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A central role of IKK2 and TPL2 in JNK activation and viral B-cell transformation

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Supplementary Figures, Tables and References



Supporting evidence for the differential requirement of IKK1 and IKK2 in JNK activation by LMP1. a The siRNA-mediated knockdown of IKK2, but not of IKK1, blocks JNK1 activation by LMP1. Wildtype MEF:NGFR-LMP1wt cells were transfected twice with siRNA targeting IKK1 (siIKK1), IKK2 (siIKK2), or non-targeting control siRNA (siCTRL) in six-well-plates. One day after the last transfection, NGFR-LMP1 was activated by antibody crosslinking and JNK activation was monitored. The knockdown of IKK1 or IKK2 was confirmed by immunoblotting using the indicated antibodies. b No defects in JNK activation by LMP1 in an additional CRISPR/Cas9 IKK1 knockout clone. *IKK1*^{crK0}MEF:NGFR-LMP1wt clones 62 and 69 were induced by antibody crosslinking and analysed by immunoblotting as indicated. The knockout of IKK1 was verified at the protein level by the IKK1 antibody and by sequencing (see Supplementary Table 2).



TAK1 and NEMO mediate signaling complex formation and IKK2 recruitment at LMP1-CTAR2 a The knockout of TAK1 prevents LMP1 interaction with IKK2. The experiment was performed as described in Figure 3f, except that coimmunoprecipitation of LMP1 and IKK2 was performed vice versa. HA-LMP1 was immunoprecipitated via the HA (3F10) antibody and co-precipitating Flag-IKK2 was detected by the IKK2 antibody. **b** NEMO is required for the CTAR2-induced interaction of TAK1 with IKK2. NEMO was targeted by CRISPR/Cas9 in HEK293 cells. HEK293 wildtype and *NEMO*^{crK0} (clone 28) cells were transfected with Flag-IKK2 and HA-TAK1 pSV-LMP1(Y384G). together with wildtype pSV-LMP1 or HA-TAK1 was immunoprecipitated via the HA (3F10) antibody and interacting Flag-IKK2 was detected by the H-470 antibody.



Supportive data for the differential role of TPL2 in JNK and NF-κB activation by LMP1. a The knockout of TPL2 in HEK293 cells interferes with LMP1's ability to induce the JNK pathway and exogenous TPL2 expression rescues JNK activation. The *TPL2* gene was targeted in HEK293 cells by CRISPR/Cas9. Wildtype HEK293 cells and the TPL2 knockout clones 1, 6 and 7 were transfected with HA-JNK1 together with LMP1 wildtype, the inactive AAA/Y384G mutant, or empty vector. Where indicated, TPL2-myc was co-transfected. HA-JNK1 was immunoprecipitated and its activity was monitored in *in vitro* kinase assays using GST-c-Jun as substrate. Quantification of JNK activity is given as x-fold induction versus wildtype cells transfected with AAA/Y384G, normalised to the amounts of immunoprecipitated HA-JNK. Ectopic expression of kinase-active TPL2-myc itself caused a certain activation of JNK. However, TPL2-myc facilitated high levels of JNK activation by LMP1 in TPL2-deficient cells. *TPL2* gene targeting was verified by immunoblotting and sequencing (see Supplementary Table 2). **b** The knockout of TPL2 has no negative effect on LMP1-induced p65 NF- κ B translocation into the nucleus or p65 NF- κ B phosphorylation at serine 536. NGFR-LMP1 was induced in wildtype and *TPL2*^{crK0} (clone 8) cells for the indicated times. Cytoplasmic and nuclear fractions were prepared and analysed by immunoblotting. **c** The knockdown of TPL2 does not affect LMP1-induced p65 NF- κ B phosphorylation at serine 536 or its translocation into the nucleus. Wildtype MEF:NGFR-LMP1wt cells were transfected twice with siRNA targeting murine TPL2 (siTPL2) or non-targeting siRNA (siCTRL). NGFR-LMP1 was induced by antibody crosslinking for the indicated times. Cytoplasmic and nuclear fractions were prepared and further analysed by immunoblotting.

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LMP1 and CD40 signaling in B-cells differ with regard to the functions of TAK1. a, b BL41:NGFR-LMP1wt cells were treated with solvent (DMSO) or 500 nM (5Z)-7-oxozeaenol (TAK1-IH). In (a) NGFR-LMP1 activity was induced by antibody crosslinking (X-link), in (b) CD40 was activated with 600 ng/ml soluble CD40 ligand (CD40L) for the indicated times. JNK, ERK and NF- κ B activation was detected in total cell lysates using the indicated antibodies.



Effects of pharmacological IKK and TPL2 inhibition on lymphoblastoid cells. a IKK inhibition interferes with proliferation of LCLs. LCL721 and LCL 1C3 lymphoblastoid cell lines were either kept in culture without further treatment, in the presence of solvent (DMSO) or 10 μ M ACHP. Cell proliferation was measured at the indicated times as MTT conversion. Data are mean values ±SD of 5 biological replicates. **b** IKK and TPL2 inhibition blocks proliferation of LCLs driven by NGFR-LMP1. LCL.NGFR-LMP1.6 cells were kept under permanent antibody crosslink to activate NGFR-LMP1 signaling (w/o). As indicated, the cells were additionally incubated with DMSO, 10 μ M ACHP, or 10 μ M TC-S7006 (TPL2-IH). MTT assays were performed to monitor proliferation. Data are mean values ±SD of 5 biological replicates. **a**, **b** Statistical analysis was performed with two-way ANOVA at alpha 0.05, p-values: *p≤0.05, **p≤0.01, ***p≤0.001, ****p≤0.0001.

		PxQxT 212	
PTLD880	187	HGQRHSDEHHHDDSLPHPQQATDDSAHESDSNSNEGRHHLLVSGAGDGPPLCSQNLGAPG	246
PTLD099	187	HGQRHSDEHHHDDSLPHPQQATHNSSHESDSNSNEGRHHLLVSGAGDGPPLCSQNLGSPG	246
LMP1 B95.8	187	HGQRHSDEHHHDDSLPHPQQATDDSGHESDSNSNEGRHHLLVSGAGDGPPLCSQNLGAPG	246

PTLD880	247	${\tt GGPDNGPQDPDNTDDNGPQDPDNTDDNGPHDPLPQDPDNTDDNGPQDPDNTDDNGPQDPLPQDPDNTDDNGPQDPDNTDDNGPQDPDNTDDNGPQDPDNTDDNGPQDPDNTDDNGPQDPDNTDDNGPQDPDNTDDNGPQDPDNTDDNGPQDPDNTDDNGPQDPDNTDDNGPQDPDNTDDNGPQDPDNTDDNGPQDPDNTDDNGPQDPDNTDDNGPQDPQDPDNTDDNGPQDPDNTDDNGPQDPDNTDDNGPQDPDNTDDNGPQDPDNTDDNGPQDPQDPDNTDDNGPQDPDNTDDNGPQDPQDPDNTDDNGPQDPQDPDNTDDNGPQDPQDPDNTDDNGPQDPQDPDNTDDNGPQDPQDPDNTDDNGPQDPQDPDNTDDNGPQDPQDPDNTDDNGPQDPQDPDNTDDNGPQDPQDPDNTDDNGPQDPQDPQDPDNTDDNGPQDPQDPQDPDNTDDNGPQDPQDPQDPDNTDDNGPQDPQDPQDPQDPQDPQDPQDPQDPQDPQDPQDPQDPQDP$	306
PTLD099	247	GGPDNGPQDPDNTDDNGPQDPDNTDDNGPHDPL	279
LMP1 B95.8	247	GGPDNGPQDPDNTDDNGPQDPDNTDDNGPHDPL	279

PTLD880	307	PQDPLPQDPDNTDDNGPHDPLPQDPDNTDDNGPQDPDNTDDNGPHDPLPHSPSDSAGNDG	366
PTLD099	280	PQDPDNTDDNGPQDPDNTDDNGPHDPLPHSPSDSAGNDG	318
LMP1 B95.8	280	PQDPDNTDDNGPQDPDNTDDNGPHDPLPHSPSDSAGNDG	318

		328 366	
PTLD880	367	GPPQLTEEVQNKGGDQGPPLMTDGGGGHSHDSGHRGGDPHLPTLLLGTSGSGGDDDDPHG	426
PTLD099	319	${\tt GPPQLTEEV} {\tt Q} {\tt NKGGDQGPPLMTDGGGGHSHDSGHGGGDPHLPTLLLGT} {\tt SGSGGDDDDPHG}$	378
LMP1 B95.8	319	${\tt GPPQLTEEVENKGGDQGPPLMTDGGGGHSHDSGHGGGDPHLPTLLLGSSGSGGDDDDPHG}$	378

PTLD880	427	PVQLSYYD* 434	
PTLD099	379	PVQLSYYD* 386	
LMP1 B95.8	379	PVQLSYYD* 386	

Signaling domains of LMP1 proteins expressed in PTLD099 and PTLD880 cells established from post-transplantation lymphoproliferative disease tumour biopsies. EBV-positive B-cells were isolated from two independent PTLD tumour biopsies derived from two PTLD patients. Genomic DNA was isolated from PTLD099 and PTLD880 cells, the *LMP1* genes were amplified by PCR and the LMP1 signaling domains of both samples were sequenced. Primer sequences are given in Supplementary Table 1. Both tumour-derived LMP1 versions carry mutations as compared to proto-type B95.8 LMP1, which have previously been observed in *LMP1* genes of field isolates ¹⁻³. Most stinkingly, PTLD880 LMP1 carries an insertion of 33 bp repeats after Leu 279 comprising 48 amino acids. The mutational hotspots Gly 212 (destruction box), Glu 328 (JAK3 box 2) and Ser 366 are altered in both tumour-derived LMP1 proteins. Interestingly, PTLD099 carries an unusual mutation of two amino acids proximal to the TRAF interaction site PxQxT of CTAR1. Aspartates 209 and 210 are replaced in PTLD099 LMP1 by histidine and asparagine. Numbering of LMP1 residues refers to amino acid positions in B95.8 LMP1. The PxQxT motif is framed. Mutations in PTLD LMP1 proteins versus B95.8 LMP1 are highlighted in red.

