

Supplementary Materials for

The kinase Itk and the adaptor TSAd change the specificity of the kinase Lck in T cells by promoting the phosphorylation of Tyr¹⁹²

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Fig. S1. Identification by fluorescence imagery of conjugates between Raji cells and transfected JCAM 1.6 cells.

Fig. S2. Distribution of Lck-SH2 domain binding preference to given phosphotyrosine motifs.

Table S1. List of Lck-interacting proteins.

Table S2. Summary per protein of peptide array screening of the binding of Lck-SH2 and Lck-SH2-Y192E to 431 phosphopeptides from Lck-interacting proteins.

Supplementary Figure 1

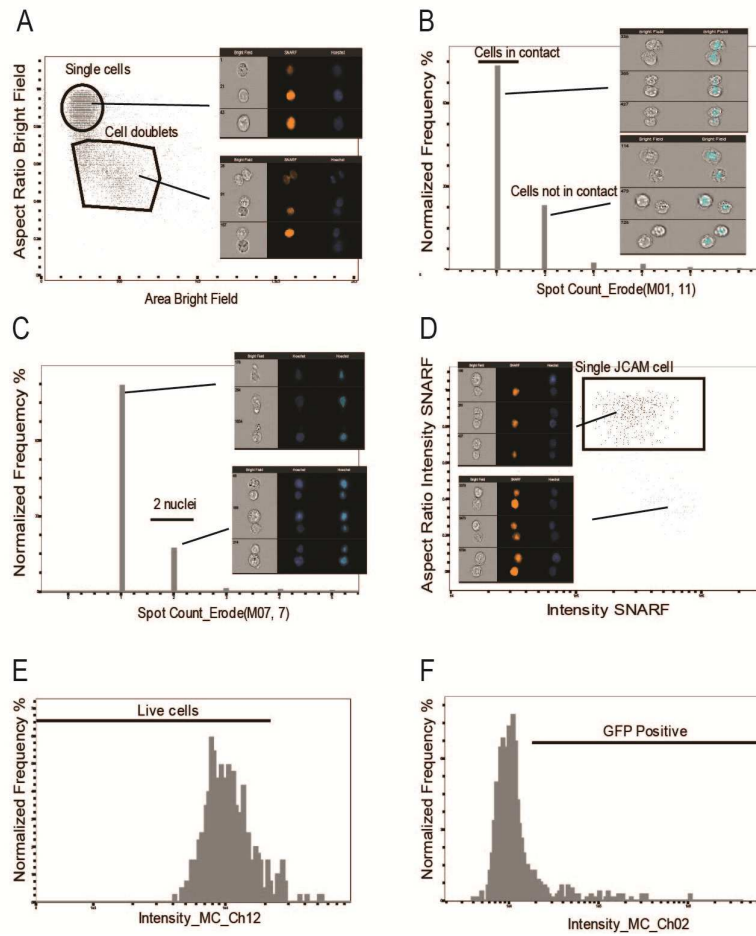


Fig. S1. Identification by fluorescence imagery of conjugates between Raji cells and transfected JCAM 1.6 cells. (A to F) Gating strategy of (A) cell doublets excluding (B) cells that are not in contact and including (C) only those doublets with two nuclei present and (D) that had only one JCAM 1.6 cell present. (E) Only live cells were included, and (F) only GFP⁺ cells were analyzed.

Supplementary Figure 2

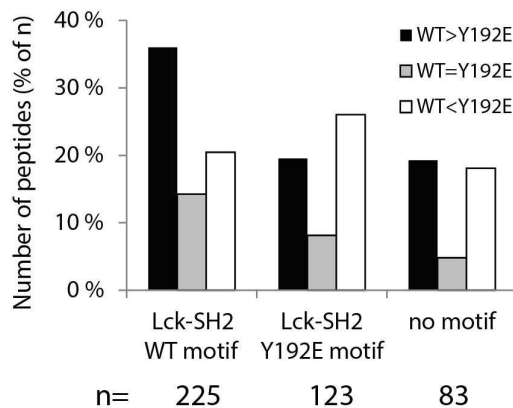


Fig. S2. Distribution of Lck-SH2 domain binding preference to given phosphotyrosine motifs. Graph shows the frequency (percentage) of peptides with a given motif that bound preferentially to one or other of the two tested Lck-SH2 domains, as indicated. The numbers of peptides (n) with the given motif is given below the graph.

Table S1. List of Lck-interacting proteins. List contains the Lck-interacting proteins that were reported in the HPRD database as of April 2009 with 431 phosphotyrosine sites supported by five or more references (<http://www.phosphosite.org>).

