

DYNAMIC CROSS TALK MODEL OF THE EPITHELIAL INNATE IMMUNE RESPONSE TO DOUBLE-STRANDED RNA STIMULATION: COORDINATED DYNAMICS EMERGING FROM CELL-LEVEL NOISE

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SUPPLEMENT FILE

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ST1: System of Ordinary Differential Equations defining the model

$$\dot{\text{dsRNA}} = -h_1 \cdot \text{dsRNA} \cdot \text{RIGI} - h_{16} \cdot \text{dsRNA} \cdot \text{TLR3i} \quad (1)$$

$$\dot{\text{RIGIg}} = -h_{39} \cdot \text{RIGIg} \cdot \text{IRF7an} + h_{40} \cdot \text{RIGIg_IRF7an} \quad (2)$$

$$\dot{\text{RIGIg_IRF7an}} = h_{39} \cdot \text{RIGIg} \cdot \text{IRF7an} - h_{40} \cdot \text{RIGIg_IRF7an} \quad (3)$$

$$\dot{\text{RIGIt}} = h_{41} \cdot \text{RIGIg_IRF7an} + h_{42} \cdot \text{RIGIg} - h_{43} \cdot \text{RIGIt} \quad (4)$$

$$\dot{\text{RIGI}} = -h_2 \cdot \text{dsRNA} \cdot \text{RIGI} + h_{44} \cdot \text{RIGIt} - h_{45} \cdot \text{RIGI} \quad (5)$$

$$\dot{\text{RIGIub}} = h_2 \cdot \text{dsRNA} \cdot \text{RIGI} - h_3 \cdot \text{RIGIub} - h_4 \cdot \text{RIGIub} \cdot \text{MAVS} \quad (6)$$

$$\dot{\text{MAVSg}} = -h_{46} \cdot \text{MAVSg} \cdot \text{TLR3dTFan} + h_{47} \cdot \text{MAVSg_TLR3dTFan} \quad (7)$$

$$\dot{\text{MAVSg_TLR3dTFan}} = h_{46} \cdot \text{MAVSg} \cdot \text{TLR3dTFan} - h_{47} \cdot \text{MAVSg_TLR3dTFan} \quad (8)$$

$$\dot{\text{MAVSt}} = h_{48} \cdot \text{MAVSg_TLR3dTFan} + h_{49} \cdot \text{MAVSg} - h_{50} \cdot \text{MAVSt} \quad (9)$$

$$\dot{\text{MAVS}} = -h_4 \cdot \text{RIGIub} \cdot \text{MAVS} + h_{51} \cdot \text{MAVSt} - h_{52} \cdot \text{MAVS} \quad (10)$$

$$\dot{\text{RIGI_MAVS}} = h_4 \cdot \text{RIGIub} \cdot \text{MAVS} - h_5 \cdot \text{RIGI_MAVS} - h_6 \cdot \text{RIGI_MAVS} \cdot \text{TRAF3} \quad (11)$$

$$\dot{\text{TRAF3g}} = 0 \quad (12)$$

$$\dot{\text{TRAF3t}} = h_{135} \cdot \text{TRAF3g} - h_{136} \cdot \text{TRAF3t} \quad (13)$$

$$\dot{\text{TRAF3}} = -h_6 \cdot \text{RIGI_MAVS} \cdot \text{TRAF3} + h_{137} \cdot \text{TRAF3t} - h_{138} \cdot \text{TRAF3} \quad (14)$$

$$\dot{\text{RIGI_MAVS_TRAF3}} = h_6 \cdot \text{RIGI_MAVS} \cdot \text{TRAF3} - h_7 \cdot \text{RIGI_MAVS_TRAF3} \quad (15)$$

$$\dot{\text{IKK1g}} = -h_{53} \cdot \text{IKK1g} \cdot \text{TLR3dTFan} + h_{54} \cdot \text{IKK1g_TLR3dTFan} \quad (16)$$

$$\dot{\text{IKK1g_TLR3dTFan}} = h_{53} \cdot \text{IKK1g} \cdot \text{TLR3dTFan} - h_{54} \cdot \text{IKK1g_TLR3dTFan} \quad (17)$$

$$\dot{\text{IKK1t}} = h_{55} \cdot \text{IKK1g_TLR3dTFan} + h_{56} \cdot \text{IKK1g} - h_{57} \cdot \text{IKK1t} \quad (18)$$

$$\dot{\text{IKK1i}} = -h_8 \cdot \text{RIGI_MAVS_TRAF3} \cdot \text{IKK1i} + h_{58} \cdot \text{IKK1t} - h_{59} \cdot \text{IKK1i} \quad (19)$$

$$\dot{\text{IKK1a}} = h_8 \cdot \text{RIGI_MAVS_TRAF3} \cdot \text{IKK1i} - h_9 \cdot \text{IKK1a} - h_{10} \cdot \text{IKK1a} \cdot \text{TNFAIP3} \quad (20)$$

$$\dot{\text{IRF3g}} = -h_{67} \cdot \text{IRF3g} \cdot \text{RelAn} + h_{68} \cdot \text{IRF3g_RelAn} - h_{69} \cdot \text{IRF3g} \cdot \text{TLR3dTFan} + h_{70} \cdot \text{IRF3g_TLR3dTFan} \quad (21)$$

$$\dot{\text{IRF3g_TLR3dTFan}} = h_{69} \cdot \text{IRF3g} \cdot \text{TLR3dTFan} - h_{70} \cdot \text{IRF3g_TLR3dTFan} \quad (22)$$

$$\dot{\text{IRF3g_RelAn}} = h_{67} \cdot \text{IRF3g} \cdot \text{RelAn} - h_{68} \cdot \text{IRF3g_RelAn} \quad (23)$$

$$\dot{\text{IRF3t}} = h_{71} \cdot \text{IRF3g_TLR3dTFan} + h_{72} \cdot \text{IRF3g} - h_{73} \cdot \text{IRF3t} \quad (24)$$

$$\dot{\text{IRF3ii}} = h_{74} \cdot \text{IRF3t} - h_{75} \cdot \text{IRF3ii} - h_{76} \cdot \text{IRF3ii} \quad (25)$$

$$\dot{IRF3i} = -h_{11} \cdot IKK1a \cdot IRF3i + h_{76} \cdot IRF3ii - h_{77} \cdot IRF3i - h_{78} \cdot IRF3i + h_{79} \cdot IRF3in \quad (26)$$

$$\dot{IRF3in} = h_{78} \cdot IRF3i - h_{79} \cdot IRF3in - h_{80} \cdot IRF3in \quad (27)$$

$$\dot{IRF3a} = h_{11} \cdot IKK1a \cdot IRF3i - h_{12} \cdot IRF3a - h_{13} \cdot IRF3a + h_{14} \cdot IRF3an \quad (28)$$

$$\begin{aligned} \dot{IRF3an} = h_{13} \cdot IRF3a - h_{14} \cdot IRF3an - h_{15} \cdot IRF3an - h_{81} \cdot IRF3an \cdot RelAg + \\ h_{82} \cdot RelAg_IRF3an - h_{117} \cdot IRF3an \cdot ISG56g + \\ h_{118} \cdot ISG56g_IRF3an - h_{125} \cdot IRF3an \cdot IFNbg_RelAn + \\ h_{126} \cdot IFNbg_RelAn_IRF3an \end{aligned} \quad (29)$$

