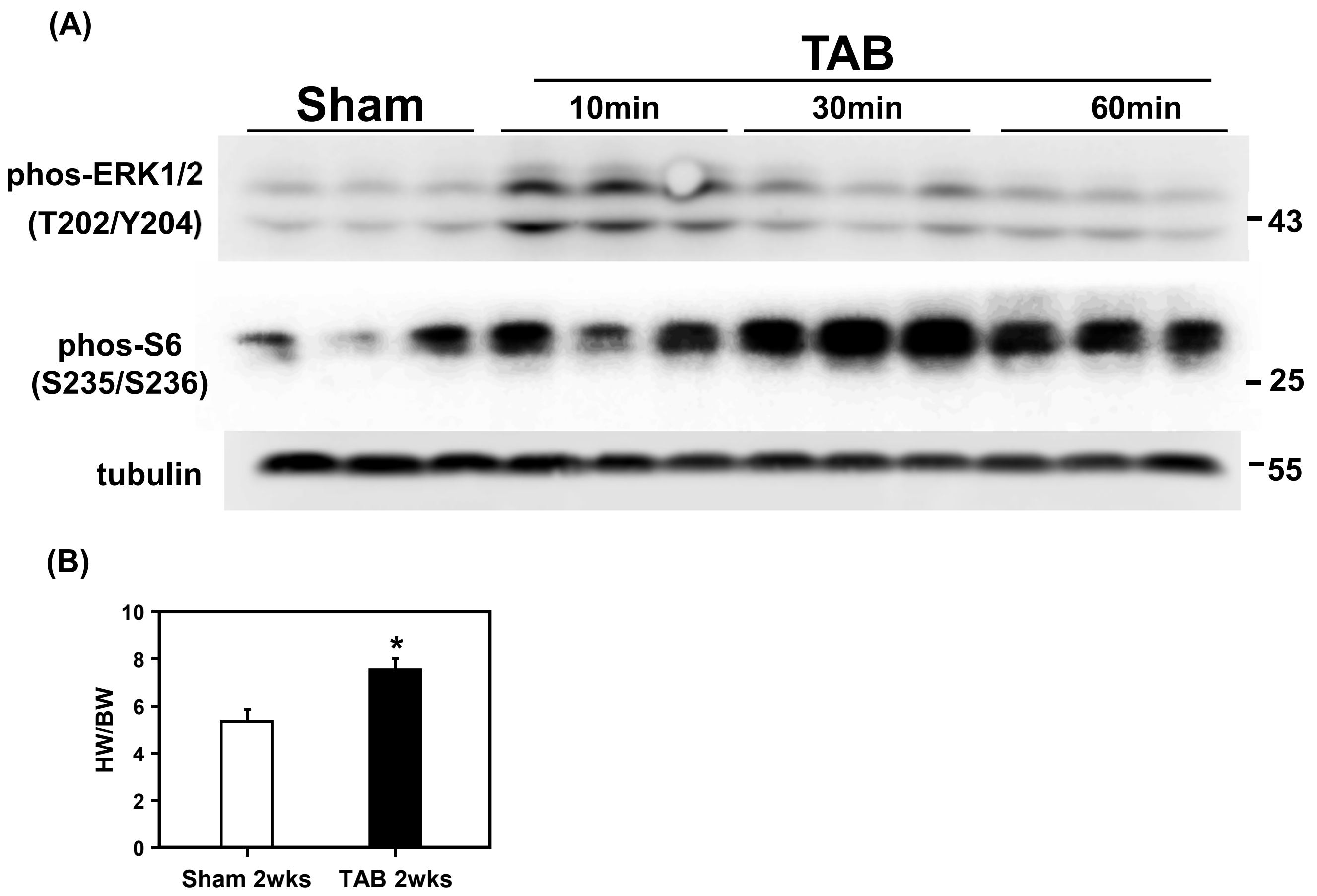
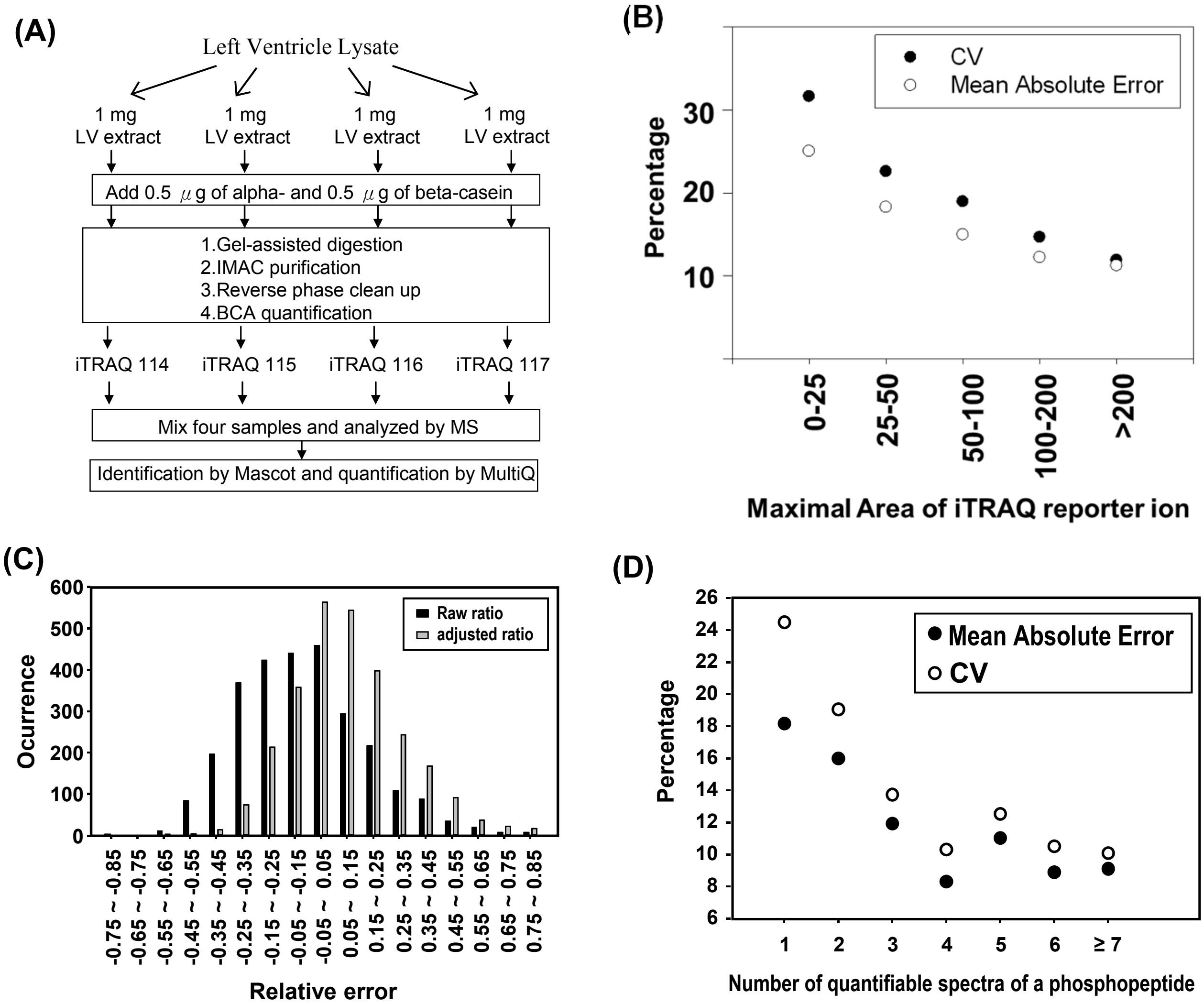
Supplemental material :

