

**Table S3. STAT3/6 dependent gene regulation by *Toxoplasma* ROP16 in BMDMs**

Gene Title	Gene Symbol	Fold change ROP16	Fold STAT6	Fold STAT3
tumor necrosis factor receptor superfamily, member 9 (4-1BB)	Tnfrsf9	3.13	1.16	1.82
B-cell translocation gene 3	Btg3	2.67	1.10	1.99
DEAH (Asp-Glu-Ala-His) box polypeptide 30	Dhx30	2.61	-1.20	3.75
platelet-derived growth factor, C polypeptide	Pdgfc	2.59	1.57	1.94
signal transducer and activator of transcription 4	Stat4	2.54	1.31	2.08
proteasome (prosome, macropain) 26S subunit, non-ATPase, 3	Psmd3	2.49	-1.21	2.29
runt related transcription factor 2	Runx2	2.39	1.61	2.13
BCL2-associated athanogene 2	Bag2	2.35	1.32	2.22
cytochrome P450, family 27, subfamily a, polypeptide 1	Cyp27a1	2.27	-1.63	4.22
suppressor of cytokine signaling 4	Socs4	2.04	1.43	2.73
NCK-associated protein 1	Nckap1	2.03	1.07	2.22
breast cancer 1	Brca1	2.01	1.29	1.94
FK506 binding protein 3	Fkbp3	1.80	1.21	1.84
NLR family, pyrin domain containing 3	Nlrp3	-1.76	-1.19	-1.88
chemokine (C-X-C motif) receptor 3	Cxcr3	-1.82	-1.44	-2.08
regulator of G-protein signaling 18	Rgs18	-1.83	-1.34	2.06
TAO kinase 3	Taok3	-1.86	-1.28	-1.97
tumor necrosis factor receptor superfamily, member 13b (TACI)	Tnfrsf13b	-1.94	1.02	-2.16
plexin D1	Plxnd1	-1.95	-1.29	-2.32
interferon-induced protein 35	Ifi35	-1.98	-1.14	-1.93
mammary tumor virus receptor 2	Mtvr2	-2.00	-1.33	-1.87
interleukin 18 binding protein	Il18bp	-2.03	1.31	-2.45
ADP-ribosylation factor-like 6 interacting protein 5	Arl6ip5	-2.05	-1.32	-1.97
activating transcription factor 6	Atf6	-2.13	-1.06	-1.99
SLAM family member 9	Slamf9	-2.31	-1.65	-2.06
histocompatibility 2, class II, locus Mb1/2	H2-DMb1/b2	-2.32	-1.37	-3.70
myxovirus (influenza virus) resistance 1	Mx1	-2.39	1.14	-2.02
mitogen-activated protein kinase kinase kinase 11	Map3k11	-2.39	-1.36	-2.21
carnitine palmitoyltransferase 1a, liver	Cpt1a	-2.41	1.07	-2.27
toll-like receptor 7	Tlr7	-2.53	-1.67	-1.94
T-cell specific GTPase /// T-cell specific GTPase 2	Tgtp / Tgtp2	-2.55	-1.06	-1.82
histocompatibility (minor) HA-1	Hmha1	-2.65	-1.52	-2.18
linker for activation of T cells family, member 2	Lat2	-2.78	-1.17	-2.56
tumor necrosis factor (ligand) superfamily, member 12 (TWEAK)	Tnfsf12	-2.96	-1.06	-2.10
TRAF-interacting protein with forkhead-associated domain	Tifa	-2.97	-1.55	-1.95
Nfat activating molecule with ITAM motif 1	Nfam1	-3.11	-1.74	-2.15
triggering receptor expressed on myeloid cells 2	Trem2	-3.17	-1.59	-3.08
interferon-induced protein with tetratricopeptide repeats 3	Ifit3	-3.82	-1.20	-1.97
coagulation factor V	F5	-4.01	-1.57	2.03
thioredoxin interacting protein	Txnip	-4.71	-1.45	-3.46

