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Supplementary Materials for

Innate immune memory and homeostasis may be conferred through crosstalk between the TLR3 and TLR7 pathways

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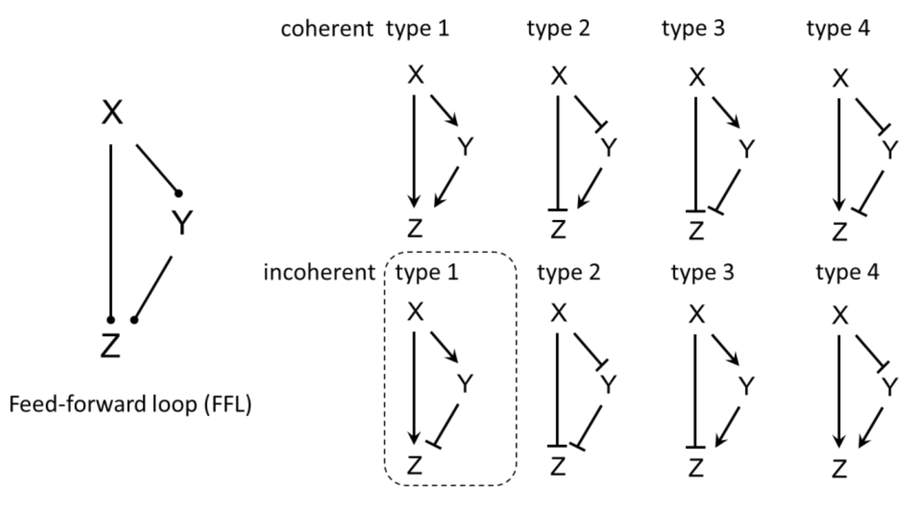
The I1-FFL

The feed-forward loop (FFL) is one of the most common network motifs in biomolecular regulatory networks (*66*, *68*). For example, suppose that transcription factor X stimulates expression of the gene encoding transcription factor Y and that both X and Y stimulate the expression of a target gene encoding Z. Then, X, Y, and Z form a FFL. Because each of the three transcriptional interactions in a FFL can be either positive (activation) or negative (inhibition), there are eight possible combinations of positive or negative interactions. They have been named as coherent or incoherent type 1 to 4 FFLs (see below). The abundance and functionality of different FFLs have been studied and discussed previously (*78*). Of particular interest in our context is the inherent type 1 FFL (I1-FFL), a circuit in which X activates the genes that encode Z and Y, and Y inhibits the genes encoding Z. It has been previously noted (*27*) that the roles of a I1-FFL include: (i) shortening of gene-circuit response time; (ii) generation of gene expression pulses; (iii) distinguishing between time-varying inputs; (iv) filtering out noise; (v) detecting the fold-change in the abundance of an input signal; and (vi) generating nonmonotonic input-output relations. The behavior resulting from (vi) is also called a biphasic response, which can be time-dependent: as time progresses, the output response initially increases but then subsequently decreases. A biphasic response can also be dose-dependent: Over a certain range of input dose, the output response first increases but subsequently decreases. The parameters that induce biphasic responses are highly limited (*77*). In the signaling network studied in this work, we showed that the I1-FFL mediated by STAT1 induced a dose-dependent biphasic response, which was crucial to both amplifying the immune response and avoiding an excessive response.



The ODE model

$$\frac{d([\text{TLR7}])}{dt} = -k_1[\text{R848}][\text{TLR7}]$$

$$\frac{d([\text{TLR*}])}{dt} = k_1[\text{R848}][\text{TLR7}] - k_2[\text{TLR7*}]$$

$$\frac{d([\text{MyD88*}])}{dt} = k_3[\text{TLR7*}][\text{MyD88}] - k_4[\text{MyD88*}][\text{IRAK1/4}][\text{TRAF6}]$$

$$\frac{d([\text{MyD88}])}{dt} = -k_3[\text{TLR7*}][\text{MyD88}] + k_7[\text{MyD88*:IRAK1/4:TRAF6}]$$

$$\frac{d([\text{IRAK1/4}])}{dt} = k_{19}[\text{IRAK1/4*:TRAF6}] - k_4[\text{MyD88*}][\text{IRAK1/4}][\text{TRAF6}]$$

$$\frac{d(\text{TRAF6}])}{dt} = k_{19}[\text{IRAK1/4*:TRAF6}] - k_4[\text{MyD88*}][\text{IRAK1/4}][\text{TRAF6}] - k_{26}[\text{TRAF6}][\text{A20}] + k_{27}[\text{TRAF6:A20}]$$
$$-k_{60}[\text{TRIF*}][\text{TRADD:FADD:RIP1:TRAF6}] - k_{70}[\text{TRIF*:TRADD:FADD:RIP1:TRAF6}]$$

$$\frac{d([\text{MyD88*:IRAK1/4:TRAF6}])}{dt} = k_4[\text{MyD88*}][\text{IRAK1/4}][\text{TRAF6}] - k_7[\text{MyD88*:IRAK1/4:TRAF6}]$$

$$\frac{d([\text{A20}])}{dt} = k_{35}[\text{A20mRNA}] - k_{26}[\text{TRAF6}][\text{A20}] + k_{27}[\text{TRAF6:A20}] - k_{37}[\text{A20}]$$

$$\frac{d([\text{TRAF6:A20}])}{dt} = k_{26}[\text{TRAF6}][\text{A20}] - k_{27}[\text{TRAF6:A20}]$$

$$\frac{d([\text{IRAK1/4*:TRAF6}])}{dt} = -k_{19}[\text{IRAK1/4*:TRAF6}] + k_7[\text{MyD88*:IRAK1/4:TRAF6}]$$
$$-k_9[\text{IRAK1/4*:TRAF6}]:[\text{TRAF3}] + k_{28}[\text{IRAK1/4*:TRAF6:TRAF3}]$$

$$\frac{d([\text{TRAF3}])}{dt} = -k_{144}[\text{IPS1}][\text{TRAF3}] - k_{145}[\text{IPS1*:TRAF3}] - k_{58}[\text{TRIF*}][\text{TRAF3}] + k_{59}[\text{TRIF*:TRAF3}]$$
$$-k_9[\text{IRAK1/4*:TRAF6}]:[\text{TRAF3}] + k_{28}[\text{IRAK1/4*:TRAF6:TRAF3}] + k_{69}[\text{TRIF*:TRAF3}]$$

$$\frac{d([\text{MKK1/2}])}{dt} = k_{24}[\text{MKK1/2*}] - \frac{k_{10}[\text{Tak1:Tab2:Tab3*}][\text{MKK1/2}]}{k_{77} + [\text{MKK1/2}]}$$

$$\frac{d([\text{MKK3/6}])}{dt} = k_{25}[\text{MKK3/6*}] - \frac{k_{11}[\text{Tak1:Tab2:Tab3*}][\text{MKK3/6}]}{k_{78} + [\text{MKK3/6}]}$$

$$\frac{d([\text{ERK}])}{dt} = k_{18}[\text{ERK*}] - k_{12}[\text{ERK}][\text{MKK1/2}]$$

$$\frac{d([\text{ERK*}])}{dt} = -k_{18}[\text{ERK*}] + k_{12}[\text{ERK}][\text{MKK1/2}]$$

$$\frac{d([\text{MKK1/2*}])}{dt} = -k_{24}[\text{MKK1/2*}] + \frac{k_{10}[\text{Tak1:Tab2:Tab3*}][\text{MKK1/2}]}{k_{77} + [\text{MKK1/2}]}$$

$$\frac{d([\text{MKK3/6*}])}{dt} = -k_{25}[\text{MKK3/6*}] + \frac{k_{11}[\text{Tak1:Tab2:Tab3*}][\text{MKK3/6}]}{k_{78} + [\text{MKK3/6}]}$$

$$\frac{d([\text{p38}])}{dt} = k_{13}[\text{p38*}] - k_{12}[\text{p38}][\text{MKK3/6}]$$

$$\frac{d([\text{p38*}])}{dt} = -k_{13}[\text{p38*}] + k_{12}[\text{p38}][\text{MKK3/6}]$$

$$\frac{d([\text{AP1}])}{dt} = -k_{20}[\text{ERK*}][\text{AP1}] - k_{14}[\text{p38*}][\text{AP1}] - k_{32}[\text{JNK*}][\text{AP1}] + k_{29}[\text{AP1*}]$$

