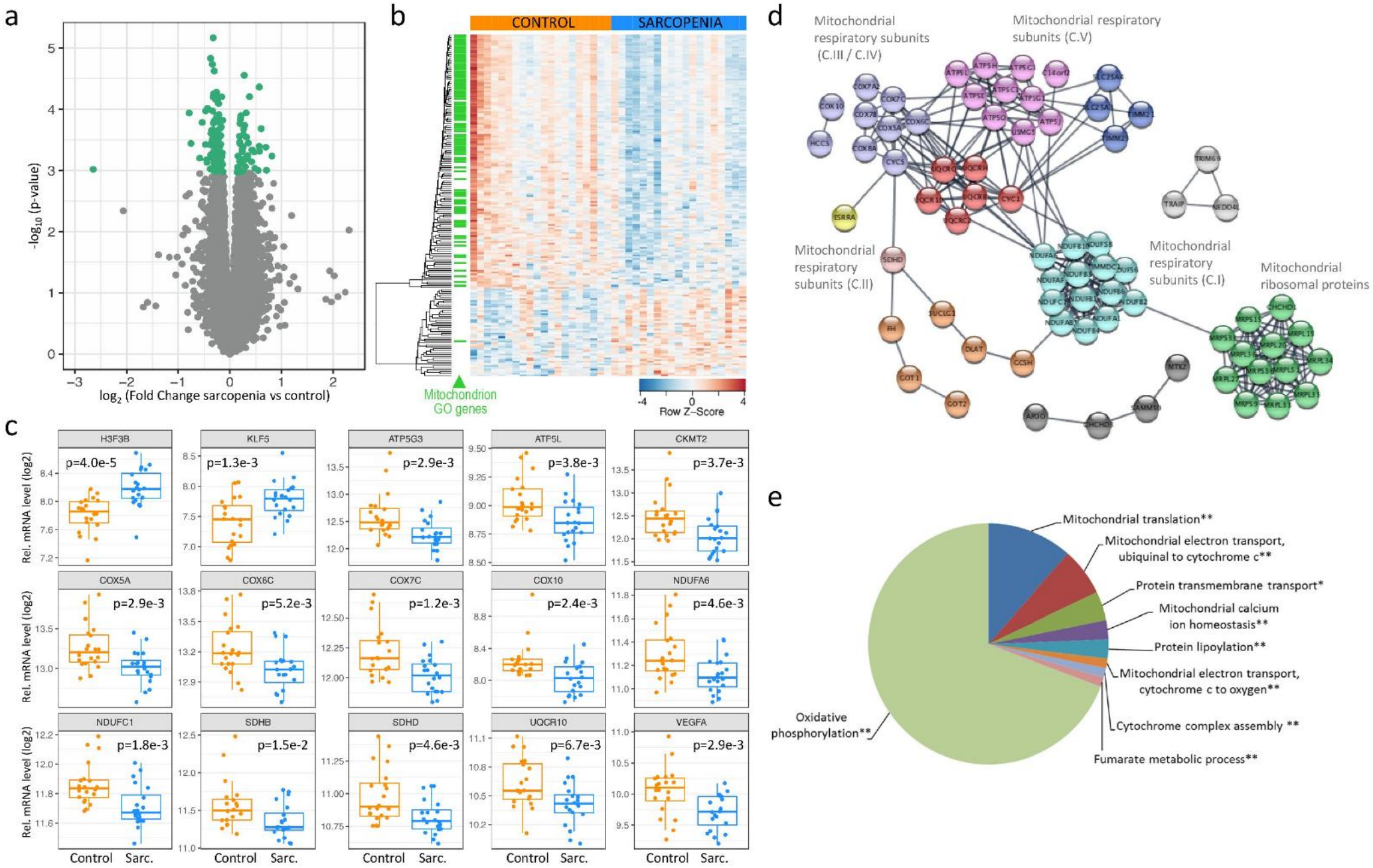
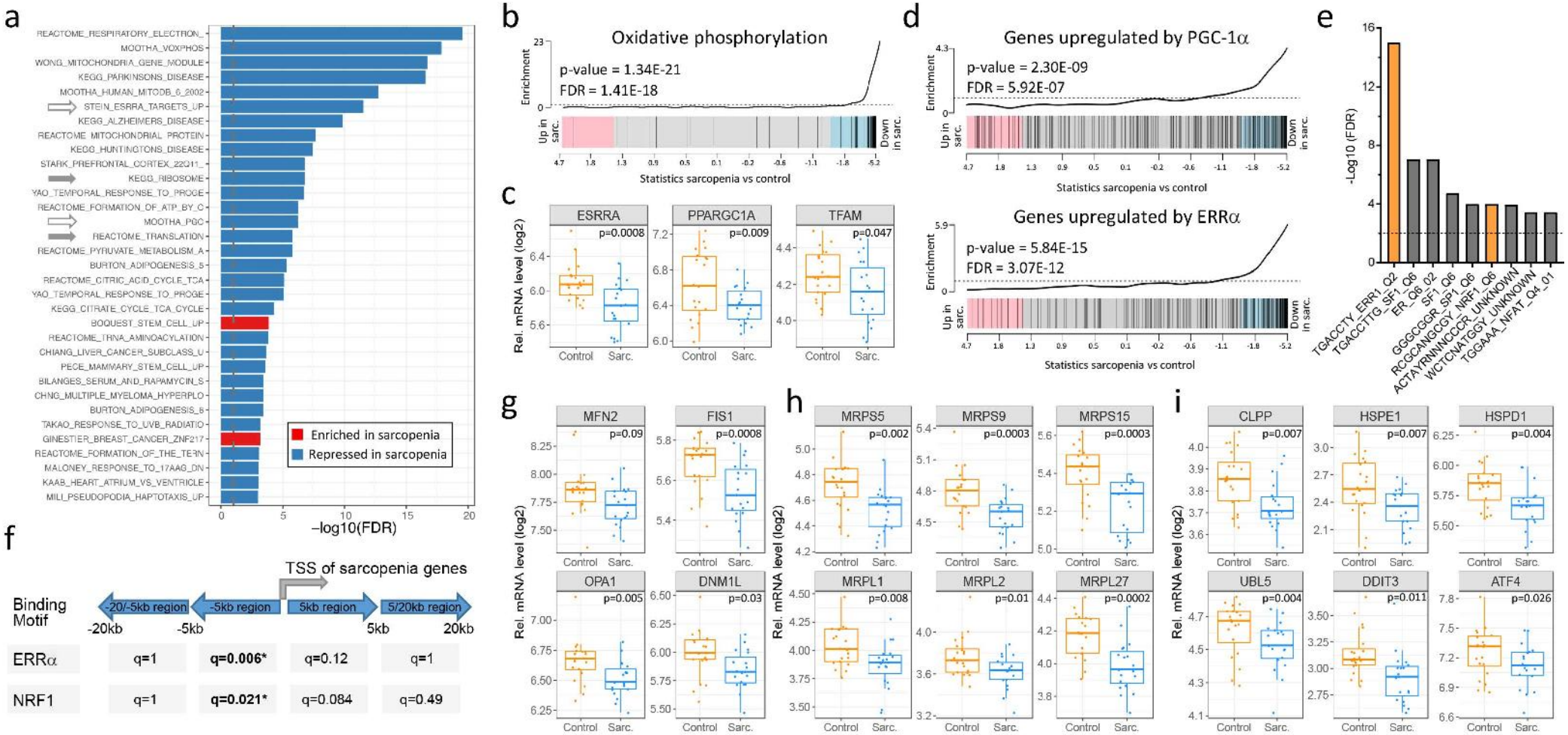
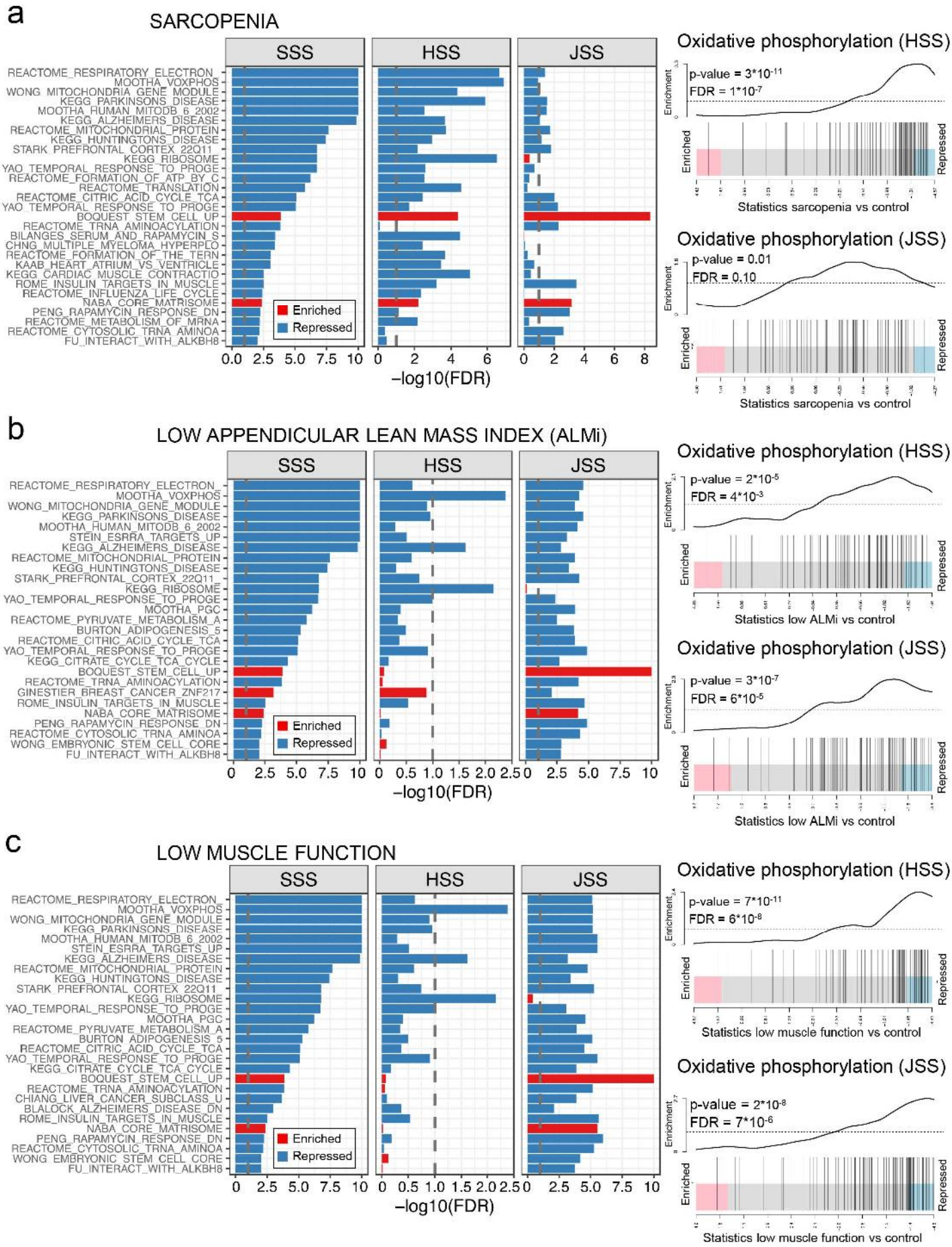
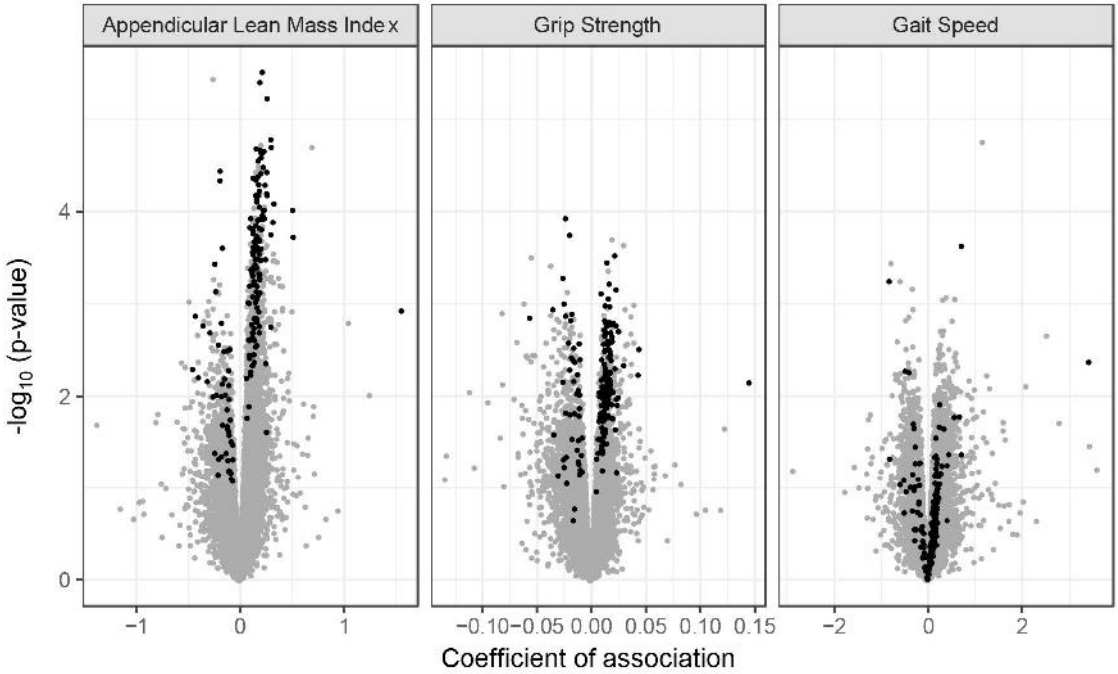

a
-log10 (p-value)
log2 (Fold Change sarcopenia vs control)
b
CONTROL
SARCOPENIA
Mitochondrion GO genes
Row Z-Score
c
H3F3B
p=4.0e-5
KLF5
p=1.3e-3
ATP5G3
p=2.9e-3
ATP5L
p=3.8e-3
CKMT2
p=3.7e-3
COX5A
p=2.9e-3
COX6C
p=5.2e-3
COX7C
p=1.2e-3
COX10
p=2.4e-3
NDUFA6
p=4.6e-3
NDUFC1
p=1.8e-3
SDHB
p=1.5e-2
SDHD
p=4.6e-3
UQCR10
p=6.7e-3
VEGFA
p=2.9e-3
Rel. mRNA level (log2)
Control
Sarc.
