

Supplemental Figure 1. Cardiac characterization of control and YAPchKO mice after 2 days of

TAC. (**A**–**D**) Relative mRNA levels in the left ventricles. n = 5–6 mice. (**E**) LVW/TL. n = 6 mice. (**F**) LungW/TL. n = 6 mice. (**G**–**T**) Relative protein levels in the left ventricles (**G**–**P**) and representative immunoblots (**Q**–**T**). α -tubulin and YAP (**Q**), α -tubulin (**R**), α -tubulin and AMPK (**S**), and α -tubulin and ACC1/2 (**T**) blots, serving as loading controls, were run in parallel and contemporaneously with other blots. n = 5–6 mice. *p < 0.05 by 1-way ANOVA with Tukey's test. Error bars represent SEM.



Supplemental Figure 2. Schematic representation of glycolysis and its auxiliary pathways.



Supplemental Figure 3. Altered levels of glucose metabolic gene mRNAs in control and YAPchKO mice after 2 days of TAC. Relative mRNA levels in the left ventricles were evaluated by qPCR. n = 5-6 mice. *p < 0.05 by 1-way ANOVA with Tukey's test. Error bars represent SEM. See also Supplemental Table 1.





Supplemental Figure 4. Representative immunoblots of glucose metabolic proteins in the left ventricles from control and YAPchKO mice subjected to either sham operation or 2 days of TAC. α -tubulin blots, serving as loading controls, were run in parallel and contemporaneously with other blots. Relative protein expression levels of glucose metabolic proteins are shown in Supplemental Figure 5. See also Table 1.



Supplemental Figure 5. Altered levels of glucose metabolic proteins in control and YAPchKO mice after 2 days of TAC. Relative protein expression levels in the left ventricles were evaluated by immunoblotting. n = 5-6 mice. *p < 0.05 by 1-way ANOVA with Tukey's test. Error bars represent SEM. See also Supplemental Figure 4.



Supplemental Figure 6. Representative immunoblots of glucose metabolic proteins in NRVMs transduced with Ad-LacZ or Ad-FLAG-YAP. α -tubulin blots, serving as loading controls, were run in parallel and contemporaneously with other blots. Relative protein expression levels of glucose metabolic proteins are shown in Supplemental Figure 7B. See also Table 2.



Supplemental Figure 7. Altered mRNA and protein levels of glucose metabolic factors in NRVMs overexpressing YAP. NRVMs were transduced with Ad-LacZ or Ad-FLAG-YAP for 6 days in serum-free DMEM/F12 medium. (A) Relative mRNA expression levels. n = 5-6 dishes from 5-6 independent experiments. (B) Relative protein expression levels. n = 5-6 dishes from 5-6 independent experiments. *p < 0.05 by Student's *t* test. Error bars represent SEM. See also Supplemental Figure 6.



Supplemental Figure 8. Knockdown of YAP decreased glycolytic function in NRVMs. (A–C) YAP was downregulated in NRVMs transduced with Ad-shYap for 6 days compared to in those transduced with Ad-shControl (A). Data are representative of 3 independent blots. Measurement of ECAR (B) and the summary of glycolytic function (C). n = 26–31 wells from 3 independent experiments. *p < 0.05 by Student's *t* test. Error bars represent SEM. (D) Representative immunoblots of NRVMs transduced with Ad-shControl or Ad-shYap are shown. α -tubulin blots, serving as loading controls, were run in parallel and contemporaneously with other blots (A and D). Relative protein expression levels of glucose metabolic proteins are shown in Supplemental Table 3.



Supplemental Figure 9. Altered mRNA and protein levels of mitochondrial oxidative phosphorylation complex components in NRVMs overexpressing YAP. (A–C) Relative mRNA and protein expression levels of oxidative phosphorylation complex components were evaluated by qPCR (n = 5–6 dishes from 5–6 independent experiments) (A) and immunoblotting (n = 5–6 dishes from 5–6 independent experiments) (B and C), respectively. Representative immunoblots are shown (C). An α -tubulin blot, serving as a loading control, was run in parallel and contemporaneously with other blots. *p < 0.05 by Student's *t* test. Error bars represent SEM.



Supplemental Figure 10. Confirmation of knockdown of glucose metabolic genes in NRVMs. (A–O) Knockdown of glucose metabolic genes in NRVMs transfected with indicated siRNAs was confirmed by immunoblotting. Data are representative of 3 independent blots. α -tubulin blots, serving as loading controls, were run in parallel and contemporaneously with other blots (A, G, J, K, N, and O). See also Figure 7.



Supplemental Figure 11. Overexpressed YAP upregulated H3K4me3 and GSH. (A–C) NRVMs were transduced with Ad-LacZ or Ad-FLAG-YAP in the presence or absence of 30 μ M CBR-5884, a selective PHGDH inhibitor. Representative immunoblots (A) and the summary of quantification (B) are shown. A H3 blot, serving as a loading control, was run in parallel and contemporaneously with other blots. n = 6 wells from 6 independent experiments. n = 6 wells from 6 independent experiments. Relative GSH levels are shown (C). n = 7 wells from 7 independent experiments. *p < 0.05 by 1-way ANOVA with Tukey's test. Error bars represent SEM.

