

**NIAAA Extramural Advisory Board
Consensus Recommendations
Alcohol and Cancer
June 2010**

The sense of the panel and the Extramural Advisory Board was to focus on tissues for which human epidemiological data suggests increased cancer risk. It is also recommended that an increased investment be made in public health awareness about alcohol and cancer risk. Recommendations are not listed in terms of priority.

1. Systems approaches to tissue specific contributions of ethanol to the development and progression of cancer.
 - a. Comprehensive, coordinated and systematic approach to understanding dose, time, sex and tissue specific differences in effects of alcohol and metabolites on cancer
 - b. Tissue specific metabolites
 - c. Signaling pathways/targets
 - d. Genetic interactions that underlie alcohol-specific responses
 - e. Biomarkers
 - f. Direct carcinogenic mechanisms (e.g acetaldehyde)
 - i. DNA mutation/loss/translocation
 - ii. Epigenetic effects
 - iii. Transcriptome
 - iv. Proteome
 - v. Metabolome

2. Molecular mechanisms. Effects of alcohol and/or its metabolites on cancer development and progression. Roles of :
 - a. Oxidative stress,
 - b. Inflammation / immunity
 - c. Retinoid homeostasis,
 - d. Epithelial mesenchymal transition and fibrosis
 - e. Ethanol metabolism---Cyp2E1, ADH,ALDH
 - f. Stem cells

3. Adapt / exploit established preclinical cancer models for studying alcohol-related carcinogenesis e.g.
 - a. P53 null mouse, MMTV-WNT, C-MYC HCC, RIP-Tag
 - b. Stem Cells

4. Cell and molecular basis for enhanced cancer risks of alcohol with other agents.
 - a. Mechanism underlying relationships with:
 - i. Viruses
 - ii. Tobacco
 - iii. Obesity
 - iv. Ovarian hormones
 - v. Microbes

5. Epidemiology and genotype-phenotype correlations
 - a. Work with other Institutes pursuing cancer related studies by exploiting technologies and resources to address alcohol-related question [cancer] e.g., large scale genomics (GWAS). Correlate genotypes with large scale epidemiologic studies.
 - b. NIAAA should have input into larger [cancer] epidemiology and intervention studies to get good reliable information on alcohol consumption.
 - c. Collect information on cancer in ongoing epidemiologic studies
 - d. Construct studies in high-risk populations to address alcohol-cancer mechanisms and health disparities e.g.
 - i. Esophageal cancer in ALDH2 deficient Asian individuals.
 - ii. ASPD in Koreans with ALDH2 allele encourages drinking could theoretically lead to cancer?
 - iii. Hispanics, high rates of cirrhosis, high rates of HCC?
 - iv. Cancers in Native Americans with very high rates of alcoholism, smoking, and diabetes?
 - v. High cancer families e.g. BRCA1 carriers.
 - vi. Collect cancer information in COGA