Supplemental Figure 1



Supplemental Figure 1. A, Western blot analysis of phosphorylated ERK1/2 and S6 from left ventricle tissues of mouse hearts with acute pressure overload. The position of molecular weight marker is showed to the right of immunoblot. B, Quantification of ratio of heart weight to body weight (HW/BW) in mice that underwent sham operation or transverse aortic banding (TAB) for 2 weeks.

Supplemental Figure 2



Supplemental Figure 2. Validation and assessment of the quantification strategy by a 1:1 experiment. A, Experimental scheme used for validation of quantification strategy. The same left ventricle lysates were used. The same amount of standard phosphoproteins and bovine α and β caseins was added to each 1 mg lysates. B, Quantification accuracy and reproducibility of phosphopeptides by peak area of iTRAQ reporter ion according to mean absolute error (MAE) and coefficient of variation (CV) of ratio of phosphopeptides. Only spectrum with iTRAQ reporter ion peak area≥25 was quantifiable. C, Quantitative bias adjusted by phosphopeptide ratio of the standard bovine α and β caseins. Only quantifiable spectra were used for calculation. D, Quantification accuracy and reproducibility of number of quantifiable spectra for a phosphopeptide according to MAE and CV of ratio of phosphopeptides. MSMS spectra for iTRAQ reporter ions with intensity ≥25. Only quantifiable spectra were used for calculation.

