List of Supplementary files

CAPTURING CELL-FATE DECISIONS FROM THE MOLECULAR SIGNATURES OF A RECEPTOR-DEPENDENT SIGNALING RESPONSE

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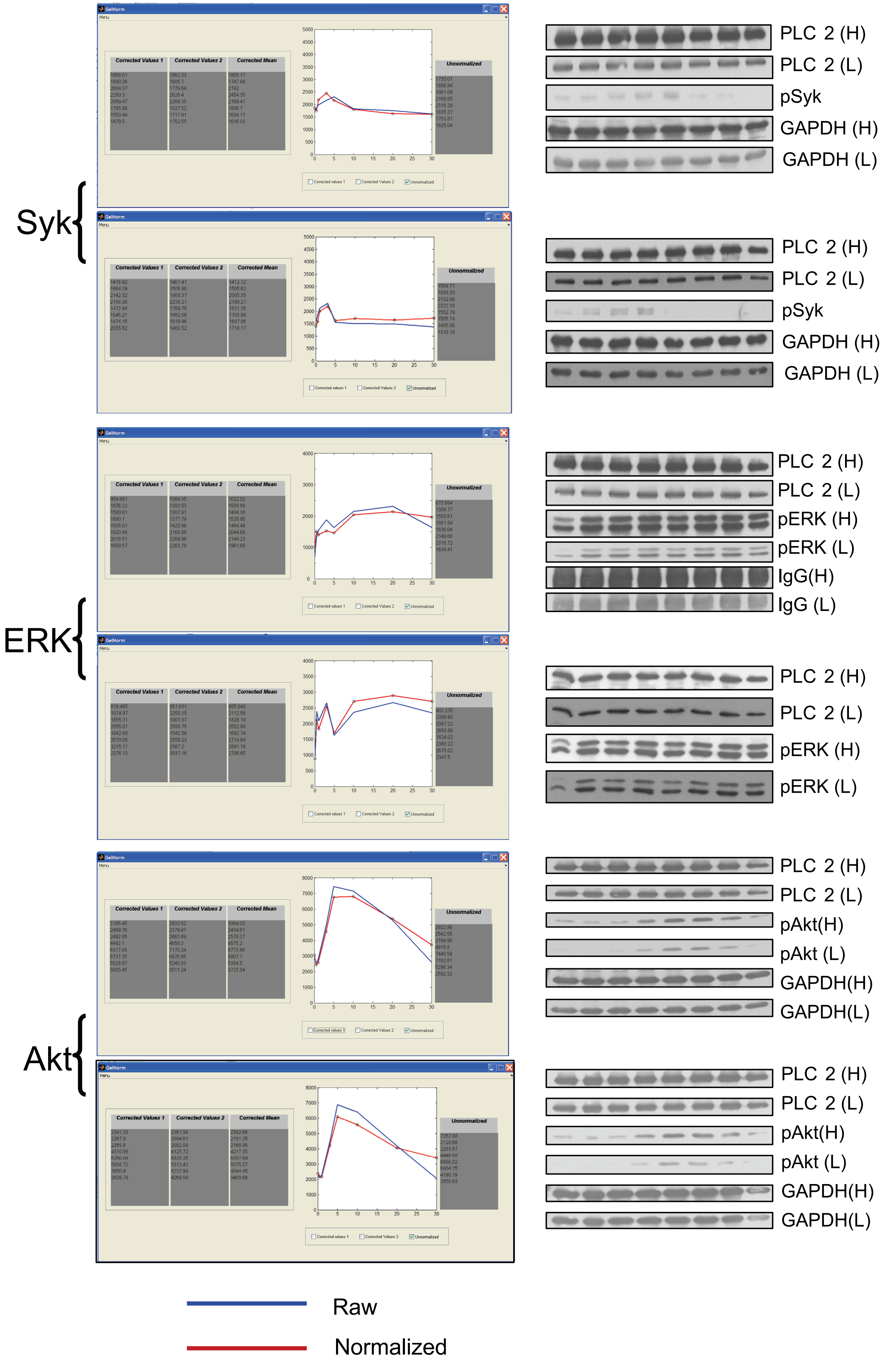
Supplementary Figure S1. Normalization of western blot



Normalization of Western blot data. For the purposes of normalization, each Western blot also included the detection of two additional proteins – whose levels remain unchanged over the course of the experiment – as internal reference standards. In most cases the two molecules were PLCγ2 (as a high molecular mass reference) and GAPDH (as a low molecular mass reference). In the occasional instances where the mass of either of these reference standards coincided with the molecule to be studied, we monitored for the surface IgG receptor of A20 cells as a substitute. Western blots obtained were scanned by PDSI personal densitometer from GE biosciences. Scanning was carried out at 50 pixel resolution and 12 bits. These scanned blots were then quantitated by Molecular Dynamics Imagequant software version 5.2. Numerical values for band intensities thus obtained were then checked for noise versus signal ratio. We were able to extract precise noise to signal ratio since we had different exposure times (low and high) for every blot. The numerical data was then corrected for noise using the calculated ratio. The intensity profile thus generated was then taken into a Toolbox in MATLAB platform developed by us using our own algorithm that normalizes the intensity of specific bands using the two different normalizers (i.e. our reference standards) (manuscript submitted). The variations of the normalizers are captured and the median of these variations is computed as the central reference value. Fluctuations in band intensities of the protein of interest due to errors are calculated by their variations with respect to that of the normalizers and are corrected systematically. Errors in the blots are identified as the deviation of the normalizers from the central reference value and the deviations are removed correspondingly from the data. These normalized values were then further analyzed to calculate changes in phosphorylation level compared to unstimulated condition (see main text). In a perfect blot concentration of normalizers are supposed to be constant (i.e. without much variations). In our case we fix a reference value *μi* (how the concentration of the normalizer would be if there were no errors) for each lane *i*. The error function (*fi*) is the computed error across all lanes due to handling and blotting errors given by.

$$f_i = \frac{\mu_i - n_i}{n_i} P_i$$

where *μi* is the reference value for *ni* for each lane. *ni* is the quantified normalizer concentration, *Pi* is the quantified concentration of protein of interest, *i* being the lane number

The normalized values for *Pi* is given by

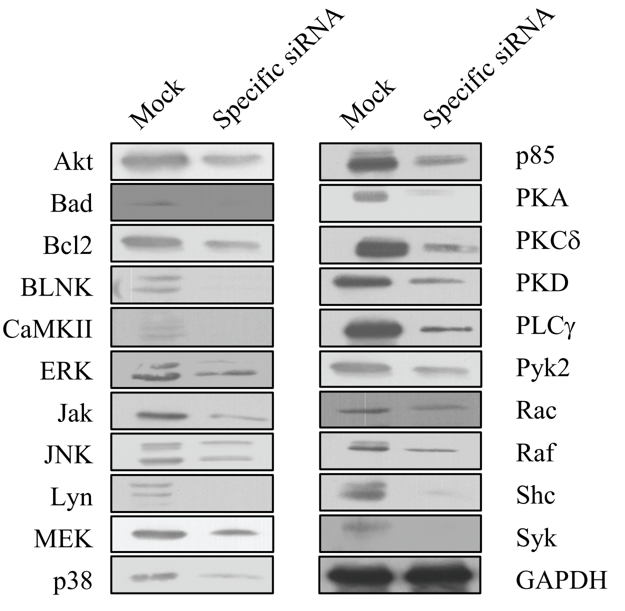
$$P_i = P_i + f_i$$

The mean of *Pi* obtained using both the normalizers gives the final normalized profile. The extent of noise was determined as the standard deviation of the ratio of band intensities obtained at high and low exposure times of the blots.

$$N_i = \sqrt{\frac{\Sigma(\frac{H_i}{L_i})^2}{i^2}}$$

The noise reduction step was applied when the standard deviation was more than a threshold value of 0.05 i.e. when Ni is greater then 0.05. where Hi and Li represent high and low exposure at each time point respectively. Here the low intensity data was decremented by the same ratio for noise reduction, and the new data for normalizers was then used for treating the general profile. The normalized profile data can be stored directly in an excel sheet and all the figures can be stored in any of the standard formats such as JPEG, TIFF etc.

Supplementary Figure S2: Specific knockdown of signaling intermediates using siRNA.



The twenty-one selected signaling molecules were individually depleted by using specific siRNA (Santa Cruz and Dharmacon Inc). We used HiPerfect (Qiagen) reagent for transfection of cells with specific siRNAs and we followed the protocol provided by the manufacturer to silence specific genes in suspension cells. For lanes marked mock, a non-specific siRNA (against GFP) was used. The general efficiency of silencing obtained was 70-90%.

Supplementary Figure S3-5: Signaling events downstream of BCR following depletion of specific intermediates

