

Supplementary Material

includes 2 supplementary figures and 3 supplementary tables.

Supplementary Figure Legends

Supplementary Figure S1. The antibody against Pgam1 also served as that against Pgam2 with a similar sensitivity.

FLAG-tagged murine Pgam1 or Pgam2 was transfected into murine embryonic fibroblasts defective in p53. Total cellular lysates were analyzed by western blotting. The antibodies used were anti-Pgam1 (1:1000; Abcam, Cambridge, UK; Ab2220) and anti-FLAG (1:1000; Sigma, St. Louis, MO, USA; F1804). The similar sensitivities of the anti-Pgam1 antibody against the two isoforms of Pgam proteins were confirmed.

Supplementary Figure S2. Mitochondrial morphology and a marker of ROS were normal in the heart tissue of Pgam2 mice.

(A) Ultrastructural analysis of Pgam2 mice. Electron micrographs of histological sections of the left ventricle prepared from 12-week-old Pgam2 mice and non-transgenic littermates. The insets on the right panel are high-magnification images of the indicated portions (squares) of the images on the left. The morphology of mitochondria in Pgam2 mice was normal. Nucl.: nucleus. The bar represents 1 μm . The density (number per 100 μm^2) and the size (μm^2) of mitochondria within a cardiomyocyte were observed by electron microscopy (lower panels). Values are the mean $\pm$ SEM (n = 3 for each groups). **(B)** TBARS as a marker of oxidative stress. Thiobarbituric acid reactive substances (TBARS) levels were normal in the heart tissue of Pgam2 mice. Values are the mean $\pm$ SEM. NTg mice: n = 7; Pgam2 mice: n = 8.

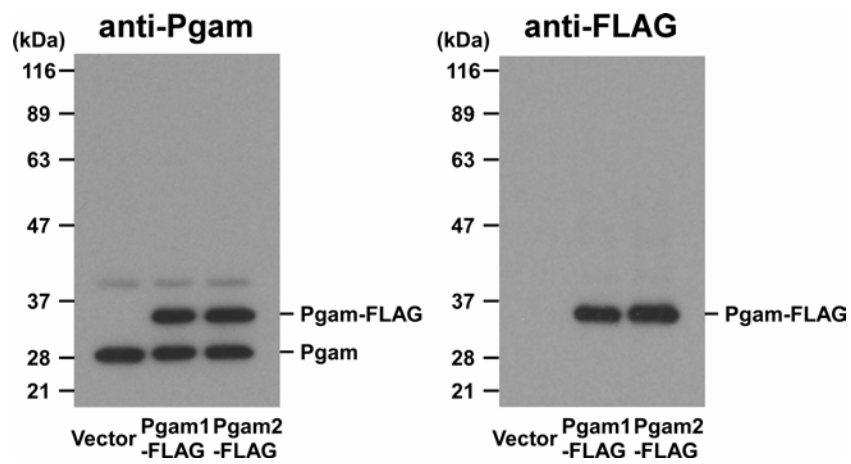
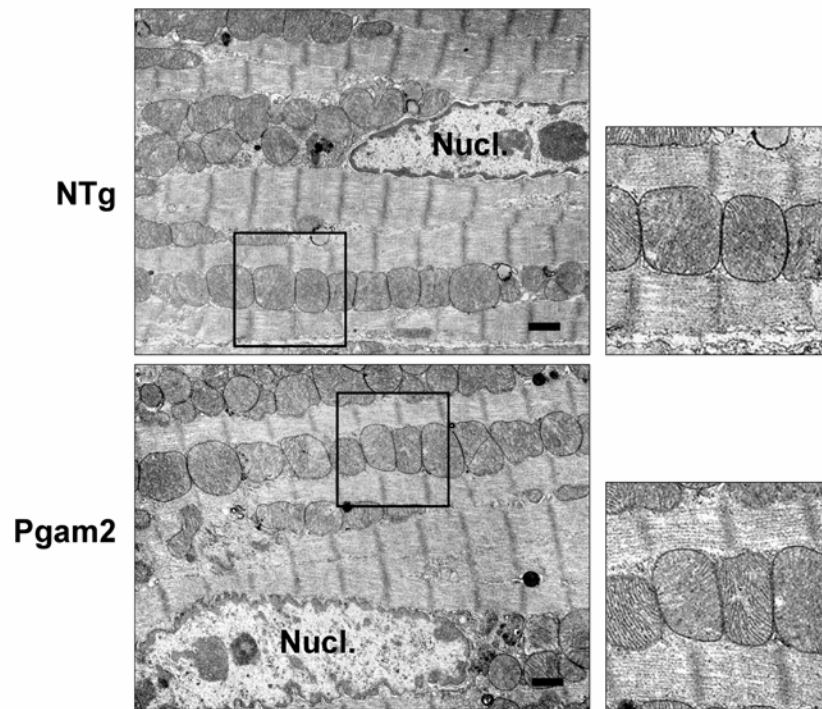
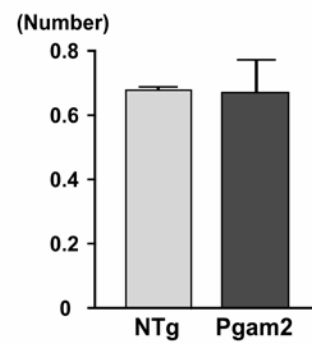


