Team finds two pathways through which chromosomes are rearranged

September 8 2013

Edward (Paul) Hasty, D.V.M., of the School of Medicine at The University of Texas Health Science Center at San Antonio, and colleagues discovered two pathways for chromosomal rearrangements to occur. This represents a novel target for potential development of anti-cancer therapies. Credit: Lester Rosebrock/The University of Texas Health Science Center at San Antonio

Biologists reported today in *Nature* that they have identified two pathways through which chromosomes are rearranged in mammalian cells. These types of changes are associated with some cancers and inherited disorders in people.

"Our finding provides a target to prevent these rearrangements, so we could conceivably prevent cancer in some high-risk people," said senior author Edward P. (Paul) Hasty, D.V.M., of the School of Medicine at The University of Texas Health Science Center at San Antonio. Partial funding came from the Cancer Therapy & Research Center at the UT Health Science Center San Antonio.

The two pathways rearrange chromosomes by recombining DNA repeats that are naturally found in the genome, Dr. Hasty said. DNA, the chemical substance of genes, denatures and replicates during cell division and other processes. Repeats are sequences of DNA that are duplicated.

Both pathways are important for the synthesis of DNA. "Therefore, we propose that chromosomal rearrangements occur as DNA is being synthesized," Dr. Hasty said.

The experiments were conducted with mouse embryonic stem cells grown in tissue culture. The team measured the incidence of DNA repeats recombining in normal cells. This is called "repeat fusion." The scientists then looked for incidence of repeat fusion in cells affected by several genetic mutations. This analysis identified the two pathways and showed large, complicated rearrangements that involved DNA repeats on multiple chromosomes.

During cell division, DNA is coiled into pairs of threadlike structures called the chromosomes. Each human cell has 22 numbered pairs of chromosomes called autosomes. The sex chromosomes are the 23rd pair

in cells and determine a person's gender. Females have two X chromosomes, while males have an X and a Y chromosome.

"We hope the new findings will help us better understand the mechanisms that cause chromosomal instability, which causes some cancers in people," Dr. Hasty said.

At the Health Science Center, Dr. Hasty is a professor in the Department of Molecular Medicine, has a laboratory at the UT Institute of Biotechnology, and is a faculty member of the Barshop Institute for Longevity and Aging Studies.

More information: Two Replication Fork Maintenance Pathways Fuse Inverted Repeats to Rearrange Chromosomes, DOI: 10.1038/nature12500

Provided by University of Texas Health Science Center at San Antonio