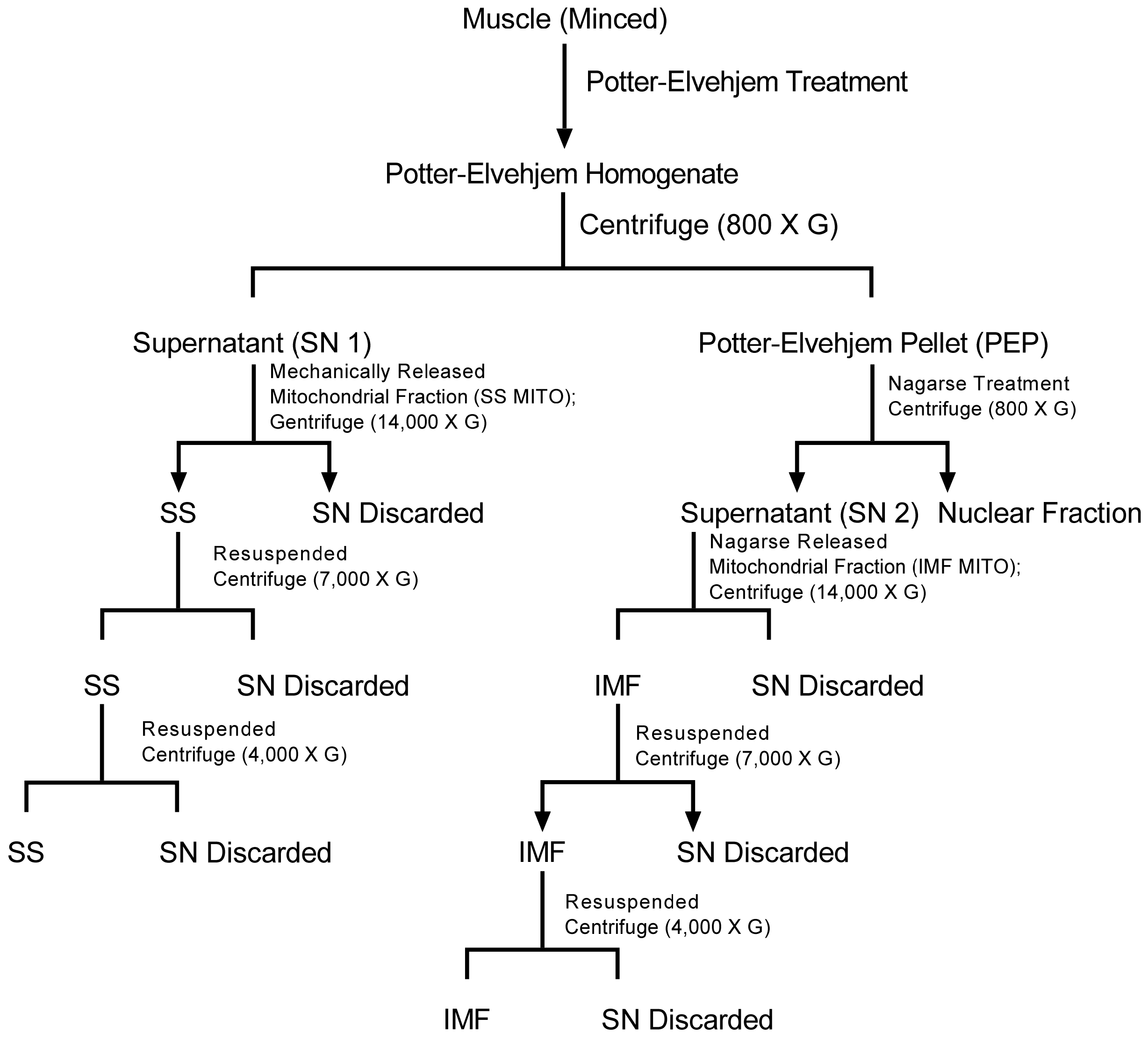
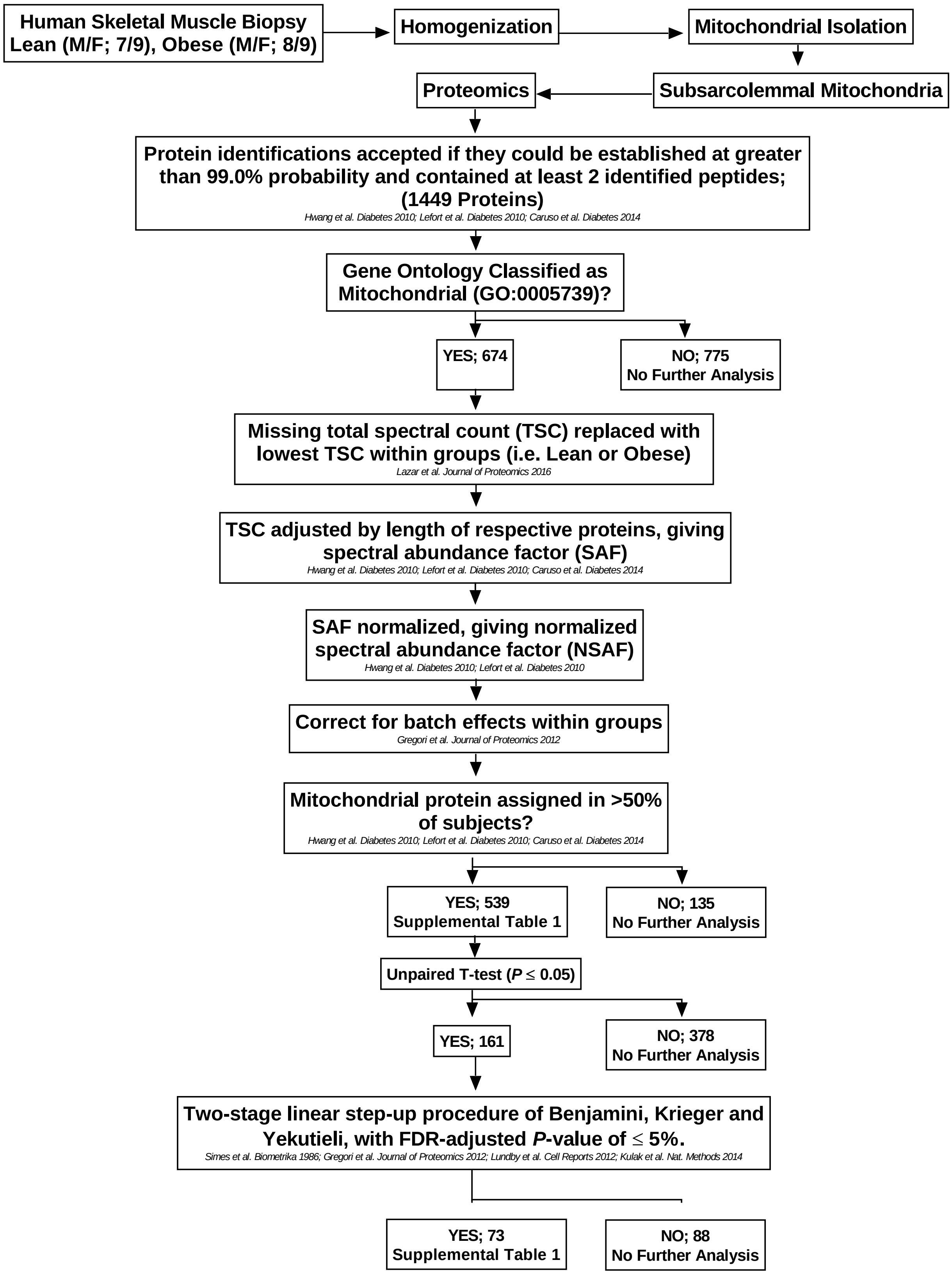
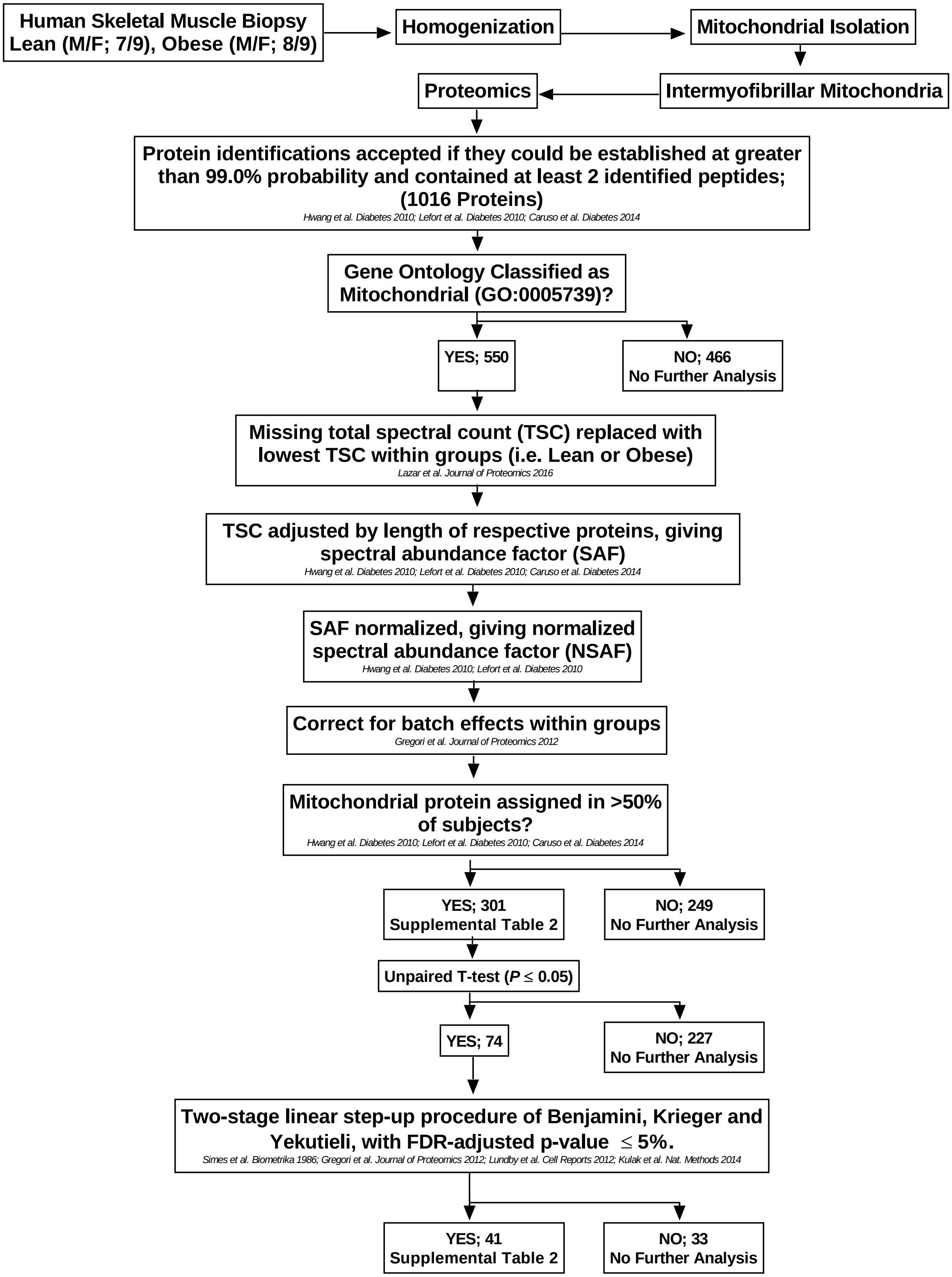


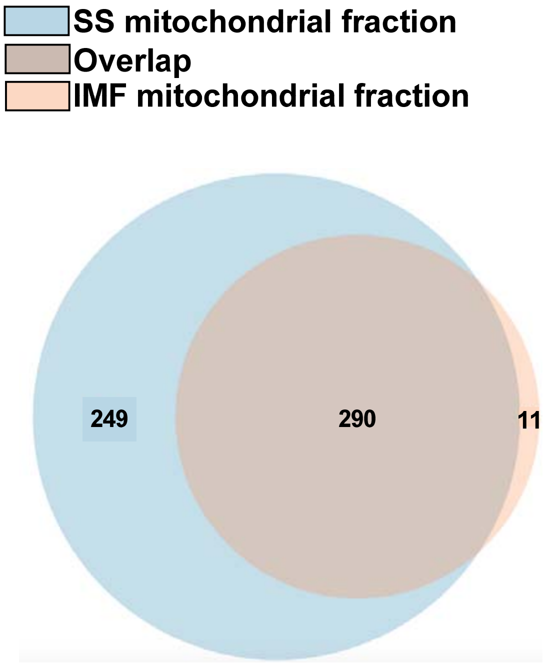
Supplemental Figure 1 – Schematic workflow showing the isolation of skeletal muscle subsarcolemmal (SS) and intermyofibrillar (IMF) mitochondria (SN, supernatant).



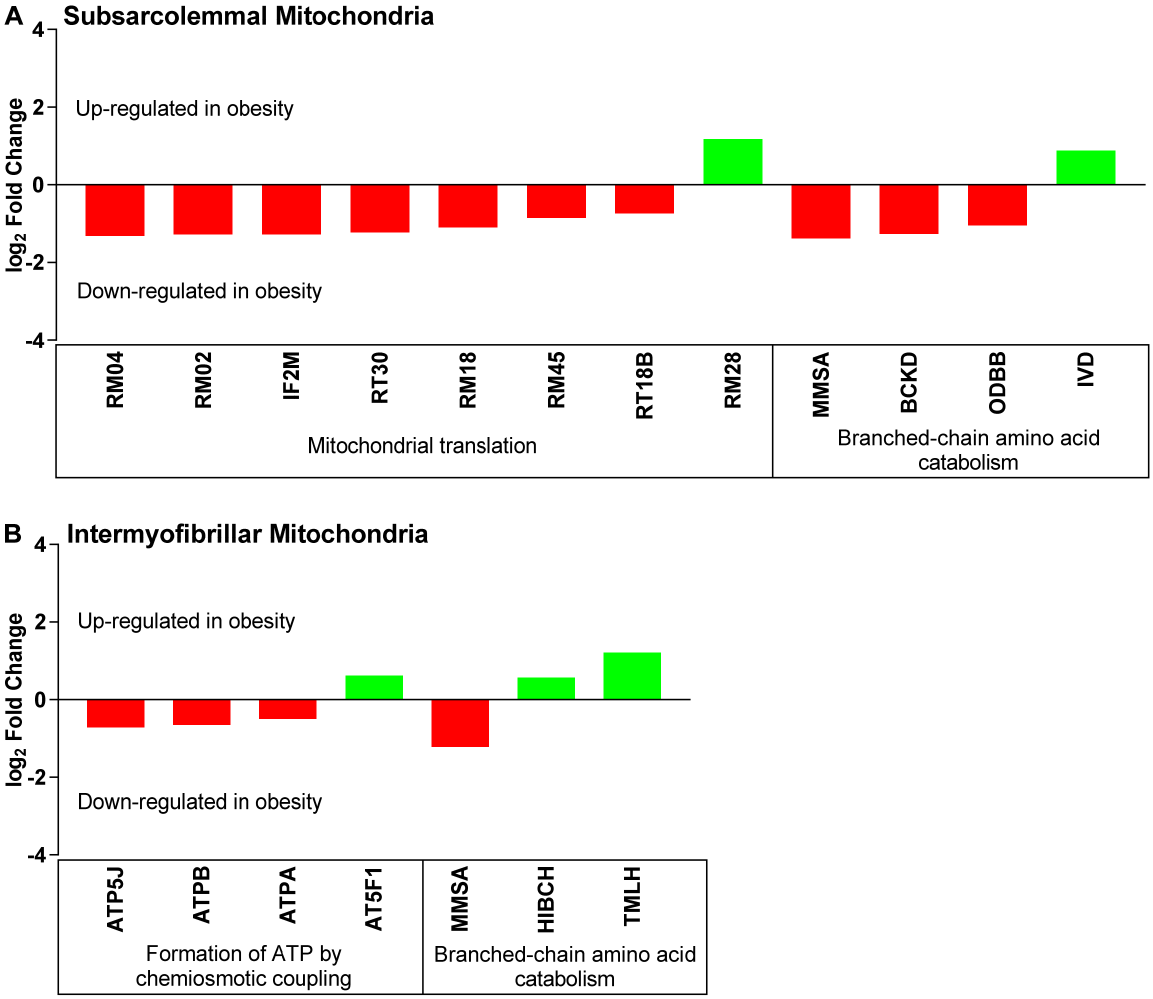
Supplemental Figure 2 – Workflow depicting the quantification of differentially expressed mitochondrial proteins in the subsarcollemal mitochondrial fraction *(please refer to the References list of the main document for references indicated in the steps of this workflow).*



