Finding may explain link between alcohol and certain cancers

August 3 2005

Drinking alcoholic beverages has been linked to an increased risk of upper gastrointestinal cancer and other types of cancer. Researchers looking for the potential biochemical basis for this link have focused on acetaldehyde, a suspected carcinogen formed as the body metabolizes alcohol.

In the journal Nucleic Acids Research, scientists from the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the National Institute of Standards and Technology (NIST) report that polyamines – natural compounds essential for cell growth – react with acetaldehyde to trigger a series of reactions that damage DNA, an event that can lead to the formation of cancer.

"We've long suspected acetaldehyde's role in the carcinogenicity of alcohol beverage consumption, but this study gives us important new clues about its involvement," says Ting-Kai Li, M.D., director of the NIAAA, part of the National Institutes of Health. "This work provides an important framework for understanding the underlying chemical pathway that could explain the association between drinking and certain types of cancer."

The research team, led by P.J. Brooks, Ph.D., of NIAAA and Miral Dizdaroglu, Ph.D., of NIST, examined acetaldehyde's reaction with polyamines, small molecules found in all cells. "Polyamines are usually considered 'good guys,' because they have been shown to protect DNA from oxidative damage," says Dr. Brooks. Yet the researchers found the

polyamines facilitated the conversion of acetaldehyde into crotonaldehyde (CrA), an environmental pollutant that has been shown to cause cancer in animals. This chemical in turn altered DNA, generating an abnormal, mutagenic DNA base called a Cr-PdG adduct. Dr. Brooks says, "We concluded that polyamines stimulated the formation of Cr-PdG adducts from acetaldehyde, and this may provide a mechanism to explain how alcohol consumption increases the risk of some types of cancer."

Previous studies had shown acetaldehyde could be converted to mutagenic Cr-PdG, but those studies used very high acetaldehyde concentrations. "We were able to demonstrate that these reactions can take place with acetaldehyde concentrations that have been measured in human saliva during alcohol consumption," says Dr. Brooks.

An important part of this research was a new chemical analysis method developed at NIST. According to Dr. Dizdaroglu, "This novel chemical assay is a powerful method that accurately measures the Cr-PdG adduct."

George Kunos, M.D., Ph.D., director of NIAAA's Division of Intramural Clinical and Biological Research, says, "These findings also have significant implications for researchers seeking to understand how genes affect the risk for cancer." Many studies have shown that certain genetic variants that affect alcohol and acetaldehyde metabolism can also affect individual susceptibility to alcohol-related gastrointestinal cancer. Dr. Kunos adds, "This work could serve as a roadmap for future studies to investigate other genetic factors, particularly those that influence DNA repair pathways, in relation to alcohol consumption and cancer."

Source: NIH/National Institute on Alcohol Abuse and Alcoholism