$$\frac{d([\text{NEMO:IKK}\beta\text{:IKK}\alpha])}{dt} = -k_{75}[\text{NEMO:IKK}\beta\text{:IKK}\alpha][\text{Tak1:Tab2:Tab3}] + k_{21} - k_{49}[\text{NEMO:IKK}\beta\text{:IKK}\alpha] - k_{94}[\text{NEMO:IKK}\beta\text{:IKK}\alpha][\text{AKT*}]$$

$$\frac{d([\text{NEMO:IKK}\beta\text{*:IKK}\alpha])}{dt} = -k_{15}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha][\text{I}\kappa\text{B}\alpha\text{:NF}\kappa\text{B}] + k_{54}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha\text{:NF}\kappa\text{B:I}\kappa\text{B}\alpha]$$
$$-k_{39}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha][\text{I}\kappa\text{B}\alpha] + k_{40}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha\text{:I}\kappa\text{B}\alpha] - k_{41}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha] + k_{50}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha]$$
$$-k_{53}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha][\text{A20}] + k_{76}[\text{NEMO:IKK}\beta\text{:IKK}\alpha\text{:Tak1:Tab2:Tab3*}] + k_{94}[\text{NEMO:IKK}\beta\text{:IKK}\alpha][\text{AKT*}]$$

$$\frac{d([\text{I}\kappa\text{B}\alpha])}{dt} = -k_{17}[\text{I}\kappa\text{B}\alpha][\text{NF}\kappa\text{B}] + k_{47}[\text{I}\kappa\text{B}\alpha\text{mRNA}] - k_{48}[\text{I}\kappa\text{B}\alpha] - k_{39}[\text{I}\kappa\text{B}\alpha][\text{NEMO:IKK}\beta\text{*:IKK}\alpha] - k_{44}[\text{I}\kappa\text{B}\alpha] + k_{45}[\text{I}\kappa\text{B}\alpha\text{n}]$$

$$\frac{d([\text{I}\kappa\text{B}\alpha\text{:NF}\kappa\text{B}])}{dt} = -k_{15}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha][\text{I}\kappa\text{B}\alpha\text{:NF}\kappa\text{B}] + k_{17}[\text{I}\kappa\text{B}\alpha][\text{NF}\kappa\text{B}] - k_{38}[\text{I}\kappa\text{B}\alpha\text{:NF}\kappa\text{B}] + k_{54}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha\text{:NF}\kappa\text{B:I}\kappa\text{B}\alpha]$$

$$\frac{d([\text{NF}\kappa\text{B}])}{dt} = -k_{17}[\text{I}\kappa\text{B}\alpha][\text{NF}\kappa\text{B}] - k_{16}[\text{NF}\kappa\text{B}] + k_{38}[\text{I}\kappa\text{B}\alpha\text{:NF}\kappa\text{B}]$$

$$\frac{d([\text{A20mRNA}])}{dt} = k_{52}[\text{NF}\kappa\text{Bn}] - k_{36}[\text{A20mRNA}]$$

$$\frac{d([\text{I}\kappa\text{B}\alpha\text{mRNA}])}{dt} = k_{55}[\text{NF}\kappa\text{Bn}] - k_{46}[\text{I}\kappa\text{B}\alpha\text{mRNA}]$$

$$\frac{d([\text{IRF7}])}{dt} = -k_5[\text{IRAK1/4:TRAF6:TRAF3}][\text{IRF7}] + k_6[\text{IRF7}]$$

$$\frac{d([\text{JNK}])}{dt}=k_{33}[\text{JNK*}]-k_{30}[\text{JNK}][\text{MKK4/7}]$$

$$\frac{d([\text{MKK4/7*}])}{dt}=-k_{34}[\text{MKK4/7*}]+\frac{k_{31}[\text{Tak1:Tab2:Tab3*}][\text{MK4/7}]}{k_{79}+[\text{MKK4/7}]}$$

$$\frac{d([\text{JNK*}])}{dt}=-k_{33}[\text{JNK*}]+k_{30}[\text{JNK}][\text{MKK4/7}]$$

$$\frac{d([\text{MKK4/7}])}{dt}=k_{34}[\text{MKK4/7*}]-\frac{k_{31}[\text{Tak1:Tab2:Tab3*}][\text{MK4/7}]}{k_{79}+[\text{MKK4/7}]}$$

$$\frac{d([\text{IRAK1/4*:TRAF6:TRAF3}])}{dt}=k_{9}[\text{IRAK1/4*:TRAF6}]:[\text{TRAF3}]-k_{28}[\text{IRAK1/4*:TRAF6:TRAF3}]$$

$$\frac{d([\text{I}\kappa\text{B}\alpha^*])}{dt}=k_{38}[\text{I}\kappa\text{B}\alpha\text{:NF}\kappa\text{B}]+k_{54}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha\text{:NF}\kappa\text{B:I}\kappa\text{B}\alpha]+k_{40}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha\text{:I}\kappa\text{B}\alpha\text{:}]-k_{140}[\text{I}\kappa\text{B}\alpha^*]$$

$$\frac{d([\text{NEMO:IKK}\beta\text{*:IKK}\alpha\text{:NF}\kappa\text{B:I}\kappa\text{B}\alpha])}{dt}=k_{15}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha][\text{I}\kappa\text{B}\alpha\text{:NF}\kappa\text{B}]-k_{54}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha\text{:NF}\kappa\text{B:I}\kappa\text{B}\alpha]$$

$$\frac{d([\text{NEMO:IKK}\beta\text{*:IKK}\alpha\text{:I}\kappa\text{B}\alpha])}{dt}=k_{39}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha][\text{I}\kappa\text{B}\alpha]-k_{40}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha\text{:I}\kappa\text{B}\alpha]$$

$$\frac{d([\text{inactiveIKK}])}{dt}=k_{41}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha]-k_{51}[\text{inactiveIKK}]+k_{53}[\text{NEMO:IKK}\beta\text{*:IKK}\alpha][\text{A20}]$$

$$\frac{d([\text{TLR3}])}{dt}=-k_{56}[\text{poly(I:C)}][\text{TLR3}]$$

$$\frac{d([\text{TLR3*}])}{dt}=k_{56}[\text{poly(I:C)}][\text{TLR3}]-k_{67}[\text{TLR3}]$$

$$\frac{d([\text{TRIF}])}{dt}=-k_{57}[\text{TLR3*}][\text{TRIF}]+k_{69}[\text{TRIF*:TRAF3}]+k_{70}[\text{TRIF*:TRADD:FADD:RIP1:TRAF6}]$$

$$\frac{d([\text{TRIF*}])}{dt}=k_{57}[\text{TLR3*}][\text{TRIF}]-k_{58}[\text{TRIF*}][\text{TRAF3}]-k_{59}[\text{TRIF*:TRAF3}]-k_{60}[\text{TRIF*}][\text{TRIF*:TRADD:FADD}][\text{TRAF6}]$$

$$\frac{d([\text{TRIF*:TRAF3}])}{dt}=k_{58}[\text{TRIF*}][\text{TRAF3}]+k_{59}[\text{TRIF*:TRAF3}]-k_{69}[\text{TRIF*:TRAF3}]$$

$$\frac{d([\text{TRADD:FADD:RIP1}])}{dt}=-k_{60}[\text{TRIF*}][\text{TRIF*:TRADD:FADD}][\text{TRAF6}]+k_{70}[\text{TRIF*:TRADD:FADD:RIP1:TRAF6}]$$

$$\frac{d([\text{TRIF*:TRADD:FADD:RIP1:TRAF6}])}{dt}=k_{60}[\text{TRIF*}][\text{TRIF*:TRADD:FADD}][\text{TRAF6}]-k_{70}[\text{TRIF*:TRADD:FADD:RIP1:TRAF6}]$$

$$\frac{d([\text{IKK}\varepsilon])}{dt}=-k_{62}[\text{IKK}\varepsilon][\text{TRIF*:TRAF3}]+k_{66}[\text{TBK1*:IKK}\varepsilon]-k_{146}[\text{IKK}\varepsilon][\text{IPS3*:TRAF3}]$$

$$\frac{d([\text{IKK}\varepsilon^*])}{dt}=k_{62}[\text{IKK}\varepsilon][\text{TRIF*:TRAF3}]-k_{64}[\text{TBK1*}][\text{IKK}\varepsilon]+k_{146}[\text{IKK}\varepsilon][\text{IPS3*:TRAF3}]$$

