

Supplementary Table 1

Count	Patient #	Sex	PDC Lymph	PDC Fb	PDC Musc	Gene	Mutation	Protein
1	1	M	0.08	0.68	0.10	PDHA1	c.1133G>A	R378H
2	2	M	ND	0.32	0.23	PDHA1	c.650C>T	P217L
3	3	M	0.99	ND	0.16	PDHA1	c.1133G>A	R378H
4	4	M	ND	0.00	ND	PDHA1	c.933-935 del	R311 del
5	5	M	0.02	0.11	0.27	PDHA1	c.628A>G	M210V
6	6	M	ND	0.13	0.06	PDHA1	c.530T>C	I177T
7	7	M	0.01	0.36	0.14	PDHA1	c.380G>A	R127Q
8	8	M	0.50	1.24	ND	PDHA1	c.787C>G	R263G
9	9	M	0.01	0.74	0.56	PDHA1	c.1045G>A	A349T
10	11	M	1.06	0.36	ND	PDHA1	c.491A>G	N164S
11	13	M	ND	0.33	ND	PDHA1	c.1133G>A	R378H
12	17	M	ND	0.47	0.52	PDHA1	c.1159-60 ins dup 1121-59	
13	22	M	ND	0.62	1.95	PDHA1	c.1157-58 ins 4 dup	fs term
14	23	M	1.13	0.99	1.13	PDHA1	c.592G>A	skips exon 6
15	24	M	0.68	2.08	0.07	PDHA1	c.405+5G>A	
16	25	M	ND	1.10	3.05	PDHA1	c.847G>A	E283K
17	26	M	ND	0.48	ND	PDHA1	c.1159-60 ins dup 1137-59	fs term
18	27	M	ND	0.56	0.11	PDHA1	c.1132C>T	R378C
19	28	M	ND	0.24	ND	PDHA1	c.380G>A	R127Q
20	34	M	ND	0.42	0.05	PDHA1	c.1133G>A	R378H
21	35	M	0.26	1.58	ND	PDHA1	c.1157-58 ins 4 dup	fs term
22	40	M	ND	0.41	ND	PDHA1	c.629T>C	M210T
23	43	M	ND	0.23	0.06	PDHA1	c.1133G>A	R378H
24	45	M	ND	0.78	ND	PDHA1	c.977-78 ins dup 963-77	
25	52	M	ND	0.50	ND	PDHA1	c.383G>A	G128D
26	53	M	ND	0.67	0.80	PDHA1	c.491A>G	N164S
27	55	M	0.92	0.31	ND	PDHA1	pathogenic*	
28	57	M	ND	0.93	ND	PDHA1	c.787C>G	R263G
29	59	M	ND	1.11	ND	PDHA1	c.491A>G hz	N164S
30	61	M	0.30	1.21	ND	PDHA1	c.677G>A	R266
31	62	M	ND	0.48	ND	PDHA1	c.1147T>C	W383R
32	63	M	0.00	2.15	ND	PDHA1	c.1132C>T	R378C
33	66	M	1.06	0.42	ND	PDHA1		F205L
34	67	M	0.22	0.35	ND	PDHA1		A236T
35	76	M	0.80	ND	ND	PDHA1	c.788G>A	R263Q
36	78	M	ND	1.16	ND	PDHA1	pathogenic*	
37	82	M	ND	ND	0.89	PDHA1	c.1095_1118dup	N366_L373dup
			Range Cutoff	Range Cutoff	Range Cutoff			
			<0.98	<1.26	<1.20			

Supplementary Table 1 (continue)

