This report describes the isolation of a heretofore uncharacterized aldehyde dehydrogenase (ALDH) with retinal dehydrogenase activity from rat kidney and the cloning and expression of a cDNA that encodes its human ortholog, the previously unknown ALDH12. The human ALDH12 cDNA predicts a 487-residue protein with the 23 invariant amino acids, four conserved regions, cofactor binding motif (G^{209}XG^{30}G), and active site cysteine residue (Cys^{287}) that typify members of the ALDH superfamily. ALDH12 seems at least as efficient (V_{max}/K_m) in converting 9-cis-retinal into the retinoid X receptor ligand 9-cis-retinoic acid as two previously identified ALDHs with 9-cis-retinal dehydrogenase activity, rat retinal dehydrogenase (RALDH1) 1 and RALDH2. ALDH12, however, has ~40-fold higher activity with 9-cis-retinal than with all-trans-retinal, whereas RALDH1 and RALDH2 have equivalent and ~4-fold less efficiencies for 9-cis-retinal versus all-trans-retinal, respectively. Therefore, ALDH12 is the first known ALDH to show a preference for 9-cis-retinal relative to all-trans-retinal. Evidence consistent with the possibility that ALDH12 could function in a pathway of 9-cis-retinoic acid biosynthesis in vivo includes biosynthesis of 9-cis-retinoic acid from 9-cis-retinol in cells co-transfected with cDNAs encoding ALDH12 and the 9-cis-retinol/androgen dehydrogenase, cis-retinoid/androgen dehydrogenase type 1. Intense ALDH12 mRNA expression in adult and fetal liver and kidney, two organs that reportedly have relatively high concentrations of 9-cis-retinol, reinforces this notion.

The ligand-activated transcription factors retinoic acid receptor and retinoid X receptor control expression of diverse genes essential for embryonic development and throughout the life spans of vertebrates (1–4). tRA\(^1\) seems to function as the major ligand of retinoic acid receptor in vivo but does not bind with retinoid X receptor. 9cRA, in contrast, can serve as a high-affinity ligand for both retinoic acid receptor and retinoid X receptor in vitro and has been identified as a retinoid X receptor ligand in cells treated with tRA (5, 6). tRA derives from the major parent retinoid in animals, all-trans-retinol. Sequential reactions generate tRA from all-trans-retinol: reversible dehydrogenation of all-trans-retinol into all-trans-retinal, and irreversible dehydrogenation of all-trans-retinal into tRA (7). Dietary all-trans-retinyl esters and all-trans-β-carotene provide all-trans-retinol and serve as the major sources of vitamin A activity for mammals. Diet also contains substantial 9-cis-β-carotene, which can undergo metabolism into 9-cis-retinal (8, 9). Several short-chain alcohol dehydrogenases convert all-trans- and/or 9-cis-retinol into all-trans- and 9-cis-retinal, respectively (10), and RALDH isoforms convert both all-trans- and 9-cis-retinol into tRA and 9cRA, respectively (11).

The RALDH isoforms belong to the ALDH superfamily, which consists of 86 eukaryotic members, including 54 animal enzymes that catalyze the metabolism of diverse aldehydes (12). Substrates include acetaldehyde, aromatic and fatty aldehydes, other metabolic intermediates (e.g., succinic semialdehyde, glutamic-γ-semialdehyde, and 4-amino butyraldehyde), and additional xenobiotics (e.g., aldophosphamide) (13). ALDH1 also serves as crystallins in the lens and cornea of vertebrates (14, 15). ALDHs that catalyze the conversion of all-trans-retinol into tRA include the orthologs rat RALDH1 (16–19), mouse AH2D2 (20), and human ALDH1 (21, 22); the orthologs rat RALDH2 (23, 24) and human ALDH11 (15); and human ALDH6 (13). However, only human ALDH1, mouse AH2D2, rat RALDH1, and rat/mouse RALDH2 have been characterized to any extent as RALDHs. The other candidates, ALDH6 and ALDH11, remain largely uncharacterized for a role in retinoic acid biosynthesis, and additional uncharacterized RALDHs occur (16).

