Supplemental Table 1: sgRNA sequences for *MUT* and *PCCA.* The upstream PAM sequences, not included in the guide sequence, are highlighted in red.

Gene	**Exon**	**sgRNA1 (5' – 3')**	**sgRNA2(5' – 3')**
MUT	5	CACACTGTCAGACATCTGGA (TGG)	CCTAAAAACTCAAAATCTCT (TCT)
PCCA	12	TGGGACCGTGGAGTTCCTTG (TGG)	CCAGAGCAGTAAAATATTCC (TCT)

Supplemental Table 2: Primer sequences for Surveyor Assay screening and sequencing of edited clones.

Gene	**Exon**	**Forward Primer (5' – 3')**	**Reverse Primer (5' – 3')**
MUT	5	TGTACGTGCACTGATCTTAATTC	TTAACCACCAGAGGGAGACAA
PCCA	12	AAAGTTGACTTATTTGAGCATGTTATG	GATGTCTTAGCACAAGCATAAAAAC

Supplemental Table 3: qRT-PCR Primer sequences for mRNA expression in HEK293 cells.

Gene	**Forward (5' – 3')**	**Reverse (5' – 3')**
SLC3A2	CTGGTGCCGTGGTCATAATC	TGCTCAGGTAATCGAGACGCC
SLC7A5	TCATCATCCGGCCTTCATCG	TCACGCTGTAGCAGTTCACG
PSAT1	TCTACGTCATGGGCTTGGTTC	TCTTGCTTCTATTTTGGGGCTC
CBS	GGGTCCCCAGAGGATAAGGA	GGGGTGTCCCCGATTTTCTT
ASNS	TGTTGGATGGTGTGTTTGCAT	TCGCGGAGTGCTTCAATGTA
S18	CGGCGACGACCCATTCGAAC	GAATCGAACCCTGATTCCCCGTC

Supplemental Table 4A: Significantly enriched GO terms and KEGG pathways identified by DAVID analysis of proteins with reduced abundance in fibroblast cells from individuals with methylmalonic acidemia (MMA).

Functional Annotation of Proteins with Reduced Abundance in MMA fibroblast cells vs Control	
Term	**P-Value**
GO Terms, Biological Process	
extracellular matrix disassembly	1.00E-04
oxidation-reduction process	2.70E-04
cyclooxygenase pathway	1.60E-03
autophagy	9.10E-03
response to vitamin B1	1.20E-02
positive regulation of reactive oxygen species metabolic process	1.40E-02
response to hypoxia	2.10E-02
negative regulation of extracellular matrix disassembly	2.40E-02
negative regulation of cell proliferation involved in contact inhibition	2.40E-02
renal absorption	2.40E-02
cell-cell adhesion	2.60E-02
muscle contraction	2.80E-02
response to oxidative stress	3.00E-02
positive regulation of adaptive immune response	3.00E-02
proteolysis	3.40E-02
proteolysis involved in cellular protein catabolic process	3.50E-02
doxorubicin metabolic process	4.80E-02
response to selenium ion	4.80E-02
daunorubicin metabolic process	4.80E-02
response to calcium ion	4.90E-02
KEGG Pathways	
Pyruvate metabolism	3.80E-03
Valine, leucine and isoleucine degradation	6.00E-03
Amino sugar and nucleotide sugar metabolism	6.40E-03
Arachidonic acid metabolism	1.30E-02
Histidine metabolism	1.40E-02
Metabolic pathways	2.60E-02
Pentose and glucuronate interconversions	3.30E-02
Tryptophan metabolism	4.00E-02
Fatty acid degradation	4.80E-02

Supplemental Table 4B: Significantly enriched GO terms and KEGG pathways identified by DAVID analysis of proteins with increased abundance in fibroblast cells from individuals with methylmalonic acidemia (MMA).