Gene Title	Gene Symbol	Fold change ROP16	Fold STAT6	Fold STAT3
chitinase 3-like 3	Chi3l3	9.24	53.67	2.03
arginase, liver	Arg1	6.99	2.86	-3.44
signaling lymphocytic activation molecule family member 1	Slamf1	5.80	4.53	2.05
preproenkephalin	Penk	4.33	1.88	2.07
lymphocyte antigen 75	Ly75	3.71	2.21	-2.19
cytochrome P450, family 1, subfamily b, polypeptide 1	Cyp1b1	2.93	3.47	-1.85
matrix metalloproteinase 12	Mmp12	2.25	2.04	-1.82
chemokine (C-X3-C) receptor 1	Cx3cr1	2.01	-1.92	1.90
intraflagellar transport 20 homolog (Chlamydomonas)	Ift20	-1.74	-1.93	-2.23
Fc receptor, IgG, low affinity IIb	Fcgr2b	-1.89	-2.00	-2.51
allograft inflammatory factor 1	Aif1	-2.20	-1.95	-1.96
serum amyloid A 3	Saa3	-2.24	-1.79	-1.77
complement factor B	Cfb	-2.24	-2.07	-2.02
apolipoprotein E	ApoE	-2.96	-1.81	-2.48
signal transducer and activator of transcription 2	Stat2	-3.64	1.75	-3.65
growth arrest specific 6	Gas6	-3.65	-2.20	-1.91
resistin like alpha	Retnla	26.98	20.33	1.44
eosinophil-associated, ribonuclease A family, member 11	Ear11	23.59	11.88	-1.21
chitinase 3-like 3 /// chitinase 3-like 4	Chi3l3/Chi3l4	12.23	33.05	1.27
programmed cell death 1 ligand 2 (B7-DC)	Pdcd1lg2	8.71	5.76	1.31
chemokine (C-C motif) ligand 8	Ccl8	5.36	16.25	-1.59
chitinase 3-like 4	Chi3l4	5.25	4.46	-1.31
chemokine (C-C motif) ligand 24	Ccl24	3.86	5.57	1.43
serine (or cysteine) peptidase inhibitor, clade A, member 3G	Serpina3g	3.30	2.48	1.14
prostaglandin-endoperoxide synthase 1 (COX-1)	Ptgs1	3.11	1.98	-1.45
heparin-binding EGF-like growth factor	Hbegf	3.01	2.86	-1.29
splA/ryanodine receptor domain and SOCS box containing 1	Spsb1	2.92	3.91	1.54
vitamin D receptor	Vdr	2.74	1.81	-1.35
matrix metalloproteinase 13	Mmp13	2.73	6.96	-1.67
integrin alpha X	Itgax	2.49	1.99	1.33
interleukin 2 receptor, alpha chain	Il2ra	2.11	1.81	-1.25
tetraspanin 7	Tspan7	2.00	1.82	-1.44
serine (or cysteine) peptidase inhibitor, clade B, member 9	Serpib9	1.88	1.75	1.55
CD36 antigen	Cd36	1.81	2.32	1.27
mannose receptor, C type 1	Mrc1	1.80	2.05	1.02
interleukin 11 receptor, alpha chain 1	Il11ra1/ra2	1.74	1.96	1.54
matrix metalloproteinase 14 (membrane-inserted)	Mmp14	-1.76	-1.76	-1.13
ATG2 autophagy related 2 homolog A (S. cerevisiae)	Atg2a	-1.76	-1.77	-1.55
HtrA serine peptidase 1	Htra1	-1.77	-1.75	1.56
interleukin 1 receptor, type I	Il1r1	-1.81	2.00	-1.54
chemokine (C-C motif) receptor 1	Ccr1	-1.81	1.79	-1.65

