Expression of a cDNA Isolated from Rat Brown Adipose Tissue and Heart Identifies the Product as the Muscle Isoform of Carnitine Palmitoyltransferase I (M-CPT I)

M-CPT I IS THE PREDOMINANT CPT I ISOFORM EXPRESSED IN BOTH WHITE (EPIDIDYMAL) AND BROWN ADIPOCYTES*

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We set out to determine if the cDNA encoding a carnitine palmitoyltransferase (CPT)-like protein recently isolated from rat brown adipose tissue (BAT) by Yamazaki et al. (Yamazaki, N., Shinohara, Y., Shima, A., and Terada, H. (1995) FEBS Lett. 363, 41-45) actually encodes the muscle isoform of mitochondrial CPT I (M-CPT I). To this end, a cDNA essentially identical to the original BAT clone was isolated from a rat heart library. When expressed in COS cells, the novel cDNA and our previously described cDNA for rat liver CPT I (L-CPT I) gave rise to products with the same kinetic characteristics (sensitivity to malonyl-CoA and K_m for carnitine) as CPT I in skeletal muscle and liver mitochondria, respectively. When labeled with [3H]etomoxir, recombinant L-CPT I and putative M-CPT I, although having approximately the same predicted masses (88.2 kDa), migrated differently on SDS gels, as did CPT I from liver and muscle mitochondria. The same was true for the products of in vitro transcription and translation of the L-CPT I and putative M-CPT I cDNAs. We conclude that the BAT cDNA does in fact encode M-CPT I.

Northern blots using L- and M-CPT I cDNA probes revealed the presence of L-CPT I mRNA in liver and heart and its absence from skeletal muscle and BAT. M-CPT I mRNA, which was absent from liver, was readily detected in skeletal muscle and was particularly strong in heart and BAT. Whereas the signal for L-CPT I was more abundant than that for M-CPT I in RNA isolated from whole epididymal fat pad, this was reversed in purified adipocytes from this source. These findings, coupled with the kinetic properties and migration profiles on SDS gels of CPT I in brown and white adipocytes, indicate that the muscle form of the enzyme is the dominant, if not exclusive, species in both cell types.

Transport of long chain fatty acyl groups into the mitochondrial matrix to undergo β-oxidation is effected by the mitochondrial carnitine palmitoyltransferase (CPT)1 enzyme system. CPT I, an integral outer membrane protein, catalyzes the transfer of an acyl group from coenzyme A to carnitine, the acylcarnitine product traversing the inner membrane by means of a specific translocase. The transesterification is then reversed by CPT II, associated with the matrix face of the inner membrane. CPT I has been the focus of particular attention due to its unique inhibition by malonyl-CoA, a property of the enzyme that is central to the physiological regulation of the β-oxidation pathway (1, 2). As a consequence, CPT I has aroused interest as a potential site for pharmacological inhibition of fatty acid oxidation in the liver in states where this process occurs at excessive rates (such as poorly controlled diabetes (3, 4)) or in the ischemic heart, where elevated levels of acylcarnitines have been associated with arrhythmias (5).

Whereas CPT II appears to be the same protein in all tissues (6), CPT I exists as at least two isoforms (6, 7). Two of these have been designated L-CPT I (expressed in liver and fibroblasts (9, 10)) and M-CPT I (expressed in skeletal muscle (6)). The heart expresses both forms, the muscle variant becoming increasingly predominant during neonatal development in the rat (7, 11, 12). A fuller understanding of the tissue distribution and properties of CPT I isoforms has been impeded by the fact that although cDNAs for L-CPT I and CPT II have been cloned from both rats (9, 13) and humans (10, 14), the same goal has not been achieved with certainty in the case of M-CPT I.

Recently, a cDNA encoding a CPT I-like protein was isolated from rat brown adipose tissue (BAT) (15). This was obtained by a subtractive cloning strategy aimed at identifying proteins expressed in BAT, but not in white adipose tissue (WAT). The derived product was predicted to be a protein of 772 amino acids having 62.6% identity to rat L-CPT I (773 amino acids). Northern blot analysis indicated high levels of expression in BAT, skeletal muscle, and heart (15). However, the study cited left unanswered three important questions. First, does this cDNA in fact correspond to M-CPT I or to an additional member of the growing family of carnitine acyltransferases that have been characterized in recent years (16-19)? Second, if the

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1 The abbreviations and trivial names used are: CPT, mitochondrial carnitine palmitoyltransferase; L-CPT I, liver-type CPT I; M-CPT I, muscle-type CPT I; BAT, brown adipose tissue; WAT, white adipose tissue; etomoxir, 2-[6-(4-chlorophenoxy)hexyl]oxirane-2-carboxylic acid; DNP-etomoxir, 2-[6-(2,4-dinitrophenox)hexyl]oxirane-2-carboxylic acid; PCR, polymerase chain reaction; PAGE, polyacrylamide gel electrophoresis.