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LMP1-dependent carcinoma cells derived from LMP1-transgenic mice show a significant increase in apoptosis after TPL2 inhibition. The LMP1-negative murine carcinoma line 53.217 and the corresponding LMP1-dependent carcinoma line 53.234a, which was established from *LMP1*-transgenic (*LMP1tg*) mice, were treated with 10 μ M TC-S7006 (TPL2-IH) or DMSO for 24 h. Cells were stained with propidium iodide (PI) and Annexin V-Cy5, and further analysed by flow cytometry. PI-/AnV-Cy5+ cell numbers indicate apoptosis rates. Combined apoptosis rates of six independent experiments are given as mean values ± SD. Statistical analysis was performed with two-way ANOVA at alpha 0.05, p-value: ****p≤0.0001.

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Gating strategy. Lymphocytes and carcinoma cells within the indicated gate were further analysed for PI and AnV-Cy5 staining. By this gating strategy all cells were included into the analysis whereas cell debris was excluded.

Supplementary Table 1 PCR and sequencing primers used in this study.

Name	Sequence	Application
AK549	CACCACTATGCCTGGCTTGA	murine <i>NEMO</i> ex3 forward primer
AK550	TCTGGATGGTTCTTGGGCAC	murine NEMO ex3 reverse primer
AK551	TGCTGTGAATGGAAGTCTAG	murine NEMO ex3 sequencing primer
AK552	AGGCCCTTTGGTCTCCAATG	murine TPL2 ex2 forward primer
AK553	TGGCAGCCATTCTTAAGCCA	murine <i>TPL2</i> ex2 reverse primer
AK554	CAAACACATTATAGTGAAGG	murine TPL2 ex2 sequencing primer
SV008	ATAGGAACCGCACGCACGAT	murine <i>IKK1</i> ex1 forward primer
SV009	TCTAGTCCAGTCTCCAGTGG	murine <i>IKK1</i> ex1 reverse primer
SV010	GACTCTGCATGCGGAAGCTA	murine <i>IKK1</i> ex1 sequencing primer
AK555	TCCCATGGGTCTTGAATGCA	human TPL2 ex2 forward primer
AK556	CATGTTGGCCAGACTGGTCT	human TPL2 ex2 reverse primer
AK557	TGCAAGTGAAGAGCCAGCAG	human TPL2 ex2 sequencing primer
AK558	AGCACCTCCCTTTGGAATGG	human NEMO ex2 forward primer
AK559	ACAGAGGCCTGGACATGTTG	human <i>NEMO</i> ex2 reverse primer
AK560	GCATCCTGATACACTAGGTG	human NEMO ex2 sequencing primer
AK575	TGCTTCTTAGCTTACTCCAC	human TAK1 ex1 forward primer
AK576	CACAGCCCTCAGTAACGTGG	human <i>TAK1</i> ex1 reverse primer
AK577	AAAACGCAGCGGAGCCAGAG	human TAK1 ex1 sequencing primer
AK605	CAACTGCCTTGCTCCTGACACAC	LMP1 forward primer
AK606	GGGAGTGTGTGCCAGTTAAGGTG	LMP1 reverse primer
AK607	GTGATTAGCTAAGGCATTCC	LMP1 sequencing primer

Cell lineª and gene	Accession number	Sigma-Aldrich gRNA ID	Ex ^b	Mutations at gRNA targeting site
MEF	NM_007700.2	MM0000145296	1	Indel, frameshift
<i>IKK1</i> ^{crK0} cl. 62				
MEF	NM_007700.2	MM0000145296	1	Indel, frameshift
<i>IKK1</i> crK0 cl. 69				
MEF IKK2 -/-	NM_007700.2	MM0000145296	1	Indel, frameshift
<i>IKK1</i> ^{crK0} cl.8				
MEF	NC_000086.7	MM0000125118	3	Indel, frameshift
<i>NEMO</i> ^{crK0} cl.2				
MEF	NC_000086.7	MM0000125118	3	Indel, frameshift
<i>NEMO</i> ^{crK0} cl.7			-	
MEF	NC_000086.7	MM0000125118	3	Indel, frameshift
NEMOCIKO CI.19				
MEF	NC_000084.6	MM0000226028	2	Indel, frameshift
TPL2 ^{crK0} cl.8	NG 000010 11	1100000000000000	2	
HEKZ93	NC_000010.11	HS0000206639	Z	Indel, frameshift
	NC 00001011	1100000000000000	n	
HEKZ93	NC_000010.11	HS0000206639	Z	Indel, frameshift
	NC 00001011	450000206620	2	Indol framachift
TDI 2 crK0 cl 7	NC_000010.11	П30000200039	Z	muel, mameshint
	NC 011066 2	4500000272768	1	Indol framoshift
TAK1 crK0 cl 3	NG_011900.2	11300000272700	1	muel, mameshint
HFK202	NG 0098961	HSUUUUU	2	Indel translational
NEMO ^{crK0} cl.28	114_0000001	110000077007	2	start site deleted

Supplementary Table 2 Sequencing results of CRISPR/Cas9-mediated gene knockout cell clones.

NEMO^{crK0} cl.28 ^a All mouse embryonic fibroblast lines express NGFR-LMP1 ^b Exon targeted by gRNA

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Supplementary Table 3. Quantification and statistics of immunoblots (Figures 1 to 6)

n, number of biological replicates SD, standard deviation

Figure	Antibody	Sample	X-link	Mean (n=3)	±SD p-value	e (Y ₃₈₄ G vs. corresponding wt)
Figure 1c	P-JNK	NGFR-LMP1wt	0 min	0.03	0.02	
-	-		20 min	0.05	0.05	
			30 min	0.06	0.07	
			45 min	0.26	0.15	
			60 min	0.54	0.20	
			90 min	0.89	0.14	
			[§] 120 min	1.00	0.00	
			180 min	0.91	0.03	
			360 min	0.84	0.31	
			600 min	0.42	0.14	
		NGFR-LMP1(Y ₂₈₄ G)	0 min	0.03	0.04	
			20 min	0.04	0.04	p = 0.80
			30 min	0.03	0.04	p = 0.58
			45 min	0.04	0.04	p = 0.067
			60 min	0.04	0.05	*p = 0.014
			90 min	0.04	0.05	***p = 0.00059
			120 min	0.06	0.07	****p = 0.000019
			180 min	0.05	0.06	****p = 0.000018
			360 min	0.12	0.11	*p = 0.018
			600 min	0.04	0.04	*p = 0.011
			[§] set to 1		T-test,	unpaired, two-tailed
	Antibody	Sample	X-link	Mean (n=3)	±SD p-value	e (Y ₃₈₄ G vs. corresponding wt)
	ΙκΒα	NGFR-LMP1wt	[§] 0 min	1.00	0.00	
			20 min	0.75	0.12	
			30 min	0.63	0.18	
			45 min	0.39	0.29	
			60 min	0.28	0.14	
			90 min	0.28	0.19	
			120 min	0.31	0.17	
			180 min	0.31	0.16	
			360 min	0.29	0.26	
			600 min	0.48	0.17	
		NGFR-LMP1(Y ₃₈₄ G)	[§] 0 min	1.00	0.00	
			20 min	1.21	0.13	**p = 0.01
			30 min	1.13	0.08	*p = 0.011
			45 min	1.10	0.09	*p = 0.016
			60 min	0.94	0.15	**p = 0.0049
			90 min	0.83	0.20	*p = 0.026
			120 min	1.11	0.38	*p = 0.029
			180 min	1.14	0.38	*p = 0.025
			360 min	1.07	0.43	p = 0.054
			600 min	0.87	0.46	p = 0.24
			[§] set to 1		T-test,	unpaired, two-tailed
		Commite	V link	Maar (g. 2)		
	Antibody	Sample	X-link	Mean $(n=3)$	±SD p-value	e (1 ₃₈₄ G vs. corresponding wt)
Figure 1d	TRAF3	NGFR-LMP1wt	³ 0 min	1.00	0.00	
			60 min	0.40	0.07	
			$120 \min_{s_{2}}$	0.43	0.00	
		NGFR-LMP1(Y ₃₈₄ G)	°0 min	1.00	0.00	
			60 min	0.37	0.20	p = 0.82
			120 min	0.40	0.29	p = 0.86
			[§] set to 1		T-test,	unpaired, two-tailed

Figure 1e	Antibody	Sample	X-link	Mean (n=6)	±SD p-value (I	<i>KK2</i> -/- vs. corresponding WT)
	ΙκΒα	WT	[§] 0 min	1.00	0.00	
			30 min	0.87	0.15	
			60 min	0.46	0.23	
			90 min	0.40	0.26	
			120 min	0.46	0.26	
			180 min	0.49	0.15	
		IKK2 -/-	[§] 0 min	1.00	0.00	
			30 min	0.94	0.13	p = 0.43
			60 min	1.09	0.49	*p = 0.016
			90 min	0.97	0.32	**p = 0.008
			120 min	1.05	0.41	*p = 0.015
			180 min	1.11	0.79	p = 0.085
			[§] set to 1		T-test, unj	paired, two-tailed
	Antibody	Sample	X-link	Mean (n=2)	±SD p-value (I	<i>KK2</i> -/- nucleus vs. corresponding WT nucleus)
Figure 1f	p65	WT. cytoplasm	[§] 0 h	1.00	0.00	, 1 0 ,
i igui e il	poo		0 h 1 h	0.55	0.26	
			2 h	0.50	0.24	
		<i>IKK2</i> - /-, cytoplasm	[#] 0 h	1 00	0.00	
			0 n 1 h	0.87	0.01	
			2 h	0.84	0.18	
				0.01		