$$\frac{d([\text{TBK1}])}{dt}=-k_{63}[\text{TBK1}][\text{TRIF*:TRAF3}]+k_{66}[\text{TBK1*:IKK}\varepsilon]-k_{147}[\text{TBK1}][\text{IPS3*:TRAF3}]$$

$$\frac{d([\text{TBK1*}])}{dt}=k_{63}[\text{TBK1}][\text{TRIF*:TRAF3}]-k_{64}[\text{TBK1*}][\text{IKK}\varepsilon]+k_{147}[\text{TBK1}][\text{IPS3*:TRAF3}]$$

$$\frac{d([\text{TBK1*:IKK}\varepsilon])}{dt}=k_{64}[\text{TBK1*}][\text{IKK}\varepsilon]-k_{66}[\text{TBK1*:IKK}\varepsilon]$$

$$\frac{d([\text{IRF3}])}{dt}=-k_{65}[\text{TBK1*:IKK}\varepsilon][\text{IRF3}]+k_{69}[\text{IRF*}]$$

$$\frac{d([\text{IL6I1}])}{dt}=-k_{105}[\text{IL6I1}]-k_{71}[\text{IL6I1}]+k_{118}\left(0.0001+0.9999\left(1-\frac{1}{1+k_{120}[\text{RELBp52}]}\right)\right)$$

$$+k_{102}\left(1-\frac{1}{1+k_{98}[\text{NF}\kappa\text{B}]}\frac{1}{1+k_{97}[\text{NF}\kappa\text{Bn}][\text{AP1*}][\text{FACY}]^{1.5}}\frac{1}{1+k_{100}[\text{AP1}]}\frac{1}{1+k_{96}[\text{FACX}][\text{NF}\kappa\text{Bn}][\text{AP1*}]}\right)$$

$$\frac{d([\text{IL6I2}])}{dt}=k_{71}[\text{IL6I1}]-k_{72}[\text{IL6I2}]$$

$$\frac{d([\text{IL6I3}])}{dt}=k_{72}[\text{IL6I2}]-k_{73}[\text{IL6I3}]$$

$$\frac{d([\text{IL12I2}])}{dt}=k_{71}[\text{IL12I1}]-k_{72}[\text{IL12I2}]$$

$$\frac{d([\text{IL12I3}])}{dt}=k_{72}[\text{IL12I2}]-k_{73}[\text{IL12I3}]$$

$$\frac{d([\text{IL6mRNA}])}{dt}=k_{73}[\text{IL6I3}]-k_{74}[\text{IL6mRNA}]-k_{123}[\text{IL6mRNA}][\text{STAT3}]-k_{114}[\text{TPP}][\text{IL6mRNA}]$$

$$\frac{d([\text{IL12mRNA}])}{dt}=k_{73}[\text{IL12I3}]-k_{74}[\text{IL12mRNA}]-k_{122}[\text{IL12mRNA}][\text{STAT3}]-k_{114}[\text{TPP}][\text{IL12mRNA}]$$

$$\frac{d([\text{Tak1:Tab2:Tab3}])}{dt}=-k_{8}[\text{IRAK1/4*:TRAF6}][\text{Tak1:Tab2:Tab3}]+k_{22}[\text{Tak1:Tab2:Tab3*}]$$

$$-k_{61}[\text{TRIF*:TRADD:FADD:RIP1:TRAF6}][\text{Tak1:Tab2:Tab3}]$$

$$\frac{d([\text{NEMO:IKK}\beta\text{:IKK}\alpha\text{:Tak1:Tab2:Tab3*}])}{dt} = -k_{76}[\text{NEMO:IKK}\beta\text{:IKK}\alpha\text{:Tak1:Tab2:Tab3*}] + k_{75}[\text{NEMO:IKK}\beta\text{:IKK}\alpha][\text{Tak1:Tab2:Tab3*}]$$

$$\frac{d([\text{Tak1:Tab2:Tab3*}])}{dt} = k_{8}[\text{IRAK1/4*:TRAF6}][\text{Tak1:Tab2:Tab3}] + k_{61}[\text{TRIF*:TRADD:FADD:RIP1:TRAF6}][\text{Tak1:Tab2:Tab3}]$$

$$+k_{76}[\text{NEMO:IKK}\beta\text{:IKK}\alpha\text{:Tak1:Tab2:Tab3*}] - k_{75}[\text{NEMO:IKK}\beta\text{:IKK}\alpha][\text{Tak1:Tab2:Tab3*}] - k_{22}[\text{Tak1:Tab2:Tab3}]$$

$$\frac{d([\text{IL12I1}])}{dt} = -k_{105}[\text{IL12I1}] - k_{71}[\text{IL12I1}] + k_{118}\left(0.0001 + 0.9999\left(1 - \frac{1}{1 + k_{119}[\text{RELBp52}]}\right)\right)$$

$$+k_{102}\left(1 - \frac{1}{1 + k_{98}[\text{NF}\kappa\text{B}]}\frac{1}{1 + k_{99}[\text{NF}\kappa\text{Bn}][\text{AP1*}][\text{FACY}]^{1.5}}\frac{1}{1 + k_{100}[\text{AP1*}]}\frac{1}{1 + k_{101}[\text{FACY}][\text{NF}\kappa\text{Bn}][\text{FACTX}]}\right)$$

$$\frac{d([\text{IFNI1}])}{dt} = -k_{106}[\text{IFNI1}] - k_{110}[\text{IFNI1}] + k_{81}\left(0.0001 + 0.9999\left(1 - \frac{1}{1 + k_{153}[\text{IRF5*}]}\right)\right) + k_{115}\left(0.0001 + 0.9999\left(1 - \frac{1}{1 + k_{153}[\text{IRF7*}]}\right)\right)$$

$$+k_{80}\left(1 - \frac{1}{1 + k_{82}[\text{IRF3*}]}\frac{1}{1 + 0.0001[\text{NF}\kappa\text{Bn}][\text{AP1*}][\text{IRF3*}]}\right)$$

$$\frac{d([\text{IFNI2}])}{dt} = k_{106}[\text{IFNI1}] - k_{107}[\text{IFNI2}]$$

$$\frac{d([\text{IFNI3}])}{dt} = k_{107}[\text{IFNI2}] - k_{108}[\text{IFNI3}]$$

$$\frac{d([\text{Type1IFN}])}{dt} = k_{108}[\text{IFNI3}] - k_{109}[\text{Type1IFN}] + k_{89}\left(0.0001 + 0.9999\left(1 - \frac{1}{1 + k_{90}[\text{STAT1:STAT2n*}]}\right)\right)$$

$$\frac{d([\text{TYK2:JAK1}])}{dt} = k_{85}[\text{TYK2:JAK1*}] - k_{83}[\text{TYK2:JAK1}][\text{Type1IFN}]$$

$$\frac{d([\text{TYK2:JAK1*}])}{dt} = -k_{85}[\text{TYK2:JAK1*}] + k_{83}[\text{TYK2:JAK1}][\text{Type1IFN}]$$

$$\frac{d([\text{STAT1:STAT2}])}{dt} = k_{86}[\text{STAT1:STAT2*}] - k_{84}[\text{STAT1:STAT2}][\text{TYK2:JAK1*}]$$

$$\frac{d([\text{STAT1:STAT2*}])}{dt} = -k_{86}[\text{STAT1:STAT2*}] + k_{84}[\text{STAT1:STAT2}][\text{TYK2:JAK1*}] - k_{87}[\text{STAT1:STAT2*}] + k_{88}[\text{STAT1:STAT2n*}]$$

$$\frac{d([\text{PI3K}])}{dt} = -k_{91}[\text{PI3K}][\text{Type1IFN}] + k_{93}[\text{PI3K*}]$$

$$\frac{d([\text{PI3K*}])}{dt} = k_{91}[\text{PI3K}][\text{Type1IFN}] - k_{93}[\text{PI3K*}]$$

$$\frac{d([\text{AKT}])}{dt} = -k_{92}[\text{AKT}][\text{PI3K*}] + k_{95}[\text{AKT*}]$$

$$\frac{d([\text{AKT*}])}{dt} = k_{92}[\text{AKT}][\text{PI3K*}] - k_{95}[\text{AKT*}]$$

$$\frac{d([\text{NIK}])}{dt} = -k_{112}[\text{NIK}][\text{Type1IFN}] + k_{141}[\text{NIK*}]$$

$$\frac{d([\text{NIK*}])}{dt} = k_{112}[\text{NIK}][\text{Type1IFN}] - k_{141}[\text{NIK*}]$$

