

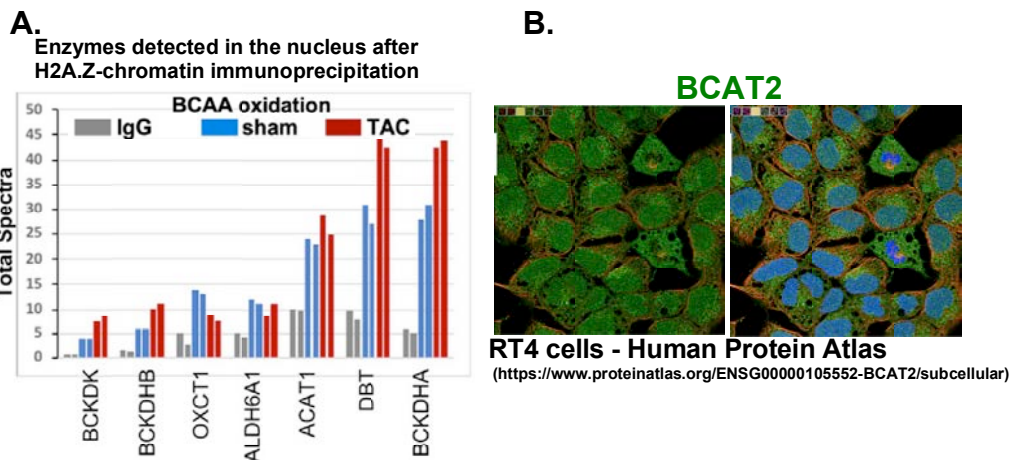


Figure 1S. BCAA oxidation enzymes are detected in the nucleus. A. Mice were subjected to either a sham operation or transverse aortic constriction (TAC) for 1 week. Chromatin was extracted and analyzed by anti-H2A.Z immunoprecipitation followed by mass spectrometry. This identified BCAA oxidation enzymes in the nucleus. The graph shows the total spectra identified for each of the indicated enzymes in the control IgG (grey bars), the sham heart (blue bars), and the hearts subjected to TAC (red bars). Note, not all the BCAA oxidation enzymes were identified by this approach, as their abundance and strength of association with chromatin influences their detection. **B.** Immunofluorescence staining of BCAT2 (green), nuclei (blue), microtubules (red), in human RT4 cells, showing its mitochondrial as well as nuclear localization (Human Protein Atlas, see link to webpage below the image).

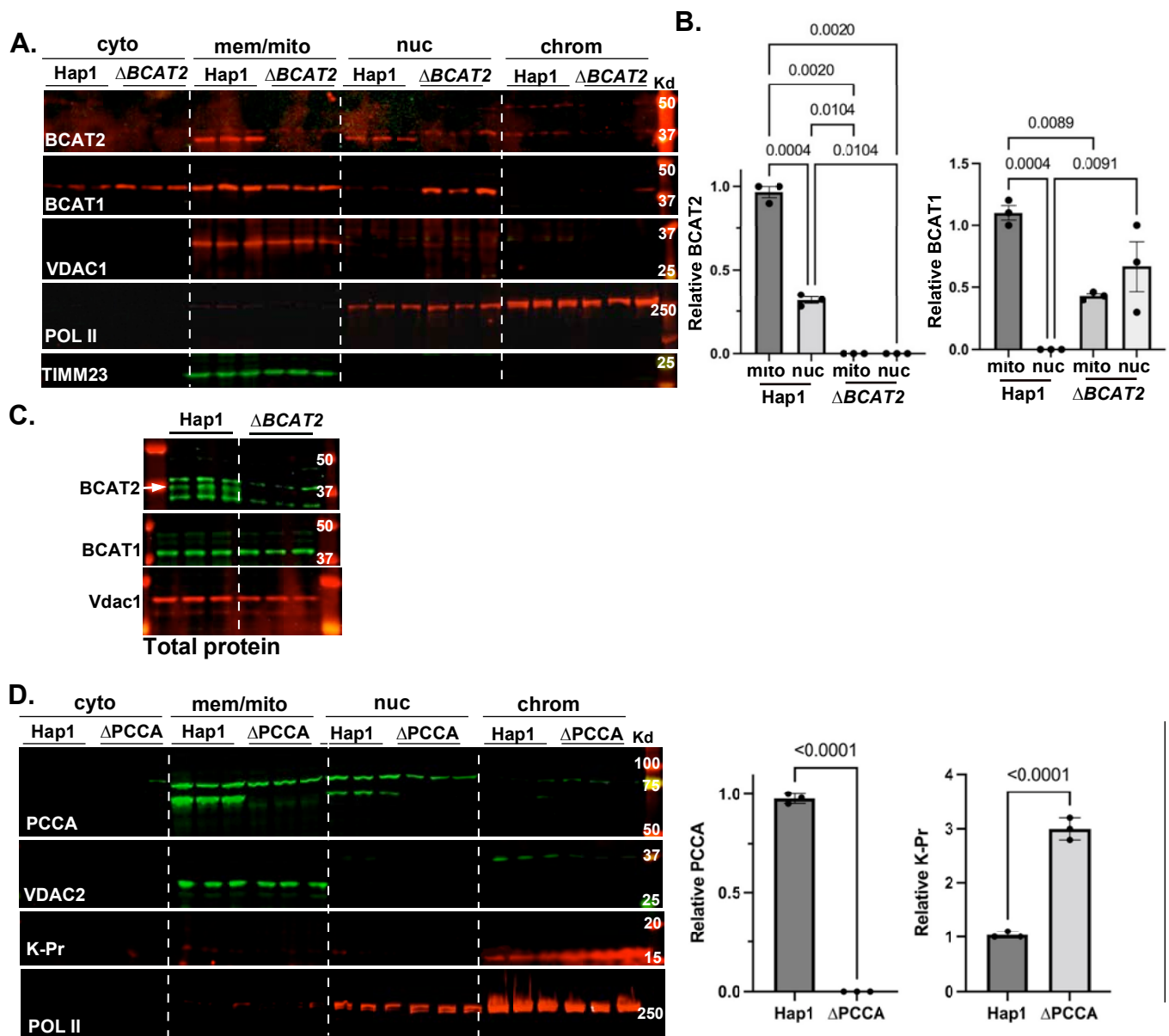


Figure 2S. Confirming BCAT2 and PCCA gene knockouts in Hap1 cells. **A, C.** Cultures of Hap1 and Hap1 $\Delta BCAT2$ cells, or **D.** Hap1 and Hap1 $\Delta PCCA$ cells, were **A., D.** harvested, and fractionated into cytoplasm (cyto), membrane, which contains mitochondria (mem/mito), nucleoplasm (nuc), and chromatin (chrom) fractions, or **C.** collected and total protein extracted. The protein was analyzed by WB with the antibodies listed on the left in each panel. **B, E.** BCAT2, BCAT1, and PCCA in the mito and nuc fractions on the WB were quantitated, normalized to Vdac1 or Vdac2 and H3 (or pol II), respectively, and plotted as relative values after adjusting the signal of 'mito' samples to 1 (n=3). The data were analyzed by one-way Anova and the p values of those that are ≤ 0.05 are indicated on the graph (n=3, each). The results confirm the absence of BCAT2 in the membrane/mitochondria and nucleoplasm fractions of the BCAT2 knockout cells, whereas BCAT1, which is not detected in the nucleoplasm in the parent Hap1 cells, translocates to the nucleus in Hap1 $\Delta BCAT2$, plausibly compensating for BCAT2's function, at least partially. This might explain the residual H3K23Pr signal observed in the presence of BCAA in these cells (main Fig. 1A).

Figure 2S

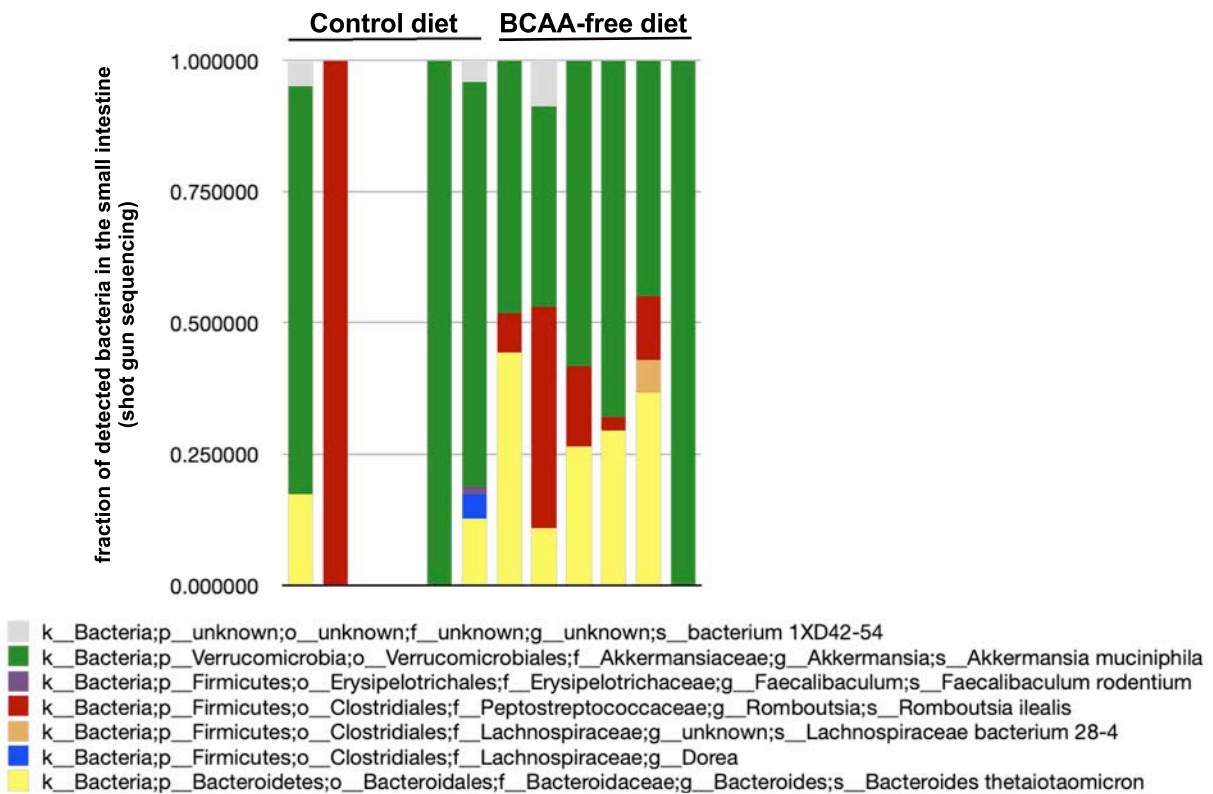


Figure 3S. Firmicutes and Bacteroidetes are more prevalent in mice guts on a BCAA-free diet. Mice were fed a BCAA-control or BCAA-free diet for 10 days. The small intestines were isolated and subjected to shotgun metagenomics. The results are presented in the stacked bar graph, showing the fractions of the bacterial families detected in each mouse. The color scheme for the family classification is listed below the graph.

Figure 3S

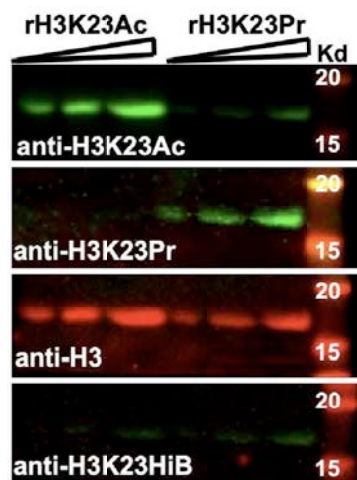


Figure 4S. Specificity of the H3K23-propionyl (H3K23Pr) antibody. Fifty, 100, and 200 nM of recombinant (r) nucleosomes harboring either rH3K23Ac or rH3K23Pr, as indicated on the top, were analyzed by Western blots for the antibodies listed on each panel.

2W-TAC

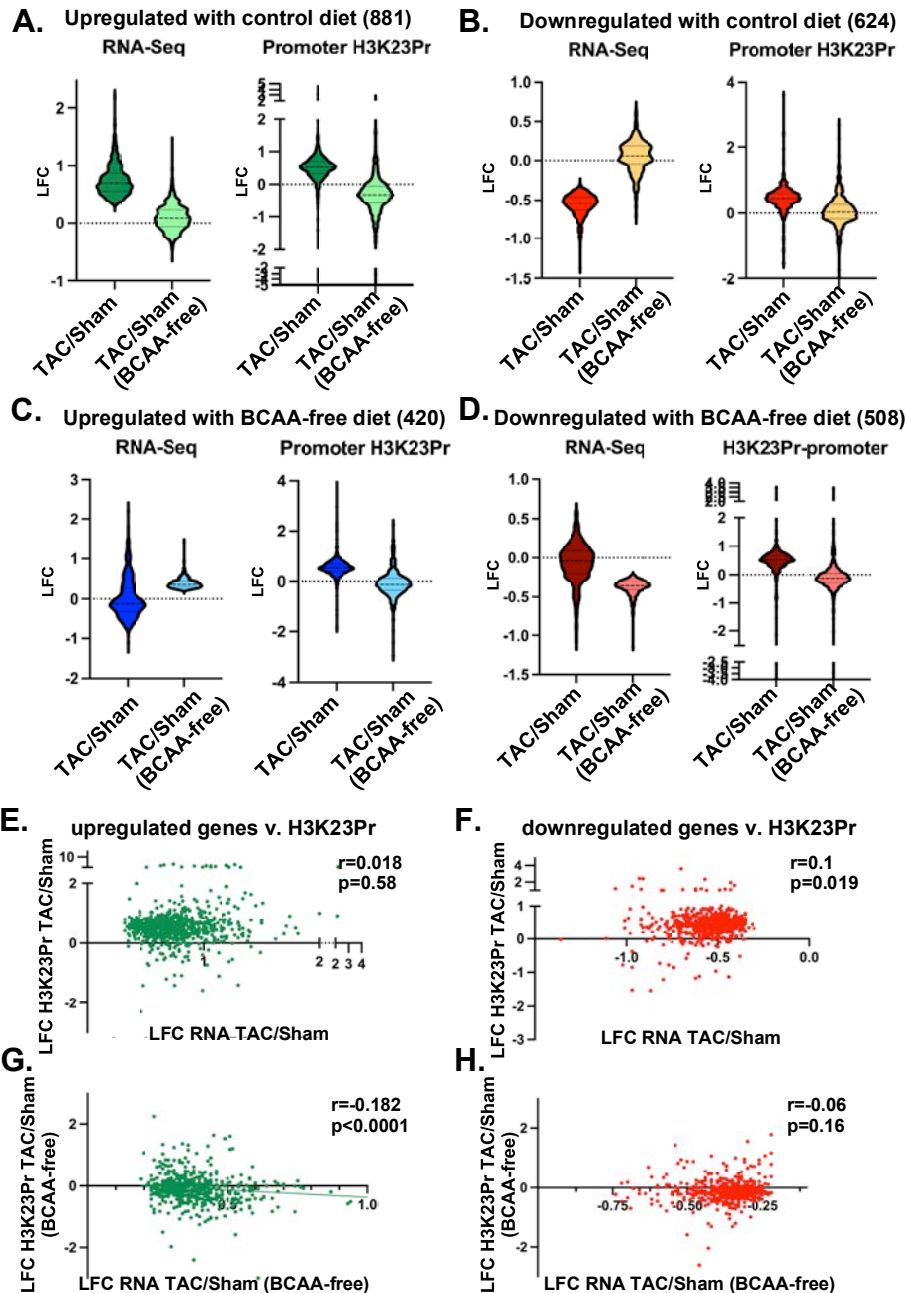


Figure 5S. The increase in promoter-H3K23Pr persists after 2W of pressure overload. H3K23Pr ChIP-Seq (-1000 to +1000) and RNA-Seq data from the 2W TAC experiment described in Fig. 3 (main text) were aligned by gene name and then sorted according to the genes' mRNA LFC TAC/sham that were significantly **A.** upregulated ($\text{padj} \leq 0.05$) in the hearts of mice on a control diet, or **C.** on a BCAA-free diet, or **B.** downregulated ($\text{padj} \leq 0.05$) in the hearts of mice on a control diet or **D.** on a BCAA-free diet. The log2 fold change (LFC) of RNA expression (RNA-Seq, left) and promoter-H3K23Pr (right) changes in the heart of TAC/Sham from these mice are presented as violin plots. **E-H.** Spearman's correlation analyses of LFC RNA expression v. LFC of promoter-H3K23Pr of TAC/Sham of significantly **E., G.** upregulated genes and **F., H.** downregulated genes. **G-J.** The RNA-Seq data from the 1W TAC on the BCAA-control and BCAA-free diets were analyzed by Gene Set Expression Analysis (GSEA). **G. I.** A complete list of the GO term enrichment. **H., J.** Examples of enrichment plots for some of the GO terms that are upregulated or downregulated during TAC.

Figure 5S

G.

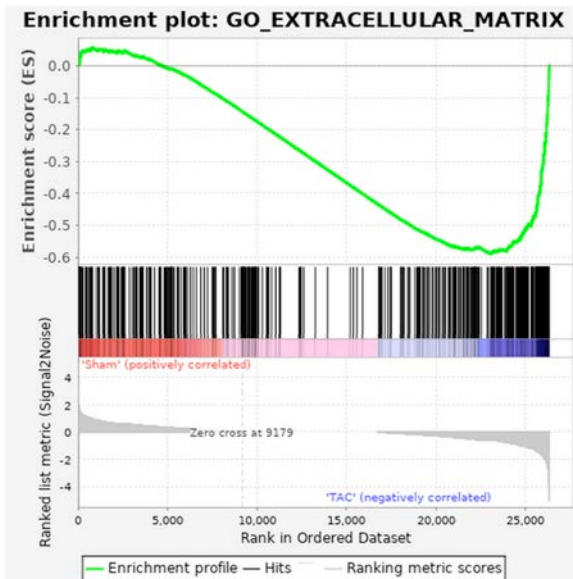
GO gene set enrichment analysis (GSEA) - TCA v Sham, BCAA-control diet (alphabetical order)

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enplot_GO_BONE_REMODELING_84.png
enplot_GO_BONE_RESORPTION_78.png
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enplot_GO_COLLAGEN_TRIMER_63.png
enplot_GO_COMPLEX_OF_COLLAGEN_TRIMERS_114.png
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enplot_GO_ENDOPLASMIC_RETICULUM_LUMEN_93.png
enplot_GO_EXTRACELLULAR_MATRIX_90.png
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enplot_GO_TRICARBOXYLIC_ACID_CYCLE_36.png
enplot_GO_VACUOLAR_LUMEN_117.png

Figure 5S-cont'

H, Enrichment plots - TCA v Sham, BCAA-control diet

Upregulated during TAC



Downregulated during TAC

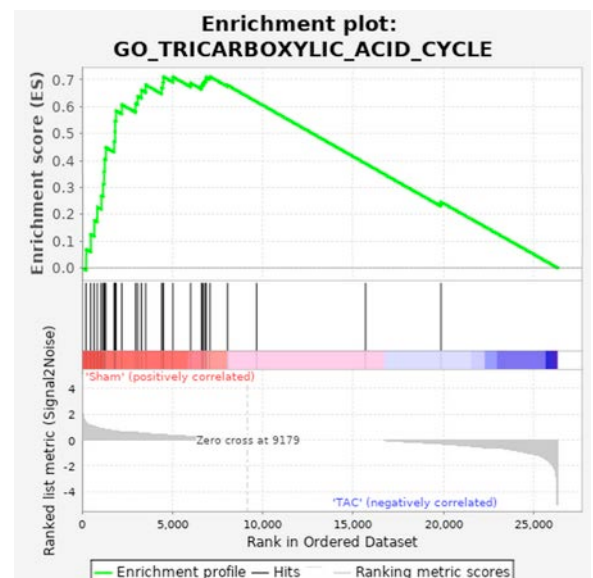
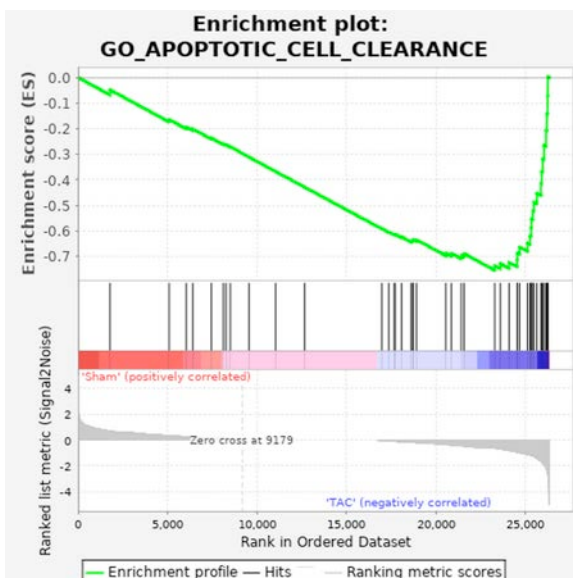
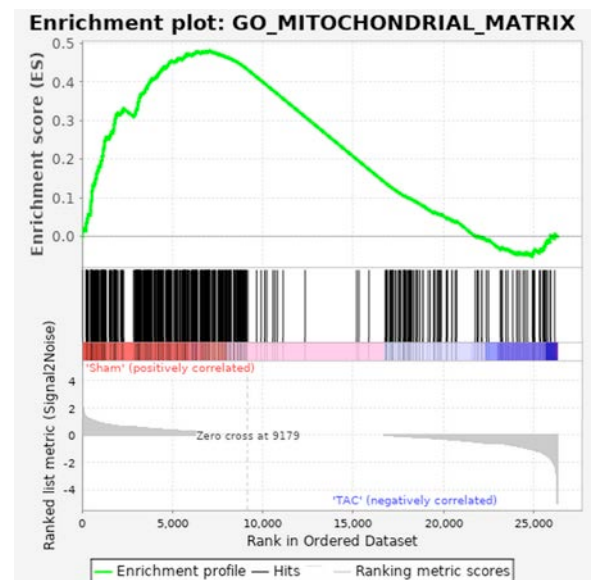
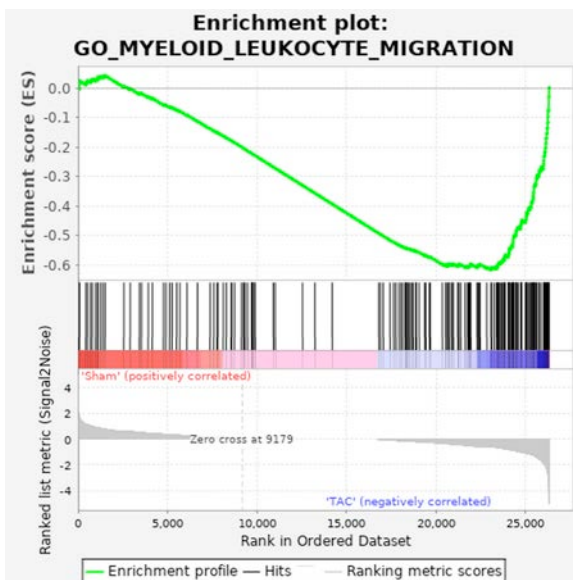
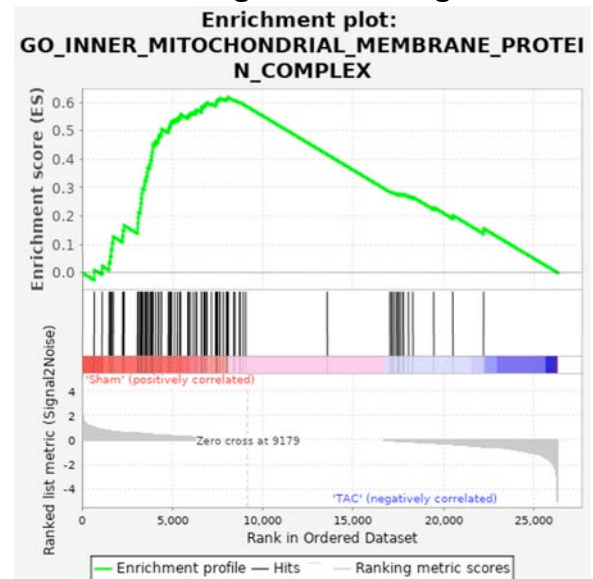


Figure 5S-cont'

I.

GO gene set enrichment analysis (GSEA) - TCA v Sham, BCAA-free diet (alphabetical order)

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Figure 5S-cont'

J. Enrichment plots - TCA v Sham, BCAA-free diet
Upregulated during TAC **Downregulated during TAC**

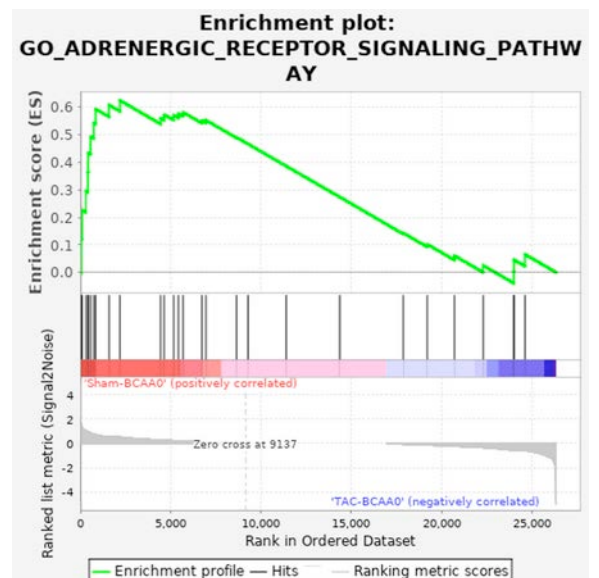
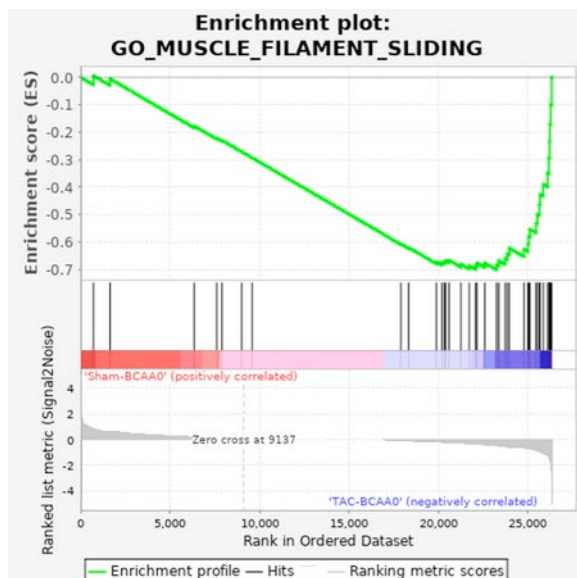
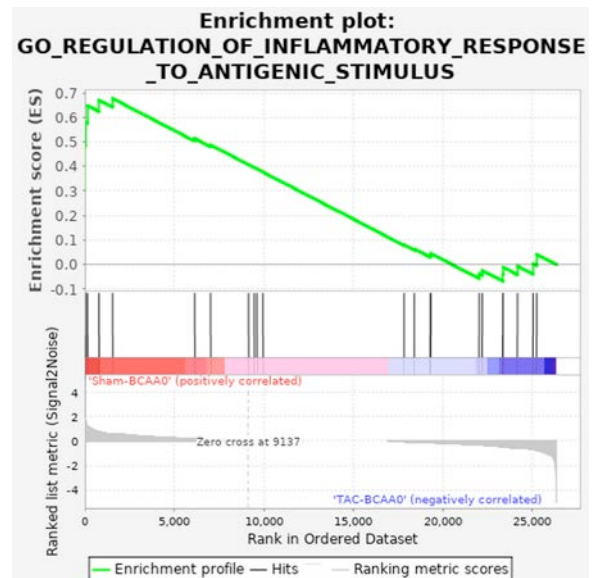
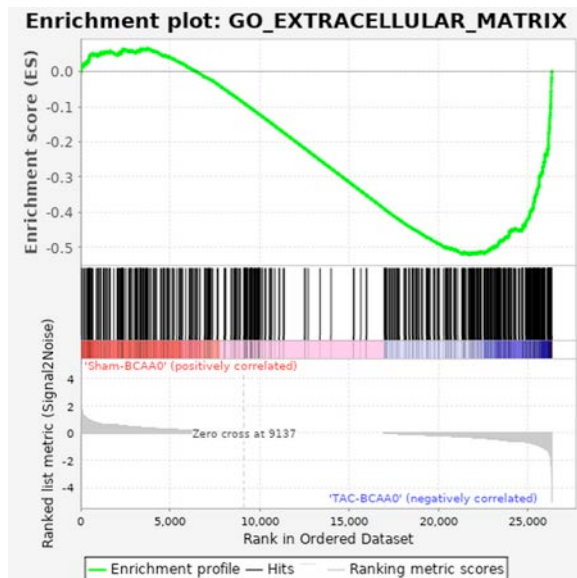
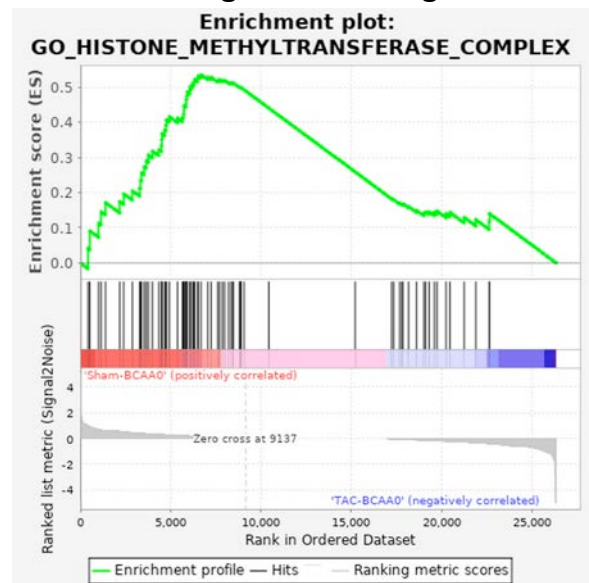
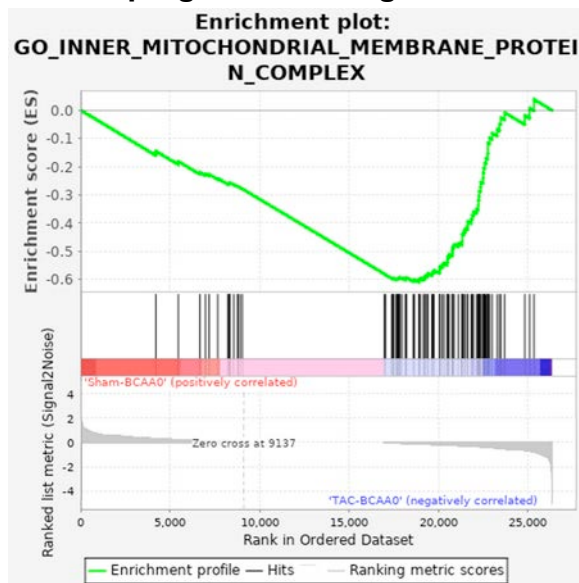


Figure 5S-cont'

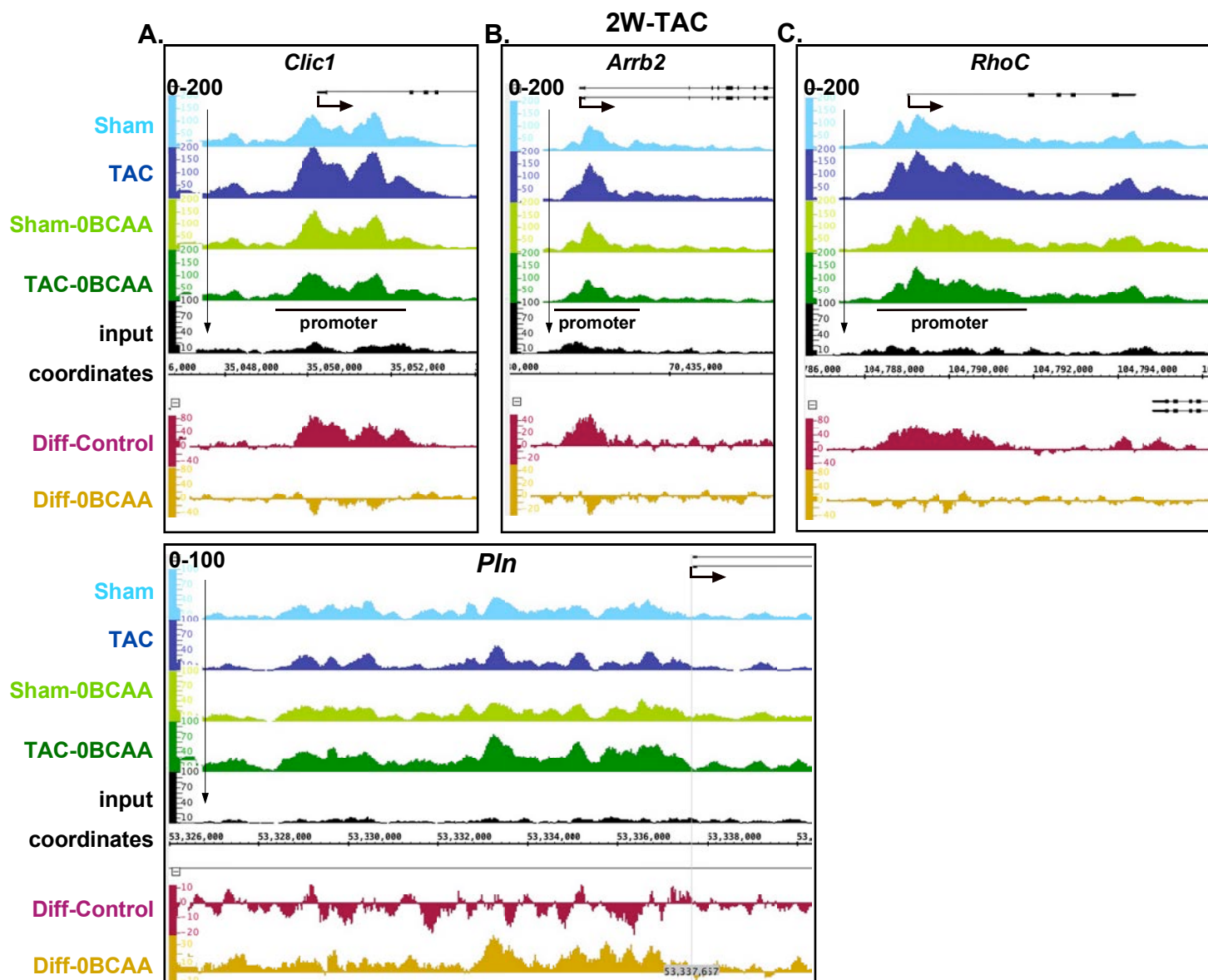


Figure 6S. TAC-induced upregulation of promoter-H3K23Pr is completely abrogated by a BCAA-free diet after 2W of pressure overload. Integrated genome browser images showing H3K23Pr ChIP-sequence tags from the 2W sham and TAC hearts of mice on the different diets, aligned across **A. *Clic1***, **B. *Arrb2***, **C. *RhoC***, and **D. *Pln***, gene coordinates. The labels on the left of each track indicate the surgical and diet conditions applied in mice; Sham and TAC surgeries with the BCAA-control diet (blue tracks), with the BCAA-free diets (green tracks); the differences (Diff) in the H3K23Pr sequence tags of TAC minus sham are shown in separate tracks for the control diet (Diff-Control, brown track) and BCAA-free diet (Diff-0BCAA, gold track).