Figure S3

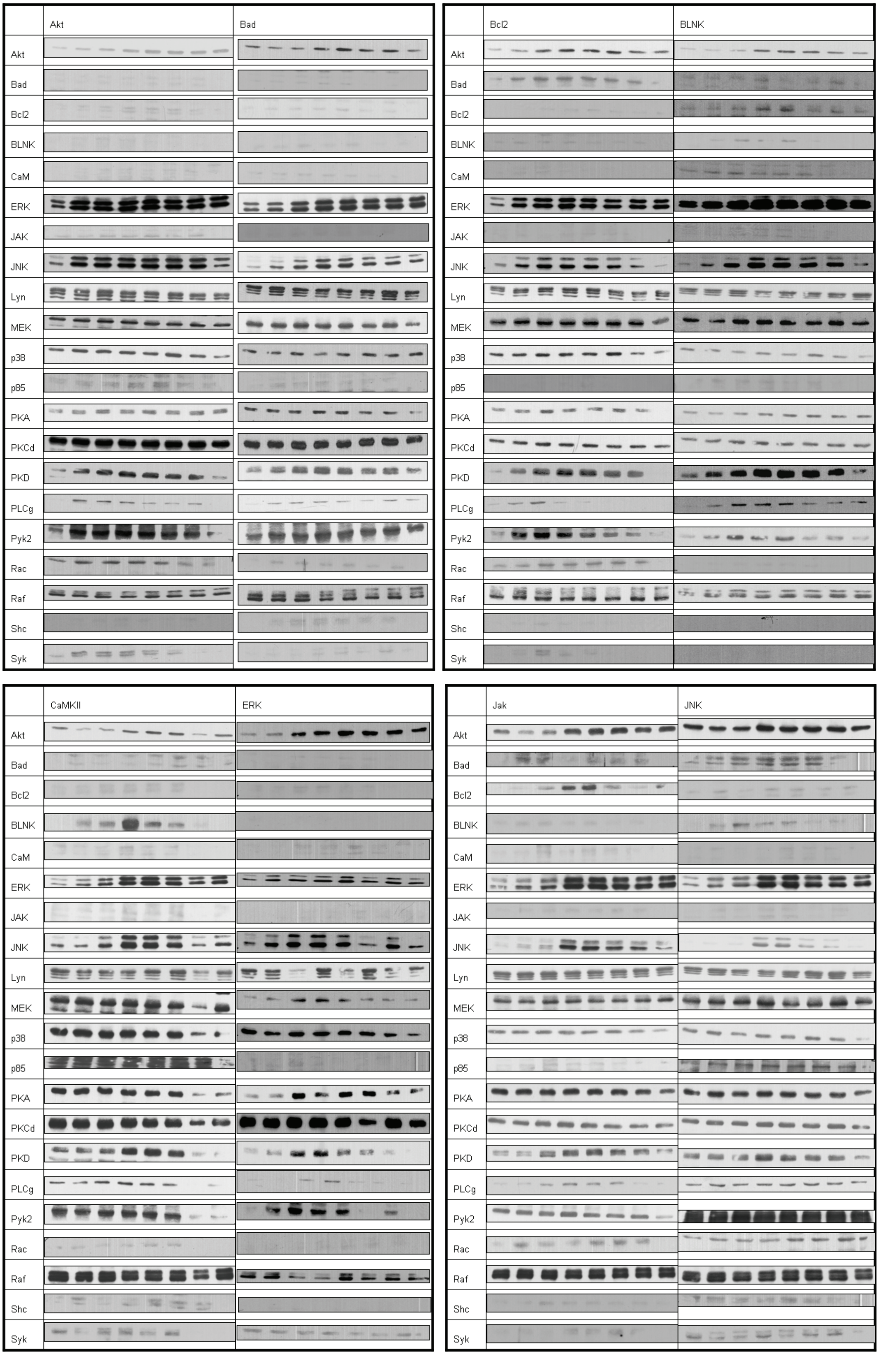


Figure S4

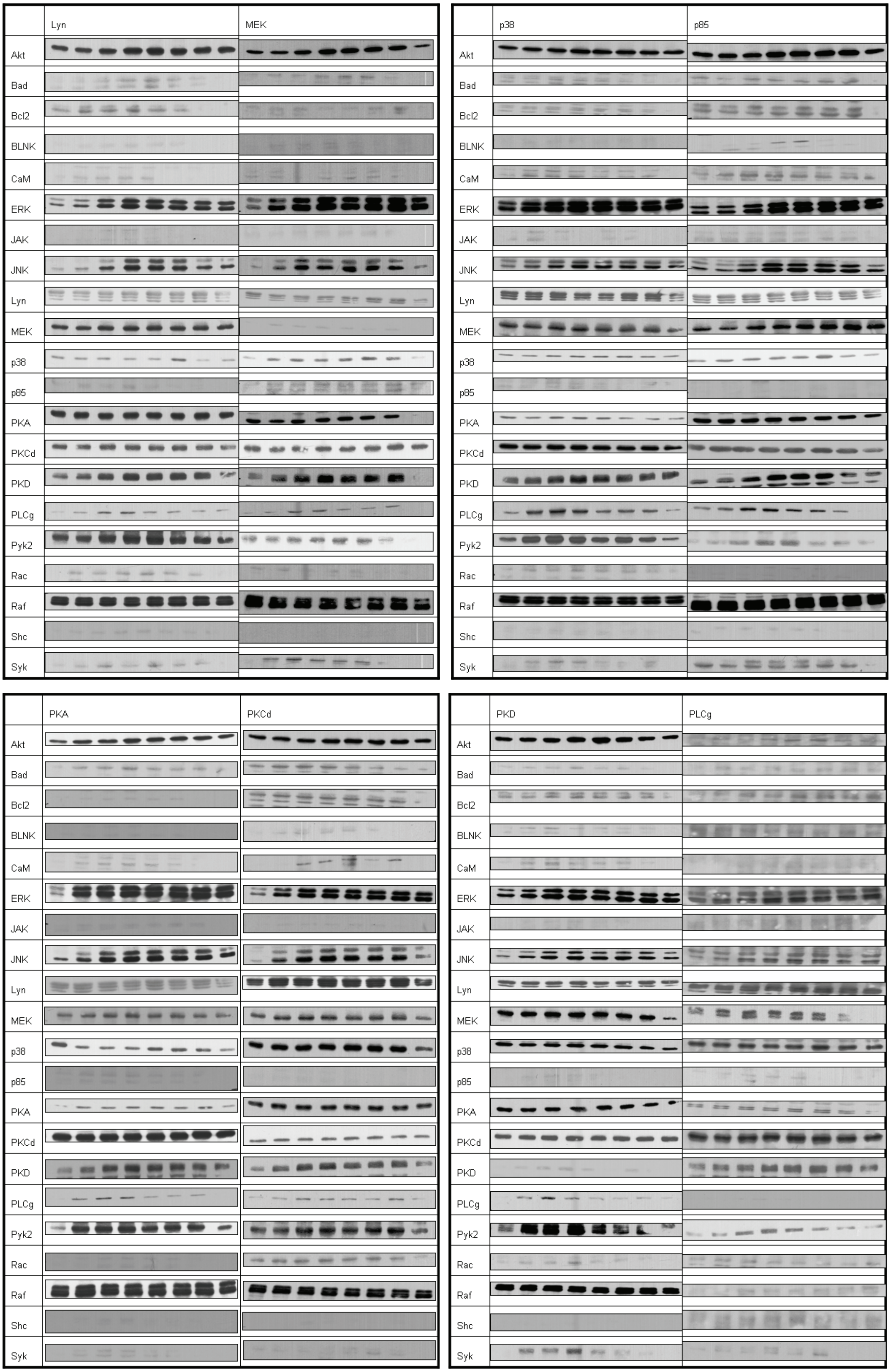
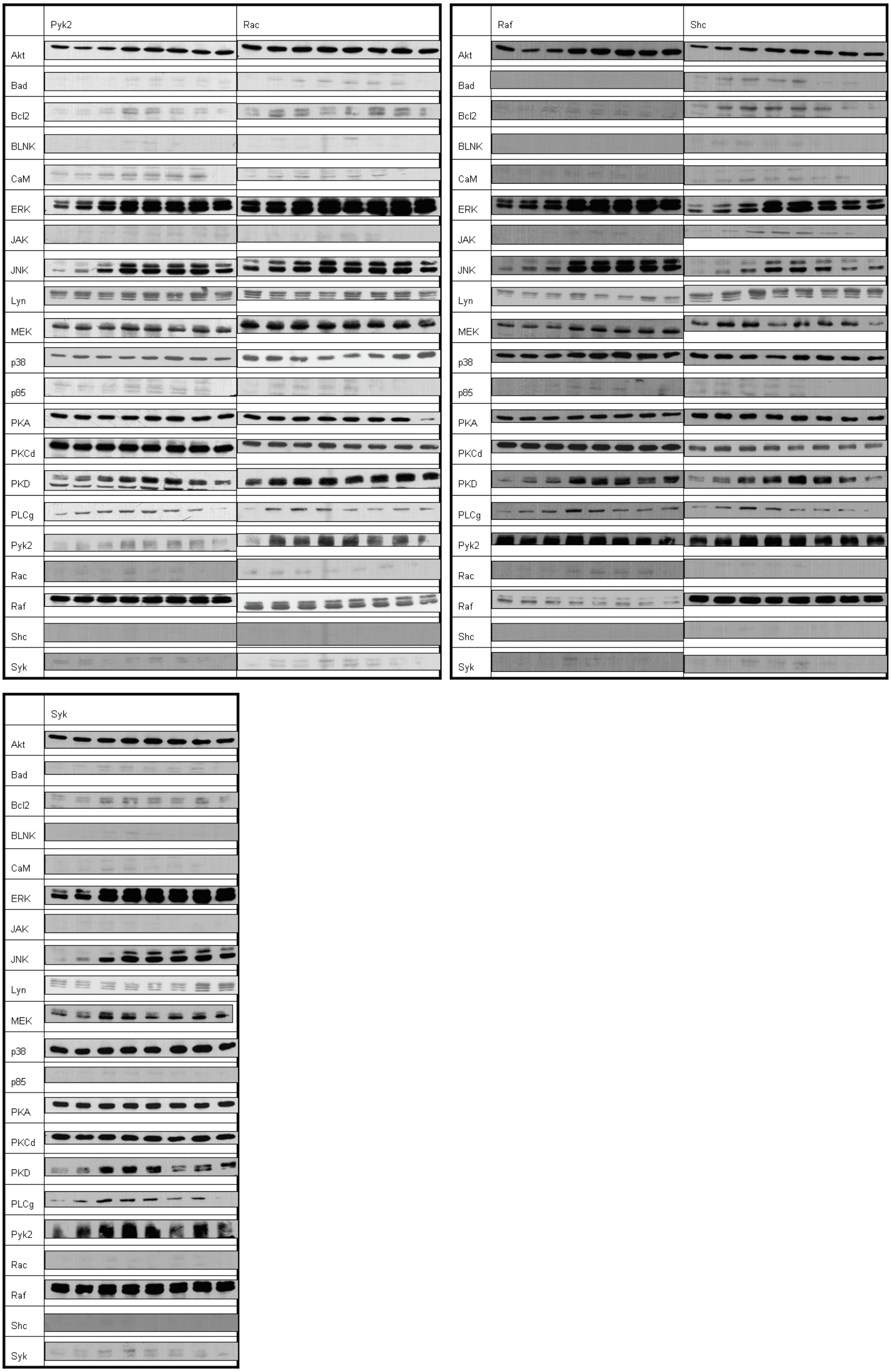

Lyn
MEK
p38
p85
PKA
PKCd
PKD
PLCg
Akt
Bad
Bcl2
BLNK
CaM
ERK
JAK
JNK
Lyn
MEK
p38
p85
PKA
PKCd
PKD
PLCg
Pyk2
Rac
Raf
Shc
Syk

Figure S5



Pyk2
Rac
Akt
Bad
Bcl2
BLNK
CaM
ERK
JAK
JNK
Lyn
MEK
p38
p85
PKA
PKCd
PKD
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Pyk2
Rac
Raf
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Syk
Akt
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Bcl2
BLNK
CaM
ERK
JAK
JNK
Lyn
MEK
p38
p85
PKA
PKCd
PKD
PLCg
Pyk2
Rac
Raf
Shc
Syk

Original scans of Western blots for phosphorylated signaling molecules under all the twenty-one siRNA conditions obtained are shown here. These blots are directly copied from Imagequant. There are a few cases where bands cannot be visualized by the naked eye, due to inhibition in phosphorylation of that molecule. Even in such cases, however, the high sensitivity and resolution of Imagequant allowed for quantitation. In all these latter instances, we confirmed the inhibition of phosphorylation by immunoblotting for the corresponding protein molecule in the same blot, after stripping (following the exact protocol recommended by Cell Signaling Technologies, data not shown). In some instances we also observed phosphorylation of the siRNA-targeted molecule, although these levels very low in comparison with the mock siRNA-treated group. In such cases the basal phosphorylation of that molecule in the siRNA treated group was generally assumed to represent 25% of that obtained for the mock siRNA-treated group, based on the range of silencing observed for the various molecules in Supplementary Figure S2.

Supplementary Table S6: List of antibodies used and their target specificities

S.No.	Molecule	Phosphorylation Site	References
1	Akt	Ser473	Franke, T. F. (1997) Cell 88, 435-437
			Burgering,B.T. and Coffer,P.J.(1995) Nature 376,599-602
2	Bad	Ser112	Yang,E. et al.(1995) Cell 80,285-291
			Zha,J.et al.(1996) Cell 87,619-628
3	Bcl2	Ser70	Murphy,K.M. et al.(2000) Cel death differ.7,102-111
			Zhu,L.et al.(1999) J.Biol.Chem.274,33267-33273
4	Blnk	Tyr96	Kurosaki, T. and Tsukada, S. (2000) *Imı*
			Fu, C. et al. (1998) *Immunity* 9, 93-103.
5	CamKll	Thr286	Hughes,K. et al. (2001) J.Biol.Chem.276,36008-36013
			Barria,A..et al(1997) Science276,2042-2045
6	ERK	Thr202/Tyr204	Marshal,C.J.(1995) cell80,179-185
			Hunter,T.(1995) Cell 80,225-236
7	Jak1	Tyr1022/1023	Leonard,W.J. and O'Shea,J.J.(1998) Annu.Rev.Immunol.16,293-332
			Darnell,J.E.(1997) Science277,1630-1635
8	Jnk	Thr183/Tyr185	Davis,R.J.(1999)Biochem.Soc.Symp.64,1-12
			Ichijo,H.(1999) Oncogene 18,6087-6093
9	Lyn	Tyr416	Hunter,T. (1987) *Cell* 49, 1-4
			Yamanshi,Y.et al.(1991) Science251,192-194
10	Mek1/2	Ser217/221	Crews,C.M.et al. (1992) Science258,478-480
			Alessi,D.R.et al.(1994) EMBO J.13,1610-1619
11	p38	Thr180/Tyr182	Han,J.et al. (1994) Science265,808-811
			Lee,J.C.et al.(1994) Nature372,739-746
12	p85	Tyr 508	Hayashi et al.(1991) Bioche J. 280, 769-775
			Kavanaug et al.(1992) Mol. Cell Bio.12, 3415-3424
13	PKA C	Thr197	Montminy,M.(1997) Annu.Rev.Biochem.66,807-822
			Dell'Acqua,M.L. and Scott,J.I (1997)J.Biol.Chem.272,12881-12884
14	PKCd	Thr505	Nishizuka,Y.(1984) nature 308,693-698
			Keranen,L.M.(1995) Curr.Biol.5,1394-1403
15	PKD	Ser744/748	Nishizuka,Y.(1984) Nature 308,693-698
			Keranen,L.M.(1995) Curr.Biol.5,1394-1403
16	Plcg2	Tyr1217	Singer, W. D. et al. (1997) *Annu. Rev. Biochem.* 66, 475-509.
			Smrcka, A. V. et al. (1991) *Science* 251, 804-807.
17	Pyk2	Tyr402	Avarham,S.et al.(1995) J.Biol.Chem.270,27742-27751
			Lev,S. et al.(1995) Nature376,737-745
18	Rac1	Ser71	Kwon,T.etal.(2000) J.Biol.Chem.275,423-428
19	Raf	Ser259	Avruch,J.et al.(1994) Trends Biochem.Sci.19,279-283
			Chong,H.et al.(2001) EMBO J.20,3716-3727
20	Shc	Tyr317	Pellici,G.et al.(1992 Cell 70,93-104
			Migliacciao,E.et al.(1997) EMBO J.16,706-716
21	Syk	Tyr352	Gunterman, C. and Alexander, D.R. (2002) *J. Immunol.* 168, 4420-4429
			Shade, A. E. and Levine, A.D. (2002) *J. Immunol* 168,2233-2239.