d
Mitochondrial respiratory subunits (C.III / C.IV)
Mitochondrial respiratory subunits (C.V)
Mitochondrial respiratory subunits (C.II)
Mitochondrial respiratory subunits (C.I)
Mitochondrial ribosomal proteins
e
Mitochondrial translation**
Mitochondrial electron transport, ubiquinal to cytochrome c**
Protein transmembrane transport*
Mitochondrial calcium ion homeostasis**
Protein lipoylation**
Mitochondrial electron transport, cytochrome c to oxygen**
Cytochrome complex assembly **
Fumarate metabolic process**
Oxidative phosphorylation**

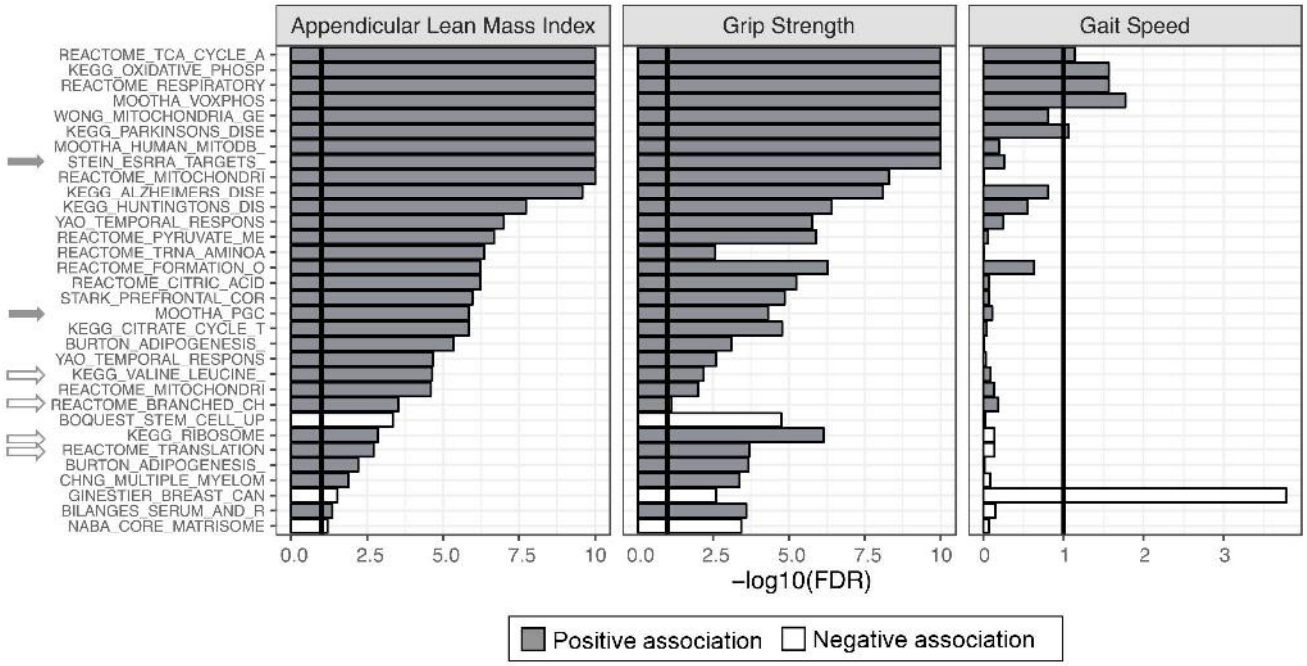

a
REACTOME_RESPIRATORY_ELECTRON_
MOOTHA_VOXPHOS
WONG_MITOCHONDRIA_GENE_MODULE
KEGG_PARKINSONS_DISEASE
MOOTHA_HUMAN_MITODB_6_2002
STEIN_ESRRA_TARGETS_UP
KEGG_ALZHEIMERS_DISEASE
REACTOME_MITOCHONDRIAL_PROTEIN
KEGG_HUNTINGTONS_DISEASE
STARK_PREFRONTAL_CORTEX_22Q11_
KEGG_RIBOSOME
YAO_TEMPORAL_RESPONSE_TO_PROGE
REACTOME_FORMATION_OF_ATP_BY_C
MOOTHA_PGC
REACTOME_TRANSLATION
REACTOME_PYRUVATE_METABOLISM_A
BURTON_ADIPOGENESIS_5
REACTOME_CITRIC_ACID_CYCLE_TCA
YAO_TEMPORAL_RESPONSE_TO_PROGE
KEGG_CITRATE_CYCLE_TCA_CYCLE
BOQUEST_STEM_CELL_UP
REACTOME_TRNA_AMINOACYLATION
CHIANG_LIVER_CANCER_SUBCLASS_U
PECE_MAMMARY_STEM_CELL_UP
BILANGES_SERUM_AND_RAPAMYCIN_S
CHNG_MULTIPLE_MYELOMA_HYPERPLO
BURTON_ADIPOGENESIS_6
TAKAO_RESPONSE_TO_UVB_RADIATIO
GINESTIER_BREAST_CANCER_ZNF217
REACTOME_FORMATION_OF_THE_TERN
MALONEY_RESPONSE_TO_17AAG_DN
KAAB_HEART_ATRIUM_VS_VENTRICLE
MILI_PSEUDOPODIA_HAPTOTAXIS_UP
Enriched in sarcopenia
Repressed in sarcopenia
−log10(FDR)
b
Oxidative phosphorylation
p-value = 1.34E-21
FDR = 1.41E-18
Enrichment
Up in sarc.
