

## SUPPLEMENTARY FIGURE LEGENDS

**Supplementary Figure S1. Effect of Bosutinib and Dasatinib on CREB-dependent gene transcription.** BMDMs were treated with vehicle control, 3  $\mu$ M Bosutinib or 0.3  $\mu$ M Dasatinib for 1 h and then stimulated with LPS for the indicated times. Expression of IL-10 and Nurr77 were measured by qPCR. mRNA levels were normalised to 1 in unstimulated cells (mean  $\pm$  SEM, n=4).

**Supplementary Figure S2. Bosutinib and Dasatinib do not affect the Pam<sub>3</sub>CSK<sub>4</sub>-stimulated phosphorylation of CREB.** BMDMs were treated with vehicle control, 3  $\mu$ M Bosutinib, 0.3  $\mu$ M Dasatinib or 0.5  $\mu$ M HG-9-91-01 for 1 h and then stimulated with Pam<sub>3</sub>CSK<sub>4</sub> for 0, 10, 30 or 60 min. Cell lysates were immunoblotted using the indicated antibodies.

**Supplementary Figure S3. Effect of Bosutinib and Dasatinib on the kinetics of cytokine secretion in mouse macrophages.** Bone marrow-derived macrophages were treated with 3000 nM Bosutinib or 300 nM Dasatinib for 1 h and then stimulated for the times indicated with 100 ng/ml LPS. The concentration of (A) IL-10, (B) TNF $\alpha$ , (C) IL-6 and (D) IL-12p40 released into the cell culture supernatant was measured using the Bioplex system (Bio-Rad) (mean  $\pm$  SEM, n=4).

**Supplementary Figure S4. Induction of ‘regulatory’-like macrophages by Bosutinib and Dasatinib in response to Pam<sub>3</sub>CSK<sub>4</sub>.** (A) Effect of Bosutinib and Dasatinib on cytokine secretion. Bone marrow-derived macrophages were treated with vehicle control, 3  $\mu$ M Bosutinib or 0.3  $\mu$ M Dasatinib for 1 h and then stimulated with Pam<sub>3</sub>CSK<sub>4</sub> for 8 h. The concentration of the different cytokines in the culture supernatant was measured using the BIOPLEX system. The data are depicted as the fold-change in cytokine secretion in the presence of the drug (n=4, mean  $\pm$  SEM). Statistical significance was determined by comparing each data set to 0 using one sample t-test. (B) Effect of Bosutinib and Dasatinib on markers of ‘regulatory’-like macrophages. BMDMs were treated with vehicle control, 3  $\mu$ M Bosutinib or 0.3  $\mu$ M Dasatinib for 1h and then stimulated with Pam<sub>3</sub>CSK<sub>4</sub> for 4 h (SPHK1, LIGHT) or 8 h (Arg1) prior to mRNA extraction. Gene expression was measured by qPCR. mRNA levels were normalised to 1 in unstimulated cells (mean  $\pm$  SEM, n=4).

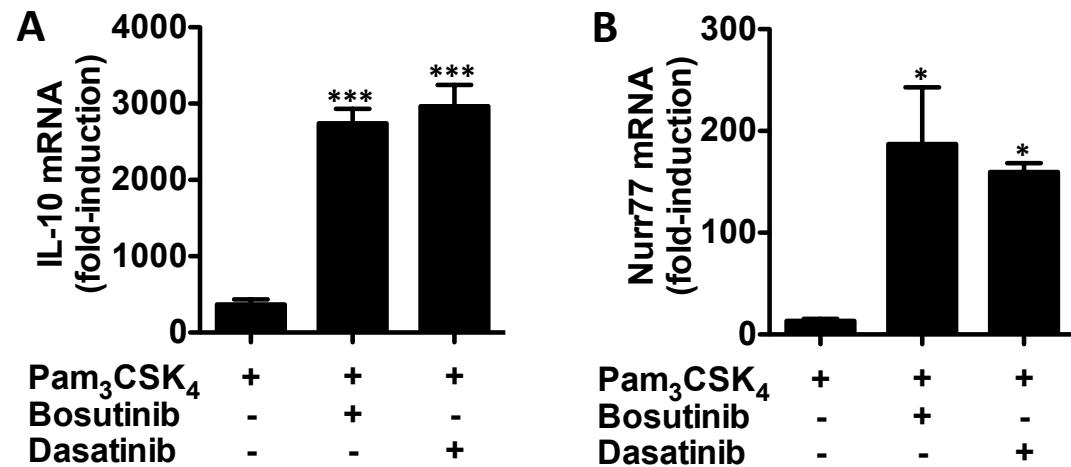
**Supplementary Figure S5. Bosutinib and Dasatinib do not affect the TLR-stimulated activation of NF $\kappa$ B and IRF3 pathways.** BMDMs were treated with vehicle control, 3  $\mu$ M Bosutinib, 0.3  $\mu$ M Dasatinib or 0.5  $\mu$ M HG-9-91-01 for 1 h and then stimulated with (A,B,C) LPS or (D,E) Pam<sub>3</sub>CSK<sub>4</sub> for 0, 10, 30 or 60 min. Cell lysates were immunoblotted using the indicated antibodies. The panels depict the following signaling cascades: A and D- activation of NF $\kappa$ B; B- activation of IRF3; C and E, activity of selected protein tyrosine kinases.