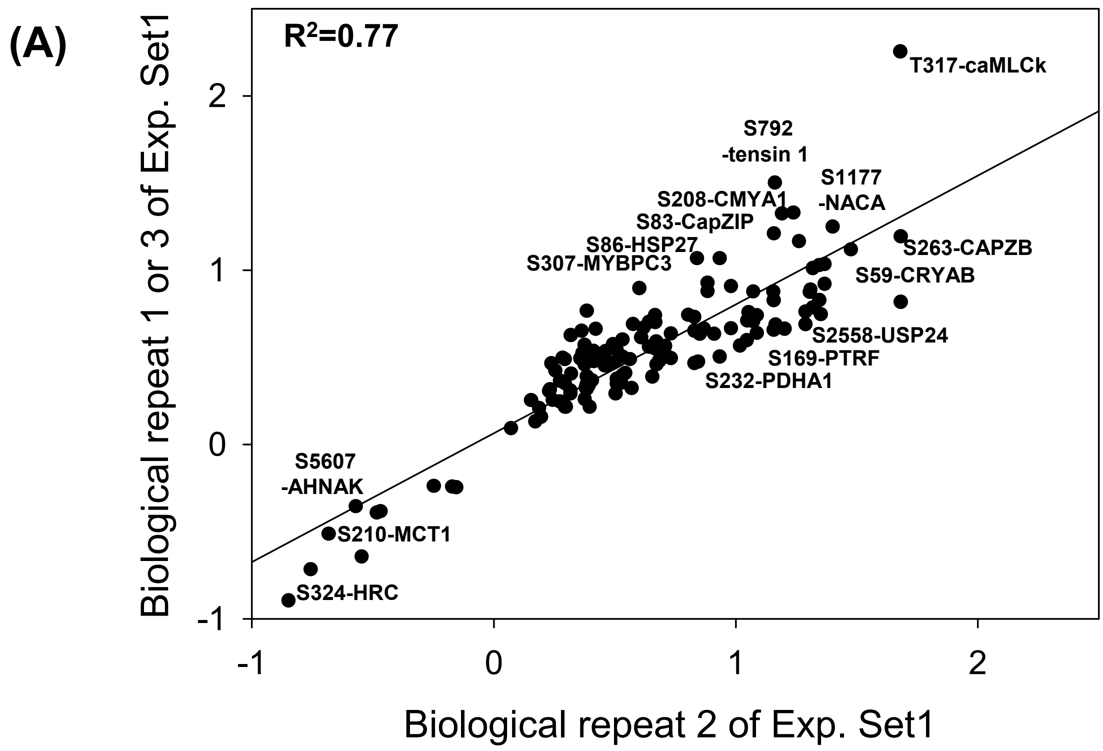
Supplemental Figure 3

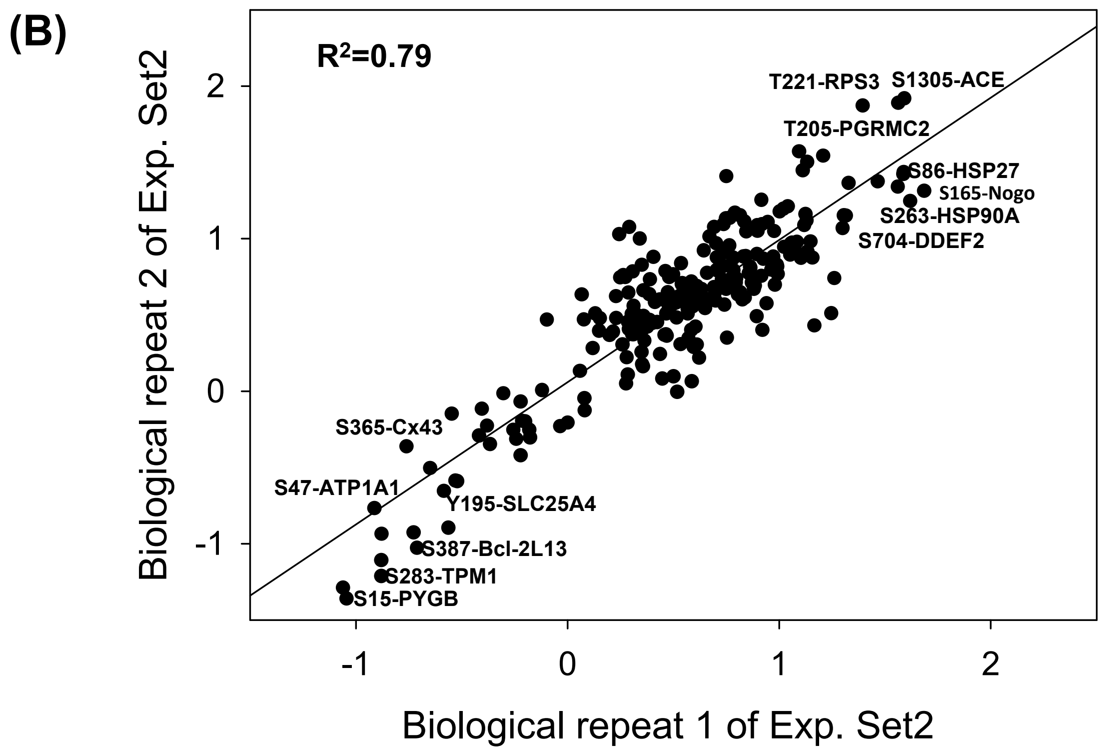
	TAB10min/sham	TAB30min/sham	TAB60min/sham
Exp. Set1 repeat 1	0.17	0.17	0.18
Exp. Set1 repeat 2	0.23	0.25	0.2
Exp. Set1 repeat 3	0.23	0.2	0.21

	Hypertrophy1/sham1	Hypertrophy2/sham1	Sham2/sham1
Exp. Set2 repeat 1	0.2	0.21	0.25
Exp. Set2 repeat 2	0.23	0.17	0.16

Supplemental Figure 3. The CV of casein phosphopeptides in each experiment of Figure 1A as an index of the quantification reproducibility for each experimental operation.