$$\frac{d([\text{RELBp100}])}{dt} = -k_{112}[\text{NIK*}][\text{RELBp100}] + k_{141}[\text{RELBp100*}]$$

$$\frac{d([\text{RELBp100*}])}{dt} = k_{112}[\text{NIK*}][\text{RELBp100}] - k_{141}[\text{RELBp100*}]$$

$$\frac{d([\text{RELBp50*}])}{dt} = k_{112}[\text{RELBp50}][\text{RELBp100*}] - k_{141}[\text{RELBp50*}]$$

$$\frac{d([\text{FACZ}])}{dt} = k_{139}[\text{STAT1:STAT2n*}] - k_{150}[\text{FACZ}]$$

$$\frac{d([\text{IL10}])}{dt} = -k_{127}[\text{IL10}] - k_{112}[\text{TPP}][\text{IL10}] + k_{130}[\text{MSK1/2}][\text{STAT1:STAT2n*}]$$

$$\frac{d([\text{MSK1/2}])}{dt} = -k_{131}[\text{MSK1/2}][\text{ERK*}] + k_{131}[\text{MSK1/2*}] - k_{112}[\text{MSK1/2}][\text{p38*}]$$

$$\frac{d([\text{MSK1/2*}])}{dt} = k_{131}[\text{MSK1/2}][\text{ERK*}] - k_{131}[\text{MSK1/2*}] + k_{112}[\text{MSK1/2}][\text{p38*}]$$

$$\frac{d([\text{STAT3}])}{dt} = -k_{126}[\text{STAT3}][\text{IL10}] + k_{129}[\text{STAT3*}]$$

$$\frac{d([\text{STAT3*}])}{dt} = k_{126}[\text{STAT3}][\text{IL10}] - k_{129}[\text{STAT3*}]$$

$$\frac{d([\text{PREFACY}])}{dt} = -\frac{k_{124}[\text{STAT1:STAT2n*}][\text{PREFACY}]}{k_{125} + [\text{PREFACY}]}$$

$$\frac{d([\text{IL1amRNA}])}{dt} = k_{132}[\text{IL6I3}] - k_{134}[\text{IL1amRNA}] - k_{133}[\text{IL1amRNA}][\text{STAT3}] - k_{114}[\text{TPP}][\text{IL1amRNA}]$$

$$\frac{d([\text{CSF3mRNA}])}{dt} = -k_{150}[\text{CSF3mRNA}] - k_{113}[\text{CSF3mRNA}][\text{TTP}] - k_{138}[\text{CSF3mRNA}][\text{STAT3}]$$

$$+k_{102}\left(1 - \frac{1}{1+k_{98}[\text{NF}\kappa\text{B}]}\frac{1}{1+k_{135}[\text{NF}\kappa\text{Bn}][\text{AP1*}][\text{FACY}]^{1.5}}\frac{1}{1+k_{136}[\text{AP1*}]}\frac{1}{1+k_{137}[\text{FACTX}]}\right)$$

$$\frac{d([\text{MDA5}])}{dt} = -k_{142}[\text{MDA5}][\text{poly(I:C)}]$$

$$\frac{d([\text{MDA5*}])}{dt} = k_{142}[\text{MDA5}][\text{poly(I:C}] - k_{142}[\text{MDA5*}]$$

$$\frac{d([\text{IPS1}])}{dt} = -k_{143}[\text{IPS1}][\text{MDA5*}] + k_{149}[\text{IPS1*}] - k_{117}[\text{IPS1}][\text{RIG-I*}]$$

$$\frac{d([\text{IPS1*}])}{dt} = k_{143}[\text{IPS1}][\text{MDA5*}] - k_{149}[\text{IPS1*}] + k_{117}[\text{IPS1}][\text{RIG-I*}] - k_{144}[\text{IPS1*}][\text{TRAF3}] + k_{145}[\text{IPS1*:TRAF3}]$$

$$\frac{d([\text{IPS1*:TRAF3}])}{dt} = k_{144}[\text{IPS1*}][\text{TRAF3}] - k_{145}[\text{IPS1*:TRAF3}]$$

$$\frac{d([\text{RIG-I}])}{dt} = -k_{152}[\text{RIG-I}][\text{poly(I:C)}]$$

$$\frac{d([\text{RIG-I*}])}{dt} = k_{152}[\text{RIG-I}][\text{poly(I:C}] - k_{116}[\text{RIG-I*}]$$

$$\frac{d([\text{MK2}])}{dt} = -k_{154}[\text{MK2}][\text{p38*}]$$

$$\frac{d([\text{TTP}])}{dt} = k_{155}[\text{MK2*}] - k_{157}[\text{TTP}]$$

$$\frac{d([\text{MK2*}])}{dt} = k_{154}[\text{MK2*}][\text{p38*}]$$

$$\frac{d([\text{IRF5}])}{dt} = -k_{151}[\text{IRAK1/4*:TRAF6:TRAF3}][\text{IRF5}]$$

$$\frac{d([\text{IRF5*}])}{dt} = k_{151}[\text{IRAK1/4*:TRAF6:TRAF3}][\text{IRF5}]$$

$$\frac{d([\text{I}\kappa\text{B}\alpha\text{n}])}{dt} = -k_{42}[\text{NF}\kappa\text{Bn}][\text{I}\kappa\text{B}\alpha\text{n}] + k_{44}[\text{I}\kappa\text{B}\alpha] - k_{45}[\text{I}\kappa\text{B}\alpha\text{n}]$$

$$\frac{d([\text{I}\kappa\text{B}\alpha\text{n:NF}\kappa\text{Bn}])}{dt} = k_{42}[\text{NF}\kappa\text{Bn}][\text{I}\kappa\text{B}\alpha\text{n}] - k_{43}[\text{I}\kappa\text{B}\alpha\text{n:NF}\kappa\text{Bn}]$$

$$\frac{d([\text{NF}\kappa\text{Bn}])}{dt} = k_{16}[\text{NF}\kappa\text{B}] - k_{42}[\text{NF}\kappa\text{Bn}][\text{I}\kappa\text{B}\alpha\text{n}]$$

$$\frac{d([\text{AP1*}])}{dt} = k_{20}[\text{ERK*}][\text{AP1}] + k_{32}[\text{JNK*}][\text{AP1}] + k_{14}[\text{p38*}][\text{AP1}] + k_{29}[\text{AP1*}]$$

$$\frac{d([\text{STAT1:STAT2n*}])}{dt} = k_{87}[\text{STAT1:STAT2*}] - k_{88}[\text{STAT1:STAT2n*}] - k_{128}[\text{STAT1:STAT2n*}]$$

$$\frac{d([\text{FACX}])}{dt} = k_{103}[\text{IRF3*}] - k_{104}[\text{FACX}]$$

$$\frac{d([\text{FACY}])}{dt} = \frac{k_{124}[\text{STAT1:STAT2n*}][\text{PREFACY}]}{k_{125} + [\text{PREFACY}]}$$

$$\frac{d([\text{IRF3*}])}{dt} = k_{65}[\text{IRF3}][\text{TBK1*:IKK}\varepsilon] - k_{68}[\text{IRF3*}]$$

$$\frac{d([\text{IRF7*}])}{dt} = k_{5}[\text{IRF7}][\text{IRAK1/4*:TRAF6:TRAF3}] - k_{6}[\text{IRF7*}]$$

