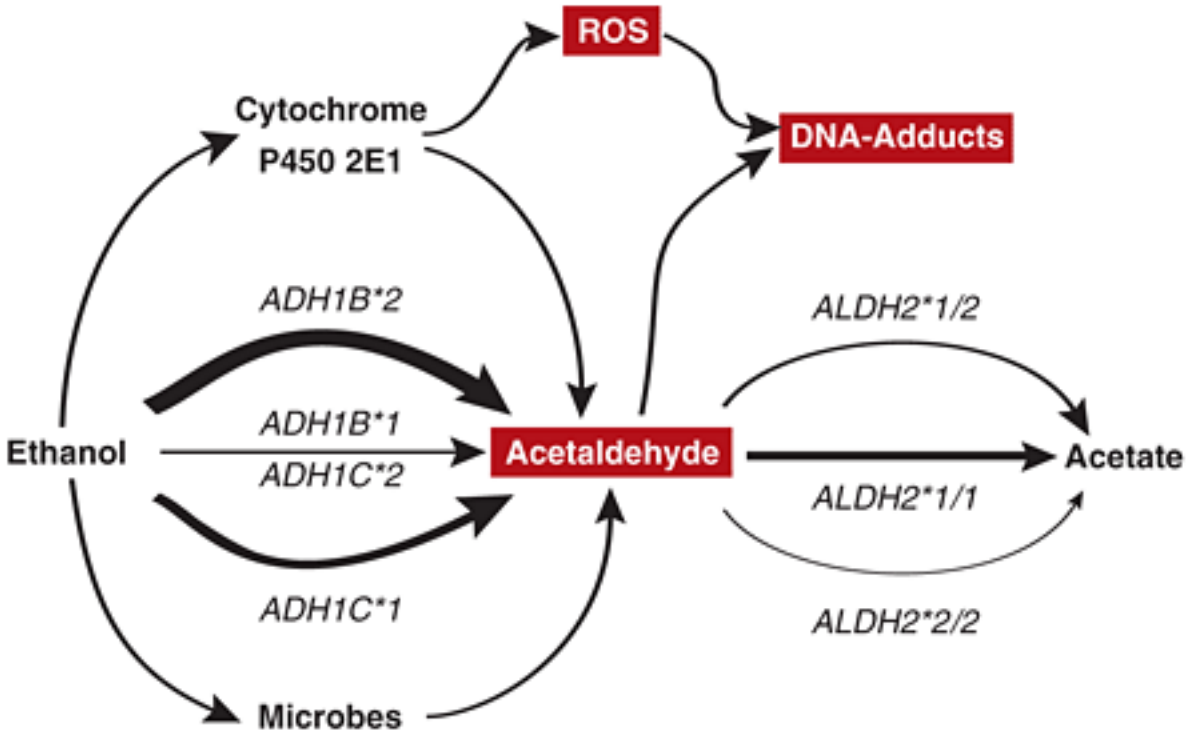
Pathways of ethanol metabolism and their role in carcinogenesis



Ethanol is oxidized to acetaldehyde through the actions of various alcohol dehydrogenase (ADH) enzymes (e.g., enzymes encoded by the *ADH1B* and *ADH1C* genes), through the microsomal enzyme cytochrome P450 2E1 (CYP2E1), and by microbes living in the human gastrointestinal tract (e.g., mouth and colon). The relative contributions of these pathways and the differences in activity between enzymes encoded by different *ADH1B* and *ADH1C* alleles is represented by the thickness of the arrows. Acetaldehyde is oxidized to acetate primarily by the enzyme aldehyde dehydrogenase 2 (ALDH2). Again, the thickness of the arrows indicates the rate of acetaldehyde oxidation in people carrying two active *ALDH2*1* alleles, one active *ALDH2*1* and one inactive *ALDH2*2* allele, or two inactive *ALDH2*2* alleles, respectively. Cancer-inducing substances (i.e., carcinogens) generated during the various pathways of alcohol metabolism are highlighted. These include acetaldehyde; highly reactive, oxygen-containing compounds (reactive oxygen species [ROS]) generated by CYP2E1; and adducts formed by the interactions of acetaldehyde or ROS with DNA.

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