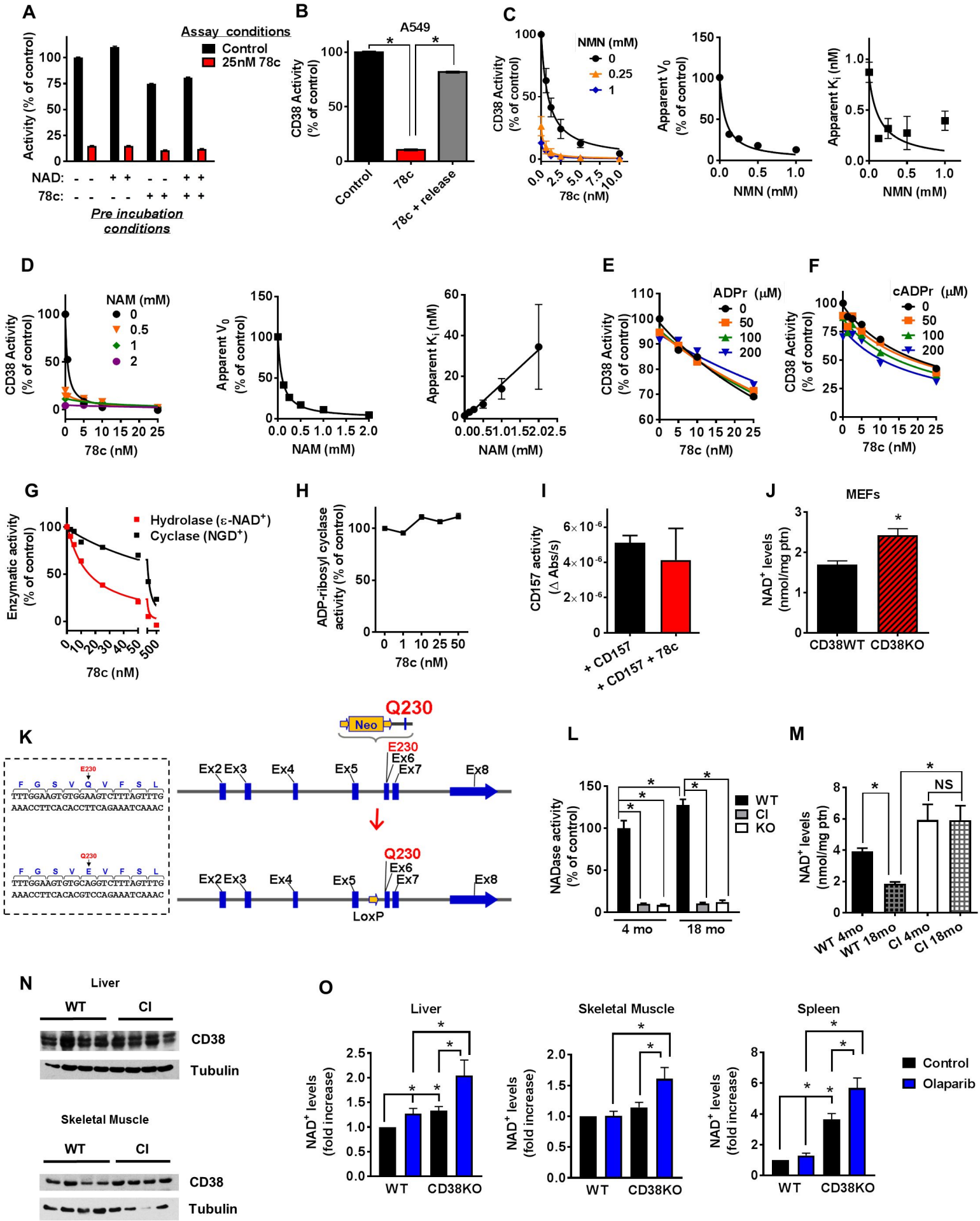
# SUPPLEMENTARY FIGURES


A
Assay conditions
Control
25nM 78c
Activity (% of control)
NAD:
78c:
Pre incubation conditions
B
A549
CD38 Activity (% of control)
Control
78c
78c + release
C
NMN (mM)
0
0.25
1
CD38 Activity (% of control)
78c (nM)
Apparent V0 (% of control)
NMN (mM)
Apparent Ki (nM)
NMN (mM)
D
NAM (mM)
0
0.5
1
2
CD38 Activity (% of control)
78c (nM)
Apparent V0 (% of control)
NAM (mM)
Apparent Ki (nM)
NAM (mM)
E
ADPr (μM)
0
50
100
200
CD38 Activity (% of control)
78c (nM)
F
cADPr (μM)
0
50
100
200
CD38 Activity (% of control)
78c (nM)
G
Hydrolase (ε-NAD+)
Cyclase (NGD+)
Enzymatic activity (% of control)
78c (nM)
H
ADP-ribosyl cyclase activity (% of control)
78c (nM)
I
CD157 activity (Δ Abs/s)
+ CD157
+ CD157 + 78c
J
MEFs
NAD+ levels (nmol/mg ptn)
CD38WT
CD38KO
K
Q230
Neo
E230
Ex2
Ex3
Ex4
Ex5
Ex6
Ex7
Ex8
LoxP
L
NADase activity (% of control)
WT
CI
KO
4 mo
18 mo
M
NAD+ levels (nmol/mg ptn)
NS
WT 4mo
WT 18mo
CI 4mo
CI 18mo
N
Liver
WT
CI
CD38
Tubulin
Skeletal Muscle
WT
CI
CD38
Tubulin
O
Liver
Skeletal Muscle
Spleen
NAD+ levels (fold increase)
WT
CD38KO
Control
Olaparib

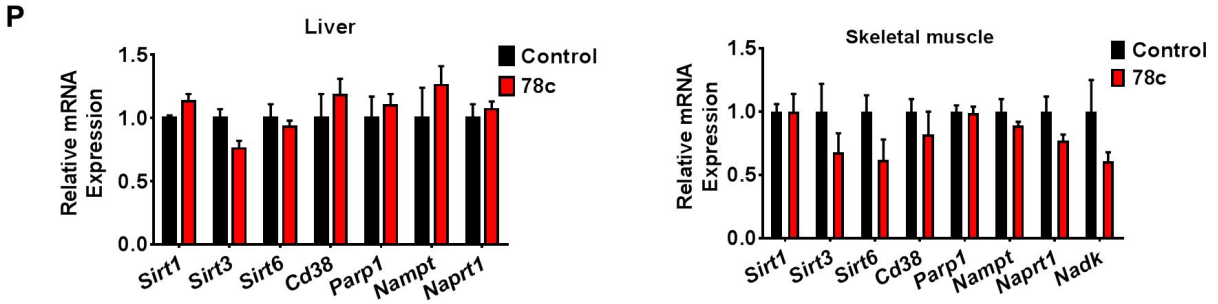
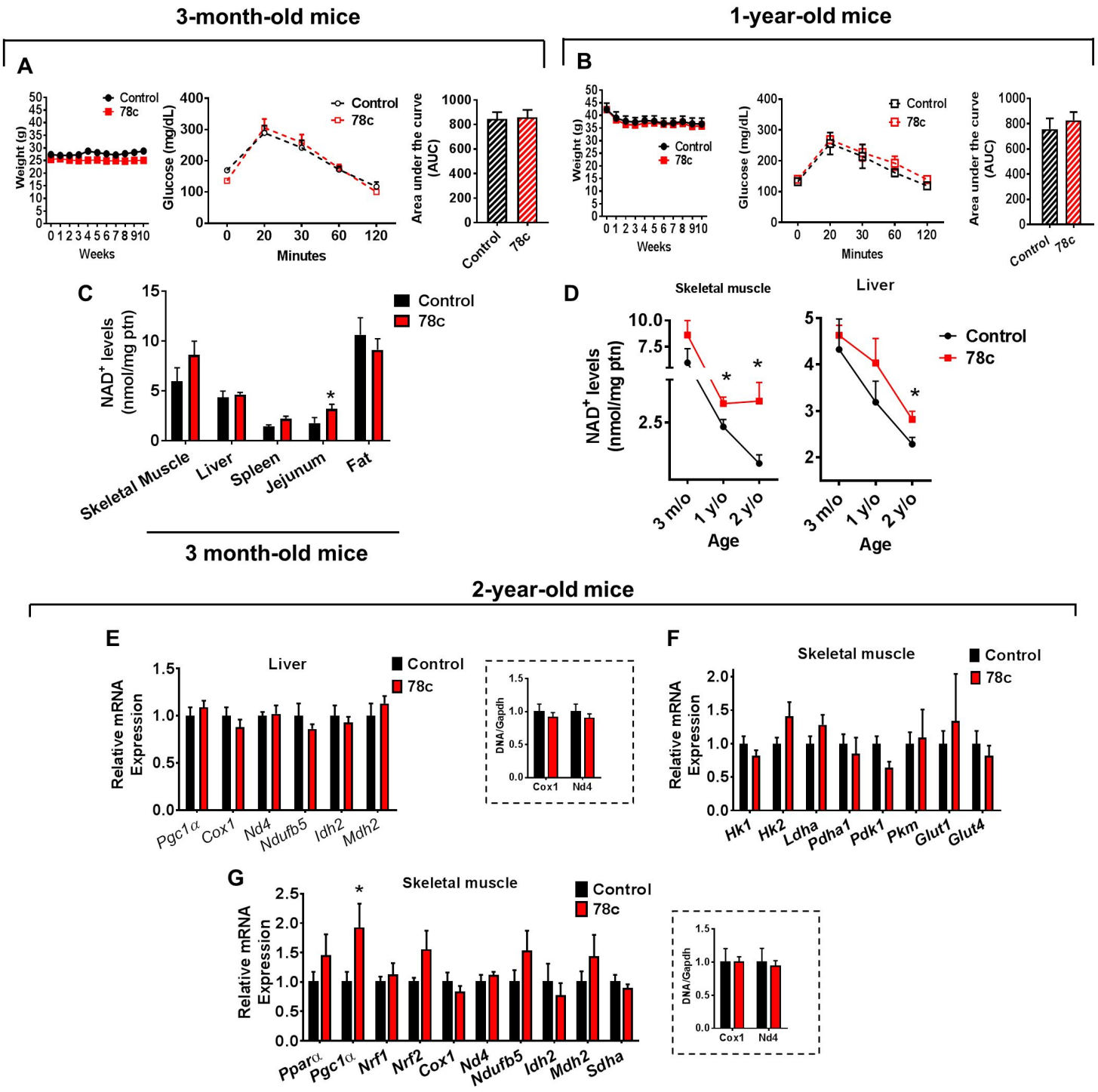