Reference HPRD§	Phosphosite*	Sequence#	pY motif Lck-SH2α	pY motif Lck-SH2Y192Eα
3BP2	Y174-p	YPTDNEDYEHDDDED		yXXD
3BP2	Y183-p	HDDEDDSYLEPDSPE	yXXP	
3BP2	Y448-p	GDDSDEDYEKVPLPN	yXXV	
ACP1	Y131-p	QLIIEDPYGNDSDF		YXXN
ACP1	Y132-p	LIIEDPYGNDSDFE		yXXD
ACP1	Y142-p	DSDFETVYQQCVRCC		
ADAM15	Y715-p	LVMLGASYWYRARLH		
AXL	Y474-p	RRKKETRYGEVFEP	yXXV	
AXL	Y691-p	FGLSKKIYNGDYRQ		yXXD
AXL	Y695-p	KKIYNGDYRQGRIA		YXXQ
AXL	Y696-p	KIYNGDYRQGRIAK		yXXG
AXL	Y719-p	ESLADRVYTSKSDVW		
AXL	Y752-p	GVENSEIYDYLROGN	yXXL	
AXL	Y754-p	ENSEIYDYLROGNRL		YXXQ
AXL	Y814-p	QEPDEILYVNMDEGG	yXXM	
AXL	Y859-p	EVHPAGRYVLCPSST		
CAS-L	Y12-p	NLMARALYDNVPECA	yXXV	
CAS-L	Y92-p	TFGQQKLYQVPNPQA	yXXP	
CAS-L	Y106-p	AAPRDTIYQVPPSYQ	yXXP	
CAS-L	Y112-p	IYQVPPSYQNQGIYQ		YXXQ
CAS-L	Y118-p	SYQNQGIYQVPTGHG	yXXP	
CAS-L	Y164-p	PVRTGHGYVYEYPSR		
CAS-L	Y166-p	RTGHGYVYEYPSRYQ	yXXP	
CAS-L	Y168-p	GHGYVYEYPSRYQKD		
CAS-L	Y172-p	VYEYPSRYQKDVYDI		yXXD
CAS-L	Y177-p	SRYQKDVYDIPPSHT	yXXP	
CAS-L	Y189-p	SHTTQGVYDIPPSA	yXXP	
CAS-L	Y214-p	EIKPQGVYDIPPTKG	yXXP	
CAS-L	Y241-p	AGLREKDYDFPPMR	yXXP	
CAS-L	Y261-p	DLRPEGVYDIPPTCT	yXXP	
CAS-L	Y317-p	VGSQNDAYDVPRGVQ	yXXP	
CAS-L	Y345-p	PQERDGVYDVPLHNP	yXXP	
CAS-L	Y629-p	ERSWDDYDYVHLQG	yXXV	
CAS-L	Y631-p	SWDDYDYVHLQGKE	yXXL	
Cbl	Y368-p	IKVTQEQYELYCEMG		yXXY
Cbl	Y371-p	TQEQYELYCEMGSTF	yXXM	
Cbl	Y455-p	EGAPSPNYDDDDER		yXXD
Cbl	Y552-p	PPPPDRPYSVGAESR		yXXG
Cbl	Y-674	SSSANAIYSLAARPL		yXXA

Cbl	Y-700	EGEEDTEyMTPSSRP	yXXP	
Cbl	Y-731-p	QQIDSCTyEAMYNIQ	yXXM	
Cbl	Y774-p	SENEDDGyDVPKPPV	yXXP	
Cd152 (CTLA-4)	Y201-p	SPLTTGVyVKMPPTTE	yXXM	
Cd152 (CTLA-4)	Y218-p	CEKQFQPyFIPIN	yXXP	
CD28	Y191-p	SRLHSDyMNMTPRR	yXXM	
CD28	Y206-p	PGPTRKHyQPYAPPR		yXXY
CD28	Y209-p	TRKHYPyAPPRDFA	yXXP	
CD28	Y218-p	PPRDFAAyRS		
CD31 (PECAM)	Y290-p	RHGKAVySVMAMVE	yXXM	
CD31 (PECAM)	Y690-p	PLNSDVQyTEVQVSS	yXXV	
CD31 (PECAM)	Y713-p	KKDTETVySEVRKAV	yXXV	
CD31 (PECAM)	Y728-p	PDAVESRySRTEGSL		yXXT
CD3e	Y188-p	PPVNPDPyEPIRKGQ	yXXI	
CD3e	Y199-p	RKGQRDLySGLNQRR	yXXL	
CD3z	Y064-p	RSADAPAyQQGQNQL		yXXG
CD3z	Y072-p	QQGQNQLyNELNLGR	yXXL	
CD3z	Y083-p	NLGRREEyDVLDKRR	yXXL	
CD3z	Y111-p	KNPQEGLyNELQKDK	yXXL	
CD3z	Y123-p	KDKMAEAySEIGMKG	yXXI	
CD3z	Y142-p	GKGHDGLyQGLSTAT	yXXL	
CD3z	Y153-p	STATKDTyDALHMQA	yXXL	
CD45	Y705-p	NGDAGSNyINASYID		yXXA
CD45	Y710-p	SNYINASyIDGFKEP		yXXG
CD45	Y978-p	RNSNVIPyDYNRVPL		YXXN
CD45	Y980-p	SNVIPYDyNRVPLKH	yXXV	
CD45	Y1216-p	MVSTFEQyQFLYDVI	yXXL	
CD5	Y453-p	ASHVDNEySQPPRNS	yXXP	
CD5	Y465-p	RNSRLSAyPALEGVL	yXXL	
CD5	Y487-p	DNSSDSDyDLHGAQR		
Csk	Y184-p	VAAQDEFyRSGWALN		yXXG
Csk	Y263-p	VEEKGLyIVTEYMA		yXXT
CTNND2	Y292-p	SAPEGATyAAPRGSS	yXXP	
CTNND2	Y499-p	AAGPASNyADPYRQL	yXXP	
CTNND2	Y503-p	ASNYADPyRQLQYCP	yXXL	
CTNND2	Y516-p	CPSVESPySKSGPAL		yXXS
CTNND2	Y1124-p	NTGISTLyRNSYGAP		yXXS
CTNND2	Y1128-p	STLYRNSyGAPAEDI	yXXP	
CTNND2	Y1154-p	QEPSRKDyETYQPFQ		yXXY
CTNND2	Y1197-p	GLKSTGNyVDFYSAA		
DAPP1	Y139-p	KVEEPSIyESVRVHT	yXXV	
Dok1	Y146-p	EMLENSLySPTWEGS		yXXT
Dok1	Y296-p	LDSPPALyAEPLDSL	yXXP	
Dok1	Y315-p	CPSQDSLySDPLDST	yXXP	
Dok1	Y337-p	VQRKKPLyWDLYEHA	yXXL	
Dok1	Y341-p	KPLYWDLyEHAQQQL		yXXA