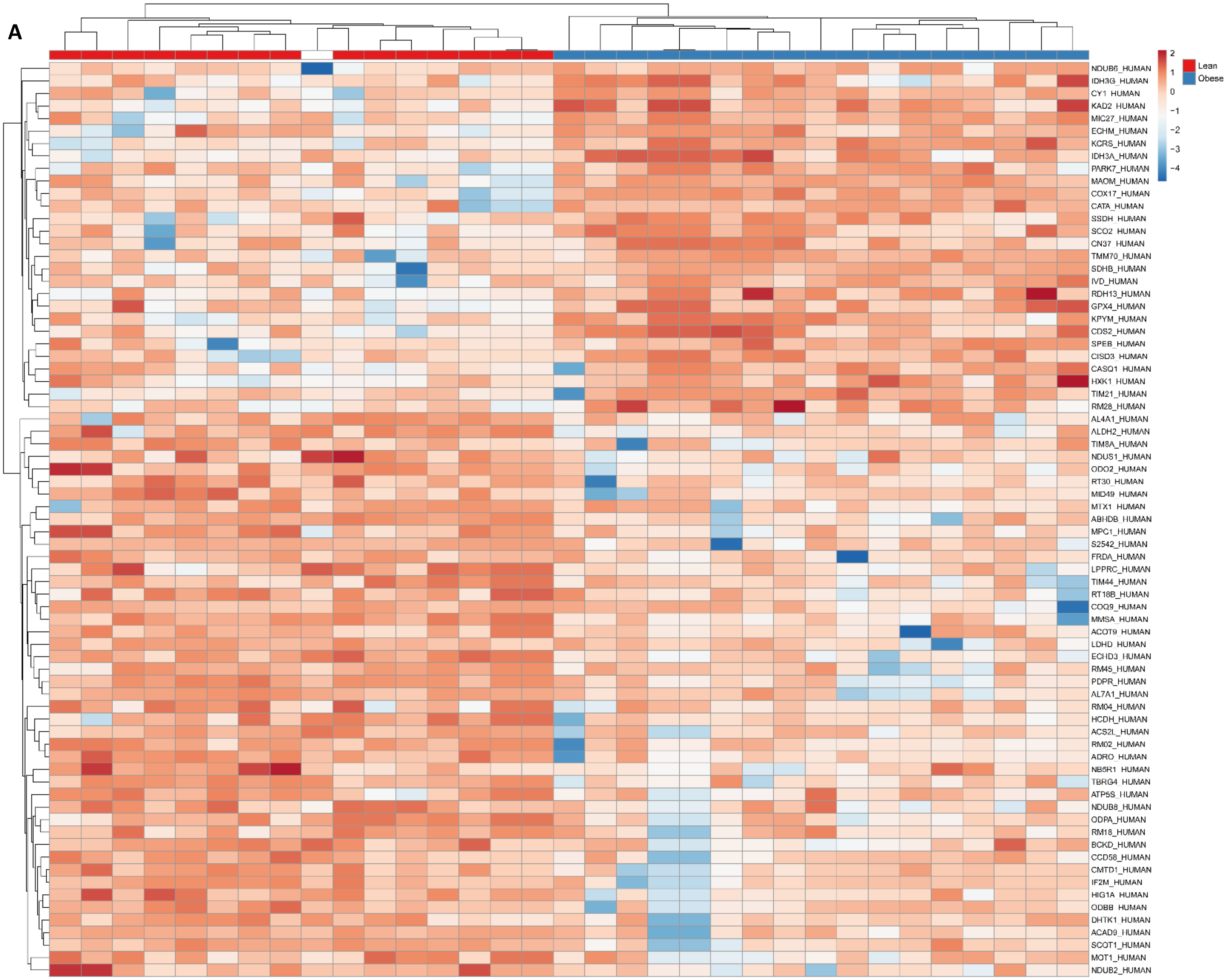
Supplemental Figure 3 – Workflow depicting the quantification of differentially expressed mitochondrial proteins in the intermyofibrillar mitochondrial fraction *(please refer to the References list of the main document for references indicated in the steps of this workflow).*

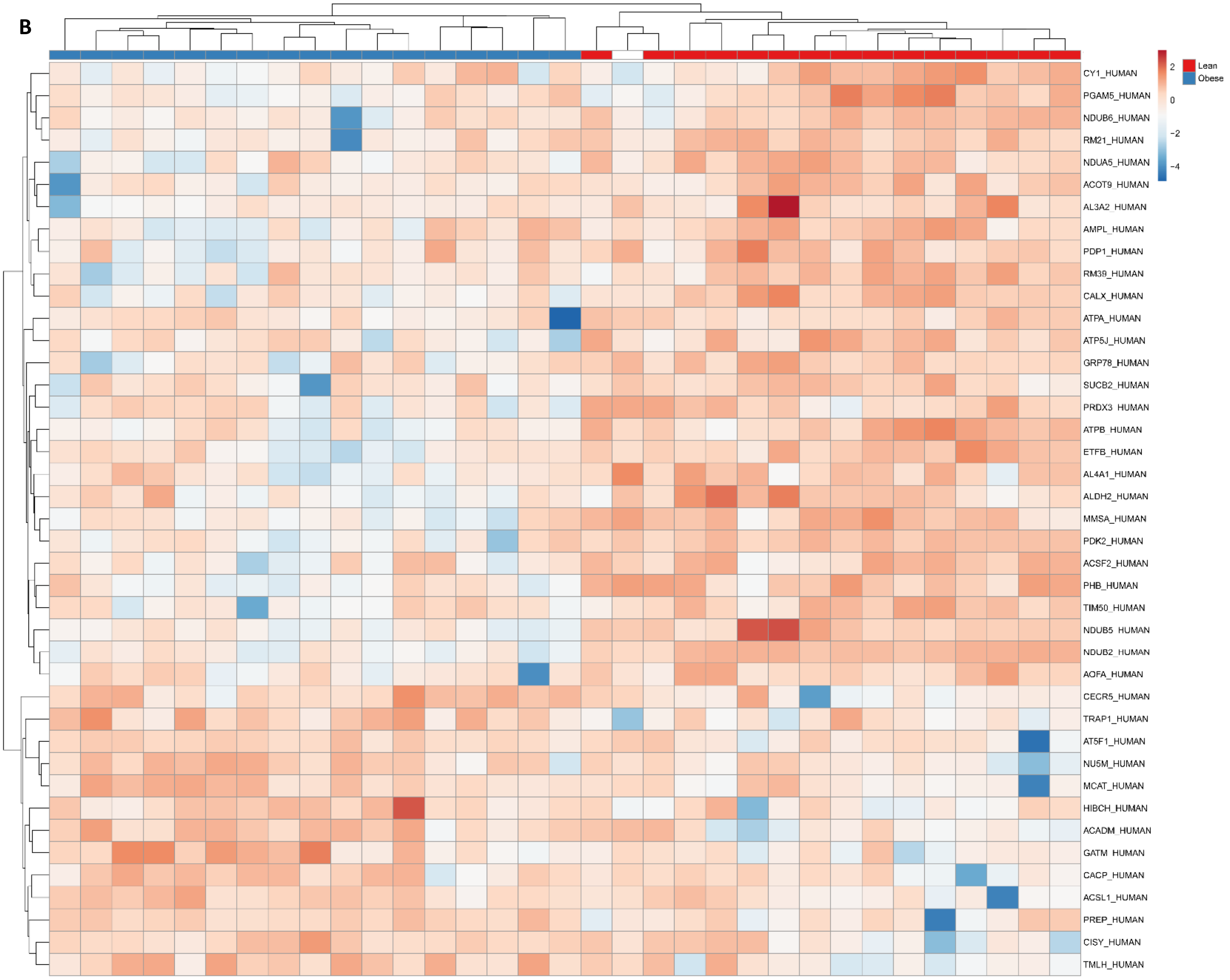


Supplemental Figure 4 – Mitochondrial proteins identified in mitochondrial subsarcolemmal (SS) and intermyofibrillar (IMF) fractions isolated from skeletal muscle in subjects with obesity and lean controls. Area-proportional Venn diagram showing mitochondrial proteins identified in isolated muscle subsarcolemmal (SS) and intermyofibrillar (IMF) mitochondrial fractions in > 17 subjects (i.e., > 50% of the subjects). A total of 539 identified proteins were assigned to mitochondria by gene ontology (GO:0005739) in the SS mitochondrial fraction, while a total of 301 identified proteins were assigned to mitochondria in the IMF mitochondrial fraction, with 290 identified proteins overlapping between the SS and IMF mitochondrial fractions.

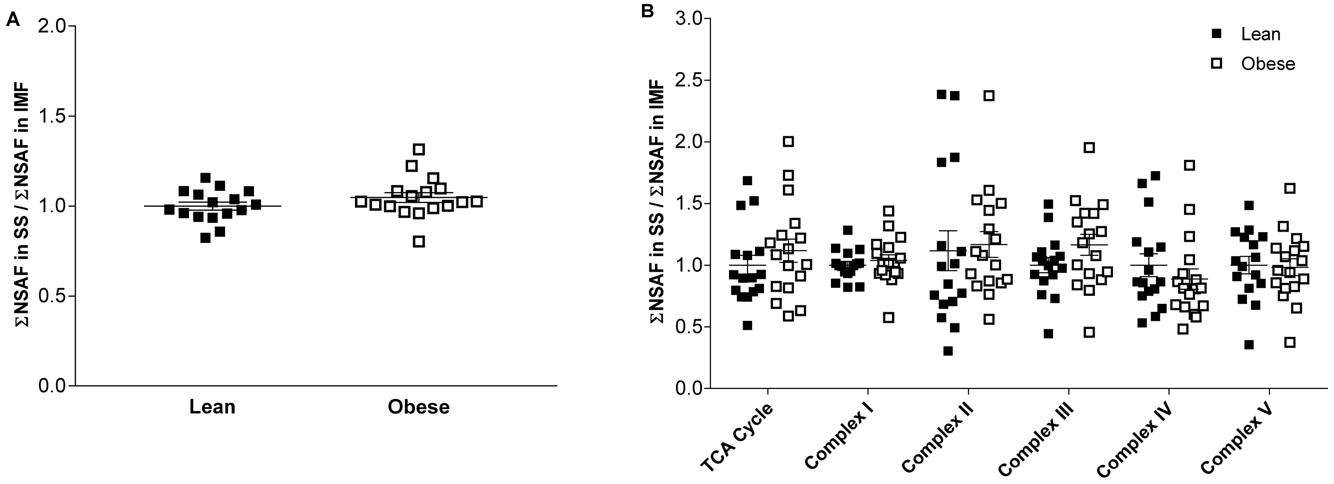


Supplemental Figure 5 – Differentially expressed proteins in subjects with obesity relative to lean controls assigned to metabolic pathways that were enriched differentially in the subsarcolemmal (A) and intermyofibrillar (B) mitochondria between groups based on the Reactome pathway database analyses. Data are presented as $\log_2$-fold difference between lean subjects and subjects with obesity. Bars represent statistically significant (FDR adjusted p-value ≤ 0.05) up- and down-regulated protein expression in subjects with obesity.

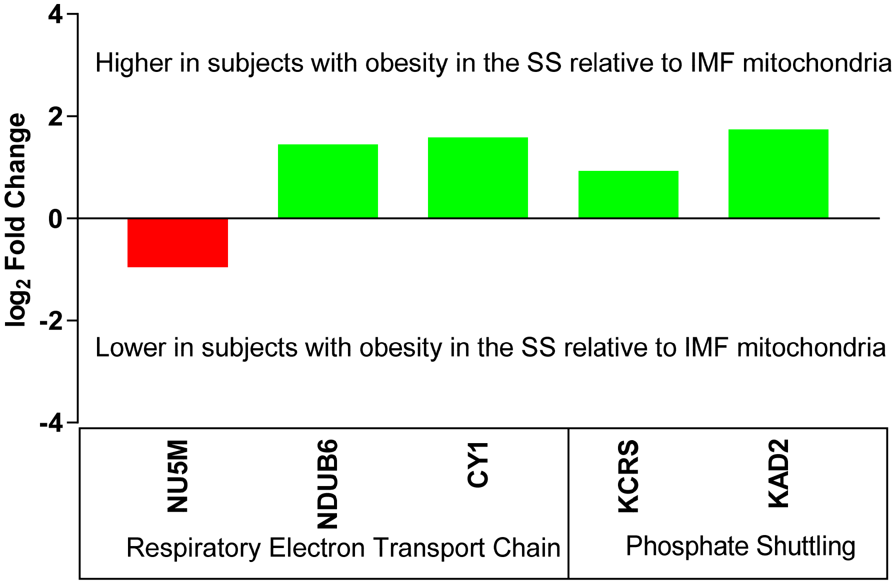

A
2
1
0
−1
−2
−3
−4
Lean
Obese
NDUB6_HUMAN
IDH3G_HUMAN
CY1_HUMAN
KAD2_HUMAN
MIC27_HUMAN
ECHM_HUMAN
KCRS_HUMAN
IDH3A_HUMAN
PARK7_HUMAN
MAOM_HUMAN
COX17_HUMAN
CATA_HUMAN
SSDH_HUMAN
SCO2_HUMAN
CN37_HUMAN
TMM70_HUMAN
SDHB_HUMAN
IVD_HUMAN
RDH13_HUMAN
GPX4_HUMAN
KPYM_HUMAN
CDS2_HUMAN
SPEB_HUMAN
CISD3_HUMAN
CASQ1_HUMAN
HXK1_HUMAN
TIM21_HUMAN
RM28_HUMAN
AL4A1_HUMAN
ALDH2_HUMAN
TIM8A_HUMAN
NDUS1_HUMAN
ODO2_HUMAN
RT30_HUMAN
MID49_HUMAN
MTX1_HUMAN
ABHDB_HUMAN
MPC1_HUMAN
S2542_HUMAN
FRDA_HUMAN
LPPRC_HUMAN
TIM44_HUMAN
RT18B_HUMAN
COQ9_HUMAN
MMSA_HUMAN
ACOT9_HUMAN
LDHD_HUMAN
ECHD3_HUMAN
RM45_HUMAN
PDPR_HUMAN
AL7A1_HUMAN
RM04_HUMAN
HCDH_HUMAN
ACS2L_HUMAN
RM02_HUMAN
ADRO_HUMAN
NB5R1_HUMAN
TBRG4_HUMAN
ATP5S_HUMAN
NDUB8_HUMAN
ODPA_HUMAN
RM18_HUMAN
BCKD_HUMAN
CCD58_HUMAN
CMTD1_HUMAN
IF2M_HUMAN
HIG1A_HUMAN
ODBB_HUMAN
DHTK1_HUMAN
ACAD9_HUMAN
SCOT1_HUMAN
MOT1_HUMAN
NDUB2_HUMAN



Supplemental Figure 6 - Heatmaps for differentially expressed muscle subsarcolemmal (A) and intermyofibrillar (B) mitochondrial proteins in subjects with obesity and lean controls. Rows have been centered and unit variance scaling has been applied to rows. Columns represent each subject in the study. Both rows and columns are clustered using correlation distance and average linkage. N = 33 data points (columns 1 – 17, subjects with obesity; columns 18 – 33, lean controls).



