

Table S2

Name of model node	Initial condition (in # of molecules)	Equation (d[x]/dt=)	Initial condition Refs.
VEGF	5223	$v111-v112$	Estimated from (1)
IFN γ	358	$v37-v41$	Estimated from (2)
IFNGR/JAK	20376	$v40-v41$	Total IFNGR estimated from (3, 4)
IFNGR	106	$-v40+v48$	Fitted
IFN γ /R	1	$v50+v54-v51$	Fitted
IFN γ /R/JAK	0	$v41-v42-v43+v51-v52$	Fitted
pIFN γ /R/JAK	0	$v42-v44$	Fitted
STAT1	397262	$-v44+v59+v60$	Total STAT1 estimated from (4, 5)
pIFN γ /R/JAK/STAT1	84	$v44-v45$	Fitted
pSTAT1	41	$v45-v60-2*v55$	Fitted
pSTAT1D	81	$v55-v56-v95$	Fitted
pSTAT1D_n	80	$v56-v57-v97$	Fitted
STAT1D_n	84	$v57+v99-v58$	Fitted
STAT1_n	1673	$2*v58-v59$	Fitted
SOCS1	3169	$v127-v128-v17+v18+v21-v27+v28-v43+v49$	Total SOCS1 estimated from (6)
IFN γ /R/JAK/SOCS1	9	$v43-v49-v50$	Fitted
IFN γ /R_lyso	1	$v46-v47-v48+v49+v53$	Fitted
SOCS1/JAK	3	$v50+v19-v21$	Fitted
IRF9	2674	$v93-v94-v95-v98$	Total IRF9 estimated from (4)
IRF9_n	27001	$v98-v97+v99$	Fitted
pSTAT1D/IRF9	26	$v95-v96$	Fitted
pSTAT1D/IRF9_n	203	$v96-v99+v97$	Fitted
SOCS3	1735	$v129-v130-v23+v24+v26-v29+v30-v52+v53$	Total SOCS3 estimated from (6)
IFN γ /R/JAK/SOCS3	3	$v52-v53-v54$	Fitted
SOCS3/JAK	8	$v54+v25-v26$	Fitted
IL4	288	$v1-v7$	Estimated from (7)
IL4R	16	$v2-v6+v12$	Fitted
IL4/R	0	$v19+v25-v22$	Fitted
IL4R/JAK	3478	$v6-v7$	Total IL4R estimated from (4)
IL4/R/JAK	0	$v7-v8$	Fitted
pIL4/R/JAK	0	$v8-v9$	Fitted
pIL4/R/JAK_i	0	$v9-v10-v13+v14-v17+v22-v23$	Fitted
IL4/R/JAK/SOCS1_i	0	$v17-v18-v19$	Fitted
IL4/R_lyso	0	$v10-v11-v12+v18+v20+v24+v28+v30$	Fitted

IL4/R/JAK/SOCS3_i	0	v23-v24-v25	Fitted
IL4/R/JAK/SOCS1	2	v27-v28	Fitted
IL4/R/JAK/SOCS3	0	v29-v30	Fitted
STAT6	59874	v35+v36-v13	Total STAT6 estimated from (4, 6)
pIL4/R/JAK/STAT6	0	v13-v14	Fitted
pSTAT6	26	v14-v36-2*v31	Fitted
pSTAT6D	1	v31-v32	Fitted
pSTAT6D_n	39	v32-v33	Fitted
STAT6D_n	0	v33-v34	Fitted
STAT6_n	16	2*v34-v35	Fitted
PTEN	64899	v84-v85	Estimated from (4)
IRF4	16460	v100-v101	Estimated from (4)
IL10	571	v119-v120	Estimated from (8)
JAK	99297	v4-v5-v6+v10+v18-v22+v24+v28+v30-v40+v46+v49+v53	Total JAK estimated from (4)
ARG1	875428	v115-v116	Estimated from (4)
miR3473	1180	v79-v80-v81+v82	Estimated from (9)
mPTEN	8	v83-v86-v81	Total mPTEN estimated from (10)
miR3473/mPTEN	6	v81-v82	Fitted
iNOS	538	v113-v114	Fitted
HIF1 α	640	v61-v63-v71+v72	Total HIF1 α estimated from (11)
HIF1 α _n	178	v63-v65	Fitted
HIF1 α / β _n	44	v65	Fitted
HIF1 α _OH	42	v71-v72-v73	Fitted
HIF2 α	878	v62-v64-v74+v75	Total HIF2 α estimated from (11)
HIF2 α _n	244	v64-v66	Fitted
HIF2 α / β _n	61	v66	Fitted
HIF2 α _OH	22	v74-v75-v76	Fitted
HIF1 β _n	14897	-v65-v66	Total HIF1 β estimated from (4)
PPARG	1437	v102-v103+v104-v106	Total PPARG estimated from (12)
aPPARG	782	v103-v104-v105	Fitted
IRF1	614	v77-v78	Estimated from (4)
PHD	5470	v67-v68-v69	Total PHD estimated from (4)
O ₂	1.204e8	Constant	Estimated from (11)
O ₂ /aPHD	3088	v70-v71-v74	Fitted
aPHD	38846	v69-v70+v71+v74	Fitted
TNF α	619	v117-v118	Estimated from (13-15)
CXCL9	54	v123-v124	Fitted

mIRF9	9	$v91-v92-v89$	Total mIRF9 estimated from (16)
miR93/mIRF9	5	$v89-v90$	Fitted
miR93	841	$v87-v88-v89+v90$	Fitted
IL12	58	$v121-v122$	Estimated from (17)
mCXCL10	12	$v125-v126$	Estimated from (16)
AKT	198060	$-v15+v16$	Total AKT estimated from (4)
pAKT	11942	$v15-v16$	Fitted
IRG1	3522	$v107-v108$	Estimated from (4)
Itaconate	6.214e7	$v109-v110$	Estimated from (18)
IRF9T (repeated assignment)	29904	$[IRF9T]=[IRF9]+[IRF9_n]+[pSTAT1D/IRF9]+[pSTAT1D/IRF9_n]$	Fitted

Table S2. Differential equations and initial conditions of all model nodes. A summary of the model equations and initial conditions in terms of absolute copy numbers of all 80 model nodes (proteins, RNAs, complexes, etc.) derived from the 34 functionally unique species. The initial levels (and also the steady state levels) of 31 out of 34 unique species are estimated and calibrated with respect to literature data (using both direct measurements and indirect observations), and the model is simulated in control condition without external stimulation until equilibrium to obtain the initial levels (e.g. copy numbers) of all 80 model nodes. A cell volume of 1 pL is assumed when doing unit conversion calculations for O₂ and itaconate (19, 20). To reduce model complexity, it is assumed that transcription factors and enzymes in Hill-type reactions are not consumed, mRNAs are not consumed during translation, and oxygen level is constant during each simulation run.

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