2 In this article, the terms CPT I and CPT II refer exclusively to the mitochondrial enzymes, although it is recognized that proteins with CPT activity are also associated with peroxisomes and microsomes (8).
new cDNA does encode M-CPT I with a predicted mass of 88,227 Da, which is almost identical to the value of 88,150 Da predicted for L-CPT I (9), why do the two proteins (when labeled with [3H]etomoxir) migrate so differently on SDS gels (6, 7)? Third, should brown and white fat express different CPT I isoforms?

The studies outlined below leave little doubt that the CPT I expressed in rat BAT is the muscle isoform of the enzyme. They also address the question of why the liver and muscle forms of CPT I behave differently on SDS gels. Finally, the new findings allow refinement of the pattern of CPT I isof orm expression in brown and white fat.

**EXPERIMENTAL PROCEDURES**

**Animals**—Male Sprague-Dawley rats were fed a standard laboratory chow (4% fat, w/w) with lighting from 10.00 to 22.00 h. For studies on BAT (interscapular), the animals were used at a body weight of 100–120 g; in all other cases, body weight ranged from 180 to 220 g. Organs were removed from anesthetized or cervically dislocated animals between 10.00 and 11.00 h.

**General Molecular Biology Methods**—Standard molecular biological techniques were employed (20). cDNA clones were sequenced by the dideoxy chain termination method (21) using the Sequenase T7 DNA polymerase kit from U.S. Biochemical Corp. First strand cDNA was synthesized from total RNA by reverse transcriptase using the kit from Life Technologies, Inc.

**Cloning Methodology**—Two oligonucleotides were synthesized in order to amplify, by the polymerase chain reaction (PCR) method (22), a fragment of the clone reported by Yamazaki et al. (15). The forward primer, 5′-GGGTTACCAGCTGTGCTGACTAAACC-3′, extended from nucleotides 919 to 938, and the reverse primer, 5′-GTGTTCGTCTCCTGTCCAGC-3′, extended from nucleotides 940 to 509, and the reverse primer, 5′-GTGTTCGTCTCCTGTCCAGC-3′, extended from nucleotides 1054 to 1720 (9).

**Northern Blots**—Total RNA was extracted with guanidinium thiocyanate followed by centrifugation in cesium chloride solution (25). Poly(A)^+ RNA was isolated by oligo(dT)-cellulose chromatography. Northern blots were performed as described (26) and hybridized with PhosphorImager (Ref. 15). BAT cDNA was used as template. The PCR product was synthesized from total RNA by reverse transcription using the kit from Life Technologies, Inc.

**CPT Assay**—CPT activity was measured in crude homogenates of the cells 48 h after transfection. CPT activity is expressed as nanomoles of palmitoyl-[14C]carnitine product formed per minute per milligram of protein.

**Plasmid**

| Exp. 1 | Control | + Malonyl-CoA | + OG* | + OG + Malonyl-CoA |
|--------|---------|--------------|------|--------------------|
| Plasmid | 0.14     | 0.13 (13%)   | 0.38 | 0.13 (18%)         |
|        | 0.14     | 0.13 (13%)   | 0.38 | 0.13 (18%)         |
|        | 0.20     | 0.07 (14%)   | 0.07 | 0.07 (14%)         |
|        | 0.20     | 0.07 (14%)   | 0.07 | 0.07 (14%)         |
|        | 0.20     | 0.07 (14%)   | 0.07 | 0.07 (14%)         |
|        | 0.20     | 0.07 (14%)   | 0.07 | 0.07 (14%)         |

*OG, octyl glycoside.