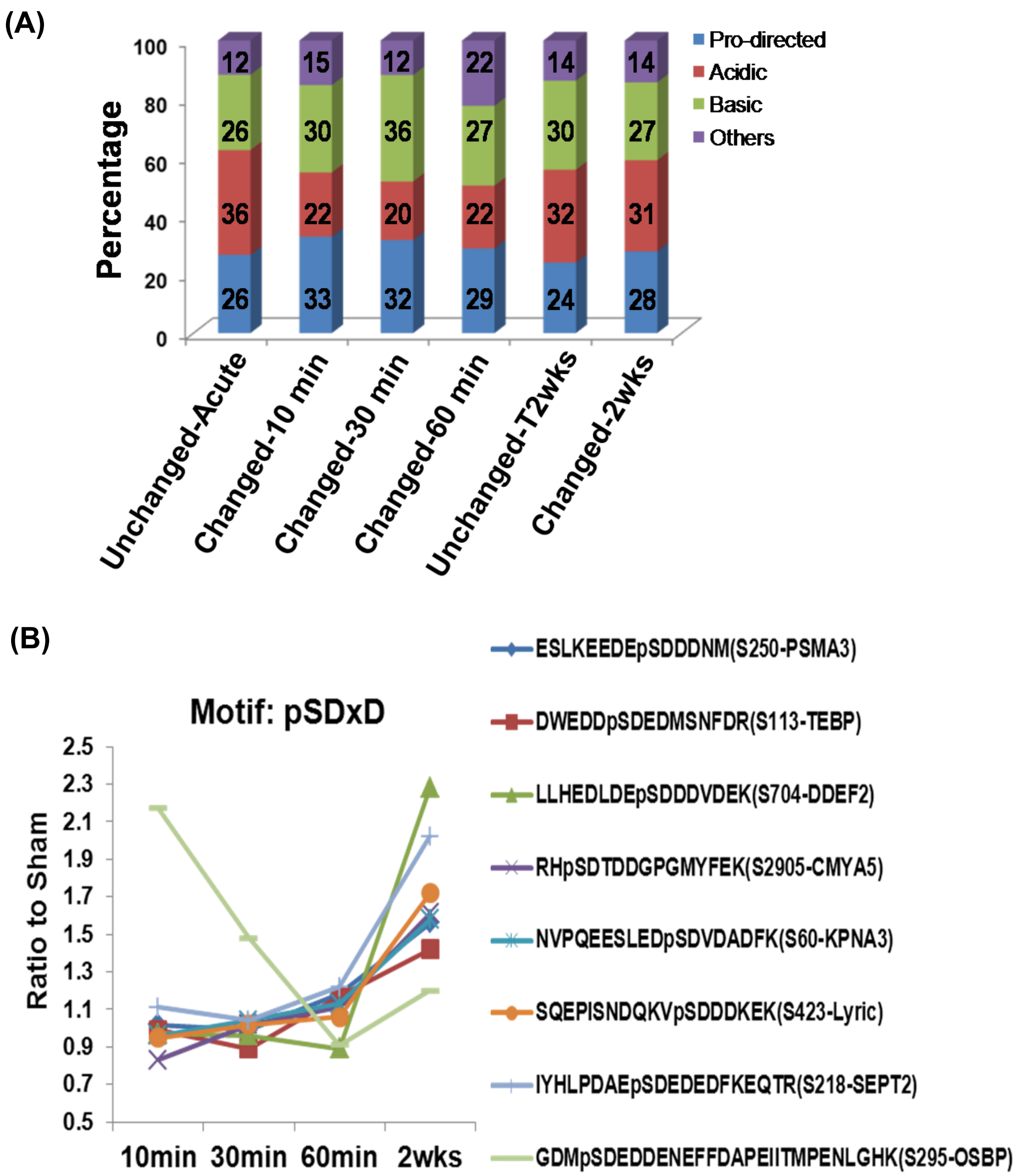
Supplemental Figure 4





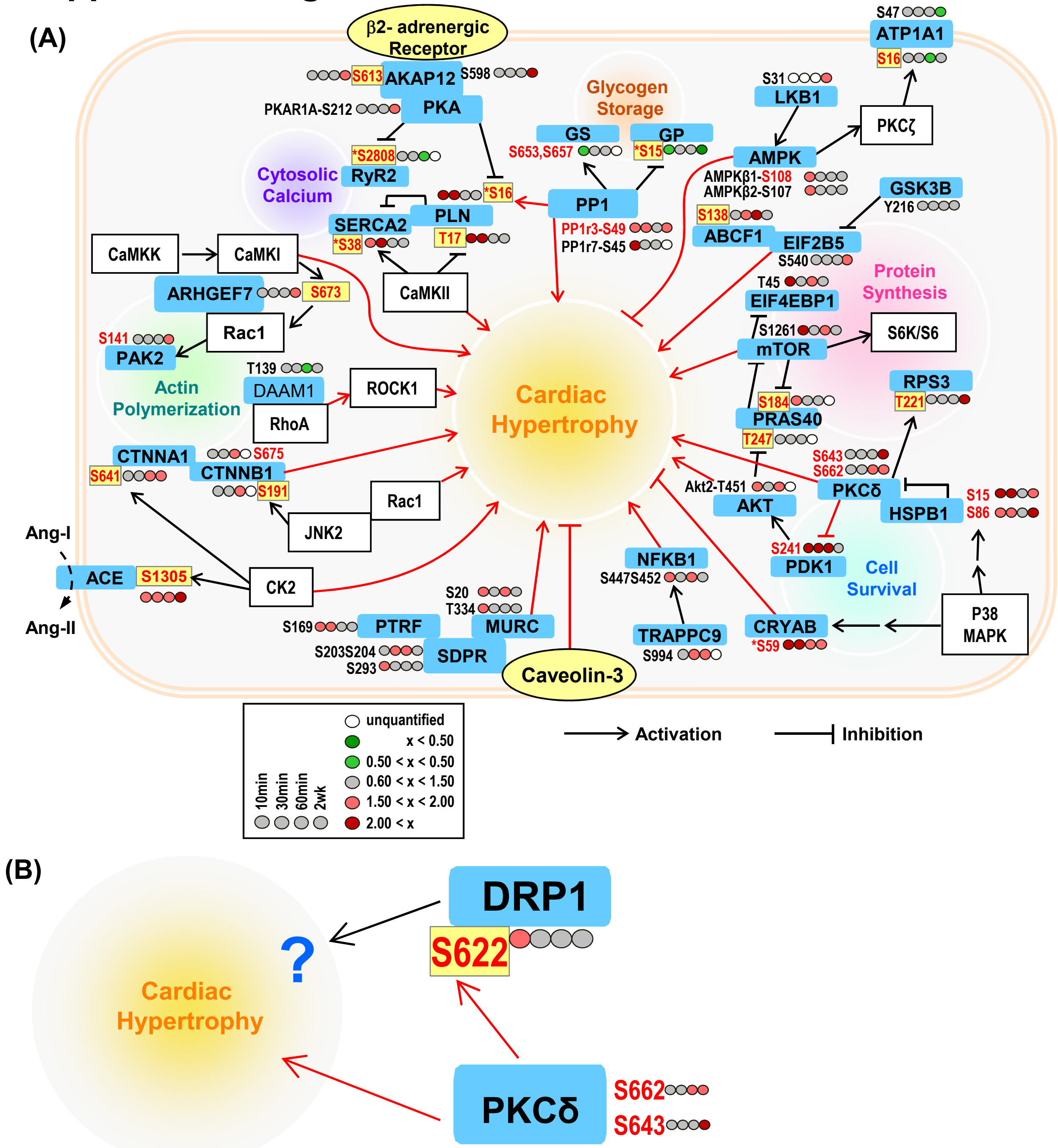
Supplemental Figure 4. (A) and (B) show correlation of ratios of biological significant changed phosphopeptides in acute pressure overload and hypertrophic hearts.

Supplemental Figure 5



Supplemental Figure 5. Kinase recognition motif analysis. A, Percentage of phosphorylated amino acid sites with 3 general kinase recognition motifs at different times of TAB. The motif classes include proline-directed (Pro-directed), acidic, basic and others. Data are percentage of kinase recognition motifs in each group.
B, Temporal pattern of pSDxD, a casein kinase II recognition motif, with TAB. pS, phosphoserine; D, aspartic acid; x, any amino acid residue. The sequences of quantified phosphopeptides are listed and the phosphorylated sites with protein names are in parentheses.

Supplemental Figure 6



Supplemental Figure 6. A, Pressure-overload–induced dynamic phosphoproteomic alteration in pathways related to cardiac hypertrophy. The fold change in phosphorylation level of indicated amino acid sites at 4 TAB times are in the inset. Proteins with blue background were quantified. Red arrows indicate events occurring in mouse hearts or rat cardiomyocytes. Black arrows indicate events not demonstrated in hearts or cardiomyocytes. Symbols or colors on amino acids: * known function of phosphorylation in cardiomyocytes; black, unknown effect of phosphorylation on proteins; red, known effect of phosphorylation on protein; rectangle box, amino acid sites are directly phosphorylated by the kinases upstream in this figure. B, DRP1 S622 is phosphorylated by prohypertrophic kinase PKC-δ. The role of DRP1 in cardiac hypertrophy was tested (Figure 3-5).