$$\dot{IRF7g} = -h_{110} \cdot I(dsRNA) \cdot IRF7g \cdot RelAn + h_{111} \cdot IRF7g_RelAn \quad (30)$$

$$\dot{IRF7g_RelAn} = h_{110} \cdot I(dsRNA) \cdot IRF7g \cdot RelAn - h_{111} \cdot IRF7g_RelAn \quad (31)$$

$$\dot{IRF7t} = h_{112} \cdot IRF7g_RelAn - h_{113} \cdot IRF7t \quad (32)$$

$$\dot{IRF7a} = h_{114} \cdot IRF7t - h_{115} \cdot IRF7a \quad (33)$$

$$\dot{IRF7an} = -h_{39} \cdot RIGIg \cdot IRF7an + h_{40} \cdot RIGIg_IRF7an + h_{115} \cdot IRF7a - h_{116} \cdot IRF7an \quad (34)$$

$$\dot{TLR3g} = 0 \quad (35)$$

$$\dot{TLR3t} = h_{131} \cdot TLR3g - h_{132} \cdot TLR3t \quad (36)$$

$$\dot{TLR3i} = -h_{17} \cdot dsRNA \cdot TLR3i + h_{133} \cdot TLR3t - h_{134} \cdot TLR3i \quad (37)$$

$$\dot{TLR3a} = h_{17} \cdot dsRNA \cdot TLR3i - h_{18} \cdot TLR3a - h_{19} \cdot TLR3a \cdot TRIF \quad (38)$$

$$\dot{TRIFg} = 0 \quad (39)$$

$$\dot{TRIFt} = h_{143} \cdot TRIFg - h_{144} \cdot TRIFT \quad (40)$$

$$\dot{TRIF} = -h_{19} \cdot TLR3a \cdot TRIF + h_{145} \cdot TRIFT - h_{146} \cdot TRIF \quad (41)$$

$$\dot{TLR3_TRIF} = h_{19} \cdot TLR3a \cdot TRIF - h_{20} \cdot TLR3_TRIF - h_{21} \cdot TLR3_TRIF \cdot TRAF6 \quad (42)$$

$$\dot{TRAF6g} = 0 \quad (43)$$

$$\dot{TRAF6t} = h_{139} \cdot TRAF6g - h_{140} \cdot TRAF6t \quad (44)$$

$$\dot{TRAF6} = -h_{21} \cdot TLR3_TRIF \cdot TRAF6 + h_{141} \cdot TRAF6t - h_{142} \cdot TRAF6 \quad (45)$$

$$\dot{TLR3_TRIF_TRAF6} = h_{21} \cdot TLR3_TRIF \cdot TRAF6 - h_{22} \cdot TLR3_TRIF_TRAF6 \quad (46)$$

$$\dot{IKK2g} = -h_{60} \cdot IKK2g \cdot TLR3dTFan + h_{61} \cdot IKK2g_TLR3dTFan \quad (47)$$

$$\dot{IKK2g_TLR3dTFan} = h_{60} \cdot IKK2g \cdot TLR3dTFan - h_{61} \cdot IKK2g_TLR3dTFan \quad (48)$$

$$\dot{IKK2t} = h_{62} \cdot IKK2g_TLR3dTFan + h_{63} \cdot IKK2g - h_{64} \cdot IKK2t \quad (49)$$

$$\dot{IKK2i} = -h_{26} \cdot TLR3_TRIF_TRAF6 \cdot IKK2i + h_{65} \cdot IKK2t - h_{66} \cdot IKK2i \quad (50)$$

$$\dot{IKK2a} = h_{26} \cdot TLR3_TRIF_TRAF6 \cdot IKK2i - h_{27} \cdot IKK2a - h_{28} \cdot IKK2a \cdot TNFAIP3 \quad (51)$$

$$\dot{TLR3dTFg} = 0 \quad (52)$$

$$\dot{TLR3dTFt} = h_{147} \cdot TLR3dTFg - h_{148} \cdot TLR3dTFt \quad (53)$$

$$\dot{TLR3dTFi} = -h_{23} \cdot TLR3_TRIF_TRAF6 \cdot TLR3dTFi + h_{149} \cdot TLR3dTFt - h_{150} \cdot TLR3dTFi \quad (54)$$

$$\dot{TLR3dTFa} = h_{23} \cdot TLR3_TRIF_TRAF6 \cdot TLR3dTFi - h_{24} \cdot TLR3dTFa \quad (55)$$

$$\begin{aligned} \dot{TLR3dTFan} = h_{24} \cdot TLR3dTFa - h_{25} \cdot TLR3dTFan - h_{46} \cdot MAVSg \cdot TLR3dTFan + \\ h_{47} \cdot MAVSg_TLR3dTFan - h_{53} \cdot IKK1g \cdot TLR3dTFan + \\ h_{54} \cdot IKK1g_TLR3dTFan - h_{60} \cdot IKK2g \cdot TLR3dTFan + \\ h_{61} \cdot IKK2g_TLR3dTFan - h_{69} \cdot IRF3g \cdot TLR3dTFan + \\ h_{70} \cdot IRF3g_TLR3dTFan - h_{83} \cdot TLR3dTFan \cdot RelAg + \\ h_{84} \cdot RelAg_TLR3dTFan \end{aligned} \quad (56)$$

Supplemental Table ST2: Reaction constants. These reaction constants are the same as in Table ST1 (they are numbered identically). Their dimensions are : 1 /(# molecules s) for second-order and 1/s for first-order reactions.