**RESULTS**

Expression of Putative M-CPT I cDNA—Oligonucleotides were designed on the basis of the published sequence of the CPT I-like protein and used to amplify a portion of the CPT I cDNA by PCR. This was then labeled and used as a probe to screen a rat heart cDNA library, resulting in the isolation of several positive clones. The longest one was subjected to DNA sequencing, revealing complete identity to the published sequence (15). However, it was found to be short at the 5′-end, lacking codons for the first two amino acids (including the initiator methionine) and all of the 5′-untranslated region. To generate the full-length construct necessary for expression studies, PCR was again used, this time to amplify the 5′-end of the sequence from BAT cDNA. DNA sequencing of this product revealed only two silent mutations (or amplification errors) at positions 496 and 540 of the published sequence. The full-length construct was then assembled in the mammalian expression vector pCMV6 to form pCMV6-M-CPT I as described under “Experimental Procedures.”

**COS-M6 cells** were transfected with plasmid pCMV6-M-CPT I (encoding rat L-CPT I) and pCMV6-M-CPT I (encoding rat L-CPT I). Mock transfections contained no plasmid. Table I shows the CPT activity measured in crude homogenates of the cells 48 h after transfection in two independent experiments. pCMV6-R-CPT I...
cause a 6–7-fold induction of CPT I activity (i.e. activity measured in the absence of octyl glucoside), consistent with previous results (9). A 5-fold induction was observed with pCMV6-rM-
CPT I. Both activities were substantially inhibited in the presence of 100 μM malonyl-CoA. Putative M-CPT I was the more sensitive, residual activity being similar to that in untransfected cells. For assay of CPT II, the membranes were solubilized in 1% octyl glucoside. Under these conditions, no change was observed in pCMV6-rM-CPT I-transfected relative to untransfected cells. For assay with pCMV6-rL-CPT I, enzyme activity in the presence of octyl glucoside did rise ~1.5-fold. This may represent incomplete inactivation of the induced L-CPT I by the detergent or up-regulation of endoge-
nous CPT II.

A more detailed analysis of the kinetic properties of the two expressed CPTs is presented in Fig. 1. A gross difference in sensitivity to malonyl-CoA is apparent, with I50 values (con-
centration needed for 50% inhibition) of ~8 and 0.15 μM, re-
spectively, for the recombinant L-CPT I and putative M-CPT I variants (Fig. 1A). The response of each enzyme to increasing concentrations of carnitine is shown in Fig. 1B. Expressed L-CPT I saturated rapidly (Km = 25 μM), whereas the other enzyme displayed a much more gradual response (higher Km). In the case of expressed M-CPT I, the presence of endogenous COS cell CPT I (probably the liver isoform) rendered the corresponding Eadie-Hofstee plot markedly nonlinear (more than one component), preventing simple calculation of an accurate Km. It is clear, however, that the exogenous CPT in this case contributed a high Km, M-CPT I-like component.

Transfected and untransfected COS cells were incubated for 6 h in medium containing 3 μM [3H]etomoxir to covalently label the expressed CPT I isoforms. Total cell membrane extracts were then analyzed by SDS-PAGE and subsequent fluorogra-
phy (Fig. 2A). Both types of transfected cells contained highly induced labeled bands. Labeled L-CPT I migrated more slowly than its presumed muscle-type counterpart (~88 and ~82 kDa, respectively), mirroring the behavior of [3H]etomoxir-labeled CPT I isoforms in mitochondria from rat liver and muscle (see below). Only a faint labeled band, of approximately the size of the L-CPT I expression product, was visible in untransfected cells.

To address the question of the differential mobility of the two enzymes during SDS-PAGE, we used an in vitro transcription and translation system to synthesize 35S-labeled protein prod-
ucts from the two CPT I clones. These would not be subject to post-translational modification, as might occur in the whole cell (e.g. upon mitochondrial import). In this system also, the radioactive proteins migrated differently (Fig. 2B). Further-
more, the apparent sizes of the in vitro synthesized 35S-labeled proteins were indistinguishable from those of the correspond-
ing [3H]etomoxir-labeled enzymes from rat liver and muscle mitochondria.