Supplemental Table II

Supplemental Table II. References of signaling pathways of Supplemental Figure 6

Classification	Pathway	Reference
Cytosolic calcium	CaMKII=>S38 of SERCA	Toyofuku T, Curotto Kurzydlowski K, Narayanan N, MacLennan DH. Identification of Ser38 as the site in cardiac sarcoplasmic reticulum Ca(2+)-ATPase that is phosphorylated by Ca2+/calmodulin-dependent protein kinase. J Biol Chem. 1994;269(42):26492-26496.
Cytosolic calcium	PKA=>S2808 0f RyR2	Shan J, Kushnir A, Betzenhauser MJ, Reiken S, Li J, Lehnart SE, Lindegger N, Mongillo M, Mohler PJ, Marks AR. Phosphorylation of the ryanodine receptor mediates the cardiac fight or flight response in mice. J Clin Invest.120(12):4388-4398.
Cytosolic calcium	PP1=>S16 of PLN	Carr AN, Schmidt AG, Suzuki Y, del Monte F, Sato Y, Lanner C, Breeden K, Jing SL, Allen PB, Greengard P, Yatani A, Hoit BD, Grupp IL, Hajjar RJ, DePaoli-Roach AA, Kranias EG. Type 1 phosphatase, a negative regulator of cardiac function. Mol Cell Biol. 2002;22(12):4124-4135.
Cytosolic calcium	CaMKII=>T17 of PLN and PKA=>S16 of PLN	Mattiazzi A, Mundina-Weilenmann C, Guoxiang C, Vittone L, Kranias E. Role of phospholamban phosphorylation on Thr17 in cardiac physiological and pathological conditions. Cardiovasc Res. 2005;68(3):366-375.
Glycogen storage	S49 of PP1r3=>S15 of GP and PP1=>GS1	Dent P, Lavoinne A, Nakielny S, Caudwell FB, Watt P, Cohen P. The molecular mechanism by which insulin stimulates glycogen synthesis in mammalian skeletal muscle. Nature. 1990;348(6299):302-308.
Protein synthesis	Akt=>T247 of PRAS40 => mTOR =>eIF4EBP and S6K/S6	Vander Haar E, Lee SI, Bandhakavi S, Griffin TJ, Kim DH. Insulin signalling to mTOR mediated by the Akt/PKB substrate PRAS40. Nat Cell Biol. 2007;9(3):316-323.
Protein synthesis	mTOR=>S184 of PRAS40	Wang L, Harris TE, Lawrence JC, Jr. Regulation of proline-rich Akt substrate of 40 kDa (PRAS40) function by mammalian target of rapamycin complex 1 (mTORC1)-mediated phosphorylation. J Biol Chem. 2008;283(23):15619-15627.
Protein synthesis	PKC delta=>T221 of rpS3	Kim TS, Kim HD, Kim J. PKCdelta-dependent functional switch of rpS3 between translation and DNA repair. Biochim Biophys Acta. 2009;1793(2):395-405.
Protein synthesis	ABCF1=>eIF2	Paytubi S, Morrice NA, Boudeau J, Proud CG. The N-terminal region of ABC50 interacts with eukaryotic initiation factor eIF2 and is a target for regulatory phosphorylation by CK2. Biochem J. 2008;409(1):223-231.
Protein synthesis	Akt=>AMPK in heart	Kovacic S, Soltys CL, Barr AJ, Shiojima I, Walsh K, Dyck JR. Akt activity negatively regulates phosphorylation of AMP-activated protein kinase in the heart. J Biol Chem. 2003;278(41):39422-39427.
Actin polymerization	CaMKK=>CaMKI=>S673 of Arhgef7=>Rac1=>PAK	Saneyoshi T, Wayman G, Fortin D, Davare M, Hoshi N, Nozaki N, Natsume T, Soderling TR. Activity-dependent synaptogenesis: regulation by a CaM-kinase kinase/CaM-kinase I/betaPIX signaling complex. Neuron. 2008;57(1):94-107.

Supplemental Table II. Continued

Classification	Pathway	Reference
Actin polymerization	Wnt=>DAAM1=>RhoA	Habas R, Kato Y, He X. Wnt/Frizzled activation of Rho regulates vertebrate gastrulation and requires a novel Formin homology protein Daam1. Cell. 2001;107(7):843-854
Actin polymerization	alpha Catenin=>actin-filament assembly	Drees F, Pokutta S, Yamada S, Nelson WJ, Weis WI. Alpha-catenin is a molecular switch that binds E-cadherin-beta-catenin and regulates actin-filament assembly. Cell. 2005;123(5):903-915.
Cell survival	aAR=>PKCdelta=>PDK1=>Akt	Guo J, Sabri A, Elouardighi H, Rybin V, Steinberg SF. Alpha1-adrenergic receptors activate AKT via a Pyk2/PDK-1 pathway that is tonically inhibited by novel protein kinase C isoforms in cardiomyocytes. Circ Res. 2006;99(12):1367-1375.
Cell survival	hspb1=>PKC delta	Lee YJ, Lee DH, Cho CK, Bae S, Jhon GJ, Lee SJ, Soh JW, Lee YS. HSP25 inhibits protein kinase C delta-mediated cell death through direct interaction. J Biol Chem. 2005;280(18):18108-18119.
Cell survival	p38 MAPK=>MAPKAPK2=>S59 of Crayab	Morrison LE, Hoover HE, Thuerauf DJ, Glembotski CC. Mimicking phosphorylation of alphaB-crystallin on serine-59 is necessary and sufficient to provide maximal protection of cardiac myocytes from apoptosis. Circ Res. 2003;92(2):203-211.
Cardiac Hypertrophy	PP1=>cardiac hypertrophy	Carr AN, Schmidt AG, Suzuki Y, del Monte F, Sato Y, Lanner C, Breeden K, Jing SL, Allen PB, Greengard P, Yatani A, Hoit BD, Grupp IL, Hajjar RJ, DePaoli-Roach AA, Kranias EG. Type 1 phosphatase, a negative regulator of cardiac function. Mol Cell Biol. 2002;22(12):4124-4135.
Cardiac Hypertrophy	RhoA=> ROCK=>cardiac hypertrophy	Higashi M, Shimokawa H, Hattori T, Hiroki J, Mukai Y, Morikawa K, Ichiki T, Takahashi S, Takeshita A. Long-term inhibition of Rho-kinase suppresses angiotensin II-induced cardiovascular hypertrophy in rats in vivo: effect on endothelial NAD(P)H oxidase system. Circ Res. 2003;93(8):767-775.
Cardiac Hypertrophy	Rac=>cardiac hypertrophy	Pracyk JB, Tanaka K, Hegland DD, Kim KS, Sethi R, Rovira, II, Blazina DR, Lee L, Bruder JT, Kovesdi I, Goldshmidt-Clermont PJ, Irani K, Finkel T. A requirement for the rac1 GTPase in the signal transduction pathway leading to cardiac myocyte hypertrophy. J Clin Invest. 1998;102(5):929-937.
Cardiac Hypertrophy	mTOR=>cardiac hypertrophy	Shioi T, McMullen JR, Tarnavski O, Converso K, Sherwood MC, Manning WJ, Izumo S. Rapamycin attenuates load-induced cardiac hypertrophy in mice. Circulation. 2003;107(12):1664-1670.
Cardiac Hypertrophy	AMPK=>mTOR/S6K/S6 and cardiac hypertrophy	Dolinsky VW, Chan AY, Robillard Frayne I, Light PE, Des Rosiers C, Dyck JR. Resveratrol prevents the prohypertrophic effects of oxidative stress on LKB1. Circulation. 2009;119(12):1643-1652.
Cardiac hypertrophy	NFkB=>cardiac hypertrophy	Gupta S, Purcell NH, Lin A, Sen S. Activation of nuclear factor-kappaB is necessary for myotrophin-induced cardiac hypertrophy. J Cell Biol. 2002;159(6):1019-1028.
Cardiac hypertrophy	PKC delta=>cardiac hypertrohy	Chen L, Hahn H, Wu G, Chen CH, Liron T, Schechtman D, Cavallaro G, Banci L, Guo Y, Bolli R, Dorn GW, 2nd, Mochly-Rosen D. Opposing cardioprotective actions and parallel hypertrophic effects of delta PKC and epsilon PKC. Proc Natl Acad Sci U S A. 2001;98(20):11114-11119.

