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Cloning and mutational analysis of human malonyl-coenzyme A decarboxylase

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Abstract Malonyl coenzyme A (CoA) decarboxylase (E.C.4. 1.1.9) catalyzes the conversion of malonyl CoA to acetyl CoA. The metabolic role of malonyl CoA decarboxylase has not been fully defined, but deficiency of the enzyme has been associated with mild mental retardation, seizures, hypotonia, cardiomyopathy, vomiting, hypoglycemia, metabolic acidosis, and malonic aciduria. Here we report the isolation and sequencing of the human gene encoding malonyl CoA decarboxylase, and the identification of a mutation causing malonyl CoA decarboxylase deficiency. Human malonyl CoA decarboxylase cDNA sequences were identified by homology to the goose gene, and the intron/exon boundaries were determined by direct sequencing of a PAC clone containing the entire human gene. The 1479 basepair human cDNA is 70 percent identical to the goose sequence, and the intron/exon boundaries are completely conserved between the two species. The genetic mutation underlying malonyl CoA decarboxylase deficiency was determined in a patient with clinical features of this defect, malonic aciduria, and markedly reduced malonyl CoA decarboxylase activity.—Gao, J., L. Waber, M. J. Bennett, K. M. Gibson, and J. C. Cohen. **Cloning and mutational analysis of human malonyl-coenzyme A decarboxylase.** ***J. Lipid Res.*** **1999.** 40: **178–182.**

Supplementary key words microbodies • mitochondria • frameshift mutation • metabolism • inborn errors

Malonyl coenzyme A (CoA) decarboxylase (E.C.4.1.1.9) activity has been detected in extracts from a wide variety of animal (1–3) and bacterial cells (4). The enzyme catalyzes the conversion of malonyl CoA to acetyl CoA, but the metabolic role of this reaction has not been fully defined. In most animal tissues, malonyl CoA decarboxylase is located in mitochondria (5–7). Accordingly it has been suggested that malonyl CoA decarboxylase protects key mitochondrial enzymes such as pyruvate carboxylase and methylmalonyl-CoA mutase from inhibition by malonyl CoA (3, 5).

In humans, deficiency of malonyl CoA decarboxylase has been associated with mild mental retardation, seizures, hypotonia, cardiomyopathy, vomiting, hypoglycemia, metabolic acidosis, and malonic aciduria (8–13). Treatment with a fat-restricted diet (12, 13) and with carnitine (13) has lead to improved general health in two patients. The human gene encoding the enzyme has not been cloned, however, and the molecular basis for malonyl CoA decarboxylase deficiency has not been determined. As a first step towards elucidating the metabolic function of malonyl CoA decarboxylase in humans, we cloned and sequenced the human gene encoding the enzyme. Here we report *i*) the genomic and complementary DNA sequences of the human malonyl CoA decarboxylase gene, and *ii*) a mutation in the gene in a new case of malonyl CoA decarboxylase deficiency. Inspection of the derived amino acid sequence of human malonyl CoA decarboxylase revealed sequence motifs that may have implications for the metabolic function of the enzyme.

METHODS

Subjects

The proband was the firstborn son of unrelated parents, and was born at term after an unremarkable pregnancy (birth weight was 8 lb, 3 oz). Micropenis and hypotonia were noted at birth, and he remained in the hospital for 12 days after birth for poor respirations. At 10 months of age he was readmitted and was found to have malonic aciduria, hypertrophic cardiomyopathy, and renal dysplasia. His extended chromosomes were normal. Malonyl CoA decarboxylase activity in his primary cultured fibroblasts was less than ten percent of control values. During surgery to have a gastrostomy feeding tube placed, the patient had a cardiac arrest and could not be revived.

Assay of malonyl CoA decarboxylase in cultured fibroblasts

Malonyl CoA decarboxylase activity was assayed in fibroblasts from the patient and in control fibroblasts by following the release of $^{14}CO_2$ from [1,3-^{14}C]malonyl CoA as described by Brown et al. (8).