**Supplementary Table S1- Kinase profiling of Bosutinib and Dasatinib**

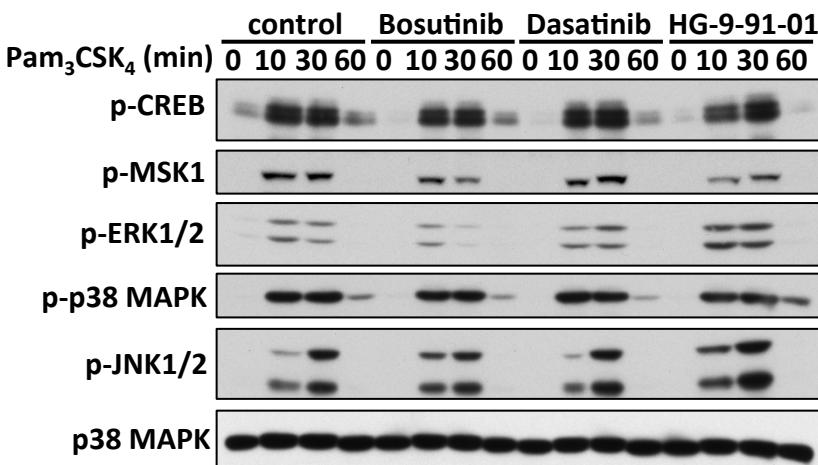
Kinase	Bosutinib		Dasatinib		Kinase	Bosutinib		Dasatinib	
	0.1 μM	1 μM	0.1 μM	1 μM		0.1 μM	1 μM	0.1 μM	1 μM
ABL	1 ± 0	0 ± 0	0 ± 0	0 ± 0	MKK6	92 ± 6	115 ± 5	104 ± 11	112 ± 4
AMPK	65 ± 4	26 ± 2	107 ± 13	120 ± 5	MLK1	52 ± 9	18 ± 4	72 ± 1	41 ± 2
ASK1	96 ± 9	106 ± 1	108 ± 7	118 ± 7	MLK3	42 ± 4	8 ± 1	76 ± 10	39 ± 6
Aurora A	95 ± 2	98 ± 6	94 ± 0	101 ± 1	MNK1	99 ± 14	105 ± 2	108 ± 0	102 ± 9
Aurora B	93 ± 13	50 ± 7	120 ± 10	108 ± 10	MNK2	87 ± 6	100 ± 9	97 ± 8	106 ± 2
BRK	88 ± 11	48 ± 0	5 ± 0	2 ± 0	MPSK1	117 ± 15	110 ± 11	101 ± 5	123 ± 1
BRSK1	101 ± 1	112 ± 5	126 ± 0	123 ± 1	MSK1	93 ± 2	102 ± 12	94 ± 4	103 ± 1
BRSK2	107 ± 12	120 ± 4	102 ± 14	108 ± 13	MST2	65 ± 6	17 ± 2	75 ± 2	81 ± 6
BTK	1 ± 0	1 ± 0	1 ± 0	1 ± 0	MST3	68 ± 0	21 ± 4	114 ± 20	93 ± 2
CAMK1	78 ± 11	74 ± 16	89 ± 16	77 ± 1	MST4	20 ± 1	7 ± 0	97 ± 10	77 ± 4
CAMKK beta	81 ± 2	27 ± 0	96 ± 4	99 ± 19	NEK2a	76 ± 4	63 ± 2	122 ± 11	98 ± 4
CDK2-Cyclin A	110 ± 32	103 ± 5	116 ± 1	112 ± 1	NEK6	102 ± 1	111 ± 3	113 ± 4	123 ± 6
CDK9-Cyclin T1	101 ± 8	125 ± 16	122 ± 8	138 ± 12	NUAK1	63 ± 12	21 ± 2	119 ± 10	118 ± 8
CHK1	91 ± 2	57 ± 0	100 ± 6	96 ± 6	OSR1	96 ± 3	65 ± 2	100 ± 1	101 ± 0
CHK2	37 ± 0	10 ± 2	98 ± 8	102 ± 1	p38 alpha MAPK	97 ± 4	72 ± 3	79 ± 15	29 ± 2
CK1 delta	86 ± 20	60 ± 7	113 ± 4	124 ± 1	p38 beta MAPK	94 ± 15	108 ± 24	105 ± 11	44 ± 4
CK1 gamma 2	117 ± 1	108 ± 4	115 ± 0	113 ± 12	p38 delta MAPK	111 ± 12	116 ± 12	118 ± 17	133 ± 1
CK2	77 ± 3	106 ± 1	95 ± 3	80 ± 28	p38 gamma MAPK	88 ± 3	109 ± 5	100 ± 4	105 ± 7
CLK2	75 ± 9	23 ± 0	120 ± 6	121 ± 6	PAK2	115 ± 6	108 ± 1	118 ± 2	119 ± 12
CSK	65 ± 7	4 ± 0	97 ± 19	8 ± 3	PAK4	110 ± 16	126 ± 1	137 ± 21	132 ± 16