Supplemental Table II. Continued

Classification	Pathway	Reference
Cardiac hypertrophy	Cryab=>cardiac hypertrophy	Kumarapeli AR, Su H, Huang W, Tang M, Zheng H, Horak KM, Li M, Wang X. Alpha B-crystallin suppresses pressure overload cardiac hypertrophy. Circ Res. 2008;103(12):1473-1482.
Cardiac hypertrophy	CaMKI=>cardiac hypertrophy	Passier R, Zeng H, Frey N, Naya FJ, Nicol RL, McKinsey TA, Overbeek P, Richardson JA, Grant SR, Olson EN. CaM kinase signaling induces cardiac hypertrophy and activates the MEF2 transcription factor in vivo. J Clin Invest. 2000;105(10):1395-1406
Cardiac hypertrophy	CaMKII=>cardiac hypertrophy	Kato T, Sano M, Miyoshi S, Sato T, Hakuno D, Ishida H, Kinoshita-Nakazawa H, Fukuda K, Ogawa S. Calmodulin kinases II and IV and calcineurin are involved in leukemia inhibitory factor-induced cardiac hypertrophy in rats. Circ Res. 2000;87(10):937-945.
Cardiac hypertrophy	Caveolin3=>cardiac hypertrophy	Koga A, Oka N, Kikuchi T, Miyazaki H, Kato S, Imaizumi T. Adenovirus-mediated overexpression of caveolin-3 inhibits rat cardiomyocyte hypertrophy. Hypertension. 2003;42(2):213-219.
Cardiac hypertrophy	Murc=>cardiac hypertrophy	Ogata T, Ueyama T, Isodono K, Tagawa M, Takehara N, Kawashima T, Harada K, Takahashi T, Shioi T, Matsubara H, Oh H. MURC, a muscle-restricted coiled-coil protein that modulates the Rho/ROCK pathway, induces cardiac dysfunction and conduction disturbance. Mol Cell Biol. 2008;28(10):3424-3436.
Cardiac hypertrophy	GSK3beat=>eIF2B5=>cardiac hypertrophy	Hardt SE, Tomita H, Katus HA, Sadoshima J. Phosphorylation of eukaryotic translation initiation factor 2Bepsilon by glycogen synthase kinase-3beta regulates beta-adrenergic cardiac myocyte hypertrophy. Circ Res. 2004;94(7):926-935.
Others	Wnt=>Rac1=>JNK2=>S191 of beta catenin	Wu X, Tu X, Joeng KS, Hilton MJ, Williams DA, Long F. Rac1 activation controls nuclear localization of beta-catenin during canonical Wnt signaling. Cell. 2008;133(2):340-353.
Others	CK2=>S641of alpha catenin=>beta catenin	Ji H, Wang J, Nika H, Hawke D, Keezer S, Ge Q, Fang B, Fang X, Fang D, Litchfield DW, Aldape K, Lu Z. EGF-induced ERK activation promotes CK2-mediated disassociation of alpha-Catenin from beta-Catenin and transactivation of beta-Catenin. Mol Cell. 2009;36(4):547-559.
Others	CK2=>S1305 of ACE=>JNK	Kohlstedt K, Brandes RP, Muller-Esterl W, Busse R, Fleming I. Angiotensin-converting enzyme is involved in outside-in signaling in endothelial cells. Circ Res. 2004;94(1):60-67.
Others	AMPK=>PKCζ=>S16 of ATP1a1	Vadasz I, Dada LA, Briva A, Trejo HE, Welch LC, Chen J, Toth PT, Lecuona E, Witters LA, Schumacker PT, Chandel NS, Seeger W, Sznajder JI. AMP-activated protein kinase regulates CO2-induced alveolar epithelial dysfunction in rats and human cells by promoting Na,K-ATPase endocytosis. J Clin Invest.
Others	beta2AR=>PKA=>S613 of AKAP12	Tao J, Wang HY, Malbon CC. Protein kinase A regulates AKAP250 (gravin) scaffold binding to the beta2-adrenergic receptor. EMBO J. 2003;22(24):6419-6429.
Others	Trappc9=>NFkB	Hu WH, Pendergast JS, Mo XM, Brambilla R, Bracchi-Ricard V, Li F, Walters WM, Blits B, He L, Schaal SM, Bethea JR. NIBP, a novel NIK and IKK(beta)-binding protein that enhances NF-(kappa)B activation. J Biol Chem. 2005;280(32):29233-29241.