Understanding how tissues maintain steady-state concentrations of retinoic acid requires identification of the enzymes that catalyze the two reactions of retinoic acid biosynthesis and when and where each functions. Because rat kidney contains multiple RALDH activities (16), we used protein purification to obtain the amino acid sequence for a heretofore uncharacterized ALDH. The rat amino acid sequence was identical with the deduced amino acid sequence of a partial human genomic clone. We generated the full-length human cDNA and expressed and characterized the enzyme as an ALDH, i.e., ALDH12. ALDH12 has considerable activity with 9-cis-retinal, has much lower activity with all-trans-retinal, and can contribute to a pathway of 9cRA biosynthesis in cells co-transfected with a cDNA that encodes CRAD1, a 9-cis-retinol dehydrogenase (25).

**EXPERIMENTAL PROCEDURES**

Identification and Sequencing of a Rat Kidney ALDH—Kidney cytosol (270 mg of protein) from male Harlan Sprague-Dawley rats (16)
was applied to a Mono-Q column (1.5 x 8 cm) in 20 mM Tris-HCl, pH 8 (buffer A). The column was washed with buffer A until protein elution ceased and then was eluted with buffer A containing 300 mM NaCl. The protein recovered was applied to Affi-Gel blue (0.75 x 15 cm) in 100 mM phosphate buffer, pH 7.5 (buffer B). The column was washed with buffer B and eluted with 2 mM NAD⁺ in buffer B. Each of the two fractions was applied to a Mono-Q HR 5/5 column (Amersham Pharmacia Biootech) in 20 mM Hepes, pH 7.5 (buffer C) and eluted at 0.5 ml/min with a NaCl gradient from 0 to 250 mM in buffer C. Active fractions were analyzed by SDS-polyacrylamide gel electrophoresis. A protein band of ~54 kDa from the NAD⁺ eluted fraction was excised and sent to Bill Lane of the Harvard Microchemistry Facility for sequence analysis.

cDNA Cloning of a Human Kidney ALDH—We identified a human genomic clone in GenBank™ (accession number AL021939) that had a partial coding sequence of an ALDH with nine of the unique peptide sequences identified in the rat protein band. To clone the cDNA, 5'-RACE (5'-AGCTGGACCTGACGGTGGCCGAATGC-3') and 3'-RACE (5'-CCAGATTTGCCCCCTGTACTTCTACC-3') were done with Human Kidney Marathon-Ready cDNA (CLONTECH). The program was as follows: 1 cycle at 94 °C for 3 min, 5 cycles at 94 °C for 30 s and 68 °C for 3 min, 5 cycles at 94 °C for 30 s and 72 °C for 3 min, 5 cycles at 94 °C for 45 s, and 72 °C for 3 min; and 1 cycle of 72 °C for 10 min.

mRNA Blots—A 334-base pair probe, corresponding to nucleotides 1361 to 1694 of the cDNA, was amplified by polymerase chain reaction, labeled with 32P, and purified using a Micro Bio-Spin 30 column (Bio-Rad). The probe was hybridized to the Human Multiple Tissue Expression Array (CLONTECH). Prehybridizations and hybridizations were done in 10 ml of ExpressHyb solution at 65 °C for 30 min and overnight, respectively. The blot was washed five times in 2× SSC (300 mM NaCl and 30 mM sodium citrate) with 1% SDS at 65 °C for 20 min and twice with 0.1× SSC/0.5% SDS at 55 °C for 20 min. The array was exposed to Kodak X-OMAT LS film for 36 h. This blot is normalized for RNA loading of each dot to account for average tissue differences in mRNA levels of eight housekeeping genes. Thus, the data show relative abundance of target transcripts in different tissues. The same probe was hybridized to the Human Multiple Tissue Northern Blot (CLONTECH). Prehybridizations and hybridizations were done in 10 ml of ExpressHyb solution at 65 °C for 30 min and 1 h, respectively. The blot was washed four times with 2× SSC/0.5% SDS for 30 min at room temperature and twice in 0.1× SSC/0.1% SDS for 30 min at 68 °C and exposed to Kodak X-OMAT LS film overnight. The blot was reprobed with a β-actin probe (CLONTECH) using the same protocol.