Down in sarc.
Statistics sarcopenia vs control
c
ESRRA
p=0.0008
PPARGC1A
p=0.009
TFAM
p=0.047
Rel. mRNA level (log2)
Control
Sarc.
d
Genes upregulated by PGC-1α
p-value = 2.30E-09
FDR = 5.92E-07
Genes upregulated by ERRα
p-value = 5.84E-15
FDR = 3.07E-12
Statistics sarcopenia vs control
e
-Log10 (FDR)
TGACCTY_ERR1_Q2
TGACCTTG_SF1_Q6
ER_Q6_02
SF1_Q6
GGGCGGR_SP1_Q6
RCGCANGCGY_NRF1_Q6
ACTAYRNNNCCCR_UNKNOWN
WCTCNATGGY_UNKNOWN
TGGAAA_NFAT_Q4_01
f
TSS of sarcopenia genes
Binding Motif
-20/-5kb region
-5kb region
5kb region
5/20kb region
-20kb
-5kb
5kb
20kb
ERRα q=1 q=0.006* q=0.12 q=1
NRF1 q=1 q=0.021* q=0.084 q=0.49
g
MFN2
p=0.09
FIS1
p=0.0008
OPA1
p=0.005
DNM1L
p=0.03
h
MRPS5
p=0.002
MRPS9
p=0.0003
MRPS15
p=0.0003
MRPL1
p=0.008
MRPL2
p=0.01
MRPL27
p=0.0002
i
CLPP
p=0.007
HSPE1
p=0.007
HSPD1
p=0.004
UBL5
p=0.004
DDIT3
p=0.011
ATF4
p=0.026

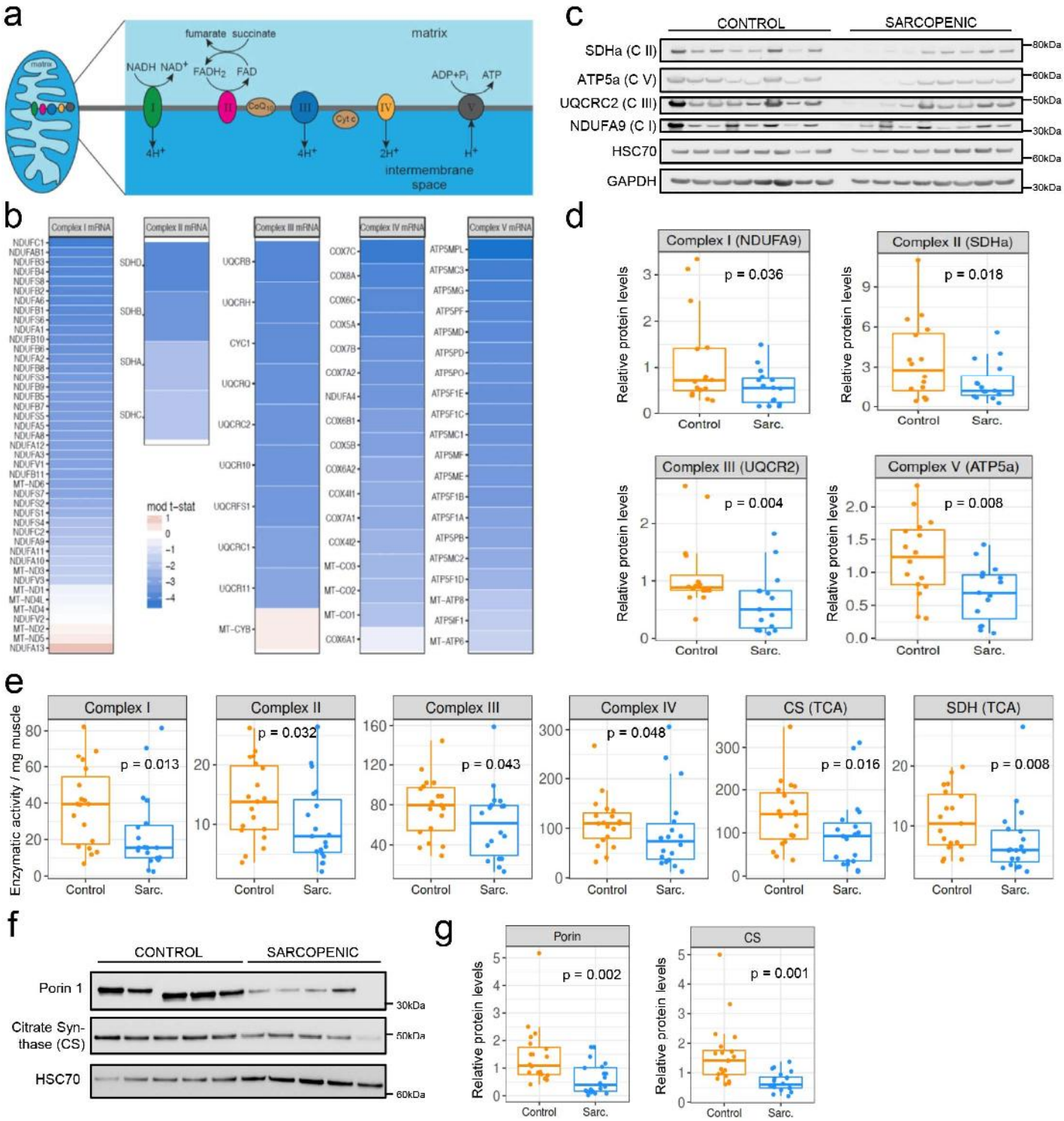

a
SARCOPENIA
SSS
HSS
JSS
REACTOME_RESPIRATORY_ELECTRON_
MOOTHA_VOXPHOS
WONG_MITOCHONDRIA_GENE_MODULE
KEGG_PARKINSONS_DISEASE
MOOTHA_HUMAN_MITODB_6_2002
KEGG_ALZHEIMERS_DISEASE
REACTOME_MITOCHONDRIAL_PROTEIN
KEGG_HUNTINGTONS_DISEASE
STARK_PREFRONTAL_CORTEX_22Q11_
KEGG_RIBOSOME
YAO_TEMPORAL_RESPONSE_TO_PROGE
REACTOME_FORMATION_OF_ATP_BY_C
REACTOME_TRANSLATION
REACTOME_CITRIC_ACID_CYCLE_TCA
YAO_TEMPORAL_RESPONSE_TO_PROGE
BOQUEST_STEM_CELL_UP
REACTOME_TRNA_AMINOACYLATION
BILANGES_SERUM_AND_RAPAMYCIN_S
CHNG_MULTIPLE_MYELOMA_HYPERPLO
REACTOME_FORMATION_OF_THE_TERN
KAAB_HEART_ATRIUM_VS_VENTRICLE
KEGG_CARDIAC_MUSCLE_CONTRACTIO
ROME_INSULIN_TARGETS_IN_MUSCLE
REACTOME_INFLUENZA_LIFE_CYCLE
NABA_CORE_MATRISOME