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cDNA analysis

A search of the Expressed Sequence Tags database (dbests) of the National Center for Biotechnology Information, Bethesda, MD, identified 22 human cDNA clones with homology to the goose malonyl CoA decarboxylase cDNA sequence (14). Oligonucleotides were derived from the human EST sequences ATCC#135110 and IMAGE Consortium cDNA clone #127540. RNA was prepared from a human liver cell line (huh7), and from primary fibroblasts from the patient, and reverse transcribed using SuperScript reverse transcriptase (Life Technologies, Gaithersburg, MD). Human cDNA corresponding to exons 2 through 5 was PCR amplified using oligonucleotides MCD8 (5′ GGTTTACTGTCAGAGCTTGCTGTTC 3′) and MCD4 (5′ GGGTTCCTGAACCTAGAACG 3′), and sequenced using a standard cycle sequencing protocol (Protocol # 402078, Applied Biosystems Inc. Foster City, CA). Partial exon 1 sequence was obtained by 5′ RACE (5′ RACE System Version 2.0, Life Technologies, Gaithersburg, MD) but no transcripts corresponding to the full length goose sequence were identified.

Genomic DNA analysis

A human PAC clone containing the entire malonyl CoA decarboxylase gene was identified by PCR screening using oligonucleotides MCD3 (5′ AGTTTTTTACAGGATGCACAGCCTC 3′) and MCD4. PAC DNA was prepared using KB-100 columns (GenomeSystems, St. Louis, MO) and the sequences of exon 1 and the in-