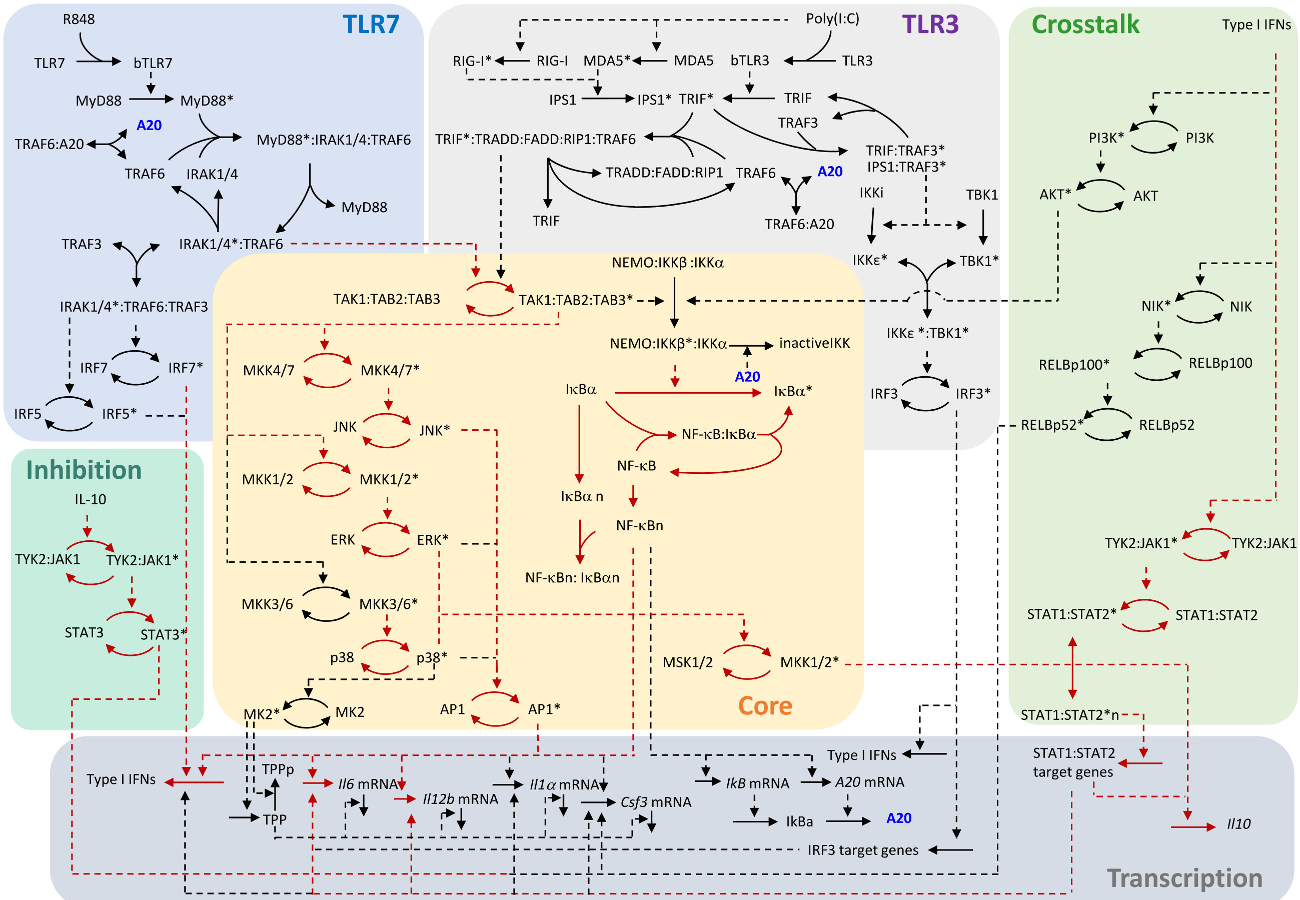


Fig. S1. The reaction schemas for the TLR3 and TLR7 signaling networks. These schemas are organized by different modules, designated as follows: TLR7-dependent, TLR3-dependent, and core interactions; inhibitory and transcriptional events: and TLR3-TLR7 crosstalk. Complexes are denoted by the names of their components, which are separated by a colon'. Single-headed solid arrows designate irreversible reactions, whereas double-headed arrows denote reversible reactions. Dotted arrows represent enzymatic reactions. The corresponding ODE model is presented. Those reactions with high global sensitivities, as identified by sensitivity analysis, are labeled in red.

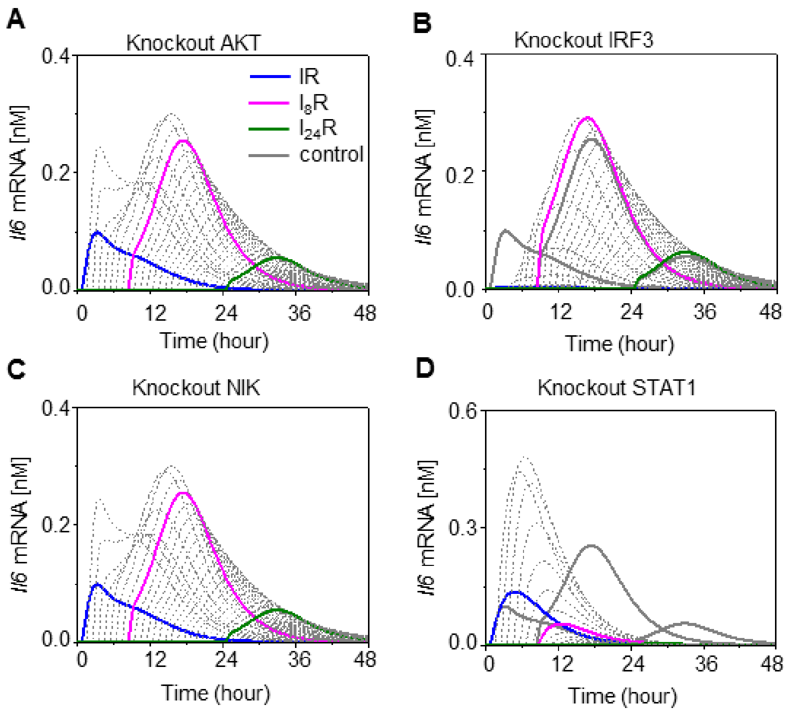


Fig. S2. Knockout simulation results. (**A** to **D**) Simulation profiles of changes in the abundance of *Il6* mRNA in the absence of (A) AKT, (B) IRF3, (C) NIK, and (D) STAT1.

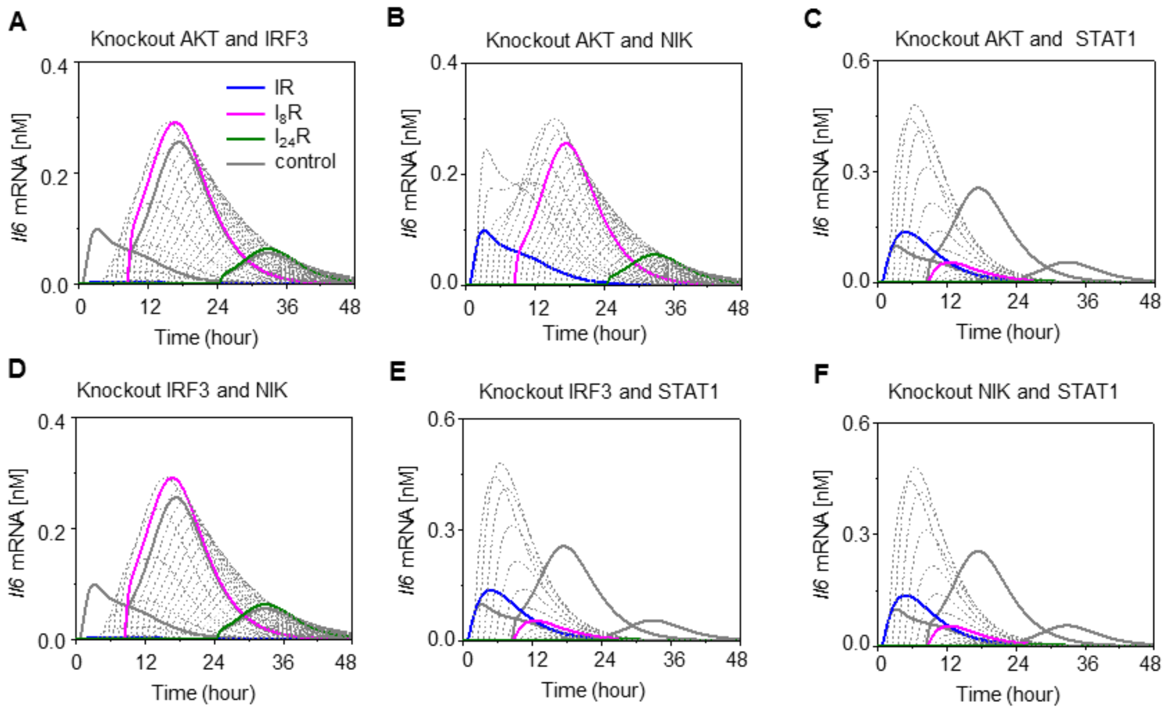


Fig. S3. Combinatorial knockout simulation results. (**A** to **F**) Simulation profiles of changes in the abundance of *Il6* mRNA in the absence of (A) AKT and IRF3, (B) AKT and NIK, (C) AKT and STAT1, (D) IRF3 and NIK, (E) IRF3 and STAT1, and (F) NIK and STAT1.