0 h 1 h

2 h

0 h

1 h

2 h

 $^{\$}$ set to 1 for WT

[#]set to 1 for *IKK2* -/-

0.00

0.84

0.80

0.00

0.01

0.00

0.00

0.46

0.09

0.00

0.01

0.00

p = 0.12

**p = 0.0056

T-test, unpaired, two-tailed

WT, nucleus

IKK2 -/-, nucleus

	Antibody	Sample	X-link	Mean $(n=6^{\dagger})$	±SD p-val	ue (<i>IKK2</i> -/- vs. corresponding WT)
Figure 2a	P-JNK	WT	0 min	0.03	0.04	
-	-		30 min	0.12	0.13	
			60 min	0.42	0.23	
			90 min	0.79	0.28	
			[§] 120 min	1.00	0.00	
			180 min	1.22	0.51	
		IKK2 -/-	0 min	0.01	0.01	
			30 min	0.01	0.02	p = 0.062
			60 min	0.02	0.03	**p = 0.0018
			90 min	0.07	0.10	***p = 0.00013
			120 min	0.09	0.13	****p = 0.000000013
			180 min	0.05	0.06	***p = 0.00024
			[§] set to 1		T-tes	t, unpaired, two-tailed
					[†] stimu into t which replic	ulation times were included he quantitative analysis, 1 were tested in all biological cates
Figuro 2h	Antibody	Sample	X-link	Mean (n=3)	±SD p-val	ue (ACHP vs. corresponding DMSO)
rigui e 20	r-jnk	DM30	0 min	0.01	0.01	
			60 min	0.02	0.01	
			90 min	0.71	0.38	
			[§] 120 min	1.00	0.00	
			120 min	0.87	0.14	
		ACHP	0 min	0.00	0.00	
			30 min	0.00	0.00	
			60 min	0.01	0.01	p = 0.14
			90 min	0.04	0.02	*p = 0.039
			120 min	0.09	0.06	****p = 0.000013
			180 min	0.12	0.13	**p = 0.0025
			[§] set to 1		T-tes	t, unpaired, two-tailed

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	Antibody	Sample	TNFα	Mean (n=3 [†])	±SD p-val	lue (<i>IKK2</i> -/- vs. corresponding WT)
Figure 2c	P-JNK	IKK2 -/-	0 min	0.03	0.04	
			10 min	0.46	0.15	**p = 0.0029
			20 min	0.64	0.19	p = 0.41
			30 min	0.13	0.09	p = 0.73
		WT	0 min	0.05	0.07	
			[§] 10 min	1.00	0.00	
			20 min	0.49	0.20	
			30 min	0.10	0.11	
			[§] set to 1		T-tes	st, unpaired, two-tailed
					[†] stim into t whic repli	nulation times were included the quantitative analysis, h were tested in all biological cates
	Antibody	Sample	ΤΝΓα	Mean (n=3*)	±SD p-val	lue (<i>IKK2 -/-</i> vs. corresponding WT)
	ΙκΒα	IKK2 - / -	[§] 0 min	1.00	0.00	
		,	10 min	0.88	0.10	***p = 0.00021
			20 min	0.79	0.17	**p = 0.0013
			30 min	0.71	0.10	***p = 0.00091
		WT	[§] 0 min	1.00	0.00	•
			10 min	0.04	0.06	
			20 min	0.01	0.02	
			30 min	0.11	0.06	
			[§] set to 1		T-tes	st, unpaired, two-tailed
					[†] stim into t whic replie	nulation times were included the quantitative analysis, h were tested in all biological cates
Figure 2d	Antibody P-INK	Sample IKK2 - /-	IL-1 0 min	Mean (n=3)	±SD p-val	lue (<i>IKK2</i> -/- vs. corresponding WT)
1 igui e 2u	1 JINIX	11112 /	5 min	0.00	0.22	n = 0.63
			10 min	0.86	0.25	n = 0.52
			15 min	1.10	0.29	p = 0.52 p = 0.71
			20 min	0.74	0.55	p = 0.46
			30 min	0.39	0.19	p = 0.81
			45 min	0.10	0.05	p = 0.74
			60 min	0.11	0.10	n = 0.76

0 min

	5 min	0.45	0.50	
	10 min	0.99	0.19	
	15 min	0.99	0.40	
	[§] 20 min	1.00	0.00	
	30 min	0.45	0.37	
	45 min	0.12	0.11	
	60 min	0.14	0.13	
	[§] set to 1		T-test, u	inpaired, two-tailed
Sample	IL-1	Mean (n=3)	±SD p-value	(<i>IKK2</i> -/- vs. corresponding WT)
IKK2 -/-	[§] 0 min	1.00	0.00	
·	5 min	0.62	0.11	p = 0.084
	10 min	0.42	0.05	***p = 0.00014
	15 min	0.24	0.08	**p = 0.0071
	20 min	0.15	0.09	p = 0.054
	30 min	0.14	0.08	p = 0.21
	45 min	0.68	0.35	p = 0.61
	60 min	0.89	0.23	p = 0.46
WT	[§] 0 min	1.00	0.00	
	5 min	0.35	0.18	
	10 min	0.00	0.01	
	15 min	0.00	0.01	
	20 min	0.01	0.01	
	30 min	0.06	0.06	
	45 min	0.55	0.24	
	60 min	1.08	0.32	
	[§] set to 1		T-test. u	inpaired, two-tailed

0.00

0.00

Antibody ΙκΒα

WT

	Antibody	Sample	X-link	Mean (n=2)	±SD p-value	(vs. corresponding WT)
Figure 2e	P-JNK	WT	0 min	0.04	0.01	
-			30 min	0.11	0.13	
			60 min	0.55	0.28	
			90 min	0.87	0.12	
			120 min	0.97	0.15	
			[§] 180 min	1.00	0.00	
		IKK1 ^{crKO}	0 min	0.00	0.00	
			30 min	0.03	0.04	p = 0.47
			60 min	0.42	0.16	p = 0.61
			90 min	0.75	0.14	p = 0.45
			120 min	0.44	0.14	p = 0.068
			180 min	0.46	0.17	*p = 0.043
		IKK2 -/-	0 min	0.00	0.00	Ĩ
			30 min	0.00	0.00	p = 0.35
			60 min	0.00	0.00	p = 0.11
			90 min	0.17	0.15	*p = 0.035
			120 min	0.19	0.16	*p = 0.037
			180 min	0.09	0.06	**p = 0.0019
		IKK1 ^{crKO} /IKK2 -/-	0 min	0.00	0.00	1
		, ,	30 min	0.00	0.00	p = 0.35
			60 min	0.01	0.01	p = 0.11
			90 min	0.19	0.16	*n = 0.041
			120 min	0.00	0.00	$p^{*} = 0.012$
			180 min	0.03	0.04	***p = 0.00094
			[§] set to 1		T-test, u	inpaired, two-tailed
	Antibody	Sample	Y-link	Mean $(n-2)$	+SD n-value	(vs. corresponding WT)
	Index		[§] 0 min	1 00		(vs. corresponding wr)
	IKDU	VV 1	0 min	1.00	0.00	
			50 min	0.09	0.27	
			90 min	0.27	0.11	
			120 min	0.15	0.10	
			120 min	0.24	0.17	
		UZIZA CrKO	\$0 min	1.00	0.00	
		IKKI	20 min	1.00	0.00	m = 0.00
			SU min	0.15	0.16	p = 0.08
			60 min	0.07	0.10	p = 0.19
			90 mm	0.14	0.05	p = 0.94
			120 min	0.21		p = 0.81
				0.26	0.15	p = 0.68
		IKKZ -/-	³ 0 min	1.00	0.00	
			30 min	0.84	0.01	p = 0.81
			60 min	0.89	0.06	*p = 0.019
			90 min	0.80	0.10	p = 0.036
			120 min	0.81	0.01	p = 0.043

IKK1 ^{crK0} /IKK2 -/-	
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180 min	0.88	0.09	*p = 0.011
[§] 0 min	1.00	0.00	
30 min	1.95	0.34	p = 0.073
60 min	1.84	0.21	*p = 0.01
90 min	2.06	0.73	p = 0.067
120 min	1.22	0.59	p = 0.15
180 min	0.97	0.47	p = 0.18

			Μ	ean (n=2 WT,		
	Antibody	Sample	X-link n=5 NEM	10 ^{crK0} clones)	±SD p-value	(<i>NEMO</i> ^{crKO} vs. corresponding WT)
Figure 2f	P-JNK	WT	0 min	0.01	0.01	
			30 min	0.15	0.22	
			60 min	0.48	0.35	
			90 min	0.84	0.40	
			[§] 120 min	1.00	0.00	
			180 min	0.61	0.21	
		NEMO ^{crKO}	0 min	0.00	0.00	
			30 min	0.00	0.00	p = 0.12
			60 min	0.00	0.00	*p = 0.015
			90 min	0.00	0.00	**p = 0.0024
			120 min	0.04	0.08	****p = 0.000015
			180 min	0.08	0.16	*p = 0.013
			[§] set to 1		T-test, ι	inpaired, two-tailed

