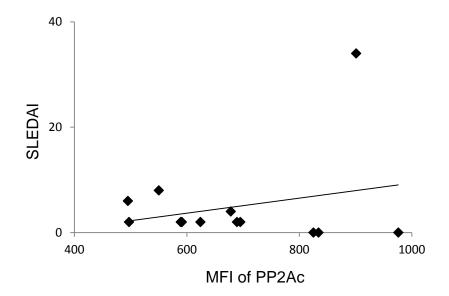
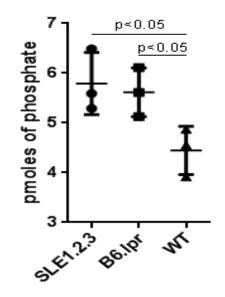


Supplementary Figure 1. Increased PP2A expression in B cells from lupus-prone mice.

- A. Western blot analysis on the expression of both scaffold (PP2A_A) and catalytic (PP2A_C) subunits in splenic B cells from indicated mice.
- B. Quantification of western blots (n=3).

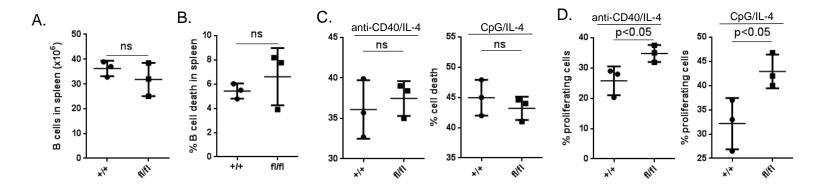


Supplementary Figure 2. Correlation between SLEDAI scores and mean fluorescence intensity (MFI) of PP2Ac in total circulating B cells from SLE patients.



Supplementary Figure 3. Increased PP2A activity in B cells from lupus-prone mice.

PP2A phosphatase activity was quantified using a kit from R&D. The activity of PP2A is presented as the rate of phosphate release (pmol x 10²).



Supplementary Figure 4. Equal proliferation and surviving rates of B cells from *flox/flox* mice and control mice with or without indicated stimulations.

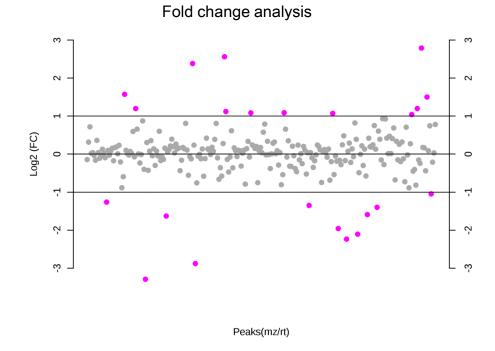
61-2-20 11-20 11

Baseline WT vs. KO (n=3 each)