Supplemental Figure 7 – Protein abundance in subsarcolemmal (SS) mitochondria relative to that in the intermyofibrillar (IMF) mitochondria in skeletal muscle from subjects with obesity and lean controls. Ratio describing the abundance of a total of 290 mitochondrial proteins detected in the SS mitochondrial fraction relative to the abundance of the same proteins detected in the IMF mitochondrial fraction (A). Ratio describing the abundance of manually curated groups of proteins assigned to the TCA cycle and mitochondrial protein complexes I-V (B). Protein abundance reflects the sum of normalized spectral abundance factors (ΣNSAF) of the respective groups of mitochondrial proteins in each isolated mitochondrial fraction. Values are mean ± SEM. All data have been adjusted to the lean group data for each variable.



Supplemental Figure 8 – Differentially expressed protein abundance in subsarcolemmal (SS) mitochondria relative to that in the intermyofibrillar (IMF) mitochondria and assigned to metabolic pathways that were enriched differentially between subjects with obesity and lean controls based on the Reactome pathway database analyses. Data are presented as $\log_2$-fold difference in the SS-to-IMF mitochondrial protein abundance ratio between lean subjects and subjects with obesity. Bars represent statistically significant (FDR adjusted p-value ≤ 0.05) up- and down-regulated SS-to-IMF mitochondrial protein abundance ratios in subjects with obesity.

Supplemental Table 1
Spectral counts and batch-corrected NSAF values for 539 proteins identified in subsarcolemmal mitochondria in >50% individuals with at least 2 unique peptides. Available at https://dataverse.harvard.edu/api/access/datafile/3174318

Supplemental Table 2
Spectral counts and batch-corrected NSAF values for 301 proteins identified in intermyofibrillar mitochondria in >50% individuals with at least 2 unique peptides. Available at https://dataverse.harvard.edu/api/access/datafile/3174319

Supplemental Table 3

73 differentially expressed mitochondrial proteins between lean and obese subjects identified in subsarcolemmal mitochondria

Uniprot ID	Protein Name	Gene Symbol(s)	Ratio Obese/Lean	log$_2$ O/L Ratio	p Value	FDR-corrected p Value/*q* Value
Q8NFV4	Protein ABHD11 (EC 3.-.-.-) (Alpha/beta hydrolase domain-containing protein 11) (Abhydrolase domain-containing protein 11) (Williams-Beuren syndrome chromosomal region 21 protein)	ABHD11, WBSCR21, PP1226	0.28	-1.84	0.0000	0.0002
Q8NCN5	Pyruvate dehydrogenase phosphatase regulatory subunit, mitochondrial (PDPr)	PDPR, KIAA1990	0.29	-1.78	0.0000	0.0001
P22570	NADPH:adrenodoxin oxidoreductase, mitochondrial (AR) (Adrenodoxin reductase) (EC 1.18.1.6) (Ferredoxin--NADP(+) reductase) (Ferredoxin reductase)	FDXR, ADXR	0.33	-1.62	0.0000	0.0001
P05091	Aldehyde dehydrogenase, mitochondrial (EC 1.2.1.3) (ALDH class 2) (ALDH-E2) (ALDHI)	ALDH2, ALDM	0.35	-1.53	0.0000	0.0017
O95178	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 2, mitochondrial (Complex I-AGGG) (CI-AGGG) (NADH-ubiquinone oxidoreductase AGGG subunit)	NDUFB2	0.35	-1.52	0.0018	0.0195
Q86VU5	Catechol O-methyltransferase domain-containing protein 1 (EC 2.1.1.-)	COMTD1, UNQ766/PRO1558	0.38	-1.41	0.0004	0.0065
Q02252	Methylmalonate-semialdehyde dehydrogenase [acylating], mitochondrial (MMSDH) (Malonate-semialdehyde dehydrogenase [acylating]) (EC 1.2.1.18) (EC 1.2.1.27) (Aldehyde dehydrogenase family 6 member A1)	ALDH6A1, MMSDH	0.39	-1.38	0.0000	0.0001
P55809	Succinyl-CoA:3-ketoacid coenzyme A transferase 1, mitochondrial (EC 2.8.3.5) (3-oxoacid CoA-transferase 1) (Somatic-type succinyl-CoA:3-oxoacid CoA-transferase) (SCOT-s)	OXCT1, OXCT, SCOT	0.39	-1.34	0.0003	0.0055
Q9H845	Acyl-CoA dehydrogenase family member 9, mitochondrial (ACAD-9) (EC 1.3.99.-)	ACAD9	0.40	-1.34	0.0001	0.0017
Q9BYD3	39S ribosomal protein L4, mitochondrial (L4mt) (MRP-L4) (Mitochondrial large ribosomal subunit protein uL4m)	MRPL4, CDABP0091, CGI-28	0.40	-1.31	0.0047	0.0421
Q5T653	39S ribosomal protein L2, mitochondrial (L2mt) (MRP-L2) (Mitochondrial large ribosomal subunit protein uL2m)	MRPL2, CGI-22	0.41	-1.27	0.0000	0.0002
P46199	Translation initiation factor IF-2, mitochondrial (IF-2(Mt)) (IF-2Mt) (IF2(mt))	MTIF2	0.42	-1.27	0.0005	0.0081
O14874	[3-methyl-2-oxobutanoate dehydrogenase [lipoamide]] kinase, mitochondrial (EC 2.7.11.4) (Branched-chain alpha-ketoacid dehydrogenase kinase) (BCKD-kinase) (BCKDHKIN)	BCKDK	0.42	-1.26	0.0082	0.0547
Q969Z0	Protein TBRG4 (Cell cycle progression restoration protein 2) (Cell cycle progression protein 2) (FAST kinase domain-containing protein 4) (Transforming growth factor beta regulator 4)	TBRG4, CPR2, FASTKD4, KIAA0948	0.42	-1.24	0.0000	0.0003
Q9NUB1	Acetyl-coenzyme A synthetase 2-like, mitochondrial (EC 6.2.1.1) (Acetate--CoA ligase 2) (Acetyl-CoA synthetase 2) (AceCS2) (Acyl-CoA synthetase short-chain family member 1)	ACSS1, ACAS2L, KIAA1846	0.43	-1.23	0.0005	0.0080
Q96C03	Mitochondrial dynamics protein MID49 (Mitochondrial dynamics protein of 49 kDa) (Mitochondrial elongation factor 2) (Smith-Magenis syndrome chromosomal region candidate gene 7 protein)	MIEF2, MID49, SMCR7	0.43	-1.23	0.0012	0.0153
Q9NP92	39S ribosomal protein S30, mitochondrial (MRP-S30) (S30mt) (Mitochondrial large ribosomal subunit protein mL65) (Mitochondrial large ribosomal subunit protein mS30) (Programmed cell death protein 9)	MRPS30, PDCD9, BM-047	0.43	-1.22	0.0012	0.0153
P49419	Alpha-aminoadipic semialdehyde dehydrogenase (Alpha-AASA dehydrogenase) (EC 1.2.1.31) (Aldehyde dehydrogenase family 7 member A1) (EC 1.2.1.3) (Antiquitin-1) (Betaine aldehyde dehydrogenase) (EC 1.2.1.8) (Delta1-piperideine-6-carboxylate dehydrogenase) (P6c dehydrogenase)	ALDH7A1, ATQ1	0.45	-1.14	0.0000	0.0014
Q9H0U6	39S ribosomal protein L18, mitochondrial (L18mt) (MRP-L18) (Mitochondrial large ribosomal subunit protein uL18m)	MRPL18, HSPC071	0.47	-1.10	0.0079	0.0545
P36957	Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex, mitochondrial (EC 2.3.1.61) (2-oxoglutarate dehydrogenase complex component E2) (OGDC-E2) (Dihydrolipoamide succinyltransferase component of 2-oxoglutarate dehydrogenase complex) (E2K)	DLST, DLTS	0.48	-1.06	0.0000	0.0017
Q4VC31	Coiled-coil domain-containing protein 58	CCDC58	0.48	-1.06	0.0040	0.0377
P21953	2-oxoisovalerate dehydrogenase subunit beta, mitochondrial (EC 1.2.4.4) (Branched-chain alpha-keto acid dehydrogenase E1 component beta chain) (BCKDE1B) (BCKDH E1-beta)	BCKDHB	0.49	-1.04	0.0012	0.0153
Q96DC8	Enoyl-CoA hydratase domain-containing protein 3, mitochondrial	ECHDC3, PP1494, PP8332	0.49	-1.03	0.0000	0.0001
Q9Y5U8	Mitochondrial pyruvate carrier 1 (Brain protein 44-like protein)	MPC1, BRP44L, CGI-129, HSPC040, PNAS-115	0.49	-1.02	0.0002	0.0044
Q9Y241	HIG1 domain family member 1A, mitochondrial (Hypoxia-inducible gene 1 protein) (RCF1 homolog A) (RCF1a)	HIGD1A, HIG1, HSPC010	0.51	-0.98	0.0001	0.0019
Q86VD7	Mitochondrial coenzyme A transporter SLC25A42 (Solute carrier family 25 member 42)	SLC25A42	0.52	-0.96	0.0002	0.0044
Q96HY7	Probable 2-oxoglutarate dehydrogenase E1 component DHKTD1, mitochondrial (EC 1.2.4.2) (Dehydrogenase E1 and transketolase domain-containing protein 1)	DHTKD1, KIAA1630	0.52	-0.93	0.0082	0.0547
P53985	Monocarboxylate transporter 1 (MCT 1) (Solute carrier family 16 member 1)	SLC16A1, MCT1	0.53	-0.92	0.0024	0.0248
O43615	Mitochondrial import inner membrane translocase subunit TIM44	TIMM44, MIMT44, TIM44	0.53	-0.92	0.0019	0.0201
P08559	Pyruvate dehydrogenase E1 component subunit alpha, somatic form, mitochondrial (EC 1.2.4.1) (PDHE1-A type I)	PDHA1, PHE1A	0.53	-0.91	0.0002	0.0044
Q99766	ATP synthase subunit s, mitochondrial (ATP synthase-coupling factor B) (FB) (Mitochondrial ATP synthase regulatory component factor B)	ATP5S, ATPW	0.54	-0.89	0.0051	0.0426
Q86WU2	Probable D-lactate dehydrogenase, mitochondrial (DLD) (Lactate dehydrogenase D) (EC 1.1.2.4)	LDHD	0.54	-0.89	0.0032	0.0316
Q13505	Metaxin-1 (Mitochondrial outer membrane import complex protein 1)	MTX1, MTX, MTXN	0.54	-0.89	0.0037	0.0354
Q16595	Frataxin, mitochondrial (EC 1.16.3.1) (Friedreich ataxia protein) (Fxn) [Cleaved into: Frataxin intermediate form (i-FXN); Frataxin(56-210) (m56-FXN); Frataxin(78-210) (d-FXN) (m78-FXN); Frataxin mature form (Frataxin(81-210)) (m81-FXN)]	FXN, FRDA, X25	0.54	-0.89	0.0007	0.0103
Q9BRJ2	39S ribosomal protein L45, mitochondrial (L45mt) (MRP-L45) (Mitochondrial large ribosomal subunit protein mL45)	MRPL45	0.56	-0.84	0.0024	0.0248