		Mea	an (n=2 WT,			
Antibody	Sample	X-link n=5 <i>NEMO</i>	^{crKO} clones)	±SD p-value (<i>NEMO</i> ^{crKO} vs. corresponding WT)		
ΙκΒα	WT	[§] 0 min	1.00	0.00		
		30 min	0.65	0.33		
		60 min	0.32	0.41		
		90 min	0.14	0.03		
		120 min	0.44	0.37		
		180 min	0.10	0.11		
	NEMO ^{crKO}	[§] 0 min	1.00	0.00		
		30 min	0.76	0.16	p = 0.56	
		60 min	0.70	0.43	p = 0.34	
		90 min	0.54	0.18	*p = 0.03	
		120 min	0.54	0.22	p = 0.66	
		180 min	0.81	0.57	p = 0.16	
		[§] set to 1		T-test, unpa	iired, two-tailed	

	Antibody	Sample	X-link	Mean (n=3)	±SD	p-value (TAK1-IH vs. corresponding DMSO)
Figure 3a	P-JNK	DMSO	0 min	0.00	0.00	
			30 min	0.08	0.13	
			60 min	0.43	0.68	
			90 min	0.86	0.61	
			[§] 120 min	1.00	0.00	
		TAK1-IH	0 min	0.00	0.00	
			30 min	0.03	0.04	p = 0.56
			60 min	0.00	0.00	p = 0.33
			90 min	0.00	0.01	p = 0.073
			120 min	0.04	0.06	****p = 0.000011
			[§] set to 1			T-test, unpaired, two-tailed
	Antibody	Sample	X-link	Mean (n=3)	±SD]	p-value (TAK1-IH vs. corresponding DMSO)
	ΙκΒα	DMSO	[§] 0 min	1.00	0.00	
			30 min	0.61	0.20	
			60 min	0.36	0.27	
			90 min	0.21	0.08	
			120 min	0.20	0.05	
		TAK1-IH	[§] 0 min	1.00	0.00	
			30 min	0.64	0.16	p = 0.85
			60 min	0.26	0.11	p = 0.59
			90 min	0.16	0.11	p = 0.55
			120 min	0.07	0.07	p = 0.077
			[§] set to 1			T-test, unpaired, two-tailed
	Antibody	Sampla	V link	$M_{000}(n-2)$	+5D	n value (vs. IMP1 wt. WT)
Figuro 3h	P_IKK2 \$177/181	WT + TAK1-IH	X-IIIK Vector	0.00		p-value (vs. LMI 1 wt, wij
i igui e 55	1 IRR2 51777101		LMP1 wt	0.86	0.36	n = 0.57
			AAA/Y ₂₀₄ G	0.15	0.24	p 0.07
		WT	vector	0.00	0.00	
			[§] I MP1 wt	1.00	0.00	
				1.00	0.00	
		TTAKA CrKO	AAA/ 1 384U	0.09	0.00	
		IAKI	vector	0.00	0.00	
			LMP1 wt	0.00	0.00	no p-value determinable vs. WT
			AAA/Y ₃₈₄ G	0.00	0.00	
			[§] set to 1		,	T-test, unpaired, two-tailed

				Mean (n=4 DMSO,		
	Antibody	Sample	St MD4	ACHP, n=3 TAK1-IHJ	±SD p-value	(VS. LMP1 Wt, DMSO)
Figure 3d	P-IKK2 S177/181	DMSO	^o LMP1 Wt	L 0.10	0 22	
		аснр	I MP1 wt	0.19	0.23	***n – 0 0002
		AGIII	vector	0.13	0.00	p – 0.0002
		ТАК1-ІН	LMP1 wt	1.18	0.49	p = 0.50
			vector	0.28	0.37	F
			[§] set to 1		T-test, v	unpaired, two-tailed
Figuro 3o	Antibody	Sample	w/o	Mean (n=2)	±SD p-value	(vs. LMP1 wt, WT)
rigule se	obiquitin		LMP1 wt	0.09	0.07	n = 0.083
		WT	w/o	0.19	0.27	p = 0.003
			[§] LMP1 wt	1.00	0.00	
		TAK1 ^{crKO}	w/o	0.03	0.04	
			LMP1 wt	0.07	0.09	**p = 0.0049
			[§] set to 1		T-test, ı	unpaired, two-tailed
Figure 3f	Antibody	Sample		Mean (n=3)	±SD p-value	(vs. LMP1wt WT)
	LMP1	WT	[§] LMP1 wt	1.00	0.00	
		WT	LMP1 AAA/Δ371	0.03	0.04	
		TAK1 ^{crKO}	LMP1wt	0.03	0.04	**** p < 0.0001
		TAK1 ^{crKO}	LMP1 AAA/Δ371	0.00	0.00	
				$^{\$}$ set to 1	T-test, v	unpaired, two-tailed
Figure 4a	Antibody		Sample	Mean (n=4)	±SD p-value	(vs. LMP1 WT)
	P-TPL2 S400		[§] LMP1 WT	1	0	
			LMP1 AAA/Y ₃₈₄ G	0.48	0.36	*p = 0.029
			[§] set to 1		T-test, ı	unpaired, two-tailed

Figure 4b	Antibody		X-link	n=1		
	P-TPL2 S400		0 min	0		
			[§] 30 min	1		
			60 min	0		
			[§] set to 1			
	Antibody	Sample	X-link lean (n=5	5, n=2 for 3 h)	±SD p-value	(vs. 0 h)
Figure 4c	TPL2	NGFR-LMP1wt	[§] 0 h	1	0	
-			1 h	0.36	0.23	**p = 0.0032
			2 h	0.10	0.07	****p < 0.00001
			3 h	0.06	0.07	*p = 0.032
			[§] set to 1		T-test, u	npaired, two-tailed

	Antibody	Sample	X-Link	Mean (n= 2^{\dagger})	±SD p-va	alue (60 min vs. 0 min)
Figure 4d	TPL2	TPL2 coIP	[§] 0 min	1	0	
		TPL2 coIP	60 min	0.42	0.26	p = 0.086
			[§] set to 1		T-te	est, unpaired, two-tailed
					[†] stir into whi biol	mulation times were included o the quantitative analysis, ch were tested in both ogical replicates
	Antibody	Sample	X-Link	Mean (n=2)	+SD n-v	alue (siIKK2 vs. corresponding siCTRL)
Figure 4e	TPI 2	siCTRI	[§] 0 h	1 00	1000 p v	and (sinking vs. corresponding storing)
rigure r e	11 62	SIGTICE	0 h 1 h	0.31	0.00	
			2 h	0.26	0.24	
		siIKK2	[§] 0 h	1.00	0.00	
		SHIKKZ	0 h 1 h	1.00	0.11	n = 0.055 ** $n = 0.0072$
			2 h	0.93	0.11	p = 0.072 * $p = 0.015$
			[§] set to 1		T-te	est, unpaired, two-tailed two-way ANOVA
	Antibody	Sample	X-Link	Mean (n=2)	±SD p-va	alue (ACHP vs. corresponding DMSO)
Figure 4f	TPL2	DMSO	[§] 0 h	1.00	0.00	
C			1 h	0.32	0.34	
			2 h	0.10	0.12	
		ACHP	[§] 0 h	1.00	0.00	
			1 h	1.04	0.20	p = 0.12
			2 h	0.88	0.20	*p = 0.041
			[§] set to 1		T-te	est, unpaired, two-tailed
	Antibody	Sample	X-Link	Mean (n=2)	±SD p-va	alue (<i>IKK2</i> -/- vs. corresponding WT)
Figure 4g	TPL2	WT	[§] 0 h	1 00	0.00	
- 1941 C 15			1 h	0.50	0.24	
			2 h	0.14	0.15	
			3 h	0.08	0.09	
		IKK2 - / -	[§] 0 h	1.00	0.00	
		/	1 h	1.01	0.10	p = 0.1
			2 h	0.93	0.14	*p = 0.033
			3 h	1.33	0.06	**p = 0.0037

Figure 5a	Antibody P-JNK	Sample siCTRL	X-Link 0 min	Mean (n=3 [†]) 0.00	±SD p-value (siTPL 0.00	.2 vs. corresponding siCTRL)
-			30 min	0.00	0.00	
			60 min	0.04	0.04	
			[§] 120 min	1.00	0.00	
		siTPL2	0 min	0.00	0.00	
			30 min	0.00	0.00	
			60 min	0.04	0.05	p = 0.91
			120 min	0.42	0.12	**p = 0.0011
			[§] set to 1		T-test, unpaire	ed, two-tailed
					[†] stimulation ti into the quant which were te replicates	mes were included itative analysis, sted in all biological
	Antibody	Sample	X-Link	Mean (n=3 [†])	±SD p-value (siCT)	RL vs. corresponding siTPL2)
	ΙκΒα	siCTRL	[§] 0 min	1.00	0.00	
			30 min	0.74	0.34	
			60 min	0.29	0.23	
			120 min	0.20	0.12	
		siTPL2	[§] 0 min	1.00	0.00	
			30 min	0.75	0.20	p = 0.96
			60 min	0.31	0.24	p = 0.92
			120 min	0.24	0.20	p = 0.77
			[§] set to 1		T-test, unpaire	ed, two-tailed
					[†] stimulation ti into the quant which were te replicates	mes were included itative analysis, sted in all biological
Figure 5b	Antibody P-JNK	Sample DMSO	X-Link 0 min 20 min	Mean (n=4) 0.02	±SD p-value (TPL2 0.04 0.04	-IH vs. corresponding DMSO)
			50 min	0.03	0.04	
			90 min	0.11	0.00	
			$\frac{9120}{1}$ min	1 00	0.00	
			120 IIIII 180 min	1.00	0.00	
		трі 2-ін	Ω min	1.14	0.12	
		11 44-111	30 min	0.00	0.00	n = 0.16
			60 min	0.00	0.05	p = 0.10 n = 0.6
			90 min	0.21	0.11	*n = 0.025

