

# RNA interference against aldehyde dehydrogenase-2: development of tools for alcohol research

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Liver alcohol dehydrogenase oxidizes ethanol to acetaldehyde, which is further oxidized to acetate by aldehyde dehydrogenase-2 (ALDH2\*1). Individuals who carry a low-activity ALDH2 (ALDH2\*2) display high blood acetaldehyde levels after ethanol consumption, which leads to dysphoric effects, such as facial flushing, nausea, dizziness, and headache ("Asian alcohol phenotype"), which result in an aversion to alcohol and protection against alcohol abuse and alcoholism. Mimicking this phenotype may reduce alcohol consumption in alcoholics. RNA interference (RNAi) is a cell process in which a short interfering RNA (siRNA) of 21-25 bp guides the degradation of a complementary target mRNA. Thus, siRNAs may be useful in mimicking the Asian phenotype by inhibiting ALDH2 gene expression. We determined the inhibitory effect of three chemically synthesized siRNAs targeted against rat ALDH2 mRNA in human embryonic kidney cells (HEK-293 cell lines) transfected with a plasmid carrying the rat ALDH2 cDN