Figure 6S

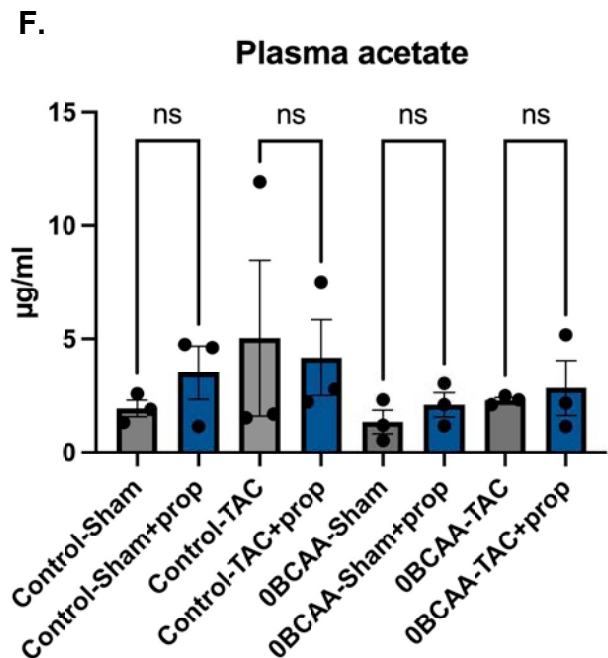
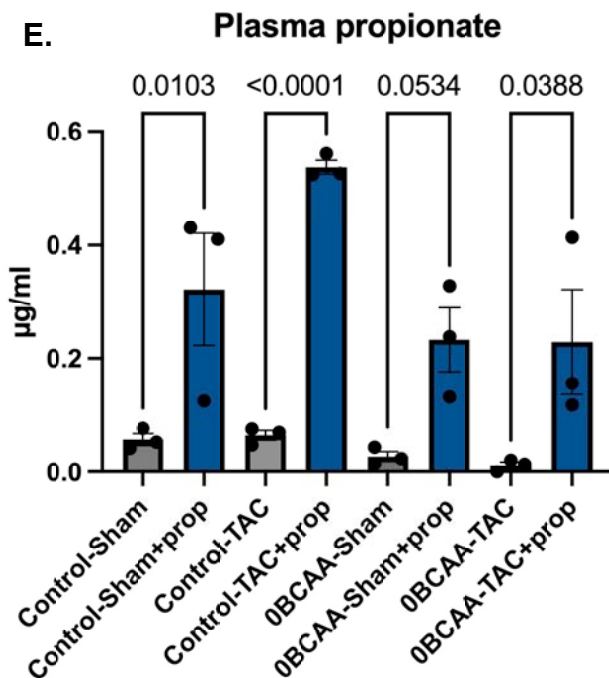


Figure 6S-E-F. Dietary propionate increases circulating propionate levels. Mice were fed a control or BCAA-free (0BCAA) diet without (grey bars) or with 1% dietary propionate (prop, blue bars) supplement for 4 days, before subjecting them to a sham or TAC operation. After 1 W the mice were analyzed with echocardiography, sacrificed, the plasma collected from the left ventricle, and the levels of short chain fatty acids measured (Creative Proteomics). Briefly, “samples were diluted in water containing labelled internal standards for each chain length (C2-C6). The free short chain fatty acids were derivatized using methyl chloroformate in 1-propanol yielding propyl esters before subsequent liquid-liquid extraction into hexane and analysis on a SLB-5ms (30 × 0.25 mm × 1.0 µm) column and detection using GC-El-MS in SIM-mode. The analytes were quantified using 8-point calibration curves.” Creative Proteomics, n=3, each. The results for plasma propionate (left) and acetate (right) concentrations (µg/ml) were plotted as bar graphs. Error bars represent S.E.M. The data were analyzed by one-way Anova using multiple pairwise comparisons of samples of those with vs. without propionate, for each of the conditions.

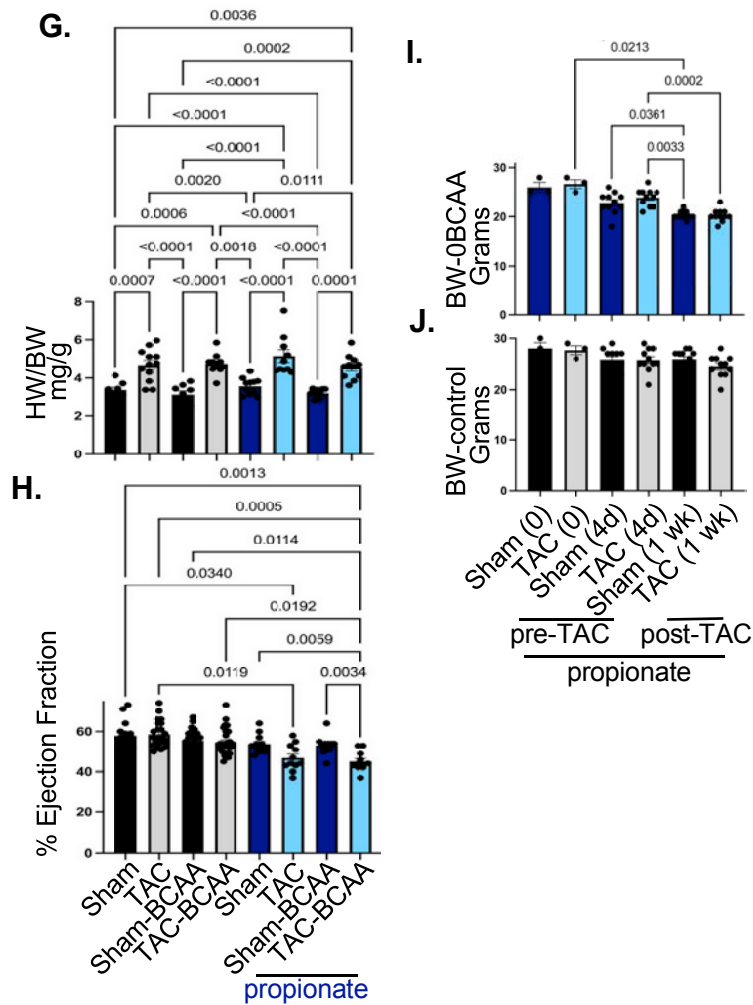


Figure 6S-G-J. Mice were fed a BCAA-control or BCAA-free diet without or with 1% propionate. After 4d they were subjected to a sham or TAC surgery. After 1W, mice were examined by echocardiography and the **G.** heart weight/body weight (HW/BW, mg/g) was calculated and graphed. **H.** Ejection fraction (EF) was graphed as %EF. **I-J.** BW (g) was measured and graphed. All results were analyzed by one-way Anova, and the p values of those that are ≤ 0.05 are listed above the brackets encompassing the bars.

Figure 6S (cont')

K.

TAC-induced upregulation of gene expression after addition of propionate to the BCAA-free diet

LFC	Gene	LFC	Gene	LFC	Gene	LFC	Gene	LFC	Gene	LFC	Gene	LFC	Gene	LFC	Gene	LFC	Gene	LFC	Gene	LFC	Gene	LFC	Gene	LFC	Gene	LFC	Gene	LFC	Gene	LFC	Gene
0.59	45174.00	0.40	Arhgef25	1.27	Ccr5	0.31	Cxcl6a2	1.21	Efr3	0.38	Ga13a3	0.60	Htra3	0.54	Ltlat	0.41	Mt1	0.52	mt-T1	0.79	Podtbl2	2.16	Ptprv	0.39	Rab34	0.70	Scln1	1.57	Strap	0.55	Tppb3
0.57	160000203Rik	1.07	Artic5	0.57	Cd14	0.93	Cpxm1	0.93	Egfr8	0.62	Gains	0.33	Lmb1	0.58	Mt2	0.61	Lmm1	0.58	Mt2	0.94	Pocb1b	1.30	Pycr1	0.40	Rab31l1	0.57	Sden1	0.35	Srebf2	1.14	Tppb2
0.73	1700017805Rik	0.50	Armcx2	1.15	Cd248	0.69	Cebd3l1	0.55	Egfr	0.58	Gaint16	0.31	ler3	0.61	Lmcc1	0.33	Mthfr	0.58	Mt2	0.42	Pogf1	0.60	Pyygo2	1.19	Rac2	0.41	Selenow	0.81	Spx	0.65	Traf4
0.81	1700020124Rik	0.85	Arntl	0.93	C3u04r	0.41	Crip1	0.85	Eyr1	0.57	Qain17	0.33	eyr1	0.87	Loxl1	0.61	Lnovd1	0.33	Mthfr	0.84	Fucos1	0.50	Rab13	0.58	Rap1ayap	1.13	Selyu	0.64	Spx2	1.24	Trem2
0.72	17002120014Rik	0.45	Arpc1b	1.30	Cd300l3b	0.35	Crip2	1.05	Egr2	1.30	Gaint6	0.67	lerf51	0.58	Lpar1	0.97	Lxot1	0.72	Mu61	0.81	Poyx11	0.40	Rab23	0.82	Rap2z	0.37	Serna3g	0.51	Srm4	0.72	Tfr1
0.16	2000002001Rik	1.09	Arpp21	0.58	Cd33	1.61	Crmpt1	0.56	Efr2d	0.94	Gas7	0.51	lef2	0.31	Lrg1	0.50	Mu81	0.20	Mu81	0.32	Pde4d	0.40	Rab34	0.37	Rapsn	0.71	Sernafc	0.37	Sxnt1	0.57	Tril
1.14	2210047318Rik	0.34	Armb1	0.90	Cd52	0.47	Crtap	0.33	Elk3	0.41	Gats2	0.40	lf227	0.48	Lrp1	0.31	Lrg1	0.34	Myadm	0.67	Pdgfra	0.40	Rab33l1	0.58	Rara	1.46	Sernc2	1.01	Sec5d	0.39	Trim26
0.31	2310022805Rik	0.68	Armb2	0.71	Cd68	0.32	Csf1	1.60	Elh1	0.83	Gdf11	0.39	lfm12	0.37	Lrp10	0.48	Lrp1	0.83	Mypc2	0.56	Pdgfrb	1.20	Rac2	0.32	Rarg	1.91	Sernc3a3	0.66	Sh4	0.42	Trim47
0.42	3632451006Rik	0.46	Arsa	1.61	Egr2	0.72	Csf1r	0.32	Elkf1	1.41	Gf3a3	0.60	lfm3a	0.34	Lrc1r2	0.37	Lrp10	0.44	Myt1	0.46	Pdgfrb	0.60	Rap1g1p	0.60	Rasl12	1.45	Sernc3a	0.52	S3gal1	0.50	Trp53
1.06	463242713Rik	0.37	Altg2a	1.03	Cd84	0.90	Cs2rb2b	0.52	Elwv1	1.02	Gf2a	0.30	lfm12a	0.72	Lrc1r7	0.34	Lrc1r4	0.49	Myd88	0.59	Pdia5	0.80	Rap2b	0.64	Rbm12	2.39	Sernb1a1a	0.48	Sl5	0.54	Ths22
1.78	53049046M23Rik	0.66	Altzb2	0.39	Cd93	1.46	Cst2rb2b	0.47	Ernp3	0.67	Gpcx4	0.46	lfm46	1.22	Lrc2z5	0.72	Lrc1r21	1.14	Myh11	0.41	Pdm3a	0.40	Hapsn	0.49	Hbm35	0.42	Sernc2	0.49	Stab1	0.31	Isku
1.51	54304311A17Rik	0.35	Altz2a3	1.03	Cd20	0.54	Csk	0.39	Erg	0.49	Glt5	0.95	lf1	0.66	Lrc2z5	1.22	Lrc2z5	0.43	Myh9	0.63	Pdm17	0.60	Rara	0.63	Rc2	0.56	Sernc1g	1.80	Star	0.39	Tsyp1b
0.94	Abec3	0.39	Abn7	0.58	Cd25b	0.66	Cepg4	0.56	Egrasee	0.49	Gimap1	0.67	lgf2	0.74	Lrc75a	0.66	Lrc75a	0.41	My12b	0.60	Pdpn	0.30	Rarg	0.79	Rcn	0.56	Seen2	0.62	Snm2	0.41	Tesc4
0.41	Abcd1	0.38	Abp97n3b	0.32	Cd42ap1	0.46	Carp1	0.48	Ert2p2	0.46	G1a1	0.69	lgf2b2p2	0.59	Lrm2	0.74	Lrc75a	0.36	My16	0.53	P14	0.60	Rasl12	0.41	Recq35	0.36	Seft1b	0.55	Sxbp2	1.60	Tic25
0.52	Abhd14b	0.48	AUO20206	0.58	Cd42ap2	0.57	Csrp2	1.03	Ephb6	0.91	Ga5	0.74	lgf2p4	0.60	Lp1	0.59	Lrm2	0.67	My19	0.44	Pgghg	0.60	Rbm12	0.48	Rela	0.42	S3a2	0.39	Supt7	0.41	Thy3
0.26	Acad11	0.35	Aup1	0.45	Cd422se1	0.40	Ctsa	0.75	Epsb2	0.34	Gbt1	0.58	lgf2p5	0.52	Lbp3	0.60	Lsp1	0.86	Myk	0.31	Pgls	0.50	Rbm33	0.58	Rem1	1.28	Sn	1.20	Susd2	0.86	Tubb2b
0.31	Acot7	0.36	Aut2	0.36	Cdk2ap1	0.40	Ctsb	0.32	Erjct1	0.70	Gli1	0.64	Igsf3	0.66	Ltca8	0.52	Ltp3	0.44	Myo1d	0.32	Pnc2	0.60	Rcc2	0.39	Rest	0.53	Slnk3	0.70	Susd5	1.36	Tubb3
1.20	Acta2	0.35	Axl	0.93	Cd01	0.54	Ctsa	0.32	Ety11	0.80	Glipr2	0.44	Igsf8	0.44	Ltca8	0.66	Ltca8	0.61	Myo1e	0.18	Pnc1g	0.80	Rcn3	0.37	Retn	1.03	Sghn	0.40	Swap70	1.18	Tubb4a
1.05	Actb	0.74	B3galnt1	0.83	Cd2f1	0.85	Ctsa	0.42	Ets1	0.62	Ets1	1.10	Igsf9	0.56	Ltca8	0.43	Ly8a	0.81	Myo1f1	0.19	Piang	0.40	Recq35	0.37	Retreg2	1.00	Sh2b2	0.41	Syde1	0.67	Tusc5
0.50	Actg1	0.92	D4galnt1	0.70	Cebp3a	0.50	Ctsa	0.40	Cv1a	0.40	Gltm	0.71	Ibkke	0.70	Ly1	0.50	Ly2e	1.36	Mypocap1	0.31	P3a3	0.50	Rela	0.30	Retreg3	0.98	Ticb2g3	0.35	Ys1	0.7	Tut1
1.45	Actg2	0.34	B4gal1	0.30	Celf2	0.40	Cxd3c1	0.34	Cvc	0.38	Gltm	0.90	I1bke	0.52	Ly22	0.70	Ly1	0.40	Naga	0.85	Pk3cd2	0.60	Rem1	0.50	Rltb3	0.58	Shcbp1	0.44	SY11	0.36	Txndc-2
0.36	Actn1	0.44	B4gal1	0.34	Cep170b	1.30	Cx3c1	1.14	Ev2a	0.59	Gm447283	0.69	I1b	0.62	Maf	0.52	Ly22	0.40	Naga	0.93	P3b	0.40	Rest	0.34	Rtk1	0.90	Sh5cx2b	0.37	T31	0.78	Tyms
0.44	Actv11	0.56	Bbc3	1.14	Ceracam	0.35	Cxcl12	0.34	Ext1	0.61	Gmf5	0.58	I17ra	0.33	Maged2	0.62	Maf	0.32	Naga	0.59	P3r	0.40	Retn	0.34	Rtkarx	0.30	Sharpin	0.71	Tagin	0.54	Tyrob
1.34	Adam12	0.53	BC017158	1.63	Cld	0.70	Cxcl16	0.63	Faap20	0.55	Gmp1	0.52	I3ra	0.61	Map1a	0.33	Maged2	0.62	Nat14	0.30	P3pnm1	0.40	Retreg2	0.31	Rgt1	0.79	Shis4a	0.47	Tagin2	0.43	Ube2w
0.35	Adam15	0.47	Bcar3	0.44	Cbl1	0.49	Cxcl4	0.30	Fad31	0.52	Gngt2	0.32	I4ra	0.36	Map1s	0.81	Map1a	0.62	Nol1	0.52	Pxnk2	0.30	Retreg3	0.41	Rgm1	0.73	Shis4a5	0.31	Taloid1	0.95	Ubun16
0.54	Adam19	0.52	Bcl2l11	0.48	Cfp	0.46	Cybsf3	0.78	Fads2	0.79	Gpc3	0.63	I6ra	0.53	Map3k14	0.36	Map1s	0.92	Ncam1	0.75	P2a15y1	0.50	Rltb3	0.90	Rgs10	0.36	Sip1	0.74	Tabpp	0.50	Unc113b
0.65	Adam33	0.46	Bcl2l12	1.03	Cnao	0.40	Cyba	0.54	Fem102a	0.93	Gpr132	0.50	lppsd5	1.23	Map3k7c1	0.53	Map3k14	0.44	Ndn	0.43	P2a16	0.40	Rtk1	1.52	Rgs11	0.47	Sipa	0.42	Ticc101ot	0.56	Unc54
1.21	Adam8	0.98	Bcl3	0.31	Cdh3	0.31	Cybb	1.33	Fem105a	0.31	Gpr137	0.37	lppsd5	0.43	Map6	1.23	Map3k7c1	0.59	Nf2	0.65	P2a17g	0.30	Rtkrank	0.51	Rgs4	0.70	Six1	0.42	Ticd15	0.73	Unc93o1
0.62	Adam15s1	0.43	Bcl6	0.37	Cypl	0.37	Cypt27a1	0.37	Fam1209b	0.47	Gpr153	0.43	lpp5	1.08	Marpe	0.43	Map6	0.56	Nf2	1.53	P2a1r2	0.30	Rgt1	0.29	Rhoc	0.41	Sixt	0.35	T2	0.80	Usp49
0.33	Adam15s4	0.43	Bcr	0.33	Cypl2	0.93	Cytp2b1	0.88	Fam181b	1.66	Gpr181b	0.38	lr3	0.31	Marvld1	1.08	Marcks	1.21	Nf4	0.43	P2c12	0.40	Rgmra	0.74	Rhog	0.63	Slc16a3	0.31	Tax5	0.64	Vasn
0.55	Adam5	0.89	Bgn	0.60	Chat1	0.39	Cy2p1	0.56	Fam193a	0.78	Gpr19	0.38	lr8	1.60	Mahn1	0.31	Marvld1	0.82	Nkap11	0.48	P2d3	0.30	Rgs10	0.48	Rhoj	0.78	Slc16a9	0.34	Tf3	0.33	Vasp
0.67	Adam1s1	0.53	Bln1	0.82	Chat12	1.16	Cypt4	1.68	Fam196a	0.58	Gpr4	0.42	Irgm2	0.38	Mcam	1.60	Mahn4	0.49	Nkap5f1	0.85	P2d4	1.50	Rgs11	0.69	Rhou	1.06	Slc13a3	0.50	Targ1	0.58	Vat1
0.53	Adcy4	1.09	Bln1	0.41	Cisd3	0.98	Cyfh18	0.72	Fam206a	1.20	Gpr65	0.62	I4ra	0.50	Mcom	0.38	Mcam	0.48	Nkap5d	0.48	P2k3b	0.40	Rgs14	0.52	Rian	0.91	Slc25a1	0.33	Tn2	0.33	Vegfb
0.59	Adcyap11	0.42	Blnrb	0.55	Cited4	0.32	D17HES53E	0.46	Fam210b	0.61	Gprc5c	0.44	Ilgam	0.34	Mcsr1	0.50	Mcom3	0.60	N3n	0.49	P2k3h3	0.30	Rhoc	0.30	Rin2	0.42	Slc25a23	0.52	Tic3	0.69	Vim
0.87	Adgri1	0.37	Bmp1	0.49	Ckap4	0.44	Dab2	0.46	Fam222b	0.72	Gpm33	0.50	Ibt2	0.69	Meg3	0.34	Mcsr1	0.63	N3futa412	0.79	P2k3h2	0.70	Rhog	0.94	Rip3r1	0.65	Slc25a45	0.44	Tybl1	0.49	Vkore1
0.74	Adgri1	0.49	Bt2	0.47	Ckb	1.26	Dac2	0.45	Fem44a	0.50	Gpx1	0.31	Ibt5	0.67	Metnl1	0.60	Meg3	0.30	N3fub7	0.46	Pod3	0.40	Thcy	0.36	Pnash2b	0.50	Slc27a4	0.55	Tybl1	0.45	Vmac
0.64	Adgri3	0.54	Bcl2	0.77	Clec10a	0.44	Dap	1.19	Fam43c	0.57	Gpx7	1.47	Ilt4	0.33	Metl1	0.37	Metl1	0.45	Natf1	0.42	P3rc3	0.70	Rhou	0.54	Rn2d2	1.19	Slc27a4	0.55	Tybl2	0.48	Vps18
0.34	Adm1	1.64	Bt2	0.85	Clec12a	0.80	Dhb	0.36	Fam53b	0.31	Ghrpr	0.44	Iltg1p1	0.43	Metl2b	0.33	Metl1	0.72	Nis	0.71	P3p	0.50	Rian	0.43	Rnf157	0.47	Slc25a2	0.79	T3f1	0.55	Vn
1.46	Adipoq	0.37	Bud13	0.38	Clec3b	0.50	Dcackd	1.52	Fen	0.52	Griks	0.43	Ja1g1	1.22	Map12	0.43	Map12b	0.35	Naur1	0.59	P3r	0.30	Rin2	0.68	Rnf2e	0.49	Slc1b1	0.49	Tb3s3	0.82	Was
0.50	Adora2a	1.43	C130023A14Rik	1.18	Clec4	0.37	Deaf1	0.70	Festk5d	0.33	Grina	0.39	Jmg1	0.45	Mge3	1.22	Map2	0.80	Naur1	1.63	Pnla1p	0.90	Rip3r3	0.35	Rnpeo	0.59	Slc8a2	0.82	Ty1	0.74	Wdcd17
0.79	Aebp1	0.87	C1q	1.22	Clec4	0.31	Dendmta	0.51	F2bn2	0.59	Gm	0.51	Jun	0.57	Mfsd10	0.45	Mlpe8	0.83	Nat4	0.33	Pnd1	0.40	Rnaseh2c	0.38	Rp24	0.77	Sera9	1.49	T4b	0.58	Wf1
0.45	Agpat1	0.80	C1q	0.38	Clec4n	0.46	Des	0.44	Fbln5	0.63	Grrp1	0.48	Junb	0.47	Mfsd12	0.57	Mfsd10	0.40	N1b	0.32	P3cd1	0.50	Rnd2	0.30	Rp2E	0.36	Slc2cb1	1.81	Tmp1	0.38	Wp12
0.70	Agpat4	0.50	C1q	0.37	Clic1	0.31	Dgcr2	1.37	Pltnr1	1.38	Gstm1	0.31	Junb	0.21	Mtr1	0.47	Mst12	0.47	N13	0.34	P3cd1p3	0.40	Rnf157	0.34	Rp41	0.77	Slr2	0.35	Tmp2	0.38	Wz
0.68	Ag1	0.59	C1qtnf2	0.48	C1p2	0.20	Dhcr2c4	1.14	Pltn2	0.50	Gstm2	0.34	Kat2a	0.27	Micaf1	0.57	Mst1	0.46	Ns2	0.47	P3r2a	0.90	Rnd2	0.33	Rp23	0.47	Slr2	0.			

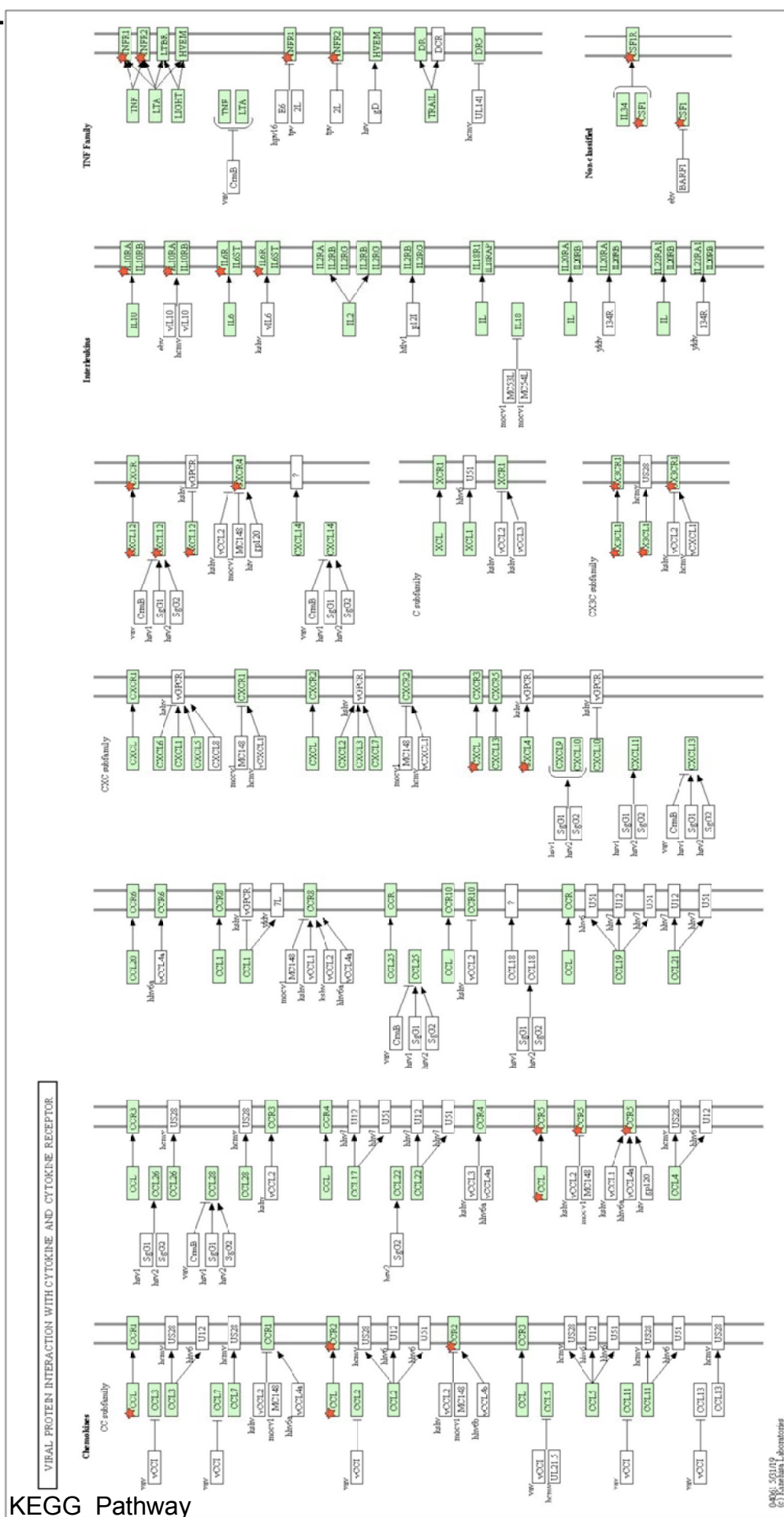
Figure 6S-K-O. Supplementing the BCAA-free diet with propionate substitutes for BCAA, enhancing gene expression in the heart during pressure overload. K. RNA was extracted and sequenced (RNA-Seq) from the hearts of mice on a BCAA-free diet or a BCAA-free diet supplemented with 1% propionate, subjected to sham or TAC surgeries. The LFC of the RNA reads from the TAC, BCAA-free plus 1% propionate / TAC, BCAA-free were calculated and those with significant increases in LFC of > 0.3 are presented in the heatmap, showing the LFC values and the gene names for each. The color scale bar for LFC is shown below the heatmap. **L-O.** The genes identified (listed in the heatmap) were analyzed by DAVID Bioinformatics Resources for functional pathways. Some of these pathway networks (KEGG_Pathway) include **L.** ECM-receptor interaction, **M** Signaling in cancer, **N.** Viral protein interaction with cytokine and cytokine receptor, and **O.** Apoptosis. Genes labeled with a red star are from the analysis list.

Figure 6S (cont')

ECM-RECEPTOR INTERACTION

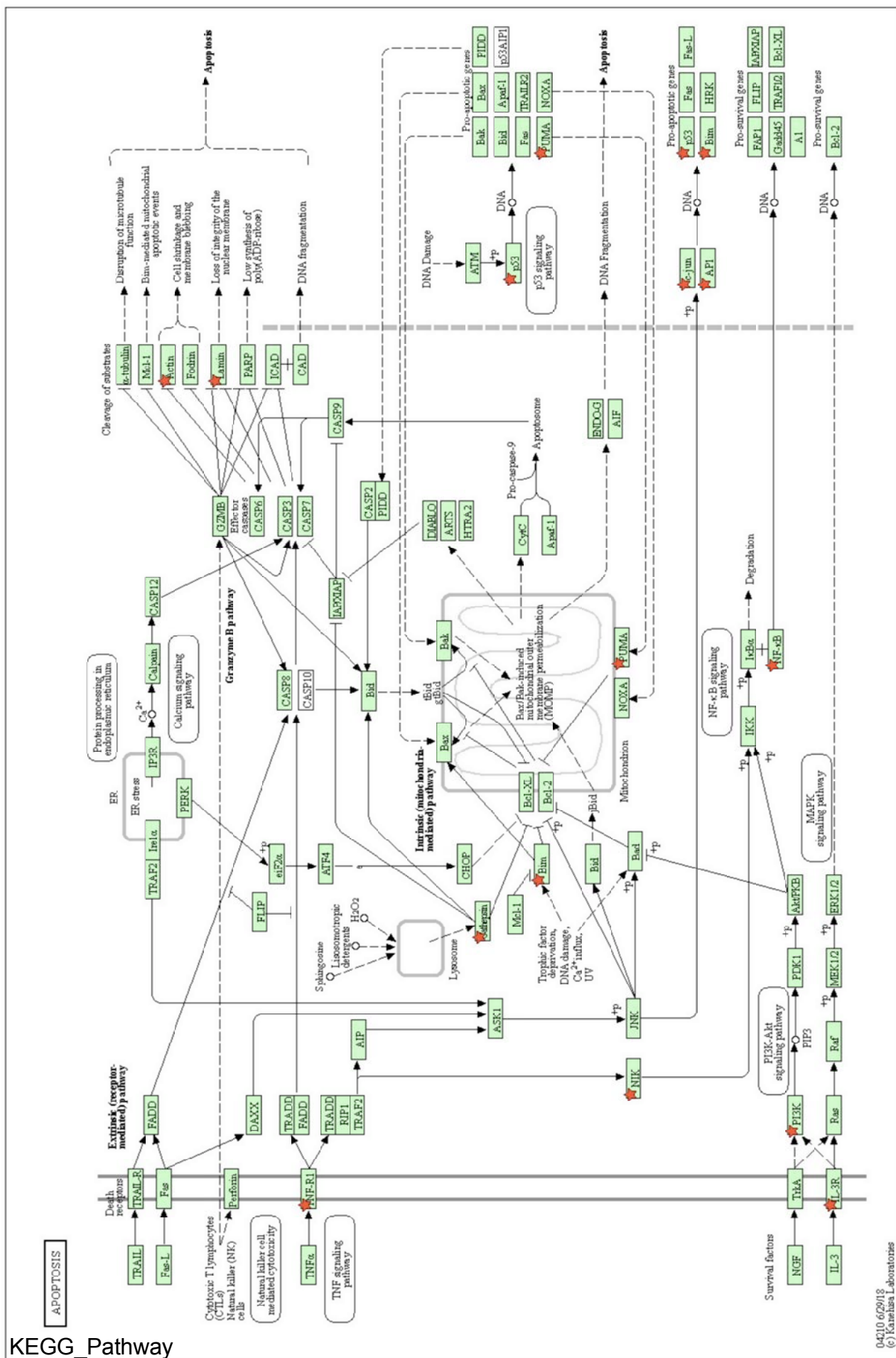


Figure 6S (cont')



upregulated by TAC in the heart of mice on a BCAA-free diet plus 1% propionate v. BCAA-free without propionate

Figure 6S (cont')



KEGG_Pathway

★ upregulated by TAC in the heart of mice on a BCAA-free diet plus 1% propionate v. BCAA-free without propionate

Figure 6S (cont')

Sarcomeric proteins

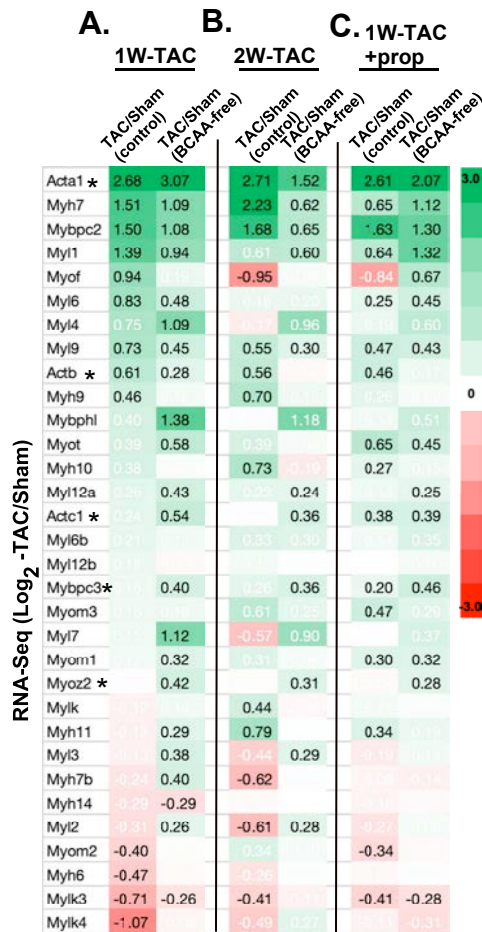


Figure 7S. Pressure overload uniquely increases cardiac actin, myosin binding protein c3, and myozenin2 in the heart, with a BCAA-free vs. BCAA-control diet. Mice were treated as described in figure 2 (in main text) **A.**, **B.** without or **C.** with 1% dietary propionate supplement. **A.**, **C.** 1W or **B.** 2W post-TAC, the hearts were isolated, RNA extracted and sequenced (n=3, each). The heatmaps show the LFC of TAC/Sham (control) and TAC/Sham (BCAA-free), for cardiac sarcomeric proteins. The values displayed in black are those with padj of ≤0.05. The color code bar is shown on the right. **D-I.** Integrated genome browser images showing H3K23Pr ChIP sequence Tags from the **D-F.** 1W, or **G-I.** 2W, sham and TAC hearts of mice on the different diets, aligned across *Actc1*, *Actb*, and *Acta1* gene coordinates, and sham and TAC hearts aligned across *Actc1*, *Actb*, and *Acta1*. The labels on the left of each track indicate the surgical and diet conditions applied in mice; Sham and TAC surgeries with the BCAA-control diet (blue tracks), with the BCAA-free diets (green tracks); the differences (Diff) in the H3K23Pr sequence tags of TAC minus sham are shown in separate tracks for the control diet (Diff-Control, brown track) and BCAA-free diet (Diff-0BCAA, gold track).