All the phospho-specific antibodies used in the present study were from Cell Signaling Technologies. The target phosphorylation sites were selected from information available in the literature, and were based on the fact that phosphorylations at these sites have been implicated in the activation/ altered functioning of the corresponding molecule. The table lists the specific antibodies used, along with the relevant references.

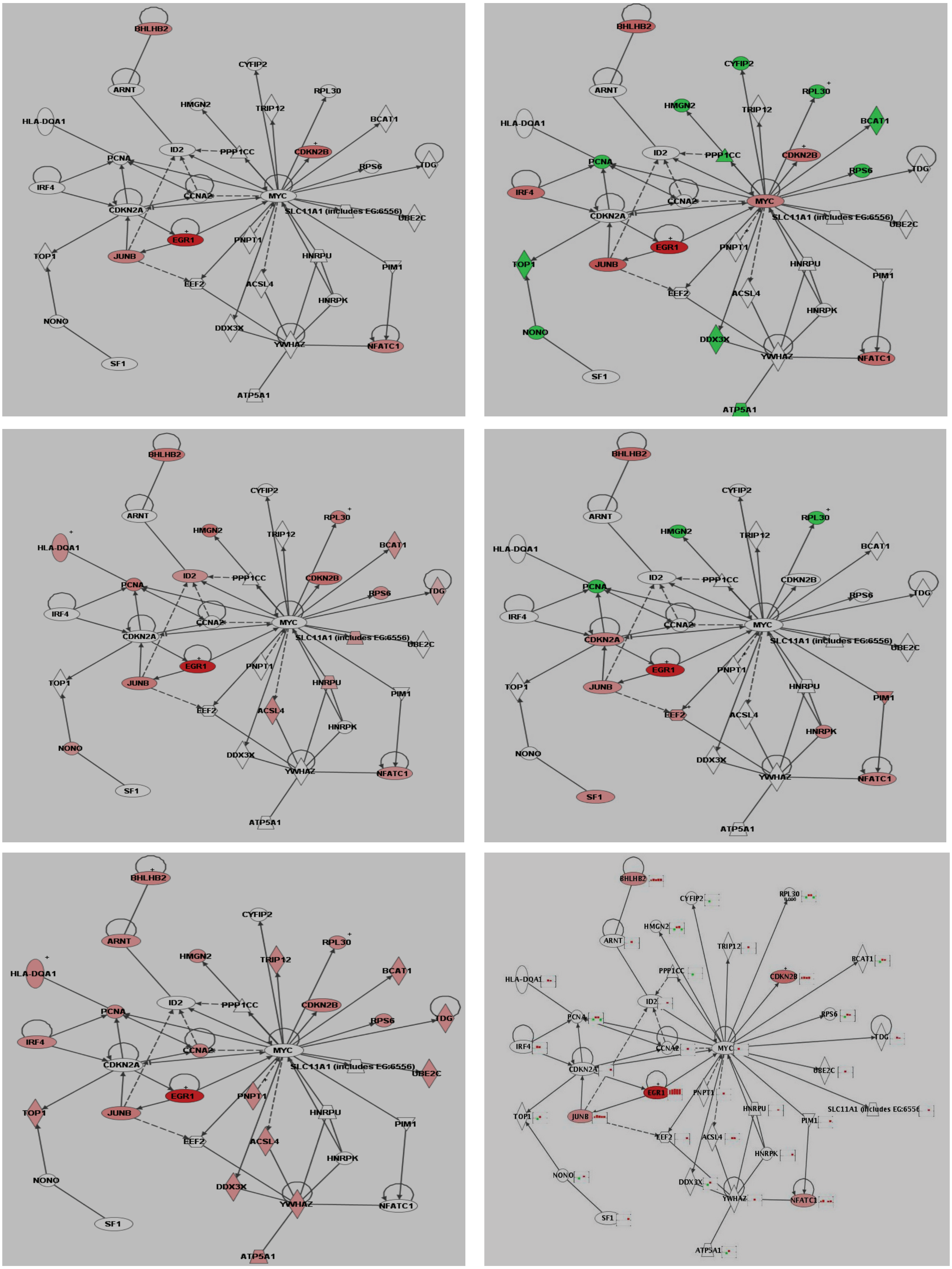
Supplementary Table S7: Microarray profiling of gene expression in cells depleted of select signaling intermediates

Gene	Nor	CaMKII	PKCd	PLCg	Pyk2
"Egr1"	2.8	3.0	3.1	2.8	3.0
"Egr2"	1.9	2.1	2.1	1.8	2.2
"Nfkbiz"	1.8	1.8	1.5	1.9	1.6
"Cd83"	1.8	2.0	1.4	1.8	1.6
"Traf1"	1.5	1.4	1.1	1.4	1.1
"Fos"	1.4	1.4	0.0	1.0	1.4
"4930431E	1.5	1.3	1.0	1.4	1.3
"Il4i1"	1.4	1.4	1.0	1.5	1.1
"Tnfaip3"	1.3	1.6	1.3	1.3	1.3
"Nfkbia"	1.0	2.1	1.5	1.1	1.2
"Cdkn2b"	1.3	1.3	1.1	1.2	0.0
"BC02453	1.3	0.8	0.0	1.0	1.3
"AY07806	1.1	1.2	0.0	1.2	1.2
"Bhlhb2"	1.0	1.2	1.1	1.3	1.3
"Cd69"	1.2	1.1	0.0	0.0	1.1
"Mmp10"	1.0	0.0	0.0	0.0	0.0
"Nfatc1"	1.0	0.9	0.0	1.2	1.0
"Pbef1"	1.0	1.0	1.0	0.0	0.0
"Junb"	1.0	1.1	1.2	1.5	1.0
"LOC3811	1.0	0.9	0.0	1.3	1.1
"Nfkbie"	1.0	0.0	0.0	0.0	0.0
"Irf4"	0.0	0.0	1.0	1.2	0.0
"Myc"	0.0	0.0	0.0	1.0	0.0
"Dusp2"	0.0	1.1	1.0	1.0	0.0
"Rabgef1"	0.0	0.0	0.0	1.0	0.0
"Gdap10"	0.0	1.2	1.0	1.0	1.1
"LOC2447	0.0	0.9	1.0	-1.0	0.0
"LOC2417	0.0	0.9	0.0	-1.0	0.0
"Cct5"	0.0	0.7	0.0	-1.0	0.0
"LOC2147	0.0	0.9	1.0	-1.0	0.0
"Atp5a1"	0.0	0.0	1.0	-1.0	0.0
"Ddx3x"	0.0	0.0	1.0	-1.0	0.0
"Mdh2"	0.0	0.9	0.0	-1.0	0.0
"LOC3845	0.0	0.0	1.0	-1.0	0.0
"Ureb1"	0.0	0.0	0.0	-1.0	0.0
"2610041F	0.0	0.0	0.0	-1.0	0.0
"Abcd3"	0.0	0.0	0.0	-1.0	0.0
"H3f3a"	0.0	0.0	0.0	-1.0	0.0
"Hnrpa2b1	0.0	0.6	1.0	-1.0	0.0
"Dld"	0.0	0.0	1.0	-1.0	0.0
"Ndufb4"	0.0	1.0	0.0	-1.0	0.0
"Mrpl13"	0.0	0.0	0.0	-1.0	0.0
"Ctss"	0.0	0.0	0.0	-1.0	0.0
"Kpna3"	0.0	0.0	0.0	-1.0	0.0
"Hspa5"	0.0	1.2	1.0	-1.0	0.0
"1810030A	0.0	0.0	1.0	-1.0	0.0
"Calm2"	0.0	0.8	1.0	-1.0	0.0
"Cryzl1"	0.0	0.0	0.0	-1.0	0.0
"Usmg5"	0.0	1.1	1.0	-1.0	0.0
"Igk-V1"	0.0	1.0	1.0	-1.0	0.0
"Bcat1"	0.0	0.9	1.0	-1.0	0.0
"Ube2e1"	0.0	0.0	1.0	-1.0	0.0
"Fin14"	0.0	0.8	1.0	-1.0	0.0
"Hmgb1"	0.0	1.1	1.0	-1.0	-1.0
"Ppp1cc"	0.0	0.0	0.0	-1.0	0.0
"Ndufa5"	0.0	0.7	0.0	-1.0	0.0
"Cspg6"	0.0	0.0	1.0	-1.0	0.0
"Rps6"	0.0	0.9	1.0	-1.0	0.0
"Prg"	0.0	1.4	1.0	-1.0	0.0
"Eif4g2"	0.0	0.8	1.0	-1.0	0.0
"Nono"	0.0	0.8	0.0	-1.0	0.0
"Cyfip2"	0.0	0.0	0.0	-1.0	0.0
"LOC2804	0.0	0.6	0.0	-1.0	0.0
"Anp32a"	0.0	0.0	0.0	-1.0	0.0
"Ndufb5"	0.0	0.8	0.0	-1.0	0.0
"Slc25a4"	0.0	1.0	1.0	-1.0	0.0
"D11Ertd6	0.0	0.0	0.0	-1.0	0.0
"Vbp1"	0.0	0.0	0.0	-1.0	0.0
"Psmd14"	0.0	0	0.0	-1.0	0.0
"Atp5l"	0.0	1.1	1.0	-1.0	0.0
"Slc3a2"	0.0	1.0	1.0	-1.0	-1.2
"Vdac3"	0.0	0.8	1.0	-1.0	-1.2
"1110005A	0.0	0.0	1.0	-1.0	0.0
"Stmn1"	0.0	0.8	0.0	-1.0	0.0
"Atp5k"	0.0	1.3	1.0	-1.0	0.0
"Hmgn2"	0.0	1.2	1.0	-1.0	-1.1
"Top1"	0.0	0.0	1.0	-1.0	0.0
"Pcna"	0.0	1.1	1.0	-1.0	-1.4
"Rpl30"	0.0	1.1	1.0	-1.0	-1.0
"LOC2358	0.0	0.0	0.0	-1.0	0.0
"mt-Nd4l"	0.0	0.9	1.0	-1.0	-1.0
"AY07806	0.0	0.0	1.2	0.0	0.0
"Cox7b"	0.0	0.9	1.0	0.0	0.0
"Tdg"	0.0	0.6	1.0	0.0	0.0
"Twistnb"	0.0	0.0	1.0	0.0	0.0
"H2-Aa"	0.0	0.9	1.0	0.0	0.0
"Rpo1-3"	0.0	0.0	1.0	0.0	0.0
"Map2k1"	0.0	0.0	1.0	0.0	0.0
"Pnpt1"	0.0	0.0	1.0	0.0	0.0

