

Investigation of the Role of Alcohol in Intestinal Cancer

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Background: Alcoholic beverages have been classified as carcinogenic, with tumour sites related to alcohol consumption including the colorectum and upper aerodigestive tract (IARC 2007). A variety of mechanisms may be causal for the enhanced cancer risk linked to alcohol consumption, including direct genotoxic effects of ethanol and its metabolite acetaldehyde (AA). The relevance of these mechanisms in the colorectum has not been fully elucidated yet, neither has the role of different isoforms of alcohol metabolising enzymes. While Aldh2, the main enzyme for AA detoxification in the liver, has been investigated widely, little is known about Aldh1b1 which also has a high affinity for AA and is highly expressed in the GIT.

Aims: We aim to further elucidate the mechanisms of alcohol as a risk factor for cancer in the intestines, focussing on alcohol metabolising enzymes and DNA repair, and on genotoxic effects.

Methods: 20% (v/v) ethanol was administered to mice via drinking water for 3 weeks, while control groups received normal drinking water. Swiss rolls of the intestine were prepared for immunohistochemical analysis and intestinal epithelium was isolated.

Results: While Aldh2 was uniformly expressed in the intestinal epithelium, Aldh1b1 expression was preferentially located in the crypt bases. Cyp2e1 was up-regulated by alcohol in the liver, but not expressed in the intestines. Alcohol increased the number of Ki67-positive cells in the liver and small intestine. Enhanced phospho-H2AX and p53 were observed in the colon, indicating DNA damage.

Conclusions: We have established a protocol for short term treatment of mice with ethanol and we demonstrated DNA damage and enhanced proliferation after 3 weeks of ethanol treatment. This provides a good basis for further elucidation of the genotoxic mechanisms of alcohol and its metabolites, as well as the protective mechanisms involved.