Figure S1

A

**Number of mitochondria
per cardiomyocyte area**



Size of mitochondria

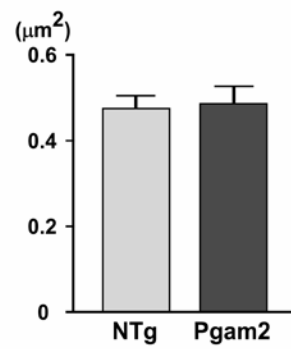
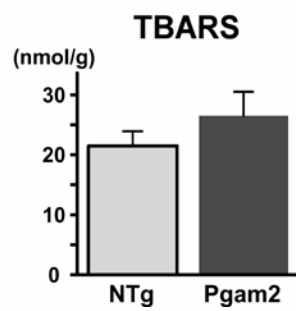
**B**

Figure S2

Supplementary Table S1. Primer sequences used for real-time quantitative RT-PCR.

Gene	Forward primer	Reverse primer
<i>18S rRNA</i>	CGGCTACCATCAAGGAA	GCTGGAATTACCGCGGCT
<i>Hexokinase 1</i>	ACGTTTTCTTCCCGTGCCGA	AGCGTCATAGTCCCCTCGCTTCT
<i>Hexokinase 2</i>	CCAGACGAAACTGGATGAGA	CAGCCACAATGTCAATGTCA
<i>Glucokinase</i>	AGAAGGAAAAGGTAGAGCAGA	TCTTTACACTGGCCTCCTGA
<i>Pfkfb1</i>	TCAGCTCGGGGCAAGCAGTATG	AGTGTCCAGGGCTTCCTCGGG
<i>Pfkfb2</i>	CCGATACCTGGTGGGGAGTCCTA	GCGCATGACAGCCTGGTGAGA
<i>Pfk1</i>	ATGGAGTGCCTGCAGGTGACCA	TCATCACGGCCACTGTGTGCAA
<i>PK</i>	GGATACAAAGGGACCTGAGA	GCAGATGTTCTTGTAGTCCA
<i>Hif-1α</i>	GATGGCTCCCTTTTTCAAGCA	CCCAGCAGTCTGCATGCTA
<i>PGC1α</i>	TTCTGGGTGGATTGAAGTGGTG	TGTCAGTGCATCAAATGAGGGC
<i>PPARα</i>	GAGAATCCACGAAGCCTACC	AATCGGACCTCTGCCTCTTT
<i>PPARδ</i>	CCGCCGACAATCCGCATGA	AGCGGATAGCGTTGTGCGACA
<i>ERRα</i>	CAAGAGCATCCCAGGCTT	GCACTTCCATCCACACACTC
<i>NRF-1</i>	GAAGTGCCAACCACAGTCAC	TTTGTTCACCTCTCCATCA
<i>Tfam</i>	CCAAAAAGACCTCGTTTCAGC	ATGTCTCCGGATCGTTTCAC
<i>CD36/FAT</i>	GGCCAAGCTATTGCGACAT	CAGATCCGAACACAGCGTAGA
<i>CPT-1b</i>	TGCCTTTACATCGTCTCCAA	AGACCCCGTAGCCATCATC
<i>MCAD</i>	GATCGCAATGGGTGCTTTTGATAGAA	AGCTGATTGGCAATGTCTCCAGCAAA
<i>IDH3α</i>	CCACAACACAAAACAGGTGA	GTCTTGAATTGCTGTGACA
<i>OgDh</i>	CCCTGGGGATTTTGATGCT	TGTAGGCCATAGAACCCTCCT
<i>SCS</i>	CAGGGAACGACGAGGCTAAT	GTACCGGACTTGGACACGAT
<i>ND4</i>	CATCACTCCTATTCTGCCTAGCAA	TCCTCGGGCCATGATTATAGTAC
<i>α-S9</i>	CCCGGGCCAGCTTACCT	GCTGCACTGCTTTCTTGATAGA
<i>SDHB</i>	CGCTGCCACACCATCATG	TTTCCGCAATCGCTTTCC
<i>Fe-S</i>	GCTGGGCGCACACTTTGT	CACTGGCCTTGCAGGAAGAA
<i>Cyt-b</i>	GCCACCTTGACCCGATTCT	TTGCTAGGGCCGCGATAAT
<i>Cyt-c</i>	GGAGGCAAGCATAAGACTGG	TCCATCAGGGTATCCTCTCC
<i>COX5a</i>	GGGTACACGAGACAGATGA	GGAACCAGATCATAGCCAACA
<i>COX7a1</i>	GTCTCCCAGGCTCTGGTCCG	CTGTACAGGACGTTGTCCATTC
<i>UCP2</i>	CTCTGCCTTGGGCCAGTACCA	GTTCCAGGATCCCAAGCGGAGA
<i>UCP3</i>	ACTCCAGCGTCGCCATCAGGATTCT	TAAACAGGTGAGACTCCAGCAACTT
<i>Mn-SOD</i>	GCGCAGATCATGCAGCTGCA	CAGGCTGAAGAGCGACCTGA