Supplemental Table 1. Relative mRNA expression of glucose metabolic genes in control and YAPchKO mice after 2 days of TAC

	mRNA					
Name	Cor	ntrol	YAPchKO			
	Sham	TAC	Sham	TAC		
Glut1	1.00	1.84 ^A	0.89	1.05 ^B		
Glut4	1.00	0.67 ^A	0.66 ^A	0.50 ^A		
Hk1	1.00	1.05	0.97	0.85		
Hk2	1.00	0.76	0.67	0.65 ^A		
Gpi	1.00	0.93	0.95	0.73		
Pfk1	1.00	0.70	1.11	0.55 ^A		
Pfk2	1.00	0.80	0.93	0.68		
Aldoa	1.00	0.79	0.84	0.65		
Gapdh	1.00	0.82	0.89	0.62 ^A		
Pgk1	1.00	0.79	0.77	0.66 ^A		
Pgam1	1.00	1.54 ^A	0.95	1.03 ^B		
Eno1	1.00	0.93	0.94	0.82		
Pkm1	1.00	0.60 ^A	0.54 ^A	0.51 ^A		
Pkm2	1.00	1.72 ^A	0.95	1.29		
Ldha	1.00	0.89	0.76 ^A	0.68 ^{AB}		
Mpc1	1.00	0.79	0.79	0.64 ^A		
Mpc2	1.00	0.79	0.77	0.65 ^A		
Pdh	1.00	0.80	0.74	0.55 ^A		
Pdk4	1.00	1.39	0.76	0.68		
Pc	1.00	0.90	0.74 ^A	0.69 ^A		
Me1	1.00	0.98	0.63 ^A	0.61 ^{AB}		
Me2	1.00	0.90	0.94	0.97		
Pck2	1.00	0.85	0.88	0.78		
G6pd	1.00	1.22	1.00	1.20		
Gfat	1.00	0.97	0.72	0.75		
Gpd	1.00	1.10	0.90	0.82		
Phgdh	1.00	1.25	1.14	1.06		
Mean values from Supplemental Figure 3 are indicated in each cell. n = 5–6 mice. ^A p < 0.05 versus the control sham group and ^B p < 0.05 versus the control TAC group by 1-						
way ANOVA with Tukey's test.						