Dok1	Y362-p	DPKEDPI y DEPEGLA	yXXP	
Dok1	Y377-p	PVPPQGL y DLPREPK	yXXP	
Dok1	Y398-p	ARVKEEG y ELPYNPA	yXXP	
Dok1	Y402-p	EEGYELP y NPATDDY		yXXA
Dok1	Y409-p	YNPATDD y AVPPPRS	yXXP	
Dok1	Y449-p	KSHNSAL y SQVQKSG	yXXV	
DOK2	Y139-p	CMEENEL y SSAVTVG		yXXA
DOK2	Y271-p	LPRPDS y SRPHDSL	yXXP	
DOK2	Y299-p	PRGQEGE y AVPFDAV	yXXP	
DOK2	Y345-p	PPRPDHI y DEPEGVA	yXXP	
DOK2	Y402-p	GWQPGTE y DNVVLKK	yXXV	
DOK3	Y208-p	PMEENSI y SSWQEVG		
DOK3	Y381-p	NDLASGL y ASVCKRA	yXXV	
DOK3	Y398-p	PPGNEHL y ENLCVLE	yXXL	
DOK3	Y-432-p	SPTTSP y HNGQDLS		yXXG
DOK3	Y453-p	DSTLEAQ y RRLLELD	yXXL	
ER-alpha	Y537-p	CKNVVPL y DLLLEML	yXXL	
ER-beta	Y488-p	CKNVVP y VDLLLEML	yXXL	
Erk1	Y204-p	HTGFLTE y VATRWR		yXXT
Erk1	Y210-p	EYVATRW y RAPEIML	yXXP	
Erk2	Y186-p	HTGFLTE y VATRWR		yXXT
Ezrin	Y146-p	KEVHKSG y LSSERLI		yXXS
Ezrin	Y191-p	KDNAMLE y LKIAQDL	yXXI	
Ezrin	Y270-p	KAPDFVF y APRLRIN		
Ezrin	Y354-p	LMLRLQD y EETKKA		
Ezrin	Y424-p	LAAELAE y TAKIALL		
Ezrin	Y478-p	PPPPPPV y EPVSYHV	yXXV	
Ezrin	Y483-p	PVYEPVS y HVQESLQ		YXXQ
FAK	Y148-p	KPTLNFF y QQVKS DY	yXXV	
FAK	Y155-p	YQQVKS y DMLEIADQ		
FAK	Y347-p	MADLIDG y CRLVNGT	yXXL	
FAK	Y397-p	SVSETDD y AEIIDEE	yXXI	
FAK	Y407-p	IIDEEDT y TMPSTRD	yXXP	
FAK	Y441-p	GDVHQGI y MSPENPA	yXXP	
FAK	Y570-p	GDFGLSR y MEDSTYY		yXXD
FAK	Y576-p	RYMEDST y YKASKGK		yXXA
FAK	Y577-p	YMEDST y YKASKGKL		yXXS
FAK	Y861-p	PIGNQHI y QPVGKPD	yXXV	
FAK	Y898-p	LSSPADS y NEGVKLQ		yXXG
FAK	Y925-p	DRSNDKV y ENVTGLV	yXXV	
FAK	Y1007-p	KMKLAQQ y VMTSLQQ		yXXT
Fas	Y091-p	PCQEGKE y TDKAHFS		
Fas	Y232-p	SDVDLSK y ITTIAGV		yXXT
Fas	Y291-p	LHGKKEA y DTLIKDL	yXXL	
Fyn	Y028-p	SLNQSSG y RYGTDPT		yXXG
Fyn	Y030-p	NQSSGYR y GTDPTPQ		yXXD