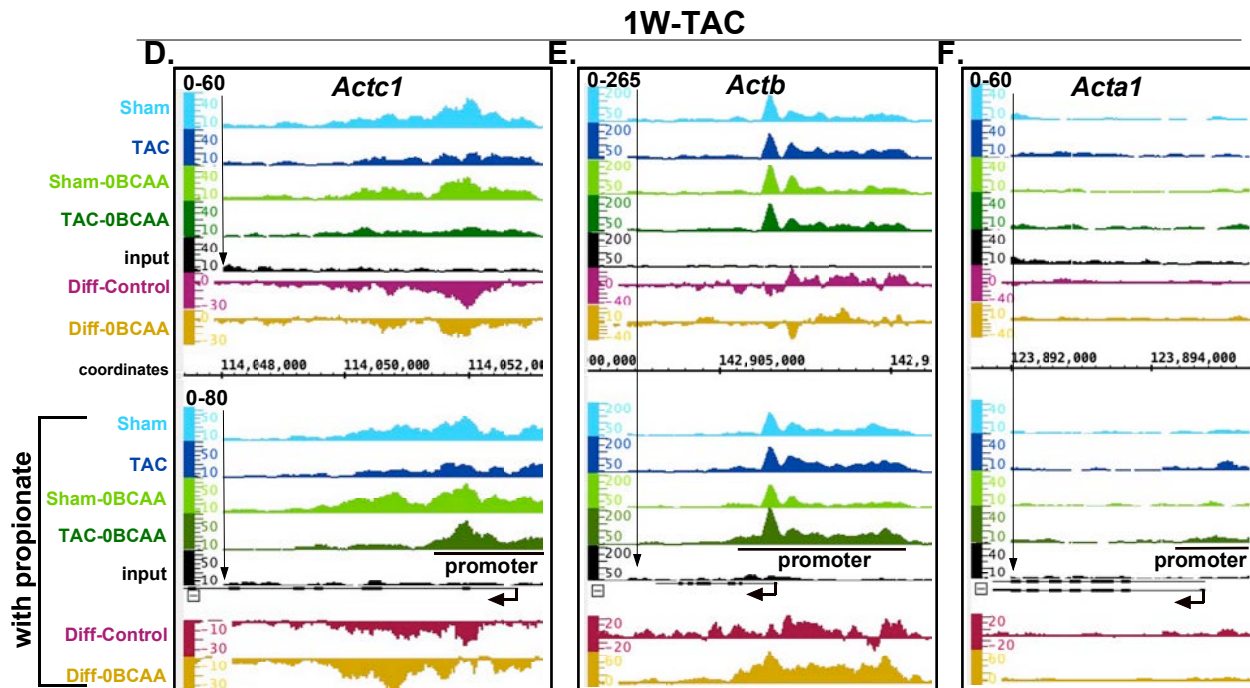


Figure 7S

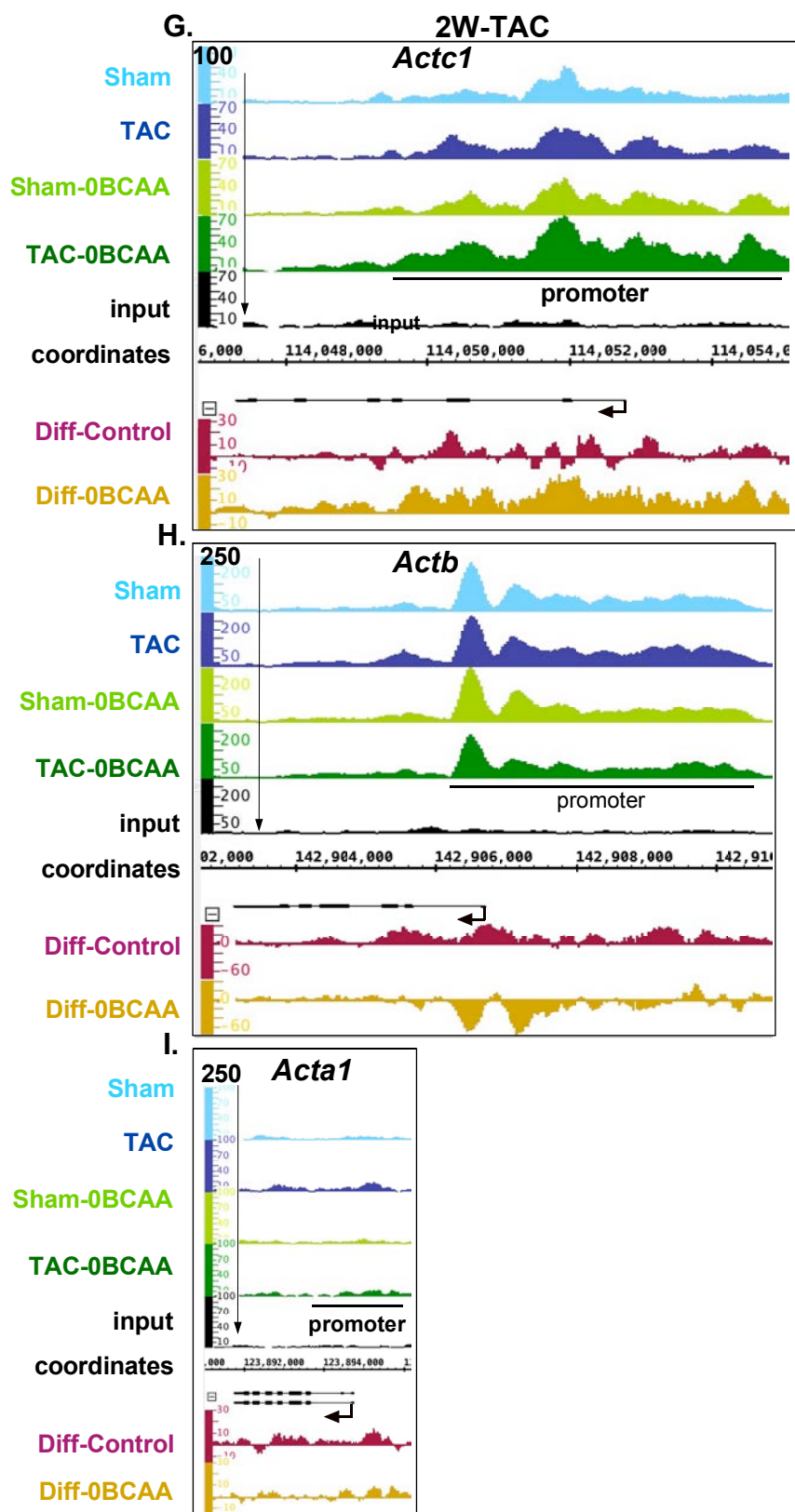


Figure 7S (continued)

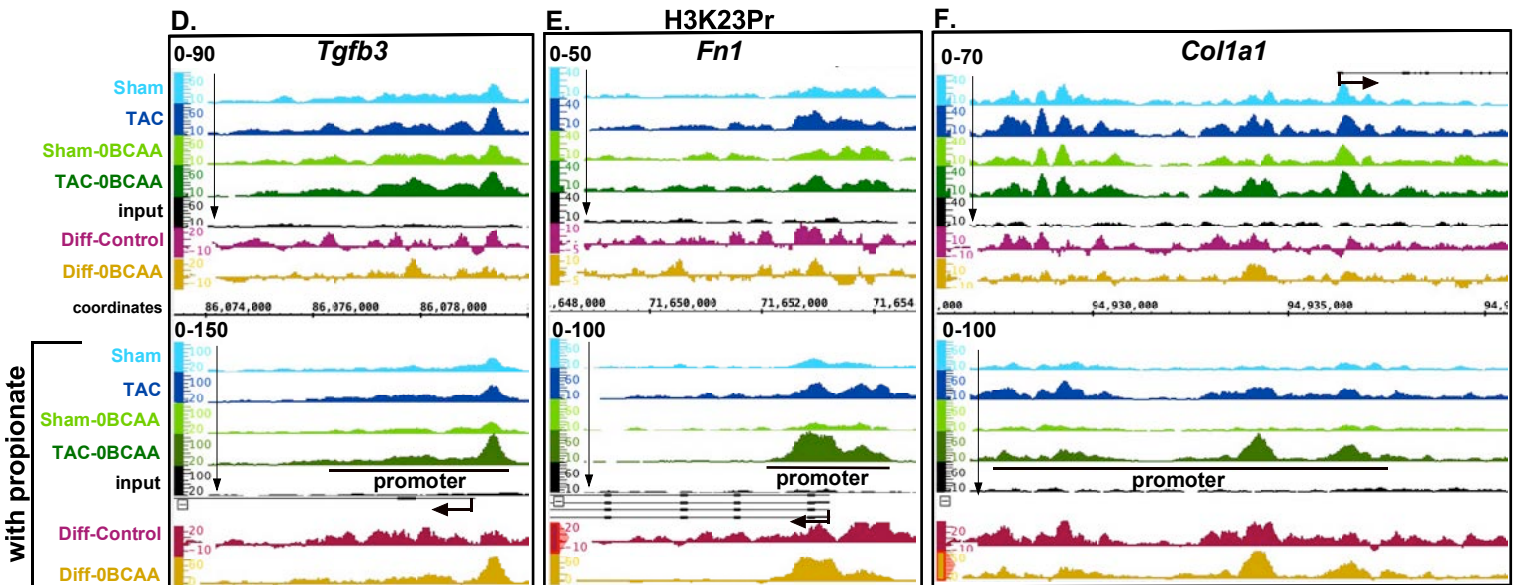
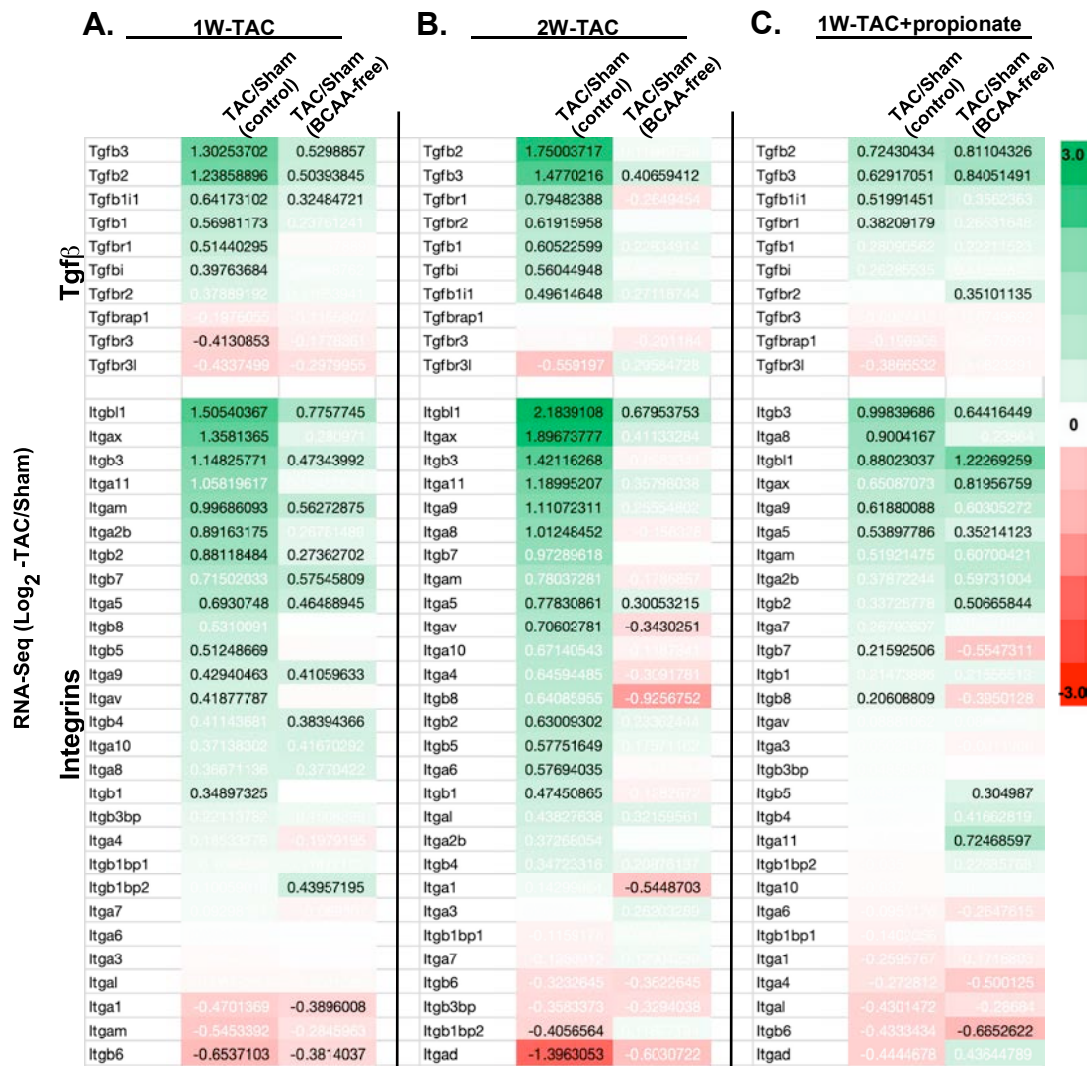
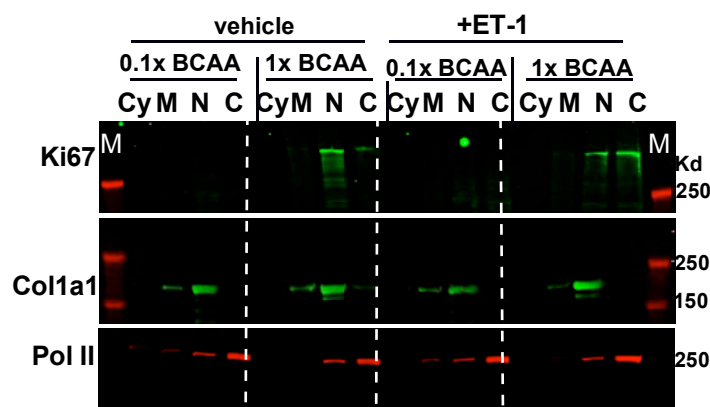


Figure 8S. TGFβ ligands, their receptors, and integrins, are upregulated by pressure overload but significantly dampened by a BCAA-free diet. Mice were treated as described in figure 2 (in main text) **A.**, **B.** without or **C.** with 1% dietary propionate supplement. **A.**, **C.** 1W or **B.** 2W post-TAC, the hearts were isolated, RNA extracted and sequenced (n=3, each). The heatmaps show the LFC of TAC/Sham (control) and TAC/Sham (BCAA-free), of the mRNA for TGFβ receptor ligand and integrin isoforms. The values displayed in black are those with padj of ≤ 0.05. The color code bar is shown on the right. **D-F.** Integrated genome browser images showing H3K23Pr ChIP sequence Tags from the 1W sham and TAC hearts of mice on the different diets, aligned across *Tgfb3*, *Fn1*, and *Col1a1* gene coordinates. See legend of Fig. 7S for more track description.

Figure 8S

A.



B.

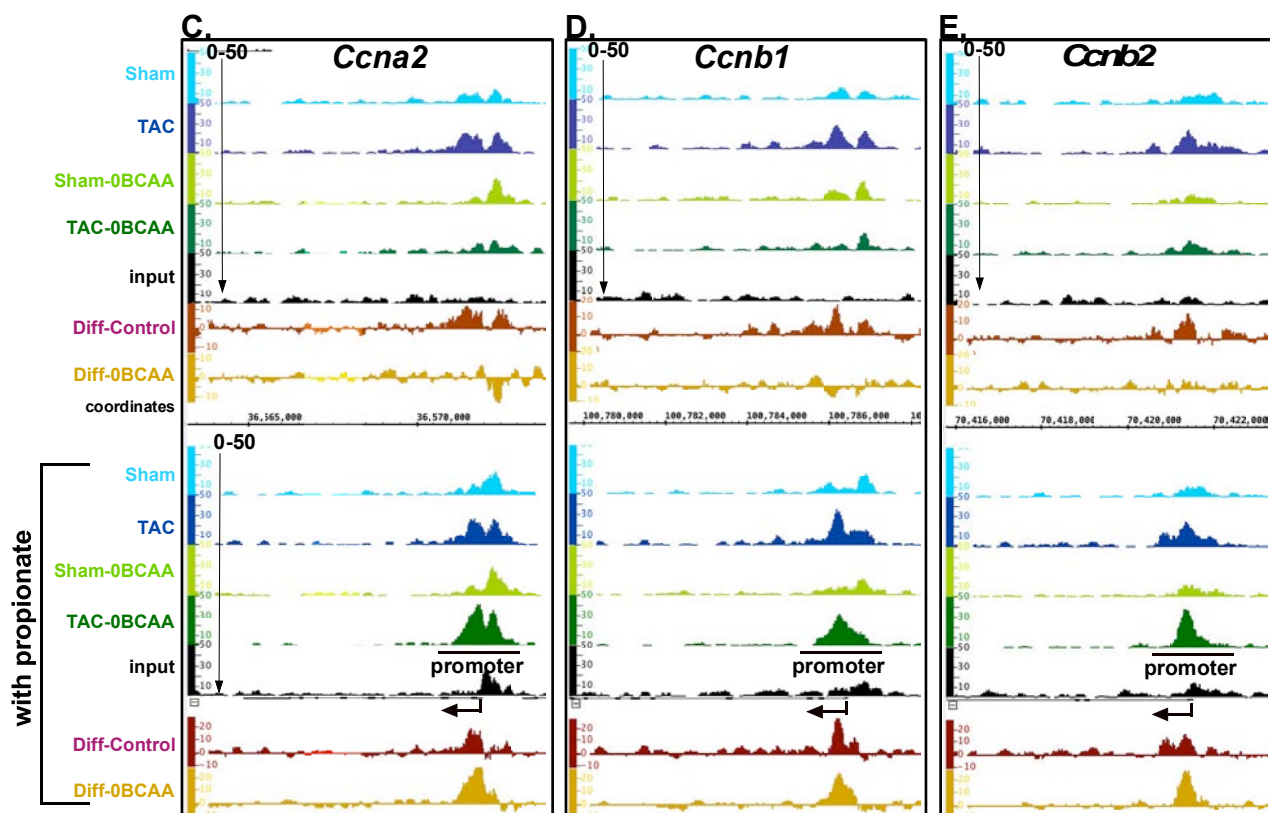
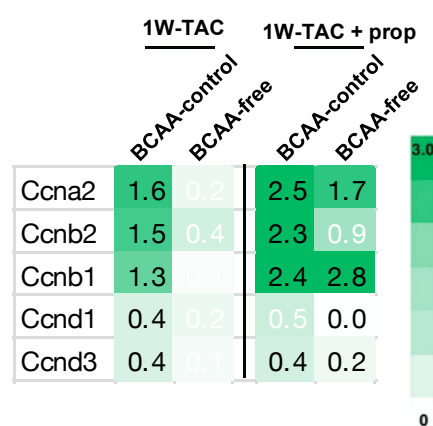


Figure 9S. Low BCAA reduces fibroblast proliferation and expression of Col1a1. Rat cardiac fibroblasts were freshly isolated and cultured in medium with the standard amount of BCAA (1x) or reduced BCAA (0.1x), in the presence or absence of 100 nM endothelin (ET-1). After 20h the protein was extracted, fractionated, and analyzed by Western blots with the Ab for the protein listed on the left. **Cy=cytoplasm, M=membrane, N=nucleoplasm, C=chromatin.** Please note that col1a1 protein is in the ER, which is in continuum with the nuclear membrane, hence its presence in the nucleoplasm fraction. **B.** The heatmaps show the LFC of TAC/Sham (control) and TAC/Sham (BCAA-free) of the mRNA for the proliferations genes *Ccna2*, *Ccnb1*, and *Ccnb2*. The values displayed in black are those with $\text{padj} \leq 0.05$. The color code bar is shown on the right. **C-E.** Integrated genome browser images showing H3K23Pr ChIP sequence Tags from the 1W sham and TAC hearts of mice on the different diets, aligned across *Ccna2*, *Ccnb1*, and *Ccnb2* gene coordinates. The labels on the left of each track indicate the surgical and diet conditions applied in mice; Sham and TAC surgeries with the BCAA-control diet (blue tracks), with the BCAA-free diets (green tracks); the differences (Diff) in the H3K23Pr sequence tags of TAC minus sham are shown in separate tracks for the control diet (Diff-Control, brown track) and BCAA-free diet (Diff-0BCAA, gold track).

Figure 9S

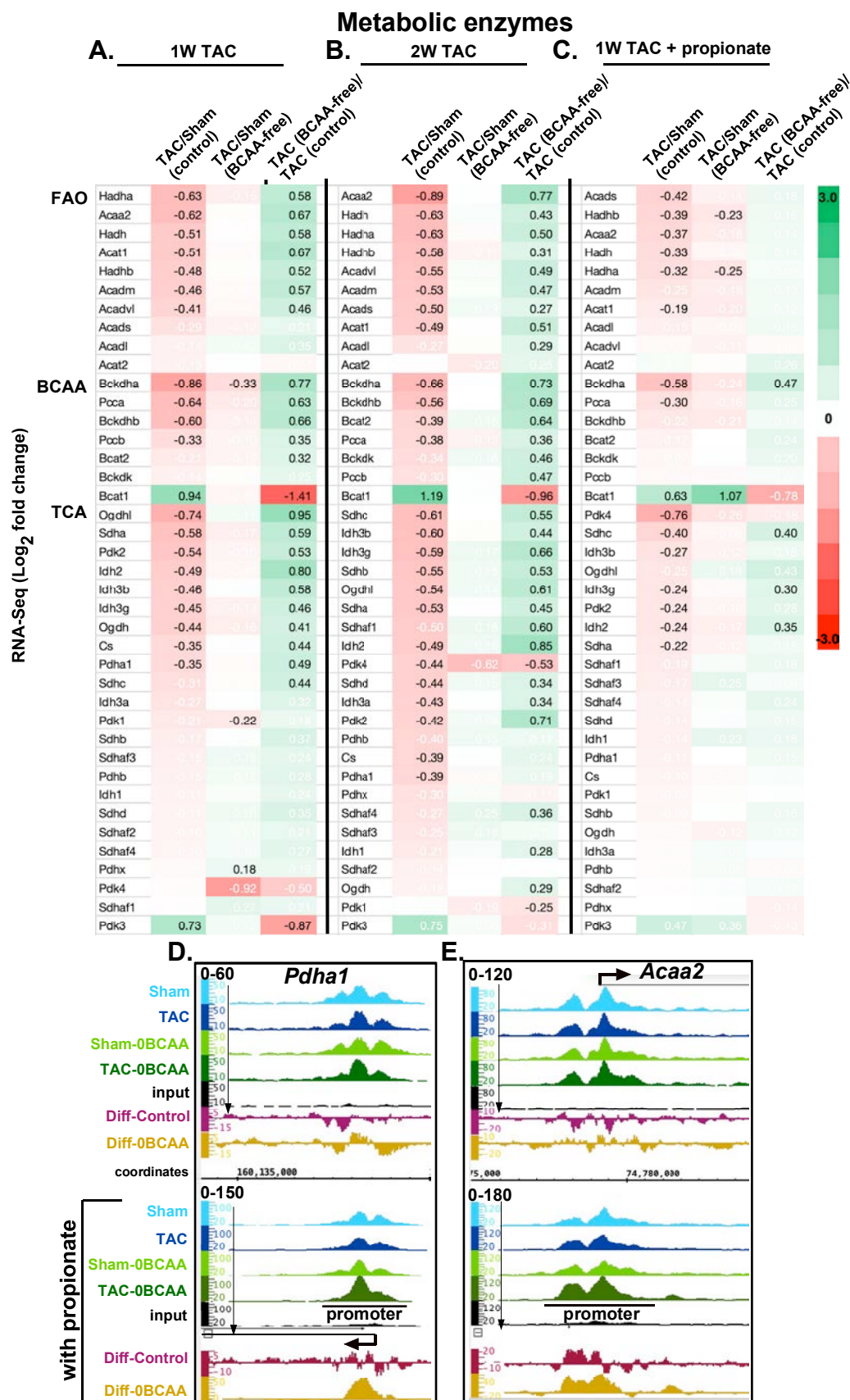


Figure 10S. Metabolic enzymes are downregulated by pressure overload, which is prevented by maintaining the mice on a BCAA-free diet. Mice were treated as described in figure 2 (in main text) **A.**, **B.** without or **C.** with 1% dietary propionate supplement. **A.**, **C.** 1Wk or **B.** 2W post-TAC, the hearts were isolated, RNA extracted and sequenced (n=3, each). The heatmaps show the LFC of TAC/Sham (control), TAC/Sham (BCAA-free), and TAC (BCAA-free)/TAC (BCAA-control) of the mRNA for metabolic enzymes. The values displayed in black are those with padj of ≤ 0.05 . The color keycode bar is shown on the right. **D-F.** Integrated genome browser images showing H3K27Pr ChIP sequence Tags from the 1W sham and TAC hearts of mice on the different diets, aligned across *Pdha1* and *Acaa2* gene coordinates. See legend of Fig. 7S for track description.

Figure 10S

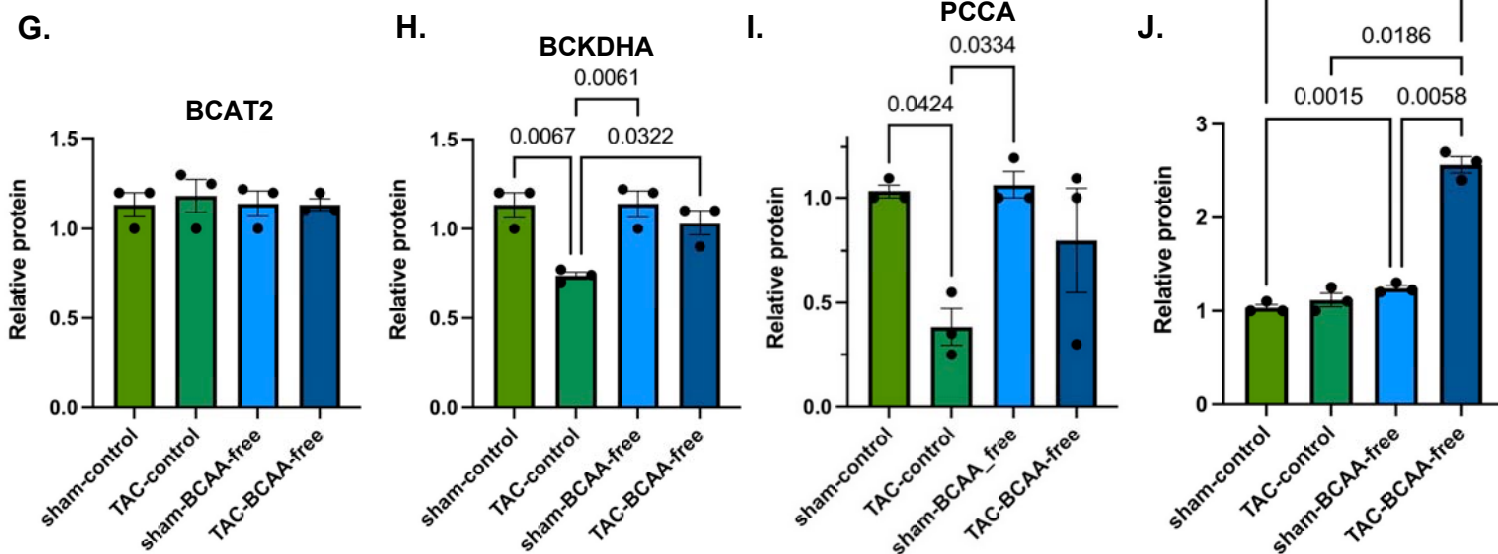
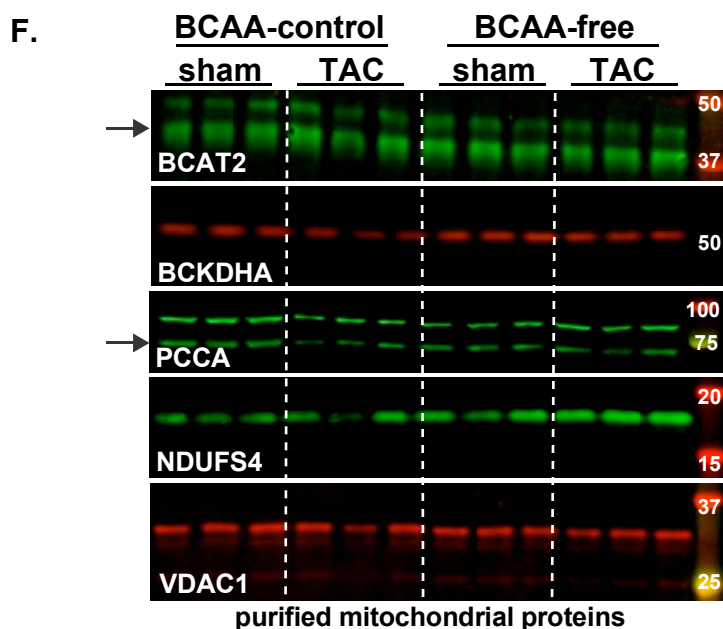


Figure 10S-F-H. Mitochondria were isolated and the protein extracted and analyzed by western blotting with the antibodies listed on the left in each panel. The signals were quantitated and normalized to VDAC1. **G-J.** The results were graphed as relative protein levels, after adjusting one of the sham control values to 1. Data were analyzed by one-way Anova (n=3, each). The p values of ≤ 0.05 are listed above the brackets encompassing the bars.

Mitochondrial electron transfer complexes

RNA-Seq (Log₂ fold change)

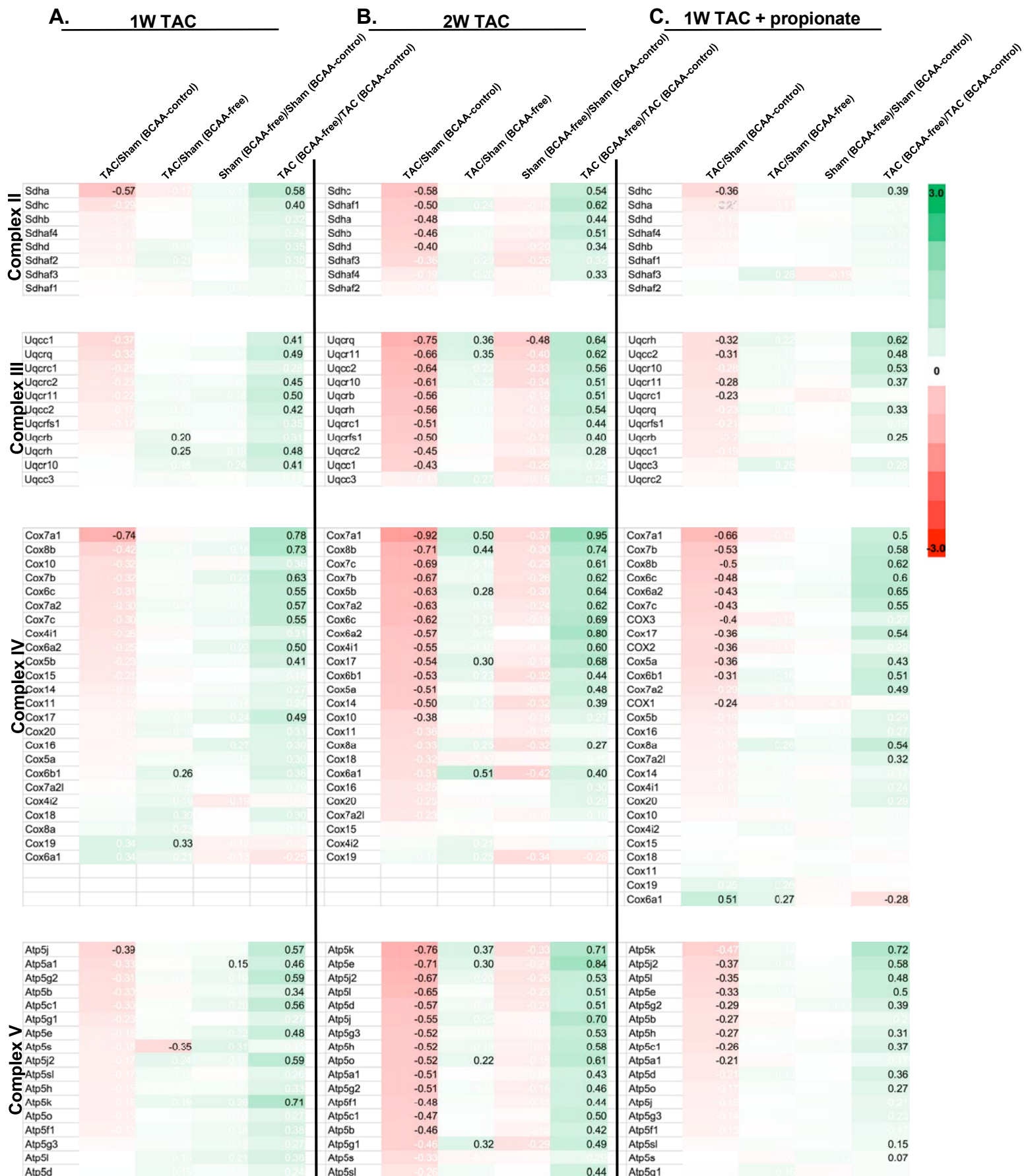


Figure 11S. Mitochondrial ETC subunits are downregulated by pressure overload, which is prevented by maintaining the mice on a BCAA-free diet. Mice were treated as described in figure 2 (main text), **A.**, **B.** without or **C.** with 1% dietary propionate supplement. **A.**, **C.** One week or **B.** 2W post-TAC, the hearts were isolated, RNA extracted and sequenced (n=3, each). The heatmaps show the LFC of TAC/Sham (control), TAC/Sham (BCAA-free), Sham (BCAA-free)/Sham (BCAA-control) and TAC (BCAA-free)/TAC (BCAA-control) of the mRNA for ETC II-IV subunits. The values displayed in black are those with p_{adj} of ≤ 0.05 . The color code bar is shown on the right.