**Figure S1 (Related to Figure 1). Characterization of the effect of 78c on CD38 and other NAD$^+$-related enzymes. (A)** Reversibility of the effect of 78c was tested using human recombinant CD38 enzyme (rhCD38). Following pre-incubation under the conditions showed in the graph, samples were diluted 100-fold in sucrose buffer alone (Control) or with 25 nM 78c. CD38 activity was measured using 1,N6-ethenoadenine dinucleotide (ε-NAD$^+$) as a substrate. Data are expressed as percent activity relative to control (n= 3 experiments). **(B)** A549 cells were treated with vehicle or 0.5 μM 78c, then washed and incubated with (78c) or without (78c+release) 0.5 μM 78c. Control cells were exposed to vehicle for the whole treatment period. CD38 activity was measured in cell lysates (n=3 experiments). **(C-F)** Effect of **(C)** nicotinamide mononucleotide (NMN), **(D)** nicotinamide (NAM), **(E)** ADP-ribose (ADPr), and **(F)** cyclic ADP-ribose (cADPr) on the kinetics of inhibition of rhCD38 by 78c (ε-NAD as a substrate, n=3 experiments for each). **(G)** Comparison of effect of 78c on rhCD38 hydrolytic activity (ε-NAD as a substrate) and cyclase activity (nicotinamide guanine dinucleotide (NGD$^+$) as a substrate, n=3 experiments). **(H)** Effect of 78c on the ADP-ribosyl cyclase activity of purified cyclase from *Aplysia* ovotestis extracts. **(I)** Effect of 78c on CD157 activity (nicotinamide riboside (NR) as substrate, n=3 experiments). **(J)** NAD$^+$ levels in WT and CD38 KO MEFs (n=11 experiments). **(K)** Schematic of CD38 knock-in construct showing the point mutation introduced in exon 6 of CD38 gene. **(L)** CD38 (NADase) activity in liver of young and old WT, CD38 CI (catalytically inactive), and CD38 KO mice (n=4 mice per group). **(M)** Liver NAD$^+$ levels in young and old WT and CI mice (n=4 mice per group). **(N)** Liver and skeletal muscle protein lysates of WT and CI mice were immunoblotted for CD38 and Tubulin (n=4 mice per group). **(O)** NAD$^+$ levels in tissues of WT and CD38 KO mice treated with the PARP inhibitor olaparib for 8 days (n=5-9 mice per group). **(P)** mRNA levels of NAD$^+$ metabolism-related genes in liver and skeletal muscle of vehicle and 78c-treated aged mice, determined by quantitative RT-PCR (n=12-15 mice per group). All values are mean ± SEM. **P*<0.05, NS=not significant.


3-month-old mice
1-year-old mice
A
B
Control
78c
Weight (g)
Weeks
Glucose (mg/dL)
Minutes
Area under the curve (AUC)
C
NAD+ levels (nmol/mg ptn)
Skeletal Muscle
Liver
Spleen
Jejunum
Fat
3 month-old mice
D
Skeletal muscle
Liver
3 m/o
1 y/o
2 y/o
Age
2-year-old mice
E
Relative mRNA Expression
Pgc1α
Cox1
Nd4
Ndufb5
Idh2
Mdh2
DNA/Gapdh
F
Hk1
Hk2
Ldha
Pdha1
Pdk1
Pkm
Glut1
Glut4
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Cox1
Nd4
Ndufb5
Idh2
Mdh2
Sdha