DAPK1	92 ± 3	105 ± 4	126 ± 10	102 ± 7	PAK5	105 ± 18	129 ± 5	131 ± 12	138 ± 7
DDR2	22 ± 1	2 ± 0	1 ± 1	0 ± 0	PAK6	103 ± 11	132 ± 7	126 ± 9	120 ± 4
DYRK1A	91 ± 3	96 ± 13	111 ± 4	126 ± 19	PDGFRA	96 ± 1	79 ± 0	6 ± 1	3 ± 1
DYRK2	71 ± 4	87 ± 5	101 ± 5	117 ± 9	PDK1	92 ± 16	98 ± 0	94 ± 9	92 ± 1
DYRK3	85 ± 11	90 ± 16	98 ± 7	104 ± 9	PHK	55 ± 0	12 ± 0	101 ± 10	103 ± 1
EF2K	81 ± 2	95 ± 6	104 ± 4	95 ± 5	PIM1	91 ± 7	94 ± 0	90 ± 1	98 ± 1
EIF2AK3	107 ± 5	103 ± 0	106 ± 6	113 ± 2	PIM2	99 ± 0	96 ± 8	104 ± 3	105 ± 1
EPH-A2	4 ± 0	1 ± 0	1 ± 0	1 ± 0	PIM3	92 ± 16	101 ± 3	96 ± 8	108 ± 5
EPH-A4	3 ± 1	1 ± 0	2 ± 0	2 ± 2	PINK	112 ± 9	125 ± 13	117 ± 1	133 ± 5
EPH-B1	12 ± 0	0 ± 2	-1 ± 1	-1 ± 2	PKA	111 ± 16	105 ± 7	110 ± 12	121 ± 27
EPH-B2	1 ± 1	0 ± 0	1 ± 0	1 ± 0	PKB alpha	110 ± 16	116 ± 30	103 ± 15	120 ± 13
EPH-B3	16 ± 0	1 ± 0	1 ± 0	1 ± 0	PKB beta	102 ± 6	90 ± 3	94 ± 11	94 ± 2
EPH-B4	10 ± 0	2 ± 0	20 ± 0	3 ± 0	PKC alpha	96 ± 5	103 ± 3	98 ± 3	105 ± 14
ERK1	98 ± 5	103 ± 1	91 ± 6	114 ± 12	PKC gamma	88 ± 6	102 ± 5	107 ± 22	114 ± 22
ERK2	104 ± 18	103 ± 15	93 ± 9	102 ± 1	PKC zeta	91 ± 2	102 ± 4	101 ± 3	109 ± 7
ERK5	74 ± 6	67 ± 10	87 ± 2	91 ± 4	PKD1	89 ± 2	86 ± 8	92 ± 21	107 ± 15
ERK8	96 ± 13	87 ± 3	90 ± 14	95 ± 11	PLK1	97 ± 12	74 ± 6	133 ± 18	99 ± 15
FGF-R1	94 ± 4	74 ± 6	88 ± 7	84 ± 6	PRAK	97 ± 2	125 ± 1	129 ± 14	128 ± 7
GCK	9 ± 2	4 ± 0	95 ± 7	56 ± 8	PRK2	86 ± 6	56 ± 3	100 ± 2	101 ± 0
GSK3 beta	109 ± 6	114 ± 22	103 ± 2	121 ± 12	RIPK2	86 ± 2	45 ± 1	5 ± 0	10 ± 12
HER4	9 ± 0	1 ± 1	27 ± 1	6 ± 0	ROCK 2	99 ± 6	74 ± 7	130 ± 10	132 ± 7
HIPK1	95 ± 0	57 ± 0	105 ± 4	122 ± 6	RSK1	90 ± 8	70 ± 3	105 ± 2	102 ± 5
HIPK2	71 ± 7	42 ± 4	95 ± 1	97 ± 5	RSK2	86 ± 6	64 ± 1	86 ± 9	101 ± 3
HIPK3	102 ± 14	66 ± 5	102 ± 3	113 ± 7	S6K1	98 ± 1	86 ± 2	108 ± 3	113 ± 11
IGF-1R	89 ± 8	79 ± 4	107 ± 6	98 ± 7	SGK1	98 ± 20	100 ± 2	87 ± 11	96 ± 7