Fyn	Y039-p	TDPTPQH y PSFGVTS		
Fyn	Y185-p	SETTKG y SLSIRDW		yXXS
Fyn	Y213-p	RKLDNGG y ITTRAQ		yXXT
Fyn	Y214-p	KLDNGG y ITTRAQF		yXXT
Fyn	Y420-p	RLIEDNE y TARQGAK		
Fyn	Y440-p	TAPEAAL y GRFTIKS		
Fyn	Y531-p	FTATEPQ y QPGENL		yXXG
GAB2	Y249-p	SGQVHG f ySLPKPSR	yXXP	
GAB2	Y266-p	TEFRDST y DLPRSLA	yXXP	
GAB2	Y293-p	ETDNEDV y TFKTPSN		
GAB2	Y324-p	PATPLSA y QIPRTFT	yXXP	
GAB2	Y409-p	RASSCET y EYPQRGG	yXXP	
GAB2	Y452-p	STNSEDN y VPMNPGS	yXXM	
GAB2	Y476-p	GDNSQSV y IPMSPGA	yXXM	
GAB2	Y584-p	SGDSEEN y VPMQNPV	yXXM	
GAB2	Y614-p	KSTGSVD y LALDFQP	yXXL	
GAB2	Y643-p	TSDEKVD y VQVDKEK	yXXV	
GCSFR	Y727-p	LPTLVQ t yVLQGDPR		YXXQ
GCSFR	Y752-p	GTSDQVL y GQLLGSP	yXXL	
GCSFR	Y767-p	TSPGPGH y LRC DSTQ		
GCSFR	Y787-p	LTPSPKS y ENLWFQA	yXXL	
GRAP2 (GADS)	Y45-p	ELGSQEG y VPKNFID		
IFNAR2	Y337-p	PRTSGGG y TMHGLTV		
IFNAR2	Y411-p	DPFPEED y SSTEGSG		yXXT
IFNAR2	Y512-p	DVDLGDG y IMR		
Ig alpha	Y182-p	GLDAGDE y EDENLYE		
Ig alpha	Y188-p	EYEDENL y EGLNLDD	yXXL	
Ig alpha	Y199-p	NLDDCSM y EDISRGL	yXXI	
Ig alpha	Y210-p	SRGLQGT y QDVGSLN	yXXV	
Ig-Beta	Y196-p	GMEEDHT y EGLDIDQ	yXXL	
Ig-Beta	Y207-p	DIDQTAT y EDIVTLR	yXXI	
IkB-alpha	Y42-p	DSMKDEE y EQMVKEL	yXXM	
IkB-alpha	Y305-p	FTEDEL p yDDCVFGG		
IL2RB	Y364-p	SCFTNQ G yFFFHLPD		
IL2RB	Y381-p	EIEACQV y FITYDPYS		yXXY
IL2RB	Y384-p	ACQVYFT y DPYSEED		yXXY
IL2RB	Y387-p	VYFTYDP y SEEDPDE		
IL2RB	Y418-p	LSGEDDA y CTFPSRD		
IL2RB	Y536-p	LPLNTDA y LSLQELQ	yXXL	
IL3RB	Y466-p	ALRFCGI y GYRLRRK		
IL3RB	Y468-p	RFCGI y YRLRRKWE		
IL3RB	Y593-p	SFDFNG p yLGPPHSR	yXXP	
IL3RB	Y628-p	PPPGSLE y LCLPAGG	yXXL	
IL3RB	Y711-p	DPGVAS G yVSSADLV		yXXS
IL3RB	Y766-p	VKSGFEG y VELPPIE	yXXL	
IL3RB	Y822-p	VLQQVGD y CFLPGLG	yXXL	

IL3RB	Y882-p	KALKQQDyLSLPPWE	yXXL	
Itk	Y180-p	ETVVIALyDYQTNDP		YXXQ
Itk	Y512-p	RFVLDDQyTSSTGTK		yXXS
JAK3	Y785-p	NSLISSDyELLSDPT	yXXL	
JAK3	Y904-p	SLRLVMEyLPSGCLR		yXXS
JAK3	Y939-p	QICKGMEyLGSRRCV		yXXS
JAK3	Y980-p	LLPLDKDyYVVREPG	yXXV	
JAK3	Y981-p	LPLDKDyYVVREPGQ		
KIR2DL2	Y101-p	LAGTYRCyGSVTHSP	yXXV	
KIR2DL2	Y109-p	GSVTHSPyQLSAPSD		yXXS
KIR2DL2	Y126-p	DIVITGLyEKPSLSA	yXXP	
KIR2DL2	Y302-p	QDPQEVTyTQLNHCV	yXXL	
KIT	Y362-p	FTDKWEDyPKSENES		yXXS
KIT	Y568-p	EEINGNNyVYIDPTQ	yXXI	
KIT	Y570-p	INGNNYyVYIDPTQLP	yXXP	
KIT	Y578-p	IDPTQLPyDHKWEFP		
KIT	Y703-p	DHAEAAlyKNLLHSK	yXXL	
KIT	Y721-p	CSDSTNEyMDMKPGV	yXXM	
KIT	Y730-p	DMKPGVSyVVPTKAD	yXXP	
KIT	Y823-p	DIKNSNyVVKGNAR		
KIT	Y900-p	EHAPAEMyDIMKTCW	yXXM	
KIT	Y936-p	SESTNHlySNLANCS	yXXL	
Lat	Y110-p	GANSVASyENEGASG		
Lat	Y156-p	ADEDEDyHNPGYLV	yXXP	
Lat	Y161-p	DDYHNPgyLVVLPDS	yXXV	
Lat	Y200-p	SMESIDyVNVPESE	yXXV	
Lat	Y220-p	SLDGSREyVNVSQEL	yXXV	
Lat	Y255-p	EEEGAPdyENLQELN	yXXL	
Lax1	Y93-p	RQRAKNIyDILPWRQ	yXXL	
Lck	Y192-p	NLDNGGfyISPRITF	yXXP	
Lck	Y394-p	RLIEDNEyTAREGAK		
Lck	Y505-p	FTATEGQyQPQP		YXXQ
LIME	Y145-p	CAGLEATySNVGLAA	yXXV	
LIME	Y200-p	AAQVDVlySRVCKPK	yXXV	
LIME	Y235-p	ALAGDLAyQTLPLRA	yXXL	
LIME	Y254-p	SGPLENVyESIRELG	yXXI	
Lyn	Y31-p	RNTERTIyVRDPTSN		yXXD
Lyn	Y116-p	EGFIPSNyVAKLNTL		
Lyn	Y192-p	RSLDNGGyYISPRIT		yXXS
Lyn	Y193-p	SLDNGGyYISPRITF	yXXP	
Lyn	Y264-p	FGEVWMgyYNNSTKV		YXXN
Lyn	Y305-p	HDKLVRLyAVVTRREE	yXXV	
Lyn	Y315-p	VTREEPIyIITEYMA		yXXT
Lyn	Y396-p	RVIEDNEyTAREGAK		
Lyn	Y459-p	MTALSQgyRMPRVEN	yXXP	
Lyn	Y472-p	ENCPDELyDIMKMCW	yXXM	