Suppleme	ntal Table 2	. Metabolomics analysis of energy	metabolis	m pathwa	ys after sha	am or 2 day	s TAC in c	control and	YAPchKO	mice
				Fold	d change		Sham	vs TAC	WT vs Y	'APchKO
Dathu	/2//	Matabolita	WT	WT	YAPchKO	YAPchKO	\ <u>\</u> /T	VAPobKO	Sham	TAC
Pathw	ay	WELADOILE	Sham	TAC	Sham	TAC			onam Duala A	
			(n = 4)	(n = 5)	(n = 5)	(n = 5)	P value	P value"	P value	P value"
		D-Fructose	1.000	1.178	1.585	1.004	0.8189	0.0390	0.0520	0.8032
Sug		D-Mannose	1.000	1.222	1.166	1.013	0.8503	0.1903	0.0468	0.9985
Suga	ar	D-Galactose	1.000	1.344	1.469	1.550	0.3506	0.9727	0.1340	0.7028
		D-Glucose	1.000	0.872	2.045	1.074	0.9425	0.0021	0.0019	0.7873
		Glucose 6-phosphate	1.000	0.728	1.396	0.971	0.7909	0.4409	0.5470	0.8160
		Fructose 6-phosphate	1.000	0.785	1.300	0.819	0.8339	0.2328	0.6513	0.9989
		Glycerol 3-phosphate	1.000	1.024	1.188	1.364	0.9990	0.7117	0.7069	0.2073
	Glycolysis	Glyceraldehyde 3-phosphate	1.000	0.562	0.576	0.842	0.9963	0.6632	0.5749	0.9785
Glucose		Phosphoenolpyruvate (PEP)	1.000	1.173	1.153	1.411	0.3212	0.0583	0.4225	0.0869
metabolism		Pyruvic acid	1.000	1.293	1.401	1.209	0.2123	0.5014	0.0568	0.9227
intermediates		L-Lactic acid	1.000	1.556	1.496	1.368	0.1384	0.9412	0.2088	0.8398
		Ribitol	1.000	0.981	1.328	1.301	0.9988	0.9957	0.0872	0.0749
	Pentose	Mvoinositol	1.000	0.863	1.328	0.941	0.8835	0.1711	0.3349	0.9707
	phosphate	Inositol phosphate	1.000	0.827	0.919	0.846	0.1613	0.7490	0.7305	0.9940
	pathway	Sedoheptulose 7-phosphate	1.000	0.708	1.675	1.271	0.8602	0.1966	0.0239	0.9754
		Citric acid	1.000	1.130	1.308	1.225	0.9700	0.9902	0.7253	0.9858
		cis-Aconitic acid	1 000	1 421	1 427	1 254	0.1702	0.7751	0.1612	0.7934
		Isocitric acid	1 000	0.834	1 279	1 725	0 9945	0 8944	0.9752	0.5159
TCA c	vcle	2-Ketoglutamic acid	1 000	1 441	1.556	1 296	0 1507	0.5091	0.0524	0.8587
	,	Succinic acid	1.000	1.067	1.316	1.200	0.9832	0.5321	0.3552	>0.9999
		Fumaric acid	1.000	1.631	1.010	1.573	0.0002	0.8695	0.0002	0.9569
		D-Malic acid	1.000	2 752	1.400	1.540	0.0101	0.0000	0.1717	0.0000
			1.000	1 / 20	1.535	1.507	0.0024	0.0000	0.0701	0.0010
			1.000	1.423	1.007	1.545	0.1700	0.9999	0.0701	0.9100
			1.000	1.473	1.507	1.545	0.5500	0.0330	0.0023	0.3303
		Choine	1.000	1.295	1.000	1.004	0.0279	0.9722	0.1452	0.4239
		Giycine	1.000	1.124	1.041	1.340	0.7420	0.0649	0.9002	0.2792
			1.000	2.093	1.595	1.043	0.0049	0.7624	0.1031	0.7503
			1.000	1.402	1.491	2.000	0.5556	0.0049	0.0260	0.3469
			1.000	1.007	1.900	2.024	0.1410	0.9940	0.0209	0.0009
			1.000	1.320	1.035	2.099	0.4910	0.1000	0.0511	0.0096
		L-Senne	1.000	2.872	1.937	1.842	0.0005	0.9917	0.0774	0.0339
Anning goid		L-Inreonine	1.000	2.028	1.651	2.657	0.0029	0.0021	0.0637	0.0560
Amino acids	s and AA		1.000	3.254	1.710	2.311	0.0001	0.3502	0.2649	0.0715
derivat	ives	L-Asparagine	1.000	0.874	1.080	1.618	0.9866	0.4533	0.9964	0.1991
		L-Aspartic acid	1.000	3.974	1.998	1.551	0.0012	0.8673	0.3988	0.0041
		L-Glutamic acid	1.000	0.913	1.370	2.416	0.9970	0.0906	0.8280	0.0107
		L-Lysine	1.000	12.134	2.328	10.184	0.7020	0.8628	0.9998	0.9492
		Pyroglutamic acid	1.000	1.289	1.245	1.412	0.0633	0.3619	0.1334	0.6075
		Ornithine	1.000	1.147	1.273	1.098	0.4858	0.2914	0.0690	0.9534
		Taurine	1.000	1.264	0.733	0.997	0.9826	0.9793	0.9820	0.9788
		Beta-Alanine	1.000	1.125	1.183	0.811	0.9170	0.2242	0.7865	0.3538
		L-Threonine2	1.000	1.981	1.754	2.020	<0.0001	0.2287	0.0004	0.9906
		Iminodiacetic acid 1	1.000	0.743	1.142	1.141	0.6786	>0.9999	0.1848	0.8084
		4-Hydroxyproline	1.000	1.398	1.469	1.303	0.0369	0.5490	0.0129	0.8660
		Capric acid	1.000	1.139	1.188	1.099	0.4789	0.7539	0.2358	0.9693
		Myristic acid	1.000	1.043	1.108	0.947	0.9953	0.7939	0.9355	0.9450
		Lauric Acid	1.000	0.969	1.223	1.118	0.9886	0.6680	0.1446	0.3983
		Palmitoleic acid	1.000	0.855	1.775	1.058	0.9702	0.1391	0.1287	0.9114
		Palmitic acid	1.000	1.110	1.332	1.200	0.7269	0.5612	0.0303	0.8036
		Linoleic acid	1.000	1.415	1.342	1.284	0.4020	0.9951	0.5605	0.9481
		Oleic acid	1.000	1.195	1.487	1.155	0.8225	0.4279	0.1802	0.9974
		Elaidic acid	1.000	0.537	0.809	0.832	0.1170	0.9992	0.7542	0.3913
		Stearic acid	1.000	1.006	1.132	1.063	>0.9999	0.9339	0.7185	0.9609
		Arachidic acid	1.000	1.046	1.227	1.119	0.9876	0.8497	0.4102	0.9480
Lipid meta	abolism	Arachidonic Acid	1.000	0.655	0.901	0.958	0.9258	0.4499	0.9720	0.9806
		Oxalic acid	1.000	1.082	1.249	1.084	0.9800	0.8450	0.6568	>0.9999
		Heptadecanoic acid	1.000	0.953	1.087	1.079	0.9638	0.9997	0.8207	0.5563
		1-Monomyristin	1.000	1.341	2.091	1.470	0.6595	0.1580	0.0101	0.9655
		2-Monopalmitoylglycerol	1.000	0.917	1.170	1.179	0.9488	>0.9999	0.6971	0.3133
		1-Palmitoylglycerol	1.000	0.907	1.156	1.204	0.9180	0.9850	0.7124	0.1798