Gene	Nor	CaMKII	PKCd	PLCg	Pyk2
"Clta"	0.0	0.9	1.0	0.0	0.0
"A530089I	0.0	0.0	1.0	0.0	0.0
"1810011C	0.0	0.8	1.0	0.0	0.0
"Strn3"	0.0	0.7	1.0	0.0	0.0
"Idi1"	0.0	0.8	1.0	0.0	0.0
"AA959742	0.0	0.8	1.0	0.0	0.0
"Ccrn4l"	0.0	0.0	1.0	0.0	0.0
"Ssfa1"	0.0	0.6	1.0	0.0	0.0
"BC02388	0.0	0.7	1.0	0.0	0.0
"Ccna2"	0.0	0.0	1.0	0.0	0.0
"Acsl4"	0.0	1.0	1.0	0.0	0.0
"2900064A	0.0	0.8	1.0	0.0	0.0
"Ywhaz"	0.0	0.0	1.0	0.0	0.0
"Ube2c"	0.0	0.0	1.0	0.0	0.0
"Ndufv2"	0.0	0.7	1.0	0.0	0.0
"Snx5"	0.0	0.9	1.0	0.0	0.0
"Sdfr1"	0.0	0.7	1.0	0.0	0.0
"E130112E	0.0	0.9	1.0	0.0	0.0
"Morf4l1"	0.0	0.0	1.0	0.0	0.0
"Paip2"	0.0	0.0	1.0	0.0	0.0
"Nup88"	0.0	1.0	1.0	0.0	-1.1
"Rbm14"	0.0	0.9	1.0	0.0	0.0
"Arnt"	0.0	0.0	1.0	0.0	0.0
"1110017C	0.0	0.8	1.0	0.0	0.0
"Ga17"	0.0	0.8	1.0	0.0	0.0
"Adrbk1"	0.0	0.0	1.0	0.0	0.0
"Trip12"	0.0	0.0	1.0	0.0	0.0
"LOC2365	0.0	0.8	1.0	0.0	0.0
"Ddx39"	0.0	0.8	1.0	0.0	0.0
"Bmyc"	0.0	0.0	1.0	0.0	0.0
"LOC2346	0.0	0.0	1.0	0.0	0.0
"Cd24a"	0.0	0.7	1.0	0.0	0.0
"LOC3820	0.0	0.9	1.0	0.0	0.0
"LOC2076	0.0	0.0	1.0	0.0	0.0
"LOC3812	0.0	1.0	1.0	0.0	0.0
"Eif3s8"	0.0	0.8	1.0	0.0	0.0
"LOC3865	0.0	0.0	1.0	0.0	0.0
"LOC3818	0.0	0.0	1.0	0.0	0.0
"Cdk5r1"	0.0	1.1	0.0	0.0	0.0
"Rpl36al"	0.0	0.9	0.0	0.0	0.0
"Tuba1"	0.0	0.9	0.0	0.0	0.0
"LOC3815	0.0	0.8	0.0	0.0	0.0
"2610511C	0.0	0.8	0.0	0.0	0.0
"LOC2456	0.0	0.7	0.0	0.0	0.0
"2900010J	0.0	0.8	0.0	0.0	0.0
"2610205H	0.0	0.8	0.0	0.0	0.0
"Hnrpu"	0.0	0.7	0.0	0.0	0.0
"Hprt"	0.0	0.8	0.0	0.0	0.0
"3300001M	0.0	0.7	0.0	0.0	0.0
"Idb2"	0.0	0.8	0.0	0.0	0.0
"Slc11a1"	0.0	0.7	0.0	0.0	0.0
"Thy28"	0.0	0.8	0.0	0.0	0.0
"Copb1"	0.0	0.7	0.0	0.0	0.0
"3110001N	0.0	0.7	0.0	0.0	0.0
"Gnb2-rs1	0.0	0.7	0.0	0.0	0.0
"D11Moh3	0.0	0.8	0.0	0.0	0.0
"Slc15a3"	0.0	0.7	0.0	0.0	0.0
"Smu1"	0.0	0.7	0.0	0.0	0.0
"D19Ertd7	0.0	0.7	0.0	0.0	0.0
"Birc3"	0.0	0.7	0.0	0.0	0.0
"LOC3850	0.0	0.0	0.0	0.0	1.8
"Prpf8"	0.0	0.0	0.0	0.0	1.2
"2610510D	0.0	0.0	0.0	0.0	1.2
"LOC3850	0.0	0.0	0.0	0.0	1.2
"Olfr887"	0.0	0.0	0.0	0.0	1.6
"Pigt"	0.0	0.0	0.0	0.0	1.1
"Slc16a6"	0.0	0.0	0.0	0.0	1.0
"Blr1"	0.0	0.0	0.0	0.0	1.1
"Ube4a"	0.0	0.0	0.0	0.0	1.1
"Got2"	0.0	0.0	0.0	0.0	1.1
"LOC3860	0.0	0.0	0.0	0.0	1.0
"Bcl2l1"	0.0	0.0	0.0	0.0	1.0
"Pim1"	0.0	0.0	0.0	0.0	1.1
"Eef2"	0.0	0.0	0.0	0.0	1.0
"Slc4a7"	0.0	0.0	0.0	0.0	3.0
"2610305J	0.0	0.0	0.0	0.0	1.0
"Csnk2a1-	0.0	0.0	0.0	0.0	1.0
"Ide"	0.0	0.0	0.0	0.0	1.0
"Vars2"	0.0	0.0	0.0	0.0	1.0
"Raly"	0.0	0.0	0.0	0.0	1.0
"Zfp162"	0.0	0.0	0.0	0.0	1.0
"Hnrpk"	0.0	0.0	0.0	0.0	1.0
"Fosb"	0.0	0.0	0.0	0.0	1.0
"LOC3821	0.0	0.0	0.0	0.0	1.0
"Cdkn2a"	0.0	0.0	0.0	0.0	1.0
"Insig1"	0.0	0.0	0.0	0.0	1.0
"1810008K	0.0	0.0	0.0	0.0	-1.0

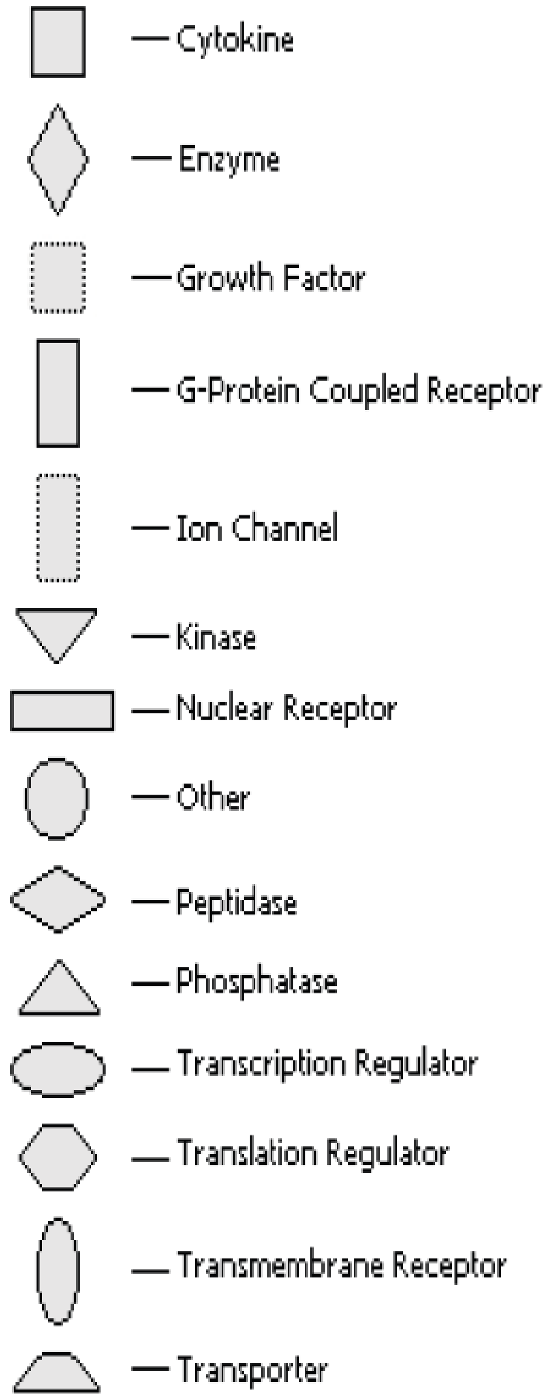
The table here shows comparative expression levels of genes regulated, in an anti-IgG-dependent manner, under the various siRNA treatment conditions indicated. Only changes of the order of at least 2-fold in all the three individual experiments are shown here, with a 2-fold variation being quantified as 1.

Supplementary Figure S8: Alteration in signal processing influence the structure of gene regulatory netwpork



We illustrate here how the perturbation-induced alterations in gene expression affect the Myc-centric gene regulatory module identified as the most significant by an IPA analysis. Those genes that are common between the components of this Myc-centric network and our gene list are marked in bold. Upregulated genes are marked in red, whereas the downregulated ones are in green. The first five networks shown (from left to right and starting from the top set of panels) correspond to results from cells treated either with mock, CaMKII, PKCδ, PLCγ, or Pyk2 specific siRNA respectively. The last panel (i.e. lower right panel) presents a summary of the comparative regulation of these Myc-centric network constituents, under these various perturbation conditions (depicted in the form of either red or green bars). The symbol code describing the role of each of the nodes of the network is listed in Supplementary Figure S9.

Supplementary Figure S9. Key for IPA network shown in Supplementary Figure S8.



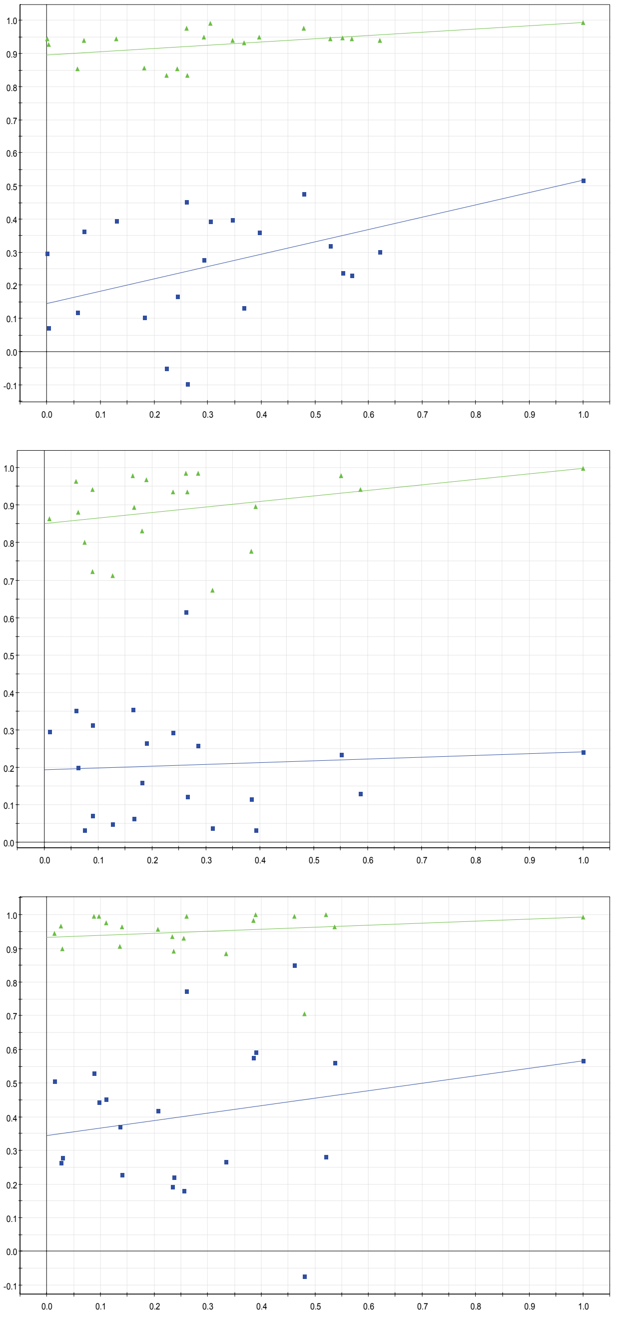
Supplementary Table S10: VIP list for all the three responses along with their VIP values