"reaction.name"	constant.value	"reaction.name"	constant.value
1 "dsRNA_db_RIGI"	1.00E-09	76 "IRF3ii_to_IRF3i"	1.00E-04
2 "RIGI_ubiq"	1.00E-09	77 "IRF3i_d"	1.00E-05
3 "RIGIub_d"	3.00E-04	78 "IRF3i_imp"	1.00E-04
4 "RIGI_b_MAVS"	1.00E-07	79 "IRF3i_exp"	0.001
5 "RIGI_MAVS_d"	3.00E-04	80 "IRF3in_d"	1.00E-05
6 "RIGI_MAVS_b_TRAF3"	1.00E-07	81 "RelAg_b_IRF3an"	2.00E-07
7 "RIGI_MAVS_TRAF3_d"	3.00E-04	82 "RelAg_IRF3an_d"	0.001
8 "IKK1i_a"	1.00E-08	83 "RelAg_a"	1.00E-07
9 "IKK1a_d"	3.00E-04	84 "RelAg_TLR3dTFFan_i"	0.01
10 "IKK1a_db_A20"	3.00E-09	85 "RelAt_t"	0.05
11 "IRF3i_a"	1.00E-08	86 "RelAt_bt"	0.001
12 "IRF3a_deg"	3.00E-04	87 "RelAt_d"	1.00E-04
13 "IRF3a_i"	0.001	88 "RelAi_s"	0.05
14 "IRF3an_e"	0.001	89 "RelAi_d"	1.00E-05
15 "IRF3an_d"	3.00E-04	90 "RelAi_to_RelA"	1.00E-05
16 "dsRNA_db_TLR3i"	1.00E-09	91 "RelA_to_RelAi"	1.00E-05
17 "TLR3i_act"	1.00E-09	92 "RelAi_to_RelA_by_IKK2a"	1.00E-09
18 "TLR3a_d"	3.00E-04	93 "RelA_d"	1.00E-05
19 "TLR3_b_TRIF"	1.00E-07	94 "RelAn_d"	1.00E-05
20 "TLR3_TRIF_d"	3.00E-04	95 "A20g_a"	8.00E-09
21 "TLR3_TRIF_b_TRAF6"	1.00E-07	96 "A20g_RelAn_i"	2.00E-07
22 "TLR3_TRIF_TRAF6_d"	3.00E-04	97 "A20t_t"	0.05
23 "TLR3dTFFi_a"	1.00E-08	98 "A20t_d"	1.00E-04
24 "TLR3dTFFa_imp"	0.001	99 "A20_s"	0.05
25 "TLR3dTFFan_d"	0.00015	100 "A20_d"	1.00E-05
26 "IKK2i_a"	1.00E-08	101 "IkBag_a"	2.5e-08
27 "IKK2a_d"	3.00E-04	102 "IkBag_RelAn_i"	2.5e-07
28 "IKK2a_db_A20"	1.5e-09	103 "IkBat_t"	0.25
29 "IkBa_d"	3.00E-06	104 "IkBat_d"	4.00E-04
30 "RelA_IkBa_d"	1.00E-05	105 "IkBa_s"	0.5
31 "RelA_IkBa_dis"	3.00E-06	106 "IkBa_d"	1.00E-04
32 "RelA_b_IkBa"	1.00E-07	107 "IkBa_imp"	0.001
33 "RelA_IkBa_sd"	1.00E-06	108 "IkBan_d"	1.00E-04
34 "RelA_i"	0.001	109 "IkBa_exp"	5.00E-04
35 "RelAn_b_IkBan"	3.42e-07	110 "IRF7g_a"	3.00E-07
36 "RelAn_IkBan_d"	1.00E-05	111 "IRF7g_RelAn_i"	0.01
37 "RelA_IkBa_i"	1.00E-04	112 "IRF7t_t"	0.05
38 "RelAn_IkBan_e"	0.001	113 "IRF7t_d"	1.00E-04
"reaction.name"	constant.value	"reaction.name"	constant.value
39 "RIGIg_a"	2.00E-09	114 "IRF7a_s"	0.05
40 "RIGIg_IRF7an_i"	2.00E-05	115 "IRF7a_imp"	0.001
41 "RIGIt_t"	0.1	116 "IRF7an_d"	0.00015
42 "RIGIt_bt"	0.001	117 "ISG56g_a"	1.00E-06
43 "RIGIt_d"	1.00E-04	118 "ISG56g_IRF3an_i"	0.01

44 "RIGI_s"	0.05	119 "ISG56t_t"	0.05
45 "RIGI_d"	1.00E-05	120 "ISG56t_d"	1.00E-04
46 "MAVSg_a"	1.00E-09	121 "ISG56_s"	0.05
47 "MAVSg_TLR3dTFab_i"	1.00E-04	122 "ISG56_d"	1.00E-05
48 "MAVSt_t"	0.075	123 "IFNbg_a_RelAn"	7.5e-08
49 "MAVSt_bt"	0.001	124 "IFNbg_RelAn_i_IkB"	2.00E-06
50 "MAVSt_d"	1.00E-04	125 "IFNbg_RelAn_a_IRF3an"	2.00E-09
51 "MAVS_s"	0.05	126 "IFNbg_RelAn_IRF3an_i"	1.00E-05
52 "MAVS_d"	1.00E-05	127 "IFNb_t"	0.25
53 "IKK1g_a"	3.00E-07	128 "IFNb_d"	1.00E-04
54 "IKK1g_TLR3dTFan_i"	0.01	129 "IFNb_s"	0.05
55 "IKK1t_t"	0.05	130 "IFNb_d"	1.00E-05
56 "IKK1t_bt"	0.001	131 "TLR3t_bt"	0.001
57 "IKK1t_d"	1.00E-04	132 "TLR3t_d"	1.00E-04
58 "IKK1i_s"	0.05	133 "TLR3i_s"	0.5
59 "IKK1i_d"	1.00E-05	134 "TLR3i_d"	1.00E-04
60 "IKK2g_a"	3.00E-07	135 "TRAF3t_bt"	0.001
61 "IKK2g_TLR3dTFan_i" x	0.05	136 "TRAF3t_d"	1.00E-04
62 "IKK2t_t"	0.05	137 "TRAF3_s"	0.5
63 "IKK2t_bt"	0.001	138 "TRAF3_d"	1.00E-04
64 "IKK2t_d"	1.00E-04	139 "TRAF6t_bt"	0.001
65 "IKK2i_s"	0.05	140 "TRAF6t_d"	1.00E-04
66 "IKK2i_d"	1.00E-05	141 "TRAF6_s"	0.5
67 "IRF3g_b_RelAn"	5.00E-07	142 "TRAF6_d"	1.00E-04
68 "IRF3g_RelAn_d"	0.01	143 "TRIF_bt"	0.001
69 "IRF3g_a"	3.00E-07	144 "TRIF_d"	1.00E-04
70 "IRF3g_TLR3dTFan_i"	0.01	145 "TRIF_s"	0.5
71 "IRF3t_t"	0.05	146 "TRIF_d"	1.00E-04
72 "IRF3t_bt"	0.001	147 "TLR3dTFT_bt"	0.001
73 "IRF3t_d"	1.00E-04	148 "TLR3dTFT_d"	1.00E-04
74 "IRF3ii_s"	0.05	149 "TLR3dTFTi_s"	0.5
75 "IRF3ii_d"	1.00E-05	150 "TLR3dTFTi_d"	1.00E-04

Supplemental Table ST3: Pseudocode.******* General constants and parameters *******

```

prot_avg      = 1e5
cyto_to_nuc_ratio = 3.42
siRNA_incr_degr_r = 1e1

prot_transl_r    = 5e-2
prot_unreg_transl_r = 5e-1

prot_degr_r     = 1e-5
prot_unreg_degr_r = 1e-4
prot_phosph_degr_r = 3e-4

prot_bind_r     = 1e-2
prot_activ_r    = 1e-3
prot_transition_r = 1e-4

prot_diss_r     = 1e-6
prot_import_r   = 1e-3
prot_export_r   = 1e-3

dsRNA_recogn_r  = 1e-4 * 5e5 / dsRNA.mean
dsRNA_degr_r    = 1e-4

```

```

gene_act_r     = 1e-2
gene_inact_r   = 1e-2

```

```

mRNA_transc_r  = 5e-2
mRNA_basal_transc_r = 1e-3
mRNA_degr_r    = 1e-4

```

RelAn_IRF3an_ratio = 2

******* Start of model definition ************** Left arm recognition of dsRNA and RIGI_MAVS_TRAF3 complex formation *******

----- dsRNA degradation induced by RIGI:
Ch.E.: RIGI + dsRNA ---> RIGI
Rt.C.: dsRNA_degr_r / prot_avg

----- RIGI ubiquitylation:
Ch.E.: dsRNA + RIGI ---> dsRNA + RIGIub
Rt.C.: dsRNA_recogn_r / prot_avg