IKK beta	92 ± 15	86 ± 8	97 ± 21	99 ± 9	SIK2	8 ± 0	3 ± 0	4 ± 1	2 ± 1
IKK epsilon	46 ± 7	6 ± 0	102 ± 5	123 ± 13	SIK3	9 ± 0	2 ± 0	9 ± 2	2 ± 0
IR	87 ± 7	107 ± 34	99 ± 2	94 ± 7	SmMLCK	88 ± 2	27 ± 1	111 ± 4	111 ± 7
IRAK1	77 ± 3	65 ± 0	96 ± 1	108 ± 3	Src	1 ± 0	1 ± 0	1 ± 0	2 ± 0
IRAK4	55 ± 3	23 ± 0	112 ± 24	102 ± 6	SRPK1	89 ± 6	109 ± 5	104 ± 9	107 ± 9
IRR	72 ± 5	59 ± 1	89 ± 4	90 ± 14	STK33	34 ± 0	17 ± 4	105 ± 6	110 ± 4
JAK2	72 ± 5	26 ± 0	94 ± 2	42 ± 1	SYK	77 ± 2	39 ± 1	97 ± 1	90 ± 0
JNK1	88 ± 15	102 ± 1	108 ± 4	121 ± 9	TAK1	41 ± 9	5 ± 0	97 ± 23	99 ± 7
JNK2	108 ± 20	108 ± 11	110 ± 10	125 ± 0	TAO1	85 ± 8	102 ± 7	120 ± 9	95 ± 7
JNK3	102 ± 3	106 ± 10	108 ± 0	113 ± 15	TBK1	75 ± 1	29 ± 1	100 ± 1	97 ± 10
Lck	1 ± 0	1 ± 0	1 ± 0	1 ± 0	TESK1	82 ± 15	61 ± 2	50 ± 3	8 ± 0
LKB1	84 ± 13	104 ± 15	96 ± 18	100 ± 14	TGFBR1	87 ± 14	101 ± 6	103 ± 1	82 ± 5
MAP4K3	3 ± 0	1 ± 0	88 ± 15	54 ± 1	TIE2	74 ± 3	64 ± 3	88 ± 7	78 ± 5
MAP4K5	0 ± 2	1 ± 0	22 ± 1	3 ± 1	TLK1	63 ± 13	35 ± 3	96 ± 4	124 ± 0
MAPKAP-K2	87 ± 5	94 ± 5	114 ± 4	111 ± 7	TrkA	25 ± 2	7 ± 0	107 ± 11	88 ± 2
MAPKAP-K3	113 ± 1	103 ± 8	117 ± 3	132 ± 1	TSSK1	67 ± 1	22 ± 2	106 ± 11	113 ± 3
MARK1	84 ± 5	76 ± 4	115 ± 3	127 ± 3	TTBK1	95 ± 2	114 ± 3	112 ± 8	112 ± 1
MARK2	89 ± 8	68 ± 1	118 ± 4	126 ± 2	TTBK2	87 ± 6	92 ± 6	110 ± 5	117 ± 7
MARK3	74 ± 10	41 ± 3	96 ± 16	104 ± 5	TTK	94 ± 0	99 ± 7	104 ± 6	109 ± 9
MARK4	101 ± 7	72 ± 5	105 ± 12	115 ± 24	ULK1	79 ± 5	44 ± 2	95 ± 9	101 ± 0
MEKK1	95 ± 5	85 ± 6	98 ± 4	102 ± 1	ULK2	78 ± 10	37 ± 1	101 ± 3	91 ± 3
MELK	95 ± 10	66 ± 1	112 ± 7	128 ± 7	VEGFR1	88 ± 5	54 ± 3	78 ± 9	53 ± 4
MINK1	5 ± 1	1 ± 0	90 ± 4	51 ± 1	WNK1	102 ± 2	104 ± 9	104 ± 4	104 ± 12
MKK1	81 ± 2	31 ± 9	118 ± 10	134 ± 16	YES1	2 ± 1	1 ± 0	1 ± 0	1 ± 0
MKK2	60 ± 3	21 ± 4	113 ± 11	91 ± 0	ZAP70	99 ± 4	109 ± 18	109 ± 1	121 ± 27