Enzyme Assays—The ADLH12 coding region was polymerase chain reaction-amplified with 5'-GGGAAGCTTATGGCTGGAACAAACGCAC-3' and 3'-RACE on the original transfection of the target band. To clone the cDNA, 5'-T-3' and 5'-AGCTGGACCTGACGGTGGCCGAATGC-3' were done with Human Kidney Marathon-Ready cDNA (CLONTECH). The program was as follows: 1 cycle at 94 °C for 3 min, 5 cycles at 94 °C for 30 s and 68 °C for 3 min, 5 cycles at 94 °C for 30 s and 72 °C for 3 min, 5 cycles at 94 °C for 45 s, and 72 °C for 3 min; and 1 cycle of 72 °C for 10 min.

RESULTS AND DISCUSSION

Identification of a Novel Rat ALDH—Two ALDH isozymes in rat kidney and liver that catalyze retinal metabolism have been cloned and characterized: (a) RALDH1, and (b) RALDH2 (16–19). To characterize another, rat kidney cytosol was applied to Mono-Q chromatography to separate the P1 fraction, which contains RALDH1, from the P2 fraction, which contains additional ALDH isozymes (16). Mono-Q does not retain P1 at pH 8 but does retain P2. P2 was eluted from the column with NaCl and separated into two fractions by Affi-Gel blue affinity chromatography. The P2 subfractions were applied separately to anion exchange chromatography. The one not retained by the Affi-Gel blue column behaved as P2c, as reported previously (16). The one that eluted with NAD⁺ behaved as P2a (Fig. 1A). P2c was not studied further because its low pI implies that it represents RALDH2, which has a pI of 5.1 (24). Fractions with...
RALDH activity from P2a were analyzed by SDS-polyacrylamide gel electrophoresis. A band that migrated with ALDHs (54 kDa) was digested in situ and sequenced (Fig. 1B). Twenty-one of the 45 sequences occur in rat pyruvate kinase (M24359), 9 occur in rat methylmalonate-semialdehyde dehydrogenase (M93401), 3 occur in Sus scrofa aldehyde reductase (U46064), 3 do not occur in known proteins, and 9 occur only in human genomic clone AL021939, which has the partial coding region of a possible ALDH. The nine peptides included NQAG-YFMLPTVITDIK, SSFANQGEICLCTSR, ISPWNLPLYLLTWWKIAPAMAFAVAGNTY, VPWNLPLYLLTTWKIAPAMAFAVAGNTY.

**cDNA Clone Encoding a Human Homolog of the Rat ALDH**—The cDNA sequence of AL021939 was generated by 5'9' - and 3'9' -RACE and polymerase chain reaction with primers to both ends with a human kidney cDNA template. The cDNA produced encodes a deduced protein of 487 amino acids with the 23 invariant amino acids and the four conserved regions that typify members of the ALDH superfamily (Fig. 2). Also included are a cofactor binding motif (G209XG3G) and a cysteine residue (Cys287) in the appropriate locus to serve as an active site nucleophile (12, 13). ALDH12 shows the closest nucleotide/amino acid similarity with the hydroxymuconic semialdehyde dehydrogenase of Pseudomonas putida but has no more than 50% similarity with other human ALDHs (Table I). Human ALDH genes 1–11 have been cloned and characterized, as have two named but unnumbered human ALDHs (succinic semialdehyde dehydrogenase and methylmalonal semialdehyde dehydrogenase); the new human ALDH therefore represents ALDH12.

**mRNA Expression of the Human ALDH**—Adult human liver and kidney expressed a 2.5-kilobase ALDH12 mRNA intensely. Expression in other tissues was below detection limits by Northern blot analysis (Fig. 3).
Table I

Comparison of nucleotide and amino acid sequences of ALDH12 with other cytosolic ALDH superfamily members

| ALDH   | Nucleotide identity (%) | Amino acid homology (%) | GenBank™ accession no. |
|--------|-------------------------|-------------------------|------------------------|
| ALDH12 (human) | 100                      | 100                      | AF303314               |
| Hydroxymucon semialdehyde (P. putida) | 45                      | 45                      | X52505                 |
| RALDH1 (rat) | 45                      | 38                      | U79118                 |
| RALDH2 (rat) | 45                      | 39                      | U60063                 |
| AHD2 (mouse) | 46                      | 38                      | M74577                 |
| PBALDH (rat) | 46                      | 39                      | M23995                 |
| ALDH1 (human) | 47                      | 39                      | J04748                 |
| ALDH5 (human) | 43                      | 38                      | M77477                 |
| ALDH6 (human) | 45                      | 39                      | U79191                 |
| ALDH9 (human) | 46                      | 38                      | U34252                 |

ALDH12 transcripts (2.5 kilobase) were detected in adult kidney and liver (lanes 7 and 8, respectively). Signals were not detected in: lane 1, brain; lane 2, heart; lane 3, skeletal muscle; lane 4, colon; lane 5, thymus; lane 6, spleen; lane 9, small intestine; lane 10, placenta; lane 11, lung; and lane 12, peripheral blood leukocytes. The 2-kilobase signal was obtained with a human β-actin probe. Faster-migrating bands in lanes 2 and 3 represent α- or γ-actin.