	2-Steroylalycerol	1.000	1,160	0.866	1.939	0.9953	0.7363	0.9968	0.6946
	1-Steroylalycerol	1 000	1 035	1 250	1 272	0.9960	0.9987	0.4099	0.4031
	Glycerol	1 000	1 311	1.200	1 277	0 3419	0.5679	0.0599	0.9971
	Cholesterol	1.000	0.865	0.880	0.082	0.3880	0.5721	0.0000	0.0071
	3-Hydroxybutyrate	1.000	1 / 85	1 820	1 60/	0.0000	0.0721	0.7406	0.4013
	Phoenhoto	1.000	1 1 1 1 0	1.029	1.034	0.3303	>0.9999	0.7400	0.0220
Inorganic phosphate	Duranhaanhata	1.000	0.952	1.030	1.244	0.4300	0.0500	0.9035	0.0050
	Hypoxanthine	1.000	0.052	1.017	1.427	0.7632	0.0505	0.9994	0.0053
	Adenosine	1.000	1 800	1.073	2 320	0.3430	0.2310	0.0036	0.4324
		1.000	0.921	1.225	1 422	0.7055	0.0400	0.9930	0.9207
	Adamina	1.000	1 202	1.090	1.433	0.9000	0.0013	0.9902	0.4902
Purines & Purimidynes	Adennie Adenosina mananhaanhata	1.000	1.303	0.756	1.417	0.0020	0.9997	0.2703	0.9407
	Adenosine monopriosphate	1.000	0.040	0.750	2.304	0.9209	<0.0001	0.7937	0.0001
		1.000	1.509	1.137	1.277	0.1556	0.9122	0.9290	0.7028
	Uracil	1.000	1.302	1.391	1.261	0.3363	0.8536	0.1522	0.9940
	Urea	1.000	1.1/1	1.105	1.165	0.6085	0.9645	0.8705	>0.9999
	Nicotinamide	1.000	1.069	0.718	1.130	0.9710	0.0602	0.3135	0.9752
	Creatinine	1.000	1.196	1.405	1.138	0.6956	0.4149	0.1492	0.9856
	Glutathione	1.000	1.678	1.050	1.567	0.6697	0.7924	0.9998	0.9971
	L-Ascorbic acid	1.000	1.035	1.957	1.299	0.9989	0.0525	0.0067	0.6682
	Galactonic acid	1.000	6.626	1.146	0.656	0.0130	0.8747	0.9816	0.0039
	Cellobiose	1.000	3.248	1.448	1.007	0.0038	0.8181	0.8362	0.0024
	D-Threitol	1.000	0.999	1.360	1.011	>0.9999	0.0475	0.0549	0.9996
	Threonic acid	1.000	1.789	1.328	1.446	0.0006	0.8480	0.1885	0.1275
	Nonanoic acid	1.000	1.230	1.319	1.213	0.2546	0.7808	0.0718	0.9987
	O-Phosphoethanolamine	1.000	1.354	1.297	1.893	0.4627	0.0740	0.6022	0.1168
	Ethanolamine1	1.000	0.874	0.937	1.060	0.8836	0.8753	0.9832	0.6711
	Allantoin	1.000	1.133	0.665	0.573	0.7719	0.9359	0.9953	>0.9999
	2-Hydroxyglutaric acid	1.000	1.716	1.376	1.271	0.0370	0.9635	0.4089	0.2293
	2-Hydroxybutyric acid	1.000	1.140	1.162	1.209	0.7529	0.9842	0.6618	0.9524
	Glycolic acid	1.000	1.495	1.283	1.253	0.0158	0.9958	0.2339	0.3104
	Putrescine	1.000	0.872	0.795	1.097	0.8349	0.1977	0.5512	0.4260
	1,6-anhydro-Glucose	1.000	1.028	1.167	1.307	0.9990	0.8811	0.8375	0.4757
	1-Octadecene	1.000	1.280	1.073	1.115	0.3334	0.9918	0.9674	0.7002
Others	2-Ketoisocaproic acid	1.000	4.501	2.287	0.612	0.5018	0.9482	0.9849	0.4072
	Adipic acid	1.000	1.329	1.257	1.412	0.0303	0.4232	0.1085	0.8343
	Azelaic acid	1.000	1.443	1.507	1.117	0.0967	0.1300	0.0497	0.2434
	Benzoic acid	1.000	1.182	1.354	1.018	0.2914	0.0119	0.0126	0.3266
	Cystathionine	1.000	1.209	0.869	0.793	0.8717	0.9878	0.9906	0.8587
	Eicosane	1.000	0.881	1.296	1.215	0.9136	0.9368	0.2337	0.8667
	Ethanolamine2	1.000	1.160	1.355	1.334	0.6793	0.9986	0.0997	0.5733
	Glyoxylic acid	1.000	0.992	1.018	1.072	>0.9999	0.9664	0.9990	0.9045
	Itaconic acid	1.000	0.984	1.022	1.065	0.9993	0.9827	0.9980	0.9015
	methyl-beta-D-Galactopyranoside	1.000	1.925	1.280	1.229	0.0011	0.9912	0.4752	0.0071
	Methylmalonic acid	1.000	1.438	1.333	1,122	0.0895	0.5706	0.2503	0.2443
	N-acetyl-L-aspartic acid	1 000	0 765	0 625	0 528	0.9531	0.9468	0.9692	0.4826
	N-acetyl-Lysine	1 000	6 238	4 342	8 749	0.6205	0.7877	0.9811	0.9899
	Nitrous Oxide	1 000	1 682	1 638	0.910	0.8396	0.7848	0.8641	0.7539
	Pyrrolidonecarboxylic acid	1 000	1 849	2 075	1 238	0 2190	0 1884	0.0874	0 4323
	Sophorose	1 000	1.050	1 418	1 337	0.9910	0 9579	0 1144	0.3275
	Trebalose	1 000	1 01/	0 710	0 022	0.7/28	0.00762	0 0084	0.8560
	Turanose	1.000	2 / 57	1 214	1 014	0.0064	0.9702	0.3304	0.0009
	alpha-D-Glucosamine 1 phosphate	1.000	1 580	1.2.14	1 924	0.0004	0.5062	0.9373	0.0043
AP value was calculated b	v 1-way ANOVA with Tukey's test	1.000	1.000	1.000	1.001	0.0031	0.0000	0.0070	0.0070