P30038	Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial (P5C dehydrogenase) (EC 1.2.1.88) (Aldehyde dehydrogenase family 4 member A1) (L-glutamate gamma-semialdehyde dehydrogenase)	ALDH4A1, ALDH4, P5CDH	0.56	-0.83	0.0048	0.0421
O60220	Mitochondrial import inner membrane translocase subunit Tim8 A (Deafness dystonia protein 1) (X-linked deafness dystonia protein)	TIMM8A, DDP, DDP1, TIM8A	0.59	-0.77	0.0063	0.0458
P42704	Leucine-rich PPR motif-containing protein, mitochondrial (130 kDa leucine-rich protein) (LRP 130) (GP130)	LRPPRC, LRP130	0.59	-0.77	0.0006	0.0082
P28331	NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial (EC 1.6.5.3) (EC 1.6.99.3) (Complex I-75kD) (CI-75kD)	NDUFS1	0.60	-0.75	0.0061	0.0458
Q9Y676	28S ribosomal protein S18b, mitochondrial (MRP-S18-b) (Mrps18-b) (S18mt-b) (28S ribosomal protein S18-2, mitochondrial) (MRP-S18-2) (Mitochondrial small ribosomal subunit protein bS18b) (Mitochondrial small ribosomal subunit protein mS40)	MRPS18B, C6orf14, HSPC183, PTD017	0.60	-0.74	0.0005	0.0080
O75208	Ubiquinone biosynthesis protein COQ9, mitochondrial	COQ9, C16orf49, HSPC326, PSEC0129	0.61	-0.72	0.0048	0.0421
O95169	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 8, mitochondrial (Complex I-ASHI) (CI-ASHI) (NADH-ubiquinone oxidoreductase ASHI subunit)	NDUFB8	0.61	-0.71	0.0017	0.0195
Q9Y305	Acyl-coenzyme A thioesterase 9, mitochondrial (Acyl-CoA thioesterase 9) (EC 3.1.2.-) (Acyl-CoA thioester hydrolase 9)	ACOT9, CGI-16	0.61	-0.71	0.0059	0.0458
Q16836	Hydroxyacyl-coenzyme A dehydrogenase, mitochondrial (HCDH) (EC 1.1.1.35) (Medium and short-chain L-3-hydroxyacyl-coenzyme A dehydrogenase) (Short-chain 3-hydroxyacyl-CoA dehydrogenase)	HADH, HAD, HADHSC, SCHAD	0.65	-0.61	0.0011	0.0142
Q9UHQ9	NADH-cytochrome b5 reductase 1 (b5R.1) (EC 1.6.2.2) (Humb5R2) (NAD(P)H:quinone oxidoreductase type 3 polypeptide A2)	CYB5R1, NQO3A2, UNQ3049/PRO9865	0.68	-0.56	0.0052	0.0430
Q8NBN7	Retinol dehydrogenase 13 (EC 1.1.1.-) (Short chain dehydrogenase/reductase family 7C member 3)	RDH13, SDR7C3, PSEC0082, UNQ736/PRO1430	1.43	0.52	0.0051	0.0426
P51553	Isocitrate dehydrogenase [NAD] subunit gamma, mitochondrial (Isocitric dehydrogenase subunit gamma) (NAD(+)-specific ICDH subunit gamma)	IDH3G	1.52	0.61	0.0082	0.0547
P51649	Succinate-semialdehyde dehydrogenase, mitochondrial (EC 1.2.1.24) (Aldehyde dehydrogenase family 5 member A1) (NAD(+)-dependent succinic semialdehyde dehydrogenase)	ALDH5A1, SSADH	1.53	0.61	0.0067	0.0478
P17540	Creatine kinase S-type, mitochondrial (EC 2.7.3.2) (Basic-type mitochondrial creatine kinase) (Mib-CK) (Sarcomeric mitochondrial creatine kinase) (S-MtCK)	CKMT2	1.56	0.64	0.0004	0.0063
O95139	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 6 (Complex I-B17) (CI-B17) (NADH-ubiquinone oxidoreductase B17 subunit)	NDUFB6	1.57	0.65	0.0016	0.0190
P31415	Calsequestrin-1 (Calmitine) (Calsequestrin, skeletal muscle isoform)	CASQ1, CASQ	1.65	0.72	0.0060	0.0458
P50213	Isocitrate dehydrogenase [NAD] subunit alpha, mitochondrial (EC 1.1.1.41) (Isocitric dehydrogenase subunit alpha) (NAD(+)-specific ICDH subunit alpha)	IDH3A	1.79	0.84	0.0001	0.0036
Q9BVV7	Mitochondrial import inner membrane translocase subunit Tim21 (TIM21-like protein, mitochondrial)	TIMM21, C18orf55, TIM21, HSPC154	1.80	0.85	0.0018	0.0195
P30084	Enoyl-CoA hydratase, mitochondrial (EC 4.2.1.17) (Enoyl-CoA hydratase 1) (Short-chain enoyl-CoA hydratase) (SCEH)	ECHS1	1.80	0.85	0.0055	0.0445
P19367	Hexokinase-1 (EC 2.7.1.1) (Brain form hexokinase) (Hexokinase type I) (HK I)	HK1	1.84	0.88	0.0030	0.0302
P26440	Isovaleryl-CoA dehydrogenase, mitochondrial (IVD) (EC 1.3.8.4)	IVD	1.86	0.89	0.0013	0.0160
P04040	Catalase (EC 1.11.1.6)	CAT	1.89	0.92	0.0060	0.0458
P08574	Cytochrome c1, heme protein, mitochondrial (Complex III subunit 4) (Complex III subunit IV) (Cytochrome b-c1 complex subunit 4) (Ubiquinol-cytochrome-c reductase complex cytochrome c1 subunit) (Cytochrome c-1)	CYC1	2.01	1.01	0.0003	0.0055
P0C7P0	CDGSH iron-sulfur domain-containing protein 3, mitochondrial (MitoNEET-related protein 2) (Miner2)	CISD3	2.06	1.04	0.0007	0.0103
Q6UXV4	MICOS complex subunit MIC27 (Apolipoprotein O-like) (Protein FAM121A)	APOOL, CXorf33, FAM121A, MIC27, UNQ8193/PRO23204	2.08	1.06	0.0001	0.0031
Q9BSE5	Agmatinase, mitochondrial (EC 3.5.3.11) (Agmatine ureohydrolase) (AUH)	AGMAT	2.10	1.07	0.0006	0.0082
Q99497	Protein/nucleic acid deglycase DJ-1 (EC 3.1.2.-) (EC 3.5.1.-) (EC 3.5.1.124) (Maillard deglycase) (Oncogene DJ1) (Parkinson disease protein 7) (Parkinsonism-associated deglycase) (Protein DJ-1) (DJ-1)	PARK7	2.11	1.08	0.0021	0.0222
P23368	NAD-dependent malic enzyme, mitochondrial (NAD-ME) (EC 1.1.1.38) (Malic enzyme 2)	ME2	2.11	1.08	0.0001	0.0025
P14618	Pyruvate kinase PKM (EC 2.7.1.40) (Cytosolic thyroid hormone-binding protein) (CTHBP) (Opa-interacting protein 3) (OIP-3) (Pyruvate kinase 2/3) (Pyruvate kinase muscle isozyme) (Thyroid hormone-binding protein 1) (THBP1) (Tumor M2-PK) (p58)	PKM, OIP3, PK2, PK3, PKM2	2.16	1.11	0.0000	0.0012
Q9BUB7	Transmembrane protein 70, mitochondrial	TMEM70	2.19	1.13	0.0000	0.0017
P21912	Succinate dehydrogenase [ubiquinone] iron-sulfur subunit, mitochondrial (EC 1.3.5.1) (Iron-sulfur subunit of complex II) (Ip)	SDHB, SDH, SDH1	2.19	1.13	0.0000	0.0012
P09543	2',3'-cyclic-nucleotide 3'-phosphodiesterase (CNP) (CNPase) (EC 3.1.4.37)	CNP	2.25	1.17	0.0062	0.0458
Q13084	39S ribosomal protein L28, mitochondrial (L28mt) (MRP-L28) (Melanoma antigen p15) (Melanoma-associated antigen recognized by T-lymphocytes) (Mitochondrial large ribosomal subunit protein bL28m)	MRPL28, MAAT1	2.27	1.18	0.0044	0.0404
O43819	Protein SCO2 homolog, mitochondrial	SCO2	2.29	1.19	0.0068	0.0478
P36969	Phospholipid hydroperoxide glutathione peroxidase, mitochondrial (PHGPx) (EC 1.11.1.12) (Glutathione peroxidase 4) (GPx-4) (GSHPx-4)	GPX4	2.37	1.25	0.0062	0.0458
Q14061	Cytochrome c oxidase copper chaperone	COX17	2.92	1.55	0.0000	0.0001
P54819	Adenylate kinase 2, mitochondrial (AK 2) (EC 2.7.4.3) (ATP-AMP transphosphorylase 2) (ATP:AMP phosphotransferase) (Adenylate monophosphate kinase) [Cleaved into: Adenylate kinase 2, mitochondrial, N-terminally processed]	AK2, ADK2	3.07	1.62	0.0001	0.0017
O95674	Phosphatidate cytidylyltransferase 2 (EC 2.7.7.41) (CDP-DAG synthase 2) (CDP-DG synthase 2) (CDP-diacylglycerol synthase 2) (CDS 2) (CDP-diglyceride pyrophosphorylase 2) (CDP-diglyceride synthase 2) (CTP:phosphatidate cytidylyltransferase 2)	CDS2	3.20	1.68	0.0002	0.0044

Supplemental Table 4

41 differentially expressed mitochondrial proteins between lean and obese subjects identified in intermyofibrillar mitochondria

Uniprot ID	Protein Name	Gene Symbol(s)	Ratio Obese/Lean	$\log_2$ O/L Ratio	p Value	FDR-corrected p Value/*q* Value
O95178	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 2, mitochondrial (Complex I-AGGG) (CI-AGGG) (NADH-ubiquinone oxidoreductase AGGG subunit)	NDUFB2	0.25	-2.01	0.0000	0.0000
Q15119	[Pyruvate dehydrogenase (acetyl-transferring)] kinase isozyme 2, mitochondrial (EC 2.7.11.2) (Pyruvate dehydrogenase kinase isoform 2) (PDH kinase 2) (PDKII)	PDK2, PDHK2	0.28	-1.81	0.0000	0.0000
P27824	Calnexin (IP90) (Major histocompatibility complex class I antigen-binding protein p88) (p90)	CANX	0.33	-1.62	0.0001	0.0038
P11021	78 kDa glucose-regulated protein (GRP-78) (Endoplasmic reticulum lumenal Ca(2+)-binding protein grp78) (Heat shock 70 kDa protein 5) (Immunoglobulin heavy chain-binding protein) (BiP)	HSPA5, GRP78	0.33	-1.59	0.0013	0.0206
Q3ZCQ8	Mitochondrial import inner membrane translocase subunit TIM50	TIMM50, TIM50, PRO1512	0.34	-1.54	0.0011	0.0201
Q96CM8	Acyl-CoA synthetase family member 2, mitochondrial (EC 6.2.1.-)	ACSF2, UNQ493/PRO1009	0.40	-1.32	0.0009	0.0184
Q7Z2W9	39S ribosomal protein L21, mitochondrial (L21mt) (MRP-L21) (Mitochondrial large ribosomal subunit protein bL21m)	MRPL21	0.41	-1.29	0.0000	0.0018
Q9NYK5	39S ribosomal protein L39, mitochondrial (L39mt) (MRP-L39) (39S ribosomal protein L5, mitochondrial) (L5mt) (MRP-L5) (Mitochondrial large ribosomal subunit protein mL39)	MRPL39, C21orf92, MRPL5, RPML5, MSTP003, PRED22	0.41	-1.29	0.0002	0.0058
O43674	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 5, mitochondrial (Complex I-SGDH) (CI-SGDH) (NADH-ubiquinone oxidoreductase SGDH subunit)	NDUFB5	0.42	-1.26	0.0001	0.0025
Q02252	Methylmalonate-semialdehyde dehydrogenase [acylating], mitochondrial (MMSDH) (Malonate-semialdehyde dehydrogenase [acylating]) (EC 1.2.1.18) (EC 1.2.1.27) (Aldehyde dehydrogenase family 6 member A1)	ALDH6A1, MMSDH	0.43	-1.22	0.0000	0.0009
P35232	Prohibitin	PHB	0.45	-1.16	0.0002	0.0052
Q96HS1	Serine/threonine-protein phosphatase PGAM5, mitochondrial (EC 3.1.3.16) (Bcl-XL-binding protein v68) (Phosphoglycerate mutase family member 5)	PGAM5	0.45	-1.15	0.0042	0.0354
Q16718	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 5 (Complex I subunit B13) (Complex I-13kD-B) (CI-13kD-B) (NADH-ubiquinone oxidoreductase 13 kDa-B subunit)	NDUFA5	0.46	-1.11	0.0002	0.0052
O95139	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 6 (Complex I-B17) (CI-B17) (NADH-ubiquinone oxidoreductase B17 subunit)	NDUFB6	0.48	-1.06	0.0001	0.0037
P38117	Electron transfer flavoprotein subunit beta (Beta-ETF)	ETFB, FP585	0.48	-1.05	0.0005	0.0110
P21397	Amine oxidase [flavin-containing] A (EC 1.4.3.4) (Monoamine oxidase type A) (MAO-A)	MAOA	0.48	-1.05	0.0029	0.0275
P51648	Fatty aldehyde dehydrogenase (EC 1.2.1.3) (Aldehyde dehydrogenase 10) (Aldehyde dehydrogenase family 3 member A2) (Microsomal aldehyde dehydrogenase)	ALDH3A2, ALDH10, FALDH	0.54	-0.89	0.0049	0.0390
Q9P0J1	[Pyruvate dehydrogenase [acetyl-transferring]]-phosphatase 1, mitochondrial (PDP 1) (EC 3.1.3.43) (Protein phosphatase 2C) (Pyruvate dehydrogenase phosphatase catalytic subunit 1) (PDPC 1)	PDP1, PDP, PPM2C	0.54	-0.89	0.0019	0.0217
P30048	Thioredoxin-dependent peroxide reductase, mitochondrial (EC 1.11.1.15) (Antioxidant protein 1) (AOP-1) (HBC189) (Peroxiredoxin III) (Prx-III) (Peroxiredoxin-3) (Protein MER5 homolog)	PRDX3, AOP1	0.56	-0.85	0.0025	0.0243
P08574	Cytochrome c1, heme protein, mitochondrial (Complex III subunit 4) (Complex III subunit IV) (Cytochrome b-c1 complex subunit 4) (Ubiquinol-cytochrome-c reductase complex cytochrome c1 subunit) (Cytochrome c-1)	CYC1	0.56	-0.84	0.0076	0.0538
P28838	Cytosol aminopeptidase (EC 3.4.11.1) (Leucine aminopeptidase 3) (LAP-3) (Leucyl aminopeptidase) (Peptidase S) (Proline aminopeptidase) (EC 3.4.11.5) (Prolyl aminopeptidase)	LAP3, LAPEP, PEPS	0.57	-0.81	0.0023	0.0234
Q96I99	Succinate--CoA ligase [GDP-forming] subunit beta, mitochondrial (EC 6.2.1.4) (GTP-specific succinyl-CoA synthetase subunit beta) (G-SCS) (GTPSCS) (Succinyl-CoA synthetase beta-G chain) (SCS-betaG)	SUCLG2	0.58	-0.79	0.0055	0.0419
P05091	Aldehyde dehydrogenase, mitochondrial (EC 1.2.1.3) (ALDH class 2) (ALDH-E2) (ALDHI)	ALDH2, ALDM	0.60	-0.74	0.0005	0.0111
P18859	ATP synthase-coupling factor 6, mitochondrial (ATPase subunit F6)	ATP5J, ATP5A, ATPM	0.61	-0.71	0.0018	0.0217
P06576	ATP synthase subunit beta, mitochondrial (EC 3.6.3.14)	ATP5B, ATPMB, ATPSB	0.64	-0.64	0.0001	0.0025
Q9Y305	Acyl-coenzyme A thioesterase 9, mitochondrial (Acyl-CoA thioesterase 9) (EC 3.1.2.-) (Acyl-CoA thioester hydrolase 9)	ACOT9, CGI-16	0.65	-0.63	0.0012	0.0201
P30038	Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial (P5C dehydrogenase) (EC 1.2.1.88) (Aldehyde dehydrogenase family 4 member A1) (L-glutamate gamma-semialdehyde dehydrogenase)	ALDH4A1, ALDH4, P5CDH	0.68	-0.55	0.0016	0.0216
P25705	ATP synthase subunit alpha, mitochondrial	ATP5A1, ATP5A, ATP5AL2, ATPM	0.71	-0.49	0.0069	0.0514
P43155	Carnitine O-acetyltransferase (Carnitine acetylase) (EC 2.3.1.7) (Carnitine acetyltransferase) (CAT) (CrAT)	CRAT, CAT1	1.46	0.55	0.0079	0.0543
Q6NVY1	3-hydroxyisobutyryl-CoA hydrolase, mitochondrial (EC 3.1.2.4) (3-hydroxyisobutyryl-coenzyme A hydrolase) (HIB-CoA hydrolase) (HIBYL-CoA-H)	HIBCH	1.48	0.56	0.0047	0.0381
P24539	ATP synthase F(0) complex subunit B1, mitochondrial (ATP synthase proton-transporting mitochondrial F(0) complex subunit B1) (ATP synthase subunit b) (ATPase subunit b)	ATP5F1	1.54	0.62	0.0076	0.0538
O75390	Citrate synthase, mitochondrial (EC 2.3.3.1) (Citrate (Si)-synthase)	CS	1.54	0.63	0.0081	0.0543
P03915	NADH-ubiquinone oxidoreductase chain 5 (EC 1.6.5.3) (NADH dehydrogenase subunit 5)	MT-ND5, MTND5, NADH5, ND5	1.70	0.76	0.0016	0.0216
O43772	Mitochondrial carnitine/acylcarnitine carrier protein (Carnitine/acylcarnitine translocase) (CAC) (Solute carrier family 25 member 20)	SLC25A20, CAC, CACT	1.93	0.95	0.0039	0.0336
Q5JRX3	Presequence protease, mitochondrial (hPreP) (EC 3.4.24.-) (Pitrilysin metalloproteinase 1) (Metalloprotease 1) (hMP1)	PITRM1, KIAA1104, MP1	2.03	1.02	0.0023	0.0234

P33121	Long-chain-fatty-acid--CoA ligase 1 (EC 6.2.1.3) (Acyl-CoA synthetase 1) (ACS1) (Long-chain acyl-CoA synthetase 1) (LACS 1) (Long-chain acyl-CoA synthetase 2) (LACS 2) (Long-chain fatty acid-CoA ligase 2) (Palmitoyl-CoA ligase 1) (Palmitoyl-CoA ligase 2)	ACSL1, FACL1, FACL2, LACS, LACS1, LACS2	2.05	1.04	0.0016	0.0216
P50440	Glycine amidinotransferase, mitochondrial (EC 2.1.4.1) (L-arginine:glycine amidinotransferase) (Transamidinase)	GATM, AGAT	2.08	1.06	0.0038	0.0336
P11310	Medium-chain specific acyl-CoA dehydrogenase, mitochondrial (MCAD) (EC 1.3.8.7)	ACADM	2.26	1.18	0.0020	0.0217
Q12931	Heat shock protein 75 kDa, mitochondrial (HSP 75) (TNFR-associated protein 1) (Tumor necrosis factor type 1 receptor-associated protein) (TRAP-1)	TRAP1, HSP75	2.28	1.19	0.0019	0.0217
Q9NVH6	Trimethyllysine dioxygenase, mitochondrial (EC 1.14.11.8) (Epsilon-trimethyllysine 2-oxoglutarate dioxygenase) (Epsilon-trimethyllysine hydroxylase) (TML hydroxylase) (TML-alpha-ketoglutarate dioxygenase) (TML dioxygenase) (TMLD)	TMLHE, TMLH	2.31	1.21	0.0016	0.0216
Q9BXW7	Haloacid dehalogenase-like hydrolase domain-containing 5 (Cat eye syndrome critical region protein 5)	HDHD5, CECR5	2.67	1.42	0.0036	0.0333

Supplemental Table 5

Mapped pathways associated with 73 differentially expressed proteins in subsarcolemmal mitochondria from obese that met false discovery rate criteria (*P* ≤0.05). Analysis was performed using the Reactome Software.

