Table S1: Model Reactions and Parameters

Reaction	Function	Rate Constant	Parameters	Units	References
[LPS]+[LBP] → [LPS-LBP]	Binding	k77_1	2.5	$nM^{-1}s^{-1}$	(2)
[LPS-LBP] → [LPS] + [LBP]	Dissociation	k77_1minus	0.0251	s^{-1}	(2)
[LPS]+[CD14] → [LPS-CD14]	Receptor binding	k77_2	2.86e-6	$nM^{-1}s^{-1}$	(2)
[LPS-CD14] → [LPS] + [CD14]	Dissociation	k77_2minus	0.0251	s^{-1}	(2)
[LPS-LBP] + [CD14] → [LPS-CD14] + [LBP]	LPS Transfer	k77_3	0.00286	$nM^{-1}s^{-1}$	(2)
[LPS-CD14] → [LPS] + [CD14]	Dissociation	k77_3minus	0.0251	s^{-1}	(2)
[TLR4]+[MD2] → [TLR4-MD2]	Helper protein binding	k77_4	6.47e-6	$nM^{-1}s^{-1}$	(2)
[TLR4-MD2] → [TLR4] + [MD2]	Dissociation	k77_4minus	3.65e-4	s^{-1}	(2)
[LPS-CD14]+[TLR4] → [AC1]	Membrane complex 1 formation	k77_5	2.33e-6	$nM^{-1}s^{-1}$	(2)
[AC1] → [LPS-CD14]+[TLR4]	Dissociation	k77_5minus	6.34e-2	s^{-1}	(2)
[LPS-CD14]+[TLR4-MD2] → [AC2]	Membrane complex 2 formation	k77_6	4.37e-4	$nM^{-1}s^{-1}$	(2)
[AC2] → [LPS-CD14]+[TLR4-MD2]	Dissociation	k77_6minus	4.03e-2	s^{-1}	(2)
[AC1]+[PI3K] → [AC-PI3K]	Binding Reaction	k79	4.80e-4	$nM^{-1}s^{-1}$	(3)
[AC2]+[PI3K] → [AC-PI3K]	Binding Reaction	k79	4.80e-4	$nM^{-1}s^{-1}$	(3)
[AC-PI3K] → sink	Complex Degradation	k80	2.81e-5	s^{-1}	(3)
[AC-PI3K] → [PI3K_P]	PI3K Phosphorylation	k81	2.82e-4	s^{-1}	(3)
[PI3K_P]+[PDK1] → [PI3K-PDK1]	Binding Reaction	k82	7.56e-5	$nM^{-1}s^{-1}$	(3)
[PI3K_P-PDK1] → sink	Complex Degradation	k83	1.05e-5	s^{-1}	(3)
[PI3K_P-PDK1] → [PDK1_P]	PDK1 Phosphorylation	k84	6.84e-4	s^{-1}	(3)
[PDK1_P]+[PKC] → [PDK1_P-PKC]	Binding Reaction	k85	0.016	$nM^{-1}s^{-1}$	(3)
[PDK1_P-PKC] → sink	Complex Degradation	k86	7.80e-8	s^{-1}	(3)
[PDK1_P-PKC] → [PKC_P]	PKC Phosphorylation	k87	0.016	s^{-1}	(3)
[PKC_P]+[PCPLC] → [PKC_P-PCPLC]	Binding Reaction	k88	2.08e-4	$nM^{-1}s^{-1}$	(4)
[PKC_P-PCPLC] → sink	Complex Degradation	k89	6.33e-4	s^{-1}	(4)
[PKC_P-PCPLC] → [PCPLC_P]	PCPLC_P Phosphorylation	k90	0.009	s^{-1}	(4)
[PCPLC_P]+[Asmase] → [PCPLC_P-Asmase]	Binding Reaction	k91	1.83e-4	$nM^{-1}s^{-1}$	(4)
[PCPLC_P-Asmase] → sink	Complex Degradation	k92	6.33e-4	s^{-1}	(4)
[PCPLC_P-Asmase] → [Asmase*]	Asmase Activation	k93	0.009	s^{-1}	(4)
[Asmase*] + [sphingomyelin] → [ceremide]	Enzymatic Reaction	k94 k95	103.83 590	nM/s nM	(5) (5)

[ceremide]+[TAK1] → [ceremide-TAK1]	Binding Reaction	k96	3.30e-4	$nM^{-1}s^{-1}$	(6)
[ceremide-TAK1] → sink	Complex Degradation	k97	2.17e-3	s^{-1}	(6)
[ceremide-TAK1] → [TAK1_P]	TAK1 Phosphorylation	k98	7.40e-3	s^{-1}	(6)
[TAK1_P]+[SEK1] → [TAK1_P-SEK1]	Binding Reaction	k99	2.57e-4	$nM^{-1}s^{-1}$	(7)