Apoptosis		Proliferation		Cytokine secretion	
Var ID (Primary)	**M1.VIP[3]**	**Var ID (Primary)**	**M2.VIP[7]**	**Var ID (Primary)**	**M3.VIP[1]**
Smax/TmaxMEK	2.46514	**Smax/Tmaxp85**	1.91071	**Smax/TmaxRaf**	2.28487
AreaPKA	2.0061	**decay rateCamKII**	1.79613	**Smax/Tmaxbad**	1.88832
Smax/Tmax akt	1.73551	**Smax/TmaxBLNK**	1.73539	**Smax/Tmaxp85**	1.7457
decay rateBLNK	1.59498	**Smax/TmaxERK**	1.51895	**AreaMEK**	1.695
Smax/TmaxERK	1.48704	**Smax/TmaxCamKII**	1.49441	**decay rateRaf**	1.66106
Smax/Tmaxbad	1.44208	**Smax/TmaxJAK**	1.47289	**Smax/TmaxShc**	1.50897
Smax/TmaxSyk	1.41977	**AreaSyk**	1.40183	**decay rateCamKII**	1.4791
AreaMEK	1.3776	**AreaCamKII**	1.36675	**decay rateBcl2**	1.43936
Smax/TmaxPKD	1.34317	**Smax/TmaxMEK**	1.3282	**decay rateMEK**	1.43019
decay ratep38	1.31144	**AreaMEK**	1.27702	**AreaAkt**	1.41659
AreaSyk	1.22515	**decay rateBLNK**	1.26634	**AreaBLNK**	1.41098
decay rateMEK	1.21238	**decay rateSyk**	1.26202	**decay rateShc**	1.38739
AreaPKCd	1.20422	**AreaRac**	1.14695	**AreaPKCd**	1.313
AreaCamKII	1.19413	**AreaPKA**	1.11748	**Smax/TmaxCamKII**	1.28783
decay rateSyk	1.13659	**decay rateMEK**	1.11396	**AreaBcl2**	1.20298
Smax/TmaxPLCg	1.12537	**AreaAkt**	1.08479	**Smax/TmaxBLNK**	1.19394
decay rateBcl2	1.11287	**Smax/TmaxRaf**	1.07696	**AreaRaf**	1.17237
Smax/TmaxJAK	1.07853	**Smax/Tmax akt**	1.07518	**AreaERK**	1.16452
AreaPKD	1.02025	**Smax/TmaxPKCd**	1.06619	**decay rateakt**	1.11286

Apoptosis		Proliferation		Cytokine secretion	
AreaBcl2	0.999468	**decay ratePKCd**	1.06018	**Area Bad**	1.09796
Smax/TmaxCamKII	0.988285	**decay rateLyn**	1.02981	**AreaShc**	1.09017
Smax/TmaxRac	0.985342	**decay ratePKD**	1.02105	**AreaSyk**	1.08216
AreaBLNK	0.952724	**AreaRaf**	1.01305	**Smax/Tmaxp38**	1.07873
Smax/TmaxBcl2	0.940998	**decay rateERK**	1.00817	**Smax/TmaxMEK**	1.00652
Smax/TmaxPKCd	0.922208	**decay ratePLCg**	0.993274	**Smax/TmaxSyk**	1.00007
Smax/TmaxShc	0.907987	**decay rateRaf**	0.967541	**decay ratePLCg**	0.988653
Smax/Tmaxp85	0.901258	**decay rateBcl2**	0.962886	**Smax/TmaxPKD**	0.954391
decay rateRaf	0.888888	**Smax/TmaxPyk2**	0.942134	**Smax/TmaxLyn**	0.932847
decay ratePKCd	0.876847	**AreaBcl2**	0.902031	**Smax/TmaxJAK**	0.930831
decay rateRac	0.870724	**Smax/TmaxBcl2**	0.887065	**AreaJAK**	0.91249
decay rateERK	0.869312	**decay ratep38**	0.876692	**Smax/Tmax akt**	0.899781
AreaAkt	0.85503	**Smax/Tmaxbad**	0.86887	**Smax/TmaxPyk2**	0.85852
Smax/TmaxBLNK	0.851156	**AreaPyk2**	0.862688	**AreaRac**	0.8389
Smax/TmaxJNK	0.850748	**Smax/TmaxShc**	0.861903	**decay rateERK**	0.822477
AreaRaf	0.842655	**Smax/TmaxSyk**	0.853338	**Smax/TmaxPLCg**	0.81799
AreaShc	0.833707	**AreaBLNK**	0.842106	**Smax/TmaxRac**	0.806834
Smax/TmaxRaf	0.819634	**AreaShc**	0.84128	**decay ratebad**	0.779393
AreaLyn	0.812357	**decay rateRac**	0.839855	**decay rateSyk**	0.762727
decay rateCamKII	0.787011	**decay ratePyk2**	0.797702	**AreaLyn**	0.687019

Apoptosis		Proliferation		Cytokine secretion	
AreaPLCg	0.754718	**Smax/TmaxPKD**	0.792058	**AreaPLCg**	0.666127
decay ratep85	0.73908	**decay ratePKA**	0.782491	**AreaCamKII**	0.65298
decay rateakt	0.72693	**AreaJAK**	0.781392	**decay ratep38**	0.638816
decay rateJAK	0.699494	**Smax/TmaxPKA**	0.775035	**AreaPKD**	0.603419
Areap38	0.69606	**decay rateJNK**	0.771048	**decay rateRac**	0.516565
AreaPyk2	0.620268	**AreaPKD**	0.746455	**decay rateJAK**	0.508252
decay rateLyn	0.611024	**AreaPKCd**	0.740828	**decay rateBLNK**	0.442473
Area Bad	0.605801	**Smax/Tmaxp38**	0.709896	**Smax/TmaxJNK**	0.435443
decay ratePKA	0.603995	**Area Bad**	0.708291	**AreaPyk2**	0.413686
AreaERK	0.600833	**Smax/TmaxRac**	0.698323	**Areap85**	0.413675
Smax/TmaxPyk2	0.584471	**Smax/TmaxPLCg**	0.69535	**decay ratePKD**	0.388072
decay rateJNK	0.583417	**Areap38**	0.694877	**Smax/TmaxERK**	0.363997
Smax/TmaxPKA	0.575646	**decay rateJAK**	0.682896	**decay rateJNK**	0.339172
decay ratePyk2	0.540636	**AreaJNK**	0.6772	**decay ratePKCd**	0.278977
decay ratePKD	0.512131	**Smax/TmaxLyn**	0.661155	**Areap38**	0.275552
decay ratePLCg	0.489846	**decay rateakt**	0.65388	**decay ratep85**	0.256031
AreaJAK	0.482896	**AreaERK**	0.641591	**Smax/TmaxBcl2**	0.220635
Smax/Tmaxp38	0.479144	**decay ratebad**	0.576052	**decay ratePyk2**	0.218541
decay rateShc	0.463192	**AreaPLCg**	0.561519	**AreaPKA**	0.207535
Smax/TmaxLyn	0.460903	**decay rateShc**	0.547926	**decay rateLyn**	0.140969
decay ratebad	0.460344	**decay ratep85**	0.454097	**Smax/TmaxPKCd**	0.12487
Areap85	0.444229	**Areap85**	0.446812	**Smax/TmaxPKA**	0.08231
AreaRac	0.440532	**AreaLyn**	0.395717	**decay ratePKA**	0.058141
AreaJNK	0.401657	**Smax/TmaxJNK**	0.339772	**AreaJNK**	0.008071

Supplementary Figure S11: Cross validation of perfect specificity in the model



Each plot represents the cross validation by iteratively retraining the model parameters and then plotting the Q2 regression line. The plots clearly show that the model becomes invalid (since Q2 regression line never makes an intercept at y axis below zero as in the case of figure 3D) when perfect specificity is assumed due to lack of variability. As a result, no meaningful information is captured by the PLS model.

Supplementary Table S12: Effect of pharmacological inhibitors on BCR-dependent signaling.

Columns represent phosphorylation profiles of the individual molecules (mentioned at the beginning of each row) in the presence of the indicated pharmacological inhibitor. These values were obtained from Imagequant analysis of the Western blot experiments. One set of data is represented as a normalized profile obtained as described for Supplementary Figure S1 (Attached as separate excel sheet).

Supplementary Table S13: Western Blot Data of all the 21 siRNA condition for each molecule along with replicates (Attached as separate excel sheet).

Supplementary Table S14: Table showing the list of siRNA and antibodies used for this study along with their sources and catalogue numbers.

S. No.	Name of the Molecule	siRNA (Cat No.)	Antibody (Cat No.)
1	Akt1	SC-29196*	SC-1618
2	Bad	SC- 29779	SC-943
3	Bcl2	SC-29215	SC-492
4	BLNK	SC-29811	SC-15345
5	CaMKIIα	SC-29901	SC-9035
6	ERK1/2	SC-29308, SC-35336	SC-94, SC-154
7	Jak1	SC-35720	3332 (Cell Signaling Technology)
8	JNK1	SC-29381	SC-474
9	Lyn	SC-35828	SC-15
10	MEK1/2	SC-35904, SC-35906	SC-219, SC-525
11	p38α	SC-29434	SC-535
12	p85α	SC-36218	SC-1637
13	PKAα	SC-36241	SC-903
14	PKCδ	SC-36246	SC-213
15	PKD	SC-36260	SC-639
16	PLCγ2	SC-36269	SC-407
17	Pyk2	SC-36333	SC-9019
18	Rac1	SC-36352	SC-95
19	Raf1	SC-29463	SC-227
20	Shc	SC-29481	SC-967
21	Syk	M_041084-00 (Dharmacon)	SC-1077

* All reagents from Santa Cruz Biotechnology, except for wherever mentioned otherwise

Supplementary Table S 15: Data of Microarray experiment

A: Mock Transfected
B: PLCγ siRNA
C: PKCδ siRNA
D: CaMKII siRNA
E: Pyk2 siRNA
SLR: Signal Log Ratio

Symbol	Accession	SLR A1 vs AC	SLR A2 vs AC	SLR A3 vs AC	SLR average
"Egr1"	NM_007913.2	2.9	2.8	2.8	2.8
"Egr2"	NM_010118.1	2.1	1.8	1.9	1.9
"Nfkbiz"	NM_030612	1.8	1.7	1.9	1.8
"Cd83"	NM_009856.1	1.7	1.7	1.8	1.8
"Traf1"	NM_009421.2	1.5	1.5	1.5	1.5
"Fos"	NM_010234.2	1.5	1.3	1.3	1.4
"4930431E	XM_207778.3	1.5	1.4	1.6	1.5
"Il4i1"	NM_010215.1	1.5	1.4	1.4	1.4
"Tnfaip3"	NM_009397.2	1.5	1.1	1.3	1.3
"Nfkbia"	NM_010907	1.4	0.9	0.7	1.0
"Cdkn2b"	NM_007670.2	1.3	1.3	1.3	1.3
"BC02453	NM_146237	1.3	1.4	1.3	1.3
"AY07806	NM_172142.1	1.1	1.0	1.1	1.1
"Bhlhb2"	NM_011498.2	1.1	0.9	1.0	1.0
"Cd69"	XM_132882.1	1.1	1.3	1.1	1.2
"Mmp10"	NM_019471.1	1.0	1.0	1.0	1.0
"Nfatc1"	NM_016791.2	1.0	0.9	1.0	1.0
"Pbef1"	NM_021524.1	1.0	0.8	1.0	0.9
"Junb"	NM_008416.1	1.0	0.9	1.1	1.0
"LOC3811	XM_355056.1	1.0	1.0	1.1	1.0
"Nfkbie"	NM_008690.2	0.8	0.9	1.0	0.9
"Pcna"	NM_011045.1	0.1	-1.0	-1.1	-0.7
"Cd24a"	NM_009846.1	-0.1	-0.8	-1.0	-0.7
"Slc3a2"	NM_008577.2	-0.2	-1.1	-1.2	-0.8
"2610041F	NM_198008.1	-0.3	-0.9	-1.0	-0.8
"LOC2346	XM_125126.3	-0.6	-0.7	-1.0	-0.8
"mt-Nd5"		-1.2	-0.7	-1.2	-1.0