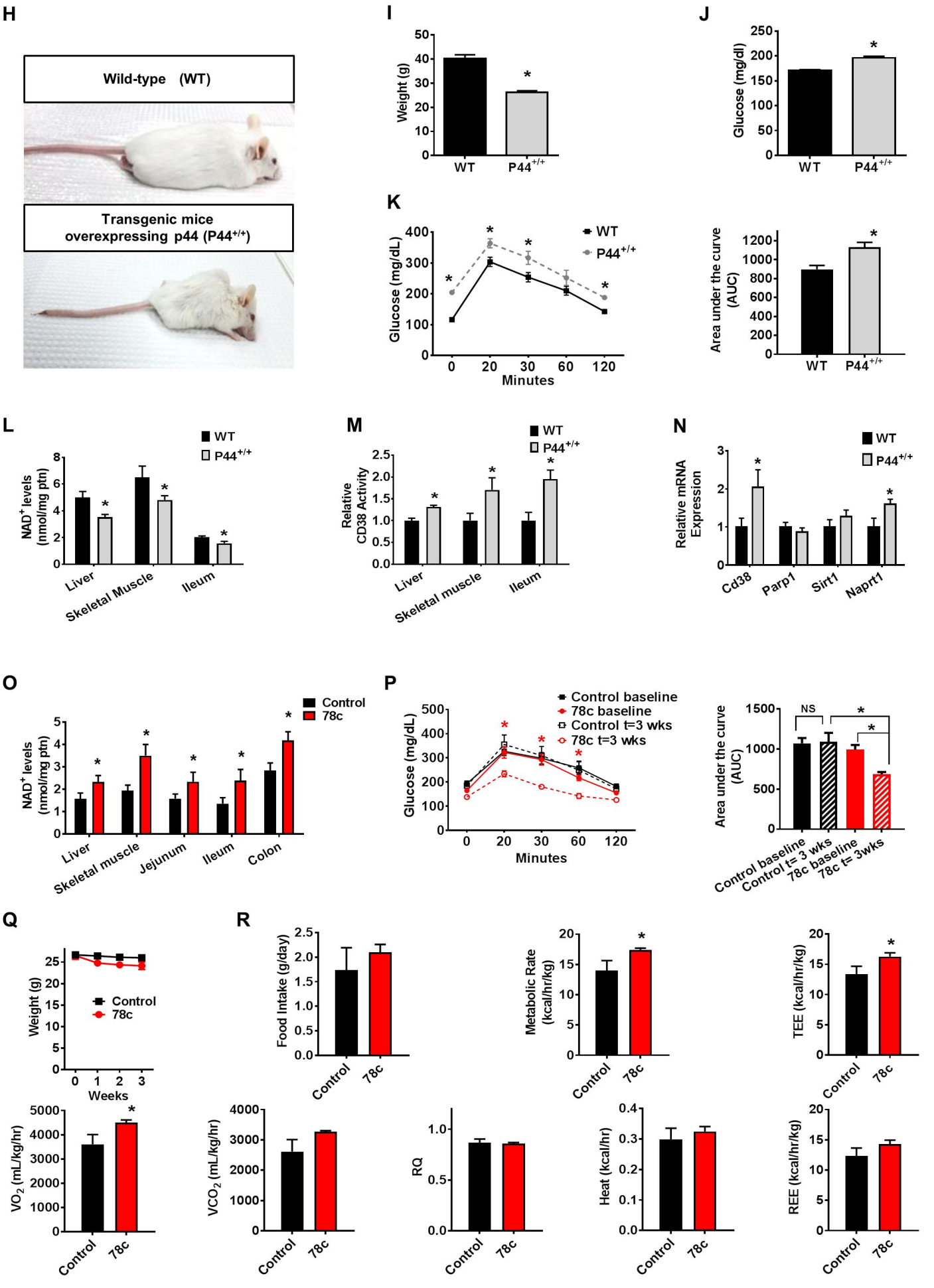
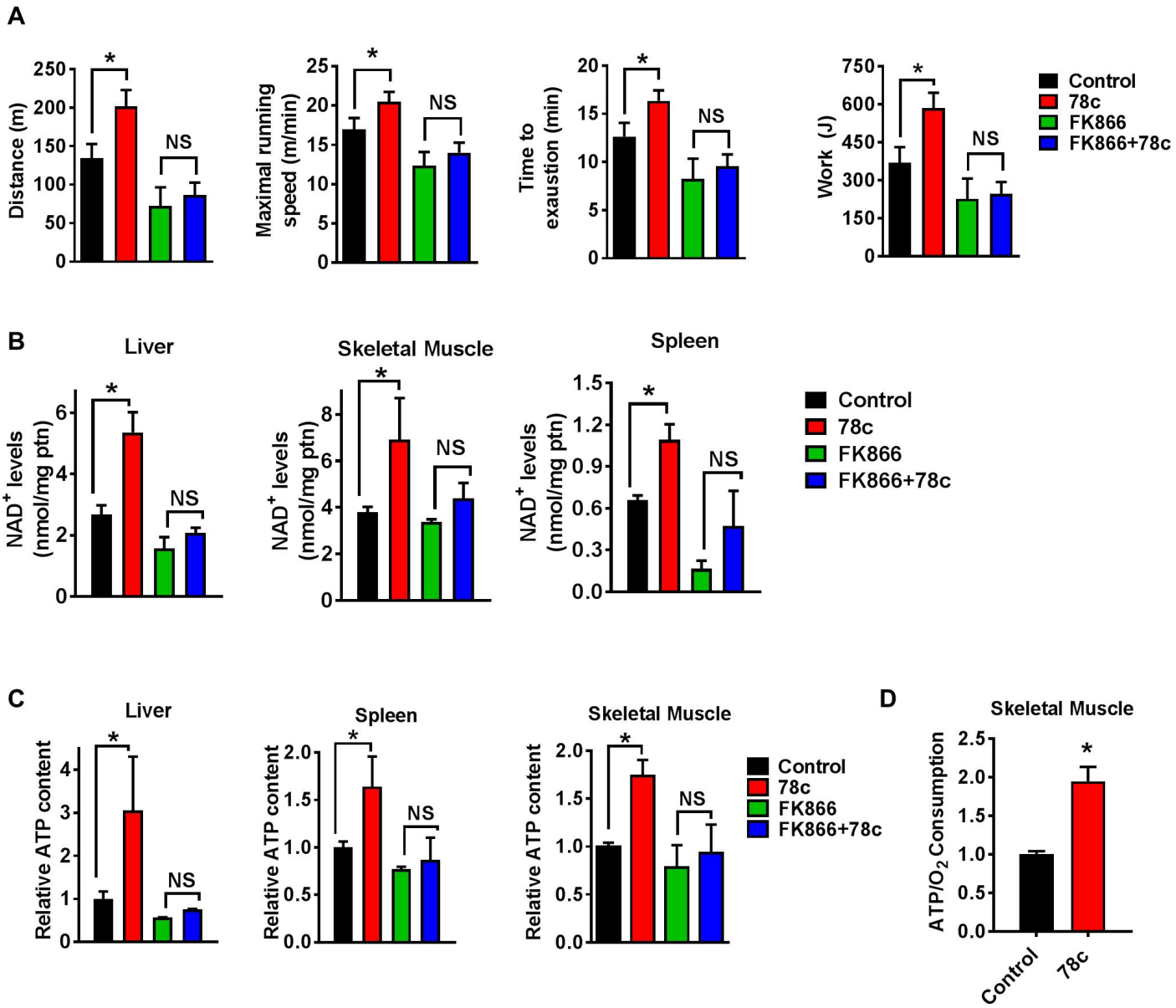
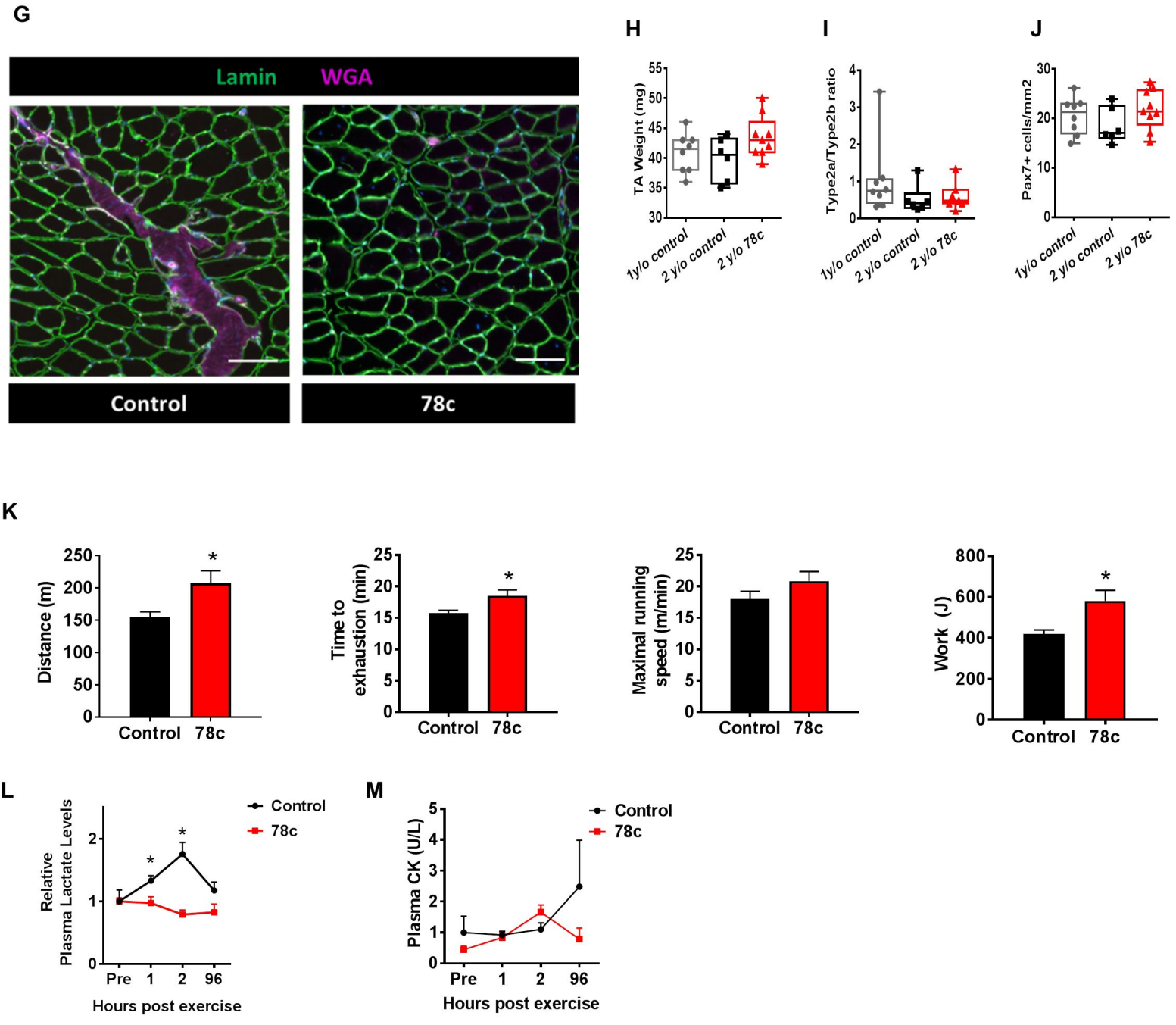
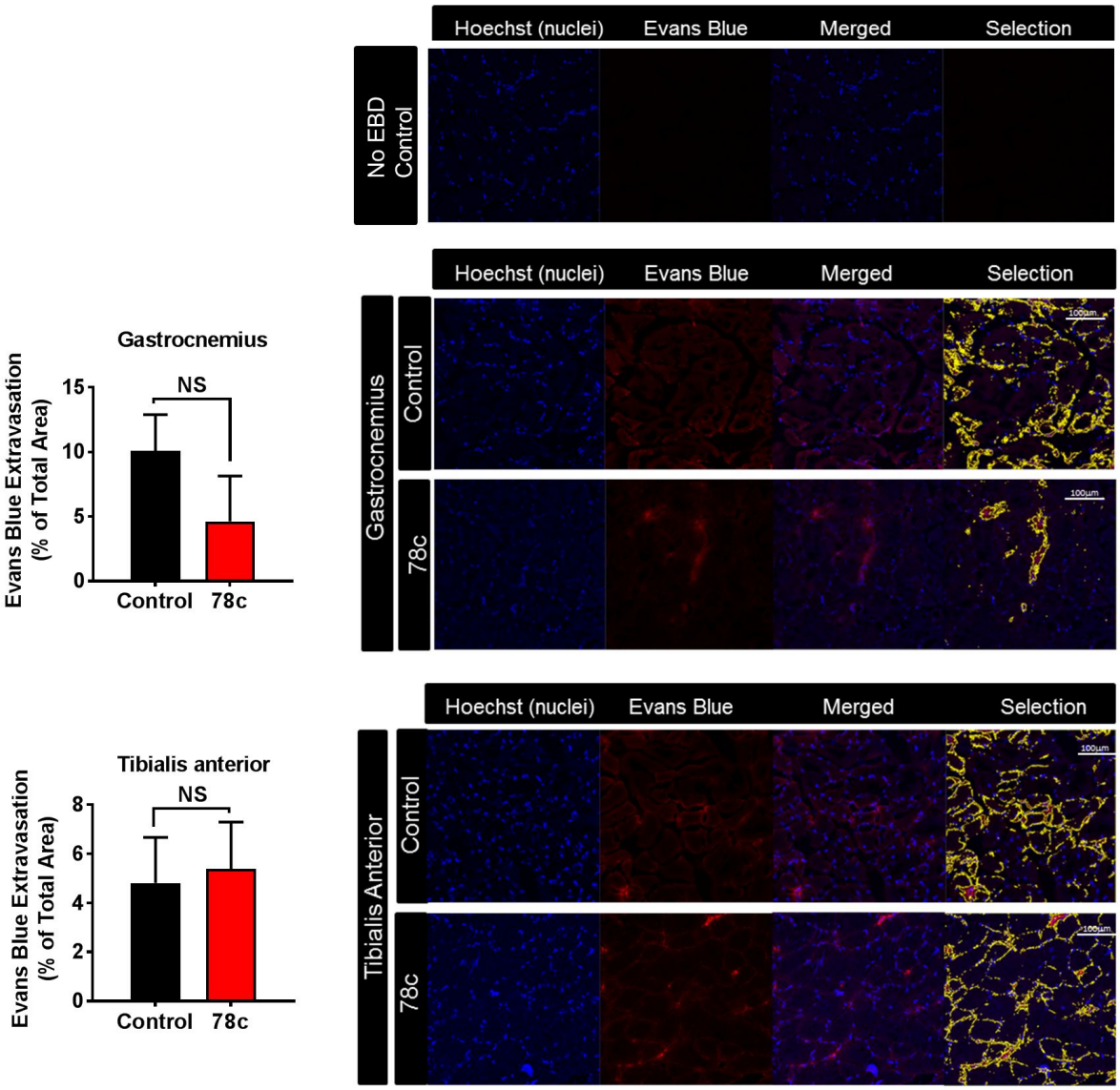