Namo	mRNA		Protein			
Name	shControl	shYap	shControl	shYap		
Glut1	1.00 ± 0.10	1.37 ± 0.13	1.00 ± 0.09	1.07 ± 0.12		
Glut4	1.00 ± 0.08	1.43 ± 0.12^{A}	1.00 ± 0.13	0.98 ± 0.16		
Hk1	1.00 ± 0.15	1.14 ± 0.08	1.00 ± 0.05	1.02 ± 0.07		
Hk2	1.00 ± 0.15	1.3 ± 0.13^{A}	1.00 ± 0.09	0.97 ± 0.14		
Gpi	1.00 ± 0.10	0.96 ± 0.06	1.00 ± 0.08	1.01 ± 0.12		
Pfk1	1.00 ± 0.11	2.3 ± 0.08^{A}	1.00 ± 0.02	1.17 ± 0.04 ^A		
Pfk2	1.00 ± 0.10	0.89 ± 0.05	1.00 ± 0.13	1.13 ± 0.06		
Aldoa	1.00 ± 0.12	0.98 ± 0.07	1.00 ± 0.08	0.75 ± 0.08		
Gapdh	1.00 ± 0.07	0.81 ± 0.05	1.00 ± 0.04	1.04 ± 0.03		
Pgk1	1.00 ± 0.03	0.73 ± 0.03^{A}	1.00 ± 0.06	0.69 ± 0.04^{A}		
Pgam1	1.00 ± 0.09	0.67 ± 0.05^{A}	1.00 ± 0.05	0.76 ± 0.06^{A}		
Eno1	1.00 ± 0.07	0.71 ± 0.05^{A}	1.00 ± 0.05	0.80 ± 0.06^{A}		
Pkm1	1.00 ± 0.09	1.75 ± 0.16^{A}	1.00 ± 0.04	0.89 ± 0.09		
Pkm2	1.00 ± 0.10	0.66 ± 0.04^{A}	1.00 ± 0.03	0.99 ± 0.04		
Ldha	1.00 ± 0.10	1.09 ± 0.03	1.00 ± 0.09	1.05 ± 0.08		
Pdh	1.00 ± 0.09	0.69 ± 0.04^{A}	1.00 ± 0.08	0.89 ± 0.07		
Pdk4	1.00 ± 0.06	1.44 ± 0.10^{A}	1.00 ± 0.03	0.94 ± 0.06		
Pc	1.00 ± 0.10	1.25 ± 0.10	1.00 ± 0.05	0.93 ± 0.09		
Me1	1.00 ± 0.06	1.07 ± 0.08	1.00 ± 0.05	0.86 ± 0.08		
Pck2	1.00 ± 0.04	0.69 ± 0.03^{A}	1.00 ± 0.02	0.86 ± 0.03^{A}		
G6pd	1.00 ± 0.14	0.96 ± 0.12	1.00 ± 0.14	0.87 ± 0.09		
Gfat	1.00 ± 0.07	0.91 ± 0.05	1.00 ± 0.17	1.04 ± 0.11		
Gpd	1.00 ± 0.10	1.52 ± 0.15 ^A	1.00 ± 0.02	0.98 ± 0.05		
Phgdh	1.00 ± 0.12	0.94 ± 0.04	1.00 ± 0.07	1.12 ± 0.05		
Mean values plus SEM are indicated in each cell. n = 5–6 dishes from 5–6						

Supplemental Table 3. Relative mRNA and protein expression of glucose metabolic factors in NRVMs transduced with Ad-shControl or Ad-shYap

Mean values plus SEM are indicated in each cell. n = 5–6 dishes from 5–6 independent experiments. A p < 0.05 versus each shControl by Student's *t* test. See also Supplemental Figure 8D.

Supplemental Table 4. Metabolomics analysis of energy metabolism pathways in NRVMs transduced with Ad-LacZ or Ad-YAP

			Fold o	Fold change		
Pat	hway	Metabolite	LacZ	YAP	P value	
			(n = 6)	(n = 6)		
		D-Glucose	1.000	1.121	0.718	
	Monosaccaride	D-Fructose	1.000	1.798	0.039	
		D-Mannose	1.000	1.869	0.053	
		Mannitol	1.000	0.751	0.106	
	Sugar alcohol (Polyol)	D-Threitol	1.000	1.755	0.000	
		Sorbitol	1.000	2.171	0.009	
		Glucose-6-phosphate	1.000	0.412	0.150	
		Fructose-6-phosphate	1.000	0.382	0.118	
Glucose metabolism		Glycerol	1.000	0.808	0.583	
		Glycerol 3-phosphate	1.000	0.718	0.023	
	Glycolytic intermediates	DHAP	1.000	1.318	0.583	
		3-Phosphoglyceric acid	1.000	1.945	0.041	
		Phosphoenolpyruvate	1.000	3.807	0.002	
		Pyruvate	1.000	0.642	0.179	
		L-Lactic acid	1.000	1.366	0.406	
	Pontoso phosphato pathway	Sedoheptulose-7-phosphate	1.000	0.622	0.360	
	r entose phosphate patriway	Ribitol	1.000	0.629	0.001	
		Citric acid	1.000	0.990	0.970	
		Isocitric acid	1.000	0.759	0.593	
		cis-Aconitic acid	1.000	1.007	0.973	
TCA	A cycle	2-Ketoglutarate	1.000	0.159	0.047	
		Succinic acid	1.000	1.249	0.108	
		D-Malic acid	1.000	2.445	0.003	
		Fumaric acid	1.000	1.497	0.108	
		L-Valine	1.000	1.269	0.254	
		L-Leucine	1.000	1.363	0.102	
		L-Isoleucine	1.000	1.452	0.027	
		L-Alanine	1.000	1.521	0.012	
		L-Aspartic acid	1.000	1.250	0.705	
		L-Glutamine	1.000	0.787	0.659	
		L-Glutamic acid	1.000	1.078	0.701	
		Glycine	1.000	1.047	0.610	
		L-Lysine	1.000	1.720	0.018	
Amine eside en		L-Methionine	1.000	1.601	0.001	
Amino acius ar	IU AA UEITVALIVES	L-Proline	1.000	1.137	0.611	
		L-Phenylalanine	1.000	1.387	0.023	
		L-Serine	1.000	1.187	0.432	
		L-Threonine	1.000	1.385	0.001	
		L-Tyrosine	1.000	1.625	0.015	
		beta-Alanine	1.000	1.017	0.965	
		2-Aminoadipic acid	1.000	0.979	0.941	
		Hypotaurine	1.000	0.928	0.627	
		Pyroglutamic acid	1.000	1.374	0.127	
		N-acetyl-L-Aspartic acid	1.000	0.378	0.053	
		Lauric acid	1.000	1.291	0.334	
		Myristic acid	1.000	1.188	0.144	
		Palmitic acid	1.000	0.985	0.908	
		Palmitoleic acid	1.000	1.099	0.767	
		Oleic acid	1.000	0.790	0.331	
Lipids		Stearic acid	1.000	0.941	0.665	