[TAK1_P-SEK1] → sink	Complex Degradation	k100	1.60e-5	s^{-1}	(7)
[TAK1_P-SEK1] → [SEK1_P]	SEK1 Phosphorylation	k101	5.64e-3	s^{-1}	(7)
[TAK1_P]+[SEK1_P] → [TAK1_P-SEK1_P]	Binding Reaction	k102	2.70e-3	$nM^{-1}s^{-1}$	(7)
[TAK1_P-SEK1_P] → sink	Complex Degradation	k103	1.60e-5	s^{-1}	(7)
[TAK1_P-SEK1_P] → [SEK1_PP]	SEK1_P Phosphorylation	k104	0.05	s^{-1}	(7)
[SEK1_PP]+[JNK] → [SEK1_PP-JNK]	Binding Reaction	k105	1.30e-3	$nM^{-1}s^{-1}$	(7)
[SEK1_PP-JNK] → sink	Complex Degradation	k106	1.60e-3	s^{-1}	(7)
[SEK1_PP-JNK] → [JNK_P]	JNK Phosphorylation	k107	0.05	s^{-1}	(7)
[SEK1_PP]+[JNK_P] → [SEK1_PP-JNK_P]	Binding Reaction	k108	1.30e-2	$nM^{-1}s^{-1}$	(7)
[SEK1_PP-JNK_P] → sink	Complex Degradation	k109	1.60e-3	s^{-1}	(7)
[SEK1_PP-JNK_P] → [JNK_PP]	JNK_P Phosphorylation	k110	0.05	s^{-1}	(7)
[JNK_PP] → [AP1]	JNK_PP Nuclear Translocation	k111	3.40e-3	s^{-1}	(8)
[AP1] → [JNK_PP]	AP1 Cytoplasmic Translocation	k167	1.60e-4	s^{-1}	(8)
[JNK_P]+[MKP1] → [JNK_P-MKP1]	Binding Reaction	k112	0.01	$nM^{-1}s^{-1}$	(9)
[JNK_P-MKP1] → sink	Complex Degradation	k113	1	s^{-1}	(9)
[JNK_P-MKP1] → [JNK]	JNK_P Dephosphorylation	k114	0.05	s^{-1}	(9)
[JNK_PP]+[MKP1] → [JNK_PP-MKP1]	Binding Reaction	k115	0.045	$nM^{-1}s^{-1}$	(9)
[JNK_PP-MKP1] → sink	Complex Degradation	k116	1	s^{-1}	(9)
[JNK_PP-MKP1] → [JNK_P]	JNK_PP Dephosphorylation	k117	0.092	s^{-1}	(9)
[JNK_P]+[MKP5] → [JNK_P-MKP5]	Binding Reaction	k118	0.011	$nM^{-1}s^{-1}$	(9)
[JNK_P-MKP5] → sink	Complex Degradation	k119	0.99	s^{-1}	(9)
[JNK_P-MKP5] → [JNK]	JNK_P	k120	0.055	s^{-1}	(9)

	Dephosphorylation				
[JNK_PP]+[MKP5] → [JNK_PP-MKP5]	Binding Reaction	k121	0.046	$nM^{-1}s^{-1}$	(9)
[JNK_PP-MKP5] → sink	Complex Degradation	k122	0.99	s^{-1}	(9)
[JNK_PP-MKP5] → [JNK_P]	JNK_PP Dephosphorylation	k123	0.093	s^{-1}	(9)
[TAK1_P]+[IKK] → [TAK1_P-IKK]	Binding Reaction	k124	8.93e-5	$nM^{-1}s^{-1}$	(10)
[TAK1_P-IKK] → sink	Complex Degradation	k125	1.0e-4	s^{-1}	(10)
[TAK1_P-IKK] → [IKK_P]	IKK Phosphorylation	k126	0.1	s^{-1}	(10)
[IkBa]+[NFkBc] → [IkBa_NFkBc]	NFkBc Deactivation	k127	0.5	$nM^{-1}s^{-1}$	(10)
[IkBa_NFkBc] → sink	Complex Degradation	k128	3.96e-4	s^{-1}	(10)
[IKK_P]+[IkBa_NFkBc]→[IKK_P-IkBa-NFkBc]	Binding Reaction	k129	0.185	$nM^{-1}s^{-1}$	(10)
[IKK_P-IkBa_NFkBc] → sink	Complex Degradation	k130	0.0125	s^{-1}	(10)
[IKK_P-IkBa_NFkBc] → [IKK_P] + [NFkBc]	NFkBc Activation	k131	0.0204	s^{-1}	(10)
[IkBa_NFkBc] → [IkBa] + [NFkBc]	Dissociation Reaction	k132	2.61e-5	s^{-1}	(10)