Supplementary Table S2. Myocardial uptake of ^{18}F FDG and ^{125}I -9MPA.

	Number of samples	¹⁸ FDG		¹²⁵ I-9MPA	
		CPM	SUV	CPM	SUV
Hearts with RI					
NTg	13	262888 ± 34414	283 ± 36	113429 ± 7510	473 ± 26
Pgam2	18	349711 ± 37166	246 ± 32	111085 ± 4514	542 ± 28
Hearts without RI					
Empty tubes	6	N.D.	N.A.	37 ± 3	N.A.
	6	N.D.	N.A.	26 ± 4	N.A.

Radioisotope (RI) counts per minute (CPM) of each sample were corrected by the average counts of the RI in hearts without RI and those of empty tubes. SUV: standard uptake value. Values are the mean $\pm$ SEM. N.D.: not determined; N.A.: not available.

Supplementary Table S3. Concentrations of metabolites in the heart identified by metabolomic analysis.

KEGG ID		NTg (n = 5)		Pgam2 (n= 5)		
	<i>Glycolysis and intermediates</i>					
C00160	Glycolate	57.30	± 6.09	60.22	± 7.22	
C00103	Glucose-1-phosphate	91.56	± 8.38	85.17	± 6.00	
C00092	Glucose-6-phosphate	743.57	± 107.63	658.36	± 95.80	
C00085	Fructose-6-phosphate	115.46	± 15.69	92.41	± 11.35	
C00354	Fructose 1,6-bisphosphate	487.44	± 43.44	472.23	± 39.00	
C00197	3-Phosphoglycerate	54.50	± 2.91	121.71	± 9.96	*
C01159	2,3-Diphosphoglycerate	63.05	± 6.34	34.69	± 3.31	*
C00631	2-Phosphoglycerate	4.41	± 0.35	12.84	± 0.90	*
C00074	Phosphoenolpyruvate (PEP)	3.19	± 0.21	7.29	± 0.42	*
C00186	Lactate	8615.59	± 358.66	8053.05	± 281.70	
C00258	Glycerate	8.84	± 1.69	54.53	± 3.30	*
	<i>TCA cycle and intermediates</i>					
C00024	Acetyl CoA	17.07	± 0.90	19.66	± 0.40	*
C00158	Citrate	461.40	± 40.15	579.37	± 37.80	
C00417	cis-Aconitate	12.89	± 1.14	17.50	± 1.55	*
C00311	Isocitrate	38.63	± 1.95	47.21	± 4.24	
C00647	Pyridoxamine 5'-phosphate	29.27	± 0.60	31.34	± 0.46	*
C02630	2-Hydroxyglutarate	35.95	± 3.81	18.73	± 2.47	*
C00042	Succinate	761.22	± 22.18	719.69	± 27.56	
C00122	Fumarate	94.26	± 5.70	71.14	± 2.77	*
C00711	Malate	518.49	± 34.07	429.33	± 19.97	
C00083	Malonyl CoA	4.00	± 0.44	4.55	± 0.44	
C00383	Malonate	2.00	± 0.31	3.00	± 0.37	
	<i>Amino acids and intermediates</i>					
C00065	Serine	427.71	± 28.89	232.13	± 9.31	*
C00263	Homoserine	4.95	± 0.29	4.44	± 0.32	
C00037	Glycine	543.12	± 18.64	511.14	± 21.58	
C00719	Betaine	86.25	± 9.99	59.96	± 5.09	*
C00114	Choline	54.85	± 1.84	58.18	± 3.64	
C00334	GABA	7.16	± 0.80	9.96	± 1.01	
C00073	Methionine	76.30	± 4.42	65.26	± 3.85	
C00127	GSSG (oxidized-form glutathione)	279.03	± 12.38	251.33	± 7.50	
C00051	GSH (reduced-form glutathione)	630.55	± 35.60	448.95	± 8.45	*
	Total glutathione (GSSG+GSH)	909.58	± 31.03	700.28	± 15.03	*
C00245	Taurine	6149.30	± 515.10	5708.18	± 563.01	
C00519	Hypotaurine	285.89	± 13.61	271.61	± 18.60	
C05123	Isethionate	36.48	± 2.63	50.24	± 3.73	*
C00041	Alanine	1951.11	± 95.33	1723.70	± 94.25	
C00049	Aspartate	1199.97	± 232.30	595.62	± 49.26	*
C03794	Adenylosuccinate	26.40	± 2.93	16.99	± 1.46	*
C00047	Lysine	512.63	± 12.42	548.75	± 38.77	
C00318	Camitine	404.31	± 27.11	348.82	± 17.47	
C00099	beta Alanine	23.73	± 3.09	16.81	± 2.73	
C00135	Histidine	257.48	± 12.44	289.99	± 6.52	*
C00388	Histamine	6.14	± 0.41	5.97	± 0.29	

