Scientists uncover function of potential cancer-causing gene product

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The Stowers Institute's Conaway Lab has uncovered a previously unknown function of a gene product called Amplified in Liver Cancer 1 (Alc1), which may play a role in the onset of cancer. The work was published yesterday by the *Proceedings of the National Academy of Science* Early Edition.

"We've been able to demonstrate that the protein encoded by the Alc1 gene is, in fact, a chromatin remodeling enzyme," explained Aaron Gottschalk, lead author on the paper and a University of Kansas Medical Center graduate student conducting research in the Conaway Lab. "By itself, this enzyme is inactive, but in the presence of a compound called NAD and another enzyme called poly (ADP-ribose) polymerase 1 (Parp1), its ability to move nucleosomes on DNA is strongly activated."

Parp1 uses NAD to build a polymeric molecule, poly(ADP-ribose), that is coupled to Parp1 itself or to other proteins. The team established that binding of a specific Alc1 region to poly(ADP-ribose) coupled to Parp1 helps recruit Alc1 to bind to and remodel nucleosomes.

"This finding is particularly interesting because Parp1 and poly(ADP-ribose) are known to play important roles in transcriptional regulation, DNA repair, and DNA replication, but how they do so is really not at all clear," said Ron Conaway, Ph.D., Investigator and co-senior author on the publication. "Finding that Parp1 and poly(ADP-ribose) recruit the chromatin remodeling enzyme Alc1 to chromatin and activate Alc1 activity suggests a mechanism by which they might function."

Medical researchers at universities and pharmaceutical companies are investigating Parp inhibitors for treatment of cancer and other diseases. The team has shown that Parp inhibitors block Alc1 activities in the test tube and cells, suggesting that the therapeutic activities of these inhibitors could be due in part to indirect affects on Alc1. If true, drugs that target Alc1 function could also be useful in the treatment of disease.

Source: Stowers Institute for Medical Research