	1-Palmitoylglycerol	1.000	1.072	0.444
	1-Steroylglycerol	1.000	1.091	0.471
	2-Monopalmitoylglycerol	1.000	1.040	0.772
	Cholesterol	1.000	0.692	0.625
	O-Phosphoethanolamine	1.000	0.265	0.000
inorganic phosphato	Phosphate	1.000	1.187	0.333
morganic prospirate	Pyrophosphate	1.000	1.038	0.893
Urea cycle	Ornithine	1.000	1.820	0.149
	Adenosine	1.000	0.842	0.488
	Inosine	1.000	1.161	0.701
	Adenine	1.000	3.358	0.078
Purine and Pyrimidine	Adenosine monophosphate	1.000	1.095	0.637
	Thymine	1.000	1.255	0.306
	Uracil	1.000	1.026	0.804
	Uridine	1.000	0.808	0.685
Katana hadu	2-Hydroxyglutaric acid	1.000	0.669	0.553
Ketone body	3-Hydroxybutyric acid	1.000	0.991	0.982
	Creatinine	1.000	1.153	0.586
	myo-Inositol	1.000	0.363	0.121
	Inositol phosphate	1.000	1.037	0.918
	Pantothenic acid	1.000	1.188	0.361
	Gluconic acid	1.000	0.525	0.054
	Nonanoic acid	1.000	1.154	0.377
	Capric acid	1.000	0.993	0.965
	Heptadecanoic acid	1.000	0.968	0.904
	2'3'-Bisphosphoglycerate	1.000	0.979	0.951
	2-Hydroxybenzoic acid	1.000	1.059	0.794
	Adipic acid	1.000	1.268	0.253
Others	Benzoic acid	1.000	1.048	0.692
Others	Cystathionine	1.000	4.314	0.001
	Disaccharide	1.000	0.740	0.623
	Ethanolamine	1.000	1.124	0.318
	Ethanolamine	1.000	1.123	0.519
	Glyoxylic acid	1.000	0.419	0.055
	Nicotinamide	1.000	1.250	0.026
	Nitrous Oxide	1.000	1.158	0.269
	Oxalic acid	1.000	1.167	0.254
	Putrescine	1.000	2.316	0.207
	Pyrrolidonecarboxylic acid	1.000	1.301	0.187
	Sarcosine	1.000	1.248	0.031
	Threonic acid	1.000	1.111	0.578
P value was calculated by 2-tailed unpaired Student	t's <i>t</i> test.			

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Supplemental	Table #	5.	Antibodies	Used	in	This Paper

Antibody	Source	Identifier	Dilution
Anti-GLUT1	Cell Signaling Technology	12939	WB 1:1.000
Anti-GLUT4	Cell Signaling Technology	2213	WB 1:1.000
Anti-HK1	Cell Signaling Technology	2024	WB 1:1.000
Anti-HK2	Cell Signaling Technology	2867	WB 1:1.000
Anti-GPI	Cell Signaling Technology	57893	WB 1:1.000
Anti-PFK1	Novus Biologicals	NBP2-75578	WB 1:1,000
Anti-PFK2	Cell Signaling Technology	13123	WB 1:1,000
Anti-ALDOA	Cell Signaling Technology	8060	WB 1:1,000
Anti-GAPDH	Cell Signaling Technology	2118	WB 1:3 000
Anti-PGK1	Abcam	ab154613	WB 1:1.000
Anti-PGAM1	Cell Signaling Technology	12098	WB 1:1,000
Anti-ENO1	Cell Signaling Technology	3810	WB 1:1,000
Anti-PKM1/2	Cell Signaling Technology	3190	WB 1:1,000
Anti-PKM1	Proteintech	15821-1-AP	WB 1:1,000
Anti-PKM2	Cell Signaling Technology	4053	WB 1:1,000
Anti-PKM2 (Tyr105)		3827	WB 1:1,000
Anti-I DHA		3582	WB 1:1,000
		3205	WB 1:1,000
		14462	WB 1:1,000
		14402	WB 1.1,000
	Cell Signaling Technology	40141	WB 1.1,000
		NBP1-07047	WB 1:1,000
		12263	WB 1:1,000
		5322	WB 1:1,000
		ab153902	WB 1:1,000
	Cell Signaling Technology	66350	WB 1:1,000
Anti-PHGDH	Novus Biologicals	NBP2-52939	WB 1:1,000
Anti-PCK2	Cell Signaling Technology	8565	WB 1:1,000
Anti-PC	Novus Biologicals	NBP1-49636	WB 1:1,000
Anti-ME1	GeneTex	GTX104122	WB 1:1,000
Anti-α-tubulin	Sigma-Aldrich	T6199	WB 1:6,000
Anti-YAP	Cell Signaling Technology	14074	WB 1:1,000
Anti-phospho-YAP	Cell Signaling Technology	4911	WB 1:1,000
(Sel127)	ABcional	A15806	WB 1:1 000
Total OXPHOS Rodent		A13000	WB 1.1,000
WB Antibody Cocktail	Abcam	ab110413	WB 1:2,000
Anti-AMPK	Cell Signaling Technology	5832	WB 1:1,000
Anti-phospho-AMPK	Cell Signaling Technology	2535	WB 1:2 000
(Thr172)		2000	
Anti-ACC	Cell Signaling Technology	3676	WB 1:1,000
Anti-phospho-ACC (Ser79)/(Ser212)	Cell Signaling Technology	11818	WB 1:1,000
Anti-Tri-Methyl-Histone H3 (Lys4)	Cell Signaling Technology	9751	WB 1:1,000
Anti-H3	Cell Signaling Technology	4499	WB 1:1,000
Anti-mouse IgG	Cell Signaling Technology	7076	WB 1:5,000
Anti-rabbit IgG	Cell Signaling Technology	7074	WB 1:5,000
Anti-TEAD1	Sigma-Aldrich	AV39521	WB 1:1,000
Anti-c-Myc	Cell Signaling Technology	5605	WB 1:1,000
Anti-HIF-1α	Cell Signaling Technology	79233	WB 1:1,000; IP 4 µg for 150 µg lysate
Control IgG	Cell Signaling Technology	5415	IP 4 µg for 150 µg lysate
Anti-FLAG	Sigma-Aldrich	F1804	IP 4 μg for 150 μg lysate
Anti-Myc-tag	MBL	M192-3	IP 4 µg for 150 µg lysate

