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DNA separates like a magician's rings

The DNA Repair Process Can Lead To Problems Like Cancer

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A new study by Stephen Kowalczykowski, a professor of microbiology at UC Davis, shows how DNA is separated like a magician's trick with interlocking rings. On a daily basis radiation, chemicals and normal cellular processes constantly damage DNA. When chromosomes repair themselves they become interlocked.

Kowalczykowski worked with yeast in a test tube, studying the DNA repair system. He found that a complex of proteins called Sgs1, Top3 and Rmi1 open the double-stranded DNA of one chromosome to allow the other one to pass through.

"This protein complex does what magicians do," Kowalczykowski said of the process.

When damaged DNA goes unrepaired, the damage can lead to cancer or birth defects. The so-called "breast cancer gene" BRCA2 can increase the risk of cancer as a result of a mutation that prevents proper DNA repair.

When damage only affects one strand out of a double-stranded chromosome, the other strand can simply serve as a template for repair. The process becomes more complicated when the damage affects both strands of a chromosome. In that case, one strand is stripped back so that the matching chromosome can attach itself to the section that is damaged. The matching chromosome is partially unwound, and each strand can now serve as a template: one for its own chromosome, the other for its matching damaged pair.

The chromosomes are now both intact but still attached at two points called "Holliday junctions." In order to separate, one ring has to pass through the other like the magician's rings.

Kowalczykowski showed how the Sgs1/Top3/Rmi1 complex of proteins attaches to the Holliday junctions and unwinds the section of DNA of one chromosome. The other chromosome can now pass through the gap and the two are cleanly separated.

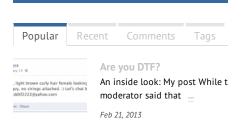
Kowalczykowski's recent research also showed that the Sgs1/Top3/Rmi1 complex of proteins also cleans the damaged section in order to leave a single strand of DNA. This is the first step of DNA repair, essential in order for the damaged DNA to attach to an intact length of DNA on another chromosome.

Properly repairing damaged DNA is what keeps cells from becoming diseased or even cancerous. The protein Sgs1 appears to be the yeast equivalent of the human protein tied to an illness called Bloom's syndrome, Kowalczykowski said.

According to The Bloom's Syndrome Foundation, patients diagnosed with Bloom's syndrome have high risks of cancer, sun sensitive lesions to the face, chronic ear and lung infections and a form of diabetes similar to adult onset diabetes but arising much earlier in life. Patients have a defective form of the protein that keeps their DNA from being unwound and properly repaired after damage occurs.

Though they have been hypothesized to be present for 26 years, Holliday junctions have only been definitively shown to exist in mitotically dividing cells – cells that make exact copies of themselves – a few months ago by Neil Hunter, associate professor of microbiology at UC Davis and senior author of a paper on Holliday junctions in the April 8 issue of Nature.

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Crossovers and Holliday junctions happen frequently in the process of meiosis, the process during which a cell divides to create four daughter cells which each have half of the DNA of the original. However, Holliday junctions are fairly rare in cell division.

"It makes sense that the double-Holliday junction pathway is a minor pathway of break repair in mitotically dividing cells because it is more likely to result in a crossover, and crossovers can cause the types of genetic changes that lead to cancer," Hunter said.

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