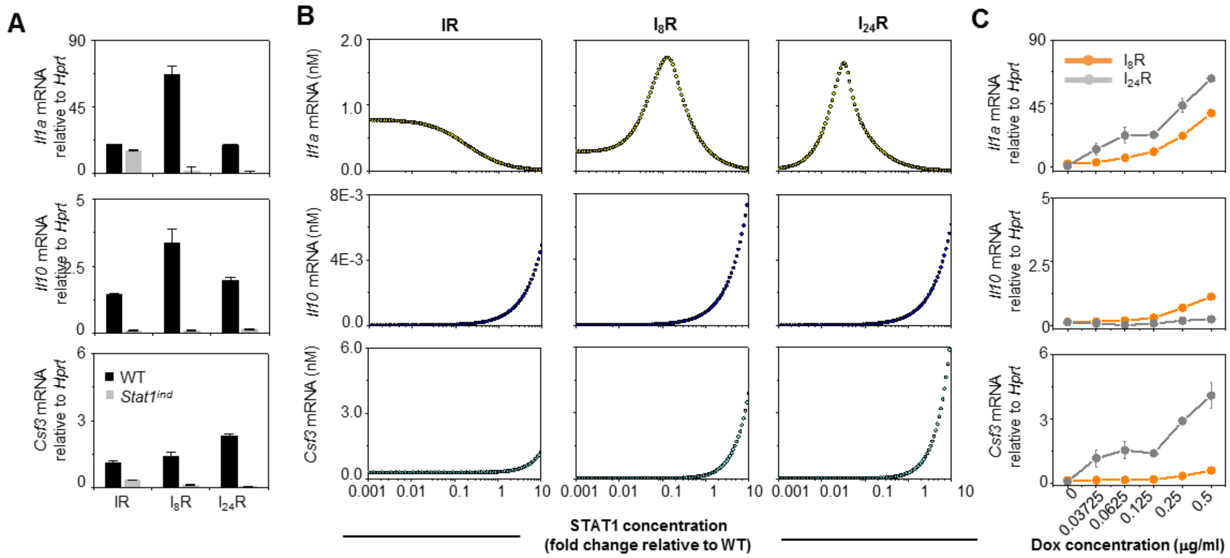


Fig. S4. Analysis of the abundances of *Il1a*, *Il10*, and *Csf3* mRNAs in response to in silico and empirical perturbation of the JAK-STAT pathway. (**A**) BMDMs isolated from wild-type (WT) and *Stat1^{ind}* mice (*Stat1* is knocked out in *Stat1^{ind}* mice in the absence of doxycycline) were subjected to the IR, I_8R, or $I_{24}R$ conditions. Eight hours after treatment with R848, the abundances of the indicated cytokine mRNAs were then determined by qRT-PCR analysis. Data are means ± SEM of three independent experiments. (**B**) Simulated response curves comparing the initial concentration of STAT1 with cytokine mRNA production under the IR, I_8R, and $I_{24}R$ conditions. (**C**) BMDMs from *Stat1^{ind}* mice were left untreated or were treated doxycycline (dox, 0.03125, 0.0625, 0.125, 0.25, or 0.5 µg/ml) for 24 hours before being subjected to either the I_8R or $I_{24}R$ conditions. Eight hours after treatment with R848, the abundances of the indicated cytokine mRNAs were then determined by qRT-PCR analysis. Data are means ± SEM of three independent experiments.

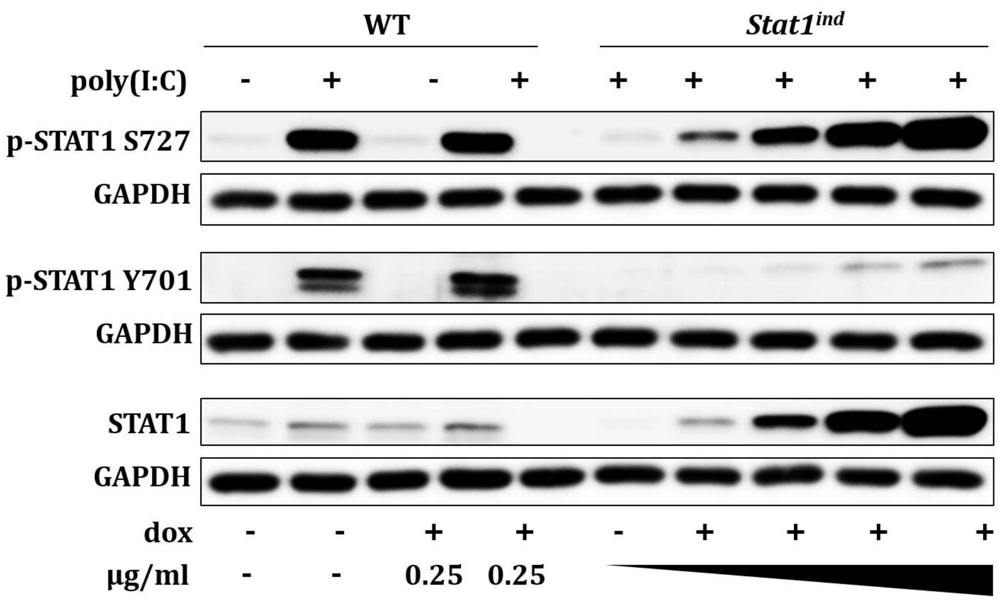


Fig. S5. Incremental induction of *Stat1* expression in BMDMs derived from S*tat1*^{ind} mice. BMDMs from WT mice were left untreated (-) or were pretreated with doxycycline (dox, 0.25 μg/ml) for 24 hours, whereas BMDMs from *Stat1*^{ind} mice were left untreated (-) or were pretreated with doxycycline (dox, 0.03125, 0.0625, 0.125, 0.25, or 0.5 μg/ml) for 24 hours. The BMDMs were then left untreated or were treated for 4 hours with poly(I:C) (10 μg/ml) as indicated. The cells were then subjected to Western blotting analysis with antibodies specific for the indicated proteins. Data are from a single experiment and are representative of three independent experiments.

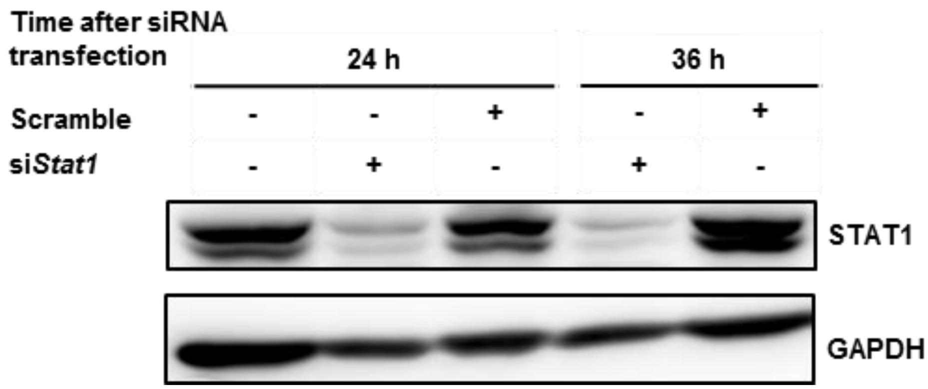


Fig. S6. Analysis of the efficiency of knockdown of *Stat1*. J774 were left untreated or were transfected with either *Stat1*-specific siRNA (si*Stat1*) or control, scrambled siRNA. Twenty-four or 36 hours later, the cells were subjected to Western blotting analysis with antibodies specific for the indicated proteins. Data are from a single experiment and are representative of two independent experiments.

Table S1. List of species and their initial concentrations.