20 20 2	SampleN		Baseline WT vs. KO (n=3 each) Low High
	HIST3H2BA MEIG1	HIST3H2BA MEIGI	histone cluster 3, H2ba meiosis expressed gene 1 homolog (mouse)
	EXTL1	EXTL1	exostoses (multiple)-like 1
	F13A1 TNFRSF1A	F13A1 TNFRSF1A	coagulation factor XIII, Al polypeptide tumor necrosis factor receptor superfamily, member là
	OCM	OCM	encomedulin
	MAGED1 LRRC23	MAGED1 LERC23	melanoma antigen family D, 1 leucine rich repeat containing 23
	SFN	SEN	stratifin
	IL13RA1	IL13RA1	interleukin 13 receptor, alpha 1
	MAGED2 ACTR3B	MAGED2 ACTR3B	melanoma antigen family D, 2 ARP3 actin-related protein 3 homolog B (yeast)
	RHPN2	RHPN2	rhophilin, Rho GTPase hinding protein 2
	CRYBA4 GPT2	GPT2	crystallin, heta A4 (Ultamic pyruytate transaminase (alanine aminotransferase) 2
		AGP7	glutamic pyruvate transaminase (alanine aminotransferase) ? aquanorin 7
	ANGPTL7 XYLB	ANGPTL7 XYLB	angionoietin-like 7 xylulokinase homolog (H. influenzae)
	COL23A1	COL23A1	côllagen, type XXIII, alpha l
	MYLPF CRLS1	CRLS1	- cardiolipin synthese l
	CD46	CD 46	CD46 molecule, complement regulatory protein membrane associated guanylate kinase, WW and PDZ domain containing 3
	MAGI3 TMOD4	MAGI3 TMOD4	membrane associated guarylate kinase, WW and PDZ domain containing 3 tropomodulin 4 (muscle)
	TRIM32	TRIM32	tripartite motif-containing 32
	PLSCR3 DNASE1	PLSCR3 DNASE1	phospholipid scramblase 3 deoxyribonuclease I
	CTNNAL1	CTNNAL1	catenin (cadherin-associated protein), alpha-like l
	FANCI ITGAE	FANCI	Fanconi anemia, complementation group I integrin, alpha E (antigen CD103, human mucosal lymphocyte antigen 1; alpha polypeptide)
	DUSP14	DUSP14	dual specificity phosphatase 14
	VCAM1 EMB1	VCAM1 EMB1	vascular cell adhesion molecule 1 egf-like module containing, mucin-like, hormone receptor-like 1
	SEPNI	SEPNI	selenoprotein N, 1
	LAG3 WDB60	LAG3 WDB60	lymphocyte-activation gene 3 WD repeat domain 60
	GAD 1	GAD 1	glutamate decarboxylase 1 (brain, 67kDa)
	TBC1D4 BRMS1L	TBC1D4 BBMS1L	TBC1 domain family, member 4 breast cancer metastasis-suppressor 1-like
	PPFIBP1	PPFIBP1	PTPRF interacting protein, binding protein 1 (liprin beta 1)
	ART3 BBS10	ART3 BBS10	ADP-ribosyltransferase 3
	SPAG1	SPAG1	Bardet-Biedl syndrome 10 sperm associated antigen 1
	CYP2U1 ABL6	CYP2U1 ABL6	cytochrome P450, family 2, subfamily II, polypeptide 1 ADP-ribosylation factor-like 6
	NMNAT1	NMNAT1	nicotinamide nucleotide adenylyltransferase 1
	IL2RB WRB	LL2RB WRB	interleukin 2 receptor, beta
	FSCN1	FSCN1	tryptophan rich basic protein fascin homolog 1, actin-bundling protein (Strongylocentrotus purpuratus)
	CASC5 INSL3	CASC5 INSL3	cancer susceptibility candidate 5
	SNCA	SNCA	insulin-like 3 (Leydig cell) symuclein, alpha (non A4 component of amyloid precursor)
	SETD6 BLOC1S3	SETD6 BLOC1S3	SET domain containing 6 biogenesis of lysosome-related organelles complex-1, subunit 3
	HIE3A	HIE3A	hypoxia inducible factor 3, alpha subunit
	LAIR1 CLEC7A	LAIRI	lenknowste-associated immunoglobulin-like receptor 1
	SLC27A4	CLEC7A SLC27A4	C-type lectin domain family 7, member A solute carrier family 27 (fatty acid transporter), member 4
	BTBDS PIK3B3	BTBD8 PIK3B3	BTB (POZ) domain containing 8
	ARRDC4	ARRDC4	arrestin domain containing 4
	PCBD2 CABYR	PCBD2 CABYR	pterin=4 alpha-carbinolamine_debydratase/dimerization_cofactor_of_hepatocyte_nuclear_factor_l_alpha_(TCF1)_2
	FANCE	FANCE	calcium hinding tyrosine-(Y)-phosphorylation regulated (fibrousheathin 2) Fanconi anemia, complementation group F
	CPNE5 ARL10	CPNE5 ABL10	copine V ADP-ribosylation factor-like 10
	CAMEL	CAMEL	calcium/calmodulin-dependent protein kinase I
	OAS3 CRIMI	CRIMI	21-51-oligoadenylate synthetase 3, 100kba custaine rich transmerkrans BND regulator 1 (chordin-like)
	SLC25A42	SLC25A42	cysteine rich transmembrane BMP regulator 1 (chordin-like) solute carrier family 25, member 42
	SPATA5L1 RPS6KL1	SPATA5L1 RPS6KL1	spermatogenesis associated 5-like 1 ribosomal protein S6 kinase-like 1
	LDHD	LDHD	lactate dehydrogenase D
	OVOL3 CITED4	OVOL3 CITED4	- Cbp/p300-interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 4
	NDNL2	NDNL2	necdin-like 2
	PLCB3	PLCB3	tyrosyl-tRNA synthetase 2 (mitochondrial) phospholipase C, beta 3 (phosphatidylinositol-specific)
	ALPL	ALPL	alkaline phosphatase, liver/bone/kidney
	SPHK1 WDTC1	SPHK1 WDTC1	sphingosine kinase l WD and tetratricopeptide repeats l
	LYRMI	LYRM1	LYR motif containing 1
	UBE2E2 OPN3	UBE2E2 OPN3	ubiquitin-conjugating enzyme E2E 2 (URC4/5 homolog, yeast) opsin 3 (encephalopsin, panopsin)
	PLLP	PLLP	plasma membrane proteolipid (plasmolipin)
	KCNMB1 DKK4	KCNMB1 DKK4	potassium large conductance calcium-activated channel, subfamily M, beta member 1 dickkopf homolog 4 (Xenopus laevis)
	ANXAG	ANXAG	annexin A9
	NPHP3 SOX4	NPHP3 SOX4	nephronophthisis 3 (adolescent) SRY (sex determining region Y)-box 4
	SUMF1	SUMF1	sulfatase modifying factor 1
	MESDC1 EN02	MESDC1 EN02	mesoderm development candidate 1 enolase 2 (gamma, neuronal)
	ZAP70	ZAP70	zeta-chain (TCR) associated protein kinase 70kDa
	GJC1 TRIM27	GJC1 TRIM27	<pre>gap junction protein, chi 1, 31.9kDa (connexin 31.9) tripartite motif-containing 27 isoleycine=rEWA synthetase 2, mitochondrial</pre>
	LARS2	LARS2	isoleucine-tENA synthetase 2, mitochondrial
	PTAFR GSTM5	PTAFR GSTM5	platelet-activating factor receptor glutathione S-transferase MS
	APOF	APOF	analisantat F