C05127	1-Methylhistamine	0.63	±	0.06	0.61	±	0.07	
C00386	Carnosine	27.71	±	2.85	71.18	±	6.10	*
C01262	Anserine	7.58	±	0.74	20.21	±	1.70	*
C00025	Glutamate	3897.49	±	132.17	4244.17	±	113.87	
C00148	Proline	92.73	±	5.00	76.96	±	3.72	*
C01015	Hydroxyproline	66.24	±	5.17	40.63	±	3.38	*
C00077	Ornithine	11.18	±	0.56	10.08	±	0.68	
C00327	Citrulline	188.82	±	6.67	188.03	±	7.65	
C03406	Argininosuccinate	4.89	±	0.25	3.63	±	0.30	*
C00062	Arginine	242.61	±	6.30	254.22	±	10.10	
C00300	Creatine	6444.53	±	265.19	6059.07	±	142.41	
C00791	Creatinine	36.87	±	3.02	31.46	±	1.04	
C00134	Putrescine(1,4-Butanediamine)	3.96	±	0.28	3.12	±	0.18	*
C00315	Spermidine	33.13	±	1.67	27.23	±	1.23	*
C00750	Spermine	5.14	±	0.81	5.20	±	0.57	
C00123	Leucine	107.70	±	6.00	94.18	±	5.00	
C00407	Isoleucine	62.67	±	5.42	52.80	±	3.69	
C00183	Valine	143.90	±	9.81	127.51	±	6.78	
C00079	Phenylalanine	64.63	±	1.72	62.18	±	2.59	
C00082	Tyrosine	90.31	±	7.71	94.23	±	6.35	
C00152	Asparagine	164.68	±	4.29	150.20	±	8.82	
C00064	Glutamine	4754.46	±	192.58	5065.96	±	112.85	
C00188	Threonine	349.37	±	12.68	324.90	±	11.86	
C00078	Tryptophan	23.69	±	1.10	25.33	±	0.57	
C00262	Hypoxanthine	16.56	±	0.81	15.07	±	1.13	
C00019	S-Adenosylmethionine	36.57	±	0.95	36.79	±	1.22	
-	Ophthalmate	0.87	±	0.09	0.82	±	0.09	
C02356	2-Aminobutyrate (2AB)	5.83	±	0.50	4.24	±	0.25	*
C00003	NAD ⁺	564.30	±	26.46	594.49	±	26.03	
C00004	NADH	272.11	±	13.95	263.20	±	19.70	
C00005	NADPH	72.81	±	5.88	93.47	±	5.47	*
C00006	NADP ⁺	43.06	±	2.94	46.83	±	3.07	

Values are expressed in nmol/g, and are presented as the mean ± SEM. NTg: non-transgenic mice; Pgam2: phosphoglycerate mutase 2 transgenic mice. *p < 0.05 versus NTg mice.