Mitochondrial membrane translocases

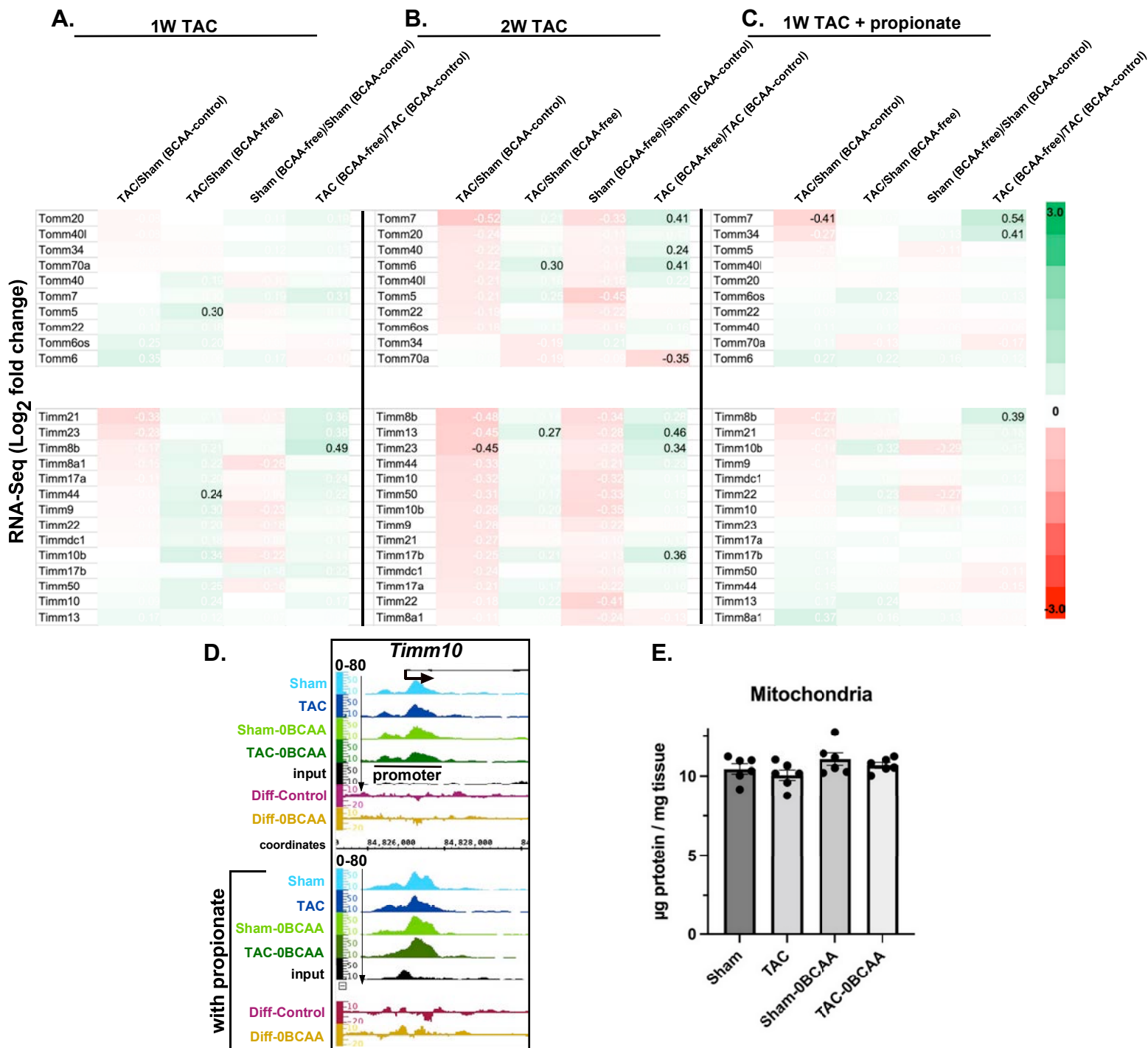


Figure 12S. There are no significant changes in mitochondrial membrane translocases mRNA expression, or total mitochondrial protein, after pressure overload. Mice were treated as described in figure 2 (in main text), **A.**, **B.** without or **C.** with 1% dietary propionate supplement. **A.**, **C.** One week or **B.** 2W post-TAC, the hearts were isolated, RNA extracted and sequenced (n=3, each). The heatmaps show the LFC of TAC/Sham (control), TAC/Sham (BCAA-free), Sham (BCAA-free)/Sham (BCAA-control) and TAC (BCAA-free)/TAC (BCAA-control) of the mRNA for mitochondrial Tomm and Timm isoforms. The color code bar is shown on the right. **D.** Integrated genome browser images showing H3K23Pr ChIP-sequence Tags from the 1W sham and TAC hearts of mice on the different diets, aligned across *Timm10* gene coordinates. The labels on the left of each track indicate the surgical and diet conditions applied in mice; Sham and TAC surgeries with the BCAA-control diet (blue tracks), with the BCAA-free diets (green tracks); the differences (Diff) in the H3K23Pr sequence tags of TAC minus sham are shown in separate tracks for the control diet (Diff-Control, brown track) and BCAA-free diet (Diff-0BCAA, gold track). **E.** Mitochondria were extracted from LV tissue, protein quantified, normalized to tissue mass, and graphed (n=6). Data were analyzed by one-way Anova, detecting no significant differences. See legend of Fig. 7S for track description.

Figure 12S

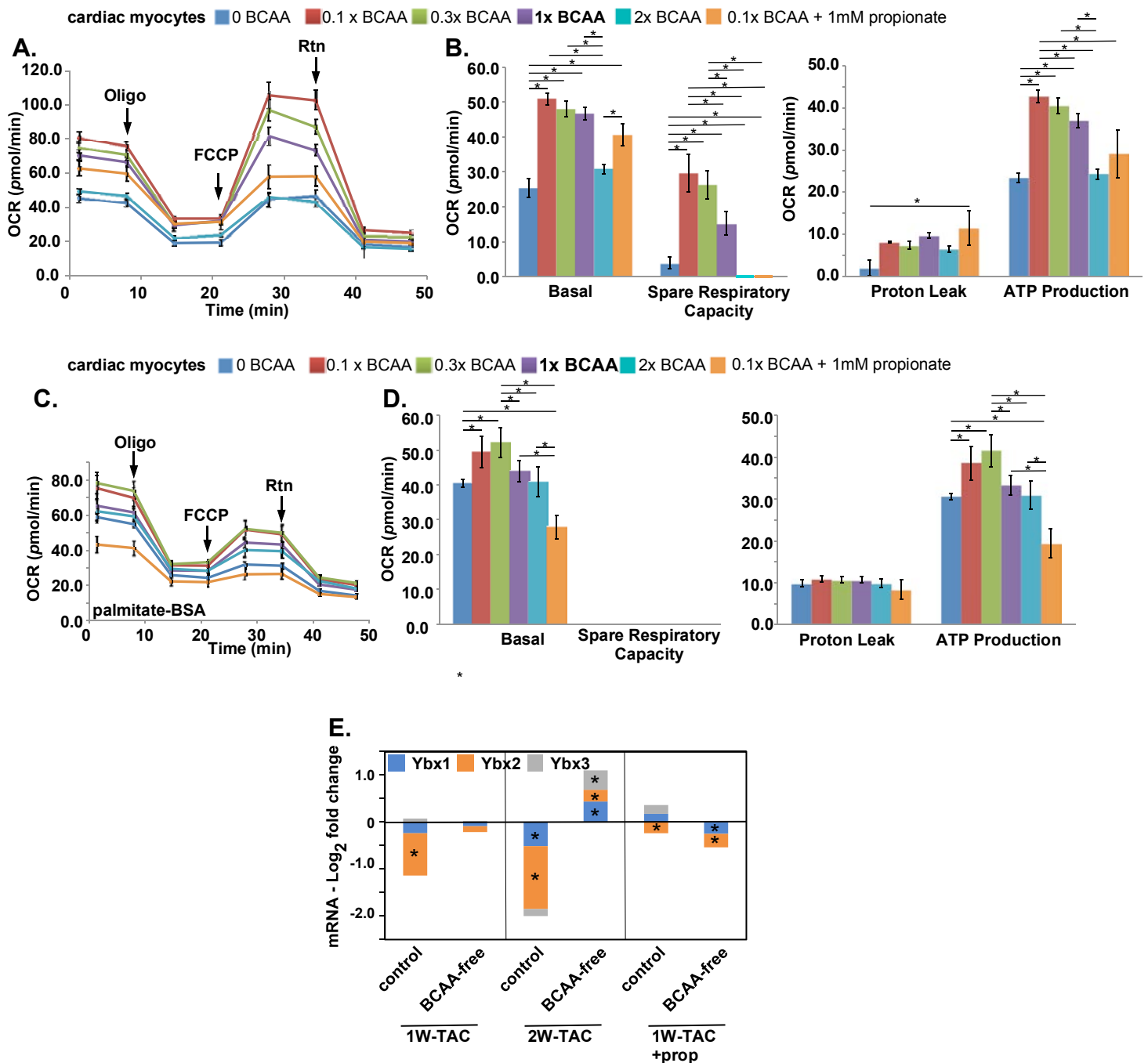


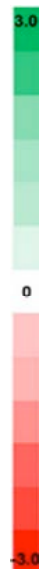
Figure 13S. Low BCAA enhances respiration. **A.** Neonatal rat cardiac myocytes were cultured in DMEM (with glucose) with either 1x or 0.1x BCAA, or 0.1x of the individual amino acids Leu, Ile, or Val, as indicated by the keycode. After 16 h, OCR (pmol/min, Y-axis) over time (X-axis) was measured by the Seahorse extracellular analyzer in the intact cells, before and after addition of oligomycin (oligo), FCCP, and rotenone (Rtn), where indicated by the arrows on the curve. **B.** The mitochondrial spare respiratory capacity, proton leak, and ATP-linked OCRs were calculated and graphed (n=3 independent cultures, n=10 replicas, each). Error bars represent S.E.M, *p ≤ 0.05, analyzed by one-way Anova. **C.** Neonatal rat cardiac myocytes were cultured in DMEM (with 100 μM palmitate-BSA, no glucose) with increasing doses of BCAA as indicated in the color keycode. After 16 h, OCR's (pmol/min, Y-axis) over time (X-axis) were measured by the Seahorse analyzer in the intact cells before and after addition of oligomycin (oligo), FCCP, and rotenone (Rtn), where indicated by the arrows on the curve. **D.** The mitochondrial basal, spare respiratory capacity, proton leak, and ATP-linked OCRs were calculated and graphed (n=3 independent cultures; n=10 measurements, each). Error bars represent S.E.M, *p ≤ 0.05, analyzed by one-way Anova. **E.** Stacked bar graph of the LFC of TAC/sham mRNA expression of the Ybx isoforms, with the different diets, 1W and 2W post-TAC, * = padj ≤ 0.05.

Figure 13S

CD surface markers

RNA-Seq (Log ₂ -TAC/Sham)	A. 1W-TAC		B. 2W-TAC		C. 1W-TAC+propionate		
	TAC/Sham (control)	TAC/Sham (BCAA-free)	TAC/Sham (control)	TAC/Sham (BCAA-free)	TAC/Sham (control)	TAC/Sham (BCAA-free)	
Cd72	1.49935452	0.78390431	Cd200r1	1.87545715	Cd72	1.18971249	1.12001013
Cd300c2	1.44666415	0.56996036	Cd109	1.87154067	Cd109	1.16587214	0.44729277
Cd52	1.29793755	0.9130529	Cd72	1.47081871	Cd84	0.89697512	0.82361162
Cd80	1.27141798	0.6446058	Cd44	1.36809886	Cd180	0.78263454	1.06277853
Cd84	1.18165239	0.42799266	Cd52	0.9506423	Cd68	0.65797777	0.74407307
Cd300lb	1.18120776	0.72272213	Cd276	0.94597941	Cd300c2	0.65775752	1.42830331
Cd200r1	1.10820672	0.6758669	Cd248	0.91228761	Cd44	0.65533665	0.4379674
Cd68	0.9546788	0.50643049	Cd74	0.85882564	Cd63-ps	0.53003383	
Cd276	0.93603022	0.28560633	Cd300c2	0.84878333	Cd14	0.42671589	0.76028149
Cd180	0.93574094	0.20108633	Cd300lb	0.74886571	Cd63	0.38403394	0.23863764
Cd109	0.84442289		Cd34	0.71458034	Cd34	0.33181926	0.41973639
Cd300a	0.82741947		Cd9	0.67602011	Cd163	0.31555813	0.59271607
Cd248	0.81718066	0.58168402	Cd83	0.66697834	Cd53	0.31253675	0.31714838
Cd24a	0.81359382	0.24933373	Cd84	0.66166318	Cd248	0.28107822	0.77388877
Cd53	0.74396309	0.4017447	Cd93	0.65406507	Cd52	0.27053978	1.22515166
Cd302	0.73077849	0.31461082	Cd53	0.6491451	Cd276	0.23033682	0.36057446
Cd34	0.65829212	0.306704	Cd48	0.59219711	Cd37	0.23631845	0.31887525
Cd44	0.63298335	0.19733335	Cd80	0.58391335	Cd200	0.2315693	0.13414689
Cd40	0.61586137	0.57483616	Cd300a	0.57591967	Cd40	0.22433587	0.43894618
Cd48	0.61540414	0.30185009	Cd38	0.55976756	Cd3eap	0.19822983	0.30886532
Cd63	0.60071127		Cd86	0.55037205	Cd33	0.19252593	0.67648124
Cd9	0.57548401	0.31693279	Cd180	0.53585034	Cd86	0.18253342	0.66037912
Cd300ld	0.56931088	0.20781287	Cd302	0.52105308	Cd300ld	0.18030192	0.71068998
Cd14	0.55934308	0.17446465	Cd33	0.48214353	Cd302	0.17830192	0.53771809
Cd86	0.41004852	0.18288630	Cd300ld	0.46092674	Cd47	0.16830192	
Cd37	0.39742447	0.3814346	Cd55	0.40268643	Cd9	0.16830192	0.22516819
Cd38	0.38468812	0.31905394	Cd14	0.38508342	Cd93	0.16830192	-0.265879
Cd3eap	0.29584619	0.13468630	Cd68	0.3344773	Cd320	0.16830192	0.13468630
Cd83	0.2917678	0.2463466	Cd63	0.33120312	Cd151	0.16830192	0.13468630
Cd200	0.28909554	0.2822309	Cd200	0.25387301	Cd2bp2	0.16830192	0.13468630
Cd33	0.28330171	0.35830673	Cd40	0.25208338	Cd24a	0.16830192	0.35532123
Cd93	0.2282476		Cd37	0.21887359	Cd81	0.16830192	
Cd163	0.2283	0.16830192	Cd63-ps	0.16830192	Cd59a	0.16830192	
Cd63-ps	0.22012362	0.13468630	Cd24a	0.16830192	Cd164	0.16830192	0.13468630
Cd81	0.18818135		Cd47	0.16830192	Cd55	0.16830192	0.13468630
Cd47	0.18830192		Cd2ap	0.16830192	Cd2ap	0.16830192	-0.2389009
Cd151	0.18830192		Cd1d1	0.16830192	Cd82	0.16830192	0.13468630
Cd2bp2	0.18830192		Cd2bp2	0.16830192	Cd28	0.16830192	-0.6949186
Cd320	0.18830192		Cd300lg	0.16830192	Cd38	0.16830192	
Cd55	0.18830192	0.13468630	Cd81		Cd48	0.16830192	0.55188075
Cd82	0.02725965	-0.4432003	Cd164		Cd1d1	0.16830192	-0.3502151
Cd74			Cd3eap		Cd300lg	0.16830192	-0.3888625
Cd300lg			Cd19		Cd36	0.16830192	-0.228517
Cd164	0.16830192	0.13468630	Cd163		Cd59b	0.16830192	-0.411247
Cd1d1	0.16830192	0.13468630	Cd151	0.16830192	Cd300a	0.16830192	-0.4297771
Cd2ap	0.16830192	0.13468630	Cd82	0.16830192	Cd74	0.16830192	-0.4802997
Cd9912	0.2027575	-0.2137939	Cd9912	0.214180	Cd83	0.16830192	-0.610113
Cd59a	0.2071381		Cd274	0.2191835	Cd46	0.16830192	-0.6124606
Cd19	0.2075188	0.5629617	Cd36	0.2364844	Cd274	0.16830192	-0.9417366
Cd59b	0.2589727	0.13468630	Cd46	0.3147544	Cd8a	0.16830192	-1.7746362
Cd36	-0.3796084	-0.1773157	Cd28	0.3473094			
Cd46	-0.6032461	-0.2826874	Cd59a	-0.4654219			
Cd28	-0.7667597	-0.6284756	Cd320	-0.4758199			
Cd274	-0.8339336	-0.3000636	Cd59b	-1.0860528			

RNA-Seq (Log₂ -TAC/Sham)



D.

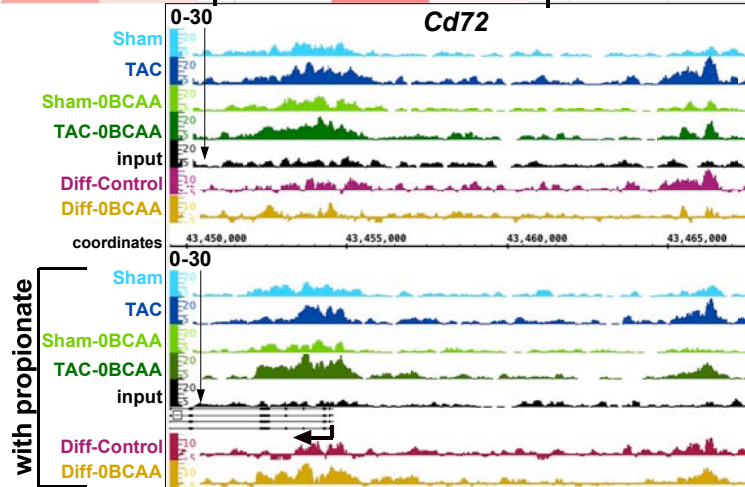


Figure 14S

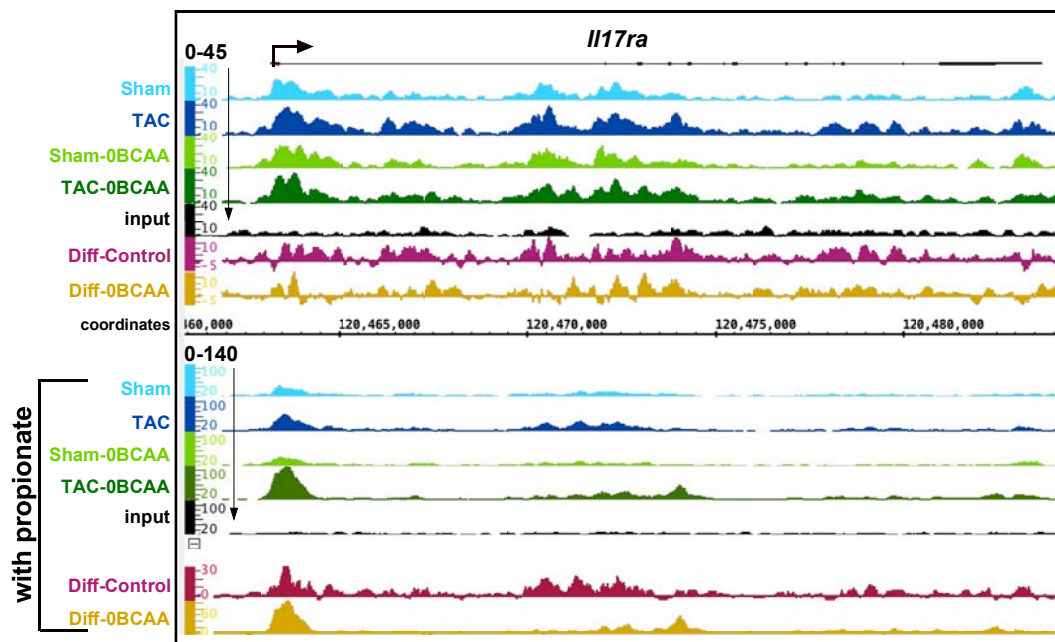


Figure 14S. CD surface markers of infiltrating cells increase after pressure overload and are diminished by a BCAA-free diet. Mice were treated as described in figure 2 (in main text), **A.**, **B.** without or **C.** with 1% dietary propionate supplement. **A.**, **C.** One week or **B.** 2W post-TAC, the hearts were isolated, RNA extracted and sequenced (n=3, each). The heatmaps show the LFC of TAC/Sham (control) and TAC/Sham (BCAA-free), of the mRNA for CD surface markers detect in the heart. The values displayed in black are those with padj of ≤ 0.05 . The color keycode bar is shown on the right. **D-E.** Integrated genome browser images showing H3K23Pr ChIP-sequence Tags from the 1W sham and TAC hearts of mice on the different diets, aligned across *CD72* and *Il17ra* gene coordinates. The labels on the left of each track indicate the surgical and diet conditions applied in mice; Sham and TAC surgeries with the BCAA-control diet (blue tracks), with the BCAA-free diets (green tracks); the differences (Diff) in the H3K23Pr sequence tags of TAC minus sham are shown in separate tracks for the control diet (Diff-Control, brown track) and BCAA-free diet (Diff-0BCAA, gold track).

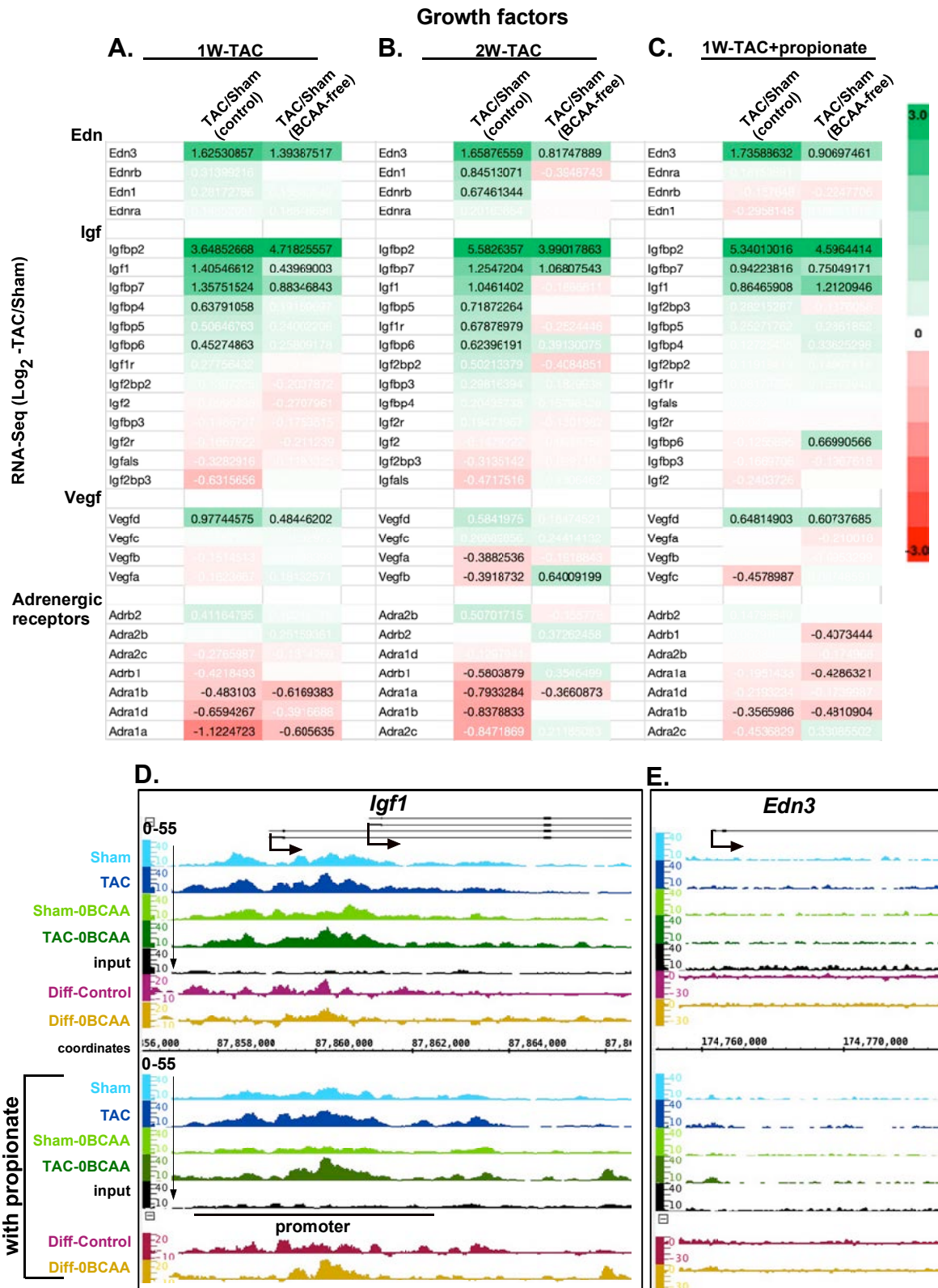


Figure 15S

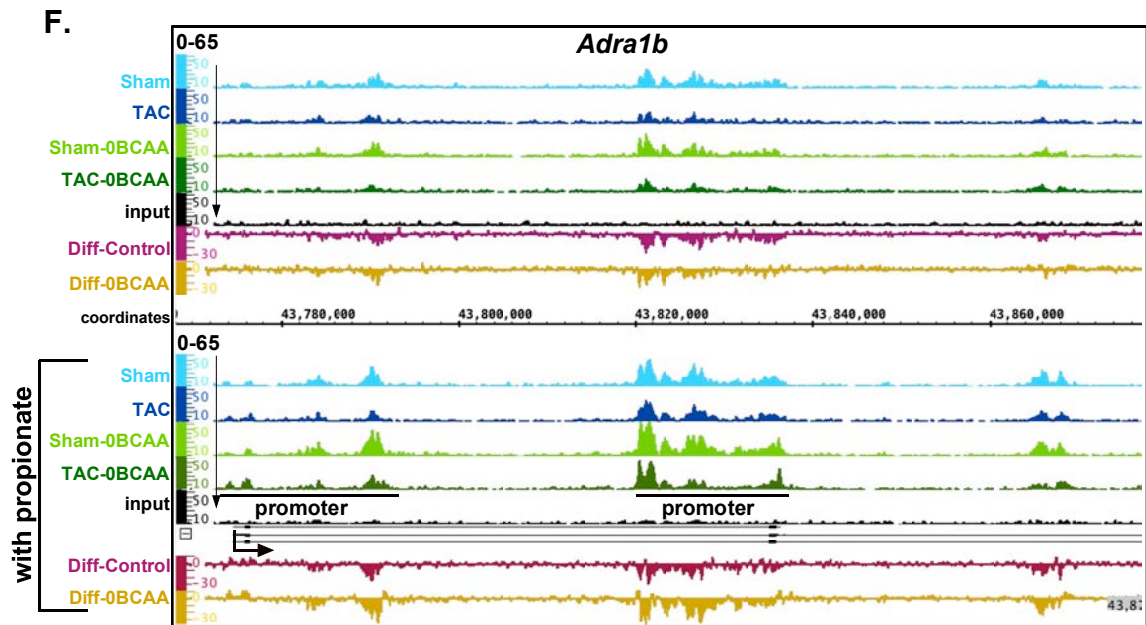


Figure 15S. Selective regulation of growth factors and their receptors by dietary BCAA. Mice were treated as described in figure 2 (in the main text), **A.**, **B.** without or **C.** with 1% dietary propionate supplement. **A.**, **C.** One week or **B.** 2W post-TAC, the hearts were isolated, RNA extracted and sequenced (n=3, each). The heatmaps show the LFC of TAC/Sham (control) and TAC/Sham (BCAA-free), of the mRNA for growth factors and their receptors detect in the heart. The values displayed in black are those with padj of ≤ 0.05 . The color keycode bar is shown on the right. **D-F.** Integrated genome browser images showing H3K23Pr ChIP-sequence Tags from the 1W sham and TAC hearts of mice on the different diets, aligned across *Igf1*, *End3*, and *Adra1b* gene coordinates. The labels on the left of each track indicate the surgical and diet conditions applied in mice; Sham and TAC surgeries with the BCAA-control diet (blue tracks), with the BCAA-free diets (green tracks); the differences (Diff) in the H3K23Pr sequence tags of TAC minus sham are shown in separate tracks for the control diet (Diff-Control, brown track) and BCAA-free diet (Diff-0BCAA, gold track).

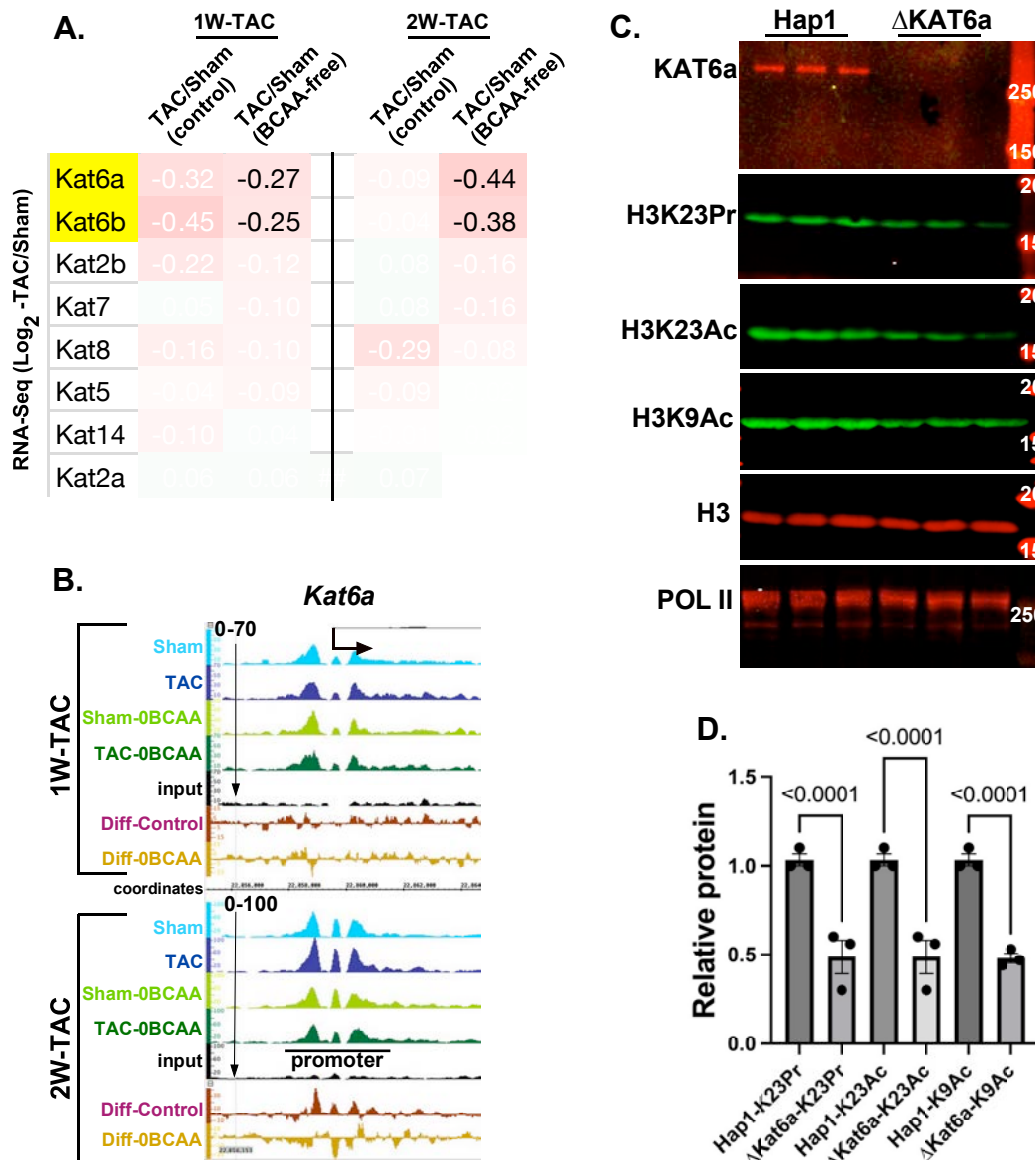


Figure 16S. TAC induce downregulation of *Kat6a* and *Kat6b* with a BCAA-free diet. A. Mice were treated as described in figure 2 (in main text). After 1W or 2W post-TAC, the hearts were isolated, RNA extracted and sequenced (n=3, each). The heatmaps show the LFC of TAC/Sham (control) and TAC/Sham (BCAA-free), of the mRNA for the Kat isoforms detect in the heart. The values displayed in black are those with padj of ≤ 0.05 . The color code bar is shown on the right. **B.** Integrated genome browser images showing H3K23Pr ChIP-sequence Tags from the 1W and 2W sham and TAC hearts of mice on the different diets, aligned across *Kat6a* gene coordinates. The labels on the left of each track indicate the surgical and diet conditions applied in mice; Sham and TAC surgeries with the BCAA-control diet (blue tracks), with the BCAA-free diets (green tracks); the differences (Diff) in the H3K23Pr sequence tags of TAC minus sham are shown in separate tracks for the control diet (Diff-Control, brown track) and BCAA-free diet (Diff-0BCAA, gold track). **C.** Hap1 and Hap Δ Kat6a cells were cultured in DMEM with 10% FBS. Cells were then harvested and chromatin-bound proteins were extracted and analyzed by Western blotting for the antibodies listed on the left. **D.** Western blot signals were quantitated and normalized to that of H3 (n=3). The relative values were calculated after adjusting one of the Hap1 signals to 1. Error bars represent SD. The results were analyzed by one-way Anova, comparing the means of Hap1 vs Δ Kat6a for each of the H3 modifications (Šídák's multiple comparisons test). The p values are listed above the brackets encompassing the bars.