H
Wild-type (WT)
Transgenic mice overexpressing p44 (P44+/+)
I
Weight (g)
WT
P44+/+
J
Glucose (mg/dl)
K
Glucose (mg/dL)
Minutes
Area under the curve (AUC)
L
NAD+ levels (nmol/mg ptn)
Liver
Skeletal Muscle
Ileum
M
Relative CD38 Activity
Skeletal muscle
N
Relative mRNA Expression
Cd38
Parp1
Sirt1
Naprt1
O
Control
78c
Jejunum
Colon
P
Control baseline
78c baseline
Control t=3 wks
78c t=3 wks
NS
Q
Weight (g)
Weeks
R
Food Intake (g/day)
Metabolic Rate (kcal/hr/kg)
TEE (kcal/hr/kg)
VO2 (mL/kg/hr)
VCO2 (mL/kg/hr)
RQ
Heat (kcal/hr)
REE (kcal/hr/kg)

**Figure S2 (Related to Figure 2). Metabolic features of 3-month-old (young), 1-year-old (middle-aged), and 2-year-old (aged) mice treated with 78c, and characterization of $NAD^+$ metabolism in an animal model of progeria**. **(A-B)** 3-month-old and 1-year-old mice were treated with vehicle (Control) or 78c. **(A)** Left panel shows weekly body weight measurements of 3-month-old mice (n= 8 mice per group) and right panel shows intraperitoneal glucose tolerance test (ipGTT) and corresponding area under the curve (AUC) after 7 weeks of treatment (n=8 mice per group). **(B)** Left panel shows weekly body weights measurements of 1-year-old mice (n=8-11 mice per group) and right panel shows ipGTT and corresponding AUC after 7 weeks of treatment (n=8-11 mice per group). **(C)** $NAD^+$ levels in multiple tissues of 3-month-old mice at the end of 14 weeks of treatment (n=8 mice per group). **(D)** $NAD^+$ levels in skeletal muscle and liver of 3-month-old, 1-year-old, and aged (2-year-old) mice treated with vehicle (Control) or 78c for up to 14 weeks. **(E-G)** Aged (2-year-old) mice treated with vehicle (Control) or 78c for up to 14 weeks. **(E)** Expression of mitochondrial biogenesis genes in liver, determined by quantitative RT-PCR (n=6-13 mice per group). Inset shows relative mtDNA content for liver, with *CoxI* and *Nd4* as mitochondrial-encoded genes normalized to *Gapdh* (n=6 mice per group). **(F-G)** Skeletal muscle mRNA levels of genes related to glucose metabolism **(F)** and mitochondrial biogenesis **(G)**, determined by quantitative RT-PCR (n=6 mice per group). Inset in G shows relative mtDNA content for skeletal muscle, with Cox I and Nd4 as mitochondrial-encoded genes normalized to *Gapdh* (n=6 mice per group). **(H-N)** 1-year-old WT and $P44^{+/+}$ progeroid mice. **(H)** Representative images of WT and $P44^{+/+}$ mice. **(I)** Body weight (n=13 mice per group). **(J)** Random fed serum glucose (n=13 mice per group). **(K)** **i**pGTT and corresponding AUC (n=10 mice per group). **(L)** $NAD^+$ levels in several tissues (n=12 mice per group). **(M)** CD38 activity in tissues (n=10 mice per group). **(N)** Liver mRNA levels of $NAD^+$ metabolism-related enzymes determined by quantitative RT-PCR (n=6 mice per group). **(O-R)** 1-year-old $P44^{+/+}$ mice treated with vehicle (Control) or 78c. Results show average of two independent experiments. **(O)** $NAD^+$ levels in several tissues at the end of 4 weeks of treatment (n=13 mice per group). **(P)** ipGTT and corresponding AUC at baseline and after 3 weeks of treatment (n=9-11 mice per group). Two-way repeated measures ANOVA with Bonferroni's post-tests shows significant interaction between the glucose curve for control and 78c-treated mice. **(Q)** Weekly body weight measurements (n=13 mice per group). **(R)** Comprehensive Laboratory Animal Monitoring System (CLAMS) measurements of food intake, metabolic rate, total energy expenditure (TEE), oxygen consumption ($VO_2$), carbon dioxide production ($VCO_2$), respiratory coefficient (RQ), heat production, and resting energy expenditure (REE) (n= 4 mice per group). All values are mean ± SEM, * $P < 0.05$. NS=not significant.

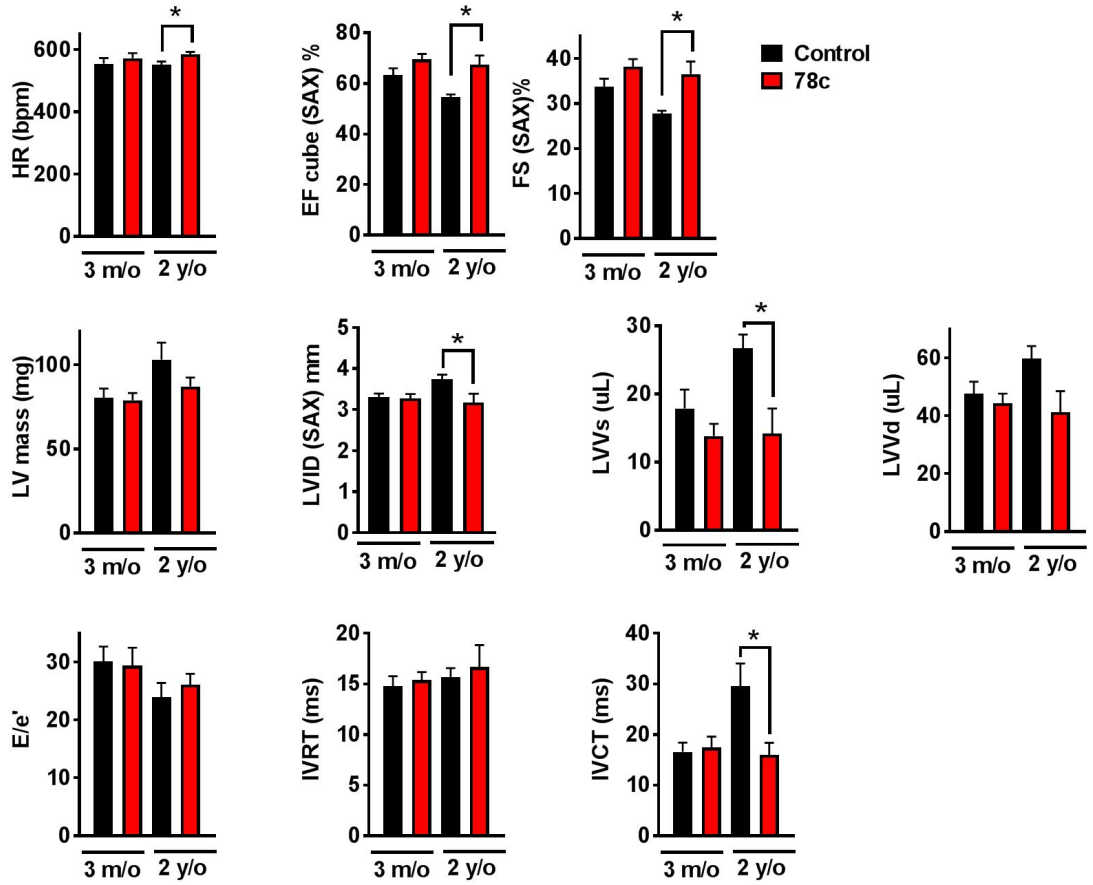

A
Distance (m)
Maximal running speed (m/min)
Time to exaustion (min)
Work (J)
NS
Control
78c
FK866
FK866+78c
B
Liver
Skeletal Muscle
Spleen
NAD+ levels (nmol/mg ptn)
C
Relative ATP content
D
Skeletal Muscle
ATP/O2 Consumption
Control
78c
3-month-old mice
E
F
Activity (counts)
Rearing (counts)
Ambulation (counts)
AEE (kcal/hr/kg)


G
Lamin
WGA
Control
78c
H
TA Weight (mg)
1y/o control
2 y/o control
2 y/o 78c
I
Type2a/Type2b ratio
1y/o control
2 y/o control
2 y/o 78c
J
Pax7+ cells/mm2
1y/o control
2 y/o control
2 y/o 78c
K
Distance (m)
Control
78c
Time to exhaustion (min)
Control
78c
Maximal running speed (m/min)
Control
78c
Work (J)
Control
78c
L
Relative Plasma Lactate Levels
Control
78c
Pre
1
2
96
Hours post exercise
M
Plasma CK (U/L)
Control
78c
Pre
1
2
96
Hours post exercise

N


Hoechst (nuclei)
Evans Blue
Merged
Selection
No EBD Control
Gastrocnemius
Control
78c
Tibialis Anterior
Evans Blue Extravasation (% of Total Area)
NS
Control
78c