Mouse TrueBlot ULTRA, Anti-mouse Ig HRP	ROCKLAND	18-8817-33	WB 1:5,000
Control IgG	Cell Signaling Technology	2729	ChIP 5 µL for 5 µg chromatin
Anti-YAP	Cell Signaling Technology	14074	ChIP 5 µL for 5 µg chromatin
Anti-TEAD1	Cell Signaling Technology	12292	ChIP 5 µL for 5 µg chromatin
Anti-HIF-1α	Cell Signaling Technology	36169	ChIP 5 µL for 5 µg chromatin
Anti-Ki-67	Cell Signaling Technology	9129	IHC 1:400
Anti-cardiac troponin T	Thermo Fisher Scientific	MA5-12960	IHC 1:400
Goat anti-mouse IgG, Alexa Fluor 488	Thermo Fisher Scientific	A-24920	IHC 1:400
Goat anti-rabbit IgG, Alexa Fluor 594	Thermo Fisher Scientific	A-11072	IHC 1:400

siRNA Name	Source	Identifier
siTead1	Thermo Fisher Scientific	MSS211219
siHif-1α	Thermo Fisher Scientific	RSS310066
sic-Myc	Thermo Fisher Scientific	RSS351381
siGlut1	Thermo Fisher Scientific	RSS332476
siHk2	Thermo Fisher Scientific	RSS302994
siGpi	Thermo Fisher Scientific	RSS307944
siPfk1	Thermo Fisher Scientific	RSS368299
siAldoa	Thermo Fisher Scientific	RSS332289
siGapdh	Thermo Fisher Scientific	s236445
siPgk1	Thermo Fisher Scientific	s128192
siPgam1	Thermo Fisher Scientific	RSS351593
siEno1	Thermo Fisher Scientific	s127698
siPkm1	Thermo Fisher Scientific	RSS340844
siG6pd	Thermo Fisher Scientific	RSS302151
siGfat	Thermo Fisher Scientific	RSS334938
siGpd1	Thermo Fisher Scientific	RSS339932
siPhgdh	Thermo Fisher Scientific	RSS339816
siPck2	Thermo Fisher Scientific	RSS323287
siControl	Thermo Fisher Scientific	12935300