Figure 16S

Supplementary table 1

A12450K, A19121601, A21123001-02, and A22041404-05

Rodent Diet w/ 10 kcal% Fat
and Same With No Added BCAAs and Sodium Propionate

Product #	A12450K	A21123001	A22041404	A19121601	A21123002	A22041405
Ingredient	gm	gm	gm	gm	gm	gm
Casein, 80 Mesh	0	0	0	0	0	0
L-Cystine	4.2	4.2	4.2	4.2	4.2	4.2
L-Isoleucine	7.6	7.6	7.6	0	0	0
L-Leucine	15.8	15.8	15.8	0	0	0
L-Lysine	13.2	13.2	13.2	13.2	13.2	13.2
L-Methionine	5.1	5.1	5.1	5.1	5.1	5.1
L-Phenylalanine	8.4	8.4	8.4	8.4	8.4	8.4
L-Threonine	7.2	7.2	7.2	7.2	7.2	7.2
L-Tryptophan	2.1	2.1	2.1	2.1	2.1	2.1
L-Valine	9.3	9.3	9.3	0	0	0
L-Histidine	4.6	4.6	4.6	4.6	4.6	4.6
L-Alanine	5.1	5.1	5.1	5.1	5.1	5.1
L-Arginine	6.0	6.0	6.0	6.0	6.0	6.0
L-Aspartic Acid	12.1	12.1	12.1	12.1	12.1	12.1
L-Glutamic Acid	38.2	38.2	38.2	38.2	38.2	38.2
Glycine	3.0	3.0	3.0	3.0	3.0	3.0
L-Proline	17.8	17.8	17.8	17.8	17.8	17.8
L-Serine	10.0	10.0	10.0	10.0	10.0	10.0
L-Tyrosine	9.2	9.2	9.2	9.2	9.2	9.2
Corn Starch	550	550	550	582.7	582.7	582.7
Maltodextrin 10	150	150	150	150	150	150
Sucrose	0	0	0	0	0	0
Cellulose, BW200	50	50	50	50	50	50
Soybean Oil	25	25	25	25	25	25
Lard	20	20	20	20	20	20
Mineral Mix S10026	10	10	10	10	10	10
DiCalcium Phosphate	13	13	13	13	13	13
Calcium Carbonate	5.5	5.5	5.5	5.5	5.5	5.5
Potassium Citrate, 1 H2O	16.5	16.5	16.5	16.5	16.5	16.5
Sodium BiCarbonate	7.5	7.5	7.5	7.5	7.5	7.5
Vitamin Mix V10001	10	10	10	10	10	10
Choline Bitartrate	2	2	2	2	2	2
Sodium Propionate	0	1.04	10.49	0	1.04	10.49
FD&C Yellow Dye #5	0	0.05	0	0	0.025	0.025
FD&C Red Dye #40	0.025	0	0	0.05	0	0.025
FD&C Blue Dye #1	0.025	0	0.05	0	0.025	0
Total	1038.45	1039.49	1048.94	1038.45	1039.49	1048.94
Diet #	A12450K	A21123001	Formula 1	A19121601	A21123002	Formula 2
gm						
Protein	178.9	178.9	178.9	146.2	146.2	146.2
Carbohydrate	710.0	710.0	710.0	742.7	742.7	742.7
Fat	45.0	45.0	45.0	45.0	45.0	45.0
Fiber	50.0	50.0	50.0	50.0	50.0	50.0
gm%						
Protein	17.2	17.2	17.1	14.1	14.1	13.9
Carbohydrate	68.4	68.3	67.7	71.5	71.4	70.8
Fat	4.3	4.3	4.3	4.3	4.3	4.3
Fiber	4.8	4.8	4.8	4.8	4.8	4.8
kcal						
Protein	716	716	716	585	585	585
Carbohydrate	2840	2840	2840	2971	2971	2971
Fat	405	405	405	405	405	405
Total	3961	3961	3961	3961	3961	3961
kcal%						
Protein	18	18	18	15	15	15
Carbohydrate	72	72	72	75	75	75
Fat	10	10	10	10	10	10
Total	100	100	100	100	100	100
kcal / gm	3.8	3.8	3.8	3.8	3.8	3.8
Sodium Propionate (g/kg diet)	0	1.00	10.00	0	1.00	10.00

Supplementary table 2



Thermo Fisher Scientific
Life Sciences Solutions
3175 Staley Road
Grand Island, New York 14072 U.S.A.
(716) 774-6726

RUTGERS THE STATE UNIV OF NEW JERSEY

DMEM Custom Formulation, SKU ME20061L1

Components	Molecular Weight	Concentration (mg/L)	mM
Amino Acids			
Glycine	75.0	30.0	0.4
L-Arginine hydrochloride	211.0	84.0	0.39810428
L-Cystine 2HCl	313.0	63.0	0.20127796
L-Glutamine	146.0	584.0	4
L-Histidine hydrochloride-H ₂ O	210.0	42.0	0.2
L-Lysine hydrochloride	183.0	146.0	0.7978142
L-Methionine	149.0	30.0	0.20134228
L-Phenylalanine	165.0	66.0	0.4
L-Serine	105.0	42.0	0.4
L-Threonine	119.0	95.0	0.79831934
L-Tryptophan	204.0	16.0	0.078431375
L-Tyrosine disodium salt dihydrate	261.0	104.0	0.39846742
Vitamins			
Choline chloride	140.0	4.0	0.028571429
D-Calcium pantothenate	477.0	4.0	0.008385744
Folic Acid	441.0	4.0	0.009070295
Niacinamide	122.0	4.0	0.032786883
Pyridoxine hydrochloride	206.0	4.0	0.019417476
Riboflavin	376.0	0.4	0.0010638298

Thiamine hydrochloride	337.0	4.0	0.011869436
i-Inositol	180.0	7.2	0.04

DMEM Custom Formulation, SKU ME20061L1
(continued)

Components	Molecular Weight	Concentration (mg/L)	mM
Inorganic Salts			
Calcium Chloride (CaCl ₂) (anhyd.)	111.0	200.0	1.8018018
Ferric Nitrate (Fe(NO ₃) ₃ ·9H ₂ O)	404.0	0.1	2.4752476E-04
Magnesium Sulfate (MgSO ₄) (anhyd.)	120.0	97.67	0.8139166
Potassium Chloride (KCl)	75.0	400.0	5.3333335
Sodium Bicarbonate (NaHCO ₃)	84.0	3700.0	44.04762
Sodium Chloride (NaCl)	58.0	6400.0	110.344826
Sodium Phosphate monobasic (NaH ₂ PO ₄ ·H ₂ O)	138.0	125.0	0.9057971
Other Components			
Phenol Red	376.4	15.0	0.039851222

Supplementary table 2. Formula for the BCAA-free DMEM. The BCAA's were added to generate 1x BCAA (0.8 mM of each, Ile, Leu, Val) , 0.1XBCAA (0.08 mM of each, Ile, Leu, and Val), 0.1XIle (0.08 mM Ile, 0.8 mM of each, Leu and Val), 0.1xLeu (0.08 mM Leu, 0.8 mM of each Ile and Val), or 0.1xVal (0.08 mM Val, 0.8 mM of each Ile and Leu), as indicated in the figure legends.

Supplementary table 3 - antibodies

Antibody	Company, catalog #
anti-H3K23Pr	Abcam, ab241466 for ChIP-Seq
anti-H3K23Pr	Active Motif, 61397
anti-H3K18Pr	PTM BIO, PTM-213
anti-H3K56Pr	PTM BIO, PTM-220RM
anti-H3K23Ac	Millipore Sigma, 07-355
anti-Lys-propionyl (K-pr)	PTM BIO, PTM-201
anti-H3	Active Motif, 61475
anti-Bcat2	Millipore Sigma, HPA054091
anti-Bcat1	Cell Signaling Technology, 88785
anti-Col1a1	Cell Signaling Technology, 72026
anti-Ki67	Abcam, ab16667
anti-Alpha smooth muscle actin	Millipore Sigma, A5228
Anti-alpha smooth muscle actin	Cell Signaling Technology, 19245
anti-Alpha-tubulin	Abcam, ab7291
anti-Myh7	Millipore Sigma, M8421
anti-Clic1	Abcam, ab229917
anti-Akt	Millipore Sigma, 07-416
anti-Myoz2	Millipore Sigma, SAB1401710
anti-Ankrd1	Santa Cruz Biotechnology, sc-30181
anti-Tnnt2	Millipore Sigma, SAB2108239
anti-Vdac1	Genscript, A01419
anti-Vdac2	Millipore Sigma, AV35113
anti-RNA polymerase II	Active Motif, 102660
anti-Timm23	Millipore Sigma, HPA031408

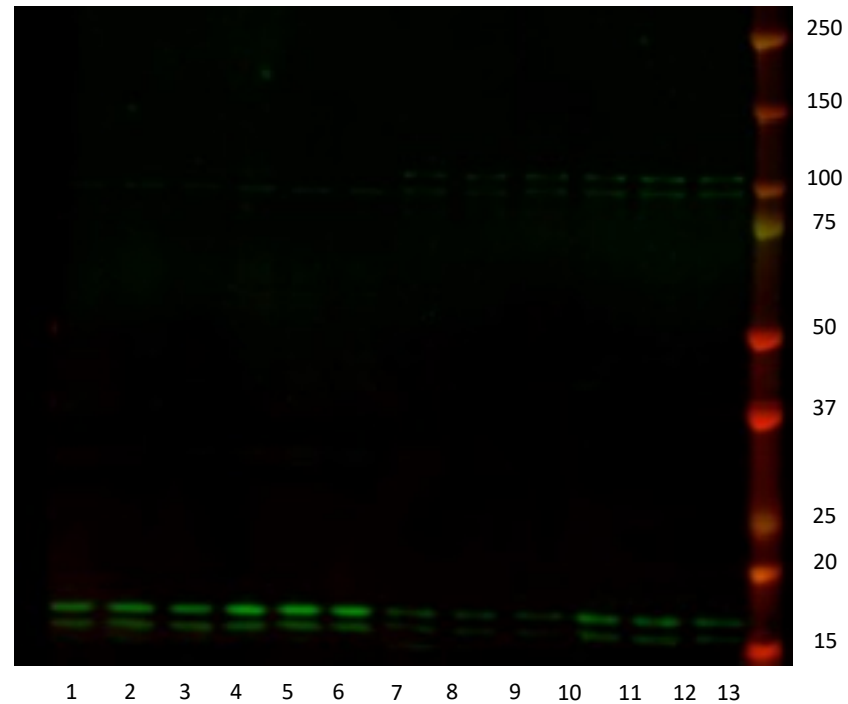
Full unedited gels for Figure 1A

Δ BCAT2 +/- BCAAs +
Glucose: H3K23Pr (Active
Motif 61397) 1:2000 Low
Exposure

- 3ug of protein loaded per well
- Expected size of H3K23Ac: ~17 kDa
 - Well 1: Hap-1 -BCAAs +G 1
 - Well 2: Hap-1 -BCAAs +G 2
 - Well 3: Hap-1 -BCAAs +G 3
 - Well 4: Hap-1 +BCAAs +G 1
 - Well 5: Hap-1 +BCAAs +G 2
 - Well 6: Hap-1 +BCAAs +G 3
 - Well 7: Δ BCAT2 -BCAAs +G 1
 - Well 8: Δ BCAT2 -BCAAs +G 2
 - Well 9: Δ BCAT2 -BCAAs +G 3
 - Well 10: Δ BCAT2 +BCAAs +G 1
 - Well 11: Δ BCAT2 +BCAAs +G 2
 - Well 12: Δ BCAT2 +BCAAs +G 3
 - Well 13: Ladder
- **G=glucose**

Full unedited gels for Figure 1A

Histone extracts

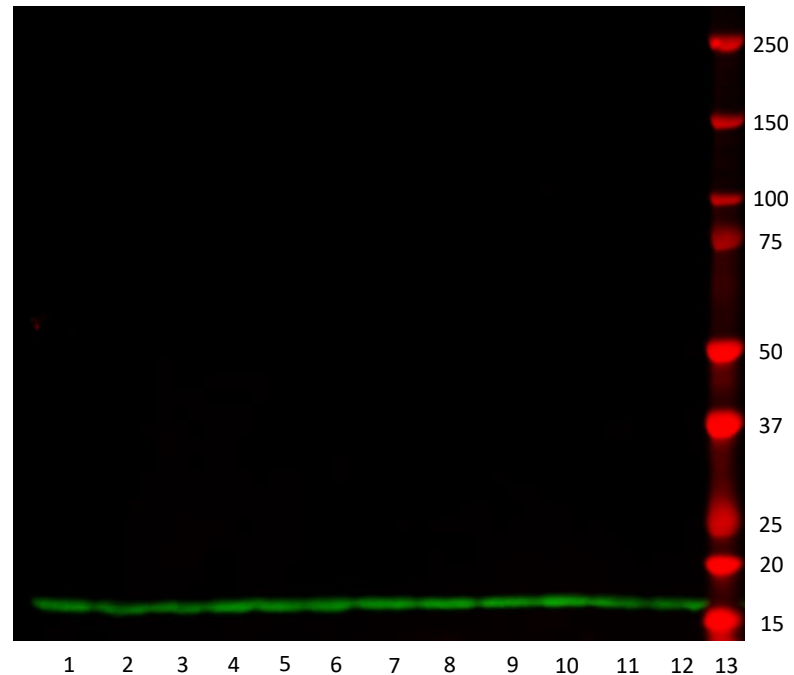


Δ BCAT2 +/- BCAAs +
Glucose: H3K23Ac
(Millipore 07-355-S) 1:1000
Low Exposure

- 3ug of protein loaded per well
- Expected size of H3K23Ac: ~17 kDa
 - Well 1: Hap-1 -BCAAs +G 1
 - Well 2: Hap-1 -BCAAs +G 2
 - Well 3: Hap-1 -BCAAs +G 3
 - Well 4: Hap-1 +BCAAs +G 1
 - Well 5: Hap-1 +BCAAs +G 2
 - Well 6: Hap-1 +BCAAs +G 3
 - Well 7: Δ BCAT2 -BCAAs +G 1
 - Well 8: Δ BCAT2 -BCAAs +G 2
 - Well 9: Δ BCAT2 -BCAAs +G 3
 - Well 10: Δ BCAT2 +BCAAs +G 1
 - Well 11: Δ BCAT2 +BCAAs +G 2
 - Well 12: Δ BCAT2 +BCAAs +G 3
 - Well 13: Ladder
- **G=glucose**

Full unedited gels for Figure 1A

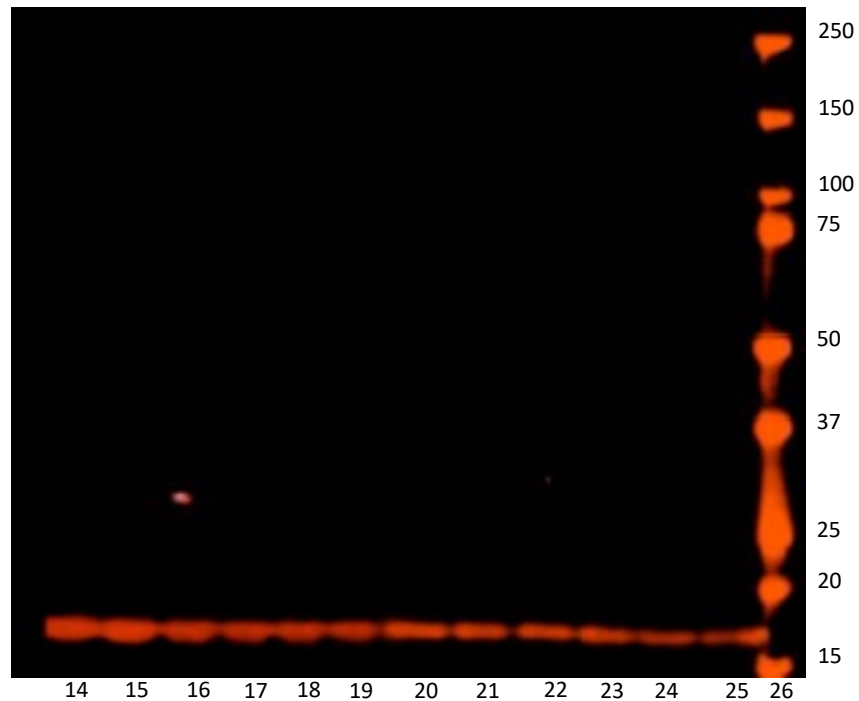
Histone extracts



Δ BCAT2 +/- BCAAs +
Glucose: H3 (Active Motif
61475) 1:30,000 Low
Exposure Reduced
Background

- 3ug of protein loaded per well
- Expected size of H3: ~ 17 kDa
 - Well 14: Hap-1 -BCAAs +G 1
 - Well 15: Hap-1 -BCAAs +G 2
 - Well 16: Hap-1 -BCAAs +G 3
 - Well 17: Hap-1 +BCAAs +G 1
 - Well 18: Hap-1 +BCAAs +G 2
 - Well 19: Hap-1 +BCAAs +G 3
 - Well 20: Δ BCAT2 -BCAAs +G 1
 - Well 21: Δ BCAT2 -BCAAs +G 2
 - Well 22: Δ BCAT2 -BCAAs +G 3
 - Well 23: Δ BCAT2 +BCAAs +G 1
 - Well 24: Δ BCAT2 +BCAAs +G 2
 - Well 25: Δ BCAT2 +BCAAs +G 3
 - Well 26: Ladder
- G=glucose

Full unedited gels for Figure 1A Histone extracts



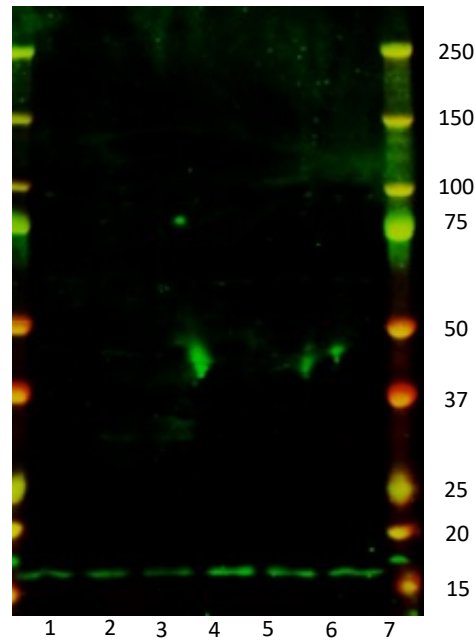
Full unedited gels for Figure 1C

Blot 1 Δ PCCA 0.1x LIV
Histones: H3K23Pr (Active
Motif 61397) 1:1000

- Expected size: ~17 kDa
- Volume of sample loaded per well determined by protein quantification using Thermo Micro BCA Protein Assay Kit; 3ug of protein
- Well 1: Hap-1 0.1X LIV 1
- Well 2: Hap-1 0.1X LIV 2
- Well 3: Hap-1 0.1X LIV 3
- Well 4: Δ PCCA 0.1X LIV 1
- Well 5: Δ PCCA 0.1X LIV 2
- Well 6: Δ PCCA 0.1X LIV 3
- Wells 7: contains the Ladder; 2.0 μ L
- **LIV = Leu, Ile, Val (BCAA)**

Full unedited gel for Figure 1C

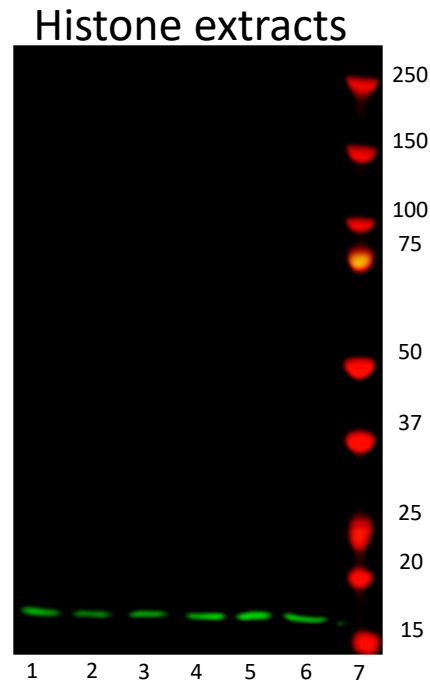
Histone extracts



Blot 2 Δ PCCA 0.1X LIV
Histones: H3K18Pr (PTM
BIO PTM-213) 1:1000 Low
Exposure

- Expected size: ~ 17 kDa
- Volume of sample loaded per well determined by protein quantification using Thermo Micro BCA Protein Assay Kit; 3 μ g of protein
- Well 1: Hap-1 0.1X LIV 1
- Well 2: Hap-1 0.1X LIV 2
- Well 3: Hap-1 0.1X LIV 3
- Well 4: Δ PCCA 0.1X LIV 1
- Well 5: Δ PCCA 0.1X LIV 2
- Well 6: Δ PCCA 0.1X LIV 3
- Wells 7: contains the Ladder; 2.0 μ L
- **LIV = Leu, Ile, Val (BCAA)**

Full unedited gel for Figure 1C

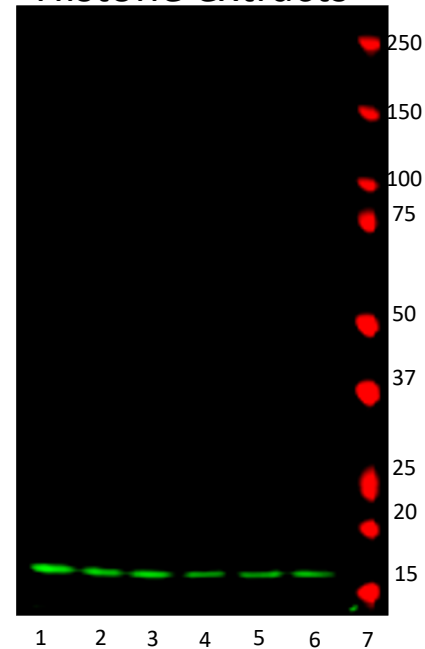


Blot 3 Δ PCCA 0.1X LIV
Histones: H3K56Pr (PTM
BIO PTM-220RM) 1:1000
Low Exposure

- Expected size: ~17 kDa
- Volume of sample loaded per well determined by protein quantification using Thermo Micro BCA Protein Assay Kit; 3ug of protein
- Well 1: Hap-1 0.1X LIV 1
- Well 2: Hap-1 0.1X LIV 2
- Well 3: Hap-1 0.1X LIV 3
- Well 4: Δ PCCA 0.1X LIV 1
- Well 5: Δ PCCA 0.1X LIV 2
- Well 6: Δ PCCA 0.1X LIV 3
- Wells 7: contains the Ladder; 2.0 μ L
- **LIV = Leu, Ile, Val (BCAA)**

Full unedited gel for Figure 1C

Histone extracts

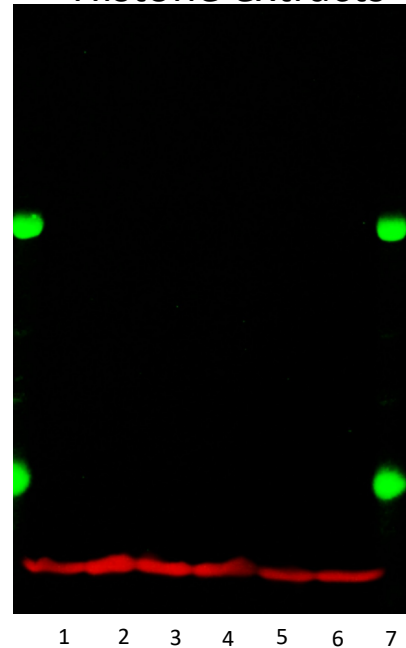


Blot 4 Δ PCCA 0.1x LIV
Histones: H3K23Ac
(Millipore 07-355) 1:1000
Low Exposure Reduced
Background

- Expected size: ~17 kDa
- Volume of sample loaded per well determined by protein quantification using Thermo Micro BCA Protein Assay Kit; 3ug of protein
- Well 1: Hap-1 0.1X LIV 1
- Well 2: Hap-1 0.1X LIV 2
- Well 3: Hap-1 0.1X LIV 3
- Well 4: Δ PCCA 0.1X LIV 1
- Well 5: Δ PCCA 0.1X LIV 2
- Well 6: Δ PCCA 0.1X LIV 3
- Wells 7: contains the Ladder; 2.0 μ L
- **LIV = Leu, Ile, Val (BCAA)**

Full unedited gel for Figure 1C

Histone extracts

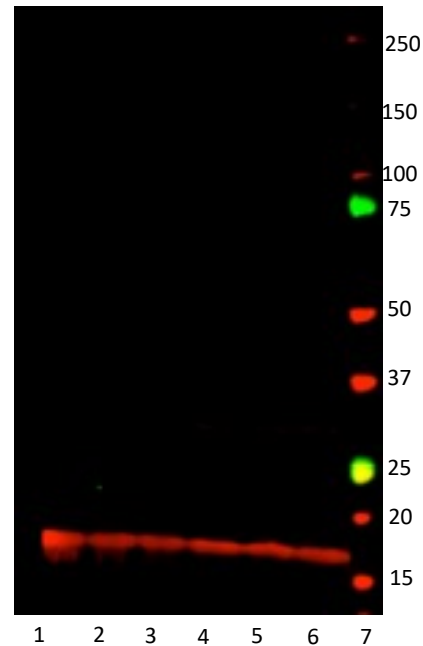


Blot 6 Δ PCCA 0.1X LIV
Histones: H3 (Active Motif
61475) 1:30,000 Low
Exposure

- Expected size: ~17 kDa
- Volume of sample loaded per well determined by protein quantification using Thermo Micro BCA Protein Assay Kit; 3 μ g of protein
- Well 1: Hap-1 0.1X LIV 1
- Well 2: Hap-1 0.1X LIV 2
- Well 3: Hap-1 0.1X LIV 3
- Well 4: Δ PCCA 0.1X LIV 1
- Well 5: Δ PCCA 0.1X LIV 2
- Well 6: Δ PCCA 0.1X LIV 3
- Wells 7: contains the Ladder; 2.0 μ L
- **LIV = Leu, Ile, Val (BCAA)**

Full unedited gel for Figure 1C

Histone extracts

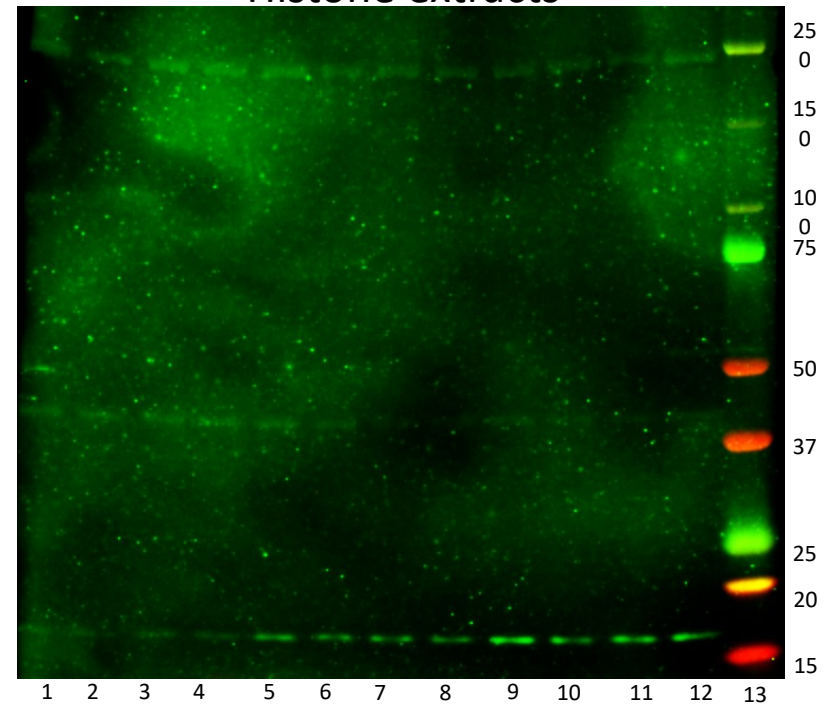


Full unedited gels for Figure 6F

Cardiac Myocytes -BCAAs +
Glucose + Sodium Propionate :
H3K23Pr (Active Motif 61397)
1:2000

- 3ug of protein loaded per well
- Expected size of H3K23Pr: ~ 17 kDa
 - Well 1: -BCAAs +Glucose 1
 - Well 2: -BCAAs +Glucose 2
 - Well 3: -BCAAs +Glucose + 0.25mM Sodium Propionate 1
 - Well 4: -BCAAs +Glucose + 0.25mM Sodium Propionate 2
 - Well 5: -BCAAs +Glucose + 0.5mM Sodium Propionate 1
 - Well 6: -BCAAs +Glucose + 0.5mM Sodium Propionate 2
 - Well 7: -BCAAs +Glucose + 0.75mM Sodium Propionate 1
 - Well 8: -BCAAs +Glucose + 0.75mM Sodium Propionate 2
 - Well 9: -BCAAs +Glucose + 1.0mM Sodium Propionate 1
 - Well 10: -BCAAs +Glucose + 1.0mM Sodium Propionate 2
 - Well 11: -BCAAs +Glucose + 1.5mM Sodium Propionate 1
 - Well 12: -BCAAs +Glucose + 1.5mM Sodium Propionate 2
 - Well 13: Ladder

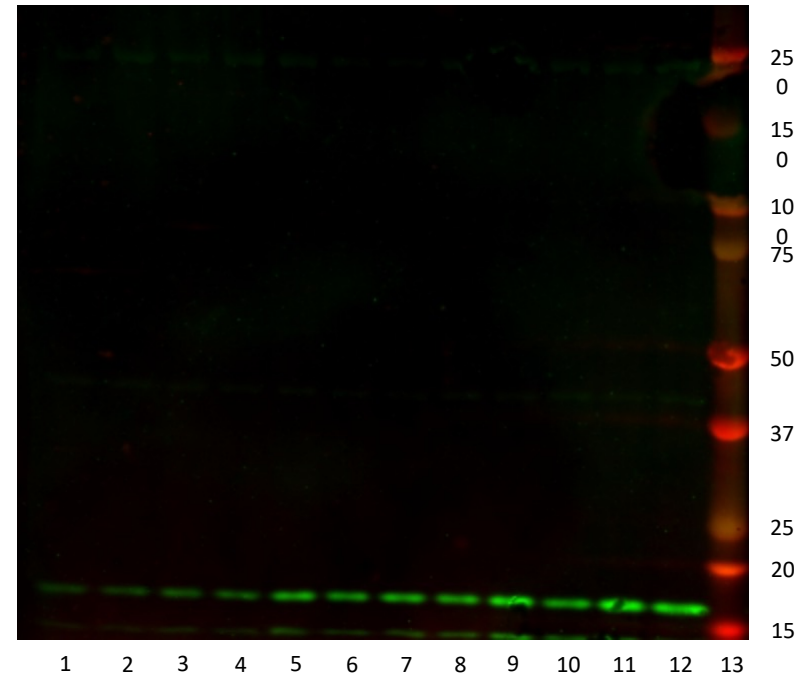
Full unedited gel for Figure 6F
Histone extracts



Cardiac Myocytes -BCAAs +
Glucose + Sodium Propionate:
KPR (PTM BIO PTM-201) 1:1000
Low Exposure

- 3ug of protein loaded per well
- Expected size of KPR: 15-17 kDa
 - Well 1: -BCAAs +Glucose 1
 - Well 2: -BCAAs +Glucose 2
 - Well 3: -BCAAs +Glucose + 0.25mM Sodium Propionate 1
 - Well 4: -BCAAs +Glucose + 0.25mM Sodium Propionate 2
 - Well 5: -BCAAs +Glucose + 0.5mM Sodium Propionate 1
 - Well 6: -BCAAs +Glucose + 0.5mM Sodium Propionate 2
 - Well 7: -BCAAs +Glucose + 0.75mM Sodium Propionate 1
 - Well 8: -BCAAs +Glucose + 0.75mM Sodium Propionate 2
 - Well 9: -BCAAs +Glucose + 1.0mM Sodium Propionate 1
 - Well 10: -BCAAs +Glucose + 1.0mM Sodium Propionate 2
 - Well 11: -BCAAs +Glucose + 1.5mM Sodium Propionate 1
 - Well 12: -BCAAs +Glucose + 1.5mM Sodium Propionate 2
 - Well 13: Ladder

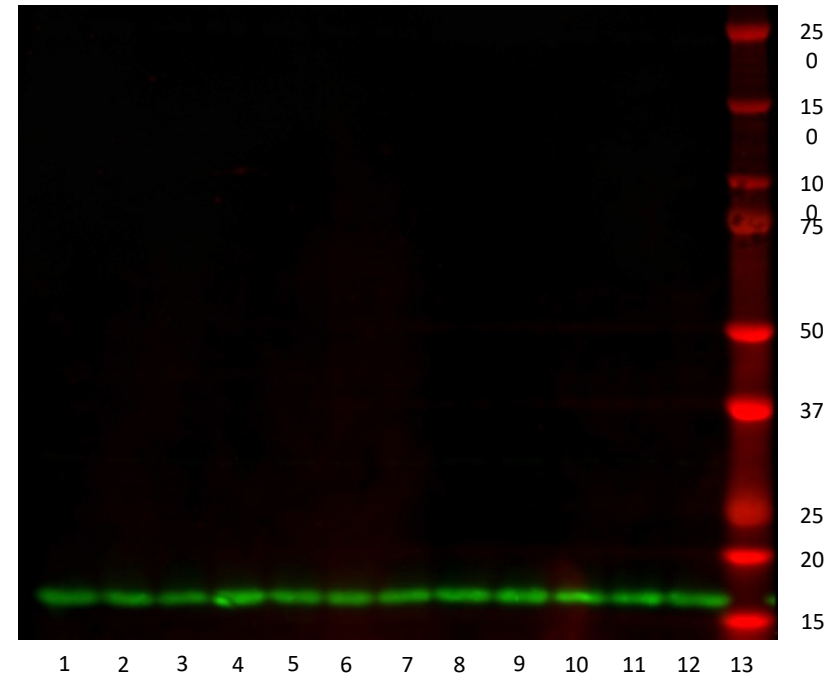
Full unedited gel for Figure 6F Histone extracts