Symbol	Accession	SLR B1 vs BC	SLR B2 vs BC	SLR B3 vs BC	SLR B3 re	SLR average
"Egr1"	NM_007913.2	2.9	2.8	3.1	2.8	2.9
"Nfkbiz"	NM_030612	1.7	1.6	1.7	1.5	1.6
"Egr2"	NM_010118.1	1.7	1.7	1.8	1.5	1.7
"Cd83"	NM_009856.1	1.6	1.4	1.3	1.5	1.4
"Junb"	NM_008416.1	1.4	1.1	1.4	1.3	1.3
"Traf1"	NM_009421.2	1.4	1.4	1.5	1.5	1.5
"Il4i1"	NM_010215.1	1.3	1.3	0.9	1.1	1.2
"4930431E	XM_207778.3	1.3	1.3	1.2	1.3	1.3
"Tnfaip3"	NM_009397.2	1.3	1.3	1.3	1.1	1.2
"BC02453	NM_146237	1.3	0.9	0.4	0.9	0.9
"LOC3811	XM_355056.1	1.2	1.1	1.0	1.0	1.1
"Cdkn2b"	NM_007670.2	1.2	1.0	1.2	1.2	1.1
"Nfkbia"	NM_010907	1.1	0.4	1.4	1.0	1.0
"Irf4"	NM_013674.1	1.1	1.0	1.1	1.2	1.1
"AY07806	NM_172142.1	1.1	1.1	1.0	0.9	1.0
"Myc"	NM_010849.2	1.0	1.0	0.5	0.8	0.8
"Fos"	NM_010234.2	1.0	1.0	0.7	0.9	0.9
"Nfatc1"	NM_016791.2	1.0	0.8	0.9	1.0	0.9
"Bhlhb2"	NM_011498.2	1.0	0.8	1.1	0.9	1.0
"Nfatc1"	NM_016791.2	1.0	0.9	1.1	1.0	1.0
"Dusp2"	NM_010090.2	0.9	1.1	1.1	1.0	1.0
"Rabgef1"	NM_019983.2	0.8	1.0	0.9	0.9	0.9

Symbol	Accession	SLR B1 vs BC	SLR B2 vs BC	SLR B3 vs BC	SLR B3 re	SLR average
"Gdap10"	NM_010268.1	0.5	0.1	1.1	0.4	0.5
"LOC2447	XM_146826.2	-0.2	-1.2	0.1	-0.4	-0.4
"LOC2417	XM_141567.3	-0.3	-1.0	0.0	-0.4	-0.4
"Cct5"	NM_007637.1	-0.4	-1.3	-0.5	-0.5	-0.7
"LOC2147	XM_125109.2	-0.5	-1.0	0.0	-0.5	-0.5
"Atp5a1"	NM_007505.1	-0.5	-1.2	-0.3	-0.6	-0.6
"Ddx3x"	NM_010028	-0.5	-1.0	-0.3	-0.5	-0.6
"Mdh2"	NM_008617.2	-0.5	-1.2	-0.2	-0.5	-0.6
"LOC3845	XM_357690.1	-0.5	-1.2	-0.1	-0.4	-0.5
"Ureb1"	XM_136108	-0.5	-1.0	-0.2	-0.4	-0.5
"2610041F	NM_198008.1	-0.5	-1.0	0.0	-0.6	-0.6
"Abcd3"	NM_008991	-0.5	-1.1	-0.1	-0.4	-0.5
"H3f3a"	NM_008210.2	-0.5	-1.1	-0.1	-0.6	-0.6
"Hnrpa2b1	NM_016806	-0.6	-1.1	-0.3	-0.7	-0.6
"Dld"	NM_007861.2	-0.6	-1.1	0.0	-0.4	-0.5
"Ndufb4"	NM_026610.1	-0.6	-1.1	-0.3	-0.7	-0.7
"Mrpl13"	NM_026759.2	-0.6	-1.0	-0.1	-0.6	-0.6
"Ctss"	NM_021281.1	-0.6	-1.1	-0.1	-0.5	-0.6
"Kpna3"	NM_008466.2	-0.6	-1.1	-0.2	-0.6	-0.6
"Hspa5"	NM_022310.2	-0.6	-1.2	0.0	-0.8	-0.6
"1810030A06Rik"		-0.6	-1.0	0.0	-0.6	-0.5
"Calm2"	NM_007589	-0.6	-1.1	-0.2	-0.5	-0.6
"Cryzl1"	NM_133679.1	-0.6	-1.1	-0.3	-0.6	-0.6
"Usmg5"	XM_123431.1	-0.6	-1.2	-0.4	-0.8	-0.7
"Igk-V1"	XM_355776.1	-0.6	-1.1	-0.1	-0.6	-0.6
"Bcat1"	NM_007532	-0.6	-1.1	-0.3	-0.7	-0.7
"Ube2e1"	NM_009455.2	-0.6	-1.1	-0.1	-0.7	-0.6
"Fin14"		-0.6	-1.1	0.1	-0.7	-0.6
"Hmgb1"	NM_010439.2	-0.6	-1.5	-0.2	-0.7	-0.8
"Ppp1cc"	NM_013636.2	-0.6	-1.2	-0.2	-0.7	-0.7
"Ndufa5"	NM_026614.1	-0.6	-1.0	-0.4	-0.7	-0.7
"Cspg6"	NM_007790.2	-0.7	-1.1	-0.2	-0.6	-0.6
"Rps6"	NM_009096.1	-0.7	-1.2	0.0	-0.5	-0.6
"Prg"	NM_011157.1	-0.7	-1.4	0.1	-0.6	-0.6
"Eif4g2"	NM_013507.2	-0.7	-1.2	-0.2	-0.7	-0.7
"Nono"	NM_023144.1	-0.7	-1.0	-0.4	-0.7	-0.7
"Cyfip2"	XM_147526.1	-0.7	-1.1	-0.1	-0.8	-0.7
"LOC2804	NM_183299	-0.7	-1.3	-0.3	-0.2	-0.6
"Anp32a"	NM_009672.2	-0.7	-1.1	-0.2	-0.7	-0.7
"Ndufb5"	NM_025316.2	-0.7	-1.1	-0.2	-0.5	-0.6
"Slc25a4"	XM_134169.4	-0.7	-1.4	-0.1	-0.7	-0.7
"D11Ertd6	NM_026023.3	-0.7	-1.1	-0.1	-0.6	-0.6
"Vbp1"	NM_011692.1	-0.7	-1.1	-0.4	-0.7	-0.7
"Psmd14"	NM_021526	-0.7	-1.0	-0.4	-0.5	-0.6
"Atp5l"	XM_125157.1	-0.8	-1.4	-0.3	-0.7	-0.8
"Slc3a2"	NM_008577.2	-0.8	-1.3	0.3	-0.6	-0.6
"Vdac3"	NM_011696.1	-0.8	-1.2	0.0	-0.7	-0.7
"1110005A	NM_025364	-0.9	-1.1	-0.6	-0.9	-0.9
"Stmn1"	NM_019641	-0.9	-1.4	-0.5	-0.9	-0.9
"Atp5k"	NM_007507	-0.9	-1.3	-0.1	-1.0	-0.8
"Hmgn2"	NM_016957.2	-1.0	-1.5	-0.5	-0.8	-0.9
"Top1"	NM_009408.1	-1.0	-1.4	-0.4	-1.0	-0.9
"Pcna"	NM_011045.1	-1.0	-1.7	-0.2	-1.2	-1.0
"Rpl30"	NM_009083.2	-1.0	-1.6	-0.3	-0.9	-1.0
"LOC2358	XM_142431.1	-1.1	-1.5	-0.8	-1.3	-1.2
"mt-Nd4l"		-1.3	-1.8	-1.1	-1.6	-1.5

Symbol	Accession	SLR C1 vs CC	SLR C2 vs CC	SLR C3 vs CC	SLR C3re	SLR average
"Egr1"	NM_007913.2	3.1	3.1	3.3	2.9	3.1
"Egr2"	NM_010118.1	2.0	2.1	2.2	2.0	2.1
"Cd83"	NM_009856.1	1.6	1.4	1.2	1.4	1.4
"Nfkbiz"	NM_030612	1.5	1.5	1.2	1.5	1.5
"Il4i1"	NM_010215.1	1.3	0.9	0.7	1.2	1.0
"AY07806	NM_172142.1	1.3	1.2	1.1	1.2	1.2
"Tnfaip3"	NM_009397.2	1.3	1.4	1.4	1.2	1.3
"Junb"	NM_008416.1	1.2	1.1	1.2	1.1	1.2
"4930431E	XM_207778.3	1.2	0.9	0.7	1.3	1.0
"Nfkbia"	NM_010907	1.2	1.7	2.0	0.9	1.5
"Traf1"	NM_009421.2	1.2	1.1	1.0	1.2	1.1
"Irf4"	NM_013674.1	1.0	0.8	0.8	1.1	0.9
"Cdkn2b"	NM_007670.2	1.0	1.1	1.2	1.0	1.1
"Dusp2"	NM_010090.2	1.0	0.8	0.8	1.0	0.9
"Bhlhb2"	NM_011498.2	0.9	1.3	1.1	0.9	1.1
"Gdap10"	NM_010268.1	0.7	1.4	1.5	0.5	1.0
"Cox7b"	NM_025379.1	0.3	0.9	1.1	-0.1	0.6
"Tdg"	NM_172552.1	0.3	0.7	1.2	0.1	0.6
"Twistnb"	NM_172253.1	0.3	0.6	1.1	-0.1	0.5
"Slc3a2"	NM_008577.2	0.2	1.4	1.9	0.0	0.9
"H2-Aa"	NM_010378.2	0.2	0.6	1.1	0.2	0.5
"Rpo1-3"	NM_181730.2	0.2	0.5	1.3	0.1	0.5
"Map2k1"	NM_008927.1	0.2	0.6	1.0	0.0	0.5
"Pnpt1"	NM_027869.1	0.2	0.5	1.1	0.0	0.4
"Clta"	NM_016760.1	0.2	1.0	1.3	0.0	0.6
"A530089I	NM_133999.1	0.2	0.3	1.1	-0.1	0.4
"1810011C	NM_025456.2	0.1	0.7	1.2	0.0	0.5
"Strn3"	NM_052973	0.1	0.8	1.1	0.0	0.5
"Hspa5"	NM_022310.2	0.1	0.9	1.7	-0.2	0.6
"Idi1"	NM_145360	0.1	0.8	1.1	-0.1	0.5
"Rpl30"	NM_009083.2	0.1	0.8	1.4	-0.4	0.5
"Fin14"		0.1	0.9	1.6	-0.1	0.6
"AA95974	NM_133807.1	0.1	0.5	1.1	-0.2	0.4
"Ccrn4l"	NM_009834.1	0.1	0.7	1.0	0.0	0.5
"Ssfa1"	XM_196564.2	0.1	0.9	1.2	-0.1	0.5
"1110005A	NM_025364	0.1	0.9	1.0	0.0	0.5
"BC02388	NM_146159.1	0.1	0.8	1.1	-0.2	0.5
"Ddx3x"	NM_010028	0.0	0.6	1.0	-0.4	0.3
"Ccna2"	NM_009828.1	0.0	0.4	1.0	0.1	0.4
"Acsl4"	NM_207625.1	0.0	1.0	1.1	-0.1	0.5
"2900064A	NM_133749.1	0.0	0.6	1.3	-0.1	0.5
"Calm2"	NM_007589	0.0	0.6	1.3	-0.4	0.4
"Ywhaz"	NM_011740.2	0.0	0.5	1.2	-0.1	0.4
"Prg"	NM_011157.1	0.0	1.1	1.7	-0.1	0.7
"Ube2c"	NM_026785.1	0.0	0.1	1.0	0.0	0.3
"Pcna"	NM_011045.1	0.0	1.3	1.8	-0.2	0.7
"Rps6"	NM_009096.1	0.0	0.7	1.3	-0.3	0.4
"Ndufv2"	XM_128725	0.0	0.6	1.3	-0.2	0.4
"Snx5"	NM_024225.2	0.0	0.7	1.3	-0.1	0.5
"Ube2e1"	NM_009455.2	0.0	0.6	1.0	-0.1	0.4
"Sdfr1"	NM_009145.1	0.0	0.5	1.0	-0.2	0.3
"Pbef1"	NM_021524.1	0.0	0.4	1.0	-0.1	0.3
"E130112E	AK053583	0.0	0.7	1.2	-0.1	0.4
"Atp5a1"	NM_007505.1	0.0	0.7	1.2	-0.2	0.4
"Morf4l1"	NM_024431	0.0	0.6	1.2	-0.2	0.4
"Bcat1"	NM_007532	0.0	0.6	1.6	-0.2	0.5
"Atp5k"	NM_007507	0.0	0.5	1.6	-0.3	0.4
"Vdac3"	NM_011696.1	0.0	0.9	1.4	-0.2	0.5