		90 min	0.21	0.11	*p = 0.025
		120 min	0.35	0.10	****p = 0.000012
		180 min	0.20	0.08	****p = 0.00001
		[§] set to 1		T-test,	unpaired, two-tailed
Antibody	Sample	X-Link	Mean (n=4)	±SD p-value	e (TPL2-IH vs. corresponding DMSO)
ΙκΒα	DMSO	[§] 0 min	1.00	1.00	
		30 min	0.50	0.50	
		60 min	0.18	0.18	
		90 min	0.22	0.22	
		120 min	0.25	0.25	
		180 min	0.29	0.29	
	TPL2-IH	[§] 0 min	1.00	0.00	
		30 min	0.64	0.21	p = 0.23
		60 min	0.43	0.23	p = 0.07
		90 min	0.28	0.22	p = 0.59
		120 min	0.36	0.31	p = 0.55
		180 min	0.29	0.19	p = 0.99
		[§] set to 1		T-test,	unpaired, two-tailed

Figure Sc P- NK TPL2 = ⁵⁶⁰ 0 mm 0.00 *p = 0.020 *p = 0.020 *p = 0.020 *p = 0.020 *p = 0.0032 *p = 0.0034 *p = 0.0034 *p = 0.0034 *p = 0.004 *p = 0.064 *p = 0.051 <t< th=""><th></th><th>Antibody</th><th>Sample</th><th>X-Link</th><th>Mean (n=2[†])</th><th>±SD p-value</th><th>(<i>TPL2</i> ^{crK0} vs. corresponding WT)</th></t<>		Antibody	Sample	X-Link	Mean (n=2 [†])	±SD p-value	(<i>TPL2</i> ^{crK0} vs. corresponding WT)
Antibody Sample Sample X-Link MT Main 30 min 30 min 30 min 30 min 30 min 30 min 40	Figure 5c	P-JNK	TPL2 ^{crKO}	0 min	0.00	0.00	
WT 60 min 90 min 0.03 0.14 0.03 $p = 0.15$ 0.00032 90 min 0.00 0.01 0.02 ****p = 0.00032 60 min 590 min 0.10 0.02 60 min 590 min 0.01 0.02 60 min 590 min 0.00 0.01 ****p = 0.00032 60 min 0.02 0.01 ****p = 0.00032 60 min 0.02 0.00 ****p = 0.00032 ****p = 0.00032 ****p = 0.00032 ****p = 0.000 ***** ************************************	0	-		30 min	0.01	0.01	*p = 0.020
WT 90 min 0 min 30 min 0.10 0.01 0.02 0.02 **** p = 0.00032 0.02 60 min 0.10 0.02 0.02 0.02 0.02 60 min 10.00 0.41 0.14 0.14 *90 min *set to 1 1.00 0.00 * *set to 1 T-test, unpaired, two-tailed into the quantitative analysis, which were tested in both biological replicates * Antibody Sample X-Link Mcan (n=2 ¹) +SD p-value (TPL2 ^{cr00} vs. corresponding WT) IkBa TPL2 ^{cr00} *60 min 0 min 1.00 0.00 p = 0.66 WT *60 min 60 min 1.20 min 0.48 0.56 * *set to 1 T-test, unpaired, two-tailed *stimulation times were included into the quantitative analysis, which were tested in both biological replicates *figure 5d Antibody Sample *LMP1 WT 1.00 0.00 *set to 1 * T-test, unpaired, two-tailed *stimulation times were included into the quantitative analysis, which were tested in both biological replicates * *120 min 0.48 0.56 * *50 p-value (TPL2 ^{cr00}) vs. WT) * p = 0.059 p50 WT,				60 min	0.10	0.14	p = 0.15
WT 0 min 30 min (0.10) 0.01 0.02 (60 min 1.00) 0.01 0.14 ⁸ 90 min 1.00 0.00 ⁴ set to 1 T-test, unpaired, two-tailed ¹ stimulation times were included into the quantitative analysis, which were tested in both biological replicates Antibody Sample 7PL2 ^{erk0} X-Link Mean (n=2 ¹) ±SD p-value (TPL2 ^{erk0} vs. corresponding WT) ikBa TPL2 ^{erk0} ⁶ 0 min 0.01 0.00 0.00 WT ⁶ 0 min 0.027 0.06 p = 0.064 120 min 0.028 0.10 p= 0.064 120 min 0.028 0.10 WT ⁶ set to 1 T-test, unpaired, two-tailed istuitation times were included into the quantitative analysis, which were tested in both biological replicates Figure 5d Antibody Sample Mean (n=3) ±SD p-value (TPL2 ^{erk0} vs. WT) ⁶ set to 1 ⁶ set to 1 T-test, unpaired, two-tailed into the quantitative analysis, which were tested in both biological replicates Figure 5d Po5 WT, nucleus ¹ LMP1 WT 1.00 0.00 7PL2 ^{erk0} , nucleus ¹ LMP1 WT 1.00 0.00 1 7PL2 ^{erk0} , nucleus ¹ LMP				90 min	0.03	0.01	****p = 0.000032
Antibody Sample X-Link Mean $(n-2^1)$ ±SD p-value (<i>TPL2</i> ^{ext0}) vs. WT) kBa <i>TPL2</i> ^{ext0} No No No No Matibody Sample X-Link Mean $(n-2^1)$ ±SD p-value (<i>TPL2</i> ^{ext0}) vs. corresponding WT) kBa <i>TPL2</i> ^{ext0} *0 min 1.00 0.00 p= 0.66 WT *0 min 0.00 0.00 p= 0.66 WT *0 min 0.00 p= 0.66 WT *0 min 0.00 p= 0.66 *0 min 0.00 0.00 p= 0.66 *0 min 0.04 0.00 p= 0.66 *0 min 0.04 0.05 p= 0.66 *0 min 0.48 0.55 0.05 *120 min 0.48 0.55 0.05 *set to 1 *set to 1 *set to 1 *set to 1 *set to 1 *set to 1 0.00 *set to 1 *set to 1 *set to 1 0.00 *set to 1 *set to 1 *set to 1 *set to 1 0.00 0.00 *set to 1 0.00 <t< th=""><th></th><th></th><th>WT</th><th>0 min</th><th>0.00</th><th>0.01</th><th></th></t<>			WT	0 min	0.00	0.01	
60 min 0.41 0.14 ⁶ 90 min 1.00 0.00 ⁸ set to 1 T-test, unpaired, two-tailed into the quantitative analysis, which were tested in both biological replicates Antibody Sample X-Link Mean (n=2 ¹) ±SD ±SD p-value (TPL2 ^{er80} vs. corresponding WT) htBa TPL2 ^{er80} ⁸ 0 min 1.00 0.00 p= 0.064 120 min 0.28 0.10 p= 0.064 120 min 0.48 0.56 WT ⁶ 0 min 0.47 0.05 120 min 0.48 0.56 T-test, unpaired, two-tailed into the quantitative analysis, which were tested in both biological replicates Mean (n=3) ±SD p-value (TPL2 ^{er80} vs. WT) test, unpaired, two-tailed istimulation times were included into the quantitative analysis, which were tested in both biological replicates Mean (n=3) ±SD p-value (TPL2 ^{er80} vs. WT) Figure 5d p65 965 WT, nucleus LMP1 WT 1.00 0.00 TPL2 ^{er80} , nucleus LMP1 WT 1.00 0.00 <t< th=""><th></th><th></th><th></th><th>30 min</th><th>0.10</th><th>0.02</th><th></th></t<>				30 min	0.10	0.02	
Figure 5d Antibody Sample X-Link Mean (n=21) $\pm SD$ p-value ($TPL2^{cR0}$ vs. corresponding WT) biological replicates Matibody Sample X-Link Mean (n=21) $\pm SD$ p-value ($TPL2^{cR0}$ vs. corresponding WT) biological replicates Matibody Sample X-Link Mean (n=21) $\pm SD$ p-value ($TPL2^{cR0}$ vs. corresponding WT) biological replicates WT $\frac{80}{90}$ min 1.00 0.00 WT $\frac{90}{10}$ min 0.00 WT $\frac{90}{10}$ min 0.00 $\frac{120}{120}$ min 0.48 0.56 Figure 5d Antibody Sample Mean (n=3) $\pm SD$ p-value ($TPL2^{cR0}$ vs. WT) $\frac{120}{120}$ min 0.48 0.56 $\frac{120}{120}$ min 0.00 Figure 5d p65 WT, nucleus $\frac{1}{140}$ HWT 1.00 0.00 $7FL2^{cR0}$, nucleus $1MP1$ WT 1.00 0.00 00 $7FL2^{cR0}$, nucleus $1MP1$ WT 1.00 0.00 00 $7FL2^{cR0}$, nucleus $1MP1$ WT 1.00 0.00 0.00 0.00 0.00 $7FL2^{cR0}$, nucleus $1MP1$ WT 1.00				60 min	0.41	0.14	
Figure 5d Antibody Sample X-Link Mean $(n=2^1)$ ±SD y-value $(TPL2^{cr60} vs. corresponding WT)$ biological replicates Mathematical Science $TPL2^{cr60}$ $\frac{8}{0}$ min 1.00 0.00 $p = 0.064$ WT $\frac{8}{0}$ min 1.00 0.00 $p = 0.064$ $p = 0.66$ WT $\frac{8}{0}$ min 1.00 0.00 $p = 0.66$ WT $\frac{8}{0}$ min 1.00 0.00 $\frac{8}{0}$ min 1.00 0.00 $p = 0.66$ WT $\frac{8}{0}$ min 1.00 0.00 $\frac{8}{2}$ min 0.05 $rest$, unpaired, two-tailed $\frac{1}{20}$ min 0.48 0.56 Figure 5d $p (5 m)^{-1}$ mcleus $FLMP1WT$ 1.00 0.00 $\frac{7}{120}^{cr60}$, nucleus $\frac{1}{1}$ MP1WT 1.02 $p = 0.59$ $p (5 m)^{-1}$ nucleus $\frac{1}{1}$ MP1WT 1.00 0.00 $m = 0.18$ $\frac{7}{712}c^{cr60}$, nucleus $\frac{1}{1}$ MP1WT 1.00 0.00 $m = 0.81$ $\frac{7}{712}c^{cr60}$, nucleus $\frac{1}{1}$ MP1WT 1.00 0.00 $m = 0.80$ $\frac{7}{712}c^{cr60}$				[§] 90 min	1.00	0.00	
Figure 5dAntibodySample TPL2 etto nucleusX-Link 9 min 1.00 Mean $(n=2^1)$ $\pm SD$ $p-value (TPL2^{-rit0} vs. corresponding WT)hcB\alphahcB\alphaTPL2^{-rit0}120 min120 min100100T-test, unpaired, two-tailedinto the quantitative analysis, which were tested in bothbiological replicatesFigure 5dMT, nucleusTPL2^{=tK0} nucleus1LMP1 WT17001000100100Figure 5dMT, nucleusTPL2^{=tK0} nucleus1LMP1 WT10001000100100p52WT, nucleus1RU2LMP1 WT100010001001000$				$^{\$}$ set to 1		T-test, ι	inpaired, two-tailed