Name	Initial State (nM)	Description
TLR7	5.31E-01 ± 2.66E-02	Toll-like receptor 7
TLR7*	0	Activate Toll-like receptor 7
R848	0	Resiquimod
MyD88*	0	Activate myeloid differentiation primary response 88
MyD88	8.74E-01 ± 4.37E-02	Myeloid differentiation primary response 88
IRAK1/4	1.29E-01 ± 6.44E-03	Interleukin-1 receptor-associated kinase 1/4
TRAF6	1.00E+00 ± 5.00E-02	TNF receptor-associated factor 6
MyD88*:IRAK1/4:TRAF6	0	A complex of active myeloid differentiation primary response 88, interleukin-1 receptor associated kinase 1/4, TNF receptor-associated factor 6
A20	4.80E-03 ± 2.40E-04	Zinc finger protein A20
TRAF6:A20	0	A complex of TNF receptor-associated factor 6 and Zinc finger protein A20
IRAK1/4*:TRAF6	0	A complex of active interleukin-1 receptor associated kinase 1/4 and TNF receptor-associated factor 6
TRAF3	2.00E-01 ± 1.00E-02	TNF receptor-associated factor 3
MKK1/2	9.93E-01 ± 4.97E-02	Mitogen-activated protein kinase 1/2
MKK3/6	1.77E-04 ± 8.86E-06	Mitogen-activated protein kinase 3/6
ERK	7.55E-02 ± 3.78E-03	Extracellular signal-regulated kinase

ERK*	0	Active extracellular signal-regulated kinase
MKK1/2*	0	Active mitogen-activated protein kinase 1/2
MKK3/6*	0	Active mitogen-activated protein kinase 3/6
p38*	0	Active p38 mitogen-activated protein kinase
p38	4.58E-01 ± 2.29E-02	p38 mitogen-activated protein kinase
AP1	2.00E-01 ± 1.00E-02	AP-1 transcription factor
NEMO:IKKβ:IKKα	2.00E-01 ± 1.00E-02	A complex of NF-κB essential modulator, inhibitor of nuclear factor kappa-B kinase subunit beta, and inhibitor of nuclear factor kappa-B kinase subunit alpha
NEMO:IKKβ*:IKKα	0	A complex of NF-kappa-B essential modulator, active inhibitor of nuclear factor kappa-B kinase subunit beta, and inhibitor of nuclear factor kappa-B kinase subunit alpha
IκBα	2.50E-03 ± 1.25E-04	Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha
IκBα:NFκB	5.92E-02 ± 2.96E-03	A complex of NF-κB and IκBα
NFκB	3.00E-03 ± 1.50E-04	Nuclear factor kappa-light-chain-enhancer of activated B cells
A20mRNA	0	Zinc finger protein A20 mRNA
IκBα mRNA	0	Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha mRNA
IRF7	2.00E-01 ± 1.00E-02	Interferon regulatory factor 7

JNK	3.20E-01 ± 1.60E-02	c-Jun N-terminal kinases
MKK4/7*	0	Active mitogen-activated protein kinase 4/7
JNK*	0	Active c-Jun N-terminal kinases
MKK4/7	6.41E-03 ± 3.21E-04	Mitogen-activated protein kinase 4/7
IRAK1/4*:TRAF6:TRAF3	0	A complex of active interleukin-1 receptor-associated kinase 1/4, TNF receptor-associated factor 6, and TNF receptor-associated factor 3
IκBα*	0	Active nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha
NEMO:IKKβ*:IKKα:NFκB:IκBα	0	A complex of NF-kappa-B essential modulator, active inhibitor of nuclear factor kappa-B kinase subunit beta, inhibitor of nuclear factor kappa-B kinase subunit alpha, nuclear factor kappa-light-chain-enhancer of activated B cells, and nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha
NEMO:IKKβ*:IKKα:IκBα	0	A complex of NF-kappa-B essential modulator, active inhibitor of nuclear factor kappa-B kinase subunit beta, inhibitor of nuclear factor kappa-B kinase subunit alpha, and nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha
inactiveIKK	0	inactive inhibitor of nuclear factor kappa-B kinase
Poly(I:C)	0	Polyinosinic:polycytidylic acid
TLR3	2.18E-01 ± 1.09E-02	Toll-like receptor 3
TLR3*	0	Activate Toll-like receptor 3
TRIF	2.00E-01 ± 1.00E-02	TIR-domain-containing adapter-inducing interferon-beta

TRIF*	0	Active TIR-domain-containing adapter-inducing interferon-beta
TRIF*:TRAF3	0	A complex of active TIR-domain-containing adapter-inducing interferon-beta and TNF receptor-associated factor 3
TRADD:FADD:RIP1	2.00E-01 ± 1.00E-02	A complex of TNFRSF1A-associated via death domain protein, Fas-Associated protein with death domain protein, and Receptor-interacting serine/threonine-protein kinase 1
TRIF*:TRADD:FADD:RIP1:TRAF6	0	A complex of active TIR-domain-containing adapter-inducing interferon-beta, TNFRSF1A-associated via death domain protein, Fas-Associated protein with death domain protein, Receptor-interacting serine/threonine-protein kinase 1, TNF receptor-associated factor 6
IKKε	2.00E-01 ± 1.00E-02	Inhibitor of nuclear factor kappa-B kinase subunit epsilon
IKKε*	0	Active inhibitor of nuclear factor kappa-B kinase subunit epsilon
TBK1	1.76E-01 ± 8.82E-03	TANK-binding kinase 1
TBK1*	0	Active TANK-binding kinase 1
TBK1*:IKKε	0	A complex of active TANK-binding kinase 1 and inhibitor of nuclear factor kappa-B kinase subunit epsilon
IRF3	1.85E-01 ± 9.24E-03	Interferon regulatory factor 3
IL6I1	0	Interleukin 6 production intermediate variable 1
IL6I2	0	Interleukin 6 production intermediate variable 2
IL6I3	0	Interleukin 6 production intermediate variable 3
IL12I2	0	Interleukin 12 production intermediate variable 2

IL12I3	0	Interleukin 12 production intermediate variable 3
IL6mRNA	0	Interleukin 6 mRNA
IL12mRNA	0	Interleukin 12 mRNA
Tak1:Tab2:Tab3	1.00E+00 ± 5.00E-02	A complex of Transforming growth factor beta activated kinase-1, Tak1 binding protein 2, and Tak1 binding protein 3
NEMO:IKKb:IKKa:Tak1:Tab2:Tab3*	0	A complex of NF-kappa-B essential modulator, inhibitor of nuclear factor kappa-B kinase subunit beta, inhibitor of nuclear factor kappa-B kinase subunit alpha, and active transforming growth factor beta activated kinase-1, Tak1 binding protein 2, and Tak1 binding protein 3
Tak1:Tab2:Tab3*	0	Active transforming growth factor beta activated kinase-1, Tak1 binding protein 2, and Tak1 binding protein 3 complex
IL12I1	0	Interleukin 12 production intermediate variable
IFNI1	0	Type 1 interferon production intermediate variable 1
IFNI2	0	Type 1 interferon production intermediate variable 2
IFNI3	0	Type 1 interferon production intermediate variable 3
Type1IFN	0	Type 1 interferon
TYK2:JAK1	2.60E-01 ± 1.30E-02	A complex of Tyrosine kinase 2 and Janus kinase 1
TYK2:JAK1*	0	Active Tyrosine kinase 2 and Janus kinase 1 complex
STAT1:STAT2	1.00E+00 ± 5.00E-02	A complex of Signal transducer and activator of transcription 1 and 2

STAT1:STAT2*	0	Active signal transducer and activator of transcription 1 and 2 complex
PI3K	6.15E-01 ± 3.08E-02	Phosphoinositide 3-kinase
PI3K*	0	Active phosphoinositide 3-kinase
AKT	2.45E-01 ± 1.22E-02	Protein kinase B
AKT*	0	Active protein kinase B
NIK	1.00E-02 ± 5.00E-04	NF-_B-inducing kinase
NIK*	0	Active NF-kappa-B-inducing kinase
RELBp52	1.00E-02 ± 5.00E-04	NF-_B Rel-like domain-containing protein/p52 heterodimer
RELBp100	1.00E-02 ± 5.00E-04	NF-_B Rel-like domain-containing protein/p100 heterodimer
RELBp100*	0	Active NF-kappaB Rel-like domain-containing protein/p100 heterodimer
RELBp52*	0	Active NF-kappaB Rel-like domain-containing protein/p52 heterodimer
FACZ	0	STAT1:STAT2 target factors that regulates *Csf3* production
IL10	0	Interleukin 10
MSK1/2	1.00E+00 ± 5.00E-02	Mitogen- and stress-activated protein kinase 1/2
MSK1/2*	0	Active mitogen- and stress-activated protein kinase 1/2
STAT3	1.00E+01 ± 5.00E-01	Signal transducer and activator of transcription 3
STAT3*	0	Active signal transducer and activator of transcription 3
IL1amRNA	0	Interleukin 1α mRNA
CSF3mRNA	0	Colony Stimulating Factor 3 mRNA