Symbol	Accession	SLR C1 vs CC	SLR C2 vs CC	SLR C3 vs CC	SLR C3re	SLR average
"Paip2"	NM_026420.1	-0.1	0.7	1.2	-0.1	0.4
"Nup88"	NM_172394.1	-0.1	0.6	1.4	-0.3	0.4
"Rbm14"	NM_019869.1	-0.1	0.7	1.1	-0.2	0.4
"Arnt"	AK037762	-0.1	0.5	1.0	-0.2	0.3
"1110017C	NM_183250.1	-0.1	0.6	1.1	-0.1	0.4
"Atp5l"	XM_125157.1	-0.1	0.9	1.7	-0.3	0.6
"Ga17"	NM_145380.1	-0.1	0.6	1.2	-0.3	0.4
"Adrbk1"	NM_130863	-0.1	0.2	1.1	-0.2	0.3
"Slc25a4"	XM_134169.4	-0.1	0.9	1.5	-0.2	0.5
"Trip12"	NM_133975.2	-0.1	0.3	1.1	-0.2	0.3
"LOC2365	XM_135705.3	-0.1	0.5	1.0	-0.2	0.3
"mt-Nd4l"		-0.1	1.1	2.1	-0.2	0.7
"Ddx39"	NM_197982.2	-0.1	0.6	1.1	-0.2	0.3
"Bmyc"	NM_023326	-0.1	0.6	1.0	-0.2	0.3
"LOC2346	XM_125126.3	-0.1	0.4	1.1	-0.4	0.3
"1810030A06Rik"		-0.1	0.6	1.1	-0.2	0.4
"Hmgn2"	NM_016957.2	-0.1	0.7	1.6	-0.3	0.5
"Hnrpa2b1	NM_016806	-0.1	0.6	1.1	-0.4	0.3
"Usmg5"	XM_123431.1	-0.1	0.7	1.3	-0.4	0.4
"Hmgb1"	NM_010439.2	-0.1	0.8	1.5	-0.4	0.4
"Dld"	NM_007861.2	-0.1	0.6	1.0	-0.2	0.3
"Cd24a"	NM_009846.1	-0.1	0.7	1.1	-0.4	0.3
"LOC3820	XM_356177.1	-0.1	0.6	1.2	-0.5	0.3
"Igk-V1"	XM_355776.1	-0.1	0.6	1.2	-0.2	0.4
"LOC2076	XM_139845.1	-0.1	0.3	1.2	-0.2	0.3
"LOC3812	XM_355183.1	-0.2	0.7	1.2	-0.3	0.3
"Eif3s8"	NM_019646.1	-0.2	0.5	1.2	-0.2	0.3
"Cspg6"	NM_007790.2	-0.2	0.5	1.1	-0.3	0.3
"LOC3845	XM_357690.1	-0.2	0.5	1.2	-0.5	0.2
"LOC3865	XM_359405.1	-0.2	0.4	1.1	-0.3	0.2
"Top1"	NM_009408.1	-0.2	0.8	1.1	-0.5	0.3
"Eif4g2"	NM_013507.2	-0.2	0.6	1.3	-0.3	0.3
"LOC3818	XM_355862.1	-0.2	0.2	1.1	-0.4	0.2
"LOC2147	XM_125109.2	-0.3	0.6	1.1	-0.6	0.2
"LOC2447	XM_146826.2	-0.5	0.5	1.4	-0.7	0.2

Symbol	Accession	SLR D1 vs DC	SLR D2 vs DC	SLR D3 vs DC	SLR D3re	SLR average
"Egr1"	NM_007913.2	3.2	3.1	2.8	2.9	3.0
"Nfkbia"	NM_010907	2.3	2.1	1.5	2.3	2.1
"Egr2"	NM_010118.1	2.3	1.9	1.9	2.2	2.1
"Cd83"	NM_009856.1	2.2	1.9	2.0	2.0	2.0
"Nfkbiz"	NM_030612	1.9	1.8	1.8	1.8	1.8
"Tnfaip3"	NM_009397.2	1.7	1.6	1.4	1.6	1.6
"Hspa5"	NM_022310.2	1.6	1.2	0.5	1.6	1.2
"Prg"	NM_011157.1	1.6	1.6	0.7	1.8	1.4
"Atp5k"	NM_007507	1.5	1.5	0.6	1.7	1.3
"Hmgn2"	NM_016957.2	1.5	1.3	0.5	1.6	1.2
"Atp5l"	XM_125157.1	1.5	1.2	0.4	1.5	1.1
"Gdap10"	NM_010268.1	1.4	1.4	0.6	1.4	1.2
"Usmg5"	XM_123431.1	1.4	1.2	0.5	1.3	1.1
"Hmgb1"	NM_010439.2	1.4	1.0	0.4	1.5	1.1
"Il4i1"	NM_010215.1	1.4	1.2	1.5	1.4	1.4
"LOC2447	XM_146826.2	1.4	0.8	0.4	1.2	0.9
"4930431E	XM_207778.3	1.4	0.9	1.3	1.4	1.3
"Pcna"	NM_011045.1	1.3	1.4	0.3	1.6	1.1
"Rpl30"	NM_009083.2	1.3	1.2	0.4	1.6	1.1
"Cdkn2b"	NM_007670.2	1.3	1.3	1.2	1.3	1.3
"Fos"	NM_010234.2	1.3	1.5	1.4	1.4	1.4
"LOC3812	XM_355183.1	1.3	1.0	0.5	1.2	1.0

Symbol	Accession	SLR D1 vs DC	SLR D2 vs DC	SLR D3 vs DC	SLR D3re	SLR average
"Junb"	NM_008416.1	1.3	1.0	1.2	1.1	1.1
"Ndufb4"	NM_026610.1	1.2	0.9	0.4	1.3	1.0
"Dusp2"	NM_010090.2	1.2	0.9	1.1	1.0	1.1
"Rbm14"	NM_019869.1	1.2	0.9	0.4	1.3	0.9
"Nup88"	NM_172394.1	1.2	0.9	0.3	1.4	1.0
"LOC2147	XM_125109.2	1.2	0.9	0.4	1.0	0.9
"Cox7b"	NM_025379.1	1.2	0.9	0.3	1.2	0.9
"Traf1"	NM_009421.2	1.2	1.2	1.6	1.5	1.4
"Igk-V1"	XM_355776.1	1.2	1.1	0.5	1.3	1.0
"Acsl4"	NM_207625.1	1.2	1.2	0.4	1.2	1.0
"Clta"	NM_016760.1	1.2	1.1	0.3	1.1	0.9
"Vdac3"	NM_011696.1	1.2	1.0	0.1	1.0	0.8
"Cdk5r1"	NM_009871.2	1.1	1.2	0.9	1.1	1.1
"Snx5"	NM_024225.2	1.1	0.9	0.3	1.1	0.9
"AY07806	NM_172142.1	1.1	1.2	1.2	1.2	1.2
"Cd69"	XM_132882.1	1.1	1.1	1.1	1.1	1.1
"Rpl36al"	NM_025589.1	1.1	1.0	0.3	1.4	0.9
"LOC2417	XM_141567.3	1.1	1.0	0.5	0.9	0.9
"Nono"	NM_023144.1	1.1	0.6	0.3	1.3	0.8
"Calm2"	NM_007589	1.1	0.7	0.3	1.2	0.8
"LOC3820	XM_356177.1	1.1	0.9	0.3	1.1	0.9
"Slc25a4"	XM_134169.4	1.1	1.2	0.3	1.4	1.0
"Eif4g2"	NM_013507.2	1.1	0.8	0.2	1.2	0.8
"Pbef1"	NM_021524.1	1.1	1.1	0.4	1.2	1.0
"Bcat1"	NM_007532	1.1	0.9	0.3	1.1	0.9
"Mdh2"	NM_008617.2	1.1	0.8	0.4	1.2	0.9
"Tuba1"	NM_011653	1.1	0.8	0.3	1.3	0.9
"H2-Aa"	NM_010378.2	1.1	0.7	0.3	1.3	0.9
"Idi1"	NM_145360	1.1	0.8	0.3	1.1	0.8
"LOC3815	XM_355538.1	1.1	0.8	0.5	0.9	0.8
"Slc3a2"	NM_008577.2	1.1	1.1	0.3	1.6	1.0
"2610511C	NM_152817.2	1.0	1.0	0.2	1.1	0.8
"LOC2365	XM_135705.3	1.0	0.9	0.5	0.9	0.8
"E130112E	AK053583	1.0	1.1	0.3	0.9	0.9
"LOC2456	XM_142259.2	1.0	0.8	0.3	0.8	0.7
"Ddx39"	NM_197982.2	1.0	0.8	0.1	1.1	0.8
"2900010J	NM_175190.2	1.0	0.7	0.3	1.0	0.8
"mt-Nd4l"		1.0	1.3	0.1	1.3	0.9
"1810011C	NM_025456.2	1.0	0.8	0.2	1.0	0.8
"Ndufv2"	XM_128725	1.0	0.6	0.2	1.0	0.7
"Bhlhb2"	NM_011498.2	1.0	1.4	1.2	1.3	1.2
"2610205H	NM_027430.1	1.0	0.8	0.3	1.1	0.8
"Rps6"	NM_009096.1	1.0	1.1	0.3	1.3	0.9
"Hnrpu"	NM_016805.1	1.0	0.7	0.2	1.0	0.7
"AA959742	NM_133807.1	1.0	1.1	0.3	1.1	0.8
"Fin14"		1.0	0.9	0.2	1.3	0.8
"Hprt"	NM_013556.1	1.0	0.7	0.3	1.1	0.8
"3300001M	NM_175113.1	0.9	0.7	0.3	1.1	0.7
"Idb2"	NM_010496.2	0.9	0.7	0.7	1.0	0.8
"Stmn1"	NM_019641	0.9	0.9	0.2	1.2	0.8
"Cct5"	NM_007637.1	0.9	0.7	0.2	1.0	0.7
"2900064A	NM_133749.1	0.9	1.0	0.2	1.0	0.8
"Eif3s8"	NM_019646.1	0.9	1.0	0.4	1.0	0.8
"Sdfr1"	NM_009145.1	0.9	1.0	0.1	0.9	0.7
"Slc11a1"	NM_013612.1	0.9	0.7	0.3	1.1	0.7
"Thy28"	NM_144543.1	0.9	0.8	0.4	1.0	0.8
"1110017C	NM_183250.1	0.9	0.8	0.3	1.2	0.8
"LOC2804	NM_183299	0.9	0.1	0.1	1.1	0.6
"Ndufb5"	NM_025316.2	0.9	0.9	0.4	1.1	0.8

Symbol	Accession	SLR D1 vs DC	SLR D2 vs DC	SLR D3 vs DC	SLR D3re	SLR average
"Copb1"	NM_033370	0.9	0.7	0.2	1.1	0.7
"Ga17"	NM_145380.1	0.8	0.7	0.3	1.3	0.8
"Strn3"	NM_052973	0.8	0.7	0.2	1.0	0.7
"Nfatc1"	NM_016791.2	0.8	0.8	0.9	1.1	0.9
"BC02388	NM_146159.1	0.8	0.9	0.2	1.0	0.7
"3110001N	NM_026517.1	0.8	0.7	0.2	1.2	0.7
"LOC3811	XM_355056.1	0.8	1.0	1.0	0.7	0.9
"Gnb2-rs1"	NM_008143.2	0.8	0.6	0.5	1.0	0.7
"Cd24a"	NM_009846.1	0.8	0.7	0.3	1.2	0.7
"D11Moh3	NM_172300	0.7	0.9	0.4	1.1	0.8
"Tdg"	NM_172552.1	0.7	0.4	0.1	1.0	0.6
"Slc15a3"	NM_023044.1	0.7	0.7	0.5	1.0	0.7
"BC02453	NM_146237	0.7	0.6	1.0	1.0	0.8
"Smu1"	NM_021535.2	0.7	0.7	0.4	1.1	0.7
"Ssfa1"	XM_196564.2	0.7	0.7	0.1	1.0	0.6
"D19Ertd7	NM_029456.1	0.6	0.7	0.3	1.1	0.7
"Birc3"	NM_007464.1	0.6	0.7	0.4	1.0	0.7
"Prg"	NM_011157.1	0.6	0.8	0.8	1.0	0.8
"Snx5"	NM_024225.2	0.6	0.7	0.4	1.1	0.7
"Hnrpa2b1	NM_016806	0.5	0.8	0.1	1.1	0.6
"Ndufa5"	NM_026614.1	0.4	1.0	0.3	1.0	0.7