Count	Patient #	Sex	PDC Lymph	PDC Fb	PDC Musc	Gene	Mutation	Protein
1	10	F	1.89	0.68	ND	<i>PDHA1</i>	c.904C>T	R302C
2	12	F	2.24	0.29	ND	<i>PDHA1</i>	1102 ins dup 1083-1102	
3	14	F	1.22	ND	0.46	<i>PDHA1</i>	952-53 ins dup 949-52	R302H
4	15	F	0.63	0.95	ND	<i>PDHA1</i>	890-91insC	fs297-303
5	16	F	2.18	0.57	1.27	<i>PDHA1</i>	c.787C>T	R263G
6	19	F	0.70	0.83	ND	<i>PDHA1</i>	c.422G>A	R141Q
7	20	F	ND	0.33	ND	<i>PDHA1</i>	982-85 ins dup 982-85	
8	21	F	ND	0.24	0.58	<i>PDHA1</i>	c.499G>A	Y167M
9	29	F	ND	0.97	ND	<i>PDHA1</i>	1145-46 dup ins 1142-45	
10	30	F	ND	0.70	ND	<i>PDHA1</i>	c.940C>T	
11	31	F	ND	1.50	0.61	<i>PDHA1</i>	c.616G>A	E205K
12	32	F	ND	0.72	ND	<i>PDHA1</i>	c.862C>T	R288C
13	33	F	ND	0.39	ND	<i>PDHA1</i>	c.847G>A	E283K
14	36	F	ND	0.57	ND	<i>PDHA1</i>	998_999ins13dup986_998	fs(334_343)
15	37	F	1.58	1.05	0.78	<i>PDHA1</i>	934-940 del	fs312-323
16	38	F	ND	0.72	2.28	<i>PDHA1</i>	c.355C>T	R119W
17	39	F	ND	0.59	ND	<i>PDHA1</i>	c.904C>T	R302C
18	41	F	0.90	ND	0.58	<i>PDHA1</i>	c.787C>G	Y243C
19	42	F	ND	0.92	0.96	<i>PDHA1</i>	c.301T>C	C101R
20	44	F	ND	0.59	ND	<i>PDHA1</i>	c.269T>C	R90S
21	46	F	ND	1.06	ND	<i>PDHA1</i>	c.901C>T	
22	47	F	ND	0.37	ND	<i>PDHA1</i>	c.1132C>T	R378C
23	48	F	1.11	0.48	ND	<i>PDHA1</i>	c.728A>G	Y243C
24	49	F	ND	0.26	ND	<i>PDHA1</i>	c.904C>T	R302C
25	50	F	ND	0.59	ND	<i>PDHA1</i>	c.738C>T	
26	51	F	ND	0.64	ND	<i>PDHA1</i>	c.905G>A	R302H
27	54	F	ND	1.10	2.38	<i>PDHA1</i>	c.900-3_922dup	Q307LfsX12
28	56	F	0.00	0.33	0.15	<i>PDHA1</i>	831+1G>A	
29	58	F	4.69	0.71	ND	<i>PDHA1</i>	899+1G>C	
30	60	F	2.36	0.56	ND	<i>PDHA1</i>	c.871G>A	G291R
31	69	F	ND	0.62	2.60	<i>PDHA1</i>	c.1153_1155dupAAG	K385dup
32	74	F	0.58	ND	2.02	<i>PDHA1</i>	c.989C>G	A330G
33	80	F	2.07	0.37	ND	<i>PDHA1</i>	c.225G>T	
			Range Cutoff	Range Cutoff	Range Cutoff			
			<0.98	<1.26	<1.20			

Supplementary Table 1. Enzymatic and genetic characteristics of the *PDHA1*-Only group by gender. 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 Molecular-First Approach group (see Supplementary Table 2). Subjects referred to CIDEM for PDC testing with limited molecular information regarding their *PDHA1* variant and found to be functionally PDC deficient are noted as pathogenic. Abbreviations: ND, not done; Lymph, lymphocytes; Fb, fibroblasts; Musc, skeletal muscle; fs, frameshift; and term, termination. *These subjects have been deceased for many years and attempts to obtain detailed *PDHA1* variant information for review and reporting were unsuccessful.