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cggcagctgttgtggggcaccATGCGAGGCTTCGGGCCAGGCTTGACGGCCAGGCGTCTCCTCCCGCTGCGGTTGCCC      57
                      M  R  G  F  G  P  G  L  T  A  R  R  L  L  P  L  R  L  P
CCGCGGCCGCCCGGGCCCCGGCTGGCGAGCGGGCAGGCGGCCGGCGCCCTGGAGCGGGCCATGGACGAGCTGCTGCGC  135
 P  R  P  P  G  P  R  L  A  S  G  Q  A  A  G  A  L  E  R  A  M  D  E  L  L  R
CGCGCGGTGCCGCCGACGCCGGCCTACGAGCTGCGCGAGAAGACACCGGCGCCCGCCGAGGGTCAGTGCGCGGACTTC  213
 R  A  V  P  P  T  P  A  Y  E  L  R  E  K  T  P  A  P  A  E  G  Q  C  A  D  F
GTGAGCTTCTACGGTGGGCTGGCCGAGACGGCCCAGCGGGCCGAACTGCTGGGCCGCCTGGCGCGGGGCTTCGGCGTG  291
 V  S  F  Y  G  G  L  A  E  T  A  Q  R  A  E  L  L  G  R  L  A  R  G  F  G  V
GACCACGGCCAGGTGGCGGAGCAGAGCGCCGGCGTGCTCCATCTGCGCCAGCAGCAGCGGGAGTCGGCGGTGCTGCTG  369
 D  H  G  Q  V  A  E  Q  S  A  G  V  L  H  L  R  Q  Q  Q  R  E  S  A  V  L  L
CAGGCCGAGGTCCGGCTGCGCTACGCGCTGGTGCCGCGCTATCGCGGCCTCTTCCACCACATCAGCAAGCTGGACGGC  447
 Q  A  E  V  R  L  R  Y  A  L  V  P  R  Y  R  G  L  F  H  H  I  S  K  L  D  G
GGCGTGCGCTTCCTGGTGCAGCTGCGGGCCGACCTGCTGGAGGCGCAGGCCCTCAAGCTGGTGGAGGGGCCGGACGTC  525
 G  V  R  F  L  V  Q  L  R  A  D  L  L  E  A  Q  A  L  K  L  V  E  G  P  D  V
CGGgtaaggggccgccgtcgacccccggcagcgcggactggccgccctcctcgagtagtcctcacttgcccctcca  528
 R
agt..>9kb..gtgcttgagtgttttcattccttgtgctgaccacaacacagagatgggcttgatctgtcgcacattg
gaggcctgggatttatcttctccttttcagGAAATGAATGGGGTGCTGAAAGGAATGCTCTCAGAATGGTTTTCCTCC  576
                                E  M  N  G  V  L  K  G  M  L  S  E  W  F  S  S
GGGTTCCTGAACCTAGAACGGGTTACCTGGCATTCACCGTGTGAAGTGCTTCAGAAAATCAGTGAgtaagtattacgg  641
 G  F  L  N  L  E  R  V  T  W  H  S  P  C  E  V  L  Q  K  I  S  E
ttttcatttctttgtacatacattttcatatatatttgtgtatgttttatattggctaaaagctaatctatctccat
tcatatgtacagttt..1.0kb..agaacttgtttgacttagacgaatagtatgaataggagtcagcagccgttgctt
gtgaattatgcatttgtcttgtctctttataaattccgccccagGGCTGAGGCTGTGCATCCTGTAAAAAACTGGATG  675
                                              A  E  A  V  H  P  V  K  N  W  M
GACATGAAGCGCCGCGTTGGGCCCTACAGAAGGTGTTACTTCTTTTCTCACTGTTCGACCCCTGGGGAGCCCCTGGTC  753
 D  M  K  R  R  V  G  P  Y  R  R  C  Y  F  F  S  H  C  S  T  P  G  E  P  L  V
GTTTTGCACGTGGCACTGACTGGTGACATCTCCAGCAACATCCAGGgtacctgcgatggtcaattcgggacaagatgg  799
 V  L  H  V  A  L  T  G  D  I  S  S  N  I  Q
gcaccccatagagccccttgtgtttattgttttgttttgtttttacttgattttatcctcct..4.0kb...cttcca
gctccttcagtgctctgagaattgtcttctcgtcccagcaacaggcttgcctcgtgggctgcagagcggccaggccac
ccttagaaccatcgttggtgttttccagCAATCGTGAAGGAACATCCTCCATCAGAAACAGAAGAGAAGAACAAAATC  849
                              A  I  V  K  E  H  P  P  S  E  T  E  E  K  N  K  I
ACTGCTGCGATCTTTTATTCCATCAGCTTGACCCAGCAGGGACTCCAAGGGGTGGAGCTGGGAACATTCCTCATAAAG  927
 T  A  A  I  F  Y  S  I  S  L  T  Q  Q  G  L  Q  G  V  E  L  G  T  F  L  I  K
CGAGTCGTCAAGGAGTTGCAGgtaagcgacacgcagggagccccggtcacgcttggcttccgtgtggtcaggtcagcg  948
 R  V  V  K  E  L  Q
aacctcgtggggtgtcaggtgccatgagggacac..2.5kb..atgtcactctgaccgctacacagcagcatgtgagc
cgtaggttaagaggtgctcctctgttggtaacgtacctgctgaatttgtgttttctccgccttcctttccaccccaac
catgctttacagAGAGAGTTTCCTCACCTTGGGGTGTTTTCAAGTCTGTCACCTATACCTGGTTTCACCAAATGGCTT  1014
              R  E  F  P  H  L  G  V  F  S  S  L  S  P  I  P  G  F  T  K  W  L
CTGGGGCTTCTGAACTCGCAAACGAAGGAGCATGGGAGGAATGAACTCTTTACAGATTCGGAATGTAAGGAAATCTCG  1092
 L  G  L  L  N  S  Q  T  K  E  H  G  R  N  E  L  F  T  D  S  E  C  K  E  I  S
GAGATCACAGGTGGCCCCATTAACGAGACCCTCAAGCTCCTCCTCAGCAGCAGCGAGTGGGTGCAGTCGGAGAAGCTG  1170
 E  I  T  G  G  P  I  N  E  T  L  K  L  L  L  S  S  S  E  W  V  Q  S  E  K  L
GTGCGGGCGCTGCAGACTCCGCTGATGAGGCTGTGCGCCTGGTACCTGTATGGAGAGAAGCACCGCGGCTACGCGCTG  1248
 V  R  A  L  Q  T  P  L  M  R  L  C  A  W  Y  L  Y  G  E  K  H  R  G  Y  A  L
AACCCCGTGGCCAACTTCCACCTGCAGAACGGGGCGGTGCTGTGGCGCATCAACTGGATGGCGGATGTGAGCCTCAGA  1326
 N  P  V  A  N  F  H  L  Q  N  G  A  V  L  W  R  I  N  W  M  A  D  V  S  L  R
GGCATCACCGGCTCCTGCGGCCTGATGGCCAACTACCGCTACTTCCTGGAGGAGACGGGCCCCAACAGCACCTCCTAC  1404
 G  I  T  G  S  C  G  L  M  A  N  Y  R  Y  F  L  E  E  T  G  P  N  S  T  S  Y
CTCGGCTCCAAGATCATCAAAGCCTCTGAGCAGGTCCTCAGCCTAGTGGCCCAGTTTCAAAAGAACAGCAAGCTCTGA  1482
 L  G  S  K  I  I  K  A  S  E  Q  V  L  S  L  V  A  Q  F  Q  K  N  S  K  L  -
cagtaaacctctcctaaagcacagggccccggctaagaaaacgatcattttcaggaggggccgggagttatgtatctg
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Fig. 1. Nucleotide and deduced amino acid sequence of the human malonyl coA decarboxylase gene. The ATG sequences corresponding to the translation initiation codons in the goose sequence, the c.638–641delGTGA mutation, and the peroxisomal targeting sequence are indicated in bold type. The sizes of introns 2, 3, and 4 were determined by PCR from the PAC, and confirmed by amplification from human genomic DNA. The size of intron 1 was estimated by Southern blotting of restriction-digested PAC DNA using oligonucleotide probes from exon 1 and exon 2.