Pathway identifier	Pathway name	#Entities found	Entities pValue	Entities FDR	Mapped entities
R-HSA-1428517	The citric acid (TCA) cycle and respiratory electron transport	17	1.45E-14	5.61E-12	Q9Y5U8;P51553;P08559;P36957;O95169;Q9H845;P28331;O95139;P50213;O95178;P53985;Q99766;P21912;O43819;Q8NCN5;P42704;P08574
R-HSA-1268020	Mitochondrial protein import	10	1.90E-11	3.66E-09	P51553;Q86WU2;O95169;Q14061;Q13505;Q9BVV7;P08574;O60220;O43615;Q16595
R-HSA-71406	Pyruvate metabolism and Citric Acid (TCA) cycle	8	2.25E-09	2.88E-07	P21912;Q8NCN5;Q9Y5U8;P51553;P36957;P08559;P50213;P53985
R-HSA-163200	Respiratory electron transport, ATP synthesis by chemiosmotic coupling, and heat production by uncoupling proteins.	10	6.00E-08	5.76E-06	Q99766;P21912;O43819;O95169;Q9H845;P42704;P28331;O95139;P08574;O95178
R-HSA-5368286	Mitochondrial translation initiation	8	9.41E-08	7.24E-06	Q9Y676;Q9NP92;Q9BYD3;P46199;Q9BRJ2;Q13084;Q9H0U6;Q5T653
R-HSA-611105	Respiratory electron transport	9	1.83E-07	1.17E-05	P21912;O43819;O95169;Q9H845;P42704;P28331;O95139;P08574;O95178
R-HSA-5368287	Mitochondrial translation	8	4.37E-07	2.41E-05	Q9Y676;Q9NP92;Q9BYD3;P46199;Q9BRJ2;Q13084;Q9H0U6;Q5T653
R-HSA-1430728	Metabolism	41	1.57E-06	7.54E-05	P26440;P36969;Q9Y305;O95674;Q9Y5U8;P08559;O75208;Q9H845;O95139;P50213;O95178;P53985;Q99766;Q8NCN5;O43819;Q9BSE5;P05091;P14618-2;P14618-1;P42704;P54819;P55809;P49419;Q16595;P30038;Q16836;P51553;O95169;P36957;P22570;P28331;Q02252;P19367;Q96HY7;P21912;P21953;P17540;P30084;P08574;O14874;Q9NUB1
R-HSA-5389840	Mitochondrial translation elongation	7	2.13E-06	8.96E-05	Q9Y676;Q9NP92;Q9BYD3;Q9BRJ2;Q13084;Q9H0U6;Q5T653
R-HSA-5419276	Mitochondrial translation termination	7	2.45E-06	9.31E-05	Q9Y676;Q9NP92;Q9BYD3;Q9BRJ2;Q13084;Q9H0U6;Q5T653
R-HSA-1362409	Mitochondrial iron-sulfur cluster biogenesis	2	5.83E-06	2.04E-04	P22570;Q16595
R-HSA-71403	Citric acid cycle (TCA cycle)	4	1.02E-05	3.27E-04	P21912;P51553;P36957;P50213
R-HSA-389661	Glyoxylate metabolism and glycine degradation	5	2.23E-05	6.48E-04	P30038;P21953;P36957;P08559;Q96HY7
R-HSA-70895	Branched-chain amino acid catabolism	4	2.72E-05	7.33E-04	P26440;P21953;Q02252;O14874
R-HSA-70268	Pyruvate metabolism	4	4.63E-05	1.16E-03	Q8NCN5;Q9Y5U8;P08559;P53985
R-HSA-6799198	Complex I biogenesis	5	1.45E-04	3.47E-03	O95169;Q9H845;P28331;O95139;O95178
R-HSA-71291	Metabolism of amino acids and derivatives	11	1.75E-04	3.85E-03	P30038;P26440;Q9BSE5;P21953;P36957;P08559;P17540;Q02252;O14874;P49419;Q96HY7
R-HSA-77348	Beta oxidation of octanoyl-CoA to hexanoyl-CoA	2	4.67E-04	8.40E-03	Q16836;P30084
R-HSA-77310	Beta oxidation of lauroyl-CoA to decanoyl-CoA-CoA	2	4.67E-04	8.40E-03	Q16836;P30084
R-HSA-77350	Beta oxidation of hexanoyl-CoA to butanoyl-CoA	2	4.67E-04	8.40E-03	Q16836;P30084
R-HSA-77352	Beta oxidation of butanoyl-CoA to acetyl-CoA	2	4.67E-04	8.40E-03	Q16836;P30084
R-HSA-77346	Beta oxidation of decanoyl-CoA to octanoyl-CoA-CoA	2	6.70E-04	1.14E-02	Q16836;P30084
R-HSA-77286	Mitochondrial fatty acid beta-oxidation of saturated fatty acids	2	2.21E-03	3.53E-02	Q16836;P30084

Supplemental Table 6

Mapped pathways associated with 41 differentially expressed proteins in intermyofibrillar mitochondria from obese that met false discovery rate criteria (*P* ≤0.05).
Analysis was performed using the Reactome Software.

Pathway identifier	Pathway name	#Entities found	Entities pValue	Entities FDR	Mapped entities
R-HSA-1428517	The citric acid (TCA) cycle and respiratory electron transport	16	9.99E-16	2.49E-13	O95139;O43674;Q12931;Q15119;P03915;Q16718;O95178;P38117;Q96I99;Q9P0J1;O75390;P25705;P18859;P24539;P08574;P06576
R-HSA-163200	Respiratory electron transport, ATP synthesis by chemiosmotic coupling, and heat production by uncoupling proteins.	12	6.53E-12	8.10E-10	P25705;P18859;P24539;O95139;O43674;Q12931;P08574;P03915;Q16718;O95178;P38117;P06576
R-HSA-611105	Respiratory electron transport	8	1.70E-07	1.41E-05	O95139;O43674;Q12931;P08574;P03915;Q16718;O95178;P38117
R-HSA-1268020	Mitochondrial protein import	6	6.37E-07	3.95E-05	Q5JRX3;O75390;Q3ZCQ8;P25705;P08574;P06576
R-HSA-1430728	Metabolism	31	8.16E-07	4.00E-05	Q9Y305;P51648-2;P51648-1;O95139;O43674;O43772;Q15119;O95178;Q96I99;Q9P0J1;O75390;P05091;Q6NVY1;P25705;Q96CM8;P18859;P24539;P43155;P50440;P30038;Q12931;Q02252;P03915;P33121;Q16718;P38117;P11310;P08574;P21397;Q9NVH6;P06576
R-HSA-163210	Formation of ATP by chemiosmotic coupling	4	1.51E-06	6.18E-05	P25705;P18859;P24539;P06576
R-HSA-6799198	Complex I biogenesis	5	3.01E-05	1.05E-03	O95139;O43674;P03915;Q16718;O95178
R-HSA-8949613	Cristae formation	4	9.99E-05	2.59E-03	P25705;P18859;P24539;P06576
R-HSA-71406	Pyruvate metabolism and Citric Acid (TCA) cycle	4	1.08E-04	2.59E-03	O75390;Q15119;Q96I99;Q9P0J1
R-HSA-70895	Branched-chain amino acid catabolism	3	2.57E-04	5.14E-03	Q6NVY1;Q02252;Q9NVH6
R-HSA-8978868	Fatty acid metabolism	7	6.13E-04	1.16E-02	Q9Y305;P51648-2;Q96CM8;O43772;P33121;P43155;P11310
R-HSA-204174	Regulation of pyruvate dehydrogenase (PDH) complex	2	2.12E-03	3.39E-02	Q15119;Q9P0J1
R-HSA-77289	Mitochondrial Fatty Acid Beta-Oxidation	3	3.61E-03	5.41E-02	Q9Y305;Q96CM8;P11310

Supplemental Table 7

Biological processes by gene ontology (GO) categories in 73 differentially expressed proteins in subsarcolemmal mitochondria from obese that met false discovery rate criteria ($P \leq 0.05$). Analysis was performed using the STRING database.