Lyn	Y500-p	QSVLDDF y TATEGQY		yXXT
Lyn	Y507-p	YTATEGQ y QQQP		yXXQ
MUC1	Y1191-p	CQCRRKN y GQLDIFP	yXXL	
MUC1	Y1203	IFPARDT y HMPSEYP	yXXM	
MUC1	Y1209-p	TYHPMSE y PTYHTHG		yXXY
MUC1	T1211-p	HMPSEYP t YHTHGRY		yXXT
MUC1	Y1212-p	PMSEYPT y HHTHGRYV		
MUC1	Y1218-p	TYHTHGR y VPPSSTD	yXXP	
MUC1	Y1229-p	SSTDRSP y EKVSAGN	yXXV	
MUC1	Y1243-p	NGGSSLS y TNPAVAA	yXXP	
P130Cas	Y12-p	NVLAKAL y DNVAESP	yXXV	
P130Cas	Y128-p	SKAQQGL y QVPGPSP	yXXP	
P130Cas	Y165-p	PSPATDL y QVPPGPG	yXXP	
P130Cas	Y222-p	PTRVGQ y VYEEAQP		
P130Cas	Y224-p	RVGQGY v YEAQAPEQ		yXXA
P130Cas	Y234-p	AQPEQDE y DIPRHLL	yXXP	
P130Cas	Y249-p	APGPQDI y DVPPVVRG	yXXP	
P130Cas	Y262-p	RGLLPSQ y GQEVYDT		
P130Cas	Y267-p	SQYQGE v YDTPPMAV	yXXP	
P130Cas	Y287-p	RDPLLEV y DVPPSVE	yXXP	
P130Cas	Y306-p	PSNHHAV y DVPPSVS	yXXP	
P130Cas	Y327-p	PLLREET y DVPPAFA	yXXP	
P130Cas	Y362-p	SPPAED v YDVPPPAP	yXXP	
P130Cas	Y372-p	PPPAPDL y DVPPGLR	yXXP	
P130Cas	Y387-p	RPGPGTL y DVPRERV	yXXP	
P130Cas	Y410-p	GVVDSGV y AVPPPAE	yXXP	
P130Cas	Y664-p	EGGWME d YDVHLQG	yXXV	
P130Cas	Y666-p	GWME d YVHLQKE	yXXL	
p85 (PIK3R1)	Y368-p	STKMHD y TLTLRKG		yXXT
p85 (PIK3R1)	Y452-p	VGKKLHE y NTQFQEK		YXXQ
p85 (PIK3R1)	Y463-p	FQEK S REYDRLYEEY	yXXL	
p85 (PIK3R1)	Y467-p	SREYDR L YEEYTRTS		yXXY
p85 (PIK3R1)	Y470-p	YDRLYEE y TRTSQEI		yXXT
p85 (PIK3R1)	Y508-p	QERYSKE y IEKFKRE		
p85 (PIK3R1)	Y528-p	IQRIMH n YDKLKSRI	yXXL	
p85 (PIK3R1)	Y556-p	LKKQAAE y REIDKRM	yXXI	
p85 (PIK3R1)	Y580-p	LRKTRDQ y LMWLTQK		
p85 (PIK3R1)	Y607-p	NENTEDQ y SLVEDDE	yXXV	
p85 (PIK3R1)	Y688-p	FAEPYN L YSSLKELV	yXXL	
PAG	Y163-p	GLGMEGP y EVLKDSS	yXXL	
PAG	Y181-p	NMVEDCL y ETVKEIK	yXXV	
PAG	Y227-p	GKAEFAE y ASVDRNK	yXXV	
PAG	Y299-p	KRFSSLS y KSREEDP		
PAG	Y317-p	EEEISAM y SSVNKPG	yXXV	
PAG	Y341-p	LTVPEST y TSIQGDP	yXXI	
PAG	Y359-p	PSSCNDL y ATVKDFE	yXXV	

