Scientists identify a cellular pathway by which alcohol may promote cancer progression

October 26 2009

Epithelial-mesenchymal transition (EMT) is essential for numerous developmental processes involving biological cells. New findings indicate that alcohol may promote cancer progression by stimulating EMT.This has implications for both cancer prevention and therapy.

Although alcohol consumption has been linked to colon and breast cancer, exactly how this occurs remains unclear. A new study has found that epithelial-mesenchymal transition (EMT) - which is essential for numerous developmental processes - may also be a cellular pathway by which alcohol-induced cancer cells aggressively progress and metastasize.

Results will be published in the January 2010 issue of *Alcoholism: Clinical & Experimental Research* and are currently available at Early View.

"Alcohol consumption is known to increase the risk of several cancers, including cancers of the oral cavity, esophagus, liver, colon, rectum, and, in women, the breast," explained Christopher B. Forsyth, assistant professor of medicine and biochemistry at Rush University Medical Center. "We also suspect an association with cancers of the pancreas and lung. However, the mechanisms by which alcohol increases the risk for these cancers have not been established. EMT is an active area of cancer research and growing evidence supports a role for EMT during cancer

progression and metastases for several cancer types but previously not for alcohol-associated cancers."

Forsyth, who is the first author of the study, was introduced to the field of alcohol research when he joined research forces with co-author Ali Keshavarzian, who had been studying alcohol effects on human and animal intestinal tract for more than 20 years.

For this study, the research team collected samples from four alcoholic and four healthy subjects, all male. They examined the effects of alcohol on a key EMT transcription factor called Snail, a protein, as well as on epidermal growth factor receptor (EGFR) signaling, a pathway known to promote cancer and EMT. They did this by treating colon and breast cancer cell lines with alcohol, then assessing them for EMT-related changes using a slate of methods.

"Our data are the first to show that alcohol turns on cell signals as well as biomarkers characteristic of EMT in cancer cells," said Forsyth. "We also show alcohol turns on the EMT pathway in non-cancer intestinal cells, thus supporting a possible role for alcohol stimulation of EMT in cancer initiation. Thus, our study supports a possible new mechanism through which alcohol may promote cancer progression by stimulating EMT. This now provides a new target for therapeutic intervention for treatment of alcohol-related cancers and for prevention of alcohol-related cancer metastasis."

"This cellular mechanism may be central to the enhanced cancer risk after alcohol exposure in these two cancers," added James L. Mulshine, professor of internal medicine and associate provost for research at Rush University Medical Center. "If confirmed, it moves the association of alcohol consumption with the risk of a major cancer to a much more firm footing … and opens up a whole variety of new studies evaluating the mechanistic basis of early carcinogenesis."

Forsyth believes that EMT may promote cancer by turning on signals in cancer cells that help them leave the main tumor, invading the bloodstream and spreading in the body. EMT may also make cancer cells more resistant to cancer-killing drugs, and increase the mutation rate in cells which can promote the spread of cancer cells.

Given that this study did not address amounts of alcohol consumption, Forsyth said that readers should decide for themselves if they want to cut back on consuming any or just large amounts of alcohol. Mulshine, on the other hand, suggested caution.

"These results suggest that women should consider managing their alcohol consumption more strictly to avoid the cancer consequences of alcohol consumption," he said.

Source: Alcoholism: Clinical & Experimental Research