Fig. 3. Northern blot analysis of ALDH12 expression in human tissues. ALDH12 transcripts (2.5 kilobase) were detected in adult kidney and liver (lanes 7 and 8, respectively). Signals were not detected in: lane 1, brain; lane 2, heart; lane 3, skeletal muscle; lane 4, colon; lane 5, thymus; lane 6, spleen; lane 9, small intestine; lane 10, placenta; lane 11, lung; and lane 12, peripheral blood leukocytes. The 2-kilobase signal was obtained with a human β-actin probe. Faster-migrating bands in lanes 2 and 3 represent α- or γ-actin.

Table II

Relative mRNA expression in human tissues of ALDH12

| Tissue                           | ALDH12 mRNA (copies/μg) |
|---------------------------------|-------------------------|
| Whole brain                     | 1 (nd)                  |
| Cerebral cortex                 | 1 (nd)                  |
| Cerebellum, left                | 1 (nd)                  |
| Cerebellum, right               | 1 (nd)                  |
| Corpus callosum                 | 1 (nd)                  |
| Thalamus                        | 1 (nd)                  |
| Hippocampus                     | 1 (nd)                  |
| Medulla                         | 1 (nd)                  |
| Caudate nucleus                 | 1 (nd)                  |
| Putamen                         | 1 (nd)                  |
| Apex of the septum              | 1 (nd)                  |
| Interventricular septum         | 1 (nd)                  |
| Pons                            | 1 (nd)                  |
| Putamen                         | 1 (nd)                  |
| Apex of the septum              | 1 (nd)                  |
| Hippocampus                     | 1 (nd)                  |
| Cerebellum, left                | 1 (nd)                  |
| Cerebellum, right               | 1 (nd)                  |
| Corpus callosum                 | 1 (nd)                  |
| Thalamus                        | 1 (nd)                  |
| Hippocampus                     | 1 (nd)                  |
| Medulla                         | 1 (nd)                  |
| Caudate nucleus                 | 1 (nd)                  |
| Putamen                         | 1 (nd)                  |
| Apex of the septum              | 1 (nd)                  |
| Interventricular septum         | 1 (nd)                  |
| Pons                            | 1 (nd)                  |
| Putamen                         | 1 (nd)                  |
| Apex of the septum              | 1 (nd)                  |
| Hippocampus                     | 1 (nd)                  |
| Cerebellum, left                | 1 (nd)                  |
| Cerebellum, right               | 1 (nd)                  |
| Corpus callosum                 | 1 (nd)                  |
| Thalamus                        | 1 (nd)                  |
| Hippocampus                     | 1 (nd)                  |
| Medulla                         | 1 (nd)                  |
| Caudate nucleus                 | 1 (nd)                  |
| Putamen                         | 1 (nd)                  |
| Apex of the septum              | 1 (nd)                  |
| Interventricular septum         | 1 (nd)                  |
| Pons                            | 1 (nd)                  |
| Putamen                         | 1 (nd)                  |
| Apex of the septum              | 1 (nd)                  |
| Hippocampus                     | 1 (nd)                  |

"nd," not detected.