Pathway ID	Pathway description	Observed gene count	False discovery rate	Matching proteins in your network (IDs)	Matching proteins in your network (labels)
GO.0055114	oxidation-reduction process	33	2.83E-21	ENSP00000217901,ENSP00000247866,ENSP00000258770,ENSP00000261733,ENSP00000262507,ENSP00000263035,ENSP00000288050,ENSP00000290597,ENSP00000299166,ENSP00000299518,ENSP00000300051,ENSP00000308334,ENSP00000312618,ENSP00000314649,ENSP00000316924,ENSP00000317159,ENSP00000320171,ENSP00000321070,ENSP00000335304,ENSP00000346103,ENSP00000356218,ENSP00000357535,ENSP00000364649,ENSP00000369134,ENSP00000369176,ENSP00000384774,ENSP00000385638,ENSP00000387123,ENSP00000392709,ENSP00000398064,ENSP00000418397,ENSP00000450436,ENSP00000462972	ACAD9, ACSS1, ALDH2, ALDH4A1, ALDH5A1, ALDH6A1, ALDH7A1, ATP5S, COQ9, CYB5R1, CYC1, DHTKD1, DLST, ECHS1, FDXR, GPX4, HADH, HIGD1A, HK1, IDH3A, IDH3G, IVD, LDHD, ME2, NDUFB2, NDUFB6, NDUFB8, NDUFS1, PDHA1, PDPR, PKM, SDHB, TBRG4
GO.0045333	cellular respiration	18	3.26E-18	ENSP00000217901,ENSP00000241052,ENSP00000247866,ENSP00000252785,ENSP00000258770,ENSP00000262507,ENSP00000263035,ENSP00000299166,ENSP00000299518,ENSP00000308334,ENSP00000314649,ENSP00000317159,ENSP00000335304,ENSP00000364649,ENSP00000366482,ENSP00000369134,ENSP00000369176,ENSP00000392709	ALDH5A1, ATP5S, CAT, COQ9, CYC1, DHTKD1, DLST, FXN, IDH3A, IDH3G, NDUFB2, NDUFB6, NDUFB8, NDUFS1, PDHA1, SCO2, SDHB, TBRG4
GO.0006091	generation of precursor metabolites and energy	21	5.59E-16	ENSP00000217901,ENSP00000241052,ENSP00000247866,ENSP00000252785,ENSP00000258770,ENSP00000261070,ENSP00000262507,ENSP00000263035,ENSP00000299166,ENSP00000299518,ENSP00000308334,ENSP00000314649,ENSP00000317159,ENSP00000320171,ENSP00000335304,ENSP00000364649,ENSP00000366482,ENSP00000369176,ENSP00000384774,ENSP00000392709,ENSP00000462972	ALDH5A1, ATP5S, CAT, COQ9, COX17, CYC1, DHTKD1, DLST, FDXR, FXN, HK1, IDH3A, IDH3G, NDUFB2, NDUFB6, NDUFB8, NDUFS1, PKM, SCO2, SDHB, TBRG4
GO.0007005	mitochondrion organization	18	3.33E-12	ENSP00000169551,ENSP00000199706,ENSP00000253099,ENSP00000263629,ENSP00000270538,ENSP00000308901,ENSP00000312599,ENSP00000312618,ENSP00000340278,ENSP00000356001,ENSP00000357360,ENSP00000361993,ENSP00000366482,ENSP00000373404,ENSP00000377470,ENSP00000379057,ENSP00000392709,ENSP00000424328	ACAD9, CNP, FXN, MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30, MTIF2, MTX1, NDUFS1, PARK7, SMCR7, TIMM21, TIMM44, TIMM8A, TMEM70
GO.0044281	small molecule metabolic process	32	3.89E-11	ENSP00000219794,ENSP00000247866,ENSP00000254035,ENSP00000261733,ENSP00000263035,ENSP00000288050,ENSP00000290597,ENSP00000299166,ENSP00000299518,ENSP00000308334,ENSP00000314649,ENSP00000317159,ENSP00000318351,ENSP00000321070,ENSP00000340278,ENSP00000346103,ENSP00000346921,ENSP00000354223,ENSP00000356218,ENSP00000357535,ENSP00000358640,ENSP00000364986,ENSP00000369176,ENSP00000377470,ENSP00000384774,ENSP00000385638,ENSP00000387123,ENSP00000392709,ENSP00000418397,ENSP00000419879,ENSP00000450436,ENSP00000462972	AGMAT, AK2, ALDH2, ALDH4A1, ALDH5A1, ALDH6A1, ALDH7A1, ATP5S, BCKDHB, BCKDK, CDS2, CKMT2, CNP, CYB5R1, CYC1, DHTKD1, ECHS1, FDXR, GPX4, HADH, HK1, IDH3A, IVD, ME2, MPC1, NDUFB2, NDUFB6, NDUFB8, NDUFS1, PARK7, PDPR, SLC16A1
GO.1901564	organonitrogen compound metabolic process	28	7.00E-11	ENSP00000199706,ENSP00000217901,ENSP00000219794,ENSP00000241052,ENSP00000247866,ENSP00000253099,ENSP00000254035,ENSP00000262507,ENSP00000263035,ENSP00000263629,ENSP00000290597,ENSP00000299166,ENSP00000308334,ENSP00000308901,ENSP00000318351,ENSP00000346921,ENSP00000356001,ENSP00000364986,ENSP00000366482,ENSP00000369134,ENSP00000369176,ENSP00000373404,ENSP00000384774,ENSP00000387123,ENSP00000392709,ENSP00000418397,ENSP00000424328,ENSP00000450436	AGMAT, AK2, ALDH4A1, ALDH6A1, ALDH7A1, ATP5S, BCKDHB, BCKDK, CAT, CKMT2, COQ9, DHTKD1, FXN, HK1, IDH3G, IVD, MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30, MTIF2, NDUFB2, NDUFB6, NDUFB8, NDUFS1, PDHA1
GO.0019752	carboxylic acid metabolic process	21	1.15E-10	ENSP00000219794,ENSP00000254035,ENSP00000263035,ENSP00000288050,ENSP00000290597,ENSP00000299518,ENSP00000314649,ENSP00000316924,ENSP00000318351,ENSP00000321070,ENSP00000340278,ENSP00000346103,ENSP00000354223,ENSP00000357535,ENSP00000358640,ENSP00000364986,ENSP00000384774,ENSP00000385638,ENSP00000387123,ENSP00000418397,ENSP00000450436	ACSS1, AGMAT, ALDH4A1, ALDH5A1, ALDH6A1, ALDH7A1, BCKDHB, BCKDK, CKMT2, DHTKD1, ECHS1, GPX4, HADH, HK1, IDH3A, IVD, ME2, MPC1, PARK7, PDPR, SLC16A1
GO.0055086	nucleobase-containing small molecule metabolic process	16	1.09E-08	ENSP00000217901,ENSP00000241052,ENSP00000247866,ENSP00000262507,ENSP00000263035,ENSP00000299166,ENSP00000308334,ENSP00000335304,ENSP00000346921,ENSP00000366482,ENSP00000369134,ENSP00000369176,ENSP00000377470,ENSP00000384774,ENSP00000392709,ENSP00000450436	AK2, ALDH6A1, ATP5S, CAT, CNP, COQ9, DHTKD1, DLST, FXN, HK1, IDH3G, NDUFB2, NDUFB6, NDUFB8, NDUFS1, PDHA1
GO.0009060	aerobic respiration	8	1.15E-08	ENSP00000217901,ENSP00000241052,ENSP00000263035,ENSP00000299518,ENSP00000335304,ENSP00000364649,ENSP00000366482,ENSP00000369134	CAT, DHTKD1, DLST, FXN, IDH3A, IDH3G, PDHA1, SDHB
GO.0046034	ATP metabolic process	11	1.18E-08	ENSP00000247866,ENSP00000262507,ENSP00000263035,ENSP00000299166,ENSP00000308334,ENSP00000346921,ENSP00000366482,ENSP00000369134,ENSP00000369176,ENSP00000384774,ENSP00000392709	AK2, ATP5S, COQ9, DHTKD1, FXN, HK1, NDUFB2, NDUFB6, NDUFB8, NDUFS1, PDHA1
GO.0044710	single-organism metabolic process	39	1.55E-08	ENSP00000199706,ENSP00000219794,ENSP00000247866,ENSP00000253099,ENSP00000254035,ENSP00000258770,ENSP00000261733,ENSP00000263035,ENSP00000263629,ENSP00000290597,ENSP00000299166,ENSP00000299518,ENSP00000300051,ENSP00000308334,ENSP00000308901,ENSP00000312618,ENSP00000317159,ENSP00000321070,ENSP00000346103,ENSP00000346921,ENSP00000354223,ENSP00000356001,ENSP00000356218,ENSP00000357535,ENSP00000364986,ENSP00000366482,ENSP00000369176,ENSP00000373404,ENSP00000377470,ENSP00000384774,ENSP00000385638,ENSP00000387123,ENSP00000392709,ENSP00000398064,ENSP00000418397,ENSP00000419879,ENSP00000424328,ENSP00000450436,ENSP00000462972	ACAD9, AGMAT, AK2, ALDH2, ALDH4A1, ALDH6A1, ALDH7A1, ATP5S, BCKDK, CDS2, CKMT2, CNP, CYB5R1, CYC1, DHTKD1, ECHS1, FDXR, FXN, GPX4, HADH, HIGD1A, HK1, IDH3A, IVD, LDHD, ME2, MPC1, MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30, MTIF2, NDUFB2, NDUFB6, NDUFB8, NDUFS1, TBRG4
GO.0022904	respiratory electron transport chain	10	1.77E-08	ENSP00000247866,ENSP00000252785,ENSP00000262507,ENSP00000299166,ENSP00000308334,ENSP00000314649,ENSP00000317159,ENSP00000364649,ENSP00000369176,ENSP00000392709	ALDH5A1, ATP5S, COQ9, CYC1, NDUFB2, NDUFB6, NDUFB8, NDUFS1, SCO2, SDHB
GO.0009117	nucleotide metabolic process	15	2.41E-08	ENSP00000217901,ENSP00000241052,ENSP00000247866,ENSP00000262507,ENSP00000263035,ENSP00000299166,ENSP00000308334,ENSP00000335304,ENSP00000346921,ENSP00000366482,ENSP00000369134,ENSP00000369176,ENSP00000377470,ENSP00000384774,ENSP00000392709	AK2, ATP5S, CAT, CNP, COQ9, DHTKD1, DLST, FXN, HK1, IDH3G, NDUFB2, NDUFB6, NDUFB8, NDUFS1, PDHA1
GO.0044282	small molecule catabolic process	12	2.90E-08	ENSP00000219794,ENSP00000261733,ENSP00000290597,ENSP00000314649,ENSP00000318351,ENSP00000335304,ENSP00000340278,ENSP00000357535,ENSP00000385638,ENSP00000387123,ENSP00000418397,ENSP00000450436	ALDH2, ALDH4A1, ALDH5A1, ALDH6A1, ALDH7A1, BCKDHB, BCKDK, DLST, ECHS1, HADH, IVD, PARK7
GO.0019637	organophosphate metabolic process	18	3.85E-08	ENSP00000217901,ENSP00000241052,ENSP00000247866,ENSP00000262507,ENSP00000263035,ENSP00000299166,ENSP00000308334,ENSP00000314649,ENSP00000335304,ENSP00000346103,ENSP00000346921,ENSP00000366482,ENSP00000369134,ENSP00000369176,ENSP00000377470,ENSP00000384774,ENSP00000392709,ENSP00000419879	AK2, ALDH5A1, ATP5S, CAT, CDS2, CNP, COQ9, DHTKD1, DLST, FXN, GPX4, HK1, IDH3G, NDUFB2, NDUFB6, NDUFB8, NDUFS1, PDHA1

GO.0044712	single-organism catabolic process	18	1.73E-07	ENSP00000219794,ENSP00000241052,ENSP00000261733,ENSP00000263035,ENSP00000290597,ENSP00000314649,ENSP00000318351,ENSP00000320171,ENSP00000335304,ENSP00000340278,ENSP00000357535,ENSP00000369134,ENSP00000377470,ENSP00000384774,ENSP00000385638,ENSP00000387123,ENSP00000418397,ENSP00000450436	ALDH2, ALDH4A1, ALDH5A1, ALDH6A1, ALDH7A1, BCKDHB, BCKDK, CAT, CNP, DHTKD1, DLST, ECHS1, HADH, HK1, IVD, PARK7, PDHA1, PKM
GO.0006099	tricarboxylic acid cycle	6	2.72E-07	ENSP00000217901,ENSP00000263035,ENSP00000299518,ENSP00000335304,ENSP00000364649,ENSP00000369134	DHTKD1, DLST, IDH3A, IDH3G, PDHA1, SDHB
GO.0044711	single-organism biosynthetic process	21	3.17E-07	ENSP00000199706,ENSP00000253099,ENSP00000262507,ENSP00000263629,ENSP00000290597,ENSP00000308334,ENSP00000308901,ENSP00000316924,ENSP00000320171,ENSP00000340278,ENSP00000346921,ENSP00000356001,ENSP00000356218,ENSP00000364986,ENSP00000366482,ENSP00000369134,ENSP00000373404,ENSP00000387123,ENSP00000419879,ENSP00000424328,ENSP00000462972	ACSS1, AGMAT, AK2, ALDH4A1, ALDH7A1, ATP5S, CDS2, COQ9, CYB5R1, FDXR, FXN, MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30, MTIF2, PARK7, PDHA1, PKM
GO.0006163	purine nucleotide metabolic process	12	3.17E-07	ENSP00000241052,ENSP00000247866,ENSP00000262507,ENSP00000263035,ENSP00000299166,ENSP00000308334,ENSP00000346921,ENSP00000366482,ENSP00000369134,ENSP00000369176,ENSP00000384774,ENSP00000392709	AK2, ATP5S, CAT, COQ9, DHTKD1, FXN, HK1, NDUFB2, NDUFB6, NDUFB8, NDUFS1, PDHA1
GO.0046395	carboxylic acid catabolic process	10	3.38E-07	ENSP00000219794,ENSP00000290597,ENSP00000314649,ENSP00000318351,ENSP00000335304,ENSP00000357535,ENSP00000385638,ENSP00000387123,ENSP00000418397,ENSP00000450436	ALDH4A1, ALDH5A1, ALDH6A1, ALDH7A1, BCKDHB, BCKDK, DLST, ECHS1, HADH, IVD
GO.0006733	oxidoreduction coenzyme metabolic process	8	5.43E-07	ENSP00000217901,ENSP00000262507,ENSP00000263035,ENSP00000320171,ENSP00000335304,ENSP00000369134,ENSP00000384774,ENSP00000462972	COQ9, DHTKD1, DLST, FDXR, HK1, IDH3G, PDHA1, PKM
GO.0009063	cellular amino acid catabolic process	8	8.28E-07	ENSP00000219794,ENSP00000290597,ENSP00000314649,ENSP00000318351,ENSP00000335304,ENSP00000387123,ENSP00000418397,ENSP00000450436	ALDH4A1, ALDH5A1, ALDH6A1, ALDH7A1, BCKDHB, BCKDK, DLST, IVD
GO.0070124	mitochondrial translational initiation	7	6.24E-06	ENSP00000199706,ENSP00000253099,ENSP00000263629,ENSP00000308901,ENSP00000356001,ENSP00000373404,ENSP00000424328	MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30, MTIF2
GO.0032787	monocarboxylic acid metabolic process	12	1.47E-05	ENSP00000263035,ENSP00000288050,ENSP00000290597,ENSP00000314649,ENSP00000316924,ENSP00000340278,ENSP00000346103,ENSP00000354223,ENSP00000357535,ENSP00000358640,ENSP00000384774,ENSP00000385638	ACSS1, ALDH4A1, ALDH5A1, DHTKD1, ECHS1, GPX4, HADH, HK1, MPC1, PARK7, PDPR, SLC16A1
GO.0006839	mitochondrial transport	8	1.63E-05	ENSP00000169551,ENSP00000270538,ENSP00000308334,ENSP00000354223,ENSP00000356001,ENSP00000357360,ENSP00000361993,ENSP00000377470	ATP5S, CNP, MPC1, MRPL18, MTX1, TIMM21, TIMM44, TIMM8A
GO.0032543	mitochondrial translation	7	2.91E-05	ENSP00000199706,ENSP00000253099,ENSP00000263629,ENSP00000308901,ENSP00000356001,ENSP00000373404,ENSP00000424328	MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30, MTIF2
GO.0006796	phosphate-containing compound metabolic process	21	3.98E-05	ENSP00000217901,ENSP00000219794,ENSP00000241052,ENSP00000247866,ENSP00000254035,ENSP00000258770,ENSP00000262507,ENSP00000263035,ENSP00000299166,ENSP00000308334,ENSP00000314649,ENSP00000335304,ENSP00000346103,ENSP00000346921,ENSP00000366482,ENSP00000369134,ENSP00000369176,ENSP00000377470,ENSP00000384774,ENSP00000392709,ENSP00000419879	AK2, ALDH5A1, ATP5S, BCKDK, CAT, CDS2, CKMT2, CNP, COQ9, DHTKD1, DLST, FXN, GPX4, HK1, IDH3G, NDUFB2, NDUFB6, NDUFB8, NDUFS1, PDHA1, TBRG4
GO.0006119	oxidative phosphorylation	6	4.00E-05	ENSP00000247866,ENSP00000262507,ENSP00000299166,ENSP00000366482,ENSP00000369176,ENSP00000392709	COQ9, FXN, NDUFB2, NDUFB6, NDUFB8, NDUFS1
GO.0006520	cellular amino acid metabolic process	10	4.25E-05	ENSP00000219794,ENSP00000254035,ENSP00000290597,ENSP00000314649,ENSP00000318351,ENSP00000335304,ENSP00000364986,ENSP00000387123,ENSP00000418397,ENSP00000450436	AGMAT, ALDH4A1, ALDH5A1, ALDH6A1, ALDH7A1, BCKDHB, BCKDK, CKMT2, DLST, IVD
GO.0006793	phosphorus metabolic process	21	5.65E-05	ENSP00000217901,ENSP00000219794,ENSP00000241052,ENSP00000247866,ENSP00000254035,ENSP00000258770,ENSP00000262507,ENSP00000263035,ENSP00000299166,ENSP00000308334,ENSP00000314649,ENSP00000335304,ENSP00000346103,ENSP00000346921,ENSP00000366482,ENSP00000368605,ENSP00000369176,ENSP00000377470,ENSP00000384774,ENSP00000392709,ENSP00000419879	ACOT9, AK2, ALDH5A1, ATP5S, BCKDK, CAT, CDS2, CKMT2, CNP, COQ9, DHTKD1, DLST, FXN, GPX4, HK1, IDH3G, NDUFB2, NDUFB6, NDUFB8, NDUFS1, TBRG4
GO.0046496	nicotinamide nucleotide metabolic process	6	9.88E-05	ENSP00000217901,ENSP00000263035,ENSP00000320171,ENSP00000335304,ENSP00000369134,ENSP00000384774	DHTKD1, DLST, HK1, IDH3G, PDHA1, PKM
GO.0043648	dicarboxylic acid metabolic process	6	0.000103	ENSP00000217901,ENSP00000290597,ENSP00000314649,ENSP00000321070,ENSP00000335304,ENSP00000364649	ALDH4A1, ALDH5A1, DLST, IDH3G, ME2, SDHB