Antibody IkBa Sample TPL2 ^{cr80} X-Link $0 min$ Mean (n=2 ^T) ±SD p-value (TPL2 ^{cr80} vs. corresponding WT) $0 min$ 0.00 0.00 p=0.064 WT $\frac{5}{0} min$ 0.00 p=0.66 WT $\frac{5}{0} min$ 0.00 0.00 $60 min$ 0.47 0.05 120 min 0.48 0.56 WT $\frac{5}{6}$ set to 1 T-test, unpaired, two-tailed $\frac{1}{5}$ stimulation times were included into the quantitative analysis, which were tested in both biological replicates $\frac{1}{5}$ set to 1 Figure 5d MT, nucleus $\frac{5}{1}$ LMP1 WT 1.00 0.00 $p50$ WT, nucleus $\frac{1}{10}$ LMP1 WT 1.22 0.32 p = 0.059 p50 WT, nucleus $\frac{1}{10}$ LMP1 WT 1.00 0.00 0.00 $p50$ WT, nucleus $\frac{1}{10}$ LMP1 WT 1.00 0.00 0.00 $p212^{cr60}$, nucleus LMP1 WT 1.00 0.00 0.00 0.00 0.00 $p50$ WT, nucleus $\frac{5}{1}$ LMP1 WT 1.00 0.00 0.00 0.00 0.00 0.00 0.00						[†] stimula into the which v biologic	ation times were included quantitative analysis, vere tested in both cal replicates
$ \begin{tabular}{ c c c c c c } \hline \begin{tabular}{ c c c c c c c } \hline & RB & $TPL2ctK0 & $TPL2ctK0 & 120 min & 0.28 & 0.10 & p = 0.064$ \\ \hline 120$ min & 0.28 & 0.10 & p = 0.66$ \\ \hline 120$ min & 0.47 & 0.05 & 120 min & 0.48 & 0.56 & 0.00 & $$120$ min & 0.48 & 0.56 & $$120$ min & $$120$ min & $$0.48$ & $$0.56$ & $$120$ min & $$120$ min & $$0.48$ & $$0.56$ & $$120$ min & $$120$ min & $$0.48$ & $$0.56$ & $$120$ min & $$120$ min & $$0.48$ & $$0.56$ & $$120$ min & $$120$ min & $$0.48$ & $$0.56$ & $$120$ min & $$120$ min & $$0.48$ & $$0.56$ & $$120$ min & $$120$ min & $$0.48$ & $$0.56$ & $$120$ min & $$120$ min & $$0.48$ & $$0.56$ & $$120$ min & $$12$		Antibody	Sample	X-Link	Mean (n=2 [†])	±SD p-value	(<i>TPL2</i> ^{crKO} vs. corresponding WT)
Figure 5d Antibody Sample Mean (n=3) \pm SD p-value (TPL2 ^{erK0} vs. WT) $p50$ WT, nucleus $\frac{1}{2}$ LMP1 WT 1.00 0.00 $p50$ WT, nucleus $\frac{1}{2}$ LMP1 WT 1.00 0.00 $p50$ WT, nucleus $\frac{1}{2}$ LMP1 WT 1.00 0.00 $p50$ WT, nucleus $\frac{1}{2}$ LMP1 WT 0.00 $p = 0.059$ $p50$ WT, nucleus $\frac{1}{2}$ LMP1 WT 0.00 $p = 0.059$ $p50$ WT, nucleus $\frac{1}{2}$ LMP1 WT 0.00 $p = 0.059$ $p50$ WT, nucleus $\frac{1}{2}$ LMP1 WT 0.00 $p = 0.059$ $p50$ WT, nucleus $\frac{1}{2}$ LMP1 WT 0.00 $p = 0.059$ $p50$ WT, nucleus $\frac{1}{2}$ LMP1 WT 0.00 $p = 0.059$ $p50$ WT, nucleus LMP1 WT 0.00 $p = 0.18$ $p52$ WT, nucleus $\frac{1}{2}$ LMP1 WT 0.00 $p = 0.80$ $p52$ WT, nucleus $\frac{1}{2}$ LMP1 WT 0.08 0.83 $p = 0.81$		ΙκΒα	TPL2 ^{crKO}	[§] 0 min	1.00	0.00	
Figure 5d Antibody Sample Mean (n=3) ±SD p-value (<i>TPL2</i> ^{orK0} vs. WT) $p50$ WT, nucleus ${}^{9}LMP1$ WT 1.00 0.00 $TPL2^{erK0}$, nucleus $LMP1$ WT 0.00 $TPL2^{erK0}$ pcleus 1.00 RelB WT, nucleus ${}^{9}LMP1$ WT 1.00 0.00 $TPL2^{erK0}$, nucleus $LMP1$ WT 1.00 0.00 $TPL2^{erK0}$, nucleus $LMP1$ WT 0.77 0.25 p = 0.18 RelB WT, nucleus ${}^{9}LMP1$ WT 1.00 0.00 1.00 $p52$ WT, nucleus ${}^{9}LMP1$ WT 0.00 1.00 0.00 1.00 $p52$ WT, nucleus ${}^{9}LMP1$ WT 0.00 0.00 1.00 0.00 $TPL2^{erK0}$, nucleus $LMP1$ WT 0.00 0.00 1.00 1.00 0.00				60 min	0.27	0.06	p = 0.064
WT ${}^{6}0$ min 1.00 0.00 60 min 0.47 0.05 120 min 0.48 0.56 5 set to 1 T-test, unpaired, two-tailed 1 stimulation times were included into the quantitative analysis, which were tested in both biological replicates Figure 5d Antibody Sample Mean (n=3) ±SD p-value (<i>TPL2</i> crK0 vs. WT) Figure 5d p65 WT, nucleus ${}^{5}LMP1$ WT 1.00 0.00 p= 0.059 p50 WT, nucleus ${}^{1}LMP1$ WT 1.00 0.00 p= 0.18 RelB WT, nucleus ${}^{1}LMP1$ WT 1.00 0.00 p= 0.80 p52 WT, nucleus ${}^{1}LMP1$ WT 1.18 1.19 p= 0.81				120 min	0.28	0.10	p = 0.66
60 min 0.47 0.05 120 min 0.48 0.56 T-test, unpaired, two-tailed s set to 1 T-test, unpaired, two-tailed t stimulation times were included into the quantitative analysis, which were tested in both biological replicates Figure 5d P65 WT, nucleus t LMP1 WT LMP1 WT 1.00 P50 WT, nucleus LMP1 WT 0.77 P50 WT, nucleus LMP1 WT 0.00 TPL2 crk0, nucleus LMP1 WT RelB WT, nucleus $TPL2 crk0, nucleus$ LMP1 WT LMP1 WT 1.00 p52 WT, nucleus $TPL2 crk0, nucleus$ LMP1 WT LMP1 WT 0.88 p52 WT, nucleus LMP1 WT 0.00 TPL2 crk0, nucleus LMP1 WT 0.00 TPL2 crk0, nucleus			WT	[§] 0 min	1.00	0.00	
I20 min 0.48 0.56 $\frac{120 \text{ min}}{100000000000000000000000000000000000$				60 min	0.47	0.05	
$^{\$}$ set to 1T-test, unpaired, two-tailed into the quantitative analysis, which were tested in both biological replicatesFigure 5dAntibodySampleMean (n=3) \pm SD p-value ($TPL2^{crK0}$ vs. WT) $P65$ WT, nucleus $^{\$}LMP1 WT$ 1.000.00 $P50$ WT, nucleus $LMP1 WT$ 1.720.32 $p = 0.059$ $p50$ WT, nucleus $^{\$}LMP1 WT$ 1.000.00 $TPL2^{crK0}$, nucleus $LMP1 WT$ 1.000.00 $P52$ WT, nucleus $^{\$}LMP1 WT$ 1.000.00 $p52$ WT, nucleus $^{\$}LMP1 WT$ 1.000.00 $p52$ WT, nucleus $^{\$}LMP1 WT$ 1.000.00 $TPL2^{crK0}$, nucleus $LMP1 WT$ 1.000.00 $p52$ WT, nucleus $^{\$}LMP1 WT$ 1.000.00 $TPL2^{crK0}$, nucleus $LMP1 WT$ 0.880.83 $p = 0.81$				120 min	0.48	0.56	
Figure 5dAntibodySampleMean (n=3) \pm SD p-value (<i>TPL2</i> ^{crK0} vs. WT)Figure 5dp65WT, nucleus 5 LMP1 WT1.000.00 $TPL2$ ^{crK0} , nucleusLMP1 WT1.720.32p = 0.059p50WT, nucleus 5 LMP1 WT1.000.00 $TPL2$ ^{crK0} , nucleusLMP1 WT0.770.25p = 0.18RelBWT, nucleus 5 LMP1 WT1.000.00 $TPL2$ ^{crK0} , nucleusLMP1 WT1.181.19p = 0.80p52WT, nucleusLMP1 WT1.000.00 $TPL2$ ^{crK0} , nucleusLMP1 WT1.000.000.00 $TPL2$ ^{crK0} , nucleusLMP1 WT1.181.19p = 0.80p52WT, nucleusLMP1 WT0.880.83p = 0.81				[§] set to 1		T-test, ι	unpaired, two-tailed
Antibody Sample Mean (n=3) \pm SD p-value ($TPL2^{crK0}$ vs. WT) Figure 5d p65 WT, nucleus $\$LMP1$ WT 1.00 0.00 p50 WT, nucleus LMP1 WT 1.72 0.32 p = 0.059 p50 WT, nucleus $\$LMP1$ WT 0.77 0.25 p = 0.18 RelB WT, nucleus $LMP1$ WT 1.00 0.00 p52 WT, nucleus LMP1 WT 1.18 1.19 p = 0.80 p52 WT, nucleus $LMP1$ WT 0.00 0.00 0.00 p54 WT, nucleus LMP1 WT 1.00 0.00 0.83 p = 0.81						[†] stimula into the which v biologic	ation times were included quantitative analysis, vere tested in both cal replicates
Figure 5dp65WT, nucleus ${}^{S}LMP1 WT$ 1.000.00TPL2 crK0, nucleusLMP1 WT1.720.32p = 0.059p50WT, nucleus ${}^{S}LMP1 WT$ 1.000.00TPL2 crK0, nucleusLMP1 WT0.770.25p = 0.18RelBWT, nucleus ${}^{S}LMP1 WT$ 1.000.00TPL2 crK0, nucleusLMP1 WT1.000.00p52WT, nucleus ${}^{S}LMP1 WT$ 1.000.00p52WT, nucleus ${}^{LMP1 WT$ 1.000.00TPL2 crK0, nucleusLMP1 WT0.880.83p = 0.81		Antibody	Sample	8	Mean (n=3)	±SD p-value	(<i>TPL2</i> ^{crKO} vs. WT)
$TPL2^{crK0}$, nucleusLMP1 WT 1.72 0.32 $p = 0.059$ p50WT, nucleus ${}^{\$}LMP1$ WT 1.00 0.00 $TPL2^{crK0}$, nucleusLMP1 WT 0.77 0.25 $p = 0.18$ RelBWT, nucleus ${}^{\$}LMP1$ WT 1.00 0.00 $TPL2^{crK0}$, nucleusLMP1 WT 1.18 1.19 $p = 0.80$ p52WT, nucleus ${}^{\$}LMP1$ WT 1.00 0.00 $TPL2^{crK0}$, nucleus ${}^{\$}LMP1$ WT 0.88 0.83 $p = 0.81$	Figure 5d	p65	WT, nucleus	^s LMP1 WT	1.00	0.00	
p50WT, nucleus ${}^{\$}LMP1$ WT1.000.00TPL2 crK0, nucleusLMP1 WT0.770.25p = 0.18RelBWT, nucleus ${}^{\$}LMP1$ WT1.000.00TPL2 crK0, nucleusLMP1 WT1.181.19p = 0.80p52WT, nucleus ${}^{\$}LMP1$ WT1.000.00p52WT, nucleus ${}^{\$}LMP1$ WT0.880.83p = 0.81			<i>TPL2</i> ^{crk0} , nucleus	LMP1 WT	1.72	0.32	p = 0.059
$TPL2^{crK0}$, nucleusLMP1 WT 0.77 0.25 $p = 0.18$ RelBWT, nucleus ${}^{\$}LMP1$ WT 1.00 0.00 $TPL2^{crK0}$, nucleusLMP1 WT 1.18 1.19 $p = 0.80$ p52WT, nucleus ${}^{\$}LMP1$ WT 1.00 0.00 $TPL2^{crK0}$, nucleusLMP1 WT 0.88 0.83 $p = 0.81$		p50	WT, nucleus	[§] LMP1 WT	1.00	0.00	
RelBWT, nucleus ${}^{\$}LMP1$ WT1.000.00 $TPL2^{crK0}$, nucleusLMP1 WT1.181.19p = 0.80p52WT, nucleus ${}^{\$}LMP1$ WT1.000.00 $TPL2^{crK0}$, nucleusLMP1 WT0.880.83p = 0.81			<i>TPL2</i> ^{crKO} , nucleus	LMP1 WT	0.77	0.25	p = 0.18
p52 $TPL2^{crKO}$, nucleus LMP1 WT 1.18 1.19 p = 0.80 WT, nucleus ${}^{\$}LMP1$ WT 1.00 0.00 $TPL2^{crKO}$, nucleus LMP1 WT 0.88 0.83 p = 0.81		RelB	WT, nucleus	[§] LMP1 WT	1.00	0.00	
p52 WT, nucleus ${}^{\$}LMP1$ WT 1.00 0.00 $TPL2^{crK0}$, nucleus LMP1 WT 0.88 0.83 $p = 0.81$			<i>TPL2</i> ^{crKO} , nucleus	LMP1 WT	1.18	1.19	p = 0.80
$TPL2^{crKO}$, nucleus LMP1 WT 0.88 0.83 $p = 0.81$		p52	WT, nucleus	[§] LMP1 WT	1.00	0.00	•
			<i>TPL2</i> ^{crKO} , nucleus	LMP1 WT	0.88	0.83	p = 0.81