E. coli

Human ALDH12 and 9-cis-Retinal Metabolism

Enzymatic Properties—ALDH12 had no detectable activity with 2 mM benzaldehyde at pH 5 or pH 6, but activity increased from pH 7 to pH 9. Activities at the physiological pH of 7.4 and the pH used for assays (pH 8–8.5) were 62% and ~88% of pH 9 activity, respectively (Fig. 5). At substrate concentrations of 2 mM, ALDH12 was most active with benzaldehyde and NAD⁺ (Table III). NADP⁺ provided lesser but substantial activity. Under these conditions, ALDH12 catalyzed the highest reaction rate with decanal among the straight-chain, aliphatic multifunctional aldehydes tested. As chain length decreased, so did activity. The addition of a second functional group to aliphatic multifunctional aldehydes had an inconsistent effect on activity. ALDH12 metabolized the four-carbon bifunctional succinic semialdehyde at a greater rate than longer-chain aliphatic bifunctional aldehydes (e.g., hexanal and octanal) but metabolized the five-carbon bifunctional aldehyde glutaraldehyde at a lower rate than shorter-chain aliphatic multifunctional aldehydes (e.g., octanal and propanal). No activity was detected with eight additional xenobiotic or naturally occurring aldehydes. Substrates were not converted into detectable products by supernatants of mock-transfected cells, with three exceptions: hexanal, decanal, and glutaraldehyde.

Hydroxymucon semialdehyde (P. putida)

Hydroxymucon semialdehyde (P. putida) was obtained with a human ALDH12 transcript (2.5 kilobase) detected in adult kidney and liver (lanes 7 and 8, respectively). Signals were not detected in: lane 1, brain; lane 2, heart; lane 3, skeletal muscle; lane 4, colon; lane 5, thymus; lane 6, spleen; lane 9, small intestine; lane 10, placenta; lane 11, lung; and lane 12, peripheral blood leukocytes. The 2-kilobase signal was obtained with a human β-actin probe. Faster-migrating bands in lanes 2 and 3 represent α- or γ-actin.
had activities in mock supernatants that were 8.5%, 74%, and 23%, respectively, of their total activities in pcDNA3/ALDH12-transfected cells.

With 10 μM retinoids, ALDH12 activity was higher with 9-cis-retinal (739 ± 21 pmol/min/mg protein, mean ± S.D., n = 3) than with 13-cis-retinal (233 ± 5 pmol/min/mg protein). Forty-fold lower activity was detected with all-trans-retinal (19 ± 2 pmol/min/mg protein).

Kinetic constants were obtained for representative substrates: benzaldehyde (most active at 2 mM), 9-cis-retinal (most active retinoid), acetaldehyde (prototypical ALDH substrate), succinic semialdehyde (high activity) (Fig. 6). ALDH12 was most efficient with benzaldehyde (highest Vmax) but had the lowest Km value with 9-cis-retinal (Table IV) and was inefficient with acetaldehyde. Note that the differences between retinoid and nonretinoid substrates reflect assay temperature differences. 9-cis-Retinal was assayed at 37 °C; the nonretinoid substrates were assayed at −22 °C. The higher temperature would increase the rate at least 5-fold.

Participation in 9cRA Biosynthesis from 9-cis-Retinol in Intact Cells—To determine whether ALDH12 would convert 9-cis-retinal generated in vivo from 9-cis-retinol into 9cRA, CHO cells were transfected with pcDNA3/ALDH12 alone or with a cDNA encoding the short-chain dehydrogenase CRAD1. CRAD1 catalyzes conversion of 9-cis-retinol into 9-cis-retinal (25). Mock-transfected cells produced 25 ± 1 (±S.D., n = 3 plates) pmol/plate/2 h of 9cRA from 1 μM 9-cis-retinol. CRAD1 alone produced 35 ± 2.5 pmol/plate/2 h (p < 0.001), a net increase of 5 pmol/plate/h. ALDH12 alone produced 42 ± 1 pmol/plate/2 h, a net increase of 8.5 pmol/plate/h (p < 0.0001). CRAD1 and ALDH12 together produced 199 ± 25 pmol/plate/2 h, a net increase of 87 pmol/plate/h (p < 0.0001) or 17- and 10-fold more 9cRA than either alone, respectively. The experiment was repeated with graded amounts of each cDNA. Transfection of CRAD1 or ALDH12 again produced only a modest amount of 9cRA (5 ± 4 and 16 ± 3 pmol/plate/h, respectively) (Fig. 7). Transfection with both was required for a marked increase in 9cRA. With fixed pcDNA3/CRAD1, a 6-fold increase in pcDNA3/ALDH12 produced a 2-fold increase in 9cRA. With fixed pcDNA3/ALDH12, a 3-fold increase of pcDNA3/CRAD1 showed no significant effect on 9cRA synthesis. Maximum 9cRA was synthesized by an ALDH12/CRAD1 ratio of 4. This suggests that the amount/activity of the ALDH determines the rate of 9cRA biosynthesis in this path, assuming equivalent transcription and translation efficiencies of the two enzymes.