Cardiac Myocytes -BCAAs +
Glucose + Sodium Propionate:
H3K23Ac (Millipore 07-355-S)
1:2000 Low Exposure

- 3ug of protein loaded per well
- Expected size of H3K23Ac: ~17 kDa
 - Well 1: -BCAAs +Glucose 1
 - Well 2: -BCAAs +Glucose 2
 - Well 3: -BCAAs +Glucose + 0.25mM Sodium Propionate 1
 - Well 4: -BCAAs +Glucose + 0.25mM Sodium Propionate 2
 - Well 5: -BCAAs +Glucose + 0.5mM Sodium Propionate 1
 - Well 6: -BCAAs +Glucose + 0.5mM Sodium Propionate 2
 - Well 7: -BCAAs +Glucose + 0.75mM Sodium Propionate 1
 - Well 8: -BCAAs +Glucose + 0.75mM Sodium Propionate 2
 - Well 9: -BCAAs +Glucose + 1.0mM Sodium Propionate 1
 - Well 10: -BCAAs +Glucose + 1.0mM Sodium Propionate 2
 - Well 11: -BCAAs +Glucose + 1.5mM Sodium Propionate 1
 - Well 12: -BCAAs +Glucose + 1.5mM Sodium Propionate 2
 - Well 13: Ladder

Full unedited gel for Figure 6F
Histone extracts

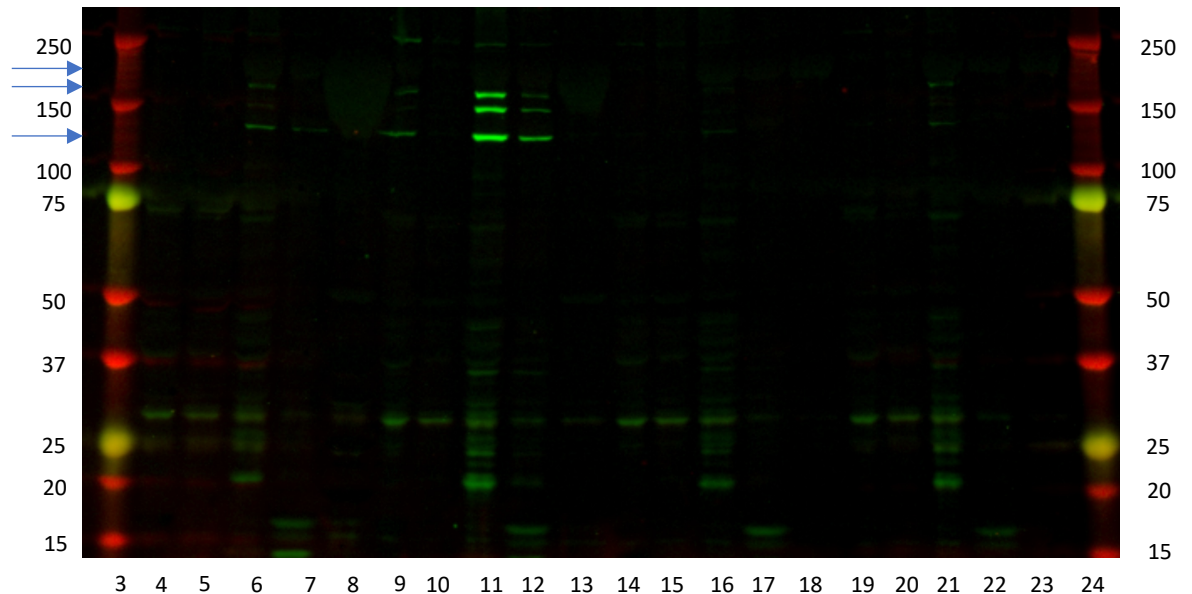


Full unedited gels for Figure 7A

Heart Tissue +/-BCAAs: Col 1A1 (Cell Signaling Technology 72026S) 1:1000

- Expected size: ~138-220 kDa
- Wells 4 through 8 contain all fractions for 1w-Sham-BCAA-control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 9 through 13 contain all fractions for 1w-TAC-BCAA-control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 14 through 18 contain all fractions for 1w-Sham-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 19 through 23 contain all fractions for 1w-TAC-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 3 and 24 contain the Ladder; 2.0 μ L

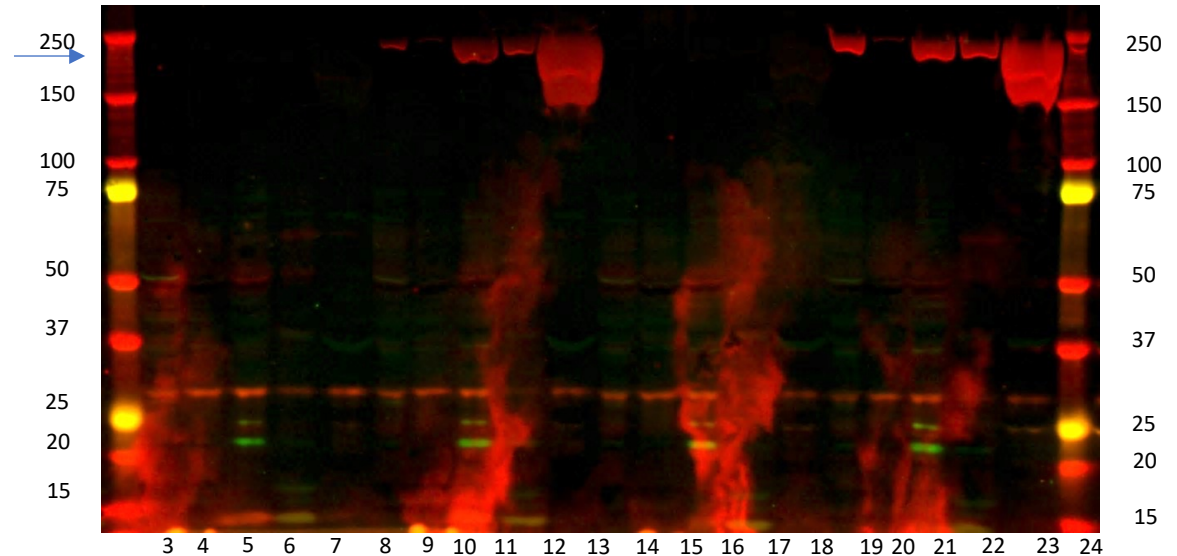
Full unedited gel for Figure 7A



Heart Tissue +/- BCAAs: Beta MHC (Sigma M8421) 1:1000

- Expected size: ~200 kDa
- Wells 4 through 8 contain all fractions for 1w-Sham- BCAAs Control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 9 through 13 contain all fractions for 1w-TAC- BCAAs Control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 14 through 18 contain all fractions for 1w-Sham-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 19 through 23 contain all fractions for 1w-TAC-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 3 and 24 contain the Ladder; 2.0 μ L

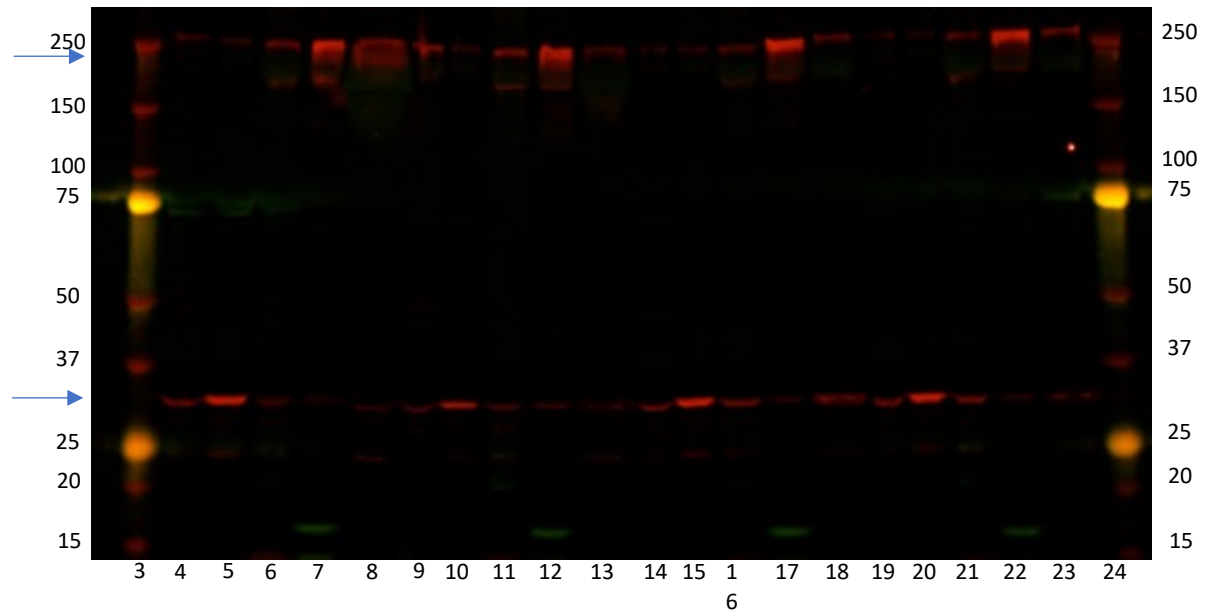
Full unedited gel for Figure 7A



Heart Tissue +/-BCAAs: VDAC1
(Genescript A01419) 1:1000 +
RNA Pol II (Active Motif
102660) 1:2000

- Expected size of VDAC1: ~34 kDa
- Expected size of RNA Pol II: ~ 240 kDa
- Wells 4 through 8 contain all fractions for 1w-Sham-BCAA-control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 9 through 13 contain all fractions for 1w-TAC-BCAA-control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 14 through 18 contain all fractions for 1w-Sham-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 19 through 23 contain all fractions for 1w-TAC-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 3 and 24 contain the Ladder; 2.0 µL

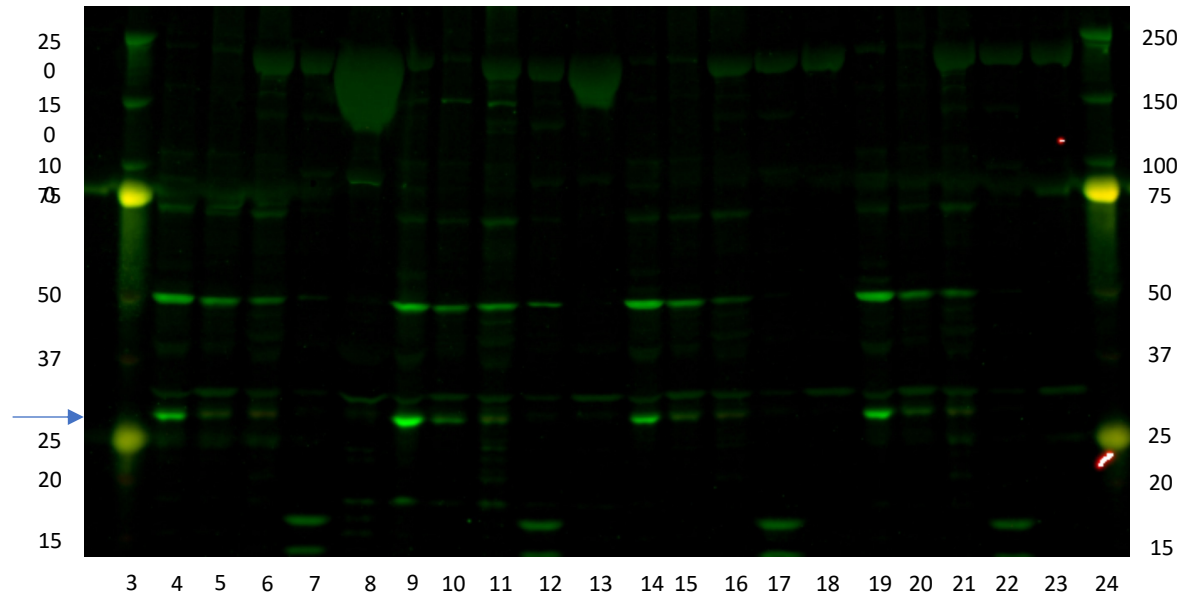
Full unedited gel for Figure 7A



Heart Tissue +/-BCAAs:
CLIC1 (abcam ab229917)
1:1000

- Expected size: ~27 kDa
- Wells 4 through 8 contain all fractions for 1w-Sham-BCAA-control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 9 through 13 contain all fractions for 1w-TAC-BCAA-control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 14 through 18 contain all fractions for 1w-Sham-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 19 through 23 contain all fractions for 1w-TAC-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 3 and 24 contain the Ladder; 2.0 μ L

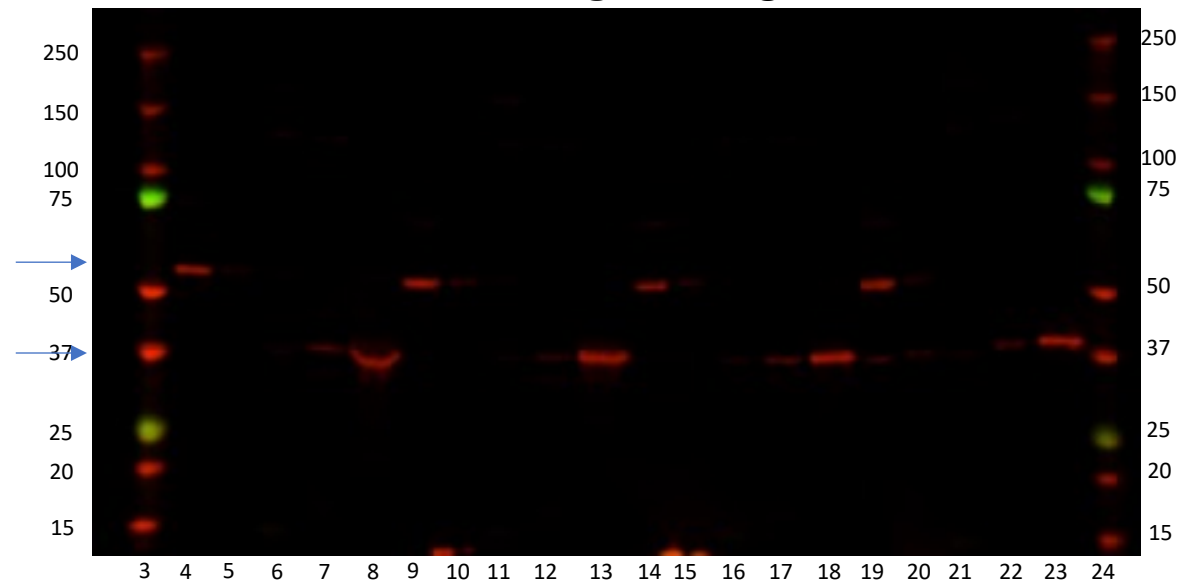
Full unedited gel for Figure 7A



1W Heart Tissue +/-BCAAs:
 AKT1 (Cell Signaling
 Technology 9272S) 1:1000 +
 TNNT2 (Sigma SAB2108239)
 1:2000

- Expected size of Akt1: ~60 kDa
- Expected size of TNNT2: ~36 kDa
- Wells 4 through 8 contain all fractions for 1w-Sham- BCAAs Control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 9 through 13 contain all fractions for 1w-TAC-BCAAs Control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 14 through 18 contain all fractions for 1w-Sham-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 19 through 23 contain all fractions for 1w-TAC-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 3 and 24 contain the Ladder; 2.0 μ L

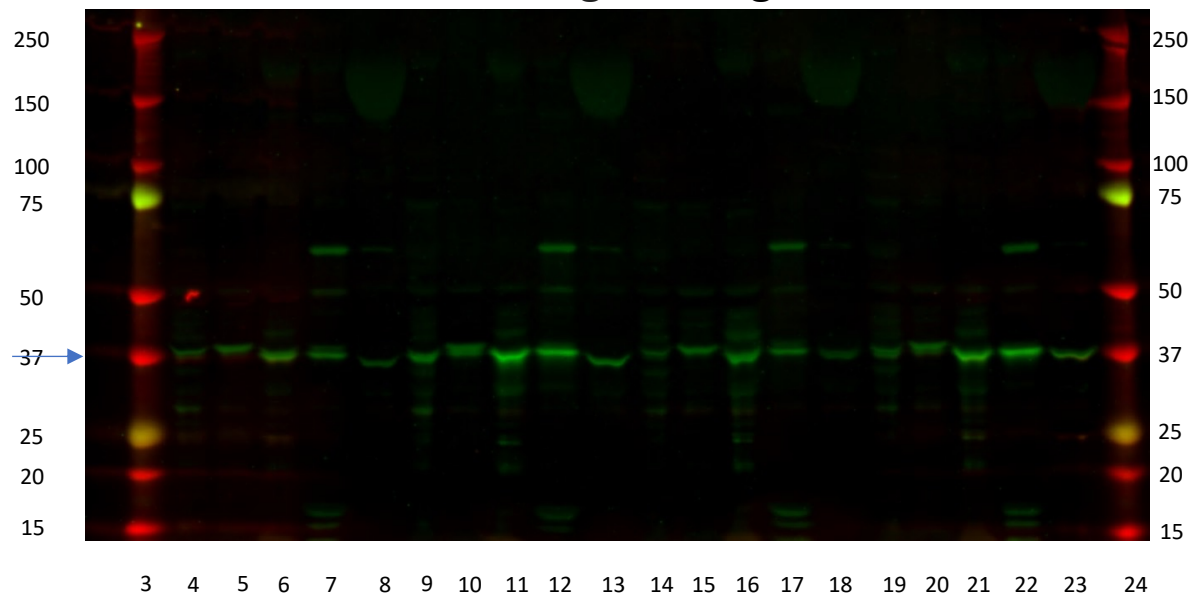
Full unedited gel for Figure 7A



Heart Tissue +/-BCAAs: ANKRD1 (Santa Cruz Biotechnology) 1:1000

- Expected size: ~36 kDa
- Wells 4 through 8 contain all fractions for 1w-Sham- BCAAs Control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 9 through 13 contain all fractions for 1w-TAC- BCAAs Control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 14 through 18 contain all fractions for 1w-Sham-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 19 through 23 contain all fractions for 1w-TAC-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 3 and 24 contain the Ladder; 2.0 μ L

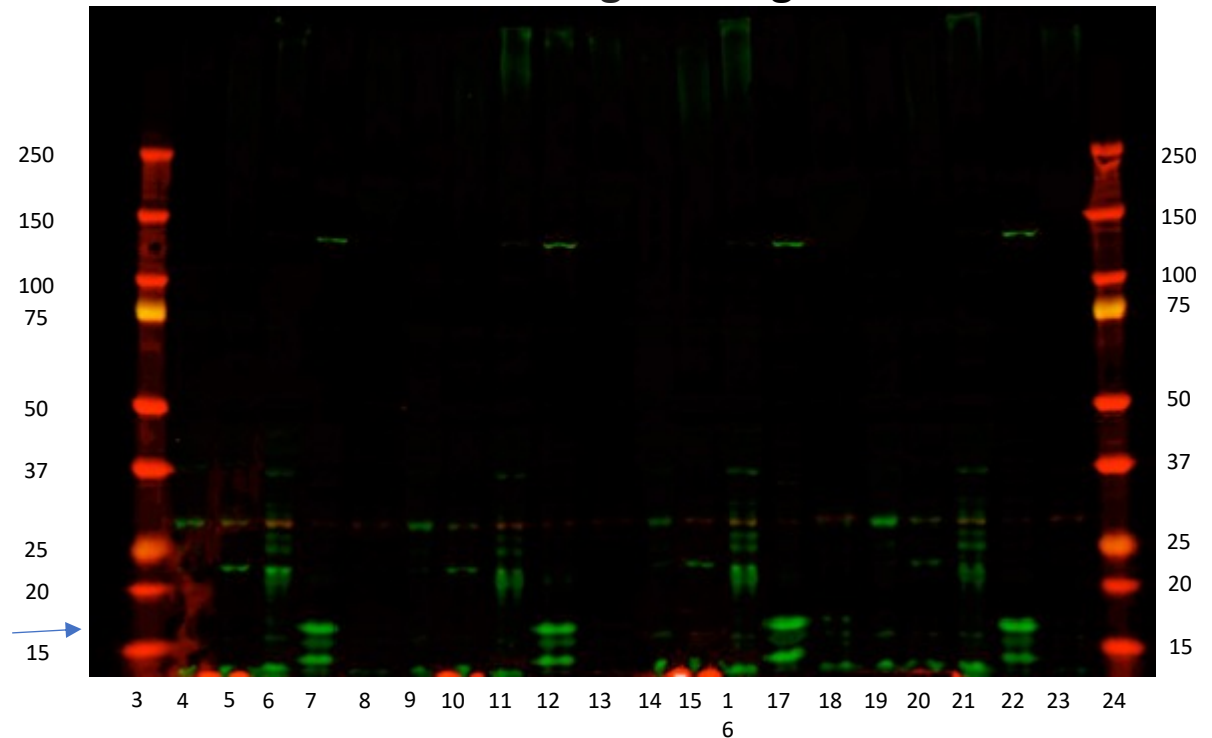
Full unedited gel for Figure 7A



1W Heart Tissue +/- BCAA:
H3K23Pr (Abcam, ab241466) +
~~HDAC9 (abcam ab109446) 1:500~~
(not included in figures)

Full unedited gel for Figure 7A

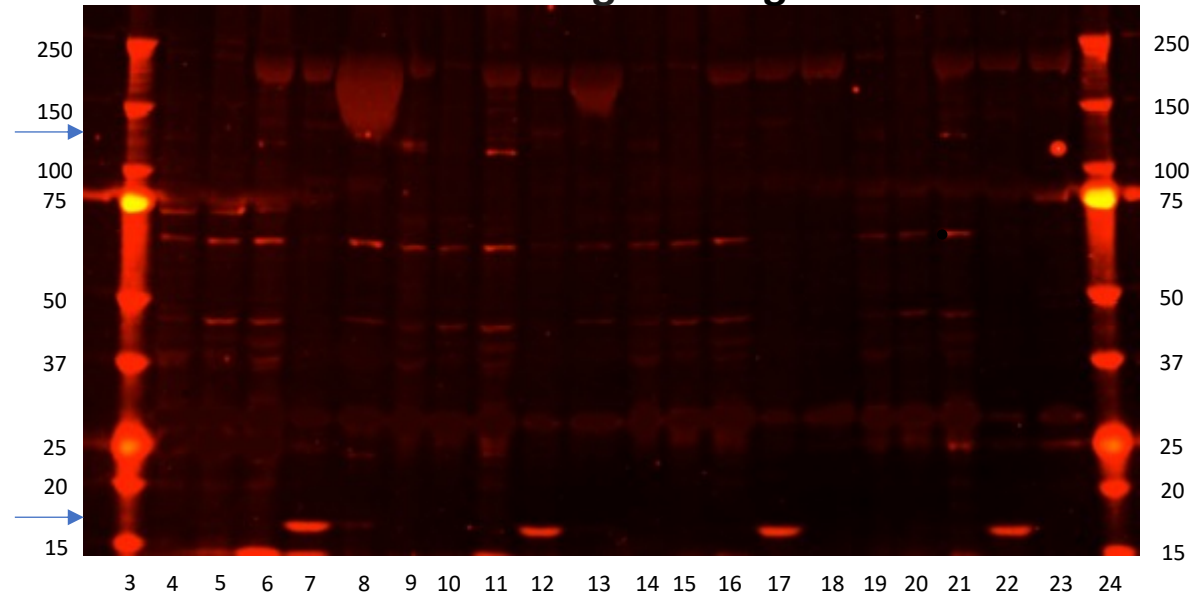
- Expected size of H3K23Pr: ~17 kDa
- Expected size of HDAC9: ~111 kDa
- Wells 4 through 8 contain all fractions for 1w-Sham- BCAAs Control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 9 through 13 contain all fractions for 1w-TAC- BCAAs Control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 14 through 18 contain all fractions for 1w-Sham-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 19 through 23 contain all fractions for 1w-TAC-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 3 and 24 contain the Ladder; 2.0 µL



Blot 1 Heart Tissue +/-
 BCAAs: H3K23Ac (Millipore,
 07-355) 1:10,000, Col VI
 (abcam-ab199720)
 1:1000(not included in
 figure)

- Expected size: H3K23ac ~17 Kd
- Expected size: Col VI ~138-220 kDa
- Wells 4 through 8 contain all fractions for 1w-Sham- BCAAs Control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 9 through 13 contain all fractions for 1w-TAC- BCAAs Control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 14 through 18 contain all fractions for 1w-Sham-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 19 through 23 contain all fractions for 1w-TAC-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 3 and 24 contain the Ladder; 2.0 μ L

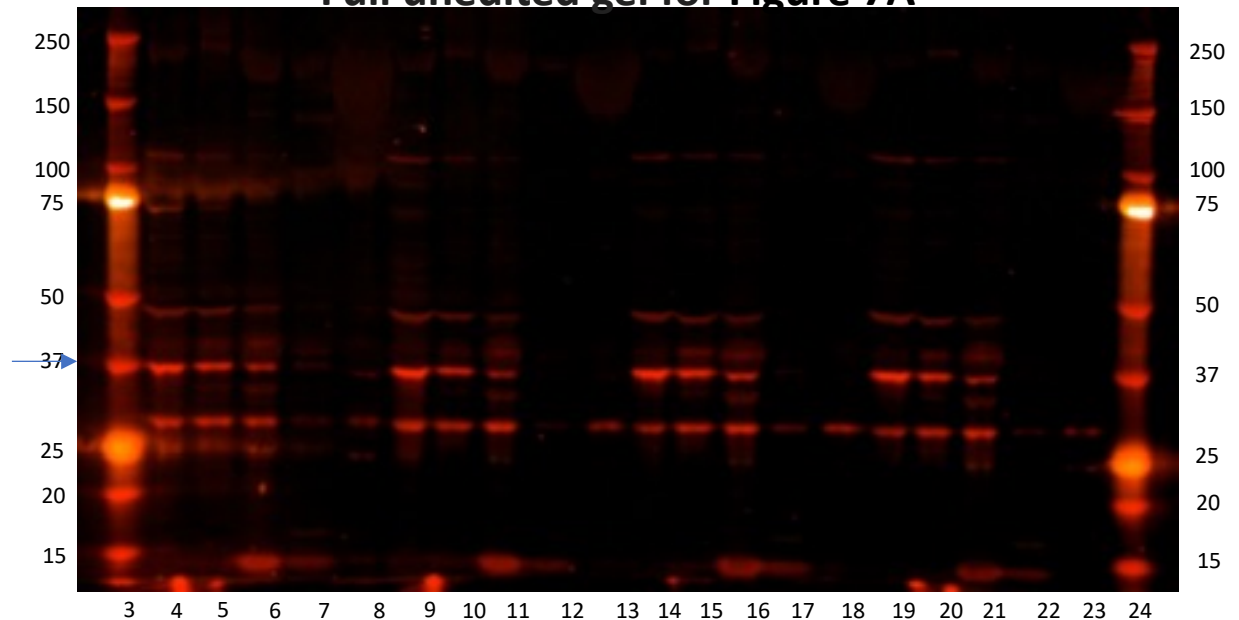
Full unedited gel for Figure 7A



Blot 3 Heart Tissue +/-
BCAAs: BCAT2 (Sigma
HPA054091) 1:1000

- Expected size: ~39 kDa
- Wells 4 through 8 contain all fractions for 1w-Sham- BCAAs Control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 9 through 13 contain all fractions for 1w-TAC- BCAAs Control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 14 through 18 contain all fractions for 1w-Sham-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 19 through 23 contain all fractions for 1w-TAC-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 3 and 24 contain the Ladder; 2.0 µL

Full unedited gel for Figure 7A

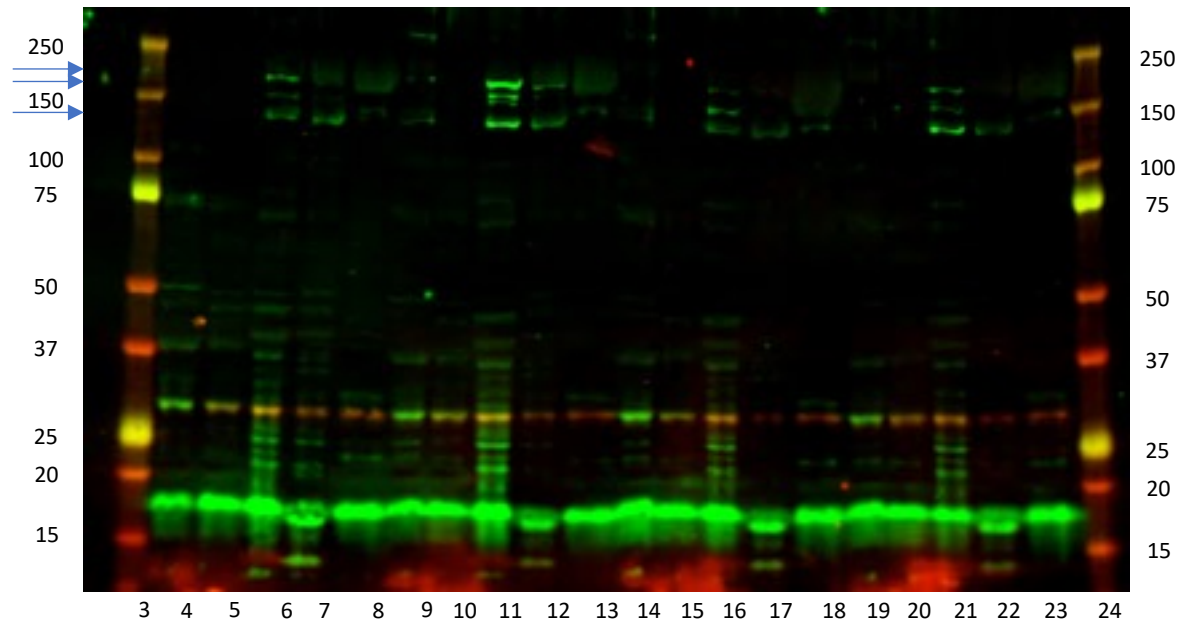


Full unedited gels for Figure 8A

1W Mouse Heart Tissue + 1%
propionate +/-BCAAs: COL 1A1
(Cell Signaling Technology
72026S) + Ndufs4 (Sigma
HPA003884) 1:1000—ignore—
was not included in figure

- Expected size of Col 1A1: ~138-220 kDa
- Expected size of Ndufs4: ~ 17 kDa ignore
- Wells 4 through 8 contain all fractions for 1w-Sham propionate BCAA-control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 9 through 13 contain all fractions for 1w-TAC propionate BCAA-control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 14 through 18 contain all fractions for 1w-Sham propionate BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 19 through 23 contain all fractions for 1w-TAC propionate BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 3 and 24 contain the Ladder; 2.0 μ L

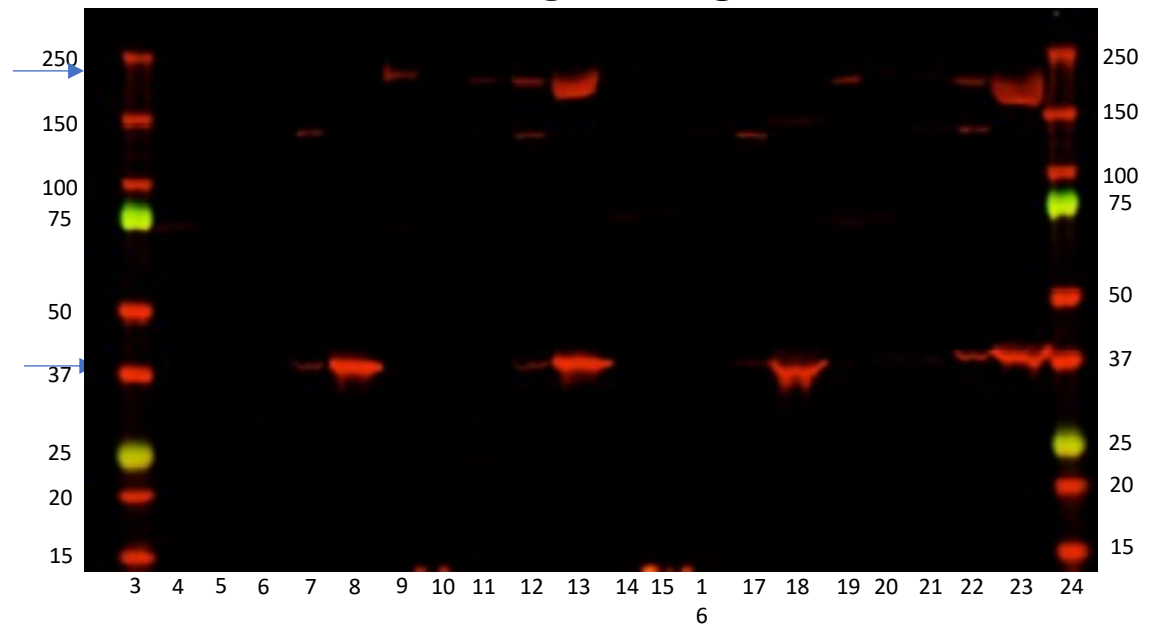
Full unedited gel for Figure 8B



1W Heart Tissue + 1%
 Propionate: MYH7 (Sigma
 M8421) 1:1000 + TNNT2
 (Sigma SAB2108239) 1:1000

- Expected size of MYH7: ~200 kDa
- Expected size of TNNT2: ~36 kDa
- Wells 4 through 8 contain all fractions for 1w-Sham Prop BCAA-control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 9 through 13 contain all fractions for 1w-TAC Prop BCAA-control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 14 through 18 contain all fractions for 1w-Sham Prop BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 19 through 23 contain all fractions for 1w-TAC Prop BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 3 and 24 contain the Ladder; 2.0 μ L