T-test, unpaired, two-tailed

	Antibody	Sample	X-link	Mean $(n=2^{\dagger})$	±SD p-	value (ACHP vs. corresponding DMSO)
Figure 6a	P-JNK	DMSO	0 min	0.06	0.08	
C	,		[§] 30 min	1.00	0.00	
			60 min	0.27	0.38	
			90 min	0.06	0.09	
			120 min	0.18	0.25	
		ACHP	0 min	0.02	0.03	
			30 min	0.19	0.24	*p = 0.041
			60 min	0.15	0.22	p = 0.75
			90 min	0.07	0.11	p = 0.92
			120 min	0.06	0.08	p= 0.59
			$^{\$}$ set to 1		T-	test, unpaired, two-tailed
					†s in wi re	timulation times were included to the quantitative analysis, hich were tested in all biological plicates
	Antibody	Sample	X-link	Mean (n=2 [†])	±SD p-	value (ACHP vs. corresponding DMSO)
	ΙκΒα	DMSO	[§] 0 min	1.00	0.00	
			30 min	0.41	0.15	
			60 min	0.35	0.00	
			90 min	0.57	0.05	
			120 min	0.49	0.28	
		ACHP	[§] 0 min	1.00	0.00	
			30 min	1.19	0.40	p = 0.12
			60 min	1.63	0.67	p = 0.11
			90 min	1.37	0.01	**p = 0.002
			120 min	1.71	0.03	*p = 0.026
			[§] set to 1		T-	test, unpaired, two-tailed
					†s in wi re	timulation times were included to the quantitative analysis, hich were tested in all biological plicates
	Antibody	Sample	X-link	Mean (n=3 [†])	±SD p-	value (DMSO vs. corresponding ACHP)
	P-ERK	DMSO	0 min	0.11	0.13	
			[§] 30 min	1.00	0.00	
			60 min	0.56	0.52	
			90 min	0.48	0.67	
			120 min	0.61	0.77	
		ACHP	0 min	0.44	0.54	
			30 min	0.38	0.33	*p = 0.032
			60 min	0.39	0.40	p = 0.67

90 min	0.29	0.43	p = 0.71
120 min	0.13	0.18	p= 0.35

T-test, unpaired, two-tailed

[†]stimulation times were included into the quantitative analysis, which were tested in all biological replicates

