# Two different genes encode δ-aminolevulinate synthase in humans: nucleotide sequences of cDNAs for the housekeeping and erythroid genes

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Submitted September 14, 1990 EMBL accession nos X56351, X56352

Human δ-aminolevulinate synthase [Succinyl-CoA:glycine *C*-succinyltransferase (decarboxylating); EC 2.3.1.37] catalyzes the first committed step of heme biosynthesis in mammals. There are two tissue-specific isozymes (1, 2) of δ-aminolevulinate synthase encoded by different structural genes in chickens (3) and in humans (4). In humans, the housekeeping gene, ALAS1, maps to chromosome band 3p21 (5, 6) while the erythroid tissue-specific gene, ALAS2, maps to the X chromosome (4, 7, 8). ALAS1 was cloned from a human adult liver cDNA library (9), kindly provided by S.Orkin, by using mixed oligonucleotide probes corresponding to conserved regions of the published sequences for chicken and yeast ALAS1. ALAS2 was cloned from a human fetal liver library (10), kindly provided by B.Forget, by using a murine erythroid cDNA graciously provided by P.Dierks.

The authenticity of human liver ALAS1 was demonstrated by its 90% amino acid sequence identity with that of rat liver δ-aminolevulinate synthase (11) and by expression of δ-aminolevulinate synthase enzymatic activity in *E. coli* (Bishop and Ioannou, unpublished). The authenticity of human ALAS2 was demonstrated by its 90% amino acid sequence identity with mouse erythroid δ-aminolevulinate synthase clone MS-6 (12, 13). In contrast, amino acid sequence comparison between human housekeeping ALAS1 and human erythroid ALAS2 showed only 59% identity. There was no homology in the amino-terminal region and about 73% homology after hepatic residue 197. Thus the peptides encoded by the human cDNAs are more homologous to their respective tissue-specific counterparts in other species than they are to each other.

Comparison of the ALAS1 sequence with that previously published (14) revealed discrepancies in the latter including mismatches, insertions and deletions resulting in amino acid substitutions and three frameshifts. The present sequence was confirmed on both strands and the predicted amino acid sequence was more homologous to that of the rat sequence (11).

## ACKNOWLEDGEMENTS

We thank S-F.Tsai, R.M.Reddy, W.Burrows and M.Lu for their expert assistance. This research was supported by a grant, R01 DK40895, from the National Institutes of Health.

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