli Institute of Nanoscience in The Netherlands have cast new light on the workings of the important cancer inhibitor topotecan. Little had been known about the underlying molecular mechanism, but the Delft scientists can now view the effects of the medicine live at the levelin of a single DNA molecule.

The research is being published this week in the journal *Nature*. The lead author of the article, Daniel Koster, will receive his PhD at TU Delft on Monday June 25, partly on the results described in the article.

The medicine investigated, topotecan, interacts with an important protein (TopoIB), causing a (cancer) cell to malfunction. The TopoIB protein is responsible for the removal of loops from DNA, which arise amongst other things during cell division. The TopoIB protein binds to the DNA molecule, clamps around it and cuts one of the two DNA strands, after which it allows it to unwind and finally joins the broken ends together.

PhD candidate Daniel Koster, Master's student Elisa Bot and researcher Nynke Dekker of the Molecular Biophysics group of the Kavli Institute of Nanoscience Delft have managed to unravel this mechanism in an extremely direct manner. In the laboratory they fixed a single DNA molecule between a glass plate and a magnetic sphere. With the help of two magnets they could both pull and twist the DNA molecule. When they added TopoIB to a twisted piece of DNA, they saw that the loops

were slowly removed.

What is exceptional is that the action of one TopoIB enzyme on one DNA molecule could be observed live. In collaboration with St. Jude Children's Research Hospital Memphis (USA) the mechanism could also be observed in living yeast cells.

Source: Delft University of Technology