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tron/exon boundaries were obtained by direct sequencing using oligonucleotides derived from the cDNA as primers.

Chromosomal localization

Oligonucleotides MCD3 and MCD4 were used to PCR amplify DNA from a mouse/human hybrid cell line (CY18) that contains human chromosome 16 (kindly provided by Dr. Roger Schultz, UT Southwestern Med. Ctr.), and from the YAC My772D12 (kindly provided by Dr. Norman Doggett, Los Alamos National Laboratory). Genomic DNA samples from mouse liver, and from a second mouse/human hybrid (A15) that does not contain human chromosome 16 sequences was used as negative controls.

Malonyl CoA decarboxylase expression

A cDNA for the human malonyl CoA decarboxylase was cloned into pCMV6 (kindly provided by Dr. David Russell at UT Southwestern Medical Center) and transiently transfected into in a human hepatoma (huh7) cell line. After 24 h the cells were lysed and the activity of the expressed enzyme was assayed by a carnitine acetyltransferase-linked assay as described by Antinozzi et al. (15).

RESULTS

Malonyl CoA decarboxylase activity

Malonyl CoA decarboxylase activity in primary cultured fibroblasts from the patient was assayed on five separate occasions. On each occasion, the activity of the enzyme was less than 10% of the activity measured in fibroblasts from five normal patients. The activity of a control enzyme (mevalonate kinase) was similar in fibroblasts from the patient and in fibroblasts from the control subjects.

Malonyl CoA decarboxylase gene sequence

Direct sequencing of the PAC revealed two in-frame ATG sequences in exon 1 that are completely conserved between human and goose. The 1479 nucleotide open reading frame (**Fig. 1**) extending from the upstream ATG codon to the stop codon (TGA) in the human sequence is 70% identical to the homologous sequence in goose, and the intron/exon boundaries are completely conserved between the two species. The deduced amino acid sequence is 68% identical (82% similar) between the two species (**Fig. 2**). BLAST searches of GenBank and SwissProt indicated that the human and goose malonyl CoA decarboxylase enzymes do not have significant homology to other known proteins. Interestingly, a putative gene (F35G12.1) identified on a cosmid from the nematode *C. elegans* (GenBank Accession number Z46242) encodes a 360 amino acid protein with 44% sequence identity to the goose malonyl CoA decarboxylase protein.