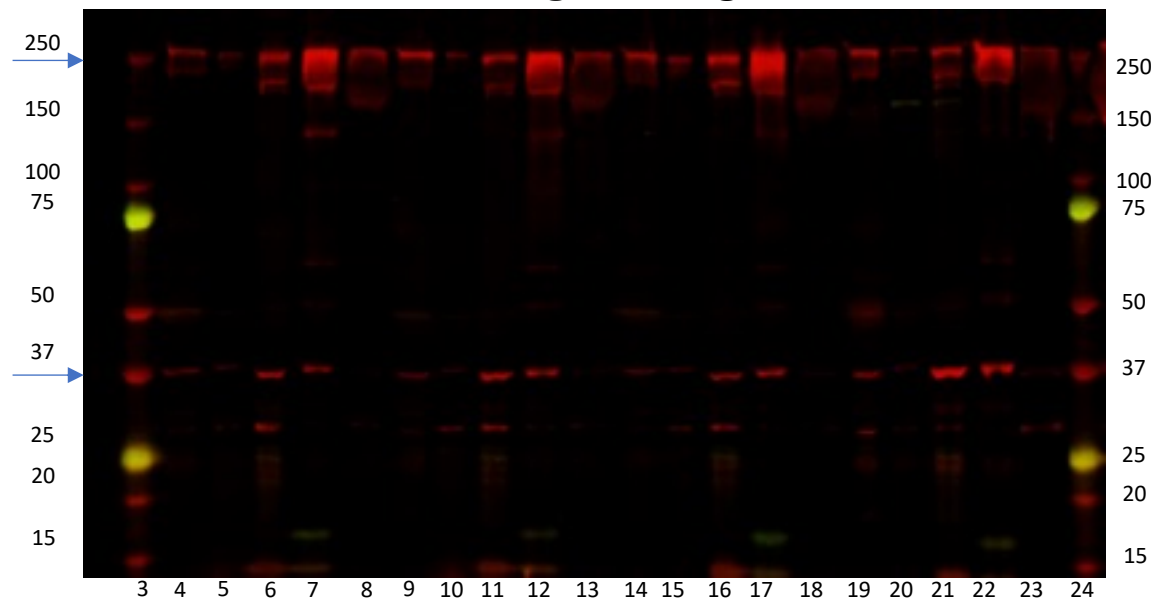
Full unedited gel for Figure 8B



1W Heart Tissue + 1%
 Propionate: ANKRD1 (Santa
 Cruz Biotechnology sc-30181)
 1:1000 + RNA Pol II (Active
 Motif 102660) 1:2000

- Expected size of AnKrd1: ~36 kDa
- Expected size of RNA Pol II: ~240 kDa
- Wells 4 through 8 contain all fractions for 1w-Sham Prop BCAA-control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 9 through 13 contain all fractions for 1w-TAC Prop BCAA-control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 14 through 18 contain all fractions for 1w-Sham Prop BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- *Wells 19 through 23 contain all fractions for 1w-TAC Prop BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 3 and 24 contain the Ladder; 2.0 μ L

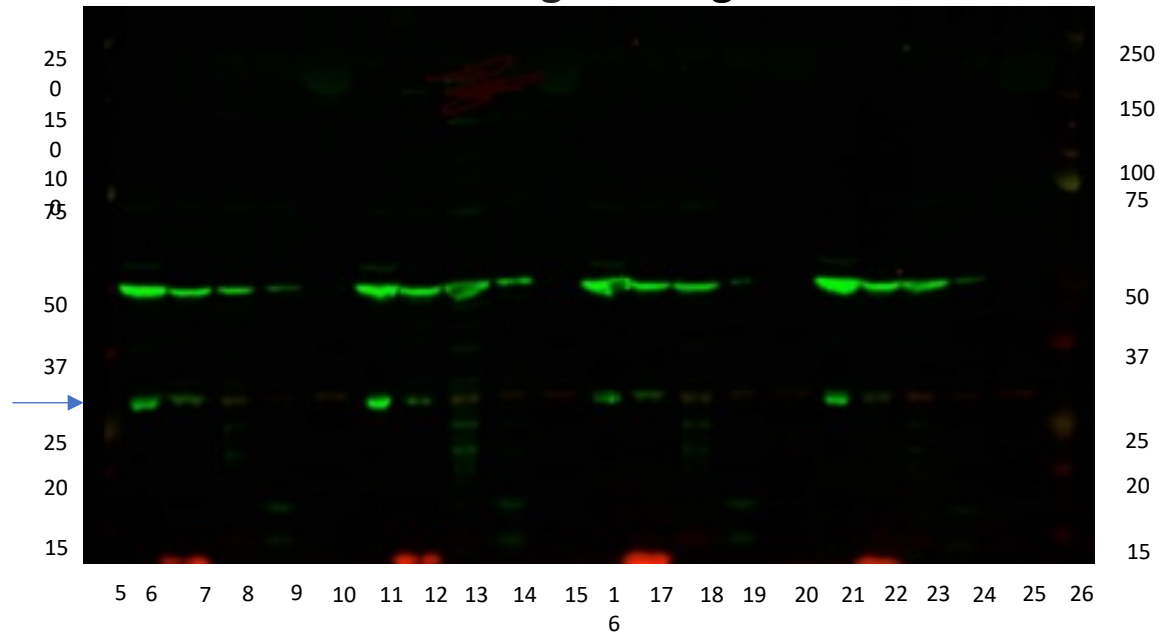
Full unedited gel for Figure 8B



1W Heart Tissue + 1%
Propionate: Clic1 (abcam
ab229917) 1:1000 Low
Exposure

- Expected size of Clic1: ~27 kDa
- Wells 6 through 10 contain all fractions for 1w-Sham Prop BCAA-control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 11 through 15 contain all fractions for 1w-TAC Prop BCAA-control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 16 through 20 contain all fractions for 1w-Sham Prop BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 21 through 25 contain all fractions for 1w-TAC Prop BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 5 and 26 contain the Ladder; 2.0 µL

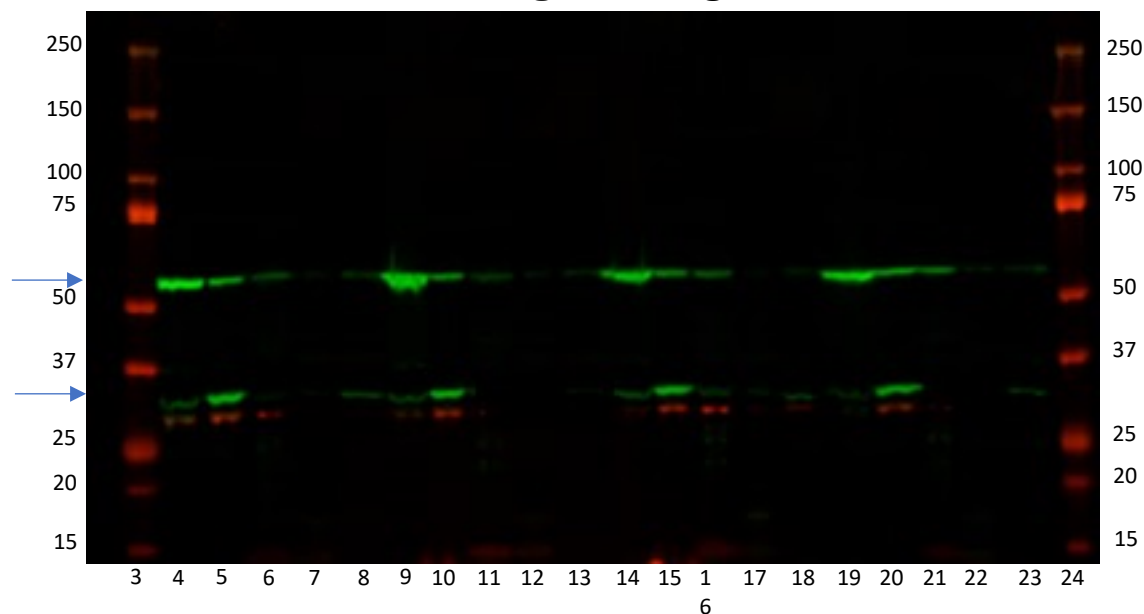
Full unedited gel for Figure 8B



1W Heart Tissue + 1%
 Propionate: AKT1 (Cell
 Signaling Technology 9272S)
 1:1000 + VDAC1 (Genescript
 A01914) 1:2000 Low Exposure

- Expected size of Akt1: ~60 kDa
- Expected size of Vdac1: ~34 kDa
- Wells 4 through 8 contain all fractions for 1w-Sham Prop BCAA-control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 9 through 13 contain all fractions for 1w-TAC Prop BCAA-control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 14 through 18 contain all fractions for 1w-Sham Prop BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 19 through 23 contain all fractions for 1w-TAC Prop BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 3 and 24 contain the Ladder; 2.0 μ L

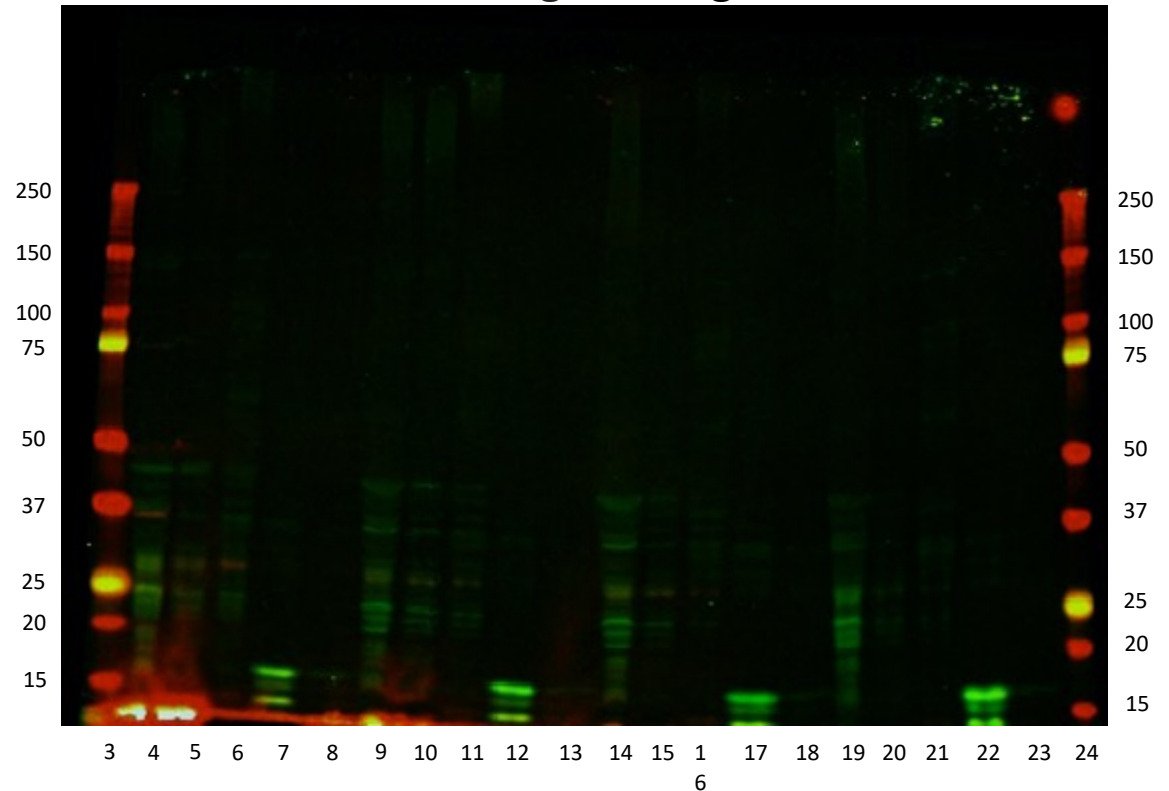
Full unedited gel for Figure 8B



1W Heart Tissue + 1%
Propionate: H3K23Pr
(Abcam, ab241466)
1:1000

- Expected size: 17~kDa
- Wells 4 through 8 contain all fractions for 1w-Sham- BCAAs Control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 9 through 13 contain all fractions for 1w-TAC- BCAAs Control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 14 through 18 contain all fractions for 1w-Sham-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 19 through 23 contain all fractions for 1w-TAC-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 3 and 24 contain the Ladder; 2.0 μ L

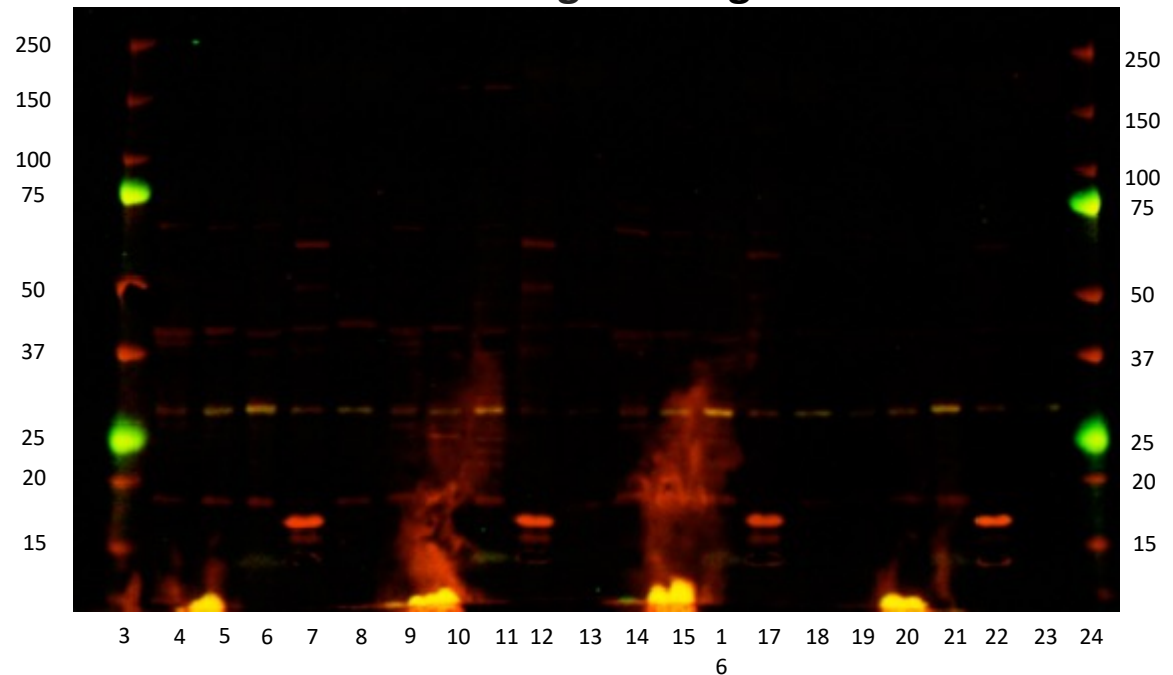
Full unedited gel for Figure 8B



1W Heart Tissue + 1%
Propionate : H3K23Ac
(Millipore, 07-355)
1:10,000

- Expected size of H3K23Pr: ~17 kDa
- Expected size: 17~kDa
- Wells 4 through 8 contain all fractions for 1w-Sham- BCAAs Control
 - The fractions are organized : cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 9 through 13 contain all fractions for 1w-TAC- BCAAs Control
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 14 through 18 contain all fractions for 1w-Sham-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 19 through 23 contain all fractions for 1w-TAC-BCAA-free
 - The fractions are organized: cytoplasmic bound proteins, membrane bound proteins, nuclear bound proteins, chromatin bound, and cytoskeletal bound.
- Wells 3 and 24 contain the Ladder; 2.0 µL

Full unedited gel for Figure 8B

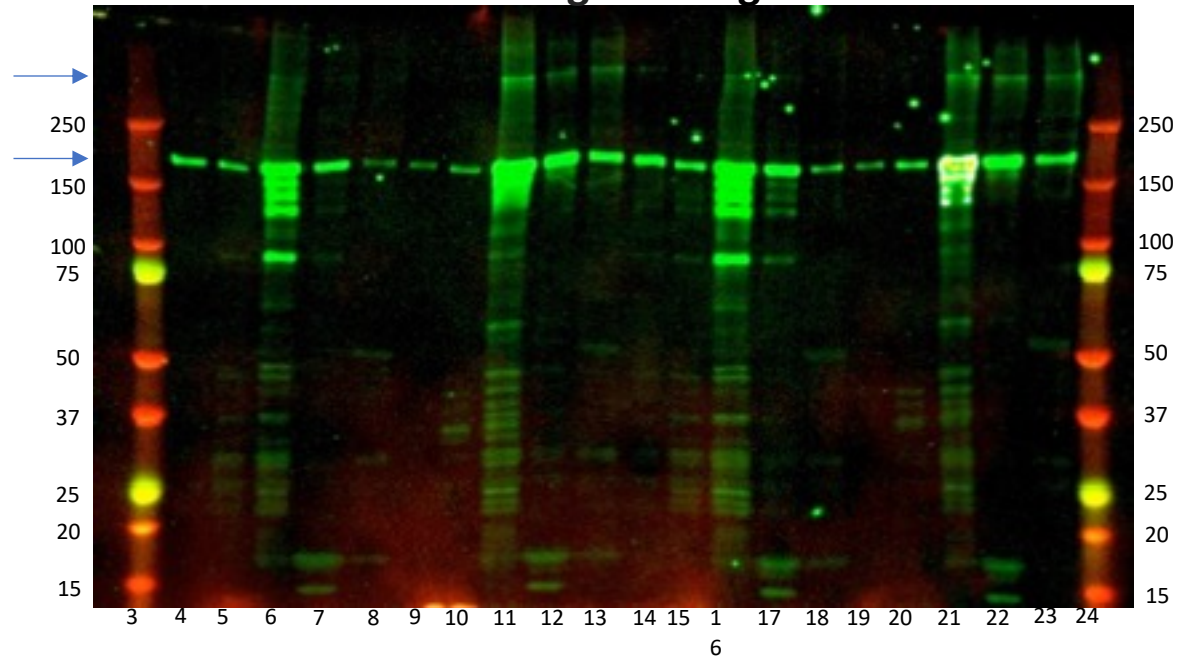


Full unedited gels for Figure 11C

Blot 2 Fibroblasts: COL1A1
 (Cell Signaling 72026s)
 1:1000 (not used in figure) +
 MKI67 (abcam ab16667)
 1:500

- Expected size of Col 1A1: ~138-220 kDa (**this was not used for the figure**)
- Expected size of Ki67: ~358 kDa
- 15uL of sample loaded per well
- Samples are organized cytoplasmic fraction, membrane bound fraction, nuclear bound fraction, chromatin bound fraction and cytoskeletal fraction as follows:
 - Wells 4 through 8 contain all fractions for Fib BF + 0.1X LIV
 - Wells 9 through 13 contain all fractions for Fib BF + 1X LIV
 - Wells 14 through 18 contain all fractions for Fib BF + 0.1X LIV + TGFb-1
 - Wells 19 through 23 contain all fractions for Fib BF + 1X LIV + TGFb-1
 - Wells 3 and 24 contain the Ladder; 2.0 μ L

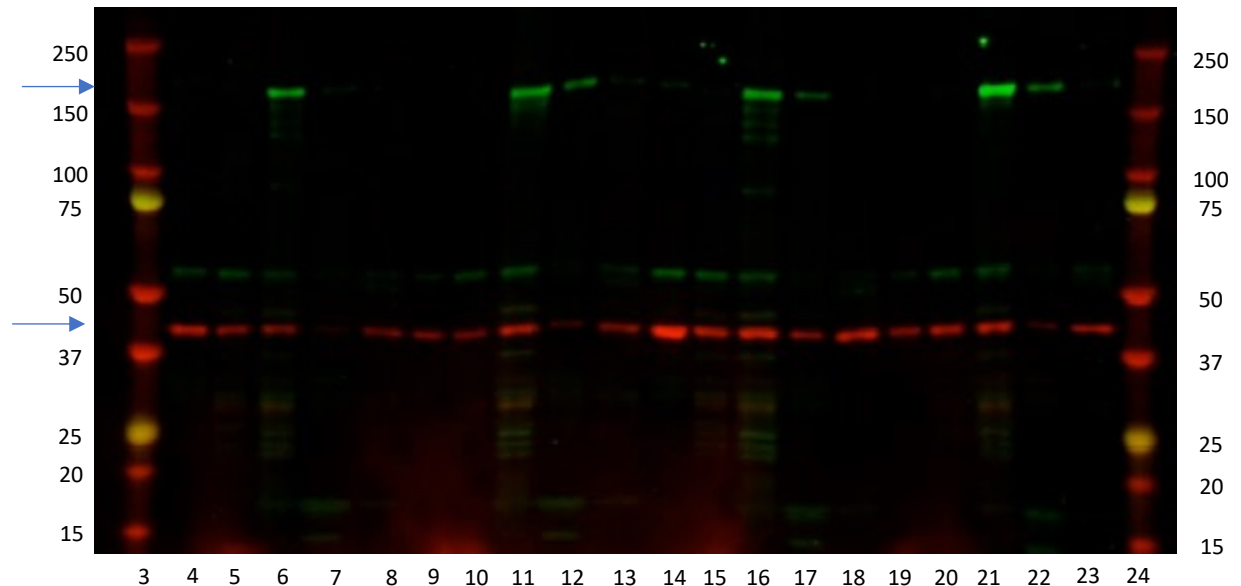
Full unedited gel for Figure 11C



Fibroblasts: COL1A1 (Cell Signaling 72026s) 1:1000 +
 αSMA (Sigma A5228) 1:1000

- Expected size of Col 1A1: ~138-220 kDa
- Expected size of αSMA: ~42 kDa
- 15uL of sample loaded per well
- Samples are organized cytoplasmic fraction, membrane bound fraction, nuclear bound fraction, chromatin bound fraction and cytoskeletal fraction as follows:
 - Wells 4 through 8 contain all fractions for Fib BF + 0.1X LIV
 - Wells 9 through 13 contain all fractions for Fib BF + 1X LIV
 - Wells 14 through 18 contain all fractions for Fib BF + 0.1X LIV + TGFb-1
 - Wells 19 through 23 contain all fractions for Fib BF + 1X LIV + TGFb-1
 - Wells 3 and 24 contain the Ladder; 2.0 μL
 - **LIV = Leu, Ile, Val**

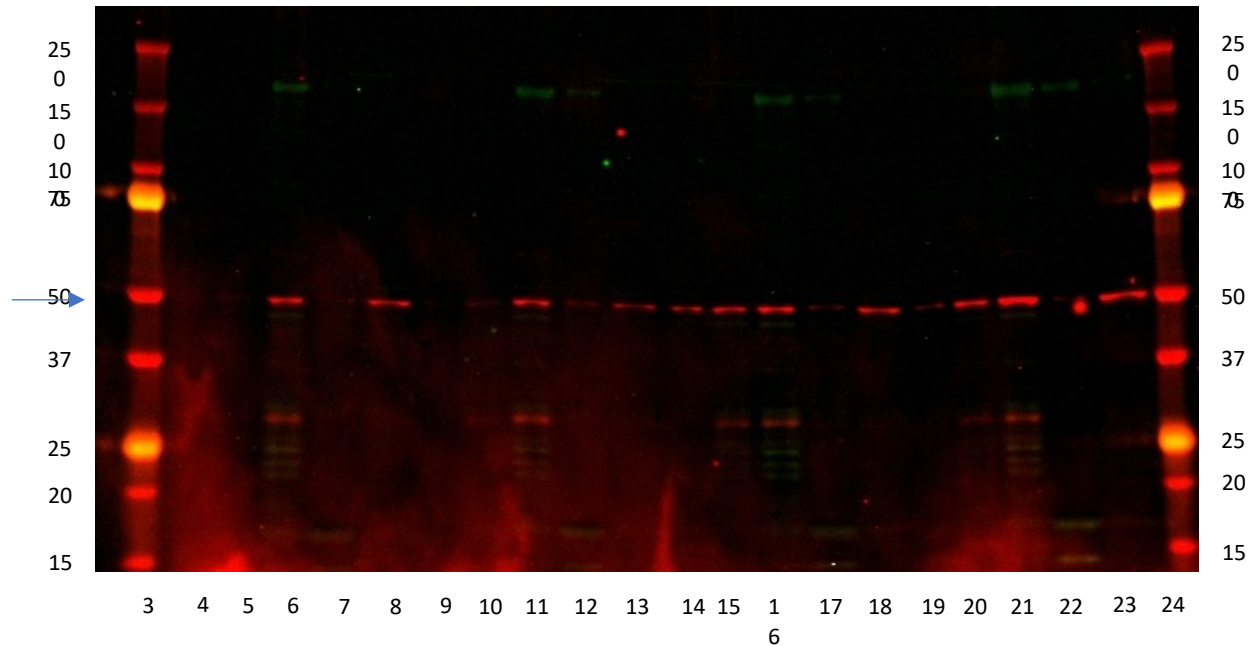
Full unedited gel for Figure 11C



Fibroblasts: alpha Tubulin
(TUBA, abcam ab7291)
1:1000

- Expected size of alpha Tubulin: ~50 kDa
- 15uL of sample loaded per well
- Samples are organized cytoplasmic fraction, membrane bound fraction, nuclear bound fraction, chromatin bound fraction and cytoskeletal fraction as follows:
 - Wells 4 through 8 contain all fractions for Fib BF + 0.1X LIV
 - Wells 9 through 13 contain all fractions for Fib BF + 1X LIV
 - Wells 14 through 18 contain all fractions for Fib BF + 0.1X LIV + TGFb-1
 - Wells 19 through 23 contain all fractions for Fib BF + 1X LIV + TGFb-1
 - Wells 3 and 24 contain the Ladder; 2.0 µL
 - **LIV = Leu, Ile, Val**

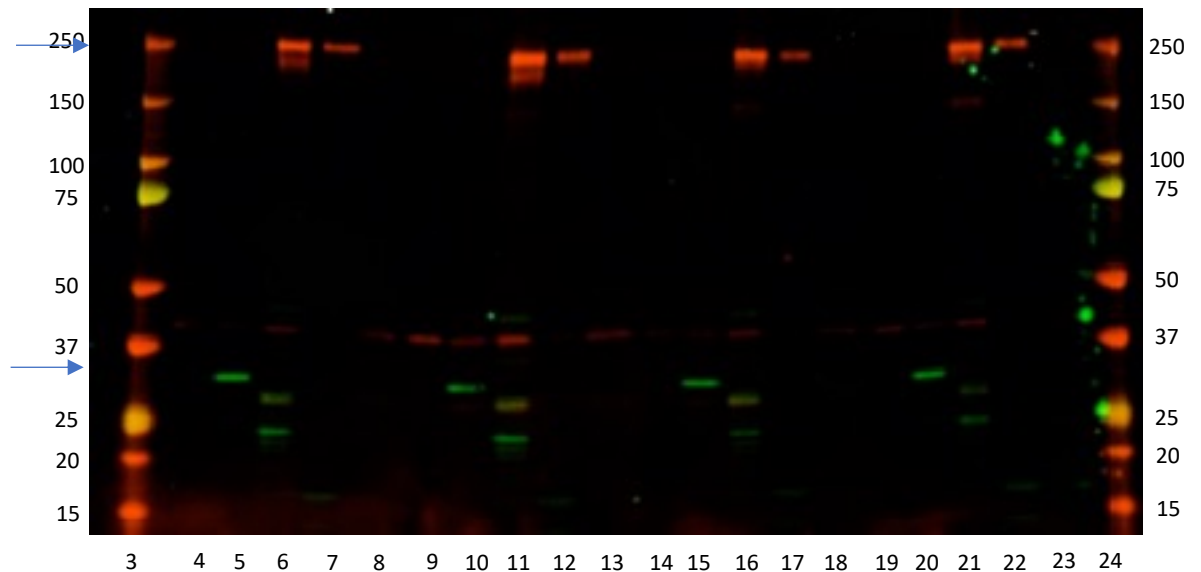
Full unedited gel for Figure 11C



Fibroblasts: VDAC1 (Sigma SAB5700655) 1:1000 + RNA Pol II (Active Motif 102660) 1:2000

- Expected size of Vdac1: ~34 kDa
- Expected size of RNA Pol II: ~240 kDa
- 15uL of sample loaded per well
- Samples are organized cytoplasmic fraction, membrane bound fraction, nuclear bound fraction, chromatin bound fraction and cytoskeletal fraction as follows:
 - Wells 4 through 8 contain all fractions for Fib BF + 0.1X LIV
 - Wells 9 through 13 contain all fractions for Fib BF + 1X LIV
 - Wells 14 through 18 contain all fractions for Fib BF + 0.1X LIV + TGFb-1
 - Wells 19 through 23 contain all fractions for Fib BF + 1X LIV + TGFb-1
 - Wells 3 and 24 contain the Ladder; 2.0 μ L
- **LIV = Leu, Ile, Val**

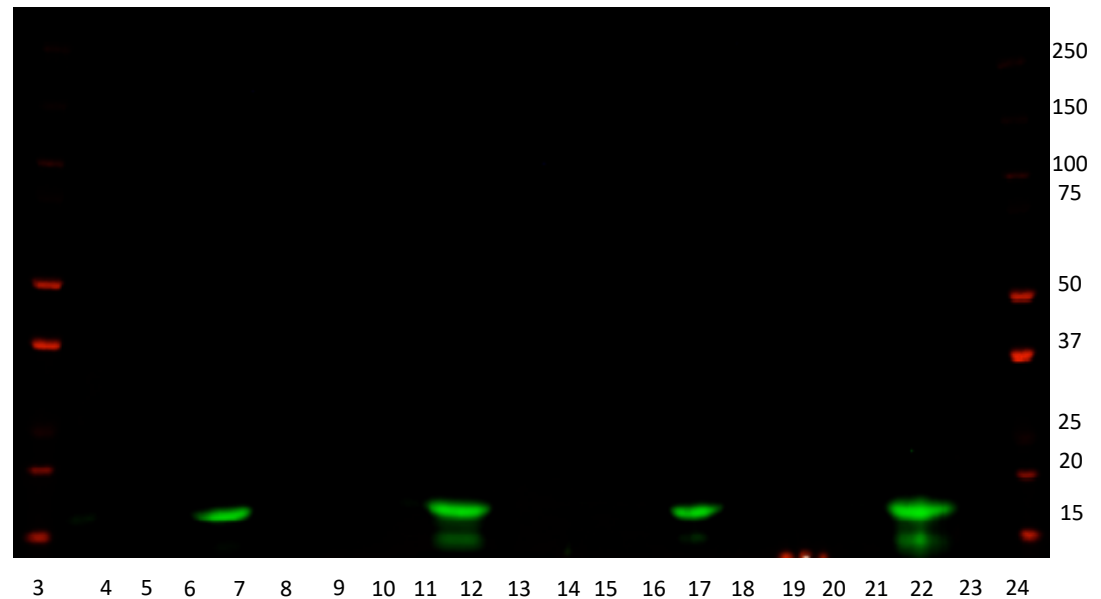
Full unedited gel for Figure 11C



Fibroblast:
H3K23Pr (Abcam,
ab241466) 1:1000

- Expected size of Vdac1: ~34 kDa
- Expected size of RNA Pol II: ~240 kDa
- 15uL of sample loaded per well
- Samples are organized cytoplasmic fraction, membrane bound fraction, nuclear bound fraction, chromatin bound fraction and cytoskeletal fraction as follows:
 - Wells 4 through 8 contain all fractions for Fib BF + 0.1X LIV
 - Wells 9 through 13 contain all fractions for Fib BF + 1X LIV
 - Wells 14 through 18 contain all fractions for Fib BF + 0.1X LIV + TGFb-1
 - Wells 19 through 23 contain all fractions for Fib BF + 1X LIV + TGFb-1
 - Wells 3 and 24 contain the Ladder; 2.0 μ L
- **LIV = Leu, Ile, Val**

Full unedited gel for Figure 11C

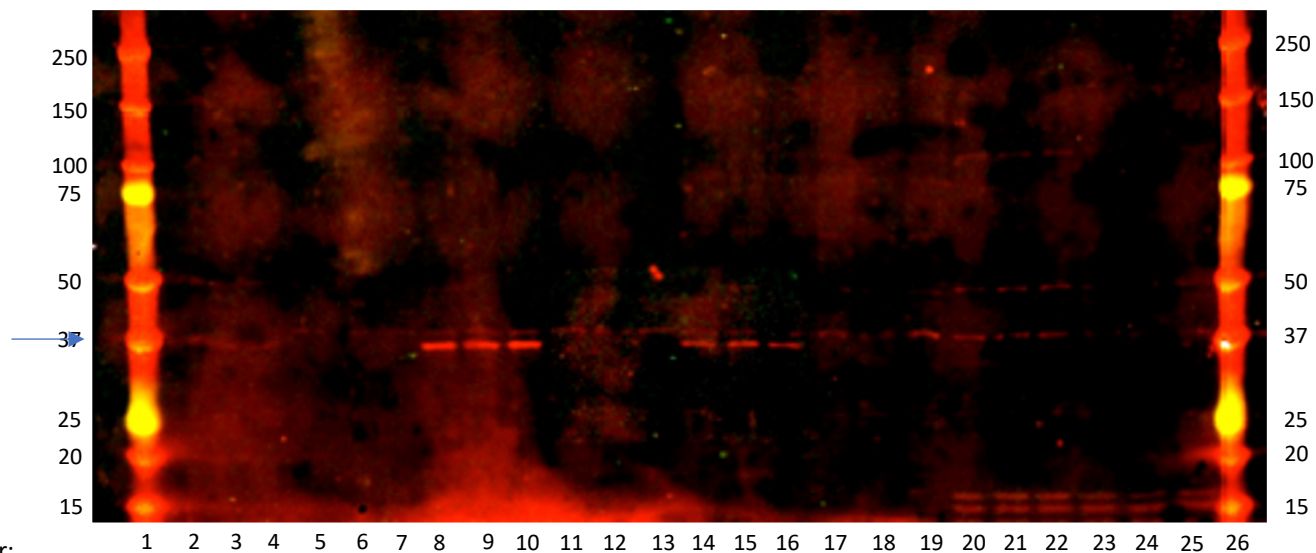


Full unedited gels for Supplementary Fig. 2S-A

BCAT2 Knockouts: BCAT2 (Sigma HPA054091) 1:1000

- Expected size: ~ 39 kDa
 - HAP-1 1
 - HAP-1 2
 - HAP-1 3
 - Δ BCAT2 1
 - Δ BCAT2 2
 - Δ BCAT2 3
- Wells 2 through 7 contain the cytoplasmic bound protein layer
- Wells 8 through 13 contain the membrane bound protein layer
- Wells 14 through 19 contain the nuclear soluble protein layer
- Wells 20 through 25 contain the chromatin bound protein layer
- Wells 1 and 26 contain the Ladder; 2.0 μ L

