SUPPLEMENTAL MATERIAL

Supplemental Table I – Selective reaction monitoring (SRM) transitions for acyl carnitine analysis

Acyl Carnitine	Transition, m/z	Retention Time
^{12}C acetyl (C2)	204.1→85	1.50-1.51
^{13}C acetyl (C2)	205.1→85	1.50-1.51
Acetyl-d_3-carnitine (internal standard)	207.1→85	1.50-1.51
^{12}C butyryl (C4)	232.1→85	5.35-5.36
^{13}C butyryl (C4)	234.1→85	5.35-5.36
^{12}C 3-hydroxybutyryl-L (L-C4OH)	248.1→85	2.43-2.44
^{13}C 3-hydroxybutyryl-L (L-C4OH)	250.1→85	2.43-2.44
^{12}C 3-hydroxybutyryl-D (D-C4OH)	248.1→85	2.94-2.95
^{12}C 3-hydroxybutyryl-D (D-C4OH)	250.1→85	2.94-2.95

Supplemental Table II – Patient characteristics

Data shown are means ± standard error of the mean

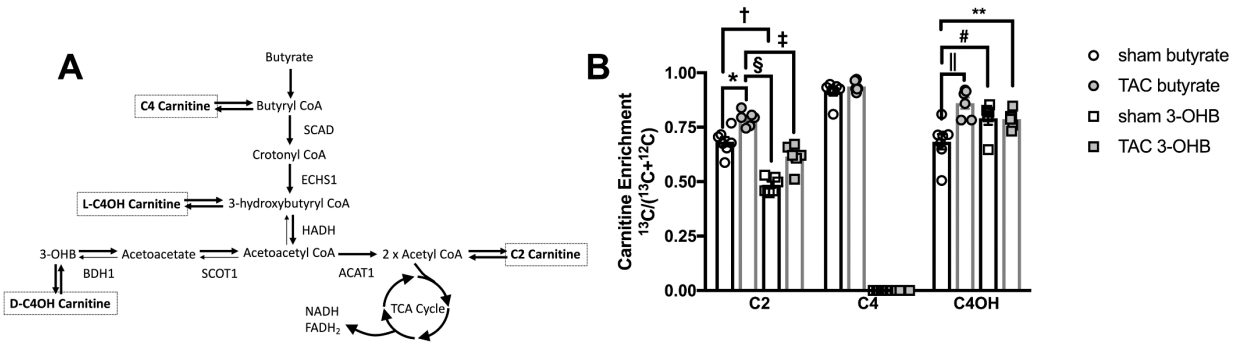
Variables	Control (n=5)	Non-ischemic cardiomyopathy (n=5)	p-value
Age at heart tissue acquisition, years	41±8	46±4	0.58
Male sex, n (%)	5 (100)	5 (100)	0.99
White or Caucasian race, n (%)	5 (100)	5 (100)	0.99
Body mass index, Kg/m^2	27±1	29±3	0.58
Diabetes mellitus, n (%)	0 (0)	0 (0)	0.99
Left ventricular ejection fraction, %	67±3	16±4	<0.0001
Left ventricular end-diastolic diameter, cm	4.5±0.3	7.3±0.4	<0.001
Cardiac index, $L/min/m^2$	4.1±0.5	1.8±0.2	<0.01