Sequencing of cDNA prepared from the patient's fibro-

```
Human      1 MRGFGPGLT--ARRLLPLRLPP------RPPGPRLASGQAAGALER---AMDELLRRAVP 49
             MRG   GL+    RL P  +P       R  GP      A    ER   +M+E+L R+VP
Goose      1 MRGLRRGLSRLGPRLGPWAVPRSLRRVLRAAGPWRGQSSAGSVSERGGASMEEVLSRSVP 60

Human     50 PTPAYELREKTPAPAEGQCADFVSFYGGLAETAQRAELLGRLARGFGVDHGQVAEQSAGV 109
               P YE +EK P PAE   A+FV +Y GL   ++RAELLG LAR FG DHG+VAE SA V
Goose     61 LLPPYETKEKAPPPAERRSAEFVRYYRGLEAGSRRAELLGCLARDFGADHGRVAEFSAKV 120

Human    110 LHLRQQQRESAVLLQAEVRLRYALVPRYRGLFHHISKLDGGVRFLVQLRADLLEAQALKL 169
             L  R+Q+RE   LLQAE R+RY L PRYR LF H+ +L+GG+RFLV+LR DL+E  A K
Goose    121 LQAREQEREQGALLQAEDRVRYYLTPRYRALFQHLGRLEGGLRFLVELRGDLVEGLAAKA 180

Human    170 VEGPDVREMNGVLKGMLSEWFSSGFLNLERVTWHSPCEVLQKISEAEAVHPVKNWMDMKR 229
             V+GP V+EM+GVLK MLSEWFS+GFLNLERVTW SPCEVLQKIS++EAVHPV+NW+D+KR
Goose    181 VDGPHVKEMSGVLKNMLSEWFSTGFLNLERVTWQSPCEVLQKISDSEAVHPVRNWVDLKR 240

Human    230 RVGPYRRCYFFSHCSTPGEPLVVLHVALTGDISSNIQAIVKEHPPSETEEKNKITAAIFY 289
             RVGPYRRCYFFSHC+ PGEPL++LHVALT DISS+IQ+IVK+    ETE+  KIT AIFY
Goose    241 RVGPYRRCYFFSHCAIPGEPLIILHVALTSDISSSIQSIVKDVESLETEDAEKITTAIFY 300

Human    290 SISLTQQGLQGVELGTFLIKRVVKELQREFPHLGVFSSLSPIPGFTKWLLGLLNSQTKEH 349
             SISL QQGLQGVELG  LIKRVVKELQ++ P +  FSSLSPIPGFTKWL+GLL+SQTKE
Goose    301 SISLAQQGLQGVELGNHLIKRVVKELQKDLPQIEAFSSLSPIPGFTKWLVGLLSSQTKEL 360

Human    350 GRNELFTDSECKEISEITGGPINETLKLLLSSSEWVQSEKLVRALQTPLMRLCAWYLYGE 409
             GRNELFT+SE +EISEIT     ETLK LL++SEWV+SEKLV+AL +PLMRLCAWYLYGE
Goose    361 GRNELFTESERQEISEITEDSTTETLKKLLTNSEWVKSEKLVKALHSPLMRLCAWYLYGE 420

Human    410 KHRGYALNPVANFHLQNGAVLWRINWMADVSLRGITGSCGLMANYRYFLEETGPNSTSYL 469
             KHRGYALNPVANFHLQNGA LWRINWM D S RGI  SCG+M NYRYFLE+T  NS +YL
Goose    421 KHRGYALNPVANFHLQNGAELWRINWMGDTSPRGIAASCGMMVNYRYFLEDTASNSAAYL 480

Human    470 GSKIIKASEQVLSLVAQFQKNSKL 493
             G+K IKASEQVLS V+QFQ+NSKL
Goose    481 GTKHIKASEQVLSFVSQFQQNSKL 504
```

Fig. 2. Alignment of the deduced amino acid sequences of the human and goose malonyl coA decarboxylase proteins. The 18 amino acids that comprise the mitochondrial targeting sequence in the goose and the conserved canonical peroxisomal targeting sequence are indicated in bold type.