Supplemental Table 6. siRNAs Used in This Paper

Supplemental Table 7	Oligonucleotide Primers	Used in This Paper

Name	Forward Primer	Reverse Primer
	aPCR primers	· · · · · · · · · · · · · · · · · · ·
Mouse Glut1	TGTGCTTCCAGTATGTGGAGC	CTTGTCACTTTGGCTGGCAC
Mouse GlutA	TATGTTGCGGATGCTATGGGTC	CTGGGTTTCACCTCCTGCTC
		GATCCTGGCTCTTAGGCGTTC
Mouse Hk2	TCATTGTTGGCACTGGAAGC	TTGCCAGGGTTGAGAGAGAG
Mouse Gni	TGATTGCCATGTATGAGCACAAG	
Mouse <i>Dfk1</i>		COTTOTOCAGACOGITICOTIG
Mouse Pfk2		
Mouse Fikz		
Mouse Aldoa		
Mouse Gapan		
Mouse Pgk1		
Mouse Pgam1		AGALULTULAGATGUTTAAUG
Mouse Eno1		ACCAGICIIGAICIGCCCAGIG
Mouse Pkm1	GTCTGGAGAAACAGCCAAGG	
Mouse Pkm2	GICIGGAGAAACAGCCAAGG	CGGAGTICCTCGAATAGCTG
Mouse Ldha	CAAGCAGGTGGTGGACAGTG	TGGGACACTGAGGAAGACATC
Mouse Mpc1	TGACTTTCGCCCTCTGTTGC	GCCGCTTACTCATCTCGTAGTTG
Mouse Mpc2	GGGATTGGTATGTGCTGGATTAG	CCTTGACCAAATAAACCCTGTAGC
Mouse <i>Pdh</i>	AGGAGATTGATGTGGAAGTGAGG	CCACCTAACAGTCACCCATTAAC
Mouse Pdk4	ATCAAGATTTCTGACCGAGGAGG	TGGCGTAGAGACGAGAAATTGG
Mouse G6pd	AAGAATGTGAAGCTCCCTGATGC	CGCGGCTGCCATATACATAGG
Mouse Gfat	GACTGCCGGACTTGATTAAGG	TCACCAGCAAGGATGCCTTC
Mouse Gpd	CTTGAAGAATATAGTGGCCGTTGG	CAGGTCGTGATGAGGTCTGC
Mouse Phgdh	CCCACTATGATTGGCCTCCTG	CCTCCAATACATGCTGCTTCC
Mouse Pc	TGCAGAGGAGTTTGAGGTTGAG	TGCATCTCCTTCATGGCCTG
Mouse Me1	TGCCCTCATAGGAGTTGCTG	TCCCTTGGTCACCTTGTAGC
Mouse Me2	TAGAAGCTGCAAAGGCGCTG	CGTATCTGGCCTTGTCCTCG
Mouse Pck2	TGCGGAGCACAAAGGAAAGAC	CACGAGCATTCTCTCCAAAGC
Mouse Ctaf	CAAAGCAGCTGCAAATACCA	GGCCAAATGTGTCTTCCAGT
Mouse Cyr61	GAGGCTTCCTGTCTTTGGCAC	GATCCGGGTCTCTTTCACCAG
Mouse Npph	GGTCCAGCAGAGACCTCAAA	CAACTTCAGTGCGTTACAGCC
Mouse Yan		TTTGCCATCTCCCAACCTGC
Rat Glut1		TCAGGIGICITIGICGCICIGG
Rat ClutA	TATGTTGCGGATGCTATGGGTC	
Rat Uk1		
Ral MZ		
Ral <i>Opi</i>		GGAGGAGTCATGGGAGGTTAC
Ral PIKI		
Rat P1K2		
Rat Aldoa		
Rat Gapdh		
Rat Pgk1	CTGGATGGGCTTGGACTGTG	TAGACGTGGCTTTCACCACC
Rat <i>Pgam1</i>	AAGCATCTGGAGGGTCTGTC	TTTACGCACGGTCTCCTCATC
Rat Eno1	TCAAGGACTACCCAGTGGTG	CTTTGAGCAGGAGGCAGTTG
Rat Pkm1	ACCGCCTGCTGTTTGAAGAG	AGCAATGATAGGAGCCCTTGG
Rat Pkm2	AGGCTGCCATCTACCACTTG	AGCAATGATAGGAGCCCTTGG
Rat Ldha	GGTGGTTGACAGTGCATACG	TGGGACGCTGAGGAAGACATC
Rat Pdh	AAGGAGATTGATGTGGAAGTGAGG	CGCCCATCCATCTAATACTCTCC
Rat Pdk4	TCAAGATTTCTGACCGAGGTGG	TAGAGACGGGAAATCGGCAAG
Rat G6pd	CGTAGTGATGAACTCAGGGAAGC	CCTCATACTGGAAGCCCACTC
Rat <i>Gfat</i>	GACTGCCGGACTTGATTAAGG	TCACCAGCAAGGATGCCTTC
Rat Gpd	ACCTCATCACGACCTGCTAC	AAGGGAAACTTGTCCACGAGG
Rat Phgdh	GGCCTCAATGTCACCACCTC	AGACAGCTCCGTTGAGCATC
Rat Pc	GGTCTTCAAGTTCTGTGAGGTG	GTCACCCGTGTAGGAGATGG
Rat Me1	AGGAGTGCTATAAAGTGACCAAGG	CTCAGTCCACAGGCCACTAC
Rat Pck2	GCTGCTGAACACAAGGGAAAG	CGGAACCAGTTGACATGGAAG
Rat Ndufs1	CGTTCCACCTCAGCTAACTATAAAAGACTTC	CTCCTCTACTGCCTGAGCGC
Rat Sdhd	CTGTGGTGGACTACTCTCTCGCT	
Rat //acrc2	GCGGCTGGAGATGTTATCAATG	ATCTCACTCAGGAAGCCCTC
Rat Cor82		GATCAAGGTGGCCTCCCAAG
Dot Ata5k		
Mayoo and Dat Drade		
wouse and Kat Rps15		GAGAACTUGUUUAGGTAGTGG
		00447070007770047007710
Kat Glut1 promoter	CACTGGUTTACAGUUUTGAAU	GCAATCIGGGTTIGGATGCTAG

Mouse Glut1 promoter	ACTCAGAGAGGTGTGCAAACCAG	CGGGGCGGGACTCTGAGA
Mouse Glut1 -7kbp	TTGCCTCAAAATGAAAACTACC	TCCTTCTATCTTCTCTCTCTGAG
Mouse Glut1 -644bp	CCTCCCGTGGTCTCTCTAATG	GGTGTTTACAACCGCGTGTG
Mouse Glut 1 -138bp	TGCTTGTAGAGTGACGATCTGAG	ACGGACGCGCTGTAACTATG









Full unedited image for Figure 13F_FLAG	Full unedited image for Figure 13H_HIF-1 α
70kDa —	100kDa —
Full unedited image for Figure 13F_FLAG	Full unedited image for Figure 13H_TEAD1
70kDa —	
Full unedited image for Figure 13F_Myc	Full unedited image for Figure 13I_HIF-1α
Full unedited image for Figure 13F_HIF-1α	Full unedited image for Figure 13I_YAP
Full unedited image for Figure 13G_FLAG	Full unedited image for Figure 13J _YAP
70kDa —	Full unedited image for Figure 13J_TEAD1
Full unedited image for Figure 13G_Myc	55kDa —
55kDa —	Full unedited image for Figure 13K_YAP
Full unedited image for Figure 13G_HIF-1 α	70kDa —
100kDa —	Full unedited image for Figure 13K_TEAD1
Full unedited image for Figure 13G_HIF-1α	55kDa —
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