RESULTS SHOW MEAN % ACTIVITY REMAINING AND STANDARD DEVIATION

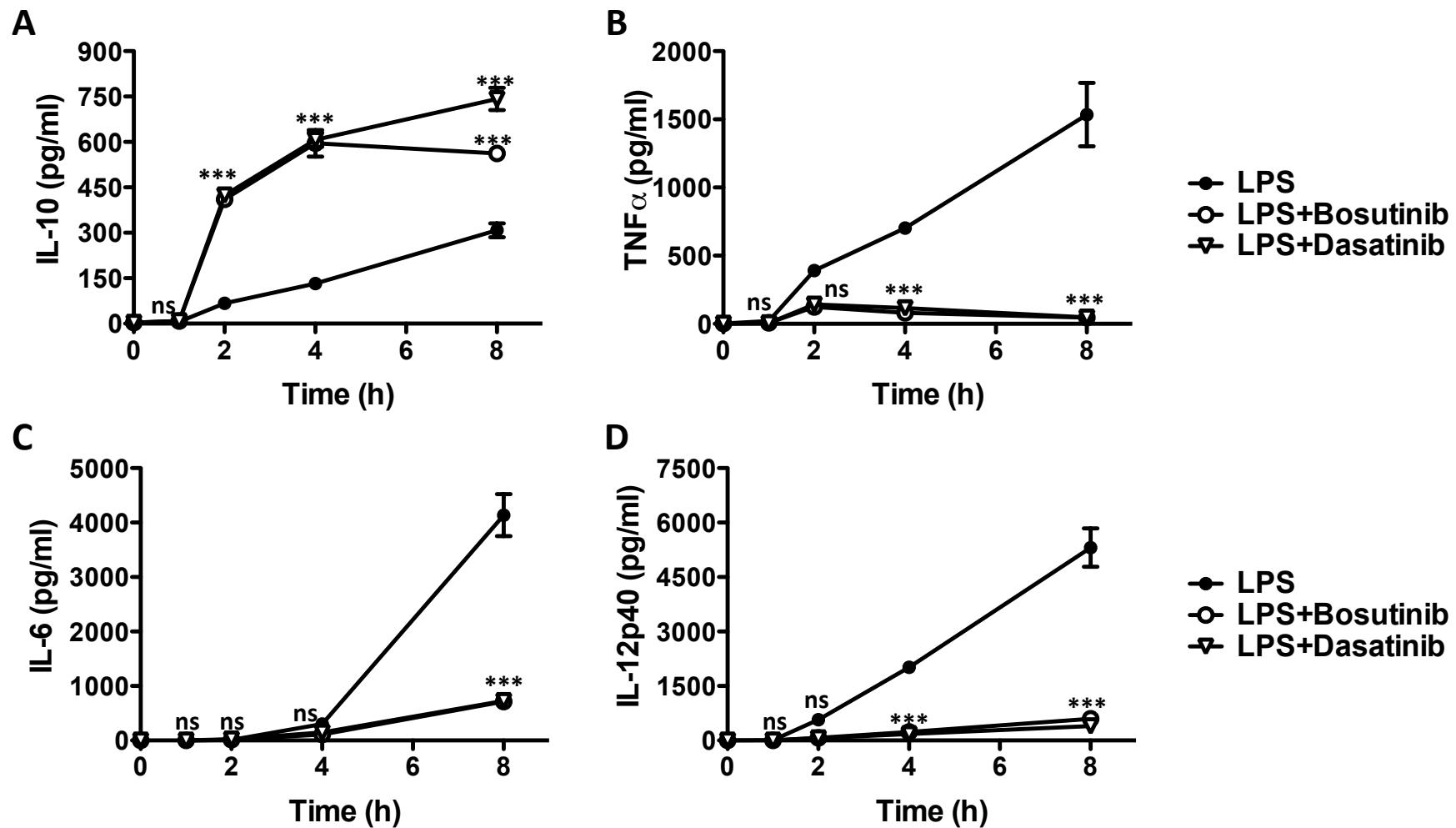
## Supplementary Figure S1



## Supplementary Figure S2

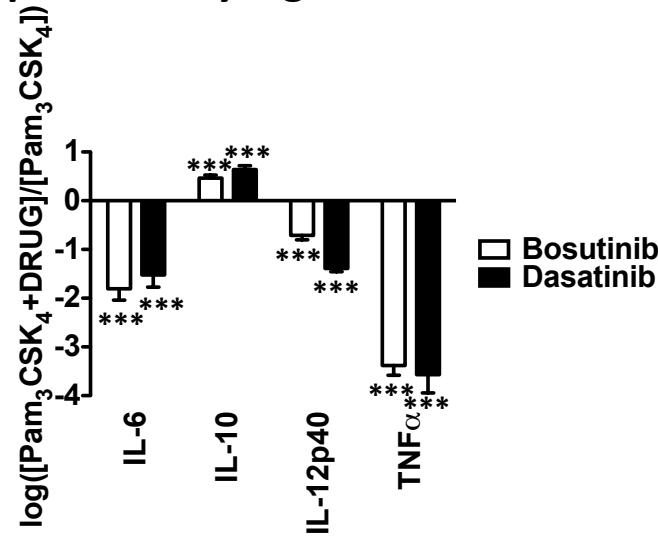