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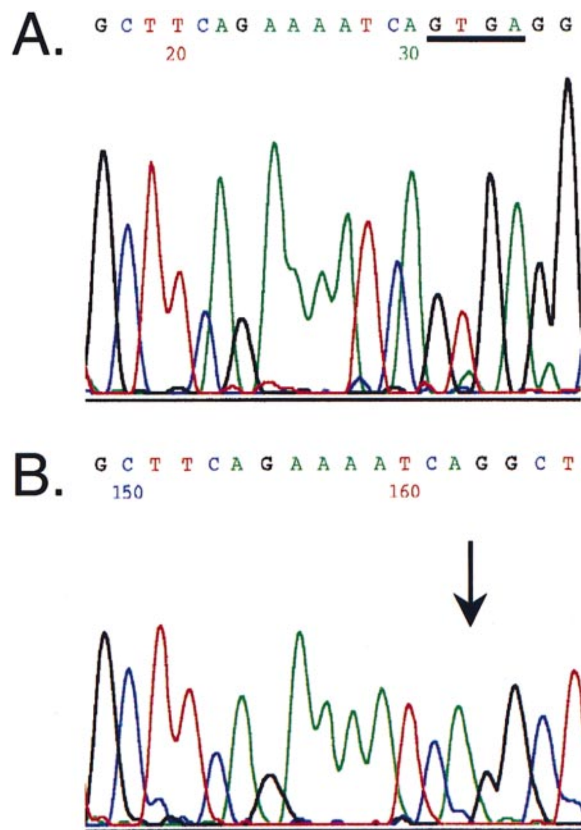

Fig. 3. Malonyl CoA decarboxylase cDNA sequence from a normal individual and a patient with malonyl CoA decarboxylase deficiency. The site of the deletion is indicated by an arrow in the mutant sequence. The deleted nucleotides are underlined in the normal sequence.

blasts indicated that four nucleotides at the 3′ end of exon 2 were deleted (c.638–641delGTGA, see Fig. 1 and **Fig. 3**). The resulting frame shift introduced a premature stop codon eight codons downstream of the deletion. The protein translated from the mutant mRNA would lack 272 carboxy terminal amino acids, therefore the mutation almost certainly abolishes malonyl CoA decarboxylase activity. The mutation was confirmed by direct sequencing of PCR amplified genomic DNA. No other mutations were identified in the coding region or in the intron exon boundaries of the gene. Genomic DNA sequencing indicated that both parents were heterozygotes for the c.638–641delGTGA mutation, therefore the patient is homozygous for this mutation.

Chromosomal localization

A human EST (IMAGE clone #127540) with strong homology to goose malonyl CoA decarboxylase cDNA has been previously mapped to 331.9 cR. from the top of chromosome 16 linkage group (Unigene Collection, National Center for Biotechnology Information). To confirm this map position, DNA from a mouse/human hybrid cell line (CY18) containing human chromosome 16 and from megaYAC My772D12 was amplified by PCR. These results indicate that the human malonyl CoA decarboxylase gene lies in a ~450 kb interval between D16S402 and D16S422 on chromosome 16q24.

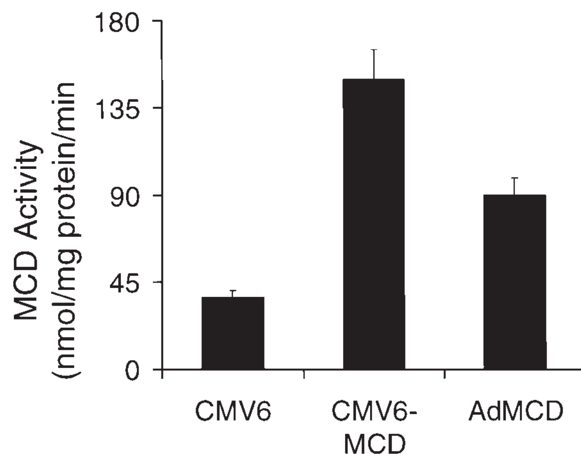

Fig. 4. Malonyl CoA decarboxylase activity in cultured cells. Huh7 cells were plated in 10-cm dishes and transfected with 10 μg of vector alone (pCMV6) as a negative control, or with 10 μg of pCMV6 containing the human malonyl CoA decarboxylase cDNA (pCMV6-MCD), or infected with 10^{10} μg of adenovirus containing the goose malonyl CoA decarboxylase (positive control). Transfected cells were incubated for 24 h, lysed, and assayed for malonyl CoA decarboxylase activity exactly as described (15).