O


HR (bpm)
EF cube (SAX) %
FS (SAX)%
Control
78c
LV mass (mg)
LVID (SAX) mm
LVVs (uL)
LVVd (uL)
E/e'
IVRT (ms)
IVCT (ms)
3 m/o
2 y/o

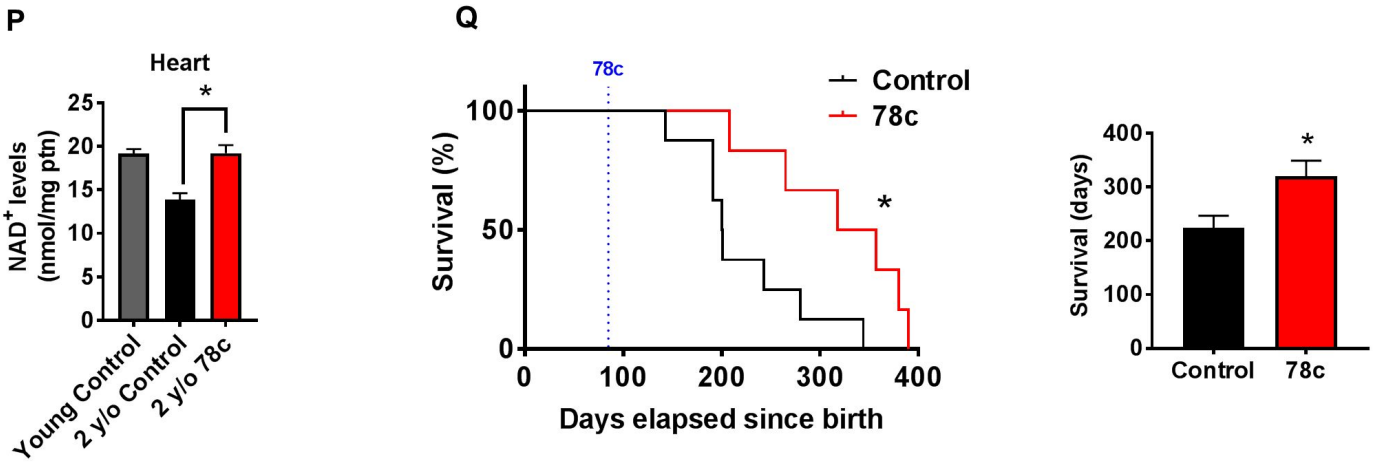
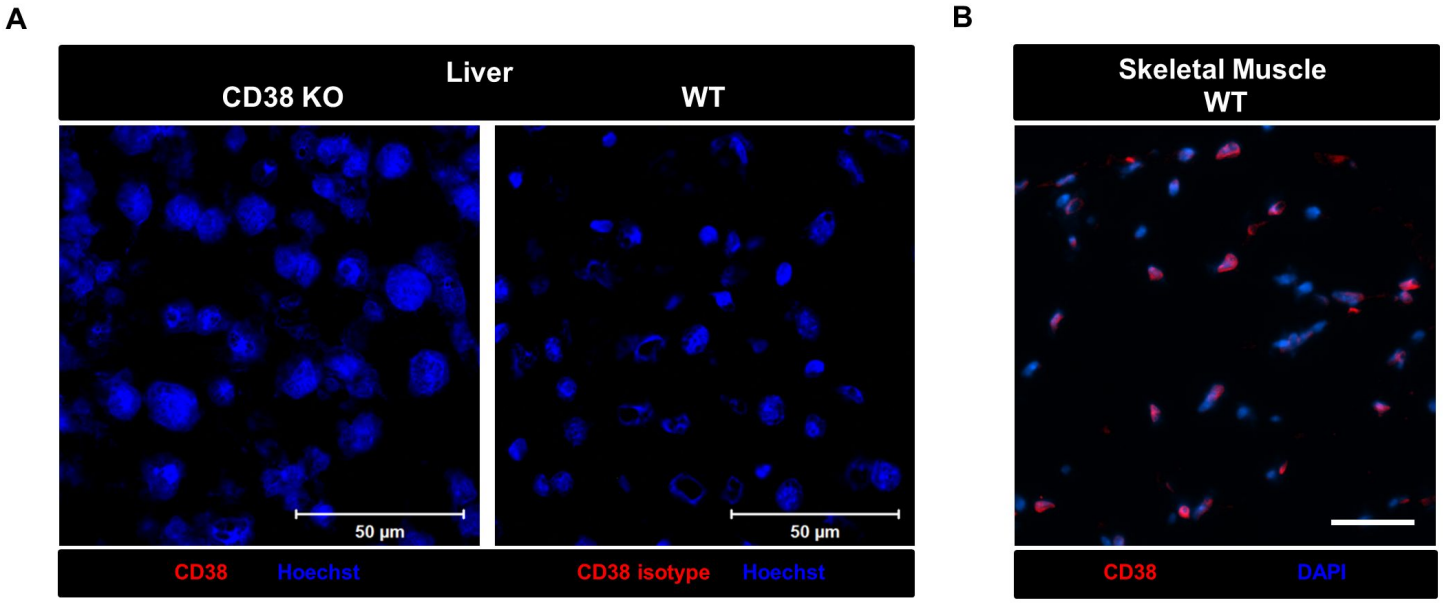
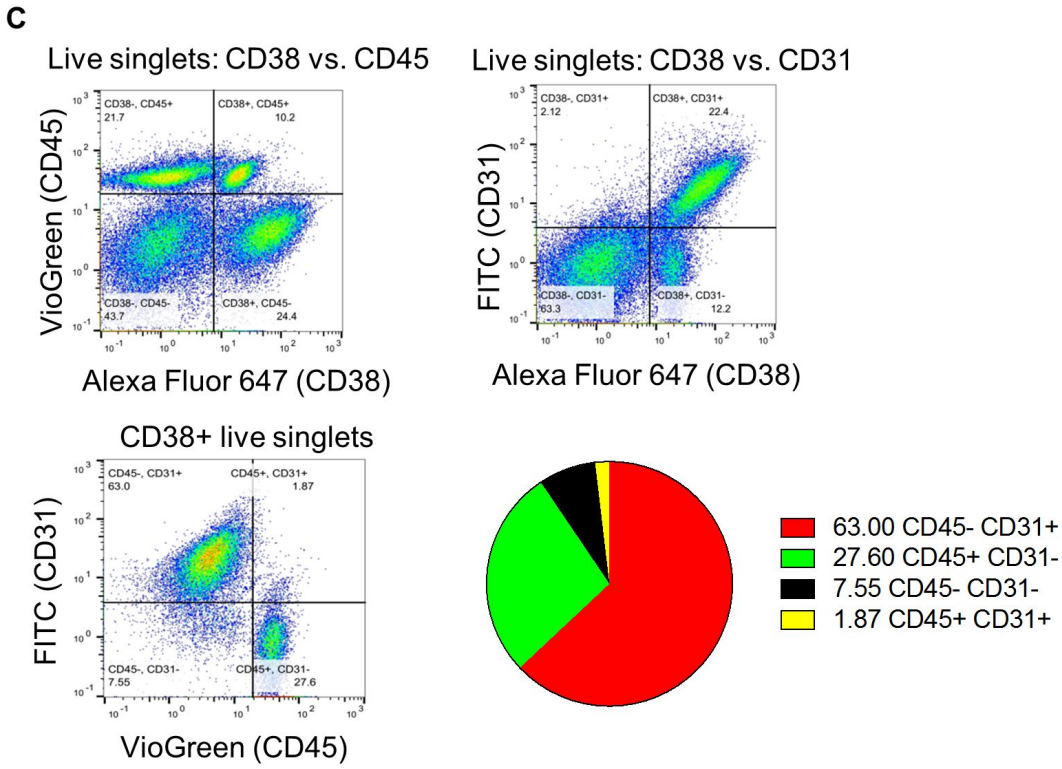
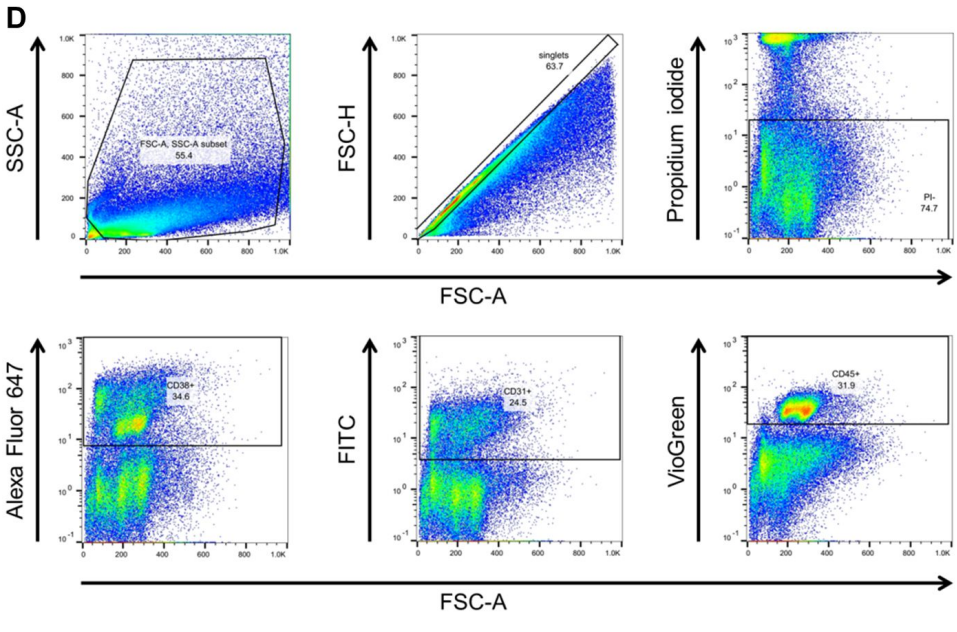