Identification of an Alternative Transcript—We identified an alternative ALDH12 transcript lacking nucleotides 910 to 1004.
Human ALDH12 and 9-cis-Retinal Metabolism

Data were obtained at ambient temperature except for 9-cis-retinal, which was assayed at 37 °C. \( K_m \) and \( V_{max} \) values represent the averages of two independent determinations obtained with six to eight substrate concentrations in duplicate or triplicate. The numbers in parentheses are the independent values (± SEM for the \( K_m \) values) determined by nonlinear regression analysis. Because data were generated from different transfections, the \( V_{max}/K_m \) ratios were normalized, setting the average \( V_{max} \) of benzaldehyde in each transfection as 100.

![Diagram](image)

**FIG. 7.** Biosynthesis of 9cRA catalyzed by CRAD1 and ALDH12 in intact CHO cells. CHO cells were transfected with a fixed amount of pcDNA3/CRAD1 and graded amounts of pcDNA3/ALDH12 (stippled bars) or a fixed amount of pcDNA3/ALDH12 and graded amounts of pcDNA3/ALDH12 (open bars). Mock transfections were performed with pcDNA3. *Numbers under the bars* indicate the micrograms of DNA added. Values are the means ± S.D. of triplicate plates.

## Table IV

| Substrate          | \( K_m \) (\( \mu \text{M} \)) | \( V_{max} \) (relative activity) | \( V_{max}/K_m \) (×10) |
|--------------------|-------------------------------|----------------------------------|--------------------------|
| Benzaldehyde       | 17.5 (19 ± 1, 16 ± 4)         | 100 (98, 102)                    | 57                       |
| Acetaldehyde       | 10,240 (9330 ± 1840, 11140 ± 2340) | 130 (140, 120)                  | 0.13                     |
| Succinic semialdehyde | 1,685 (1500 ± 400, 1870 ± 430) | 60 (60, 60)                     | 0.36                     |
| 9-cis-Retinal       | 3.15 (2.3 ± 0.3, 4 ± 0.5)     |                                  | 6.5 (6, 7)               |

These data indicate efficiencies of −27 and 38, respectively, for RALDH1 and RALDH2 with 9-cis-retinal, compared with 0.8 ((0.065 × 40 nmol/min/mg)/3.15 \( \mu \text{M} \)) for ALDH12. The lack of ALDH12 purity also must be considered because activity was measured in the 800 × g supernatant of transfected cells. Fifty-fold represents a conservative estimate for a purification factor, placing ALDH12 near or greater than RALDH1 and RALDH2 in efficiency for catalyzing 9-cis-retinal metabolism.

ALDH12 seems too restricted in substrate recognition to serve as a general xenobiotic clearing enzyme. That is, despite its seemingly disparate substrate recognition (Table III), ALDH12 showed remarkable specificity in some respects. High efficiency for benzaldehyde was eliminated by adding substrates to the phenyl ring—note the lack of detectable activity with coniferyl aldehyde and trans-4-stilbene-carboxyaldehyde—or by separating the phenyl ring from the carboxyaldehyde (no detectable activity with trans-cinnamaldehyde). Despite activity with all-trans-retinal, albeit low, ALDH12 had no detectable activity with citral, a simplified analog of retinal. Appreciable activity with short-chain aliphatic aldehydes was eliminated with the addition of functional groups (pyruvaldehyde, betaine, and malonaldehyde), except for glutaraldehyde. Taken together, these data suggest an active site structured or adaptable to specific classes of substrate(s), with recognition of short- and medium-chain aliphatic aldehydes possible because of their size and flexibility, not necessarily because they are preferred substrates. The situation might be similar to that of RALDH2, which has a protruding “arm” that wraps around all-trans-retinal to form an organized active site (29, 30); yet RALDH2 also recognizes acetaldehyde and medium-chain acylaldehydes, resulting from its initially unorganized binding pocket (23).

A function for the short transcript that translates an enzymatically inactive ALDH12 remains uncertain. It could serve as a control element for ALDH12 action (substrate sequestration?), perhaps produced under certain conditions, or it might function as a structural protein. Uses of ALDHs as crystallin and an aldehydogen-binding protein indicate that such a transcript could translate a protein with a function unrelated to aldehyde metabolism (14, 15, 31).

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