Malonyl CoA decarboxylase expression

Transfection of the human malonyl CoA decarboxylase cDNA into huh7 cells increased malonyl CoA decarboxylase activity by about 4-fold (**Fig. 4**).

DISCUSSION

Malonyl CoA decarboxylase deficiency is a rare inborn error of metabolism (8–12). To elucidate the molecular basis of this condition we cloned the human gene encoding malonyl CoA decarboxylase, and sequenced genomic and complementary DNA from a patient with clinical and biochemical features consistent with the disorder. Analysis of complementary and genomic DNA indicated that human malonyl CoA decarboxylase is a 493 amino acid protein. Transfection of the cDNA into a human hepatoma cell line confirmed that this gene encodes a protein with malonyl CoA decarboxylase activity. The cDNA and deduced amino acid sequences are highly conserved (~70% identical) between human and goose, and the locations of the intron/exon boundaries are identical between the two species. Partial sequencing (1001 nucleotides) of the mouse malonyl CoA decarboxylase gene (J. C. Cohen, unpublished results) revealed 83% identity between the human and mouse cDNA sequences. The high degree of sequence identity between the malonyl CoA decarboxylase genes from these three species indicates strong evolutionary conservation.

DNA sequence from the proband revealed a four nucleotide deletion in the gene encoding malonyl CoA decar-

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boxylase that introduced a premature stop codon and deleted the 272 carboxy terminal amino acids of the protein. This mutation almost certainly abolishes malonyl CoA decarboxylase activity. The same mutation was identified in both parents, therefore the proband is a true homozygote. The absence of any detectable chromosomal abnormality in the proband strongly indicates that his unusual phenotype was due entirely to malonyl CoA decarboxylase deficiency. Some of the clinical features observed in this individual and in previously described patients with malonyl CoA decarboxylase deficiency (e.g., seizures, hypotonia, cardiomyopathy), have also been observed in patients with mitochondrial disorders (see ref. 15 for review). Defective mitochondrial function may therefore account for some or all of the clinical sequelae of malonyl CoA decarboxylase deficiency.

Inspection of the derived amino acid sequence of human malonyl CoA decarboxylase revealed sequence motifs that may indicate alternative metabolic functions for the enzyme. In the goose, the mitochondrial and cytoplasmic forms of malonyl CoA decarboxylase are transcribed from alternate, in-frame initiation codons separated by 146 nucleotides in exon 1 (16). Transcripts from the upstream codon include an 18 amino acid N-terminal motif that forms an amphipathic alpha helix (16) constituting the mitochondrial targeting sequence. Both AUG codons are conserved in the human sequence, and both are in an appropriate sequence context for efficient initiation of translation as determined by Kozak (17). However, the putative mitochondrial targeting sequence identified in the goose protein is poorly conserved in humans (see Fig. 2). Secondary structure modeling of the N-terminus of the human protein (using the computer program Protean, DNAstar) suggests that this region does not form an amphipathic alpha helix and does not correspond to a canonical mitochondrial targeting sequence. Therefore further studies will be required to determine whether malonyl CoA decarboxylase is a mitochondrial enzyme in humans, and the extent to which the phenotype of malonyl CoA decarboxylase deficiency reflects impaired mitochondrial function. Interestingly, a canonical peroxisomal-matrix targeting sequence (SKL) at the carboxy terminus of the protein (18) is strictly conserved in human, goose, and mouse (J. C. Cohen, unpublished results). This sequence is sufficient to direct some (though not all) carrier proteins to peroxisomes (18). Therefore the human malonyl CoA decarboxylase may be targeted to peroxisomes in addition to (or possibly instead of) mitochondria.

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