Analysis of CPT I Isoform Expression in Rat Adipose Tis-
tues—[3H]Etomoxir labeling of CPT I enzymes from mitochon-
dria from several rat tissues is shown in Fig. 3A. Lanes 1–3 illustrate the established pattern of expression of CPT I iso-
enzymes in rat liver (L-CPT I), skeletal muscle (M-CPT I), and heart (predominantly M-CPT I), the muscle form migrating somewhat faster than the liver type. In BAT (lane 4), only a protein of the size of M-CPT I was detected. However, in white adipose tissue, mitochondria bands of both muscle and liver sizes were seen, L-CPT I being the major component (lane 5).3 Since the epididymal fat pad, used here as a source of white adipose tissue, contains other cell types in addition to adipocytes, it was necessary to establish whether the labeling pattern observed was a property of the adipocytes themselves. To

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3 We suspect that the minor smaller sized bands seen in Fig. 3A (lanes 1–4) represent degradation products of the major labeled proteins.
A. whole rat tissues; B, purified white adipocytes; C, effect of DNP-etomoxir preincubation on [3H]etomoxir labeling of white adipocyte mitochondria. Adipocyte mitochondria were incubated in the absence (lane 1) or presence (lane 2) of 10 μM DNP-etomoxir before exposure to 3 μM [3H]etomoxir (see “Experimental Procedures”). L and M indicate migration positions of L-CPT I and M-CPT I, respectively.

this end, similar experiments were performed using mitochondria from purified adipocytes (Fig. 3B). Under these circumstances, the expression pattern was reversed, the M-CPT I size band now predominating. To exclude the possibility that this phenomenon was an artifact due to degradation of L-CPT I during the prolonged adipocyte preparation protocol, we employed another covalent CPT I inhibitor to confirm the identities of the two labeled proteins. This agent, DNP-etomoxir, has been shown to have a high degree of specificity for the liver isoform of CPT I and to block subsequent binding of [3H]etomoxir (11). Mitochondria were prepared from adipocytes and then preincubated for 1 h in the absence or presence of 10 μM unlabeled DNP-etomoxir before exposure for an additional hour to 3 μM [3H]etomoxir. The effect of the DNP-etomoxir preincubation is shown in Fig. 3C. The minor upper L-CPT I size band was virtually eliminated. In contrast, the intensity of the lower band was unaffected by the DNP-etomoxir preincubation, consistent with its representing the muscle isoform.

The different CPT I profiles indicated by [3H]etomoxir labeling of mitochondria prepared from BAT, whole epididymal WAT, and purified white adipocytes were paralleled by differences in the kinetic properties of the enzyme from these sources. When expressed relative to mitochondrial protein (Table II), the activity of CPT I measured in liver, heart, and skeletal muscle varied over only a 2-fold range, with a proportional change in the level of CPT II, so that the CPT II/CPT I ratio remained close to unity. (It is important to note that since the K_m values for the substrates of L-CPT I, M-CPT I, and CPT II are different, the relative activities measured for the different isoenzymes will depend upon experimental conditions. The present data are intended to show that wide variation exists between tissues; however, they do not necessarily reflect the molar ratios in vivo.) In BAT mitochondria, the ratio was doubled, and in WAT and purified adipocytes, it rose to 9 and 14, respectively. This observation explains the apparent resistance to complete inhibition of CPT I activity in mitochondria from whole epididymal fat pads and adipocytes isolated from them (Table II, sixth column). Whereas inhibition of ≈90% is routine with 100 μM malonyl-CoA in “intact” mitochondria from liver, heart, and skeletal muscle, the value dropped to 83% in BAT and to only 40–50% in white adipose-derivated preparations. It is likely that in the case of each tissue or cell type, a similar small fraction of the mitochondria becomes damaged, but that the amount of malonyl-CoA-insensitive CPT II rendered overt is exaggerated in those tissues where the CPT II/CPT I ratio is highest. Accordingly, values for CPT I shown here have been assessed as the malonyl-CoA-sensitive component of overt CPT activity.

The potency of malonyl-CoA as an inhibitor of CPT I in each mitochondrial type is shown in Fig. 4. Skeletal muscle was the most sensitive (I_50 = 0.04 μM) and liver the least, with an I_50 100-fold greater (Table II, fourth column). Heart and BAT mitochondria exhibited a sensitivity close to that of skeletal muscle. CPT I from whole WAT behaved more like the liver enzyme, displaying an I_50 of 1.5 μM. However, the malonyl-CoA response curve of CPT I in mitochondria from purified adipocytes was clearly shifted to the left, the I_50 of 0.23 μM being consistent with a predominance of M-CPT I.