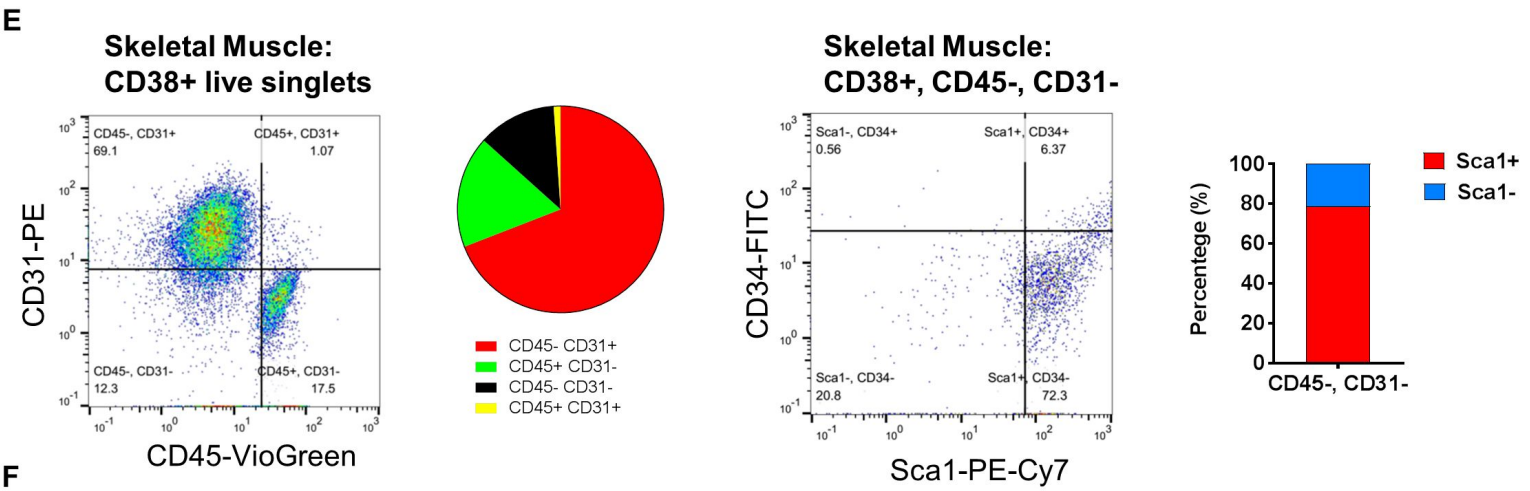

**Figure S3 (Related to Figure 3). Skeletal muscle features in mice treated with 78c**. **(A-C)** 2-year-old (aged) mice treated with vehicle (Control), 78c, FK866 (NAMPT inhibitor), or 78c+FK866. **(A)** Physical performance assessment on a motorized treadmill after 8 weeks of treatment: measurements of distance, maximal running speed, running time, and work (n=5 mice per group). **(B)** Tissue $NAD^+$ levels at end of 10 weeks of treatment (n=5 mice per group). **(C)** Tissue ATP levels at end of study, measured by a luminescence assay. **(D)** Ratio of skeletal muscle ATP level and $O_2$ consumption in isolated muscle fibers from 2-year-old mice treated with vehicle (Control) or 78c for 10 weeks (n= 4-5 mice per group). **(E-F)** 3-month-old mice treated with vehicle (Control) or 78c (n=8 mice per group). **(E)** Physical performance assessment on treadmill after 8 weeks of treatment: measurements of distance, maximal running speed, running time, and work. **(F)** Measurements of locomotor activity by CLAMS after 4 weeks of treatment: total activity, rearing counts, ambulation, AEE. **(G)** Representative images of wheat germ agglutinin (WGA) (magenta) and lamin (green) co-staining of skeletal muscle sections from aged mice treated with vehicle (Control) or 78c for 14 weeks. **(H-J)** 1-year-old mice and 2-year-old (aged) mice treated with vehicle (Control) or 78c for up to 14 weeks. **(H)** Weight of tibialis anterior muscle (TA) (n=6-9 mice per group). **(I)** Fiber-type switching in TA muscle (n=6-9 mice per group). **(J)** Number of $PAX7^+$ cells per unit of muscle area (n=6-9 mice per group). **(K-M)** 2-year-old (aged) mice were treated with vehicle (Control) or 78c. **(K)** Physical performance assessment during downhill treadmill exercise on a motorized treadmill (10° decline) after 10 weeks of treatment. Measurements of distance, maximal running speed, running time, and work (n= 5-6 mice per group). **(L)** Relative plasma lactate levels before and after downhill running exercise (n=5-6 mice per group). **(M)** Plasma creatine kinase (CK) levels before and after downhill running exercise (n=5-6 mice per group). **(N)** Evans blue dye (EBD) assessment of sarcolemmal integrity within the gastrocnemius (GA) and TA muscles of mice submitted to a downhill treadmill exhaustion protocol. Images are representative of GA and TA muscles from EBD-injected control/78c treated mice showing Hoechst (nuclei) and EBD 96 hours post injury. The yellow selection surrounds the $EBD^+$ fibers. The graphs show percentage of total area with Evans Blue extravasation. Scale bar: 100 μm. **(O)** Transthoracic echocardiography measurements in 3-month-old and aged (2-year-old) mice treated with vehicle (Control) or 78c (n=5-8 animals per group). Parameters assessed after 9 weeks of treatment were: HR- Heart Rate; EF- Ejection fraction, FS- Fractional shortening, LV mass- Left ventricular mass, LVID- Left ventricular internal dimension, LVVs- Left ventricle volume during systole, LVVd- Left ventricle volume during diastole, E/e'- Early filling (E) and early diastolic mitral annular velocity (e') ratio, IVRT- Isovolumic (or isovolumetric) relaxation time, IVCT- Isovolumic (isovolumetric) contraction time. SAX: short axis. **(P)** $NAD^+$ levels in heart of young and aged mice treated with vehicle (Control) or 78c for 10 weeks (n=4 mice per group). **(Q)** Kaplan-Meier overall survival curve of $Bub1b^{H/H}$ mice treated with vehicle (Control) and 78c for up to 10 months. Asterisk denotes significance compared to control mice using a log-rank (Mantel-Cox) test and the Gehan-Breslow-Wilcoxon test. Tick line indicates start of 78c/control treatment. Right panel shows overall survival of both groups (n=6-8 mice per group). All values are mean ± SEM. * $P < 0.05$.


A
Liver
CD38 KO
WT
50 µm
50 µm
CD38
Hoechst
CD38 isotype
Hoechst
B
Skeletal Muscle
WT
CD38
DAPI

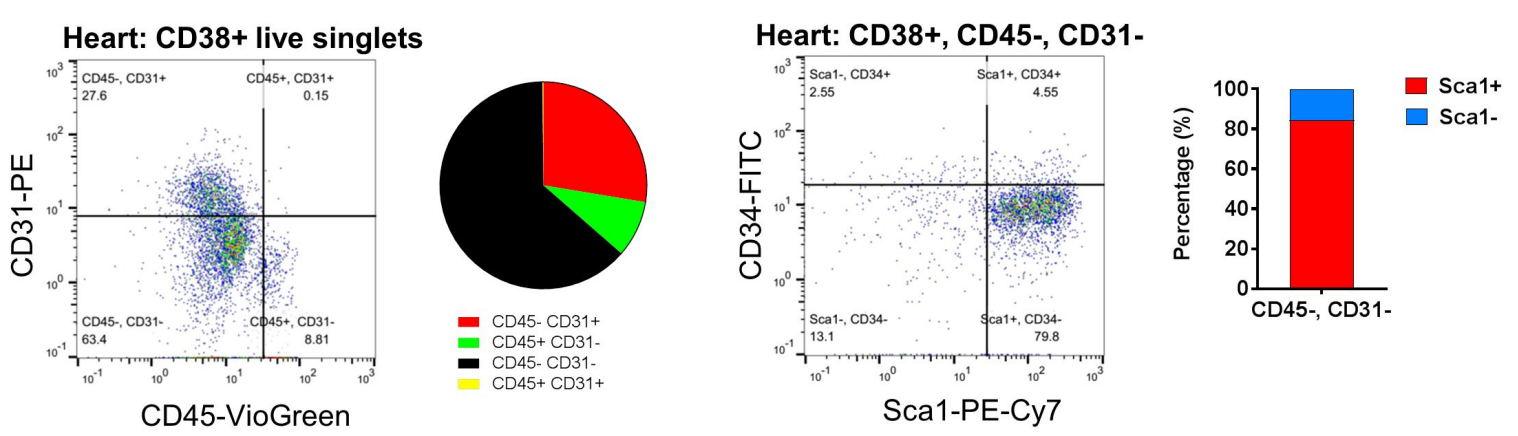

C
Live singlets: CD38 vs. CD45
VioGreen (CD45)
Alexa Fluor 647 (CD38)
CD38-, CD45+ 21.7
CD38+, CD45+ 10.2
CD38-, CD45- 43.7
CD38+, CD45- 24.4
Live singlets: CD38 vs. CD31
FITC (CD31)
Alexa Fluor 647 (CD38)
CD38-, CD31+ 2.12
CD38+, CD31+ 22.4
CD38-, CD31- 63.3
CD38+, CD31- 12.2
CD38+ live singlets
FITC (CD31)
VioGreen (CD45)
CD45-, CD31+ 63.0
CD45+, CD31+ 1.87
CD45-, CD31- 7.55
CD45+, CD31- 27.6
63.00 CD45- CD31+
27.60 CD45+ CD31-
7.55 CD45- CD31-
1.87 CD45+ CD31+