PENG_RAPAMYCIN_RESPONSE_DN
REACTOME_METABOLISM_OF_MRNA
REACTOME_CYTOSOLIC_TRNA_AMINOA
FU_INTERACT_WITH_ALKBH8
Enriched
Repressed
0.0 2.5 5.0 7.5 10
0 2 4 6
0 2 4 6 8
−log10(FDR)
Oxidative phosphorylation (HSS)
p-value = 3*10-11
FDR = 1*10-7
Enrichment
Enriched
Repressed
Statistics sarcopenia vs control
Oxidative phosphorylation (JSS)
p-value = 0.01
FDR = 0.10
Statistics sarcopenia vs control
b
LOW APPENDICULAR LEAN MASS INDEX (ALMi)
SSS
HSS
JSS
REACTOME_RESPIRATORY_ELECTRON_
MOOTHA_VOXPHOS
WONG_MITOCHONDRIA_GENE_MODULE
KEGG_PARKINSONS_DISEASE
MOOTHA_HUMAN_MITODB_6_2002
STEIN_ESRRA_TARGETS_UP
KEGG_ALZHEIMERS_DISEASE
REACTOME_MITOCHONDRIAL_PROTEIN
KEGG_HUNTINGTONS_DISEASE
STARK_PREFRONTAL_CORTEX_22Q11_
KEGG_RIBOSOME
YAO_TEMPORAL_RESPONSE_TO_PROGE
MOOTHA_PGC
REACTOME_PYRUVATE_METABOLISM_A
BURTON_ADIPOGENESIS_5
REACTOME_CITRIC_ACID_CYCLE_TCA
YAO_TEMPORAL_RESPONSE_TO_PROGE
KEGG_CITRATE_CYCLE_TCA_CYCLE
BOQUEST_STEM_CELL_UP
REACTOME_TRNA_AMINOACYLATION
GINESTIER_BREAST_CANCER_ZNF217
ROME_INSULIN_TARGETS_IN_MUSCLE
NABA_CORE_MATRISOME
PENG_RAPAMYCIN_RESPONSE_DN
REACTOME_CYTOSOLIC_TRNA_AMINOA
WONG_EMBRYONIC_STEM_CELL_CORE
FU_INTERACT_WITH_ALKBH8
Enriched
Repressed
0 2.5 5.0 7.5 10
0 0.5 1.0 1.5 2.0 2.5
0 2.5 5.0 7.5 10
−log10(FDR)
Oxidative phosphorylation (HSS)
p-value = 2*10-5
FDR = 4*10-3
Statistics low ALMi vs control
Oxidative phosphorylation (JSS)
p-value = 3*10-7
FDR = 6*10-5
Statistics low ALMi vs control
c
LOW MUSCLE FUNCTION
SSS
HSS
JSS
REACTOME_RESPIRATORY_ELECTRON_
MOOTHA_VOXPHOS
WONG_MITOCHONDRIA_GENE_MODULE
KEGG_PARKINSONS_DISEASE
MOOTHA_HUMAN_MITODB_6_2002
STEIN_ESRRA_TARGETS_UP
