

Supplementary Table 2

Count	Patient #	Sex	PDC Lymph	PDC Fb	PDC Musc	Gene	Initial designation	Mutation
1	18	F	1.38	ND	ND	<i>PDHA1</i>	VUS	unresolved
2	54	F	ND	1.10	2.38	<i>PDHA1</i>	VUS	c.900-3_922dup Q307LfsX12
3	56	F	0.00	0.33	0.15	<i>PDHA1</i>	VUS	831+1G>A
4	64	F	ND	ND	1.88	<i>PDHA1</i>	VUS	unresolved
5	68	F	3.26	ND	ND	<i>PDHA1</i>	pathogenic	c.1142_1145dup W383fs
6	69	F	ND	0.62	2.60	<i>PDHA1</i>	VUS	K385dup
7	70	F	2.09	3.16	ND	<i>PDHA1</i>	VUS	unresolved
8	73	F	1.79	ND	ND	<i>PDHA1</i>	VUS	unresolved
9	74	F	0.58	ND	2.02	<i>PDHA1</i>	VUS	A330G
10	75	F	1.63	ND	1.48	<i>PDHA1</i>	VUS	A175P
11	80	F	2.07	0.37	ND	<i>PDHA1</i>	VUS	c.225G>T
12	81	F	1.47	ND	ND	<i>PDHA1</i>	VUS	unresolved
13	55	M	0.30	0.31	ND	<i>PDHA1</i>	VUS	pathogenic*
14	57	M	ND	0.93	ND	<i>PDHA1</i>	VUS	c.787C>G R263G
15	59	M	ND	1.11	ND	<i>PDHA1</i>	VUS	c.491A>G N164S
16	61	M	0.30	1.21	ND	<i>PDHA1</i>	VUS	c.677G>A R226
17	62	M	ND	0.48	ND	<i>PDHA1</i>	VUS	c.1147T>C W383R
18	63	M	0.00	2.15	ND	<i>PDHA1</i>	pathogenic	c.1132C>T R378C
19	65	M	1.70	ND	ND	<i>PDHA1</i>	probably pathogenic	A349T
20	66	M	0.84	0.42	ND	<i>PDHA1</i>	VUS	F205L
21	67	M	0.22	0.35	ND	<i>PDHA1</i>	VUS	A236T
22	71	M	1.74	ND	ND	<i>PDHA1</i>	VUS	unresolved
23	72	M	1.46	ND	ND	<i>PDHA1</i>	VUS	unresolved
24	76	M	0.80	ND	ND	<i>PDHA1</i>	VUS	R263Q
25	77	M	ND	1.66	ND	<i>PDHA1</i>	VUS	unresolved
26	78	M	ND	1.16	ND	<i>PDHA1</i>	VUS	pathogenic*
27	79	M	2.32	ND	ND	<i>PDHA1</i>	VUS	A136T
28	82	M	ND	ND	0.89	<i>PDHA1</i>	VUS	c.1095_1118dup N366_L373dup
29	83	M	3.16	ND	ND	<i>PDHA1</i>	VUS	unresolved
			Range Cutoff	Range Cutoff	Range Cutoff			
			<0.98	<1.26	<1.20			

Supplementary Table 2. Samples with an unclassified/known *PDHA1* variant referred to CIDEM for testing (representing Molecular-First Approach group). Values in red (bold) represent PDC activity (nmol/min/mg protein) below cutoff for specific cell/tissue (see Materials and Methods Section 2.2 for cutoff values). Yellow highlights indicate samples with more than one cell/tissue type assayed. Subjects in green are also within the *PDHA1*-Only group (see Supplementary Table 1). If subjects with an unclassified/known *PDHA1* variant referred to CIDEM for PDC testing, are found to be enzymatically deficient (or not deficient), the molecular variant is reclassified as pathogenic (or unresolved). Abbreviations: ND, not done; Lymph, lymphocytes; Fb, fibroblasts; fs, frameshift; and Musc, skeletal muscle. *These subjects have been deceased for many years and attempts to obtain detailed *PDHA1* variant information for review and reporting were unsuccessful.