Symbol	Accession	SLR E1 vs EC	SLR E2 vs EC	SLR E3 vs EC	SLR E3re	SLR average
"Egr1"	NM_007913.2	2.4	3.0	3.2	3.2	2.9
"Egr2"	NM_010118.1	2.2	2.0	2.0	2.2	2.1
"LOC3850	XM_358044.1	1.7	1.5	1.8	1.6	1.6
"Nfkbiz"	NM_030612	1.6	1.6	1.6	1.5	1.6
"Cd83"	NM_009856.1	1.6	1.5	1.6	1.4	1.5
"Tnfaip3"	NM_009397.2	1.4	1.2	1.1	1.3	1.2
"Prpf8"	NM_138659.1	1.3	1.1	1.2	1.2	1.2
"Bhlhb2"	NM_011498.2	1.3				1.3
"Fos"	NM_010234.2	1.2	1.5	1.4	1.5	1.4
"2610510D	NM_146130	1.2	1.2	1.3	1.3	1.2
"4930431E	XM_207778.3	1.2	1.3	1.3	1.3	1.3
"AY07806	NM_172142.1	1.2	1.2	1.0	1.2	1.1
"Nfkbia"	NM_010907	1.2	1.0		1.2	1.1
"LOC3850	XM_358030.1	1.2	1.1	1.3	1.0	1.1
"Cd69"	XM_132882.1	1.1	1.2	1.1	1.1	1.1
"Olfr887"	NM_146423.1	1.1	1.2	1.7	1.6	1.4
"Gdap10"	NM_010268.1	1.1				
"LOC3811	XM_355056.1	1.1				
"Pigt"	NM_133779.1	1.1		1.1	1.2	1.1
"Traf1"	NM_009421.2	1.1				
"Il4i1"	NM_010215.1	1.0	1.1	1.1	1.0	1.1
"Slc16a6"	NM_134038	1.0		1.0		1.0
"Blr1"	NM_007551.2	1.0		1.3	1.1	1.1
"Ube4a"	NM_145400	1.0	1.0	1.1	1.1	1.1
"Got2"	NM_010325.1	1.0	1.1	1.3	1.1	1.1
"LOC3860	XM_359058.1	1.0		1.0	1.0	1.0
"Bcl2l1"	NM_009743.2	1.0		1.1		
"Junb"	NM_008416.1			1.0	1.0	
"Nfatc1"	NM_016791.2				1.1	
"BC02453	NM_146237		1.2	1.4	1.2	1.3
"Pim1"	NM_008842.2		1.1	1.1		1.1
"Eef2"	NM_007907.1		1.2	1.5	1.3	1.3
"Slc4a7"	XM_147798.4				1.0	
"2610305J	AK011989		1.0	1.1		
"Csnk2a1-	AK031617			1.1		

Symbol	Accession	SLR E1 vs EC	SLR E2 vs EC	SLR E3 vs EC	SLR E3re	SLR average
"Ide"	AK029089			1.3		
"Vars2"	NM_011690.2			1.1	1.0	
"Raly"	NM_023130.1			1.0		
"Zfp162"	NM_011750.1		1.0	1.1		
"Hnrpk"	NM_025279.1		1.1	1.1	1.0	1.1
"Bcl2l1"	NM_009743.2		1.0	1.0		
"Fosb"	NM_008036		1.0	1.0		
"LOC3821	XM_356263.1		1.0	1.1		
"mt-Nd4l"				-1.1		
"Cdkn2a"	NM_009877.1			1.1	1.0	
"Eef2"	NM_007907.1			1.1		
"Insig1"	NM_153526.2		1.2	1.0	1.0	
"Slc3a2"	NM_008577.2			-1.2		
"Hmgb1"	NM_010439.2			-1.0		
"Pcna"	NM_011045.1		-1.2	-1.4		
"Hmgn2"	NM_016957.2			-1.1		
"Rpl30"	NM_009083.2			-1.0		
"Nup88"	NM_172394.1			-1.1		
"Vdac3"	NM_011696.1		-1.0	-1.2		
"1810008K	NM_026929.2	-1.1		-0.2		

C: Unstimulated
1,2 and 3: Stimulated

Supplementary Table S16: Data for the three cellular responses

% Apoptotic Cells

	Cells	Fas	IgG+Fas		Cells	Fas	IgG+Fas
Akt	15	38	51	Akt	13	33	48
Bad	14	40	51	Bad	11	39	51
Bcl2	15	37	49	Bcl2	12	36	48
BLNK	22	67	66	BLNK	25	71	65
CaMKII	19	57	39	CaMKII	19	60	38
ERK	26	68	67	ERK	30	74	69
JAK	17	46	45	JAK	19	41	45
JNK	17	80	72	JNK	17	80	74
Lyn	29	77	72	Lyn	33	80	76
MEK	29	73	70	MEK	25	73	70
p38	18	75	71	p38	11	70	66
p85	17	74	71	p85	12	72	70
PKA	20	68	72	PKA	22	67	70
PKCd	6	49	36	PKCd	8	44	32
PKD	25	68	66	PKD	25	71	66
PLC	6	50	37	PLC	5	49	38
Rac	8	46	32	Rac	10	50	35
Raf	3	47	33	Raf	1	41	34
Shc	20	72	69	Shc	17	70	69
Syk	20	65	66	Syk	20	67	67
Nor	6	43	32	Nor	4	46	30

Cytokine Secretion

	IL2 Secretion (pg per million cells)					IL2 Secretion (pg per million cells)					IL2 Secretion (pg per million cells)			
Akt	30.84936	149.4391	270.694	203.4366	Akt	46.27404	224.1587	311.2981	274.6394	Akt	27.24359	107.3718	216.3462	177.6175
Bad	38.14799	192.9087	217.2047	152.0694	Bad	43.87019	192.9087	152.0433	174.8798	Bad	33.96739	174.8798	212.0536	145.2759
Bcl2	71.3141	226.3622	203.125	147.929	Bcl2	53.48558	203.726	203.125	192.3077	Bcl2	64.90385	208.3333	200.1202	161.7973
BLNK	28.04487	65.6185	70.87202	82.84684	BLNK	42.06731	121.3942	102.7644	115.9856	BLNK	12.01923	63.34459	67.14191	71.68613
CaMKII	27.711	92.42374	89.03134	85.59149	CaMKII	49.87981	134.0144	120.1923	141.226	CaMKII	14.02244	78.33223	94.81838	84.13462
ERK	33.65385	78.90886	93.29212	70.4764	ERK	33.65385	90.74519	97.95673	77.52404	ERK	15.02404	69.50251	86.99634	72.11538
Jak	23.69505	72.78312	103.1996	81.9493	Jak	41.46635	131.0096	149.6394	135.2163	Jak	15.7967	77.1234	104.8574	84.86305
JNK	24.03846	165.4412	154.533	131.7308	JNK	32.45192	140.625	162.2596	164.6635	JNK	20.47721	152.0079	164.2628	138.4615
Lyn	35.16738	138.8428	188.7464	118.5681	Lyn	47.47596	201.3221	254.8077	219.351	Lyn	17.36111	124.7513	177.6175	115.9693
MEK	42.06731	122.0901	78.58728	126.5182	MEK	33.65385	115.9856	102.1635	120.1923	MEK	30.79928	97.41903	73.9645	118.9271
p38	45.40598	109.5085	111.1779	89.74359	p38	40.86538	147.8365	133.4135	134.6154	p38	32.05128	104.1667	102.6643	88.94231
p85	25.88757	173.0769	180.8894	172.9724	p85	33.65385	173.0769	180.8894	198.9183	p85	5.547337	161.0577	186.2981	180.2885
PKA	37.15035	97.12838	149.2388	90.77682	PKA	40.86538	179.6875	179.0865	172.476	PKA	15.2972	89.33212	155.2484	91.72571
PKCd	32.39967	111.4887	111.9291	75.0469	PKCd	37.25962	161.6587	179.0865	153.8462	PKCd	36.58027	106.1008	112.6803	80.32364
PKD	51.28205	136.5041	210.7372	99.0676	PKD	38.46154	191.1058	158.0529	163.4615	PKD	52.08333	133.0701	229.1667	94.69697
PLCg	32.92224	83.65385	71.19083	69.8896	PLCg	37.86058	104.5673	92.54808	94.35096	PLCg	30.83194	76.92308	67.4926	68.99929
Pyk2	45.07212	169.9082	225.5373	111.6625	Pyk2	45.07212	186.899	191.7067	173.0769	Pyk2	16.82692	167.7229	219.8812	121.7432
Rac	33.19597	145.7985	159.413	166.6302	Rac	34.85577	167.6683	151.4423	183.2933	Rac	20.6044	151.0242	174.5951	163.8986
Raf	58.37912	139.3138	121.6346	93.03775	Raf	40.86538	153.2452	152.0433	125.601	Raf	21.46291	127.2946	112.5	84.13462
Shc	37.95547	193.109	130.5726	123.0769	Shc	36.05769	144.8317	143.6298	153.8462	Shc	25.30364	148.2372	91.78322	93.75
Syk	32.19437	143.75	84.13462	127.8846	Syk	45.07212	179.6875	126.2019	159.8558	Syk	31.33585	123.0769	75.72115	110.5769
Nor	30.04808	102.8312	159.6154	101.0188	Nor	45.07212	185.0962	199.5192	212.1394	Nor	17.62821	98.49092	157.6923	98.44322

Cell Proliferation

	IgG (12 Hr	IgG(24 Hrs	IgG(48 Hrs)		IgG (12 Hr	IgG(24 Hrs	IgG(48 Hrs)
Nor	4.3	53.4	88.6	Nor	2.3	42.8	81.2
Akt	10.9	82.0	97.4	Akt	9.6	82.7	96.8
Bad	5.5	78.2	97.4	Bad	7.1	72.7	96.6
Bcl2	4.6	63.5	96.2	Bcl2	5.2	66.8	96.8
BLNK	5.2	48.0	87.6	BLNK	1.5	40.0	82.1
CaMKII	1.5	29.3	88.4	CaMKII	1.0	26.7	89.2
ERK	5.0	38.0	90.8	ERK	4.0	35.0	89.4
JAK1	1.7	49.5	93.9	JAK1	1.0	44.8	94.1
JNK	5.6	75.6	99.5	JNK	7.5	79.3	98.4
Lyn	3.2	54.0	98.7	Lyn	2.1	49.0	96.7
MEK	1.0	5.0	89.2	MEK	0.2	16.1	87.3
p38	1.8	44.7	96.9	p38	2.0	45.0	96.5
p85	4.3	63.0	99.2	p85	3.4	51.0	98.7
PKA	4.6	44.2	90.0	PKA	1.1	35.3	80.9
PKD	0.3	21.0	75.5	PKD	0.1	16.0	62.0
PKCd	25.7	72.9	79.3	PKCd	22.0	71.6	64.8
PLC	35.0	85.1	95.0	PLC	34.8	82.1	93.9
Rac	42.5	83.4	60.6	Rac	40.0	78.0	29.5
Raf	54.8	88.9	54.2	Raf	57.4	87.6	50.2
Shc	1.3	32.7	82.5	Shc	0.6	28.7	80.4
Syk	1.0	24.9	74.5	Syk	0.4	25.1	70.3