Supplemental Table III

Supplemental Table III. TAB-phosphoprotein-related abnormal heart phenotypes

Quantified		Phosphosite Ratio >1.5 change		Gene Symbol	Mammalian Phenotype Term
Acute	2wks	Acute	2wks		
v	v	v		Acacb	small heart
v	v	v		Acadl	abnormal heart morphology
v	v	v	v	Ace	decreased heart rate,decreased heart weight,dilated heart,enlarged heart atrium,increased heart rate,increased heart weight
v				Actc1	abnormal heart development,dilated heart right ventricle,enlarged heart,heart left ventricle hypertrophy
v	v			Ak1	altered response to myocardial infarction
v	v		v	Akap12	enlarged heart
v	v			Ank1	enlarged heart
v	v	v		Ank2	increased heart rate variability
v	v			Atp1a1	decreased cardiac muscle contractility,increased cardiac muscle contractility
v	v	v		Atp2a2	abnormal heart left atrium morphology,abnormal heart left ventricle pressure,abnormal heart shape,congestive heart failure,decreased heart rate,dilated heart atrium,dilated heart left ventricle,dilated heart right ventricle,enlarged heart,heart left ventricle hypertrophy,increased heart weight,increased response of heart to induced stress
v	v	v	v	Bag3	increased cardiomyocyte apoptosis,myocardial fiber degeneration
v		v		Bnip3	altered response of heart to induced stress
v				Cacna1c	congestive heart failure,decreased heart rate,dilated heart ventricle,heart right ventricle hypertrophy,increased heart weight,irregular heartbeat
v	v	v	v	Ckm	dilated heart left ventricle,heart left ventricle hypertrophy
v	v	v	v	Ckmt2	dilated heart left ventricle,heart left ventricle hypertrophy

Supplemental Table III. Continued

Quantified		Phosphosite Ratio >1.5 change		Gene Symbol	Mammalian Phenotype Term
Acute	2wks	Acute	2wks		
	v		v	Csrp3	abnormal myocardial fiber morphology,cardiac fibrosis,cardiac hypertrophy,cardiac interstitial fibrosis,cardiomyopathy,decreased cardiac muscle contractility,dilated cardiomyopathy,enlarged myocardial fiber,increased cardiac muscle contractility,abnormal heart morphology,abnormal heart septum morphology,abnormal heart ventricle morphology,decreased heart rate,decreased response of heart to induced stress,dilated heart left ventricle,enlarged heart,increased heart weight
v	v	v	v	Ctnnb1	decreased response of heart to induced stress,small heart
v		v		Daam1	abnormal heart left ventricle morphology,abnormal heart ventricle morphology
v	v	v		Dag1	abnormal cardiac muscle contractility,cardiac fibrosis,dilated cardiomyopathy,myocardial fiber degeneration
v		v		Dnm1l	abnormal heart development,abnormal heart morphology,abnormal heart ventricle pressure,congestive heart failure,dilated heart
	v		v	Dtna	cardiac fibrosis,cardiomyopathy,myocardial fiber degeneration
v	v	v		Flna	abnormal heart morphology,decreased heart right ventricle size,dilated heart
v				Fxr1	small heart
	v			Gab1	abnormal cardiac muscle relaxation,abnormal cardiovascular system morphology,abnormal endocardium morphology,decreased cardiac muscle contractility,hemopericardium,abnormal heart left ventricle morphology,abnormal heart morphology,congestive heart failure,dilated heart,dilated heart left ventricle,dilated heart right ventricle,increased heart weight

Supplemental Table III. Continued

Quantified		Phosphosite Ratio >1.5 change		Gene Symbol	Mammalian Phenotype Term
Acute	2wks	Acute	2wks		
v		v		Gja1	abnormal heart development,abnormal heart electrocardiography waveform feature,abnormal heart morphology,abnormal heart rate,abnormal heart right ventricle morphology,abnormal heart right ventricle outflow tract morphology,abnormal heart shape,abnormal heart ventricle morphology,decreased heart rate,dilated heart left ventricle,heart inflammation,heart right ventricle hypertrophy,heart right ventricle outflow tract stenosis,increased heart rate,irregular heartbeat,small heart
v				Gtf2i	failure of heart looping
v	v	v		Hadha	abnormal myocardium layer morphology
v	v	v	v	Hrc	increased response of heart to induced stress
v	v			Hsp90ab1	absent heartbeat
v	v			Huwe1	enlarged heart,small heart
v	v	v		Igf2r	congestive heart failure,dilated heart left ventricle,dilated heart right ventricle,enlarged heart,heart hyperplasia,increased heart right ventricle size,increased heart weight
	v		v	Ivns1abp	decreased cardiac muscle contractility,increased cardiomyocyte apoptosis
v	v	v		Jph2	irregular heartbeat
v	v	v	v	Jup	abnormal heart atrium morphology,abnormal heart development,abnormal heart electrocardiography waveform feature,abnormal heart morphology,abnormal heart right ventricle morphology,abnormal heart ventricle morphology,dilated heart,dilated heart left ventricle,dilated heart right ventricle,enlarged heart,enlarged heart right atrium,heart inflammation,heart left ventricle hypertrophy,increased heart left ventricle size,increased heart rate,increased

Supplemental Table III. Continued

Quantified		Phosphosite Ratio >1.5 change		Gene Symbol	Mammalian Phenotype Term
Acute	2wks	Acute	2wks		
v	v	v		Ldb3	abnormal heart left ventricle morphology,abnormal heart morphology,abnormal heart right ventricle morphology,abnormal heart ventricle morphology,dilated heart left ventricle,dilated heart right ventricle,enlarged heart,heart vascular congestion,increased heart left ventricle size,increased heart right ventricle size,increased heart weight,increased response of heart to induced stress
v	v			Map3k5	decreased response of heart to induced stress
v	v			Mb	abnormal heart morphology,congestive heart failure,heart left ventricle hypertrophy
v	v	v		Mybpc3	abnormal heart left ventricle morphology,abnormal heart morphology,dilated heart left atrium,dilated heart left ventricle,enlarged heart,heart left ventricle hypertrophy,increased heart weight,dilated heart left ventricle
v				Myh11	dilated heart left ventricle
v		v		Myh6	abnormal heart atrium morphology,abnormal heart left ventricle morphology,abnormal heart morphology,abnormal heart ventricle morphology,abnormal heart ventricle pressure,dilated heart atrium,dilated heart left ventricle,heart left ventricle hypertrophy,irregular heartbeat

