Can DNA breaks be repaired?

A new microscopic assay has been developed by scientists at the University of North Carolina at Chapel Hill that, for the first time, allows them to see DNA breaks in chromosomes in living cells following damage to those complex, gene-filled structures. Their success is exciting because the assay should become a powerful aid for boosting understanding of chromosome damage and how it is repaired naturally or might be repaired therapeutically, notes Kerry S. Bloom, professor of biology. Chromosome damage leads to, at a minimum, hundreds of fatal or debilitating illnesses each year.

"In the course of this work, we discovered that, when breaks occur in either one or both strands of DNA, which is a complex, double-stranded, helical molecule, the chromosomes do not fragment," Bloom explains. "Proteins are recruited very quickly to the sites of DNA damage, and they keep the chromosome intact. This was hypothesized but never shown before. We also identified some of those specific proteins."

Human cells contain an amazing amount of DNA, which produces proteins for countless tasks in the body. "In fact, if you took all of the DNA in your cells and stretched it out, it would go to the sun and back. That is awesome," marvels Bloom.

"This is the first [study] that distinguishes breaks in chromosomes versus breaks in DNA," Bloom points out. "Chromosomal breaks are important in many diseases that stem from chromosomal translocation, in which genes get switched around."

Chromosomal aberrations are common outcomes of exposure to DNA-damaging chemicals such as Agent Orange, excessive sunlight, and radiation. They also result from replication disrupted in some way and can lead to such conditions as leukemia, lymphoma, sarcoma, and epithelial tumors.

"Aberrations can be greatly increased as a result of defects in DNA repair," Bloom reports. "While there was considerable information about molecular events associated with the induction and repair of a double-stranded break, little has been known about events leading to chromosome breaks or the reassociation of broken ends that results in translocations or deletions."

He likens translocations to circuits being rewired incorrectly or surgeons accidentally connecting veins to arteries. "Our new system allows for visualizing DNA ends at the site of a double-stranded break in living cells. We showed that a protein complex we call RMX holds broken ends of DNA together and counteracts forces that can be destructive to damaged chromosomes."