The K_m values for carnitine of L-CPT I and M-CPT I are ~30 and 500 μM, respectively (29). In BAT mitochondria, the K_m was found to be >400 μM, close to that of the muscle isoform of CPT I (Table II, fifth column). Unfortunately, the substantial contamination of CPT I by exposed CPT II in mitochondria from whole WAT and white adipocytes precluded accurate determination of a K_m for carnitine in either case.

CPT I isoform expression was also studied at the level of mRNA for each tissue or cell type (Fig. 5). Fig. 5 (A and B) shows a Northern blot analysis of poly(A^+) RNA isolated from liver, heart, skeletal muscle, and BAT. The L-CPT I probe generated strong signals in liver and heart, as expected, and a weak signal in BAT, while no band was detected in skeletal muscle (Fig. 5A). The M-CPT I probe revealed expression of this isoform in heart, skeletal muscle, and BAT, but not in liver (Fig. 5B). Due to the extremely low RNA yields from purified adipocytes, total RNA was used to perform Northern analysis on both adipocytes and whole WAT to allow for a direct comparison. The band representing the liver form was stronger in WAT than in adipocytes (Fig. 5C), whereas the mRNA for the muscle isoform was found to be the more abundant species in the purified cells (Fig. 5D).

DISCUSSION

The recent cloning and expression of cDNAs encoding rat and human L-CPT I and CPT II have provided considerable insight into the structure/function relationships between the CPT isoenzymes (9, 13, 24, 28, 33, 34). There are, however, a number of important but unresolved issues. Particularly intriguing is the question of why CPT I should exist in at least two forms with distinct kinetic properties and tissue distribution, and how these relate to whole body fuel homeostasis. Progress on this front has been hampered by the unavailability of a cDNA corresponding to the muscle enzyme. Our initial goal here, therefore, was to determine whether a candidate cDNA isolated from rat BAT (15) did in fact represent muscle CPT I. To this end, we used sequence information from the BAT cDNA to screen a rat heart cDNA library, and the CPT I-like sequence was confirmed in that tissue.

As with L-CPT I (9), COS cells transfected with the putative M-CPT I cDNA generated a CPT activity with characteristics typical of mitochondrial CPT I, i.e. membrane-bound and malonyl-CoA-sensitive and lost activity upon solubilization of the membranes with the detergent octyl glucoside. Malonyl-CoA response curves established that expressed putative M-CPT I was far more sensitive to the inhibitor than was the liver enzyme. Although the I_50 value observed (0.15 μM) was somewhat higher than that for CPT I from skeletal muscle mitochondria (~0.04 μM), the difference was likely due to the presence of background endogenous CPT I activity in the COS cells, which is of the less sensitive liver type. The I_50 for the ex-
Muscle Carnitine Palmitoyltransferase I

TABLE I

CPT activity in mitochondria from rat tissues

| Source          | CPT I (nmol/min/mg protein) | CPT II (nmol/min/mg protein) | CPT II/CPT I | I50 (μM) | Km (μM) | % Imax |
|-----------------|----------------------------|-----------------------------|--------------|---------|---------|--------|
| Liver           | 6.53 ± 2.20                | 6.37 ± 1.60                 | 1.01         | 4.0     | ∼30     | 90.0 ± 2.0 |
| Heart           | 11.50 ± 1.10               | 9.37 ± 2.00                 | 0.81         | 0.07    | ∼200    | 93.3 ± 0.6 |
| Skeletal muscle | 5.80 ± 0.56                | 5.95 ± 1.05                 | 1.04         | 0.04    | ∼500    | 94.4 ± 0.9 |
| Brown adipose   | 10.90 ± 0.10               | 23.4 ± 2.40                 | 2.16         | 0.07    | 416 ± 44 | 82.8 ± 4.2 |
| Epididymal fat pad | 1.15 ± 0.17               | 10.35 ± 1.54                | 9.04         | 1.5     | ND*     | 42.7 ± 0.8 |
| Adipocytes      | 0.31 ± 0.02                | 4.32 ± 0.74                 | 14.1         | 0.23    | ND*     | 51.3 ± 3.4 |

* ND, not determined.

**FIG. 4.** Effect of malonyl-CoA on CPT I in rat tissue mitochondria. Results are expressed relative to values in the absence of malonyl-CoA (mean of three independent determinations; error bars omitted for clarity). L, liver; Ad, purified adipocytes; H, heart; SM, skeletal muscle.