Supplemental Table III – Antibodies used for Western Blotting

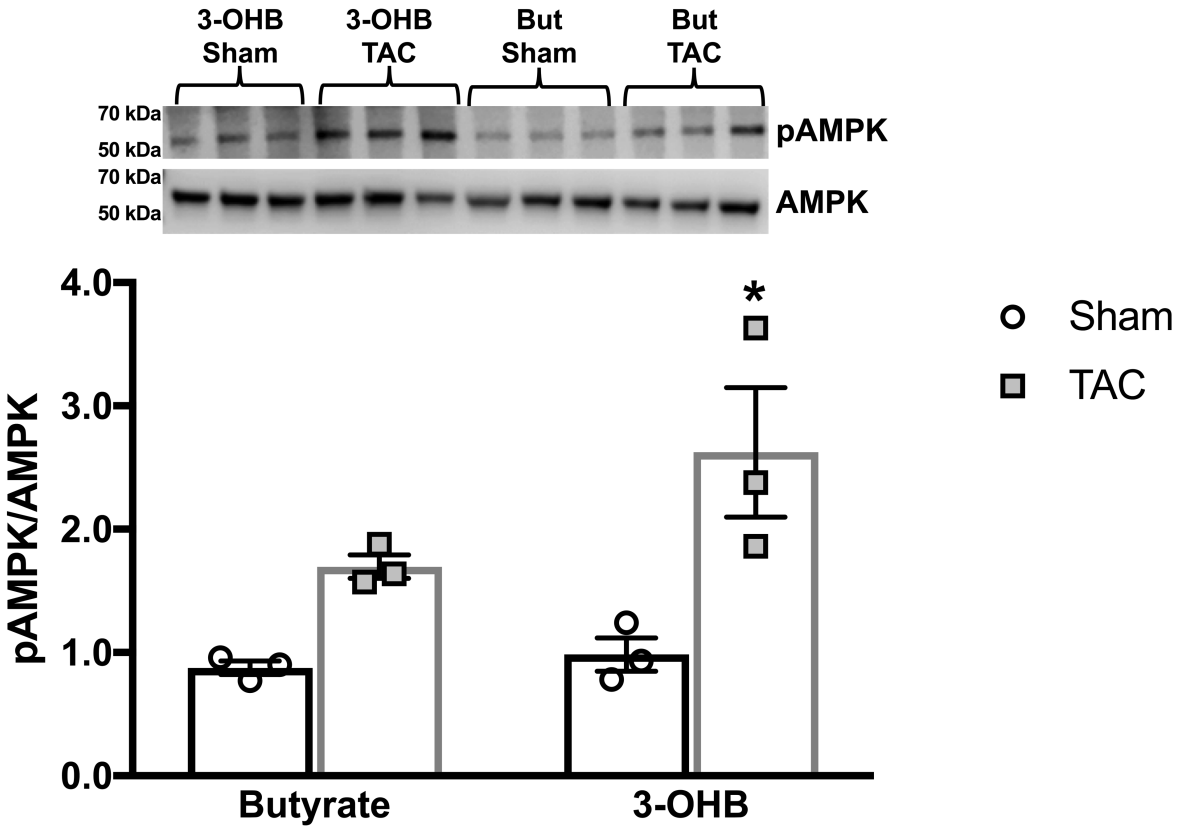
Antibody	**Vendor**	**Catalogue**
Acyl CoA synthetase medium chain family member 3 (ACSM3)	Proteintech	10168-2-AP
β-hydroxybutyrate dehydrogenase 1 (BDH1)	Proteintech	15417-1-AP
Calsequestrin (CASQ)	ThermoFisher	PA1-913
Carnitine palmitoyl transferase 1a (CPT1a)	Abcam	Ab128568
Carnitine palmitoyl transferase 1b (CPT1b)	Proteintech	22170-1-AP
Short chain acyl CoA dehydrogenase (SCAD)	GeneTex	GTX55489

Supplemental Table IV – Primer sequences for mRNA analysis

Gene	Primer Sequence
β-hydroxybutyrate dehydrogenase 1 (BDH1) rat	Forward: AGG CTG TGA CTC TGG ATT TG Reverse: AGC ATC GCC TTT GTC CTT
β-hydroxybutyrate dehydrogenase 1 (BDH1) human	TaqMan assay catalogue number Hs00366297_m1
Short chain acyl CoA dehydrogenase (SCAD) rat	Forward: CTC GAG ATT GGC GAA GAT TAC A Reverse: CAG CTC CTT CTC AGC AAA GT
Short chain acyl CoA dehydrogenase (SCAD) human	TaqMan assay catalogue number Hs00163506_m1



Supplemental Figure I – The enrichment of short chain acyl carnitine species with ^{13}C labelled carnitine. Short chain carnitine species were measured by LC/MS and the enrichment of the pool with ^{13}C carnitine species was determined. **A**, A depiction of the different short chain carnitine pools and their origination within the oxidative pathway for ketones and SCFA. **B**, Mean enrichment data for the different short chain carnitine pools with ^{13}C labeled carnitine species is shown *p=0.0029, †p<0.0001, ‡p<0.008, §p<0.0001, ||p<0.0001, #p=0.0022, **p=0.0035 with comparisons as indicated via 2-way ANOVA and Tukey's post hoc test measured in hearts perfused with either ^{13}C butyrate (n=7 sham, n=6 TAC) or ^{13}C 3-OHB (n=6 sham, n=6 TAC).



Supplemental Figure II – The phosphorylation of AMPK (pAMPK) and total AMPK measured in hearts after perfusion with either the SCFA butyrate or the ketone 3-hydroxybutyrate (3-OHB). Hearts were perfused 14 weeks after TAC or sham surgery. *p<0.05 vs. butyrate sham and 3-OHB sham via 2-way ANOVA and Tukey's post hoc test, n=3 for all groups.