GO.0009083	branched-chain amino acid catabolic process	4	0.000103	ENSP00000219794,ENSP00000318351,ENSP00000418397,ENSP00000450436	ALDH6A1, BCKDHB, BCKDK, IVD
GO.0051186	cofactor metabolic process	9	0.000128	ENSP00000217901,ENSP00000262507,ENSP00000263035,ENSP00000320171,ENSP00000335304,ENSP00000366482,ENSP00000368605,ENSP00000384774,ENSP00000462972	ACOT9, COQ9, DHTKD1, DLST, FDXR, FXN, HK1, IDH3G, PKM
GO.0070125	mitochondrial translational elongation	6	0.000128	ENSP00000199706,ENSP00000253099,ENSP00000308901,ENSP00000356001,ENSP00000373404,ENSP00000424328	MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30
GO.0070126	mitochondrial translational termination	6	0.000128	ENSP00000199706,ENSP00000253099,ENSP00000308901,ENSP00000356001,ENSP00000373404,ENSP00000424328	MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30
GO.0006120	mitochondrial electron transport, NADH to ubiquinone	5	0.000133	ENSP00000247866,ENSP00000262507,ENSP00000299166,ENSP00000369176,ENSP00000392709	COQ9, NDUFB2, NDUFB6, NDUFB8, NDUFS1
GO.0046031	ADP metabolic process	5	0.000178	ENSP00000263035,ENSP00000320171,ENSP00000346921,ENSP00000369134,ENSP00000384774	AK2, DHTKD1, HK1, PDHA1, PKM
GO.1901565	organonitrogen compound catabolic process	9	0.000231	ENSP00000219794,ENSP00000241052,ENSP00000290597,ENSP00000314649,ENSP00000318351,ENSP00000335304,ENSP00000387123,ENSP00000418397,ENSP00000450436	ALDH4A1, ALDH5A1, ALDH6A1, ALDH7A1, BCKDHB, BCKDK, CAT, DLST, IVD
GO.1901605	alpha-amino acid metabolic process	8	0.000236	ENSP00000254035,ENSP00000290597,ENSP00000314649,ENSP00000335304,ENSP00000364986,ENSP00000387123,ENSP00000418397,ENSP00000450436	AGMAT, ALDH4A1, ALDH5A1, ALDH6A1, ALDH7A1, CKMT2, DLST, IVD
GO.1901575	organic substance catabolic process	18	0.000246	ENSP00000219794,ENSP00000241052,ENSP00000261733,ENSP00000263035,ENSP00000290597,ENSP00000314649,ENSP00000318351,ENSP00000320171,ENSP00000335304,ENSP00000340278,ENSP00000357535,ENSP00000369134,ENSP00000377470,ENSP00000384774,ENSP00000385638,ENSP00000387123,ENSP00000418397,ENSP00000450436	ALDH2, ALDH4A1, ALDH5A1, ALDH6A1, ALDH7A1, BCKDHB, BCKDK, CAT, CNP, DHTKD1, DLST, ECHS1, HADH, HK1, IVD, PARK7, PDHA1, PKM
GO.0006732	coenzyme metabolic process	8	0.000266	ENSP00000217901,ENSP00000262507,ENSP00000263035,ENSP00000320171,ENSP00000335304,ENSP00000368605,ENSP00000384774,ENSP00000462972	ACOT9, COQ9, DHTKD1, DLST, FDXR, HK1, IDH3G, PKM
GO.1901566	organonitrogen compound biosynthetic process	14	0.000428	ENSP00000199706,ENSP00000253099,ENSP00000263629,ENSP00000290597,ENSP00000308334,ENSP00000308901,ENSP00000320171,ENSP00000346921,ENSP00000356001,ENSP00000364986,ENSP00000366482,ENSP00000373404,ENSP00000387123,ENSP00000424328	AGMAT, AK2, ALDH4A1, ALDH7A1, ATP5S, FXN, MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30, MTIF2, PKM
GO.0042775	mitochondrial ATP synthesis coupled electron transport	5	0.000465	ENSP00000247866,ENSP00000262507,ENSP00000299166,ENSP00000369176,ENSP00000392709	COQ9, NDUFB2, NDUFB6, NDUFB8, NDUFS1
GO.0006090	pyruvate metabolic process	5	0.000498	ENSP00000263035,ENSP00000288050,ENSP00000354223,ENSP00000358640,ENSP00000384774	DHTKD1, HK1, MPC1, PDPR, SLC16A1
GO.0006734	NADH metabolic process	4	0.00113	ENSP00000217901,ENSP00000320171,ENSP00000335304,ENSP00000384774	DLST, HK1, IDH3G, PKM
GO.0046939	nucleotide phosphorylation	5	0.00123	ENSP00000263035,ENSP00000320171,ENSP00000346921,ENSP00000369134,ENSP00000384774	AK2, DHTKD1, HK1, PDHA1, PKM
GO.0014854	response to inactivity	3	0.00123	ENSP00000241052,ENSP00000320171,ENSP00000357057	CASQ1, CAT, PKM
GO.0016310	phosphorylation	14	0.00153	ENSP00000219794,ENSP00000247866,ENSP00000254035,ENSP00000258770,ENSP00000262507,ENSP00000263035,ENSP00000299166,ENSP00000320171,ENSP00000346921,ENSP00000366482,ENSP00000369134,ENSP00000369176,ENSP00000384774,ENSP00000392709	AK2, BCKDK, CKMT2, COQ9, DHTKD1, FXN, HK1, NDUFB2, NDUFB6, NDUFB8, NDUFS1, PDHA1, PKM, TBRG4

GO.1901606	alpha-amino acid catabolic process	5	0.00172	ENSP00000290597,ENSP00000335304,ENSP00000387123,ENSP00000418397,ENSP00000450436	ALDH4A1, ALDH6A1, ALDH7A1, DLST, IVD
GO.0044238	primary metabolic process	45	0.00184	ENSP00000169551,ENSP00000196371,ENSP00000199706,ENSP00000219794,ENSP00000247866,ENSP00000252785,ENSP00000253099,ENSP00000254035,ENSP00000258770,ENSP00000260665,ENSP00000261733,ENSP00000262507,ENSP00000263035,ENSP00000263629,ENSP00000270538,ENSP00000290597,ENSP00000299166,ENSP00000299518,ENSP00000308334,ENSP00000308901,ENSP00000316924,ENSP00000318351,ENSP00000346103,ENSP00000346921,ENSP00000356001,ENSP00000356218,ENSP00000357360,ENSP00000357535,ENSP00000358640,ENSP00000361993,ENSP00000364649,ENSP00000364986,ENSP00000366482,ENSP00000369176,ENSP00000373404,ENSP00000377470,ENSP00000384774,ENSP00000385638,ENSP00000387123,ENSP00000392709,ENSP00000418397,ENSP00000419879,ENSP00000424328,ENSP00000450436,ENSP00000462972	ACSS1, AGMAT, AK2, ALDH2, ALDH4A1, ALDH6A1, ALDH7A1, ATP5S, BCKDHB, BCKDK, CDS2, CKMT2, CNP, COQ9, CYB5R1, DHTKD1, ECHS1, FDXR, FXN, GPX4, HADH, HK1, IDH3A, IVD, LRPPRC, MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30, MTIF2, MTX1, NDUFB2, NDUFB6, NDUFB8, NDUFS1, OXCT1, SCO2, SDHB, SLC16A1, TBRG4, TIMM21, TIMM44, TIMM8A
GO.0006096	glycolytic process	4	0.00198	ENSP00000263035,ENSP00000320171,ENSP00000369134,ENSP00000384774	DHTKD1, HK1, PDHA1, PKM
GO.0032984	macromolecular complex disassembly	7	0.00249	ENSP00000199706,ENSP00000253099,ENSP00000263629,ENSP00000308901,ENSP00000356001,ENSP00000373404,ENSP00000424328	MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30, MTIF2
GO.0044237	cellular metabolic process	44	0.00317	ENSP00000169551,ENSP00000199706,ENSP00000219794,ENSP00000247866,ENSP00000253099,ENSP00000254035,ENSP00000260665,ENSP00000261070,ENSP00000261733,ENSP00000263035,ENSP00000263629,ENSP00000270538,ENSP00000288050,ENSP00000290597,ENSP00000299166,ENSP00000299518,ENSP00000308334,ENSP00000308901,ENSP00000317159,ENSP00000318351,ENSP00000321070,ENSP00000346103,ENSP00000346921,ENSP00000354223,ENSP00000356001,ENSP00000357360,ENSP00000357535,ENSP00000358640,ENSP00000361993,ENSP00000364986,ENSP00000366482,ENSP00000368605,ENSP00000369176,ENSP00000373404,ENSP00000377470,ENSP00000384774,ENSP00000385638,ENSP00000387123,ENSP00000392709,ENSP00000418397,ENSP00000419879,ENSP00000424328,ENSP00000450436,ENSP00000462972	ACOT9, AGMAT, AK2, ALDH2, ALDH4A1, ALDH6A1, ALDH7A1, ATP5S, BCKDHB, BCKDK, CDS2, CKMT2, CNP, COX17, CYC1, DHTKD1, ECHS1, FDXR, FXN, GPX4, HADH, HK1, IDH3A, IVD, LRPPRC, ME2, MPC1, MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30, MTIF2, MTX1, NDUFB2, NDUFB6, NDUFB8, NDUFS1, PDPR, SLC16A1, TIMM21, TIMM44, TIMM8A
GO.0006083	acetate metabolic process	2	0.00564	ENSP00000314649,ENSP00000316924	ACSS1, ALDH5A1
GO.0008152	metabolic process	47	0.0064	ENSP00000169551,ENSP00000199706,ENSP00000219794,ENSP00000247866,ENSP00000253099,ENSP00000254035,ENSP00000260665,ENSP00000261070,ENSP00000261733,ENSP00000263035,ENSP00000263629,ENSP00000270538,ENSP00000290597,ENSP00000299166,ENSP00000299518,ENSP00000300051,ENSP00000308334,ENSP00000308901,ENSP00000312618,ENSP00000317159,ENSP00000321070,ENSP00000326693,ENSP00000346103,ENSP00000346921,ENSP00000354223,ENSP00000356001,ENSP00000356218,ENSP00000357360,ENSP00000357535,ENSP00000361616,ENSP00000361993,ENSP00000364986,ENSP00000366482,ENSP00000368517,ENSP00000368605,ENSP00000369176,ENSP00000373404,ENSP00000384774,ENSP00000385638,ENSP00000387123,ENSP00000392709,ENSP00000398064,ENSP00000418397,ENSP00000419879,ENSP00000424328,ENSP00000450436,ENSP00000462972	ACAD9, ACOT9, AGMAT, AK2, ALDH2, ALDH4A1, ALDH6A1, ALDH7A1, ATP5S, BCKDK, CDS2, CKMT2, COMTD1, COX17, CYB5R1, CYC1, DHTKD1, ECHDC3, ECHS1, FDXR, FXN, GPX4, HADH, HIGD1A, HK1, IDH3A, IVD, LDHD, LRPPRC, ME2, MPC1, MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30, MTIF2, MTX1, NDUFB2, NDUFB6, NDUFB8, NDUFS1, SLC25A42, TIMM21, TIMM44, TIMM8A
GO.0014823	response to activity	4	0.00651	ENSP00000196371,ENSP00000241052,ENSP00000252785,ENSP00000385638	CAT, HADH, OXCT1, SCO2
GO.0006626	protein targeting to mitochondrion	4	0.00734	ENSP00000169551,ENSP00000270538,ENSP00000357360,ENSP00000361993	MTX1, TIMM21, TIMM44, TIMM8A
GO.0042180	cellular ketone metabolic process	4	0.00816	ENSP00000196371,ENSP00000262507,ENSP00000340278,ENSP00000462972	COQ9, FDXR, OXCT1, PARK7
GO.0071704	organic substance metabolic process	44	0.00842	ENSP00000169551,ENSP00000199706,ENSP00000219794,ENSP00000247866,ENSP00000252785,ENSP00000253099,ENSP00000254035,ENSP00000258770,ENSP00000260665,ENSP00000261733,ENSP00000263035,ENSP00000263629,ENSP00000270538,ENSP00000288050,ENSP00000290597,ENSP00000299166,ENSP00000299518,ENSP00000308334,ENSP00000308901,ENSP00000318351,ENSP00000321070,ENSP00000346103,ENSP00000346921,ENSP00000354223,ENSP00000356001,ENSP00000356218,ENSP00000357360,ENSP00000357535,ENSP00000361993,ENSP00000364986,ENSP00000366482,ENSP00000368605,ENSP00000369176,ENSP00000373404,ENSP00000377470,ENSP00000384774,ENSP00000385638,ENSP00000387123,ENSP00000392709,ENSP00000418397,ENSP00000419879,ENSP00000424328,ENSP00000450436,ENSP00000462972	ACOT9, AGMAT, AK2, ALDH2, ALDH4A1, ALDH6A1, ALDH7A1, ATP5S, BCKDHB, BCKDK, CDS2, CKMT2, CNP, CYB5R1, DHTKD1, ECHS1, FDXR, FXN, GPX4, HADH, HK1, IDH3A, IVD, LRPPRC, ME2, MPC1, MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30, MTIF2, MTX1, NDUFB2, NDUFB6, NDUFB8, NDUFS1, PDPR, SCO2, TBRG4, TIMM21, TIMM44, TIMM8A
GO.0030150	protein import into mitochondrial matrix	2	0.0165	ENSP00000169551,ENSP00000270538	TIMM21, TIMM44
GO.0006518	peptide metabolic process	8	0.0168	ENSP00000199706,ENSP00000253099,ENSP00000263629,ENSP00000308901,ENSP00000314649,ENSP00000356001,ENSP00000373404,ENSP00000424328	ALDH5A1, MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30, MTIF2
GO.0006066	alcohol metabolic process	7	0.0227	ENSP00000241052,ENSP00000261733,ENSP00000316924,ENSP00000340278,ENSP00000356218,ENSP00000387123,ENSP00000462972	ACSS1, ALDH2, ALDH7A1, CAT, CYB5R1, FDXR, PARK7
GO.0072329	monocarboxylic acid catabolic process	4	0.0243	ENSP00000290597,ENSP00000314649,ENSP00000357535,ENSP00000385638	ALDH4A1, ALDH5A1, ECHS1, HADH

GO.0014870	response to muscle inactivity	2	0.0321	ENSP00000320171,ENSP00000357057	CASQ1, PKM
GO.0042182	ketone catabolic process	2	0.0321	ENSP00000196371,ENSP00000340278	OXCT1, PARK7
GO.0044283	small molecule biosynthetic process	7	0.04	ENSP00000262507,ENSP00000290597,ENSP00000316924,ENSP00000320171,ENSP00000340278,ENSP00000356218,ENSP00000462972	ACSS1, ALDH4A1, COQ9, CYB5R1, FDXR, PARK7, PKM
GO.0034308	primary alcohol metabolic process	3	0.0407	ENSP00000261733,ENSP00000316924,ENSP00000340278	ACSS1, ALDH2, PARK7
GO.0034641	cellular nitrogen compound metabolic process	30	0.0421	ENSP00000199706,ENSP00000217901,ENSP00000241052,ENSP00000247866,ENSP00000252785,ENSP00000253099,ENSP00000254035,ENSP00000260665,ENSP00000262507,ENSP00000263035,ENSP00000263629,ENSP00000290597,ENSP00000299166,ENSP00000308334,ENSP00000308901,ENSP00000318351,ENSP00000346921,ENSP00000356001,ENSP00000364986,ENSP00000366482,ENSP00000369134,ENSP00000369176,ENSP00000373404,ENSP00000377470,ENSP00000384774,ENSP00000387123,ENSP00000392709,ENSP00000418397,ENSP00000424328,ENSP00000450436	AGMAT, AK2, ALDH4A1, ALDH6A1, ALDH7A1, ATP5S, BCKDHB, CAT, CKMT2, CNP, COQ9, DHTKD1, FXN, HK1, IDH3G, IVD, LRPPRC, MRPL18, MRPL2, MRPL28, MRPL4, MRPL45, MRPS30, MTIF2, NDUFB2, NDUFB6, NDUFB8, NDUFS1, PDHA1, SCO2

Supplemental Table 8

Biological processes by gene ontology (GO) categories in 41 differentially expressed proteins in intermyofibrillar mitochondria from obese that met false discovery rate criteria (P≤0.05). Analysis was performed using the STRING database.