KEGG_ALZHEIMERS_DISEASE
REACTOME_MITOCHONDRIAL_PROTEIN
KEGG_HUNTINGTONS_DISEASE
STARK_PREFRONTAL_CORTEX_22Q11_
KEGG_RIBOSOME
YAO_TEMPORAL_RESPONSE_TO_PROGE
MOOTHA_PGC
REACTOME_PYRUVATE_METABOLISM_A
BURTON_ADIPOGENESIS_5
REACTOME_CITRIC_ACID_CYCLE_TCA
YAO_TEMPORAL_RESPONSE_TO_PROGE
KEGG_CITRATE_CYCLE_TCA_CYCLE
BOQUEST_STEM_CELL_UP
REACTOME_TRNA_AMINOACYLATION
CHIANG_LIVER_CANCER_SUBCLASS_U
BLALOCK_ALZHEIMERS_DISEASE_DN
ROME_INSULIN_TARGETS_IN_MUSCLE
NABA_CORE_MATRISOME
PENG_RAPAMYCIN_RESPONSE_DN
REACTOME_CYTOSOLIC_TRNA_AMINOA
WONG_EMBRYONIC_STEM_CELL_CORE
FU_INTERACT_WITH_ALKBH8
Enriched
Repressed
0 2.5 5.0 7.5 10
0 0.5 1.0 1.5 2.0 2.5
0 2.5 5.0 7.5 10
−log10(FDR)
Oxidative phosphorylation (HSS)
p-value = 7*10-11
FDR = 6*10-8
Statistics low muscle function vs control
Oxidative phosphorylation (JSS)
p-value = 2*10-8
FDR = 7*10-6
Statistics low muscle function vs control

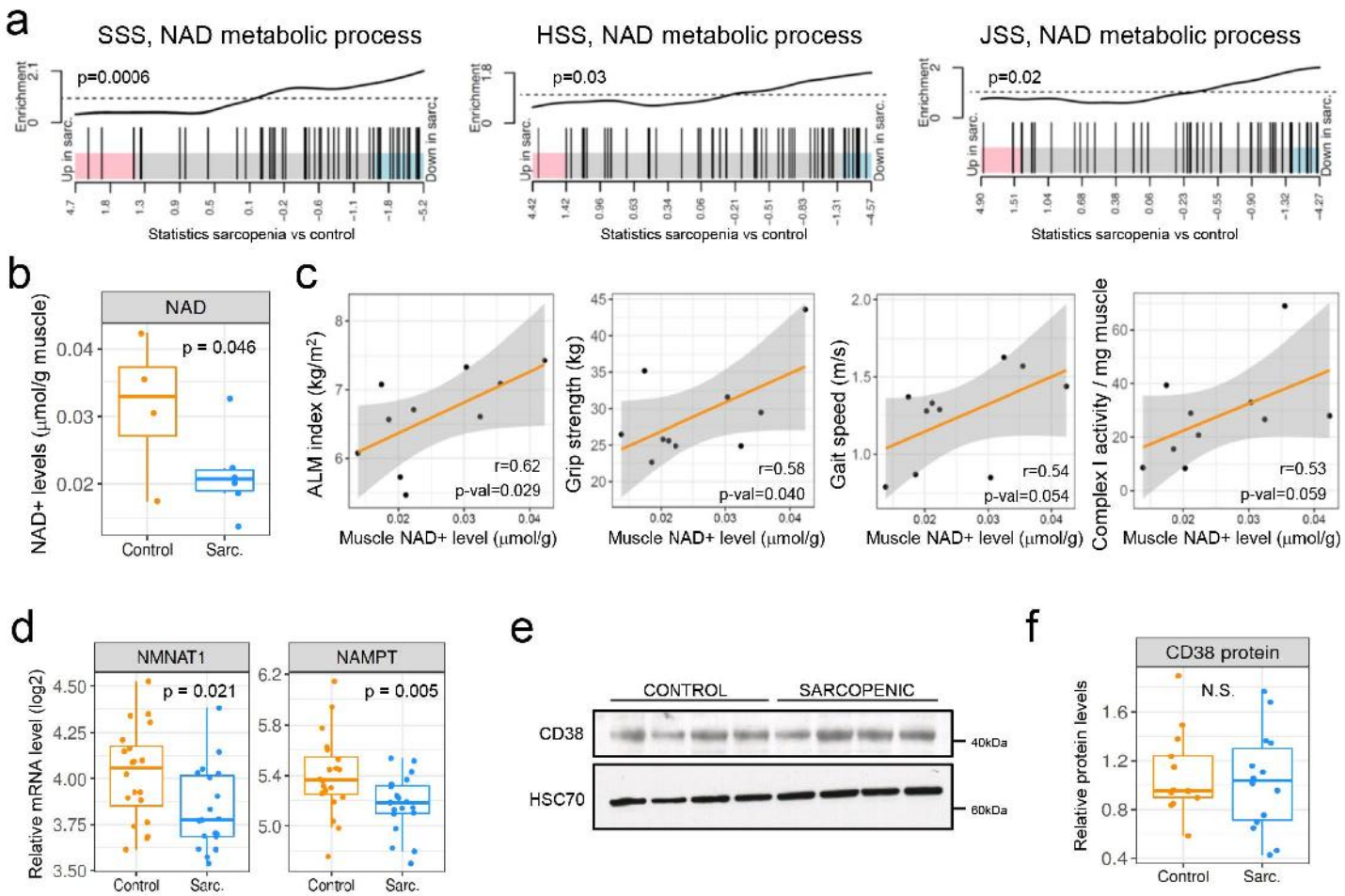
a


Appendicular Lean Mass Index
Grip Strength
Gait Speed
-log10 (p-value)
Coefficient of association

b


Appendicular Lean Mass Index
Grip Strength
Gait Speed
REACTOME_TCA_CYCLE_A
KEGG_OXIDATIVE_PHOSP
REACTOME_RESPIRATORY
MOOTHA_VOXPHOS
WONG_MITOCHONDRIA_GE
KEGG_PARKINSONS_DISE
MOOTHA_HUMAN_MITODB_
STEIN_ESRRA_TARGETS_
REACTOME_MITOCHONDRI
KEGG_ALZHEIMERS_DISE
KEGG_HUNTINGTONS_DIS
YAO_TEMPORAL_RESPONS
REACTOME_PYRUVATE_ME
REACTOME_TRNA_AMINOA
REACTOME_FORMATION_O
REACTOME_CITRIC_ACID
STARK_PREFRONTAL_COR
MOOTHA_PGC
KEGG_CITRATE_CYCLE_T
BURTON_ADIPOGENESIS_
YAO_TEMPORAL_RESPONS
KEGG_VALINE_LEUCINE_
REACTOME_MITOCHONDRI
REACTOME_BRANCHED_CH
BOQUEST_STEM_CELL_UP
