MedicalXpress

'Pinball protons' created by ultraviolet rays and other causes can lead to DNA damage

May 17 2006

Researchers have known for years that damaged DNA can lead to human diseases such as cancer, but how damage occurs--and what causes it--has remained less clear.

Now, computational chemists at the University of Georgia have discovered for the first time that when a proton is knocked off one of the pairs of bases that make up DNA, a chain of damage begins that causes "lesions" in the DNA. These lesions, when replicated in the copying mechanisms of DNA, can lead to serious disorders such as cancer.

The research, just published in the Proceedings of the National Academy of Sciences (PNAS), was led by doctoral student Maria Lind and Henry F. Schaefer III, Graham-Perdue Professor of Chemistry. Other authors on the paper are doctoral student Partha Bera, postdoctoral associate Nancy Richardson and recent doctoral graduate Steven Wheeler.

Call it a "pinball proton." While chemists have shown other causes of DNA damage, the report in PNAS is the first to report how protons, knocked away by such mechanisms as radiation or chemical exposure, can cause lesions in DNA. The work was done entirely on computers in the Center for Computational Chemistry, part of the Franklin College of Arts and Sciences at UGA.

"This kind of damage in DNA subunits is about as basic as you can get,"

said Schaefer. "This is the simplest kind of lesion possible for such a system."

The double-helix structure of DNA has been known for more than half a century. This basic building block of life can "unzip" itself to create copies, a process at the heart of cell replication and growth. DNA is made of four "bases," Adenine, Guanine, Thymine and Cytosine, and each one pairs with its opposite to form bonds where the "information" of life is stored. Thus, Guanine pairs with Cytosine, and Thymine with Adenine.

The team at the University of Georgia studied how the removal of a proton from the Guanine-Cytosine (G-C) base pair is involved in creating lesions that can lead to replication errors. This pair has 10 protons, meaning there are numerous targets for processes that knock the protons off.

The lesions are breaks in the hydrogen bonds, of which there are two in the G-C base pair. (The Adenine-Thymine pair has three hydrogen bonds.)

"Our real goal is to examine all possible lesions in DNA subunits," said Lind.

The team discovered that the base pair minus its knocked-off proton can either break entirely or change its bonding angle--something that also causes improper replication.

"The C-G subunit is usually totally planar [flat]," said Lind. "If it twists, it could simply pull apart."

Though it has already been suspected that lesions in DNA caused by both high- and low-energy electrons result in cancer cell formation, the

new study is the first evidence that protons do the same thing.

The study in PNAS also has other implications. Researchers are beginning to understand how DNA can be used as "molecular wire" in constructing electrical circuits. Such a breakthrough would allow small electronic devices to shrink even further, but how the electrical properties of DNA would work in such a context is not yet understood. The UGA research adds important knowledge about how so-called "deprotonated" DNA base pairs work and could be important in creating "DNA wire."

Source: University of Georgia