	Antibody	Sample	CD40L	Mean (n=2)	±SD p-value	(ACHP vs. corresponding DMSO)
Figure 6b	P-INK	DMSO	0 min	0.00	0.00	
0	,		5 min	0.24	0.14	
			[§] 15 min	1.00	0.00	
			30 min	0.33	0.47	
			45 min	0.02	0.02	
		ACHP	0 min	0.00	0.00	
			5 min	0.29	0.22	p = 0.8
			15 min	0.99	0.54	p = 0.98
			30 min	0.35	0.49	p = 0.98
			45 min	0.20	0.29	p = 0.46
			[§] set to 1		T-test, u	npaired, two-tailed
	Antibody	Sample	CD40L	Mean (n=2)	±SD p-value	(ACHP vs. corresponding DMSO)
	ΙκΒα	DMSO	[§] 0 min	1.00	0.00	
			5 min	0.55	0.26	
			15 min	0.22	0.23	
			30 min	0.03	0.02	
			45 min	0.60	0.11	
		ACHP	[§] 0 min	1.00	0.00	
			5 min	0.85	0.03	p = 0.24
			15 min	0.82	0.19	p = 0.10
			30 min	0.86	0.06	**p = 0.0025
			45 min	0.89	0.01	p = 0.067
			$^{\$}$ set to 1		T-test, u	npaired, two-tailed
	Antibody	Sample	CD40L	Mean (n=2)	±SD p-value	(ACHP vs. DMSO)
	P-ERK	DMSO	0 min	0.02	0.02	
			5 min	0.14	0.20	
			[§] 15 min	1.00	0.00	
			30 min	2.68	3.44	
			45 min	0.06	0.08	
		ACHP	0 min	0.07	0.09	
			5 min	0.07	0.10	p = 0.69
			15 min	0.18	0.25	*p = 0.044
			30 min	0.08	0.11	p = 0.40
			45 min	0.16	0.22	p= 0.61
			$^{\$}$ set to 1		T-test, u	npaired, two-tailed

	Antibody	Sample	X-link	Mean (n=3)	±SD p-value (TPL2-IH vs. corresponding DMSO)
Figure 6c	P-JNK	DMSO	0 min	0.29	0.35	
			[§] 30 min	1.00	0.00	
			60 min	1.06	0.93	
			90 min	0.37	0.30	
			120 min	0.19	0.21	
		TPL2-IH	0 min	0.10	0.09	
			30 min	0.23	0.18	**p = 0.0016
			60 min	0.24	0.31	p = 0.22
			90 min	0.08	0.09	p = 0.18
			120 min	0.03	0.04	p = 0.25
			[§] set to 1		T-test, ur	npaired, two-tailed
	Antibody	Sample	X-link	Mean (n=3)	±SD p-value (TPL2-IH vs. corresponding DMSO)
	ΙκΒα	DMSO	[§] 0 min	1.00	0.00	
			30 min	0.76	0.38	
			60 min	0.34	0.15	
			90 min	0.32	0.07	
			120 min	0.67	0.09	
		TPL2-IH	[§] 0 min	1.00	0.00	
			30 min	0.83	0.30	p = 0.82
			60 min	0.32	0.10	p = 0.84
			90 min	0.31	0.14	p = 0.88
			120 min	0.57	0.35	p = 0.63
			[§] set to 1		T-test, ur	npaired, two-tailed
	Antibody	Sample	X-link	Mean (n=3)	±SD p-value (TPL2-IH vs. corresponding DMSO)
	P-ERK	DMSO	0 min	0.44	0.68	
			[§] 30 min	1.00	0.00	
			60 min	1.12	1.67	
			90 min	0.31	0.45	
			120 min	0.16	0.19	
		TPL2-IH	0 min	0.18	0.30	p = 0.58
			30 min	0.28	0.26	**p = 0.0085
			60 min	0.85	1.26	p = 0.83
			90 min	0.19	0.27	p = 0.73
			120 min	0.20	0.29	p = 0.87
			[§] set to 1		T-test, ur	paired, two-tailed

Figure 6d	Antibody P-JNK	Sample DMSO	CD40L 0 min 5 min	Mean (n=2 [†]) 0.00 0.41	±SD p-value (T 0.00 0.29	PL2-IH vs. corresponding DMSO)	
			⁹ 15 min	1.00	0.00		
			30 min	0.84	0.21		
		TPL2-IH	0 min	0.01	0.01	0.00	
			5 min	0.34	0.31	$\mathbf{p} = 0.82$	
			15 min	0.85	0.18	p = 0.36	
			30 min	0.59	0.51	p = 0.59	
			[§] set to 1		T-test, unpaired, two-tailed [†] stimulation times were included into the quantitative analysis, which were tested in both biological replicates		
	Antibody	Sample	CD40L	Mean (n=2 [†])	±SD p-value (T	PL2-IH vs. corresponding DMSO)	
	ΙκΒα	DMSO	[§] 0 min	1.00	0.00		
			5 min	0.38	0.42		
			15 min	0.02	0.03		
			30 min	0.12	0.16		
		TPL2-IH	[§] 0 min	1.00	0.00		
			5 min	0.45	0.62	p = 0.91	
			15 min	0.03	0.05	p = 0.82	
			30 min	0.00	0.00	p = 0.40	
				[§] set to 1 T-test, unpaired, two-ta		paired, two-tailed	
					[†] stimulatio into the qu which wer biological	on times were included antitative analysis, e tested in both replicates	
	Antibody	Sample	CD40L	Mean $(n=2^{\dagger})$	±SD p-value (T	PL2-IH vs. corresponding DMSO)	
	P-ERK	DMSO	0 min	0.00	0.00		
			5 min	0.21	0.30		
			[§] 15 min	1.00	0.00		
			30 min	0.39	0.51		
		TPL2-IH	0 min	0.00	0.00		
			5 min	0.00	0.00	p = 0.42	
			15 min	0.14	0.20	*p = 0.026	
			30 min	0.15	0.21	p = 0.60	
			$^{\$}$ set to 1		T-test, unp	paired, two-tailed	
					[†] stimulatio	on times were included	

into the quantitative analysis, which were tested in both biological replicates

				Mean (n=3 DMSO,			
	Antibody	Sample	X-link	n=5 TPL2-IH)	±SD p-value (TPL2-IH vs. corresponding DMSO)	
Figure 6f	P-JNK	DMSO	0 min	0.00	0.01		
			30 min	0.16	0.15		
			[§] 60 min	1.00	0.00		
			90 min	0.40	0.07		
		TPL2-IH	0 min	0.01	0.01		
			30 min	0.05	0.02	p = 0.14	
			60 min	0.34	0.18	***p = 0.00076	
			90 min	0.17	0.12	*p = 0.024	
			[§] set to 1		T-test, unpaired, two-tailed		
	Antibody	Sample	X-link	Mean (n=2)	±SD p-value (TPL2-IH vs. corresponding DMSO)	
	ΙκΒα	DMSO	[§] 0 min	1.00	0.00		
			30 min	0.72	0.10		
			60 min	0.44	0.08		
			90 min	0.50	0.13		
		TPL2-IH	[§] 0 min	1.00	0.00		
			30 min	0.72	0.20	p = 0.99	
			60 min	0.43	0.09	p = 0.87	
			90 min	0.29	0.05	p = 0.17	
			[§] set to 1		T-test, unpaired, two-tailed		
	Antibody	Sample	X-link	Mean (n=2)	±SD p-value (ACHP vs. corresponding DMSO)		
	P-JNK	DMSO	0 min	0.01	0.02		
			30 min	0.18	0.12		
			[§] 60 min	1.00	0.00		
			90 min	0.55	0.32		
		ACHP	0 min	0.02	0.03		
			30 min	0.02	0.03	p = 0.20	
			60 min	0.03	0.05	**p = 0.0011	
			90 min	0.02	0.02	p = 0.14	
			[§] set to 1		T-test, unpaired, two-tailed		
	Antibody	Sample	X-link	Mean (n=3)	±SD p-value (ACHP vs. corresponding DMSO)	
	ΙκΒα	DMSO	[§] 0 min	1.00	0.00		
			30 min	0.44	0.37		
			60 min	0.40	0.08		
			90 min	0.44	0.22		
		ACHP	[§] 0 min	1.00	0.00		
			30 min	0.93	0.01	p = 0.088	
			60 min	0.89	0.11	**p = 0.004	

90 min 0.98 0.28 p = 0.058

[§]set to 1

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Supplementary Table 4. Phosphoimager quantification and statistics of kinase activities (Figures 3b and 3c)

n, number of biological replicates SD, standard deviation

	Substrate phosphorylation	Sample		Mean (n=3)	±SD p-value
Figure 3b	IKK2 kinase activity, GST-IκBα~P*	TAK1-IH	vector	0.14	0.06
			LMP1 wt	2.59	0.89 p = 0.75 (TAK1-IH vs. WT); **p = 0.008 (TAK1-IH vs. <i>TAK1</i> ^{crK0})
			AAA/Y ₃₈₄ G	0.79	0.13
		WT	vector	0.14	0.06
			LMP1 wt	2.93	1.46
			[§] AAA/Y ₃₈₄ G	1.00	0.00
		TAK1 crKO	vector	0.07	0.03
			LMP1 wt	0.06	0.04 *p = 0.027 ($TAK1^{crKO}$ vs. WT)
			AAA/Y ₃₈₄ G	0.07	0.03
			[§] set to 1		T-test, unpaired, two-tailed
	Substrate phosphorylation	Sample		Mean (n=3)	±SD p-value
Figure 3c	JNK1 kinase activity, GST-c-Jun~P*	TAK1-IH	vector	0.49	0.13
			LMP1 wt	0.78	0.73 *p = 0.037 (TAK1-IH vs. WT); p = 0.64 (TAK1-IH vs. <i>TAK1</i> ^{crK0})
			AAA/Y ₃₈₄ G	0.47	0.15
		WT	vector	0.72	0.20
			LMP1 wt	11.28	5.84
			[§] AAA/Y ₃₈₄ G	1.00	0.00
		TAK1 ^{crKO}	vector	0.81	0.50
			LMP1 wt	1.10	0.84 *p = 0.041 ($TAK1^{CrKO}$ vs. WT)
			AAA/Y ₃₈₄ G	1.23	0.71
			[§] set to 1		T-test, unpaired, two-tailed

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Supplementary References

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