

By: February 2006 World and Health News Editor

Z-DNA, the Bad DNA

The oddly shaped DNA can cause DNA breaks in mammalian cells

When otherwise normal DNA adopts an unusual shape called Z-DNA, it can lead to the kind of genetic instability associated with cancers such as leukemia and lymphoma, according to a study by researchers at The University of Texas M. D. Anderson Cancer Center. The study demonstrates for the first time that the oddly shaped DNA can cause DNA breaks in mammalian cells. Interestingly, these sequences prone to forming Z-DNA are often found in genetic "hot spots," areas of DNA known to be prone to the genetic rearrangements associated with cancer. About 90 percent of patients with Burkitt's lymphoma, for example, have DNA breaks that map to regions with the potential to form these odd DNA structures. "Our study shows that DNA itself can act as a mutagen, resulting in genetic instability. The discovery opens up a new field of inquiry into the role of DNA shape in genomic instability and cancer," says Karen Vasquez, Ph.D., lead author of the study and assistant professor of carcinogenesis at M. D. Anderson's Science Park Research Division, Smithville, Texas. Imagine untwisting the DNA ladder and then winding it up the other way. The result is a twisted mess with segments jutting out left and right, and the all important base pairs that hold the DNA code zigzagging in a jagged zipper shape. Scientists call this left-hand twist Z-DNA. This is a far cry from the graceful right-hand twisted helix that has become an iconic symbol of biology. It just doesn't look right, and it doesn't act right either, according to Vasquez. This awkward shape puts strain on the DNA, and as Vasquez and her colleagues show, can cause the DNA molecule to break completely apart. Analysis of the genome reveals that DNA sequences prone to forming the Z-DNA structure occur in 0.25 percent of the genome, according to Vasquez. "We discovered that bacterial cells and human cells process the Z-DNA in different ways. We aren't sure why, but we think that the DNA repair machinery may be involved in processing the Z-DNA structure differently in bacteria versus human cells," she says. "If we could understand the players involved in this process, we might be able to prevent the generation of these breaks. For example, if certain types of cell stress lead to breaks, we might be able to find ways to reduce those stresses and prevent breaks," says Vasquez.