Gene Title	Gene Symbol	Fold change ROP16	Fold STAT6	Fold STAT3
interleukin 6 receptor, alpha	Il6ra	-1.85	-2.03	-1.17
SLIT-ROBO Rho GTPase activating protein 2	Srgap2	-1.89	-2.36	-1.31
AXL receptor tyrosine kinase	Axl	-1.97	-1.84	-1.63
anthrax toxin receptor 1	Antxr1	-1.99	-2.26	1.17
tumor necrosis factor alpha induced protein 6	Tnfaip6	-1.99	1.78	1.48
protein tyrosine phosphatase, non-receptor type 6	Ptpn6	-2.30	-1.77	-1.19
paired immunoglobulin-like type 2 receptor alpha	Pilra	-2.37	-2.63	-1.24
paired immunoglobulin-like type 2 receptor beta 1	Pilrb1	-2.49	-3.03	-1.09
lymphoblastomic leukemia 1	Lyl1	-2.68	-2.12	1.28
cytokine inducible SH2-containing protein	Cish	4.07	1.63	1.28
tissue inhibitor of metalloproteinase 1	Timp1	3.10	1.61	1.17
cellular retinoic acid binding protein II	Crabp2	3.08	-1.22	1.18
C-type lectin domain family 4, member b1	Clec4b1	2.84	1.19	1.24
alanine and arginine rich domain containing protein	Aard	2.75	1.32	-1.15
vascular cell adhesion molecule 1	Vcam1	2.63	1.55	1.03
suppressor of cytokine signaling 2	Socs2	2.48	1.21	1.11
basic leucine zipper transcription factor, ATF-like 3	Batf3	2.23	1.10	-1.30
glutamate-rich WD repeat containing 1	Grwd1	2.18	-1.07	1.36
chemokine (C-C motif) ligand 6	Ccl6	2.15	1.30	1.46
thymic stromal lymphopoietin	Tslp	2.08	-1.12	-1.32
gap junction protein, alpha 1	Gja1	2.03	1.50	1.60
interferon regulatory factor 4	Irf4	2.02	1.46	-1.17
peroxisome proliferator activated receptor gamma	Pparg	2.00	1.46	1.32
protein tyrosine phosphatase, non-receptor type 2	Ptpn2	1.96	1.61	-1.08
aldehyde dehydrogenase 18 family, member A1	Aldh18a1	1.94	1.28	1.43
cyclin D2	Ccnd2	1.94	-1.17	-1.57
COX15 homolog, cytochrome c oxidase assembly protein (yeast)	Cox15	1.93	1.27	1.73
CD244 natural killer cell receptor 2B4	Cd244	1.91	1.09	1.10
phospholipase A2, group XV	Pla2g15	1.91	-1.33	-1.19
Von Willebrand factor homolog	Vwf	1.90	1.17	1.34
interleukin 12 receptor, beta 2	Il12rb2	1.87	1.61	1.26
leukocyte-associated Ig-like receptor 1	Lair1	1.87	-1.31	1.16
SLAM family member 8	Slamf8	1.83	1.16	-1.04
basic leucine zipper transcription factor, ATF-like	Batf	1.82	-1.65	1.12
metallothionein 1	Mt1	1.80	1.11	1.50
retinoid X receptor alpha	Rxra	1.76	-1.12	1.25
NLR family member X1	NlrX1	1.75	-1.16	1.42
Jun dimerization protein 2	Jdp2	1.74	1.69	1.29
tetraspanin 5	Tspan5	1.74	1.05	1.23
CD5 antigen-like	Cd5l	-1.74	-1.35	-1.21
integrin beta 7	Itgb7	-1.74	-1.41	-1.13

Gene Title	Gene Symbol	Fold change ROP16	Fold STAT6	Fold STAT3
forkhead box J2	Foxj2	-1.75	-1.30	-1.20
histocompatibility 2, class II antigen A, beta 1	H2-Ab1	-1.76	-1.59	-1.18
MARCKS-like 1	Marcksl1	-1.77	-1.69	-1.37
protein tyrosine phosphatase, non-receptor type 1	Ptpn1	-1.78	-1.34	-1.61
apolipoprotein B48 receptor	Apob48r	-1.79	-1.27	-1.13
arginase type II	Arg2	-1.80	-1.59	-1.32
interferon regulatory factor 7	Irf7	-1.80	-1.36	-1.53
chemokine (C-X-C motif) ligand 1	Cxcl1	-1.81	-1.25	-1.39
unc-93 homolog B1 (C. elegans)	Unc93b1	-1.81	-1.36	-1.16
interleukin 12b	Il12b	-1.81	-1.33	-1.65
FMS-like tyrosine kinase 4	Flt4	-1.81	1.32	1.64
integrin beta 5	Itgb5	-1.82	-1.18	-1.10
lectin, galactose binding, soluble 9	Lgals9	-1.82	-1.30	-1.47
protein tyrosine phosphatase, receptor type, A	Ptpa	-1.83	-1.70	-1.73
interleukin 13 receptor, alpha 1	Il13ra1	-1.83	-1.03	-1.30
cAMP responsive element modulator	Crem	-1.83	1.06	1.46
Fc receptor, IgG, low affinity IV	Fcgr4	-1.84	-1.13	-1.30
suppressor of cytokine signaling 5	Socs5	-1.84	-1.22	-1.44
mitogen-activated protein kinase kinase kinase kinase 4	Map4k4	-1.85	1.25	-1.15
purinergic receptor P2X, ligand-gated ion channel, 5	P2rx5	-1.86	-1.20	-1.68
lysosomal trafficking regulator	Lyst	-1.88	-1.02	-1.19
peptidyl arginine deiminase, type II	Padi2	-1.89	-1.15	-1.26
poly (ADP-ribose) polymerase family, member 3	Parp3	-1.90	-1.15	-1.20
creatine kinase, brain	Ckb	-1.91	-1.30	-1.53
protein tyrosine phosphatase-like A domain containing 2	Ptplad2	-1.91	-1.19	-1.15
interleukin 6	Il6	-1.92	1.05	-1.30
CD276 antigen (B7-H3)	Cd276	-1.92	-1.07	-1.34
CD72 antigen	Cd72	-1.93	-1.24	-1.47
glia maturation factor, gamma	Gmfg	-1.94	-1.53	1.42
Fc receptor, IgG, high affinity I	Fcgr1	-1.95	-1.33	-1.69
plasminogen activator, tissue	Plat	-1.96	-1.37	1.32
CD99 antigen	Cd99	-1.97	-1.22	-1.70
sequestosome 1	Sqstm1	-1.99	-1.20	-1.51
prostaglandin D2 synthase 2, hematopoietic	Ptgds2	-2.00	-1.36	-1.50
coronin, actin binding protein 1A	Coro1a	-2.02	-1.35	-1.39
CD28 antigen	Cd28	-2.04	1.36	-1.39
colony stimulating factor 2 (granulocyte-macrophage)	Csf2	-2.09	-1.65	-1.18
tissue inhibitor of metalloproteinase 2	Timp2	-2.10	-1.41	-1.28
signal-induced proliferation-associated 1 like 2	Sipa1l2	-2.11	-1.34	-1.07
ArfGAP with RhoGAP domain, ankyrin repeat and PH domain 3	Arap3	-2.12	-1.65	-1.17
CD70 antigen	Cd70	-2.13	-1.59	-1.61

