MOLECULAR CLONING AND CHARACTERIZATION OF THE MOUSE *Adh-1* GENE AND THE HUMAN β_1 ADH cDNA.

KE ZHANG

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Doctoral Committee

Howard J. Edenberg, Ph.D.
(Committee chairman)

William F. Bosron, Ph.D.

Ting-Kai Li, M. D.

Steven Larsen, Ph. D.

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ABSTRACT

In mammals, ethanol is principally oxidized in liver. The rate-limiting step is the oxidation of ethanol to acetaldehyde, which is catalyzed by alcohol dehydrogenase (ADH). ADH-A_2 is the main alcohol dehydrogenase in mouse liver, and is encoded by the *Adh-1* gene. Genetic variations in liver ADH activity have been found among different inbred strains of mice; similar variations might be present in humans. The structure of the mouse and human ADH genes, and the mechanism(s) involved in regulation of their expression, were not known. Using a mixture of oligonucleotides based on the amino acid sequence of horse ADH as the probe, we isolated cDNA clones encoding the entire mouse ADH-A_2 from a cDNA library made from the liver of DBA/2J mice. Using cloned mouse ADH cDNA as the probe, we isolated cDNA clones encoding the human β_1 ADH isoenzyme from a human liver cDNA library. Both cDNAs were completely sequenced; the deduced amino acid sequences show 85% identity between the mouse ADH-A_2 and the human β_1 isoenzyme. Genomic clones of *Adh-1* were isolated from YBR/Ki mice, which express ADH-A_2 at high levels in liver, and BALB/c mice which express ADH-A_2 at low levels in liver. Our results demonstrate that the mouse *Adh-1* gene contains 9 exons interrupted by 8 introns. The first 293 bp 5' to the coding region is identical in the *Adh-1* genes of these high- and low-expression strains. There are 288 base pairs of alternating purines and pyrimidines located in the first intron in the YBR/Ki gene. Such sequences have been reported to enhance gene expression in cultured cells. Interestingly, the

Adh-1 gene from BALB/c, a low-expression strain, lacks 101 base pairs of this sequence, and also has several transition mutations there.

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