D
SSC-A
FSC-A, SSC-A subset 55.4
FSC-H
singlets 63.7
Propidium iodide
PI- 74.7
FSC-A
Alexa Fluor 647
CD38+ 34.6
FITC
CD31+ 24.5
VioGreen
CD45+ 31.9
FSC-A

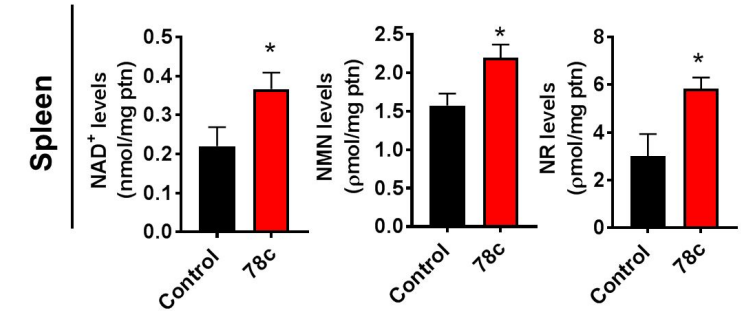
E


Skeletal Muscle:
CD38+ live singlets
CD45-, CD31+
69.1
CD45+, CD31+
1.07
CD45-, CD31-
12.3
CD45+, CD31-
17.5
CD31-PE
CD45-VioGreen
CD45- CD31+
CD45+ CD31-
CD45- CD31-
CD45+ CD31+
Skeletal Muscle:
CD38+, CD45-, CD31-
Sca1-, CD34+
0.56
Sca1+, CD34+
6.37
Sca1-, CD34-
20.8
Sca1+, CD34-
72.3
CD34-FITC
Sca1-PE-Cy7
Percentage (%)
Sca1+
Sca1-
CD45-, CD31-

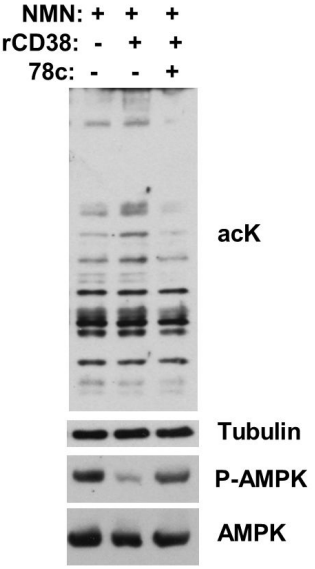
F


Heart: CD38+ live singlets
CD45-, CD31+
27.6
CD45+, CD31+
0.15
CD45-, CD31-
63.4
CD45+, CD31-
8.81
CD31-PE
CD45-VioGreen
CD45- CD31+
CD45+ CD31-
CD45- CD31-
CD45+ CD31+
Heart: CD38+, CD45-, CD31-
Sca1-, CD34+
2.55
Sca1+, CD34+
4.55
Sca1-, CD34-
13.1
Sca1+, CD34-
79.8
CD34-FITC
Sca1-PE-Cy7
Percentage (%)
Sca1+
Sca1-
CD45-, CD31-

G


Spleen
NAD+ levels (nmol/mg ptn)
NMN levels (pmol/mg ptn)
NR levels (pmol/mg ptn)
Control
78c

H


NMN: + + +
rCD38: - + +
78c: - - +
acK
Tubulin
P-AMPK
AMPK

I

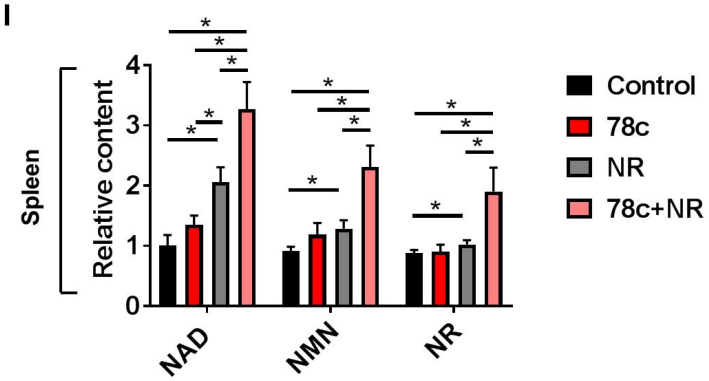
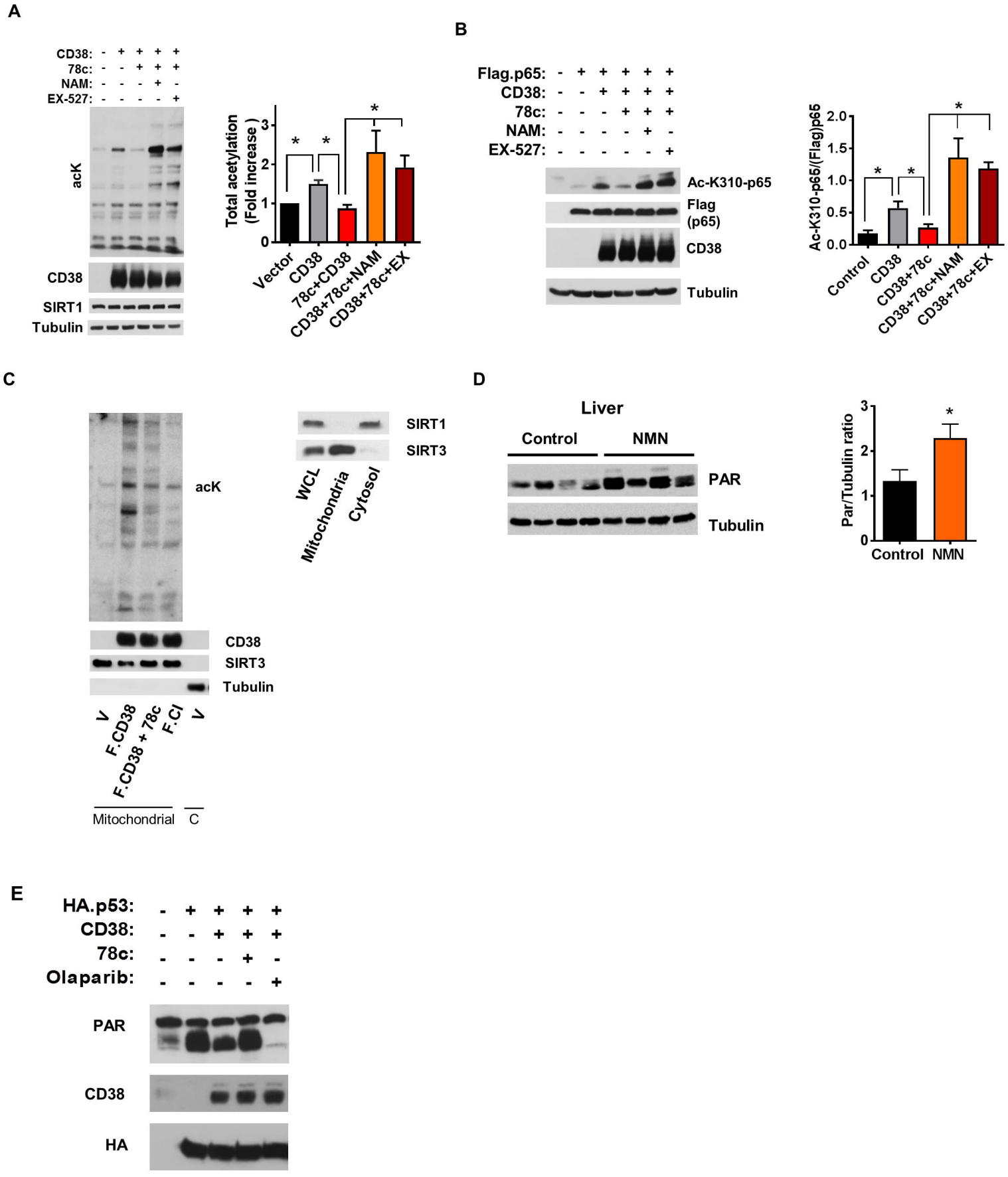
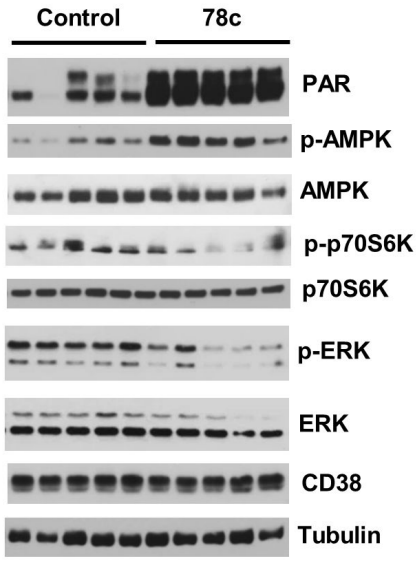
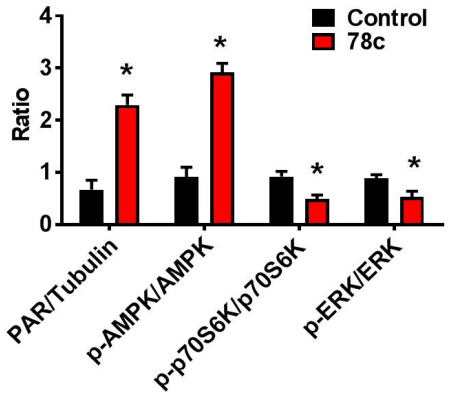