----- RIGIub degradation:
Ch.E.: RIGIub ---> 0

Rt.C.: prot_phosph_degr_r

----- RIGIub and MAVS binding:

Ch.E.: RIGIub + MAVS ---> RIGI_MAVS

Rt.C.: prot_bind_r / prot_avg

----- RIGI_MAVS degradation:

Ch.E.: RIGI_MAVS ---> 0

Rt.C.: prot_phosph_degr_r

----- RIGI_MAVS and TRAF3 binding:

Ch.E.: RIGI_MAVS + TRAF3 ---> RIGI_MAVS_TRAF3

Rt.C.: prot_bind_r / prot_avg

----- RIGI_MAVS_TRAF3 degradation:

Ch.E.: RIGI_MAVS_TRAF3 ---> 0

Rt.C.: prot_phosph_degr_r

***** IKK1 (TBK1/IKKe) activation by RIGI_MAVS_TRAF3 and regulation by A20 *****

----- IKK1i activation:

Ch.E.: RIGI_MAVS_TRAF3 + IKK1i ---> RIGI_MAVS_TRAF3 + IKK1a

Rt.C.: prot_activ_r / prot_avg

----- IKK1a degradation:

Ch.E.: IKK1a ---> 0

Rt.C.: prot_phosph_degr_r

----- IKK1a degradation due to A20:

Ch.E.: A20 + IKK1a ---> A20

Rt.C.: prot_phosph_degr_r / prot_avg

***** IRF3 activation by IKK1 and nuclear translocation *****

----- IRF3i activation:

Ch.E.: IKK1a + IRF3i ---> IKK1a + IRF3a

Rt.C.: prot_activ_r / prot_avg

----- IRF3a degradation:

Ch.E.: IRF3a ---> 0

Rt.C.: prot_phosph_degr_r

----- IRF3a import:

Ch.E.: IRF3a ---> IRF3an

Rt.C.: prot_import_r

----- IRF3a export:

Ch.E.: IRF3an ---> IRF3a

Rt.C.: prot_export_r

----- IRF3an degradation:

Ch.E.: IRF3an ---> 0

Rt.C.: prot_phosph_degr_r

***** Right arm recognition of dsRNA and TLR3_TRIF_TRAF6 complex formation *****

----- dsRNA degradation induced by TLR3i:

Ch.E.: TLR3i + dsRNA ---> TLR3i

Rt.C.: dsRNA_degr_r / prot_avg

----- TLR3i activation:

Ch.E.: dsRNA + TLR3i ---> dsRNA + TLR3a

Rt.C.: dsRNA_recogn_r / prot_avg

----- TLR3a degradation:

Ch.E.: TLR3a ---> 0

Rt.C.: prot_phosph_degr_r

----- TLR3a and TRIF binding:

Ch.E.: TLR3a + TRIF ---> TLR3_TRIF

Rt.C.: prot_bind_r / prot_avg

----- TLR3_TRIF degradation:

Ch.E.: TLR3_TRIF ---> 0

Rt.C.: prot_phosph_degr_r

----- TLR3_TRIF and TRAF6 binding:

Ch.E.: TLR3_TRIF + TRAF6 ---> TLR3_TRIF_TRAF6

Rt.C.: prot_bind_r / prot_avg

----- TLR3_TRIF_TRAF6 degradation:

Ch.E.: TLR3_TRIF_TRAF6 ---> 0

Rt.C.: prot_phosph_degr_r

***** TLR3dTF activation by TLR3_TRIF_TRAF6 *****

----- TLR3dTFi activation:

Ch.E.: TLR3_TRIF_TRAF6 + TLR3dTFi ---> TLR3_TRIF_TRAF6 + TLR3dTFa

Rt.C.: prot_activ_r / prot_avg

----- TLR3dTFa import:

Ch.E.: TLR3dTFa ---> TLR3dTFan

Rt.C.: prot_import_r

----- TLR3dTFan degradation:

Ch.E.: TLR3dTFan \rightarrow 0

Rt.C.: prot_phosph_degr_r

/ 2

***** IKK2 (IKK γ /IKK α /IKK β) activation by TLR3_TRIF_TRAF6 and regulation by A20 *****

----- IKK2i activation:

Ch.E.: TLR3_TRIF_TRAF6 + IKK2i \rightarrow TLR3_TRIF_TRAF6 + IKK2a

Rt.C.: prot_activ_r / prot_avg

----- IKK2a degradation:

Ch.E.: IKK2a \rightarrow 0

Rt.C.: prot_phosph_degr_r

----- IKK2a degradation due to A20:

Ch.E.: A20 + IKK2a \rightarrow A20

Rt.C.: prot_phosph_degr_r / prot_avg / 2

***** IKK2 degradation of IkBa, RelA nuclear translocation, RelA_IkBa binding *****

----- IkBa degradation due to IKK2a:

Ch.E.: IKK2a + IkBa \rightarrow IKK2a

Rt.C.: prot_phosph_degr_r / prot_avg * 1000

----- RelA_IkBa degradation:

Ch.E.: RelA_IkBa \rightarrow 0

Rt.C.: prot_degr_r

----- RelA dissociation (and degradation of IkBa) due to IKK2a:

Ch.E.: IKK2a + RelA_IkBa \rightarrow IKK2a + RelA

Rt.C.: prot_phosph_degr_r / prot_avg * 1000

----- RelA and IkBa binding:

Ch.E.: RelA + IkBa \rightarrow RelA_IkBa

Rt.C.: prot_bind_r / prot_avg

----- RelA_IkBa spontaneous dissociation:

Ch.E.: RelA_IkBa \rightarrow RelA + IkBa

Rt.C.: prot_diss_r

----- RelA nuclear import:

Ch.E.: RelA \rightarrow RelAn

Rt.C.: prot_import_r

----- RelAn and IkBan binding:

Ch.E.: RelAn + IkBan \rightarrow RelAn_IkBan

Rt.C.: cyto_to_nuc_ratio * prot_bind_r / prot_avg

----- RelAn_IkB degradation:

Ch.E.: RelAn_IkB ---> 0

Rt.C.: prot_degr_r

----- RelA_IkBa import:

Ch.E.: RelA_IkBa ---> RelAn_IkB

Rt.C.: prot_import_r / 10

----- RelAn_IkB export:

Ch.E.: RelAn_IkB ---> RelA_IkBa

Rt.C.: prot_export_r

******* IRF7 dependent genes *******

******* RIGI production and degradation *******

----- RIGIg activation:

Ch.E.: IRF7an + RIGIg ---> RIGIg_IRF7an

Rt.C.: gene_act_r / prot_avg / 500 * 10

----- RIGIg_IRF7an inactivation:

Ch.E.: RIGIg_IRF7ab ---> RIGIg + IRF7an

Rt.C.: gene_inact_r / 500

----- RIGIt transcription:

Ch.E.: RIGIg_IRF7an ---> RIGIg_IRF7an + RIGIt

Rt.C.: mRNA_transc_r * 2

----- RIGIt basal transcription:

Ch.E.: RIGIg ---> RIGIg + RIGIt

Rt.C.: mRNA_basal_transc_r

----- RIGIt degradation:

Ch.E.: RIGIt ---> 0

Rt.C.: ifelse(RIGIt_siRNA, 8 * siRNA_incr_degr_r, 1) * mRNA_degr_r

----- RIGI synthesis:

Ch.E.: RIGIt ---> RIGIt + RIGI

Rt.C.: prot_transl_r

----- RIGI degradation:

Ch.E.: RIGI ---> 0

Rt.C.: prot_degr_r

******* TLR3dTF dependent genes *******

******* MAVS production and degradation *******

----- MAVSg activation:

Ch.E.: TLR3dTFan + MAVSg ---> MAVSg_TLR3dTFan

Rt.C.: gene_act_r / prot_avg / 100

----- MAVSg_TLR3dTFan inactivation:

Ch.E.: MAVSg_TLR3dTFab ---> MAVSg + TLR3dTFan

Rt.C.: gene_inact_r / 100

----- MAVSt transcription:

Ch.E.: MAVSg_TLR3dTFan ---> MAVSg_TLR3dTFan + MAVSt

Rt.C.: mRNA_transc_r * 1.5

----- MAVSt basal transcription:

Ch.E.: MAVSg ---> MAVSg + MAVSt

Rt.C.: mRNA_basal_transc_r

----- MAVSt degradation:

Ch.E.: MAVSt ---> 0

Rt.C.: mRNA_degr_r

----- MAVS synthesis:

Ch.E.: MAVSt ---> MAVSt + MAVS

Rt.C.: prot_transl_r

----- MAVS degradation:

Ch.E.: MAVS ---> 0

Rt.C.: prot_degr_r

******* IKK1 (TBK1/IKKe) production and degradation *******

----- IKK1g activation:

Ch.E.: TLR3dTFan + IKK1g ---> IKK1g_TLR3dTFan

Rt.C.: gene_act_r / prot_avg * 3

----- IKK1g_TLR3dTFan inactivation:

Ch.E.: IKK1g_TLR3dTFab ---> IKK1g + TLR3dTFan

Rt.C.: gene_inact_r

----- IKK1t transcription:

Ch.E.: IKK1g_TLR3dTFan ---> IKK1g_TLR3dTFan + IKK1t

Rt.C.: mRNA_transc_r

----- IKK1t basal transcription:

Ch.E.: IKK1g ---> IKK1g + IKK1t

Rt.C.: mRNA_basal_transc_r

----- IKK1t degradation:

Ch.E.: IKK1t ---> 0

Rt.C.: mRNA_degr_r

----- IKK1i synthesis:

Ch.E.: IKK1t ---> IKK1t + IKK1i

Rt.C.: prot_transl_r

----- IKK1i degradation:

Ch.E.: IKK1i ---> 0

Rt.C.: prot_degr_r

***** IKK2 (IKKg/IKKa/IKKb) production and degradation *****

----- IKK2g activation:

Ch.E.: TLR3dTFan + IKK2g ---> IKK2g_TLR3dTFan

Rt.C.: gene_act_r / prot_avg * 3

----- IKK2g_TLR3dTFan inactivation:

Ch.E.: IKK2g_TLR3dTFab ---> IKK2g + TLR3dTFan

Rt.C.: gene_inact_r

----- IKK2t transcription:

Ch.E.: IKK2g_TLR3dTFan ---> IKK2g_TLR3dTFan + IKK2t

Rt.C.: mRNA_transc_r

----- IKK2t basal transcription:

Ch.E.: IKK2g ---> IKK2g + IKK2t

Rt.C.: mRNA_basal_transc_r

----- IKK2t degradation:

Ch.E.: IKK2t ---> 0

Rt.C.: ifelse(IKK2t_siRNA, 0.6 * siRNA_incr_degr_r, 1) * mRNA_degr_r

----- IKK2i synthesis:

Ch.E.: IKK2t ---> IKK2t + IKK2i

Rt.C.: prot_transl_r

----- IKK2i degradation:

Ch.E.: IKK2i ---> 0

Rt.C.: prot_degr_r

***** IRF3 production and degradation, inhibition by RelA *****

----- IRF3g inhibition:

Ch.E.: RelAn + IRF3g ---> IRF3g_RelAn

Rt.C.: gene_act_r / prot_avg * 5

----- IRF3g_RelAn inhibition release:

Ch.E.: IRF3g_RelA ---> IRF3g + RelAn

Rt.C.: gene_inact_r

----- IRF3g activation:

Ch.E.: TLR3dTFan + IRF3g ---> IRF3g_TLR3dTFan

Rt.C.: gene_act_r / prot_avg * 3

----- IRF3g_TLR3dTFan inactivation:

Ch.E.: IRF3g_TLR3dTFan ---> IRF3g + TLR3dTFan

Rt.C.: gene_inact_r

----- IRF3t transcription:

Ch.E.: IRF3g_TLR3dTFan ---> IRF3g_TLR3dTFan + IRF3t

Rt.C.: mRNA_transc_r

----- IRF3t basal transcription:

Ch.E.: IRF3g ---> IRF3g + IRF3t

Rt.C.: mRNA_basal_transc_r

----- IRF3t degradation:

Ch.E.: IRF3t ---> 0

Rt.C.: ifelse(IRF3t_siRNA, 0.50 * siRNA_incr_degr_r, 1) * mRNA_degr_r

----- IRF3ii synthesis:

Ch.E.: IRF3t ---> IRF3t + IRF3ii

Rt.C.: prot_transl_r

----- IRF3ii degradation:

Ch.E.: IRF3ii ---> 0

Rt.C.: prot_degr_r

----- IRF3ii to IRF3i:

Ch.E.: IRF3ii ---> IRF3i

Rt.C.: prot_transition_r

----- IRF3i degradation:

Ch.E.: IRF3i ---> 0

Rt.C.: prot_degr_r

----- IRF3i import:

Ch.E.: IRF3i ---> IRF3in

Rt.C.: prot_import_r / 10

----- IRF3in export:

Ch.E.: IRF3in ---> IRF3i

Rt.C.: prot_export_r

----- IRF3in degradation:

Ch.E.: IRF3in ---> 0

Rt.C.: prot_degr_r

***** RelA production and degradation, inhibition by IRF3 *****

----- RelAg inhibition by IRF3an:

Ch.E.: IRF3an + RelAg ---> RelAg_IRF3an

Rt.C.: gene_act_r / prot_avg * RelAn_IRF3an_ratio

----- RelAg_IRF3an inhibition release:

Ch.E.: RelAg_IRF3ab ---> RelAg + IRF3an

Rt.C.: gene_inact_r / 10

----- RelAg activation:

Ch.E.: TLR3dTFan + RelAg ---> RelAg_TLR3dTFan

Rt.C.: gene_act_r / prot_avg

----- RelAg_TLR3dTFan inactivation:

Ch.E.: RelAg_TLR3dTFab ---> RelAg + TLR3dTFan

Rt.C.: gene_inact_r

----- RelAt transcription:

Ch.E.: RelAg_TLR3dTFan ---> RelAg_TLR3dTFan + RelAt

Rt.C.: mRNA_transc_r

----- RelAt basal transcription:

Ch.E.: RelAg ---> RelAg + RelAt

Rt.C.: mRNA_basal_transc_r

----- RelAt degradation:

Ch.E.: RelAt ---> 0

Rt.C.: ifelse(RelAt_siRNA, 1 * siRNA_incr_degr_r, 1) * mRNA_degr_r

----- RelAi synthesis:

Ch.E.: RelAt ---> RelAt + RelAi

Rt.C.: prot_transl_r

----- RelAi degradation:

Ch.E.: RelAi ---> 0

Rt.C.: prot_degr_r

----- RelAi to RelA:

Ch.E.: RelAi ---> RelA

Rt.C.: prot_transition_r / 10

----- RelA to RelAi:

Ch.E.: RelA ---> RelAi

Rt.C.: prot_transition_r / 10

----- RelAi to RelA due to IKK2a:

Ch.E.: IKK2a + RelAi \rightarrow IKK2a + RelA

Rt.C.: prot_transition_r / prot_avg

----- RelA degradation:

Ch.E.: RelA \rightarrow 0

Rt.C.: prot_degr_r

----- RelAn degradation:

Ch.E.: RelAn \rightarrow 0

Rt.C.: prot_degr_r

***** RelA dependent genes *****

***** A20 production and degradation *****

----- A20g activation:

Ch.E.: RelAn + A20g \rightarrow A20g_RelAn

Rt.C.: gene_act_r / prot_avg * 2 / 25

----- A20g_RelAn inactivation:

Ch.E.: IkBan + A20g_RelAn \rightarrow A20g + RelAn_IkBan

Rt.C.: gene_inact_r / prot_avg * 2

----- A20t transcription:

Ch.E.: A20g_RelAn \rightarrow A20g_RelAn + A20t

Rt.C.: mRNA_transc_r

----- A20t degradation:

Ch.E.: A20t \rightarrow 0

Rt.C.: ifelse(A20t_siRNA, 6.5 * siRNA_incr_degr_r, 1) * mRNA_degr_r

----- A20 synthesis:

Ch.E.: A20t \rightarrow A20t + A20

Rt.C.: prot_transl_r

----- A20 degradation:

Ch.E.: A20 \rightarrow 0

Rt.C.: prot_degr_r

***** IkBa production and degradation *****

----- IkBag activation:

Ch.E.: RelAn + IkBag \rightarrow IkBag_RelAn

Rt.C.: gene_act_r / prot_avg / 4

----- I kB_g_RelAn inactivation:

Ch.E.: I kB_an + I kB_g_RelAb ---> I kB_g + RelAn_I kB_an
 Rt.C.: gene_inact_r / prot_avg / 2 * 5

----- I kB_at transcription:

Ch.E.: I kB_g_RelAn ---> I kB_g_RelAn + I kB_at
 Rt.C.: mRNA_transc_r * 5

----- I kB_at degradation:

Ch.E.: I kB_at ---> 0
 Rt.C.: mRNA_degr_r * 4

----- I kB_as synthesis:

Ch.E.: I kB_at ---> I kB_at + I kB_as
 Rt.C.: prot_transl_r * 10

----- I kB_as degradation:

Ch.E.: I kB_as ---> 0
 Rt.C.: prot_degr_r * 10

----- I kB_as import:

Ch.E.: I kB_as ---> I kB_an
 Rt.C.: prot_import_r

----- I kB_an degradation:

Ch.E.: I kB_an ---> 0
 Rt.C.: prot_degr_r * 10

----- I kB_an export:

Ch.E.: I kB_an ---> I kB_as
Rt.C.: prot_export_r / 2

***** IRF7 production and degradation *****

#NAME?

Ch.E.: RelAn + IRF7g ---> IRF7g_RelAn
 Rt.C.: gene_act_r / prot_avg * 3

----- IRF7g_RelAn inactivation:

Ch.E.: IRF7g_RelAn ---> IRF7g + RelAn
 Rt.C.: gene_inact_r

----- IRF7t transcription:

Ch.E.: IRF7g_RelAn ---> IRF7g_RelAn + IRF7t
 Rt.C.: mRNA_transc_r

----- IRF7t degradation:

Ch.E.: IRF7t ---> 0
 Rt.C.: ifelse(IRF7t_siRNA, 0.50 * siRNA_incr_degr_r, 1) * mRNA_degr_r

----- IRF7a synthesis:

Ch.E.: IRF7t ---> IRF7t + IRF7a

Rt.C.: prot_transl_r

----- IRF7a import:

Ch.E.: IRF7a ---> IRF7an

Rt.C.: prot_import_r

----- IRF7an degradation:

Ch.E.: IRF7an ---> 0

Rt.C.: prot_phosph_degr_r / 2

***** IRF3 dependent genes *****

***** ISG56 production and degradation *****

----- ISG56g activation:

Ch.E.: IRF3an + ISG56g ---> ISG56g_IRF3an

Rt.C.: gene_act_r / prot_avg * RelAn_IRF3an_ratio * 5

----- ISG56g_IRF3an inactivation:

Ch.E.: ISG56g_IRF3ab ---> ISG56g + IRF3an

Rt.C.: gene_inact_r

----- ISG56t transcription:

Ch.E.: ISG56g_IRF3an ---> ISG56g_IRF3an + ISG56t

Rt.C.: mRNA_transc_r

----- ISG56t degradation:

Ch.E.: ISG56t ---> 0

Rt.C.: mRNA_degr_r

----- ISG56 synthesis:

Ch.E.: ISG56t ---> ISG56t + ISG56

Rt.C.: prot_transl_r

----- ISG56 degradation:

Ch.E.: ISG56 ---> 0

Rt.C.: prot_degr_r

***** RelA/IRF3 dependent genes *****

***** IFNb production and degradation *****

----- IFNb activation by RelAn:

Ch.E.: RelAn + IFNb ---> IFNb_RelAn

Rt.C.: gene_act_r / prot_avg / 100 * 75

----- IFNb_RelAn inactivation:

Ch.E.: lkBan + IFNb_RelAn ---> IFNb + RelAn_lkBan

Rt.C.: gene_inact_r / prot_avg * 20

----- IFNb_RelAn activation by IRF3an:

Ch.E.: IRF3an + IFNb_RelAn ---> IFNb_RelAn_IRF3an

Rt.C.: gene_act_r / prot_avg * RelAn_IRF3an_ratio / 100

----- IFNb_RelAn_IRF3an inactivation:

Ch.E.: IFNb_RelAn_IRF3an ---> IFNb + IRF3an + RelAn

Rt.C.: gene_inact_r / 1000

----- IFNb transcription by IFNb_RelAn_IRF3an:

Ch.E.: IFNb_RelAn_IRF3an ---> IFNb_RelAn_IRF3an + IFNb

Rt.C.: mRNA_transc_r * 5

----- IFNb degradation:

Ch.E.: IFNb ---> 0

Rt.C.: mRNA_degr_r

----- IFNb synthesis:

Ch.E.: IFNb ---> IFNb + IFNb

Rt.C.: prot_transl_r

----- IFNb degradation:

Ch.E.: IFNb ---> 0

Rt.C.: prot_degr_r

***** Unregulated genes *****

***** TLR3 production and degradation *****

----- TLR3t basal transcription:

Ch.E.: TLR3g ---> TLR3g + TLR3t

Rt.C.: mRNA_basal_transc_r

----- TLR3t degradation:

Ch.E.: TLR3t ---> 0

Rt.C.: mRNA_degr_r

----- TLR3i synthesis:

Ch.E.: TLR3t ---> TLR3t + TLR3i

Rt.C.: prot_unreg_transl_r

----- TLR3i degradation:

Ch.E.: TLR3i ---> 0

Rt.C.: prot_unreg_degr_r

***** TRAF3 production and degradation *****

----- TRAF3t basal transcription:

Ch.E.: TRAF3g ---> TRAF3g + TRAF3t

Rt.C.: mRNA_basal_transc_r

----- TRAF3t degradation:

Ch.E.: TRAF3t ---> 0

Rt.C.: mRNA_degr_r

----- TRAF3 synthesis:

Ch.E.: TRAF3t ---> TRAF3t + TRAF3

Rt.C.: prot_unreg_transl_r

----- TRAF3 degradation:

Ch.E.: TRAF3 ---> 0

Rt.C.: prot_unreg_degr_r

***** TRAF6 production and degradation *****

----- TRAF6t basal transcription:

Ch.E.: TRAF6g ---> TRAF6g + TRAF6t

Rt.C.: mRNA_basal_transc_r

----- TRAF6t degradation:

Ch.E.: TRAF6t ---> 0

Rt.C.: mRNA_degr_r

----- TRAF6 synthesis:

Ch.E.: TRAF6t ---> TRAF6t + TRAF6

Rt.C.: prot_unreg_transl_r

----- TRAF6 degradation:

Ch.E.: TRAF6 ---> 0

Rt.C.: prot_unreg_degr_r

***** TRIF production and degradation *****

----- TRIFt basal transcription:

Ch.E.: TRIFg ---> TRIFg + TRIFt

Rt.C.: mRNA_basal_transc_r

----- TRIFt degradation:

Ch.E.: TRIFt ---> 0

Rt.C.: mRNA_degr_r

----- TRIF synthesis:

Ch.E.: TRIFt ---> TRIFt + TRIF

Rt.C.: prot_unreg_transl_r

----- TRIF degradation:

Ch.E.: TRIF ---> 0

Rt.C.: prot_unreg_degr_r

***** TLR3dTF production and degradation *****

----- TLR3dTFt basal transcription:

Ch.E.: TLR3dTFg ---> TLR3dTFg + TLR3dTFt

Rt.C.: mRNA_basal_transc_r

----- TLR3dTFt degradation:

Ch.E.: TLR3dTFt ---> 0

Rt.C.: mRNA_degr_r

----- TLR3dTFi synthesis:

Ch.E.: TLR3dTFt ---> TLR3dTFt + TLR3dTFi

Rt.C.: prot_unreg_transl_r

----- TLR3dTFi degradation:

Ch.E.: TLR3dTFi ---> 0

Rt.C.: prot_unreg_degr_r

***** End of model definition *****

Query ID	RefSeq ID	IRF1	IRF2	IRF3	IRF7	NF-kappaB	NFKB1	REL	RELA	AP1	SP1
Ikbkb-mv1	mm10_knownGene_uc009ldm.2	1	0	0	0	1	0	3	1	7	9
Ikbkb-mv2	mm10_knownGene_uc009ldq.1	0	0	0	0	2	2	4	1	6	20
DDX58-hv1hg19_knownGene_uc003zra.3		9	5	3	12	2	1	3	2	12	8
DDX58-hv2hg19_knownGene_uc010mji.3		0	1	0	1	1	1	2	0	10	4
Ddx58-mv1mm10_knownGene_uc008she.1		2	2	0	6	2	2	10	1	13	10
Ddx58-mv2mm10_knownGene_uc008shf.1		2	1	1	2	2	0	3	2	5	53

Table ST5: Effect of siRNA knockdown on dsRNA-induced NF- κ B/IRF3 gene expressions in A549 cells. Statistical significance of the difference recorded in the knockdown experiment, carried out using the 2-sample, 2-sided t-test (Welch test), corresponding to the bar charts in Figure 3. (A) Comparison of the mRNA-specific siRNA knockdown versus control (nonspecific siRNA), in dsRNA-nonstimulated and dsRNA-stimulated experiment (at 6hr). (B) Comparison of dsRNA-induced versus dsRNA-noninduced under siRNA knockdown (at 6hr). Rows: Different knockdowns. Columns: Genes expressed.

*Minus sign at the p-value denotes reduced expression. For example, -0.002 denotes p = 0.002 and reduced expression as a result of knockdown (panel A) or as result of dsRNA induction (panel B).

(A) Comparison of control (at 0 hr) and knockdown (at 6 hr)

	Rel A	IRF3	RIG-I	Ikk γ	A20	I κ B α	ISG56	IFN
RelAsiRNA	-0.002	<u>0.007</u>	<u>-0.039</u>	<u>0.017</u>	<u>-0.041</u>	-0.066	<u>-0.026</u>	-0.541
RelAsiRNA+dsRNA	0.000	<u>0.010</u>	<u>-0.006</u>	<u>0.009</u>	-0.002	-0.001	<u>0.008</u>	-0.001
IRF3siRNA	<u>0.011</u>	<u>-0.009</u>	-0.153	0.063	<u>0.045</u>	0.051	<u>-0.005</u>	<u>0.006</u>
IRF3siRNA+dsRNA	<u>0.014</u>	-0.001	-0.390	0.206	0.000	0.003	0.000	0.000
RIG1siRNA	<u>0.012</u>	<u>0.012</u>	<u>-0.006</u>	<u>0.050</u>	0.182	-0.468	-0.004	<u>0.022</u>
RIG1siRNA+dsRNA	0.561	0.139	0.000	0.273	0.043	0.101	0.000	0.000
IKK γ siRNA	0.363	0.168	-0.098	-0.001	-0.140	0.608	<u>-0.006</u>	<u>0.021</u>
IKK γ siRNA+dsRNA	-0.107	0.154	<u>-0.011</u>	-0.001	<u>-0.008</u>	<u>-0.025</u>	<u>-0.042</u>	<u>-0.007</u>

(B) Comparison of dsRNA-induced to dsRNA-noninduced under siRNA knockdown (at 6hr)

	Rel A	IRF3	RIG-I	Ikk γ	A20	I κ B α	ISG56	IFN
ConsiRNA	0.002	0.001	0.000	-0.399	0.001	0.001	0.000	0.000
RelAsiRNA	0.756	0.001	0.000	0.799	0.003	<u>0.007</u>	0.000	0.000
IRF3siRNA	0.004	<u>0.021</u>	0.000	-0.182	0.000	0.000	0.001	0.001
RIG1siRNA	<u>0.053</u>	0.002	0.005	<u>-0.038</u>	0.000	0.000	0.002	0.001
IKK γ siRNA	<u>0.022</u>	0.001	0.000	0.632	0.002	0.001	0.000	0.000