KEGG_RIBOSOME
REACTOME_TRANSLATION
BURTON_ADIPOGENESIS_
CHNG_MULTIPLE_MYELOM
GINESTIER_BREAST_CAN
BILANGES_SERUM_AND_R
NABA_CORE_MATRISOME
−log10(FDR)
Positive association
Negative association


a
matrix
fumarate succinate
NADH NAD+
FADH2 FAD
ADP+Pi ATP
I
II
CoQ10
III
Cyt c
IV
V
4H+
4H+
2H+
H+
intermembrane space
b
Complex I mRNA
Complex II mRNA
Complex III mRNA
Complex IV mRNA
Complex V mRNA
mod t-stat
c
CONTROL
SARCOPENIC
SDHa (C II)
ATP5a (C V)
UQCRC2 (C III)
NDUFA9 (C I)
HSC70
GAPDH
80kDa
60kDa
50kDa
30kDa
60kDa
30kDa
d
Complex I (NDUFA9)
p = 0.036
Complex II (SDHa)
p = 0.018
Complex III (UQCR2)
p = 0.004
Complex V (ATP5a)
p = 0.008
Relative protein levels
Control
Sarc.
e
Enzymatic activity / mg muscle
Complex I
p = 0.013
Complex II
p = 0.032
Complex III
p = 0.043
Complex IV
p = 0.048
CS (TCA)
p = 0.016
SDH (TCA)
p = 0.008
Control
Sarc.
f
CONTROL
SARCOPENIC
Porin 1
Citrate Synthase (CS)
HSC70
30kDa
50kDa
60kDa
g
Porin
p = 0.002
CS
p = 0.001
Relative protein levels
Control
Sarc.


a
SSS, NAD metabolic process
p=0.0006
HSS, NAD metabolic process
p=0.03
JSS, NAD metabolic process
p=0.02
Enrichment
Up in sarc.
Down in sarc.
Statistics sarcopenia vs control
b
NAD
p = 0.046
NAD+ levels (μmol/g muscle)
Control
Sarc.
c
ALM index (kg/m²)
r=0.62
p-val=0.029
Grip strength (kg)
r=0.58
p-val=0.040
Gait speed (m/s)
r=0.54
p-val=0.054
Complex I activity / mg muscle
r=0.53
p-val=0.059
Muscle NAD+ level (μmol/g)
d
NMNAT1
p = 0.021
NAMPT
p = 0.005
Relative mRNA level (log2)
Control
Sarc.
e
CONTROL
SARCOPENIC
CD38
HSC70
40kDa
60kDa
f
CD38 protein
N.S.
Relative protein levels
Control
Sarc.