

# Gene therapy reduces ethanol intake in an animal model of alcohol dependence

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Background: Some gene polymorphisms strongly protect against the development of alcoholism. A large proportion of East Asians carry a protective inactivating mutation in aldehyde dehydrogenase (ALDH2\*2). These subjects display high levels of blood acetaldehyde when consuming alcohol, a condition that exerts a 66 to 99% protection against alcohol abuse and alcoholism. Present knowledge allows the incorporation of therapeutic genes that can modify the expression of disease predisposing genes, an effect that can last from months to years. In line with the above, we have tested if inhibiting the expression of the aldehyde dehydrogenase gene (ALDH2) by an anti-Aldh2 antisense gene can curtail the drive of alcohol-dependent animals to consume alcohol. Methods: Wistar-derived rats bred as high alcohol drinkers (UChB; Universidad de Chile Bibulous) were rendered alcohol dependent by a 2-month period of voluntary ethanol (10%) intake, subjected to a 3-day withdrawal period and further allowed a