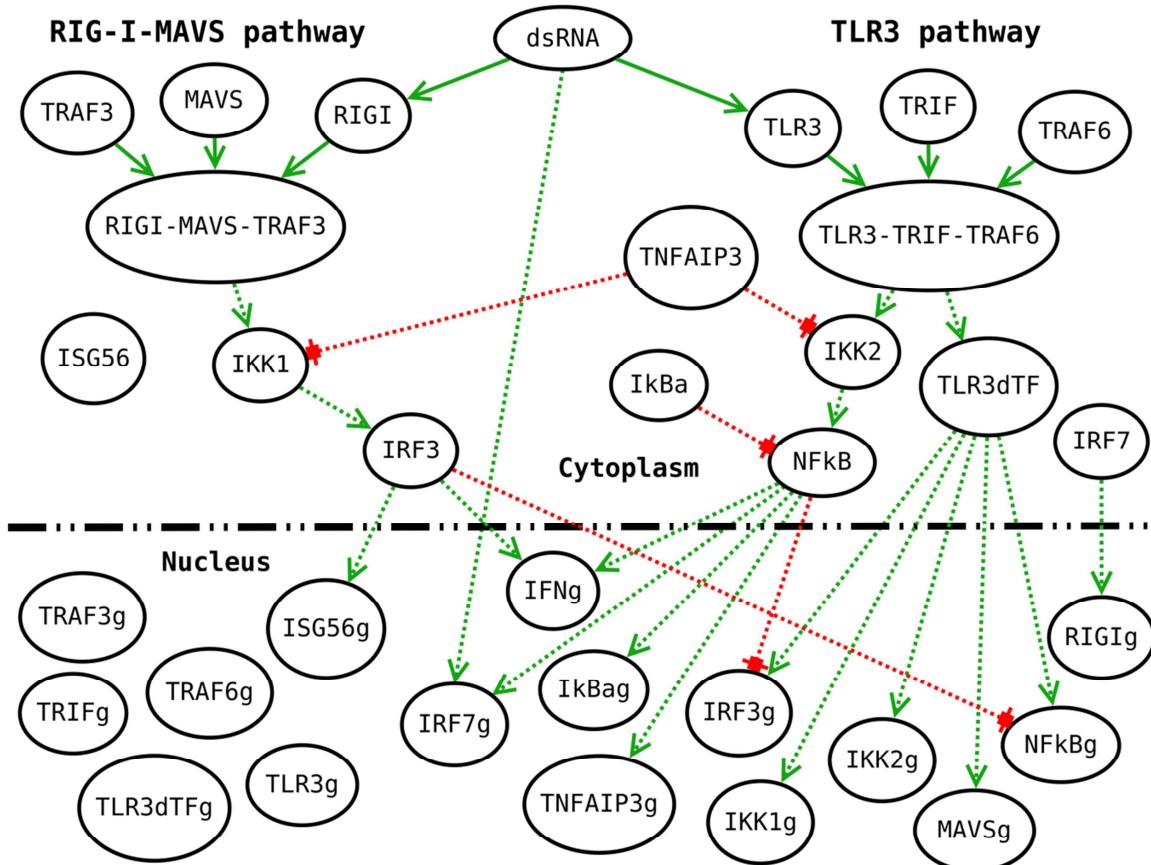
p-values

italics, underscored ≤ 0.05

italics, boldface ≤ 0.01

p = **0.000** denotes *p* < 0.001

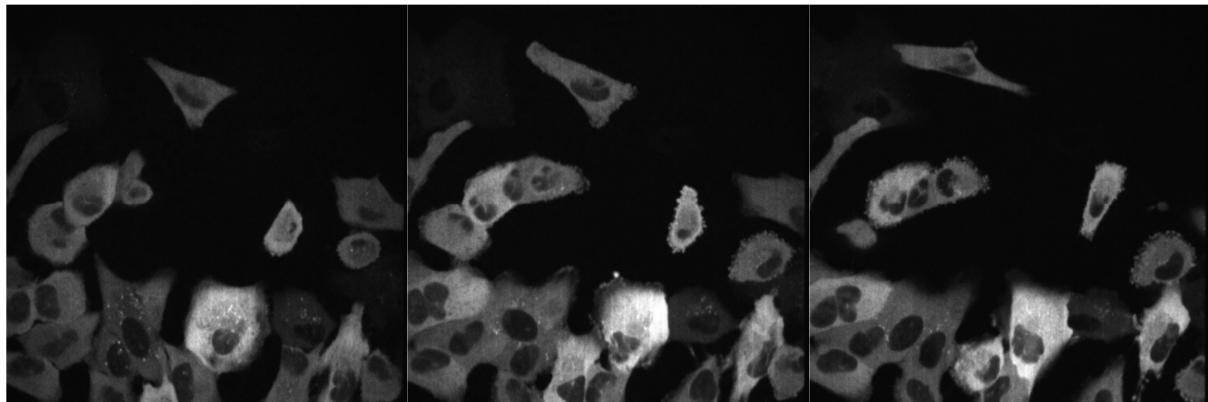
SF1: Wiring diagram corresponding to the pseudocode and differential equation system defining the mathematical model of innate immune response.



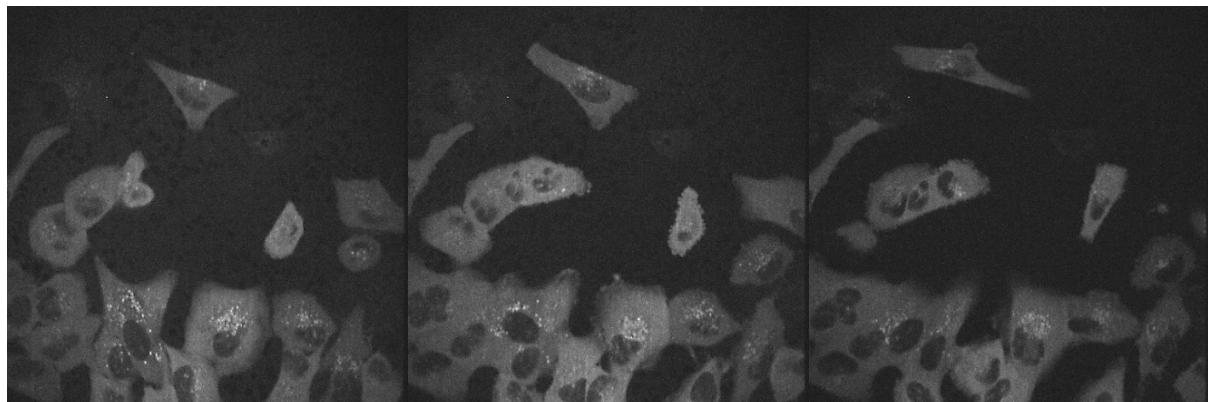
Notes

- Solid lines denote binding reactions
- Dot lines denote activation (green) or inhibition (red). The special case of a dotted line from dsRNA to IRF7g, means that NFkB only activates IRF7g in presence of dsRNA (in the differential equation system, this appears as $I(dsRNA)$, meaning the indicator of dsRNA).
- We show only cytosolic proteins, without making difference if they are active or inactive. For example, there exist IRF3ii, IRF3i, and IRF3a, and we show IRF3. Translocation of the protein to nucleus is implicit in its action on a nuclear gene.
- We do not show the complex NFkB-IkB α
- We do not show mRNA

SF2: Snapshots of RelA-specific and IRF3-specific labeling in A549 cells at different times in non dsRNA-induced experiment.



(A) RelA-specific labeling at times $t = 0, 3$ and 6 hr. No translocation from cytoplasm to nucleus has been observed.



(B) IRF3-specific labeling at times $t = 0, 3$ and 6 hr. No translocation from cytoplasm to nucleus has been observed.