Functional Annotation of Proteins with Increased Abundance in MMA fibroblast cells vs Control	
Term	**P-Value**
GO Terms, Biological Process	
cellular amino acid biosynthetic process	1.10E-04
response to virus	7.50E-03
negative regulation of cell proliferation	1.40E-02
hydrogen sulfide biosynthetic process	1.40E-02
nuclear transport	1.80E-02
transsulfuration	1.80E-02
establishment of integrated proviral latency	2.90E-02
organ morphogenesis	4.40E-02
neutral amino acid transport	4.60E-02
KEGG Pathways	
Biosynthesis of amino acids	2.30E-03
Cysteine and methionine metabolism	8.20E-03
Metabolic pathways	2.30E-02
Biosynthesis of antibiotics	4.00E-02
Glycerophospholipid metabolism	4.60E-02

Supplemental Table 4C: Significantly enriched GO terms and KEGG pathways identified by DAVID analysis of proteins with reduced abundance in fibroblast cells from individuals with propionic acidemia (PA).

Functional Annotation of Proteins with Reduced Abundance in PA fibroblast cells vs Control	
Term	**P-Value**
GO Terms, Biological Process	
extracellular matrix disassembly	8.10E-05
response to hypoxia	5.10E-04
oxidation-reduction process	2.40E-03
positive regulation of osteoblast differentiation	5.20E-03
branched-chain amino acid catabolic process	5.40E-03
protein localization	5.40E-03
memory	5.70E-03
response to cadmium ion	9.30E-03
angiogenesis	9.90E-03
response to vitamin B1	1.20E-02
positive regulation of I-kappaB kinase/NF-kappaB signaling	1.50E-02
positive regulation of vasoconstriction	1.50E-02
apoptotic process	1.80E-02
protein homooligomerization	2.00E-02
negative regulation of cell proliferation involved in contact inhibition	2.30E-02
valine catabolic process	2.30E-02
negative regulation of extracellular matrix disassembly	2.30E-02
negative regulation of protein ubiquitination	2.40E-02
response to oxidative stress	2.70E-02
proteolysis	2.70E-02
cellular response to lipopolysaccharide	2.80E-02
peripheral nervous system axon regeneration	2.90E-02
positive regulation of adaptive immune response	2.90E-02
cellular response to amino acid stimulus	3.10E-02
proteolysis involved in cellular protein catabolic process	3.20E-02
response to drug	3.30E-02
leukocyte migration	3.50E-02
defense response to Gram-negative bacterium	4.10E-02
response to calcium ion	4.50E-02
response to mechanical stimulus	4.70E-02
KEGG Pathways	
Proteoglycans in cancer	1.40E-04
Valine, leucine and isoleucine degradation	4.60E-04
Glyoxylate and dicarboxylate metabolism	1.90E-02
Protein digestion and absorption	3.10E-02

Pyruvate metabolism	3.90E-02
Metabolic Pathways	4.50E-02
Fatty acid degradation	4.60E-02

Supplemental Table 4D: Significantly enriched GO terms and KEGG pathways identified by DAVID analysis of proteins with increased abundance in fibroblast cells from individuals with propionic acidemia (PA).

Functional Annotation of Proteins with Increased Abundance in PA fibroblast cells vs Control	
Term	**P-Value**
GO Terms, Biological Process	
extracellular matrix organization	3.90E-04
cell adhesion	3.90E-04
cellular amino acid biosynthetic process	7.10E-03
glycosaminoglycan metabolic process	8.80E-03
cell migration	1.00E-02
cell-cell adhesion	1.00E-02
amino acid transport	1.30E-02
adherens junction organization	1.40E-02
muscle contraction	1.50E-02
collagen fibril organization	1.60E-02
hydrogen sulfide biosynthetic process	1.90E-02
transsulfuration	2.40E-02
heterophilic cell-cell adhesion via plasma membrane cell adhesion molecules	2.50E-02
cerebral cortex development	3.10E-02
regulation of cell shape	3.10E-02
elastic fiber assembly	3.40E-02
cardiac muscle fiber development	3.80E-02
KEGG Pathways	
Focal Adhesion	3.30E-02
Vascular smooth muscle contraction	3.30E-02
Biosynthesis of antibiotics	3.60E-02
Metabolic pathways	4.80E-02
Cell adhesion molecules (CAMs)	5.10E-02
Biosynthesis of amino acids	7.10E-02