PAG	Y387-p	SEEPEPDyEAIQTLN	yXXI	
PAG	Y417-p	LVPKENDyESISDLQ	yXXI	
Paxillin (PXN)	Y31-p	FLSEETPySYPTGNH	yXXP	
Paxillin (PXN)	Y33-p	SEETPySYPTGNHTY		yXXG
Paxillin (PXN)	Y40-p	YPTGNHTyQEIAVPP	yXXI	
Paxillin (PXN)	Y88-p	PQSSSPVyGSSAKTS		yXXS
Paxillin (PXN)	Y118-p	VGEEEHVySFPNKQK	yXXP	
Paxillin (PXN)	Y181-p	PGALSPLyGVPETNS	yXXP	
Paxillin (PXN)	Y375-p	QPYCEKdyHNLFSR	yXXL	
Paxillin (PXN)	Y-434-p	KAYCRKdyFDMFAPK	yXXM	
PI3K alpha	Y317-p	RISTATPyMNGETST		yXXG
PI3K alpha	Y508-p	SREAGFSySHAGLSN		yXXA
PKC alpha	Y194-p	PNGLSDPyVKLKLIP	yXXL	
PKC alpha	Y657-p	SDFEGFSyVNPQFVH	yXXP	
PKC theta	Y90-p	SETTVELySLAERCR		yXXA
PKCdelta	Y52-p	VQKKPTMyPEWKSTF		
PKCdelta	Y64-p	STFDAHIyEGRVIQI		
PKCdelta	Y120-p	KVLMsvQyFLEDVDC		
PKCdelta	Y155-p	IKQAKIHyIKNHEFI		YXXN
PKCdelta	Y187-p	WGLNKQyKCRQCNA		
PKCdelta	Y313-p	SSEPVGyIQGFEEKT		
PKCdelta	Y334-p	MQDNSGTyGKIWEGS	yXXI	
PKCdelta	Y374-p	ELKGRGEySAIKALK	yXXI	
PKCdelta	Y514-p	TFCGTPdyIAPEILQ	yXXP	
PKCdelta	Y525-p	EILQGLKyTFSVDWW		yXXS
PKCdelta	Y567-p	IRVDTPHyPRWITKE		
PKCdelta	Y630-p	KVKSPRDySNFDQEF		
PKCdelta	Y646-p	NEKARLSySDKNLID		
PLCG1	Y379-p	PDGMPVIyHGHTLTT		
PLCG1	Y472-p	KLAEGSAyEEVPTSM	yXXV	
PLCG1	Y481-p	EVPTSMMySENDISN		yXXN
PLCG1	Y506-p	DPVNHEWyPHYFVLT		yXXY
PLCG1	Y509-p	NHEWYPHyFVLTSSK	yXXL	
PLCG1	Y771-p	IGTAEPdyGALYEGR	yXXL	
PLCG1	Y775-p	EPDYGALyEGRNPGF		
PLCG1	Y783-p	EGRNPGFyVEANPMP		yXXA
PLCG1	Y977-p	IGTERACyRDMSSFP	yXXM	
PLCG1	Y1253-p	EGSFESRyQQPFEDF	yXXP	
PLCg2	Y733-p	YRKMLRyPVTPELL		yXXT
PLCg2	Y753-p	ERDINSLyDVSRMYV		yXXS
PLCg2	Y759-p	LYDVSRMyVDPSEIN	yXXP	
PLCg2	Y780-p	TVKALYdyKAKRSDE		
PLCg2	Y1197-p	LESEEElySSCRQLR		
PLCg2	Y1217-p	LNNQLFLyDTHQNLR		
PLCg2	Y1245-p	NENQLQLyQEKCNKR		
PLD2	Y165-p	HAASKQKyLENYLNR		yXXN

PLD2	Y169-p	KQKYLEN y LNRLLT		
PLD2	Y179-p	RLLTMSF y RNYHAMT		yXXY
PLD2	y 470-p	GRWDDLH y RLTDLGD		yXXT
PTPRF	Y1311-p	VEMRRLN y QTPGMRD	yXXP	
PYK2	Y402-p	CSIESDI y AEIPDET	yXXI	
PYK2	y 440-p	EGFFGEV y EGVYTNH	yXXV	
PYK2	Y579-p	RYIEDED y YKASVTR		yXXA
PYK2	Y580-p	YIEDED y YKASVTRL		yXXS
PYK2	Y683-p	VCSLSDV y QMEKDIA		
PYK2	Y699-p	EQERNAR y RTPKILE	yXXP	
PYK2	Y756-p	TLTSPME y PSPVNSL	yXXP	
PYK2	Y834-p	KSLDPMV y MNDKSPL		yXXD
PYK2	Y849-p	TPEKEVG y LEFTGPP		
PYK2	Y881-p	DRTDDL y LVNVMELV	yXXV	
PYK2	Y906-p	CQLPPEG y VVVVKNV	yXXV	
Raf1	Y340-p	RGQRDSS y WEIEAS		
Raf1	Y341-p	GQRDSS y WEIEASE	yXXI	
RasGap	Y239-p	IIAMCGD y YIGRRF		yXXG
RasGap	y 460	TVDGKEI y NTIRRKT	yXXI	
RasGap	y 472-p	RKTKDAF y KNIVKKG	yXXI	
RasGap	Y615-p	VKHFTNP y CNIYLNS	yXXI	
Sam68	Y103-p	KMEPENK y LPELMAE		
Sam68	y 435-p	ARPVKG y AREHPYGR		
Sam68	y 440-p	GAYREHP y GRY		yXXY
Sam68	y 443-p	REHPY y GRY		
SAP97	Y110-p	PSVEKYR y QDEDTPP		
SAP97	Y399-p	KNTSDFV y LKVAKPT	yXXV	
SAP97	Y760-p	YEVDGRD y HFVTSRE	yXXV	
SHC1 iso1	y 315-p	FELRFKQ y LRNPPKL		YXXN
SHC1 iso1	Y349-p	EEPPDHQ y YNDFPKG		yXXD
SHC1 iso1	Y350-p	EPPDHQ y YNDFPGKE		
SHC1 iso1	Y427-p	ELFDDPS y VNVQNL	yXXV	
SHP-1	Y61-p	IQNSGDF y DLYGGEK		yXXY
SHP-1	Y64-p	SGDFYDL y GGEKFAT		
SHP-1	Y208-p	EASGAFV y LRQPYA		YXXQ
SHP-1	Y301-p	SNIPGSD y INANYIK		yXXA
SHP-1	Y374-p	EVGMQRA y GPYSVTN		yXXY
SHP-1	Y377-p	MQRAYGP y SVTNCGE		yXXT
SHP-1	Y390-p	GEHDTTE y KLRTLQV		
SHP-1	Y509-p	EAQYKFI y VAIAQFI	yXXI	
SHP-1	Y536-p	QKGQESE y GNITYPP	yXXI	
SHP-1	Y541-p	SEYGNIT y PPAMKNA		yXXA
SHP-1	Y564-p	SKHKEDV y ENLHTKN	yXXL	
SHP-2	Y62-p	KIQNTGD y YDLYGGE	yXXL	
SHP-2	Y63-p	IQNTGD y YDLYGGEK		yXXY
SHP-2	Y66-p	TGDYIDL y GGEKFAT		