MDA5	4.10E-01 ± 2.05E-02	Melanoma Differentiation-Associated protein 5
MDA5*	0	Active melanoma Differentiation-Associated protein 5
IPS1	4.10E-02 ± 2.05E-03	Induced by phosphate starvation1
IPS1*	0	Active Induced by phosphate starvation1
IPS1*:TRAF3	0	A complex of active Induced by phosphate starvation1 and TNF receptor-associated factor 3
RIG-I	1.31E-01 ± 6.55E-03	Retinoic acid-inducible gene 1
RIG-I*	0	Active retinoic acid-inducible gene 1)
MK2	4.00E-01 ± 2.00E-02	Mitogen-Activated Protein Kinase-Activated Protein Kinase 2
TTP	1.00E-01 ± 5.00E-03	Tristetraprolin
TTPp	0	Phosphoratled tristetraprolin
MK2*	0	Active mitogen-Activated Protein Kinase-Activated Protein Kinase 2
IRF5	6.00E-02 ± 3.00E-03	Interferon regulatory factor 5
IRF5*	0	Active interferon regulatory factor 5
IκBαn	3.40E-03 ± 1.70E-04	Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha in nucleus
IκBαn:NFκBn	1.00E-04 ± 5.00E-06	A complex of nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha and nuclear factor kappa-light-chain-enhancer of activated B cells in nucleus
NFκBn	2.30E-03 ± 1.15E-04	Nuclear factor kappa-light-chain-enhancer of activated B cells in nucleus
AP1*	0	Active AP-1 transcription factor
STAT1:STAT2n*	0	Nuclear complex of Signal transducer and activator of transcription 1 and 2

FACX	0	IRF3 target factors
FACY	0	STAT1:STAT2 target factors (e.g. IRF1)
IRF3*	0	Active interferon regulatory factor 3
IRF7*	0	Active interferon regulatory factor 7

Table. S2. List of parameters and their values.

Parameter	Value	Unit
k1	4.31303	$nM^{-1}min^{-1}$
k2	62.0718	min^{-1}
k3	79.7282	$nM^{-1}min^{-1}$
k4	18.3319	$nM^{-2}min^{-1}$
k5	0.401153	$nM^{-1}min^{-1}$
k6	0.555267	min^{-1}
k7	0.455019	min^{-1}
k8	10.2145	$nM^{-1}min^{-1}$
k9	0.114814	$nM^{-1}min^{-1}$
k10	49.5518	min^{-1}
k11	93.6679	min^{-1}
k12	11.5939	$nM^{-1}min^{-1}$
k13	83.0183	$nM^{-1}min^{-1}$
k14	0.001	$nM^{-1}min^{-1}$
k15	60	$nM^{-1}min^{-1}$
k16	0.15	min^{-1}
k17	30	$nM^{-1}min^{-1}$
k18	0.0659759	min^{-1}
k19	0.497574	min^{-1}
k20	0.001	$nM^{-1}min^{-1}$
k21	0.0015	$nMmin^{-1}$
k22	0.479795	min^{-1}
k23	0.337396	min^{-1}
k24	0.0929546	min^{-1}
k25	0.0325152	min^{-1}
k26	0.284599	$nM^{-1}min^{-1}$
k27	1.90E-08	min^{-1}
k28	0.446332	min^{-1}
k29	0.05	min^{-1}
k30	53.2169	$nM^{-1}min^{-1}$
k31	64.0901	min^{-1}
k32	0.85	$nM^{-1}min^{-1}$
k33	0.128266	min^{-1}
k34	0.127762	min^{-1}
k35	30	min^{-1}
k36	0.024	min^{-1}
k37	0.018	min^{-1}
k38	0.0012	min^{-1}

k39	12	$nM^{-1}min^{-1}$
k40	6	min^{-1}
k41	0.09	min^{-1}
k42	30	$nM^{-1}min^{-1}$
k43	0.6	min^{-1}
k44	0.085	min^{-1}
k45	0.04	min^{-1}
k46	0.024	min^{-1}
k47	30	min^{-1}
k48	0.006	min^{-1}
k49	0.0075	min^{-1}
k50	0.0075	min^{-1}
k51	0.0075	min^{-1}
k52	3.00E-05	min^{-1}
k53	6	$nM^{-1}min^{-1}$
k54	6	min^{-1}
k55	3.00E-05	min^{-1}
k56	9952	$nM^{-1}min^{-1}$
k57	0.666364	$nM^{-1}min^{-1}$
k58	0.938185	$nM^{-1}min^{-1}$
k59	0.0196567	min^{-1}
k60	1	$nM^{-2}min^{-1}$
k61	0.00616326	$nM^{-1}min^{-1}$
k62	0.88438	$nM^{-1}min^{-1}$
k63	1	$nM^{-1}min^{-1}$
k64	0.9936	$nM^{-1}min^{-1}$
k65	0.818255	$nM^{-1}min^{-1}$
k66	0.240184	min^{-1}
k67	0.0409038	min^{-1}
k68	0.018947	min^{-1}
k69	0.012172	min^{-1}
k70	1	min^{-1}
k71	0.055068	min^{-1}
k72	0.00453392	min^{-1}
k73	0.00450439	min^{-1}
k74	0.347466	min^{-1}
k75	4.17803	$nM^{-1}min^{-1}$
k76	0.0110971	min^{-1}
k77	7712.52	nM
k78	2.35374	nM

k79	19991.5	nM
k80	0.111635	dimensionless
k81	20	dimensionless
k82	0.499547	nM^{-1}
k83	0.00181387	$nM^{-1}min^{-1}$
k84	0.372414	$nM^{-1}min^{-1}$
k85	0.0407122	min^{-1}
k86	0.0169071	min^{-1}
k87	0.0387076	min^{-1}
k88	0.0131879	min^{-1}
k89	3.68E-08	dimensionless
k90	0.00104135	nM^{-1}
k91	6.00E-09	$nM^{-1}min^{-1}$
k92	0.834749	$nM^{-1}min^{-1}$
k93	0.162221	min^{-1}
k94	0.954199	$nM^{-1}min^{-1}$
k95	0.62167	min^{-1}
k96	18.5703	nM^{-3}
k97	41.8866	dimensionless
k98	0.000128926	nM^{-1}
k99	449.12	dimensionless
k100	0.182554	nM^{-1}
k101	0.04	nM^{-3}
k102	55.1036	$nMmin^{-1}$
k103	1	min^{-1}
k104	0.01	min^{-1}
k105	0.420909	min^{-1}
k106	0.121509	min^{-1}
k107	0.00796542	min^{-1}
k108	0.00692448	min^{-1}
k109	0.00817427	min^{-1}
k110	0.830381	min^{-1}
k111	0.0015	min^{-1}
k112	0.001	$nM^{-1}min^{-1}$
k113	1	$nM^{-1}min^{-1}$
k114	0.04	$nM^{-1}min^{-1}$
k115	20	dimensionless
k116	0.59	min^{-1}
k117	0.02	$nM^{-1}min^{-1}$
k118	1.00E-06	$nMmin^{-1}$

k119	1.00E-06	nM^{-1}
k120	0.76	nM^{-1}
k121	0.89	min^{-1}
k122	600	$nM^{-1}min^{-1}$
k123	600	$nM^{-1}min^{-1}$
k124	1	min^{-1}
k125	0.1	nM
k126	0.5	min^{-1}
k127	0.01	min^{-1}
k128	0.05	min^{-1}
k129	0.1	$nM^{-1}min^{-1}$
k130	0.1	$nM^{-1}min^{-1}$
k131	0.01	min^{-1}
k132	0.01	min^{-1}
k133	600	$nM^{-1}min^{-1}$
k134	1	$nM^{-1}min^{-1}$
k135	81	dimensionless
k136	0.18	nM^{-1}
k137	0.001	nM^{-1}
k138	5	$nM^{-1}min^{-1}$
k139	0.4	min^{-1}
k140	0.392884	min^{-1}
k141	0.001	min^{-1}
k142	0.11	$nM^{-1}min^{-1}$
k143	0.012	$nM^{-1}min^{-1}$
k144	0.01	$nM^{-1}min^{-1}$
k145	0.79	min^{-1}
k146	0.01	$nM^{-1}min^{-1}$
k147	0.01	$nM^{-1}min^{-1}$
k148	0.81	$nM^{-1}min^{-1}$
k149	0.76	min^{-1}
k150	0.001	nM^{-1}
k151	0.1	min^{-1}
k152	0.001	$nM^{-1}min^{-1}$
k153	0.001	nM^{-1}
k154	0.1	$nM^{-1}min^{-1}$
k155	0.1	$nM^{-1}min^{-1}$
k156	0.04	min^{-1}