Pathway ID	Pathway description	Observed gene count	False discovery rate	Matching proteins in your network (IDs)	Matching proteins in your network (labels)
GO.0044281	small molecule metabolic process	23	2.69E-11	ENSP00000247866,ENSP00000259037,ENSP00000261733,ENSP00000262030,ENSP00000281455,ENSP00000290597,ENSP00000300441,ENSP00000326305,ENSP00000335261,ENSP00000340684,ENSP00000345774,ENSP00000346173,ENSP00000347988,ENSP00000352706,ENSP00000354813,ENSP00000369176,ENSP00000379503,ENSP00000379895,ENSP00000389649,ENSP00000409612,ENSP00000419325,ENSP00000420927,ENSP00000450436	ACADM, ACSF2, ACSL1, ALDH2, ALDH3A2, ALDH4A1, ALDH6A1, ATP5B, ATP5J, ETFB, GATM, HIBCH, MAOA, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6, PDK2, PDP1, SLC25A20, SUCLG2, TMLHE
GO.0044710	single-organism metabolic process	28	9.71E-11	ENSP00000247461,ENSP00000247866,ENSP00000259037,ENSP00000261733,ENSP00000281455,ENSP00000290597,ENSP00000298510,ENSP00000300408,ENSP00000300441,ENSP00000305682,ENSP00000324173,ENSP00000326305,ENSP00000335261,ENSP00000340684,ENSP00000345774,ENSP00000346173,ENSP00000347988,ENSP00000352706,ENSP00000354580,ENSP00000354813,ENSP00000369176,ENSP00000379503,ENSP00000379895,ENSP00000389649,ENSP00000409612,ENSP00000419325,ENSP00000420927,ENSP00000450436	ACADM, ACSF2, ACSL1, ALDH2, ALDH3A2, ALDH4A1, ALDH6A1, ATP5J, CANX, ETFB, GATM, HIBCH, HSPA5, MAOA, MRPL21, MRPL39, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6, PDK2, PDP1, PHB, PRDX3, SLC25A20, SUCLG2, TMLHE
GO.0055114	oxidation-reduction process	17	1.82E-10	ENSP00000247866,ENSP00000259037,ENSP00000261733,ENSP00000262030,ENSP00000290597,ENSP00000298510,ENSP00000335261,ENSP00000340684,ENSP00000345774,ENSP00000346173,ENSP00000347988,ENSP00000354813,ENSP00000369176,ENSP00000389649,ENSP00000409612,ENSP00000419325,ENSP00000450436	ACADM, ALDH2, ALDH3A2, ALDH4A1, ALDH6A1, ATP5B, ATP5J, ETFB, MAOA, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6, PRDX3, SUCLG2, TMLHE
GO.0045333	cellular respiration	9	3.88E-08	ENSP00000247866,ENSP00000259037,ENSP00000262030,ENSP00000346173,ENSP00000347988,ENSP00000354813,ENSP00000369176,ENSP00000389649,ENSP00000419325	ATP5B, ATP5J, ETFB, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6, SUCLG2
GO.0022904	respiratory electron transport chain	8	9.34E-08	ENSP00000247866,ENSP00000259037,ENSP00000262030,ENSP00000346173,ENSP00000347988,ENSP00000354813,ENSP00000369176,ENSP00000389649	ATP5B, ATP5J, ETFB, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6
GO.0046034	ATP metabolic process	7	1.87E-05	ENSP00000247866,ENSP00000259037,ENSP00000262030,ENSP00000347988,ENSP00000354813,ENSP00000369176,ENSP00000389649	ATP5B, ATP5J, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6
GO.0006120	mitochondrial electron transport, NADH to ubiquinone	5	2.27E-05	ENSP00000247866,ENSP00000259037,ENSP00000347988,ENSP00000354813,ENSP00000369176	MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6
GO.0071704	organic substance metabolic process	30	2.32E-05	ENSP00000226299,ENSP00000246957,ENSP00000247866,ENSP00000259037,ENSP00000261733,ENSP00000281455,ENSP00000290597,ENSP00000298510,ENSP00000300441,ENSP00000305682,ENSP00000318115,ENSP00000324173,ENSP00000326305,ENSP00000335261,ENSP00000345774,ENSP00000347988,ENSP00000352706,ENSP00000354580,ENSP00000354813,ENSP00000368605,ENSP00000369176,ENSP00000370377,ENSP00000379503,ENSP00000379895,ENSP00000389649,ENSP00000409612,ENSP00000419325,ENSP00000420927,ENSP00000438465,ENSP00000450436	ACADM, ACOT9, ACSF2, ACSL1, ALDH2, ALDH3A2, ALDH4A1, ALDH6A1, ATP5J, GATM, HIBCH, HSPA5, LAP3, MRPL21, MRPL39, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6, PDK2, PDP1, PGAM5, PITRM1, PRDX3, SLC25A20, SUCLG2, TIMM50, TMLHE, TRAP1
GO.0019752	carboxylic acid metabolic process	11	2.60E-05	ENSP00000281455,ENSP00000290597,ENSP00000300441,ENSP00000335261,ENSP00000352706,ENSP00000379503,ENSP00000379895,ENSP00000409612,ENSP00000419325,ENSP00000420927,ENSP00000450436	ACADM, ACSF2, ACSL1, ALDH4A1, ALDH6A1, GATM, HIBCH, PDK2, PDP1, SUCLG2, TMLHE
GO.0044237	cellular metabolic process	29	3.70E-05	ENSP00000246957,ENSP00000247866,ENSP00000259037,ENSP00000261733,ENSP00000262030,ENSP00000290597,ENSP00000298510,ENSP00000300441,ENSP00000305682,ENSP00000318115,ENSP00000324173,ENSP00000326305,ENSP00000335261,ENSP00000345774,ENSP00000346173,ENSP00000347988,ENSP00000352706,ENSP00000354580,ENSP00000354813,ENSP00000368605,ENSP00000369176,ENSP00000379503,ENSP00000379895,ENSP00000389649,ENSP00000409612,ENSP00000419325,ENSP00000420927,ENSP00000438465,ENSP00000450436	ACADM, ACOT9, ACSF2, ALDH2, ALDH3A2, ALDH4A1, ALDH6A1, ATP5B, ATP5J, ETFB, GATM, HIBCH, HSPA5, MRPL21, MRPL39, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6, PDK2, PDP1, PGAM5, PRDX3, SLC25A20, SUCLG2, TIMM50, TMLHE, TRAP1
GO.0042775	mitochondrial ATP synthesis coupled electron transport	5	4.20E-05	ENSP00000247866,ENSP00000259037,ENSP00000347988,ENSP00000354813,ENSP00000369176	MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6
GO.0006119	oxidative phosphorylation	5	6.99E-05	ENSP00000247866,ENSP00000259037,ENSP00000347988,ENSP00000354813,ENSP00000369176	MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6
GO.0006793	phosphorus metabolic process	14	1.86E-04	ENSP00000247866,ENSP00000259037,ENSP00000262030,ENSP00000281455,ENSP00000318115,ENSP00000347988,ENSP00000354813,ENSP00000368605,ENSP00000369176,ENSP00000379503,ENSP00000389649,ENSP00000419325,ENSP00000420927,ENSP00000438465	ACOT9, ACSL1, ATP5B, ATP5J, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6, PDK2, PDP1, PGAM5, SUCLG2, TIMM50
GO.0044238	primary metabolic process	28	2.37E-04	ENSP00000226299,ENSP00000246957,ENSP00000247866,ENSP00000259037,ENSP00000261733,ENSP00000281455,ENSP00000290597,ENSP00000298510,ENSP00000300441,ENSP00000305682,ENSP00000318115,ENSP00000324173,ENSP00000326305,ENSP00000345774,ENSP00000347988,ENSP00000352706,ENSP00000354580,ENSP00000354813,ENSP00000369176,ENSP00000370377,ENSP00000379503,ENSP00000379895,ENSP00000389649,ENSP00000409612,ENSP00000419325,ENSP00000420927,ENSP00000438465,ENSP00000450436	ACADM, ACSF2, ACSL1, ALDH2, ALDH3A2, ALDH4A1, ALDH6A1, ATP5J, GATM, HIBCH, HSPA5, LAP3, MRPL21, MRPL39, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6, PDK2, PDP1, PGAM5, PITRM1, PRDX3, SLC25A20, SUCLG2, TIMM50, TRAP1
GO.1901564	organonitrogen compound metabolic process	13	2.51E-04	ENSP00000247866,ENSP00000259037,ENSP00000262030,ENSP00000290597,ENSP00000305682,ENSP00000347988,ENSP00000352706,ENSP00000354580,ENSP00000354813,ENSP00000369176,ENSP00000379895,ENSP00000389649,ENSP00000450436	ALDH4A1, ALDH6A1, ATP5B, ATP5J, GATM, HIBCH, MRPL21, MRPL39, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6
GO.0008152	metabolic process	29	4.70E-04	ENSP00000226299,ENSP00000246957,ENSP00000247866,ENSP00000259037,ENSP00000261733,ENSP00000290597,ENSP00000298510,ENSP00000300441,ENSP00000305682,ENSP00000318115,ENSP00000324173,ENSP00000326305,ENSP00000335261,ENSP00000345774,ENSP00000346173,ENSP00000347988,ENSP00000352706,ENSP00000354580,ENSP00000354813,ENSP00000368605,ENSP00000369176,ENSP00000370377,ENSP00000379503,ENSP00000389649,ENSP00000409612,ENSP00000419325,ENSP00000420927,ENSP00000438465,ENSP00000450436	ACADM, ACOT9, ACSF2, ALDH2, ALDH3A2, ALDH4A1, ALDH6A1, ATP5J, ETFB, HIBCH, HSPA5, LAP3, MRPL21, MRPL39, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6, PDK2, PDP1, PGAM5, PITRM1, PRDX3, SLC25A20, SUCLG2, TIMM50, TMLHE, TRAP1

GO.0055086	nucleobase-containing small molecule metabolic process	8	4.70E-04	ENSP00000247866,ENSP00000259037,ENSP00000262030,ENSP00000347988,ENSP00000354813,ENSP00000369176,ENSP00000389649,ENSP00000450436	ALDH6A1, ATP5B, ATP5J, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6
GO.0032787	monocarboxylic acid metabolic process	7	3.28E-03	ENSP00000281455,ENSP00000290597,ENSP00000300441,ENSP00000335261,ENSP00000379503,ENSP00000409612,ENSP00000420927	ACADM, ACSF2, ACSL1, ALDH4A1, PDK2, PDP1, TMLHE
GO.0006574	valine catabolic process	2	5.52E-03	ENSP00000352706,ENSP00000450436	ALDH6A1, HIBCH
GO.0044763	single-organism cellular process	28	6.98E-03	ENSP00000247461,ENSP00000247866,ENSP00000259037,ENSP00000261733,ENSP00000290597,ENSP00000298510,ENSP00000300408,ENSP00000300441,ENSP00000305682,ENSP00000318115,ENSP00000324173,ENSP00000326305,ENSP00000335261,ENSP00000340684,ENSP00000345774,ENSP00000346173,ENSP00000347988,ENSP00000352706,ENSP00000354580,ENSP00000354813,ENSP00000369176,ENSP00000379503,ENSP00000379895,ENSP00000409612,ENSP00000419325,ENSP00000420927,ENSP00000438465,ENSP00000450436	ACADM, ACSF2, ALDH2, ALDH3A2, ALDH4A1, ALDH6A1, CANX, ETFB, GATM, HIBCH, HSPA5, MAOA, MRPL21, MRPL39, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6, PDK2, PDP1, PGAM5, PHB, PRDX3, SLC25A20, SUCLG2, TIMM50, TMLHE
GO.0045329	carnitine biosynthetic process	2	8.81E-03	ENSP00000335261,ENSP00000409612	ACADM, TMLHE
GO.0007005	mitochondrion organization	6	1.46E-02	ENSP00000262030,ENSP00000298510,ENSP00000300408,ENSP00000305682,ENSP00000318115,ENSP00000354580	ATP5B, MRPL21, MRPL39, PHB, PRDX3, TIMM50
GO.0044282	small molecule catabolic process	5	1.68E-02	ENSP00000261733,ENSP00000290597,ENSP00000352706,ENSP00000409612,ENSP00000450436	ACADM, ALDH2, ALDH4A1, ALDH6A1, HIBCH
GO.0006796	phosphate-containing compound metabolic process	11	2.04E-02	ENSP00000247866,ENSP00000259037,ENSP00000262030,ENSP00000318115,ENSP00000347988,ENSP00000354813,ENSP00000369176,ENSP00000379503,ENSP00000389649,ENSP00000420927,ENSP00000438465	ATP5B, ATP5J, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6, PDK2, PDP1, PGAM5, TIMM50
GO.1990542	mitochondrial transmembrane transport	3	2.04E-02	ENSP00000262030,ENSP00000326305,ENSP00000389649	ATP5B, ATP5J, SLC25A20
GO.0034975	protein folding in endoplasmic reticulum	2	2.14E-02	ENSP00000247461,ENSP00000324173	CANX, HSPA5
GO.0006839	mitochondrial transport	4	3.33E-02	ENSP00000262030,ENSP00000318115,ENSP00000326305,ENSP00000389649	ATP5B, ATP5J, SLC25A20, TIMM50
GO.0006637	acyl-CoA metabolic process	3	4.19E-02	ENSP00000281455,ENSP00000368605,ENSP00000419325	ACOT9, ACSL1, SUCLG2
GO.1901135	carbohydrate derivative metabolic process	8	4.19E-02	ENSP00000247461,ENSP00000247866,ENSP00000259037,ENSP00000262030,ENSP00000347988,ENSP00000354813,ENSP00000369176,ENSP00000389649	ATP5B, ATP5J, CANX, MT-ND5, NDUFA5, NDUFB2, NDUFB5, NDUFB6
GO.0044711	single-organism biosynthetic process	9	4.31E-02	ENSP00000262030,ENSP00000281455,ENSP00000290597,ENSP00000305682,ENSP00000335261,ENSP00000354580,ENSP00000379895,ENSP00000389649,ENSP00000409612	ACADM, ACSL1, ALDH4A1, ATP5B, ATP5J, GATM, MRPL21, MRPL39, TMLHE
GO.0010510	regulation of acetyl-CoA biosynthetic process from pyruvate	2	4.44E-02	ENSP00000379503,ENSP00000420927	PDK2, PDP1

Supplemental Table 9

Mapped pathways associated with subsarcolemmal-to-intermyofibrillar mitochondrial protein abundance ratios of 290 mitochondrial identified in both mitochondrial fractions and in both the subjects with obesity and the lean controls that met false discovery rate (FDR) criteria (*P* ≤ 0.05). Analysis was performed using the Reactome Software.

Pathway identifier	Pathway name	#Entities found	Entities pValue	Entities FDR	Mapped entities
R-HSA-611105	Respiratory electron transport	3	7.56E-06	8.37E-05	NDUB6;CY1;NU5M
R-HSA-163200	Respiratory electron transport, ATP synthesis by chemiosmotic coupling, and heat production by uncoupling proteins.	3	1.40E-05	8.37E-05	NDUB6;CY1;NU5M
R-HSA-1428517	The citric acid (TCA) cycle and respiratory electron transport	3	3.51E-05	1.40E-04	NDUB6;CY1;NU5M
R-HSA-6799198	Complex I biogenesis	2	2.46E-04	5.11E-04	NDUB6;NU5M
R-HSA-1430728	Metabolism	5	2.56E-04	5.11E-04	NDUB6;KAD2;CY1;KCRS;NU5M
R-HSA-71288	Creatine metabolism	1	4.52E-03	9.05E-03	KCRS
R-HSA-499943	Interconversion of nucleotide di- and triphosphates	1	1.44E-02	1.44E-02	KAD2
R-HSA-1268020	Mitochondrial protein import	1	2.91E-02	2.91E-02	CY1
R-HSA-351202	Metabolism of polyamines	1	3.79E-02	3.79E-02	KCRS
R-HSA-15869	Metabolism of nucleotides	1	4.67E-02	4.67E-02	KAD2