**Supplementary Figure S3**

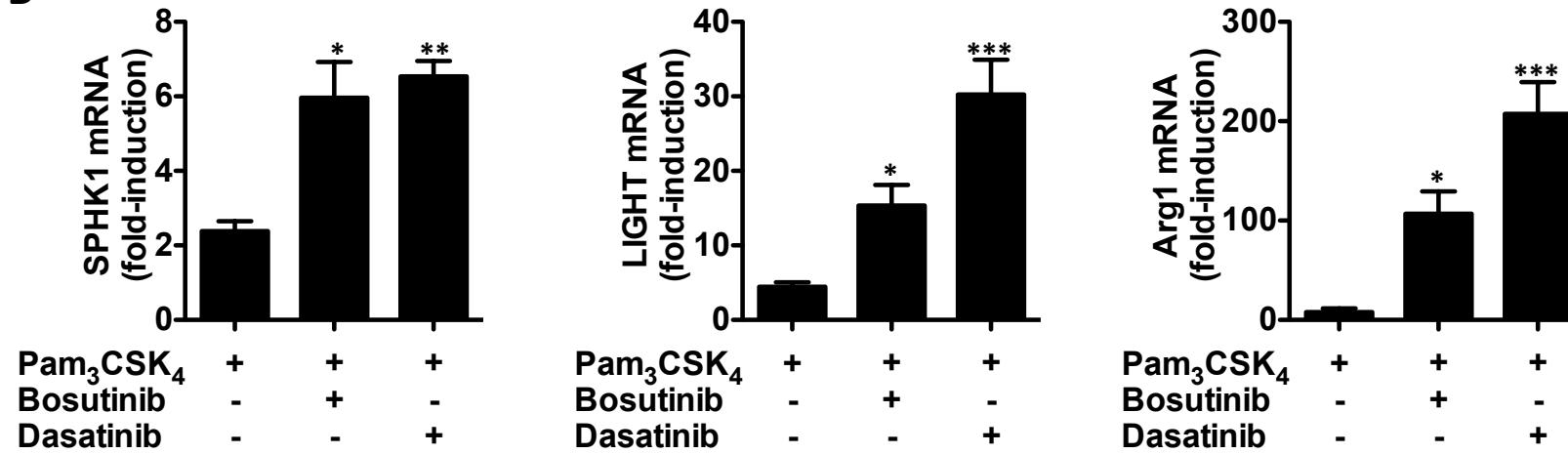


## Supplementary Figure S4

A

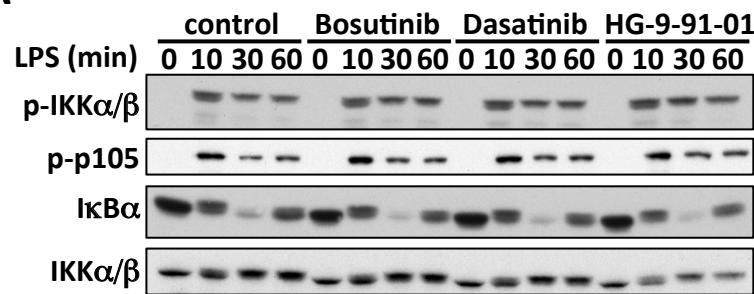


B