[NFkBc] → [NFkBn]	Nuclear transport of NFkB	k133	0.09	s^{-1}	(10)
[NFkBn] → [NFkBc]	Cytoplasmic transport of NFkB	k134	8.0e-5	s^{-1}	(10)
$[NFkB]^2$ + [STAT1n_P_STAT1n_P] → [IRF1_mRNAn]	IRF1 Gene Expression	k135 k135b k136 k137 KIirf2	4.43e-3 0.03 1.94 10 364	nM/s nM/s nM nM nM	(1, 11, 12)
[IRF1_mRNAn] → [IRF1_mRNAc]	Cytoplasmic transport of mRNA	k138	1.36e-3	s^{-1}	(1)
[IRF1_mRNAc] → [IRF1c]	Translation	k139	0.01	s^{-1}	(1)
[IRF1c] → [IRF1n]	Nuclear Transport of IRF1	k140	5e-3	s^{-1}	(1)
$[NFkB]^3$ + [AP1] → [TNFalpha_mRNAn]	TNF-a Gene Expression	k141 k142 k143	0.01 3 4	nM/s nM nM	(11, 13, 14)
$[IRF1n]^2$ + [IRF2n]→ [TNFalpha_mRNAn]	TNF-a Gene Expression	k168 k169 KIirf2	1.38e-3 4.99e-3 364	nM/s nM nM	(15-17)
[TNFalpha_mRNAn] → [TNFalpha_mRNAc]	Cytoplasmic transport of mRNA	k144	8.05e-4	s^{-1}	(1)
[TNFalpha_mRNAc] → [TNFalphac]	Translation	k145	0.01	s^{-1}	(1)
[TNFalphac] → [TNFalphaEC]	Cellular Export of TNFa	k146	0.1	s^{-1}	(1)
[TNFalphaEC] + [TR1] → [TNFR1]	Receptor Binding	k147	0.0183	$nM^{-1}s^{-1}$	(18)
[TNFR1] → [TNFalphaEC] + [TR1]	Dissociation	k148	3.5e-4	s^{-1}	(18)
[TNFR1] + [TRADD] ←→ [TNFR1_TRADD]	Membrane complex formation	k151	0.1	$nM^{-1}s^{-1}$	(18)
[TNFR1_TRADD] → [TNFR1] +	Dissociation	k152	0.1	s^{-1}	(18)

[TRADD]					
[TNFR1_TRADD] + [TAK1] → TAK1_P	TAK1 Phosphorylation by TNFR1_TRADD	k153	0.1	$nM^{-1}s^{-1}$	(18)
[TNFR1_TRADD] → sink	Complex Degradation	k153b	0.1	s^{-1}	(18)
$[NFkBn]^2$ + $[AP1]^2$ + [IRF1n] + [IRF2n] + [STAT1n_P_STAT1n_P] → [iNOS_mRNAn]	iNOS Gene Expression	k154 k155 KiNOS1 KiNOS2 KIirf2	1e-3 0.02 0.022 0.017 364	nM/s nM/s nM nM nM	(11, 13, 16, 19, 20)
[iNOS_mRNAn] → [iNOS_mRNAc]	Cytoplasmic transport of mRNA	k156	1e-3	s^{-1}	(1)
[iNOS_mRNAc] → [iNOS]	Translation	k157	0.01	s^{-1}	(1)
[iNOS] + [arg] → [NO] + [citrulline]	Enzymatic formation of NO	k158 k159	5.83e-3 2800	nM/s nM	(5)
[citrulline] → [arginosuccinate]	Enzymatic formation of arginosuccinate	k160 k161	86 4.4e4	nM/s nM	(5)
[arginosuccinate] → [arg]	Enzymatic formation of arginine	k162 k163	171.67 2.0e5	nM/s nM	(5)
$[NFkBn]^2$ → [IkBa_mRNAn]	IkBa Gene Expression	k164	1.47e-2	$nM^{-1}s^{-1}$	(10)
[IkBa_mRNAn] → [IkBa_mRNAc]	Cytoplasmic transport of mRNA	k165	1e-3	s^{-1}	(1)
[IkBa_mRNAc] → [IkBa]	Translation	k166	4.08e-3	s^{-1}	(1)
[IRF1n] → [IRF2_mRNAn]	IRF2 Gene Expression	k170 k171	0.01 400	nM/s nM	(17)
[IRF2_mRNAn] → [IRF2_mRNAc]	Cytoplasmic transport of mRNA	k172	1e-3	s^{-1}	(1)
[IRF2_mRNAc] → [IRF2c]	Translation	k173	0.01	s^{-1}	(1)
[IRF2c] → [IRF2n]	Nuclear Transport	k174	4.60e-3	s^{-1}	(17)