Supplemental Table III. Continued

Quantified		Phosphosite Ratio >1.5 change		Gene Symbol	Mammalian Phenotype Term
Acute	2wks	Acute	2wks		
v		v		Myl2	abnormal heart development,abnormal heart left ventricle morphology,abnormal heart left ventricle pressure,abnormal heart morphology,abnormal heart right ventricle morphology,abnormal heart shape,abnormal heart ventricle morphology,congestive heart failure,decreased heart rate,decreased response of heart to induced stress,dilated heart,dilated heart atrium,dilated heart left ventricle,dilated heart right ventricle,dilated heart ventricle,enlarged heart,enlarged heart atrium,heart block,heart hypoplasia,increased heart left ventricle size,increased heart weight,increased response of heart to induced stress,irregular heartbeat
v	v	v		Mylk3	abnormal heart left ventricle morphology,heart left ventricle hypertrophy,heart right ventricle hypertrophy,increased heart weight
v	v	v	v	Naca	abnormal heart ventricle morphology
v				Nos3	abnormal heart left ventricle morphology,abnormal heart morphology,abnormal heart right ventricle pressure,abnormal heart weight,congestive heart failure,decreased heart rate,dilated heart left ventricle,enlarged heart,enlarged heart atrium,heart left ventricle hypertrophy,increased heart left ventricle size,increased heart rate,increased heart right ventricle size,increased heart ventricle size,increased heart weight
v	v	v	v	Pdha1	abnormal heart left ventricle morphology,heart left ventricle hypertrophy,increased heart weight

Supplemental Table III. Continued

Quantified		Phosphosite Ratio >1.5 change		Gene Symbol	Mammalian Phenotype Term
Acute	2wks	Acute	2wks		
v	v	v		Pdpk1	abnormal cardiovascular system morphology,abnormal cardiovascular system physiology,abnormal myocardial fiber morphology,decreased cardiac muscle contractility,dilated cardiomyopathy,myocardium hypoplasia,abnormal heart morphology,abnormal heart right ventricle morphology,abnormal heart tube morphology,abnormal heart ventricle morphology,enlarged heart atrium,heart right ventricle hypertrophy,small heart
v		v		Pds5b	abnormal heart morphology,dilated heart atrium
v	v	v		Plin5	abnormal heart ventricle morphology
v	v	v		Pln	abnormal heart left ventricle pressure,abnormal heart shape,congestive heart failure,decreased heart rate,increased heart weight
v				Popdc2	altered response of heart to induced stress
v	v			Prkaca	pericardial edema
v	v			Prkar1a	abnormal heart development,abnormal heart tube morphology,decreased heart rate variability
	v			Prkca	decreased response of heart to induced stress,dilated heart left ventricle
v	v	v	v	Prkcd	abnormal cardiovascular system physiology
v				Ptpn12	abnormal heart development
v				Rasip1	abnormal cardiovascular development,abnormal endocardium morphology
v	v	v		Ryr2	abnormal heartbeat,abnormal heart morphology,altered response of heart to induced stress,decreased heart rate,enlarged heart,heart left ventricle hypertrophy,increased response of heart to induced stress,irregular heartbeat
v		v		Sgca	abnormal heart left ventricle morphology,heart inflammation

Supplemental Table III. Continued

Quantified		Phosphosite Ratio >1.5 change		Gene Symbol	Mammalian Phenotype Term
Acute	2wks	Acute	2wks		
v	v		v	Slc25a4	increased heart weight
v	v	v		Slc2a4	abnormal heart morphology,heart inflammation,increased heart weight
v	v			Slc4a3	abnormal heart rate,congestive heart failure,decreased heart rate
v	v			Slc8a1	abnormal heart atrium morphology,abnormal heart development,abnormal heart morphology,abnormal heart tube morphology,absent heartbeat,decreased heart rate,enlarged heart,heart left ventricle hypertrophy,irregular heartbeat
v		v		Speg	dilated heart,dilated heart left atrium,dilated heart right atrium,dilated heart ventricle,enlarged heart,increased heart weight
v	v		v	Sptan1	abnormal heart shape,dilated heart
v	v	v	v	Sptbn1	abnormal heart ventricle morphology,enlarged heart
v	v			Srf	abnormal heart shape,abnormal heart ventricle morphology,irregular heartbeat
	v			Srl	abnormal cardiac muscle relaxation,abnormal cardiovascular system physiology,decreased cardiac muscle contractility
v		v		Sfrs2	cardiac interstitial fibrosis,dilated cardiomyopathy
v		v		Syne1	decreased heart rate
	v			Tcea1	pericardial edema
v				Tnni3	congestive heart failure,increased heart weight
v				Tnnt2	abnormal heart development,abnormal heart electrocardiography waveform feature,abnormal heart left ventricle morphology,absent heartbeat,congestive heart failure,dilated heart,enlarged heart,failure of heart looping,increased heart rate

Supplemental Table III. Continued

Quantified		Phosphosite Ratio >1.5 change		Gene Symbol	Mammalian Phenotype Term
Acute	2wks	Acute	2wks		
v	v	v	v	Tpm1	increased heart weight
v				Tsc2	abnormal heart ventricle morphology,heart hyperplasia
v	v	v	v	Ttn	abnormal heart development,abnormal heart left ventricle morphology,abnormal heart ventricle morphology,absent heartbeat,decreased heart weight,dilated heart left ventricle,heart left ventricle hypertrophy,increased heart left ventricle size
v	v		v	Utrn	cardiomyopathy,myocardial necrosis
v		v		Vac14	abnormal heart atrium morphology
v	v	v	v	Vcl	abnormal heart development,abnormal heart electrocardiography waveform feature,abnormal heart position or orientation,abnormal heart valve morphology,congestive heart failure,dilated heart left ventricle,heart block,increased heart weight,irregular heartbeat,small heart
v				Wnk1	heart hemorrhage,heart hypoplasia
v	v	v		Xirp1	abnormal cardiac muscle contractility,abnormal cardiovascular system morphology,abnormal cardiovascular system physiology,abnormal myocardial fiber morphology,abnormal myocardium layer morphology,cardiac fibrosis,cardiac hypertrophy,decreased cardiac muscle contractility
v	v		v	Zranb2	decreased heart rate