SHP-2	Y279-p	ENKKNRyKNILPFD	yXXI	
SHP-2	Y304-p	PNEPVSdyINANIIM		yXXA
SHP-2	Y327-p	NSKPKKSyIATQGCL		yXXT
SHP-2	Y546-p	SKRKGHEyTNIKYSL	yXXI	
SHP-2	Y584-p	REDSARVyENVGLMQ	yXXV	
SIT	Y90-p	SVEEVPLyGNLHYLQ	yXXL	
SIT	Y95-p	PLYGNLHyLQTGRLS		yXXT
SIT	Y127-p	AAEEVMCyTSLQLRP	yXXL	
SIT	Y148-p	GPGTPVKySEVVLDS	yXXV	
SIT	Y169-p	SGPEPELyASVCAQT	yXXV	
SIT	Y188-p	ASFPDQAyANSQPAA		yXXS
SKAP55	Y142-p	VSRGLFyYANEKSK		YXXN
SKAP55	Y219-p	LSSLTIPyEEDEEEE		yXXD
SKAP55	Y232-p	EEEKEETyDDIDGFD	yXXI	
SKAP55	Y271-p	EKEEEDIyEVLPEDEE	yXXL	
SKAP55	Y295-p	TRRKGVDyASYQGL		yXXY
SKAP55	Y298-p	KGVDYASyYQGLWDC		yXXG
SLP76	Y113-p	SSFEEDdyESPNDQ	yXXP	
SLP76	Y128-p	DGEDDGDyESPNEEE	yXXP	
SLP76	Y145-p	PVEDDADyEPPPSND	yXXP	
SLP76	Y173-p	FPNSNSMyIDRPPSG		
SQSTM1	Y148-p	KCSVCPdyDLCSVCE		
STAT1	Y203-p	QLLLKKMyLMLDNKR	yXXL	
STAT1	Y701-p	DGPKGTGyIKTELIS		yXXT
STAT3	Y45-p	IESQDWAYAASKESH		yXXS
STAT3	Y539-p	LLGPGVnySGCQITW		
STAT3	Y686-p	KEEAFGKyCRPESQE	yXXP	
STAT3	Y705-p	DPGSAAPyLKTkFIC		yXXT
STAT5A	Y90-p	LKIKLGHyATQLQKT		yXXQ
STAT5A	Y694-p	LAKAVDgyVKPQIKQ	yXXP	
Syk	Y74-p	ERELNGTyAIAGGRT		yXXA
Syk	Y131-p	KENLIREyVKQTNWL		yXXQ
Syk	Y203-p	ARDNNGSyALCLLHE		
Syk	Y244-p	LWQLVEHySYKADGL		
Syk	Y296-p	IISRIKSySFPKPGH	yXXP	
Syk	Y323-p	STVSFNPyEPELAPW		
Syk	Y348-p	LPMDTEVyESPYADP	yXXP	
Syk	Y352-p	TEVYESPyADPEEIR	yXXP	
Syk	Y525-p	ALRADENyYKAQTHG		yXXA
Syk	Y526-p	LRADENyYKAQTHGK		yXXQ
Syk	Y568-p	LMWEAFSyGQKPYRG		
TIE2	Y897-p	GACEHRGyLYLAIEY	yXXL	
TIE2	Y992-p	LSRQEVyVKKTMGR		
TIE2	Y1048-p	GMTCAELyEKLPQGY	yXXL	
TIE2	Y1102-p	MLEERKTyVNTTLYE		yXXT
TIE2	Y1108-p	TYVNTTLyEKFTYAG		

