Supplemental Data Table S9. *In silico* analyses of variants identified in ten cases with genetic alterations irrelevant to metabolite abnormalities

Gene	NT alteration	AA alteration	ACMG category*	1000G	ExAC	ESP6500	SIFT	Polyphen2	LRT	Mutation taster	Mutation assessor	FATHMM	GERP++
OTC	c.298+5G>C	NA	LP	ND	0.0013	ND	NA	NA	NA	NA	NA	NA	NA
ETFB	c.155insT	p.P52fs	LP	ND	ND	ND	NA	NA	NA	NA	NA	NA	NA
SLC7A7	c.T498G	p.I166M	VUS	ND	ND	ND	D	B	D	P	M	D	3.88
PAH	c.C721T	p.R241C	LP	ND	0.0001	ND	D	D	D	D	M	D	5.92
PAH	c.442-1G>A	NA	P	ND	ND	ND	NA	NA	NA	D	NA	NA	6.08
DUOX2	c.T3239C	p.I1080T	LP	ND	ND	ND	D	P	D	D	M	NA	5.6
DUOX2	c.A2678G	p.N893S	VUS	ND	ND	ND	T	B	D	D	M	NA	5.69
DUOX2	c.G4232A	p.C1411Y	VUS	ND	ND	ND	D	D	D	D	M	NA	5.8
PCCB	c.C1283T	p.T428I	LP	ND	ND	ND	D	D	D	A	H	T	5.59
PCCB	c.A1316G	p.Y439C	LP	ND	ND	ND	D	D	D	D	H	D	4.64

*P, Pathogenic; LP, Likely pathogenic; VUS, variant of unknown significance.
Abbreviations: ND, not detected; NA, not applicable; D, damaging (in PolyPhen)/deleterious (in SIFT, LRT, FATHMM, and LR); P, possibly damaging (in PolyPhen); H, high (functional); M, medium (functional); N, neutral (nonfunctional); L, low (nonfunctional); T, tolerated (in SIFT); B, benign (in PolyPhen), A or D, disease-causing (in MutationTaster).