Supplementary Table. Expression pattern of indicated genes in B cells from WT vs KO

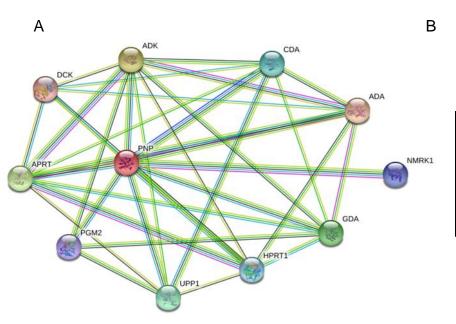


Pink dots represent >2 fold change metabolites (WT/KO).

	Fold Change
phenylpyruvate	0.10216
deoxyinosine	0.13593
putrescine	6.9171
dCDP-nega	5.9015
thymidine	5.2131
N-carbamoyl-L-aspartate	0.21229
N-acetyl-glutamate	0.23237
Pyridoxamine	0.25751
gluconolactone	0.32335
cystathionine	0.33212
acetylphosphate	2.9753
Nicotinamide Riboside	2.8328
acadesine	0.3791
N-Acetylputrescine	0.3925
nicotinate	0.41686
FAD	2.2966
Hydroxyphenylacetic acid	2.2955
5-phosphoribosyl-1-pyrophosphate	2.173
4-aminobutyrate	2.1266
dATP-nega	2.1208
2-Aminooctanoic acid	2.1019
phosphocreatine	0.48406
NAD posi	2.0606

Supplementary Figure 5. Targeted metabolomics analysis

Metabolites were extracted from cells and polar metabolomics profiling (303 metabolites) was performed by using Liquid Chromatography-Tandem Mass Spectroscopy (LC/MS). Metabolomics data was analyzed using MetaboAnalyst 4.0. Metabolites with ≥2-fold changes between groups were shown.



Name	p.value	FDR
Adenine phosphoribosyltransferase	0.00014769	0.023926
Adenosine kinase	4.67E-12	8.55E-10
Deoxycytidine kinase	0.00029112	0.046675
Phosphoglucomutase-2	7.12E-13	1.26E-10
Purine nucleoside phosphorylase	3.46E-13	8.93E-11

Supplementary Figure 6. Alteration of PNP pathway in B cells with PP2Aa deficiency.

- A. Predicted proteins directly interacting with PNP on STRING database.
- B. Genes on PNP pathways with significant alterations (P<0.05, *t*-test) obtained from RNA-seq data. FDR: false discovery rate.