TIE2	Y1113-p	TLYEKFT y AGIDCSA	yXXI	
TRPV2	Y523-p	GFQHTGI y SVMIQKV	yXXM	
TSAd	Y39-p	RSCQNLG y TAASPQA		yXXA
TSAd	Y216-p	SQDPNPQ y SPIIKQG	yXXI	
TSAd	Y280-p	PKPSNPI y NEPDEPI	yXXP	
TSAd	Y290-p	PDEPIAF y AMGRGSP		yXXG
TSAd	Y305-p	GEAPSN y VEVEDEG	yXXV	
Vav1	Y142-p	SVGDEDI y SGLSDQI	yXXL	
Vav1	Y160-p	VEEDEDL y DCVENEE	yXXV	
Vav1	Y174-p	EAEGDEI y EDLMRSE	yXXL	
Vav1	Y280-p	YKERFLV y GRYCSQV		yXXY
Vav1	Y791-p	FGTAKAR y DFCARDR		
Vav1	Y826-p	GWWRGEI y GRVGWFP	yXXV	
Vav1	Y844-p	VEEDYSE y C		
Zap-70	Y 46-p	CLRSLGG y VLSLVHD		yXXS
Zap-70	Y 69-p	ERQLNGT y AIAGGKA		yXXA
Zap-70	Y164-p	AHERMPW y HSSLTRE		yXXS
Zap-70	Y248-p	LKADGLI y CLKEACP		
Zap-70	Y292-p	DTLNSDG y TPEPARI		
Zap-70	Y315-p	MPMDTSV y ESPYS DP	yXXP	
Zap-70	Y319-p	TSVYESP y SDPEELK	yXXP	
Zap-70	Y474-p	VLLVNRH y AKISDFG	yXXI	
Zap-70	Y492-p	ALGADDS y YTARSAG		yXXA
Zap-70	Y493-p	LGADDS y YTARSAGK		

Table S2. Summary per protein of peptide array screening of the binding of Lck-SH2 and Lck-SH2-Y192E to 431 phosphopeptides from Lck-interacting proteins.

Reference HPRD§	Number of phospho peptides tested	Number of phospho peptides binding	Contains phosphopeptides with prefered binding to Lck-SH2 domains			Number of Lck SH2 motifs tested	Number of Lck SH2 Y192E motifs tested
			Preferred binding to WT	Preferred binding to Y192E	No preference		
n=	431	260				225	123
3BP2	3	3	x	x		2	1
ACP1	3	2		x		0	2
ADAM15	1	0				0	0
AXL	9	4	x	x		3	4
CAS-L	18	17	x	x		14	2
Cbl	8	6	x	x		4	4
Cd152 (CTLA-4)	2	1	x			2	0
CD28	4	2			x	2	1
CD31 (PECAM)	4	1	x			3	1
CD3e	2	1	x			2	0
CD3z	7	3	x	x		6	1
CD45	5	3	x	x		2	3
CD5	3	2	x	x		2	0
Csk	2	2	x			0	2
CTNND2	8	4	x	x		4	3
DAPP1	1	1			x	1	0
Dok1	11	9	x	x		8	3
DOK2	5	3	x	x		4	1
DOK3	5	4	x	x		3	1
ER-alpha	1	1	x			1	0
ER-beta	1	1	x			1	0
Erk1	2	0				1	1
Erk2	1	0				0	1
Ezrin	7	3	x	x		2	2
FAK	13	7	x	x		7	5
Fas	3	1	x			1	1
Fyn	9	4	x	x		0	6
GAB2	10	6	x	x		9	0
GCSFR	4	3	x	x		2	1
GRAP2 (GADS)	1	0				0	0
IFNAR2	3	2	x			0	1
Ig alpha	4	3	x			3	0
Ig-Beta	2	1		x		2	0
IkB-alpha	2	1	x			1	0
IL2RB	6	3	x	x		1	2
IL3RB	8	4	x	x		5	1

Itk	2	2		x		0	2
JAK3	5	3	x			2	2
KIR2DL2	4	4	x			3	1
KIT	10	4	x			7	1
Lat	6	6	x	x		5	0
Lax1	1	1		x		1	0
Lck	3	2	x			1	1
LIME	4	3			x	4	0
Lyn	12	7	x	x		4	6
MUC1	8	4	x	x		5	2
P130Cas	18	18	x	x		15	1
p85 (PIK3R1)	11	6		x		5	4
PAG	9	8	x	x		8	0
Paxillin (PXN)	8	4	x			6	2
PI3K alpha	2	2	x	x		0	2
PKC alpha	2	1		x		2	0
PKC theta	1	0				0	1
PKCdelta	13	5	x	x		3	2
PLCG1	10	6	x	x		5	3
PLCg2	7	2	x	x		1	2
PLD2	4	2	x	x		0	3
PTPRF	1	0				1	0
PYK2	11	4	x	x		6	3
Raf1	2	2	x	x		1	0
RasGap	4	1			x	3	1
Sam68	4	2			x	0	1
SAP97	3	1	x			2	0
SHC1 iso1	4	2	x	x		1	2
SHP-1	11	6		x		3	6
SHP-2	8	6	x	x		4	3
SIT	6	6	x	x		4	2
SKAP55	6	4	x	x		2	4
SLP76	4	3	x	x		3	0
SQSTM1	1	0				0	0
STAT1	2	0				1	1
STAT3	4	1	x			1	2
STAT5A	2	0				1	1
Syk	11	7	x	x		3	4
TIE2	6	4	x			3	1
TRPV2	1	0				1	0
TSAAd	5	3	x	x		3	2
Vav1	7	4	x	x		4	1
Zap-70	10	6	x	x		3	4
Sum	431	260				225	123