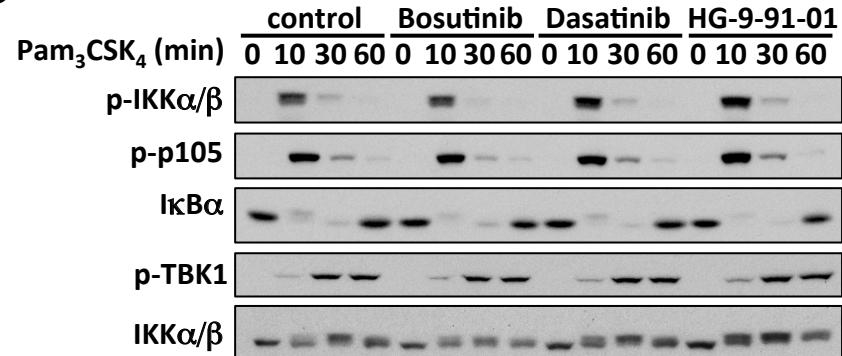


## Supplementary Figure S5

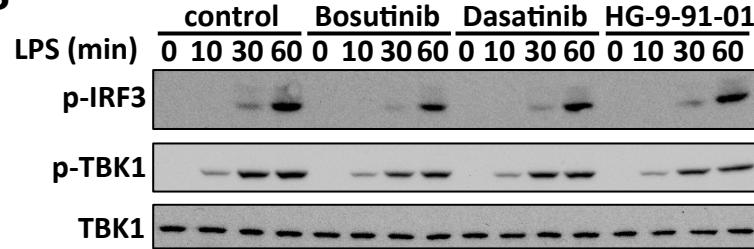
**A**



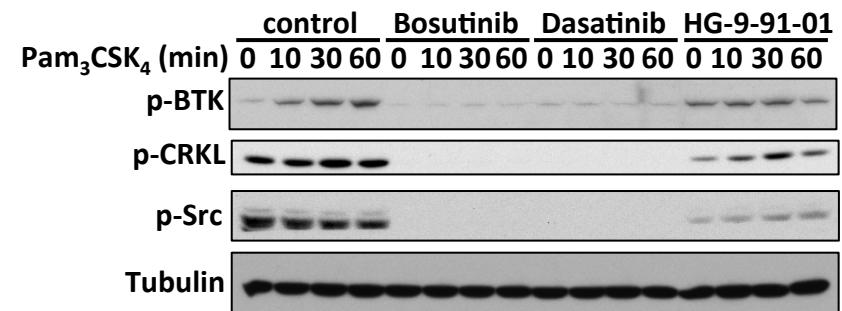
**D**



**B**



**E**



**C**

