MedicalXpress

Scientists demonstrate role of protein in distinguishing chromosome ends from DNA breaks

September 17 2009

The Stowers Institute's Baumann Lab has demonstrated how human cells protect chromosome ends from misguided repairs that can lead to cancer. The work, published in *The EMBO Journal,* a publication of the European Molecular Biology Organization, follows the team's 2007 in vitro demonstration of the role of the hRAP1 protein in preventing chromosome ends from being fused to new DNA breaks.

Chromosomes are linear. Their ends (called telomeres) should look like DNA breaks to the proteins that repair them. But somehow, cells are able to distinguish chromosome ends from DNA breaks. In this work, the team demonstrated that the human RAP1 protein plays a key role in preventing chromosome ends from being fused to new DNA breaks. Chromosome end fusions result in genomic instability, which can cause cancer. These findings suggest that RAP1 plays a critical role in cancer prevention in humans.

"Protecting naturally occurring chromosome ends from erosion and fusions may increase longevity and reduce cancer risk," said Jay Sarthy, formerly a graduate student in the Baumann Lab and lead author on the paper. "A protein that protects chromosome ends may provide an attractive target for drugs that can help to stave off aging and cancer."

"Our finding has paved the way to investigate the mechanism by which hRAP1 protects chromosome ends from undergoing fusions," said Peter

Baumann, Ph.D., Associate Investigator and senior author on the publication. "This research contributes to our understanding of chromosome stability and, thereby, tumor suppression and cancer. If partial loss of hRAP1 function causes chromosomal instability, as suggested by our current work, then mutations in RAP1 may be linked to a predisposition for cancer."

Identifying hRAP1 as a critical protector of chromosome ends was an important step in understanding how telomeres are protected from DNA repair. The Baumann Lab will move forward in their efforts to understand what hRAP1 does to protect telomeres from repair — the proteins with which it interacts, and how it inactivates DNA repair specifically at chromosome ends.

Source: Stowers Institute for Medical Research