Spleen
Relative content
NAD
NMN
NR
Control
78c
NR
78c+NR

**Figure S4 (Related to Figure 4). Cellular localization of CD38 in multiple tissues and modulation of $NAD^+$ and its precursors by 78c. (A)** Immunofluorescence analysis of liver sections from CD38KO and WT mice co-stained for CD38 or CD38 isotype (red). Hoerchst-stained nuclei are shown in blue. Scale bar represents 50 μm. **(B-D)** Representative figures of staining and gating strategy for live singlet cells present in skeletal muscle samples of WT mice. **(B)** Representative image of skeletal muscle tissue section of WT mice immunostained for CD38. **(C)** Representative fluorescent signal plots of CD38, CD45 and CD31 expressing cells in skeletal muscle. Circle chart shows percentage of CD45 and CD31 markers expression within the $CD38^+$ cells population. **(D)** Gating strategy employed to identify CD38, CD31 and CD45 expressing cells in skeletal muscle. **(E-F)** Representative fluorescent signal plots of CD38, CD45, CD31 and Sca-1 expressing cells in skeletal muscle **(E)** and heart **(F)** of WT mice. Circle chart shows percentage of CD45 and CD31 markers expression within the $CD38^+$ cells population. Column graph shows the percentage of Sca1+ cells within the $CD45^-/CD31^-$ cells population. **(G)** $NAD^+$, NMN and NR levels in spleen of aged (2-year-old) mice treated with vehicle (Control) or 78c for 10 weeks. Metabolites were measured by high-performance liquid chromatography (HPLC)-mass spec (n=5-6 mice per group). **(H)** AML12 cells were incubated for 18 hours in media containing 100 μM NMN in the presence or absence of 100 ng/ml rhCD38 and 1 μM 78c. Protein lysates were immunoblotted with specific antibodies. **(I)** $NAD^+$, NMN and NR levels in spleen of aged (2-year-old) mice treated with vehicle (Control), 78c, NR or 78c+NR. Mice received two doses of vehicle or 78c 22 hours and 6 hours prior to euthanasia. One dose of NR was given by gavage 6 hours before euthanasia. Metabolites were measured by high-performance liquid chromatography (HPLC)-mass spec (n=7-10 mice per group). All values are mean ± SEM. * $P < 0.05$.

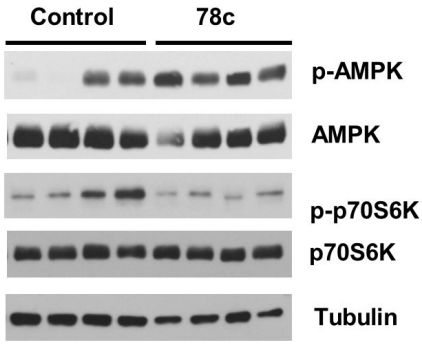

A
CD38:
78c:
NAM:
EX-527:
acK
CD38
SIRT1
Tubulin
Total acetylation (Fold increase)
Vector
CD38
78c+CD38
CD38+78c+NAM
CD38+78c+EX
B
Flag.p65:
CD38:
78c:
NAM:
EX-527:
Ac-K310-p65
Flag (p65)
CD38
Tubulin
Ac-K310-p65/(Flag)p65
Control
CD38
CD38+78c
CD38+78c+NAM
CD38+78c+EX
C
acK
SIRT1
SIRT3
WCL
Mitochondria
Cytosol
CD38
SIRT3
Tubulin
V
F.CD38
F.CD38 + 78c
F.CI
V
Mitochondrial
C
D
Liver
Control
NMN
PAR
Tubulin
Par/Tubulin ratio
Control
NMN
E
HA.p53:
CD38:
78c:
Olaparib:
PAR
CD38
HA

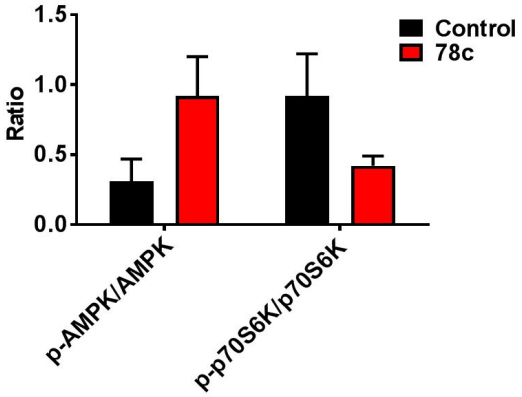
F


Control
78c
PAR
p-AMPK
AMPK
p-p70S6K
p70S6K
p-ERK
ERK
CD38
Tubulin

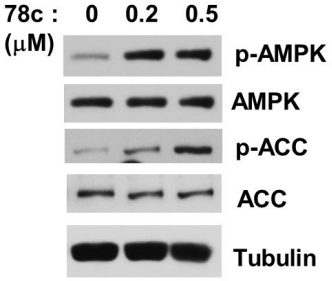

Control
78c
Ratio
PAR/Tubulin
p-AMPK/AMPK
p-p70S6K/p70S6K
p-ERK/ERK

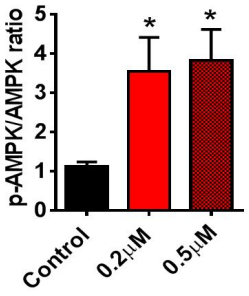
G

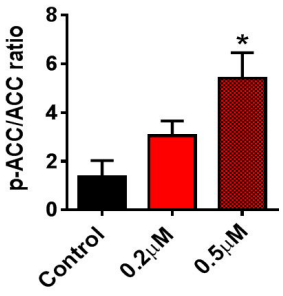

Control
78c
p-AMPK
AMPK
p-p70S6K
p70S6K
Tubulin


Control
78c
Ratio
p-AMPK/AMPK
p-p70S6K/p70S6K

H


78c : (μM)
0
0.2
0.5
p-AMPK
AMPK
p-ACC
ACC
Tubulin


p-AMPK/AMPK ratio
Control
0.2μM
0.5μM


p-ACC/ACC ratio
Control
0.2μM
0.5μM

I

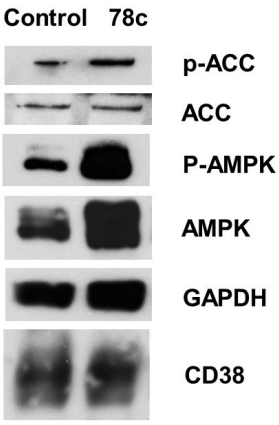

Control
78c
p-ACC
ACC
P-AMPK
AMPK
GAPDH
CD38

**Figure S5 (Related to Figure 5). 78c regulates signaling pathways involved in health span and longevity.** **(A)** 293T cells were transfected with vector or CD38 plasmid. 24 hours after transfection, cells were treated with 0.5 μM 78c in the presence or absence of 5 μM SIRT1 inhibitor EX-527 (EX) or 5 mM nicotinamide (NAM). Cell lysates were immunoblotted for lysine acetylation (acK), CD38, SIRT1, and Tubulin. Graph shows quantification of immunoblots using vector transfection as a control (n=3-6 experiments). **(B)** 293T cells were transfected with vector, Flag-p65 and/or CD38 plasmids. After 24 hours of transfection, cells were treated with 0.5 μM 78c in the presence or absence of 5 μM EX-527 (EX) or 5 mM nicotinamide (NAM). Cell lysates were immunoblotted for p65 lysine acetylation (Ac-K310-p65), Flag (p65), CD38, and Tubulin. Graph shows quantification of immunoblots using p65 transfection alone as a control (n=3-6 experiments). **(C)** 293T cells were transfected with vector, CD38 WT, or CI plasmid, and then treated with 0.5 μM 78c for 20 hours. Mitochondria were isolated, and mitochondria lysates or control cytosol (c) were immunoblotted with specific antibodies. Blot is representative of 3 experiments. Right blot shows presence of Sirt1 in cytosol and Sirt3 in mitochondrial fraction. **(D)** Mice were treated with a single dose of vehicle (Control) or NMN (500 mg/kg), and tissues collected 2 hours later. Liver lysates were immunoblotted for PAR and Tubulin. Graph shows quantification of immunoblots (n=4 mice per group. **(E)** 293T cells were transfected with vector or HA.p53 in the presence or absence of CD38 plasmid. 24 hours after transfection, cells were treated with 0.5 μM 78c or 5 μM olaparib (PARP inhibitor) for 24 hours. Cell lysates were immunoblotted for PAR, CD38, and HA (p53). Blot is representative of 3 experiments **(F-G)** 1-year-old mice were treated with 78c for 8 days. Spleen **(F)** and skeletal muscle **(G)** protein lysates were immunoblotted with specific antibodies. Graph shows quantification of immunoblots (n=4 mice per group). **(H)** A549 cells were treated with vehicle and different doses of 78c. Cell lysates were immunoblotted with specific antibodies. Graph shows quantification of immunoblots (n=3-4 experiments). **(I)** Mouse bone marrow-derived macrophages were treated with 100 ng/mL LPS (to induce CD38 expression) with and without 0.2 μM 78c for 30 hours. Cell lysates were immunoblotted with the specific antibodies. Blot is representative of 3 experiments. All values are mean ± SEM, * $P < 0.05$.