**FIG. 5.** Northern blot analysis of RNA from rat tissues. A, 5 μg of poly(A) RNA from the indicated rat tissues were analyzed as described under "Experimental Procedures" using a single-stranded liver cDNA probe. B, 8 μg of poly(A) RNA were analyzed using a single-stranded muscle cDNA probe. Twenty micrograms of total RNA from whole WAT and purified adipocytes were analyzed using a single-stranded liver (C) or muscle (D) cDNA probe. kb, kilobases.

Mitochondria were prepared and assayed as described under "Experimental Procedures." All of the data derive from three independent experiments. Values for CPT I, CPT II, I50, and Km (carnitine) (BAT only) are shown as means ± S.D. I50 is the concentration of malonyl-CoA needed for 50% inhibition of CPT I; I50 is the percent inhibition of CPT I by 100 μM malonyl-CoA. I50 values were obtained from the data of Fig. 4. Kms values for carnitine of liver, heart, and skeletal muscle CPT I are taken from Ref. 29. Note that the value of 200 μM for (adult) heart CPT I represents a composite because of the presence of a 97:3 ratio of M-CPT I to L-CPT I in this tissue (11).

That being so, the question arises as to why two highly homologous proteins with almost identical predicted molecular masses should display such distinct electrophoretic mobilities. To investigate this question, we generated 35S-labeled protein from the L-CPT I and M-CPT I clones using in vitro transcription and translation. The products were found not only to run differently, but to migrate exactly with their mitochondrial equivalents. This suggests that the phenomenon is not the result of post-translational modification, but stems from an intrinsic difference in the primary sequence of the two proteins. A comparison of the cDNA-derived polypeptide molecular masses (both ∼88 kDa) with those estimated from SDS-PAGE analysis (∼88 and ∼82 kDa for L- and M-CPT I, respectively) suggests that the muscle isoform behaves anomalously.

Our final aim was to investigate the implication of the work of Yamazaki et al. (15), that whereas M-CPT I is expressed in BAT, L-CPT I is the primary isoform in WAT. An additional consideration here was the earlier work by Saggerson and Carpenter showing that CPT I in BAT mitochondria is highly malonyl-CoA-sensitive, as is CPT I in muscle (37), but that in mitochondria from purified adipocytes, CPT I exhibits a sensitivity intermediate between that of the muscle and liver enzymes (38). A more detailed interpretation of these observations is now possible. The 3H-etomoxir labeling patterns of CPT I obtained using mitochondria prepared from whole rat epididymal fat pad and BAT appeared to conform to a model in which L- and M-CPT I are the primary isoforms in those tissues, respectively, and Northern blots appeared to support this notion. However, when the white adipocytes were separated from the bulk of the stromal and other cell types, the M-CPT I band labeled with 3H-etomoxir was seen to dominate. Moreover, kinetic analysis of CPT I in mitochondria isolated from whole fat pad and adipocytes corroborated the predomi-
nance of M-CPT I-like activity in the purified cells, and this was also reflected at the level of the mRNAs for L- and M-CPT I.

Therefore, all of the above evidence pointed to a scenario in which the muscle-type enzyme not only represents the sole species of CPT I in BAT, but is also the major isoenzyme in isolated white adipocytes from the epididymal fat pad. Furthermore, when expressed relative to mitochondrial protein, the CPT I activity of white adipocyte mitochondria is seen to be 20-40-fold lower than that of preparations from any other tissue examined (liver, heart, skeletal muscle, or BAT). This suggests that a small contamination of the adipocytes with any other cell type containing CPT I activity at a similar level to that of brown adipocytes, which both isoenzymes are to be found in a variety of tissues (liver, heart, and white and brown adipocytes). This will be a key consideration in the design of CPT I inhibitors as potential pharmaceutical agents. The diverse tissue expression of each isoform may also help to explain the multitissue symptoms exhibited by L-CPT I-deficient patients (39–41). No M-CPT I isoform may also help to explain the multitissue symptoms of M-CPT I in adipocytes, indeed, to explain the tissue-specific deficiencies have yet been described. Obviously, further studies will be needed to establish a teleological basis for the presence of M-CPT I in adipocytes, indeed, to explain the tissue-specific expression of CPT I remains to be established.

5 As used here, the term “white adipocytes” refers to fat cells isolated from the epididymal fat pad. Whether white fat cells from other body sites also express predominantly the muscle form of CPT I remains to be established.

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