Gene Title	Gene Symbol	Fold change ROP16	Fold STAT6	Fold STAT3
immunoglobulin superfamily, member 6	Igsf6	-2.14	-1.64	-1.31
Rho GTPase activating protein 9	Arhgap9	-2.20	-1.51	-1.29
plexin B2	Plxnb2	-2.23	-1.66	1.27
ATP-binding cassette, sub-family C (CFTR/MRP), member 3	Abcc3	-2.25	-1.47	-1.45
coagulation factor XIII, A1 subunit	F13a1	-2.26	-1.55	1.33
complement component 3a receptor 1	C3ar1	-2.30	-1.33	-1.46
immunity-related GTPase family M member 2	Irgm2	-2.31	1.08	-1.66
interleukin 23, alpha subunit p19	Il23a	-2.31	-1.01	-1.35
chemokine (C-X-C motif) ligand 10	Cxcl10	-2.32	1.04	-1.15
paired-Ig-like receptor A2	Pira2	-2.45	1.10	-1.50
toll-like receptor 2	Tlr2	-2.50	-1.33	-1.10
high mobility group AT-hook 2	Hmga2	-2.69	-1.11	-1.44
FBJ osteosarcoma oncogene	Fos	-2.72	-1.20	-1.32
thrombospondin 1	Thbs1	-2.72	1.37	1.36
aryl-hydrocarbon receptor repressor	Ahrr	-2.79	1.23	-1.23
Notch gene homolog 1 (Drosophila)	Notch1	-2.93	-1.41	-1.63
UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5	B3gnt5	-3.47	1.58	-1.30
DNA-damage-inducible transcript 4	Ddit4	-4.62	-1.05	-1.59

**Table S3. STAT3/6 dependent gene regulation by *Toxoplasma* ROP16 in BMDMs**

A shortened list of the 938 uniquely annotated genes whose expression was regulated by ROP16 at least 1.7 fold ( $0.8 < \text{Absolute value of the } \text{Log}_2 \text{ ratio } [+ROP16_i / \text{control infection}]$ ) when comparing type II vs. II+*ROP16<sub>i</sub>*, or II  $\Delta$ *gra15* vs. II  $\Delta$ *gra15* +*ROP16<sub>i</sub>* infected BMDMs. ‘Fold ROP16’ is the greatest difference in gene expression due to *Toxoplasma* ROP16 obtained from these comparisons. Negative values indicated ROP16 downregulated gene expression. The ‘Fold STAT3’ indicates how the ‘Fold ROP16’ value changes when comparing similar infections in wild type and STAT3 deficient macrophages ( $0.8 < \text{Absolute value of the } \text{Log}_2 [+ROP16_i / \text{control infection in wild type BMDMs}] - \text{Log}_2 [+ROP16_i / \text{control infection in } Stat3 \text{ deficient BMDMs}]$ ); ‘Fold STAT6’ is the absolute difference in gene expression between wild type and *Stat6*<sup>-/-</sup> BMDMs infected with the II+*ROP16<sub>i</sub>* strain. In order for a gene to have been categorized as STAT3 or STAT6 regulated that difference had to be at least  $\pm 1.7$  fold in the

aforementioned comparisons. Negative values indicate the gene expression or 'Fold ROP16' expression value was reduced in the wild type compared to STAT-deficient BMDMs (i.e. the STAT-pathway acted as a repressor); positive values indicate the 'Fold ROP16' expression value increased in the wild type compared to STAT-deficient BMDMs (i.e. the STAT-pathway induced gene expression). Highlighted in periwinkle are genes that are modulated by STAT3, forest green STAT6, orange by both STAT3 and STAT6, and peach neither STAT3 nor STAT6 host transcription factors.