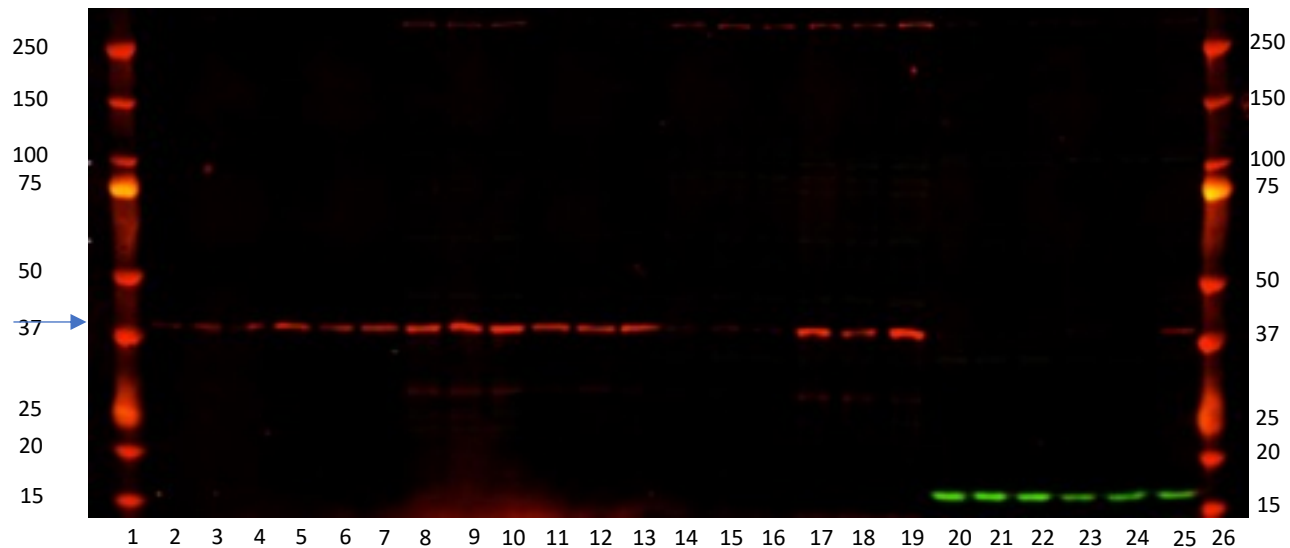
Full unedited gel for Supplementary Fig. 2S-A



BCAT2 Knockouts: BCAT1
(Cell Signaling Technology
8875S) 1:1000

- Expected size: ~ 43 kDa
 - HAP-1 1
 - HAP-1 2
 - HAP-1 3
 - Δ BCAT2 1
 - Δ BCAT2 2
 - Δ BCAT2 3
- Wells 2 through 7 contain the cytoplasmic bound protein layer
- Wells 8 through 13 contain the membrane bound protein layer
- Wells 14 through 19 contain the nuclear soluble protein layer
- Wells 20 through 25 contain the chromatin bound protein layer
- Wells 1 and 26 contain the Ladder; 2.0 μ L

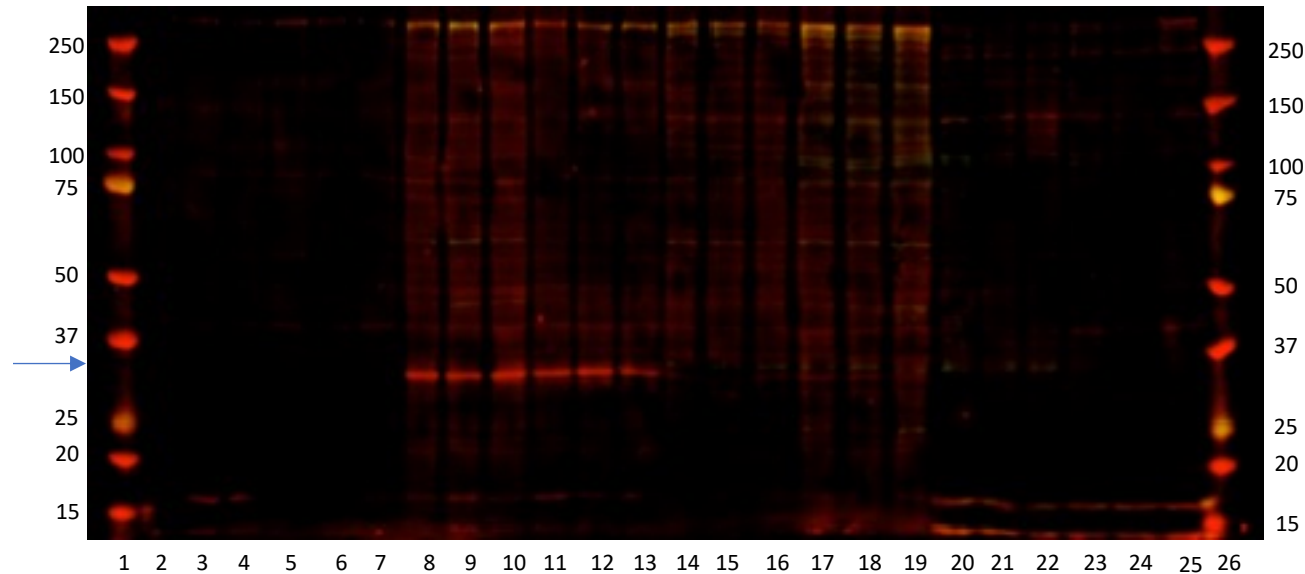
Full unedited gel for Supplementary Fig. 2S-A



BCAT2 Knockouts: VDAC1
(Genescript A01419) 1:1000

- Expected size: ~34 kDa
 - HAP-1 1
 - HAP-1 2
 - HAP-1 3
 - Δ BCAT2 1
 - Δ BCAT2 2
 - Δ BCAT2 3
- Wells 2 through 7 contain the cytoplasmic bound protein layer
- Wells 8 through 13 contain the membrane bound protein layer
- Wells 14 through 19 contain the nuclear soluble protein layer
- Wells 20 through 25 contain the chromatin bound protein layer
- Wells 1 and 26 contain the Ladder; 2.0 μ L

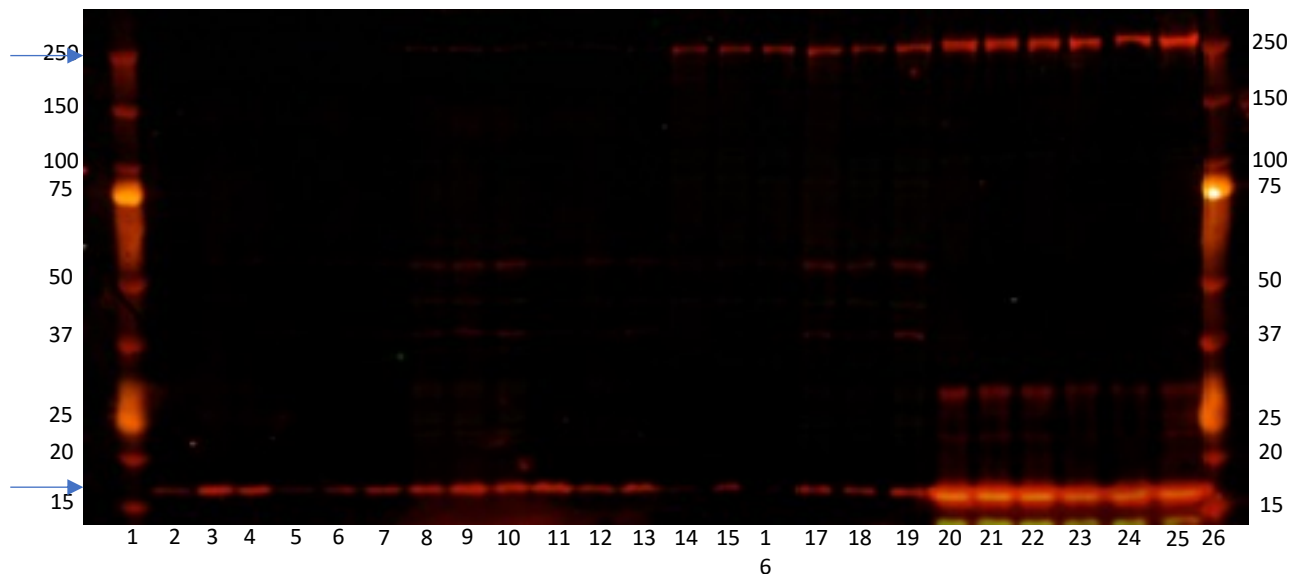
Full unedited gel for Supplementary Fig. 2S-A



BCAT2 Knockouts: RNA Pol II
 (Active Motif 102660)
 1:2000 + H3 (Active Motif
 61475) 1:30,000(not used
 in figure)

- Expected size of RNA Pol II: ~ 240 KDa
- Expected size of H3: ~ 17 kDa
 - HAP-1 1
 - HAP-1 2
 - HAP-1 3
 - ΔBCAT2 1
 - ΔBCAT2 2
 - ΔBCAT2 3
- Wells 2 through 7 contain the cytoplasmic bound protein layer
- Wells 8 through 13 contain the membrane bound protein layer
- Wells 14 through 19 contain the nuclear soluble protein layer
- Wells 20 through 25 contain the chromatin bound protein layer
- Wells 1 and 26 contain the Ladder; 2.0 μL

Full unedited gel for Supplementary Fig. 2S-A

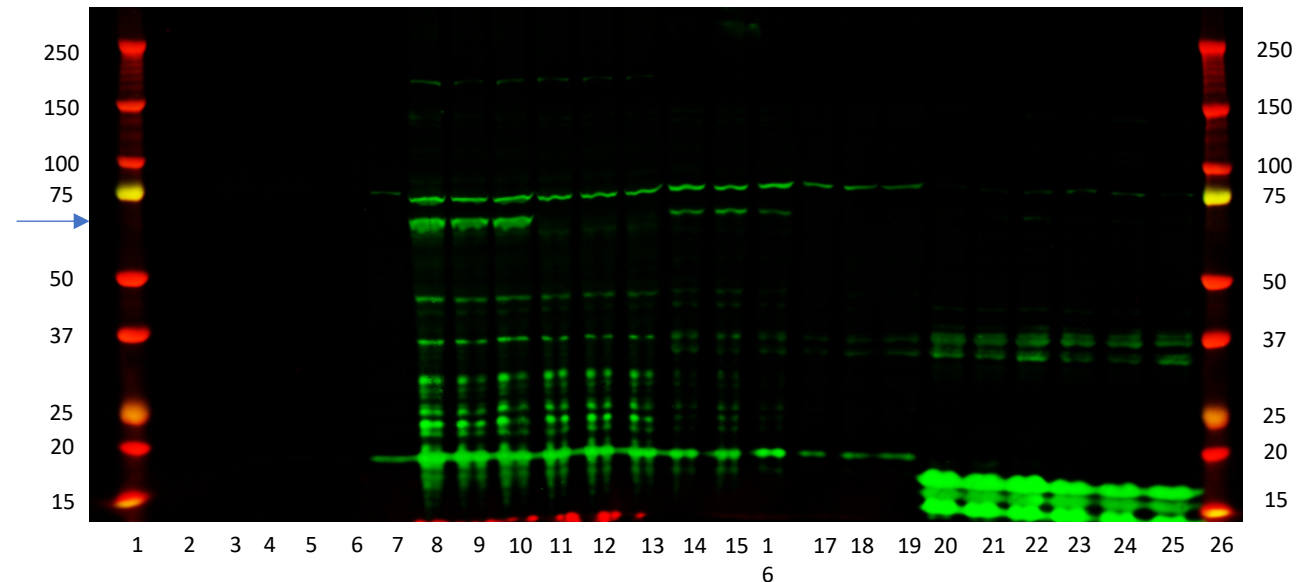


Full unedited gels for Supplementary Fig. 2S-D

Δ PCCA Cells 0.1X LIV: PCCA
(abcam ab187686) 1:1000

- Expected size of PCCA: ~70 kDa
- Samples are organized as follows for all fractions:
 - Hap-1 0.1X LIV 1
 - Hap-1 0.1X LIV2
 - Hap-1 0.1X LIV 3
 - Δ PCAA 0.1X LIV 1
 - Δ PCAA 0.1X LIV 2
 - Δ PCAA 0.1X LIV 3
- Wells 2 through 7 contain the cytoplasmic bound layer
- Wells 8 through 13 contain the membrane bound protein layer
- Wells 14 through 19 contain the nuclear bound protein layer
- Wells 20 through 25 contain the chromatin bound protein layer
- Wells 1 and 26 contain the Ladder; 2.0 μ L

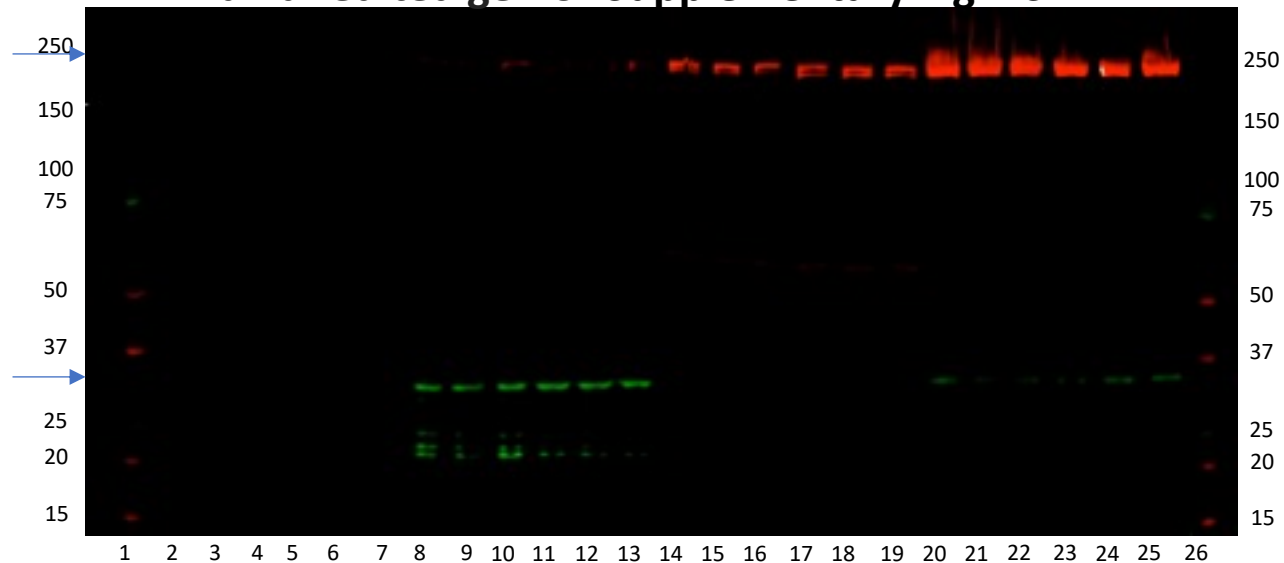
Full unedited gel for Supplementary Fig. 2S-D



ΔPCCA Cells 0.1X LIV: Vdac1
(Genscript A01419) 1:1000
+ RNA Pol II (Active Motif
102660) 1:2000 Low
Exposure

- Expected size of Vdac1: ~34 kDa
- Expected size of RNA Pol II: ~240 kDa
- Samples are organized as follows for all factions:
 - Hap-1 0.1X LIV 1
 - Hap-1 0.1X LIV2
 - Hap-1 0.1X LIV 3
 - ΔPCAA 0.1X LIV 1
 - ΔPCAA 0.1X LIV 2
 - ΔPCAA 0.1X LIV 3
- Wells 2 through 7 contain the cytoplasmic bound layer
- Wells 8 through 13 contain the membrane bound protein layer
- Wells 14 through 19 contain the nuclear bound protein layer
- Wells 20 through 25 contain the chromatin bound protein layer
- Wells 1 and 26 contain the Ladder; 2.0 μL

Full unedited gel for Supplementary Fig. 2S-D

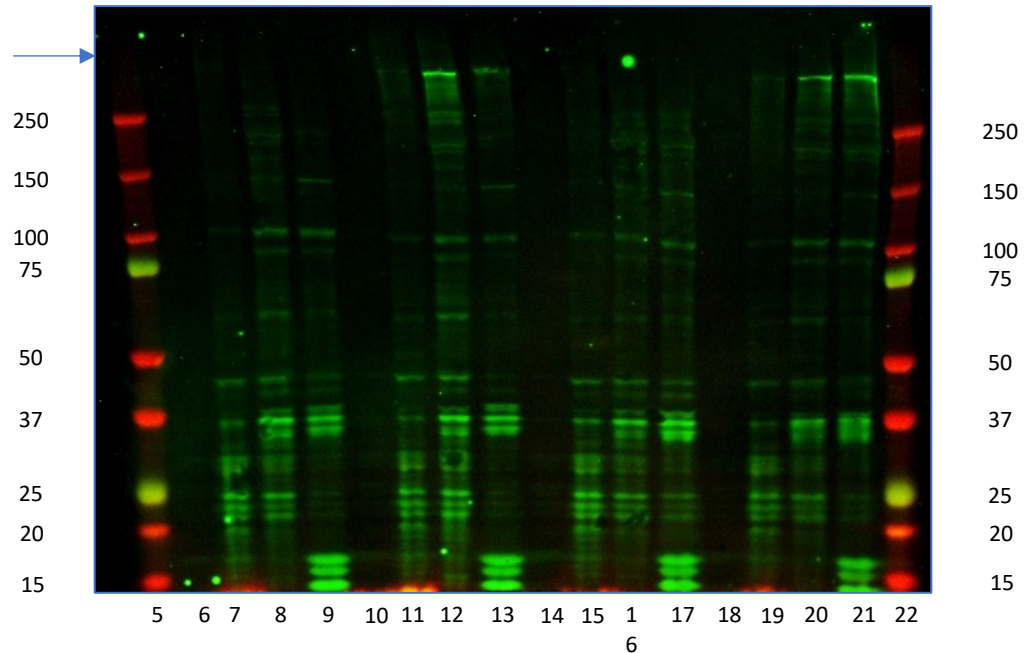


Full unedited gels for Supplementary Fig. 9S-A

Blot 3 Fibroblasts: Ki67 (abcam ab16667) 1:500

- Expected size of Ki67: ~358 kDa
- 15uL of sample loaded per well
- Samples are organized cytoplasmic fraction, membrane bound fraction, nuclear bound fraction and chromatin bound fraction as follows:
 - Wells 6 through 9 contain all fractions for Fib BF + 0.1X LIV
 - Wells 10 through 13 contain all fractions for Fib BF + 1X LIV
 - Wells 14 through 17 contain all fractions for Fib BF + 0.1X LIV + ET-1
 - Wells 18 through 21 contain all fractions for Fib BF + 1X LIV + ET-1
 - Wells 5 and 22 contain the Ladder; 2.0 μ L

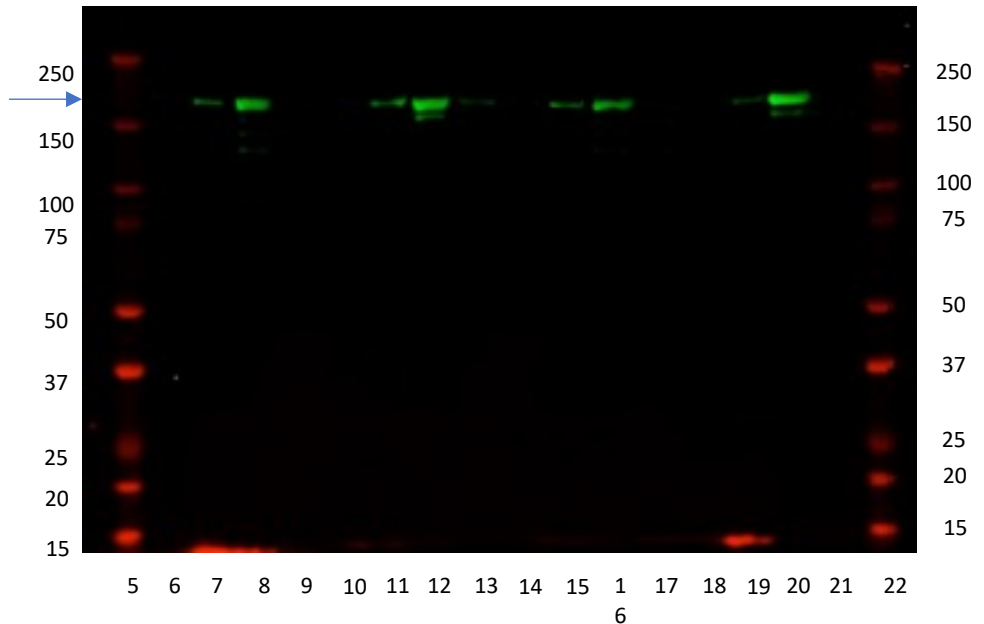
Full unedited gel for Supplementary Fig. 9S-A



Blot 4 Fibroblasts: Col 1A1
(Cell Signaling Technology
72026s) 1:1000 Low
Exposure

- Expected size of Col 1A1: ~138-220 kDa
- 15uL of sample loaded per well
- Samples are organized cytoplasmic fraction, membrane bound fraction, nuclear bound fraction and chromatin bound fraction as follows:
 - Wells 6 through 9 contain all fractions for Fib BF + 0.1X LIV
 - Wells 10 through 13 contain all fractions for Fib BF + 1X LIV
 - Wells 14 through 17 contain all fractions for Fib BF + 0.1X LIV + ET-1
 - Wells 18 through 21 contain all fractions for Fib BF + 1X LIV + ET-1
 - Wells 5 and 22 contain the Ladder; 2.0 μ L
 - **LIV = Leu, Ile, Val (BCAA)**

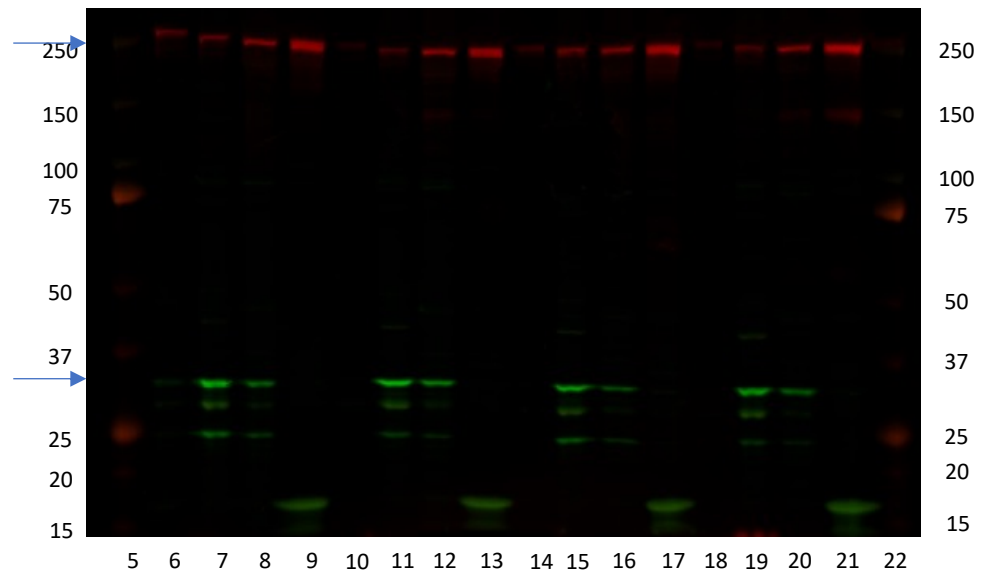
Full unedited gel for Supplementary Fig. 9S-A



Blot 1 Fibroblasts: RNA Pol II
 (Active Motif 102660)
 1:2000 + VAC1 (Sigma
 SAB5700655) 1:1000

- Expected size of RNA Pol II: ~240 kDa
- Expected size of Vdac1: ~34 kDa
- 15uL of sample loaded per well
- Samples are organized cytoplasmic fraction, membrane bound fraction, nuclear bound fraction and chromatin bound fraction as follows:
 - Wells 6 through 9 contain all fractions for Fib BF + 0.1X LIV
 - Wells 10 through 13 contain all fractions for Fib BF + 1X LIV
 - Wells 14 through 17 contain all fractions for Fib BF + 0.1X LIV + ET-1
 - Wells 18 through 21 contain all fractions for Fib BF + 1X LIV + ET-1
 - Wells 5 and 22 contain the Ladder; 2.0 µL
 - **LIV = Leu, Ile, Val (BCAA)**

Full unedited gel for Supplementary Fig. 9S-A

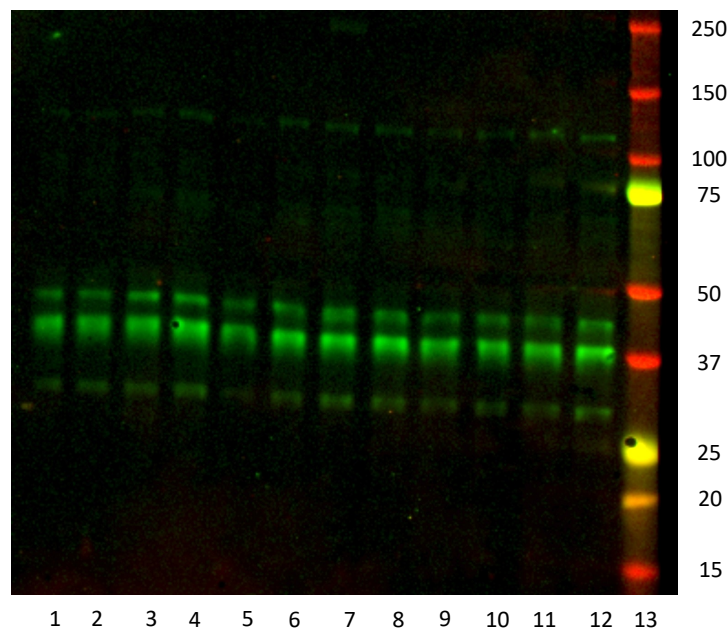


Full unedited gels for Supplementary Fig. 10S-F

Blot 1 Mouse Heart
Mitochondria +/- BCAAs:
BCAT2 (Sigma HPA054091)
1:1000 Low Exposure

- Expected size: ~39 kDa
- Volume of sample loaded per well determined by protein quantification using Thermo Micro BCA Protein Assay Kit; 10ug of protein
- Well 1: 1W-SHAM-BCAA-control
- Well 2: 1W-SHAM-BCAA-control
- Well 3: 1W-SHAM-BCAA-control
- Well 4: 1W-TAC-BCAA-control
- Well 5: 1W-TAC-BCAA-control
- Well 6: 1W-TAC-BCAA-control
- Well 7: 1W-SHAM-BCAA-free
- Well 8: 1W-TAC-BCAA-control
- Well 9: 1W-TAC-BCAA-control
- Well 10: 1W-TAC-BCAA-free
- Well 11: 1W-TAC-BCAA-free
- Well 12: 1W-TAC-BCAA-free
- Wells 13 contains the Ladder; 2.0 µL

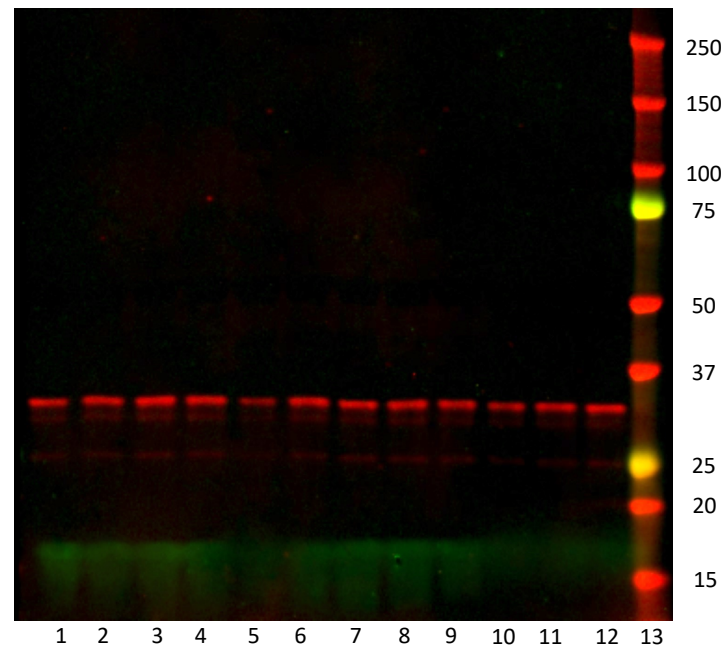
Full unedited gel for Supplementary Fig. 10S-F



Blot 4 Mouse Heart +/-
BCAAs: VDAC1 (Genescript
A01419) 1:1000

- Expected size: ~34 kDa
- Volume of sample loaded per well determined by protein quantification using Thermo Micro BCA Protein Assay Kit; 10ug of protein
- Well 1: 1W-SHAM-BCAA-control
- Well 2: 1W-SHAM-BCAA-control
- Well 3: 1W-SHAM-BCAA-control
- Well 4: 1W-TAC-BCAA-control
- Well 5: 1W-TAC-BCAA-control
- Well 6: 1W-TAC-BCAA-control
- Well 7: 1W-SHAM-BCAA-free
- Well 8: 1W-TAC-BCAA-control
- Well 9: 1W-TAC-BCAA-control
- Well 10: 1W-TAC-BCAA-free
- Well 11: 1W-TAC-BCAA-free
- Well 12: 1W-TAC-BCAA-free
- Wells 13 contains the Ladder; 2.0 µL
- Wells 13 contains the Ladder; 2.0 µL

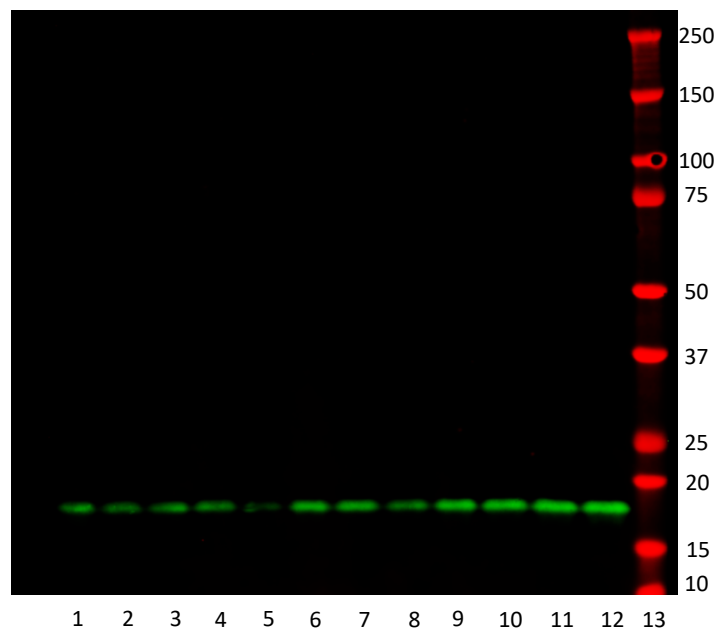
Full unedited gel for Supplementary Fig. 10S-F



Blot 3 Mouse Heart +/-BCAAs:
NDUFS4 (Sigma HPOA003884)
1:1000 Low Exposure Reduced
Background

- Expected size: ~17 kDa
- Volume of sample loaded per well determined by protein quantification using Thermo Micro BCA Protein Assay Kit; 10ug of protein
- Well 1: 1W-SHAM-BCAA-control
- Well 2: 1W-SHAM-BCAA-control
- Well 3: 1W-SHAM-BCAA-control
- Well 4: 1W-TAC-BCAA-control
- Well 5: 1W-TAC-BCAA-control
- Well 6: 1W-TAC-BCAA-control
- Well 7: 1W-SHAM-BCAA-free
- Well 8: 1W-TAC-BCAA-control
- Well 9: 1W-TAC-BCAA-control
- Well 10: 1W-TAC-BCAA-free
- Well 11: 1W-TAC-BCAA-free
- Well 12: 1W-TAC-BCAA-free
- Wells 13 contains the Ladder; 2.0 µL
- Wells 13 contains the Ladder; 2.0 µL

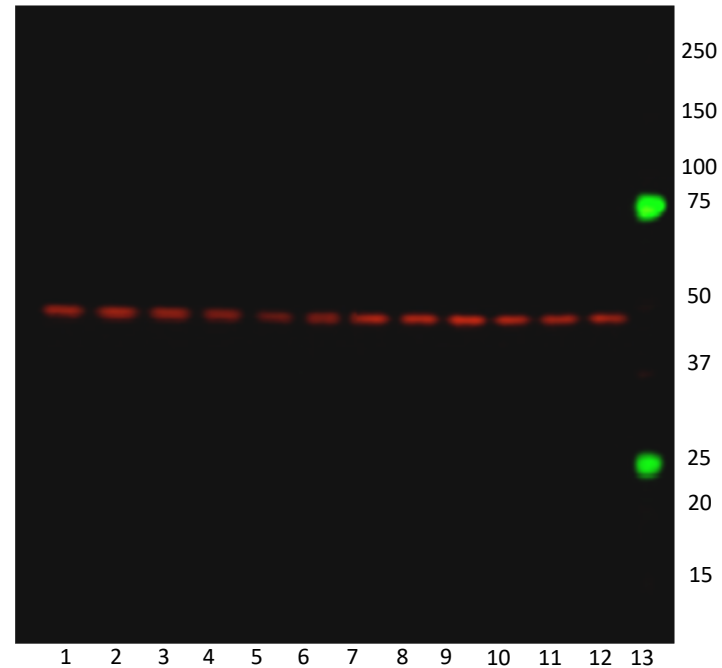
Full unedited gel for Supplementary Fig. 10S-F



Blot 2 Mouse Heart +/-
BCAAs: : BCKDHA (Sigma
SAB2104058) 1:1000

- Expected size: ~50 kDa
- Volume of sample loaded per well determined by protein quantification using Thermo Micro BCA Protein Assay Kit; 10ug of protein
- Well 1: 1W-SHAM-BCAA-control
- Well 2: 1W-SHAM-BCAA-control
- Well 3: 1W-SHAM-BCAA-control
- Well 4: 1W-TAC-BCAA-control
- Well 5: 1W-TAC-BCAA-control
- Well 6: 1W-TAC-BCAA-control
- Well 7: 1W-SHAM-BCAA-free
- Well 8: 1W-TAC-BCAA-control
- Well 9: 1W-TAC-BCAA-control
- Well 10: 1W-TAC-BCAA-free
- Well 11: 1W-TAC-BCAA-free
- Well 12: 1W-TAC-BCAA-free
- Wells 13 contains the Ladder; 2.0 µL

Full unedited gel for Supplementary Fig. 10S-F



Blot 1 Mouse Heart
Mitochondria +/- BCAAs:
PCCA 1:1000

- Expected size: ~70 kDa
- Volume of sample loaded per well determined by protein quantification using Thermo Micro BCA Protein Assay Kit; 10ug of protein
- Well 1: 1W-SHAM-BCAA-control
- Well 2: 1W-SHAM-BCAA-control
- Well 3: 1W-SHAM-BCAA-control
- Well 4: 1W-TAC-BCAA-control
- Well 5: 1W-TAC-BCAA-control
- Well 6: 1W-TAC-BCAA-control
- Well 7: 1W-SHAM-BCAA-free
- Well 8: 1W-TAC-BCAA-control
- Well 9: 1W-TAC-BCAA-control
- Well 10: 1W-TAC-BCAA-free
- Well 11: 1W-TAC-BCAA-free
- Well 12: 1W-TAC-BCAA-free
- Wells 13 contains the Ladder; 2.0 μ L

Full unedited gel for Supplementary Fig. 10S-F

