MedicalXpress

Researchers identify protein -- telomere interactions that could be key in treating cancer

August 31 2009

A team of researchers from The Wistar Institute have shown that a large non-coding RNA in mammals and yeast plays a central role in helping maintain telomeres, the tips of chromosomes that contain important genetic information and help regulate cell division. Since this RNA also facilitates the formation of DNA at telomeres -- a process that can protect aging cells and destabilize tumor cells -- manipulating its expression may be useful in treating cancer and other diseases.

The steady shortening of telomeres with each replication in somatic cells is linked to cellular aging, genetic instability, and tumor formation. This is because telomeres eventually "run out" after a certain number of cell divisions, resulting in the loss of vital genetic information from the cell's chromosome with future divisions. Scientists recently identified telomere-repeat-encoding RNA (TERRA) as an integral component of DNA within the telomeres of multiple species. The Wistar team demonstrated how TERRA mediates and partially stabilizes interactions between telomeric proteins that play essential roles in DNA replication.

"TERRA is a major component in helping protect the genome at a very sensitive place, the telomeres," said senior author Paul M. Lieberman, Ph.D., a professor in Wistar's Gene Expression and Regulation Program. "By managing TERRA levels we have the potential to regulate cellular aging and to impair the functioning of cancer cells."

TERRA associates with telomeric factors, but its precise function and mechanism of localization at telomeres had been largely unknown. In a study published on-line on August 27 in *Molecular Cell,* the Wistar scientists, led by Lieberman, describe how they discovered the telomere proteins that interact with TERRA and the processes by which they do so.

In cell cultures, through RNA affinity purification, a process that isolates a single type of protein from a complex mixture, the team identified telomeric proteins (Shelterin components TRF1 and TRF2, and origin recognition complex subunits ORC1, ORC2, and ORC4) that bound to a TERRA oligonucleotide sequence but not to control oligonucleotides. Using RNA chromatin immunoprecipitation assays (ChIPs), in which specific pieces of RNA are isolated from bound proteins, the team discovered that TERRA is bound by telomeric proteins indicating that TERRA was a component of the Shelterin complex. The findings provide important clues that point to strategies for altering the expression of TERRA as a means to treat cancer and other diseases of aging, Lieberman says.

Source: The Wistar Institute