

Table S5. Upstream regulators of SPP1 macrophages*

Upstream Regulator	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap
lipopolysaccharide	chemical drug	Activated	5.504	1.12E-79
TNF	cytokine	Activated	3.837	1.12E-50
TGFB1	growth factor	Activated	2.651	1.43E-45
CD40LG	cytokine	Activated	3.102	2.08E-39
IL33	cytokine	Activated	3.284	3.22E-37
IL1B	cytokine	Activated	3.746	2.50E-36
IL2	cytokine	Activated	2.675	1.70E-27
IL6	cytokine	Activated	3.157	6.62E-27
TNFSF11	cytokine	Activated	2.426	1.18E-25
IL15	cytokine	Activated	2.802	3.34E-24
IL3	cytokine	Activated	2.674	3.47E-22
IL5	cytokine	Activated	3.466	7.33E-22
EGF	growth factor	Activated	3.151	9.86E-22
VEGFA	growth factor	Activated	2.769	2.93E-19
HGF	growth factor	Activated	4.814	1.76E-18
IGF1	growth factor	Activated	2.634	1.56E-17
PRL	cytokine	Activated	3.323	2.96E-17
AGT	growth factor	Activated	2.013	8.18E-17
CCL5	cytokine	Activated	3.113	6.26E-16
IL17A	cytokine	Activated	3.038	1.07E-14
TFEB	transcription regulator	Activated	3.012	3.97E-14
FGF2	growth factor	Activated	2.471	6.50E-14
CNTF	cytokine	Activated	2.173	2.01E-13
IL1A	cytokine	Activated	4.093	1.81E-11
PF4	cytokine	Activated	3.264	2.33E-11
IL11	cytokine	Activated	2.085	3.11E-10
C5	cytokine	Activated	2.889	1.32E-09
TGFA	growth factor	Activated	2.282	1.36E-09
ANGPT2	growth factor	Activated	2.204	4.22E-09
TLR7	transmembrane recept	Activated	3.929	4.67E-09
TLR9	transmembrane recept	Activated	3.377	6.17E-08
SPP1	cytokine	Activated	2.031	5.92E-06
NGF	growth factor	Activated	2.424	9.92E-06
TNFSF12	cytokine	Activated	2.994	5.68E-05
AIMP1	cytokine	Activated	2.207	9.19E-05
GDF2	growth factor	Activated	2.95	1.01E-04
THPO	cytokine	Activated	2.037	1.63E-04
BMP6	growth factor	Activated	2.118	1.79E-04
IL22	cytokine	Activated	2.229	2.67E-04
IL12B	cytokine	Activated	2.008	8.07E-04
BTC	growth factor	Activated	2	1.24E-03
IL36G	cytokine	Activated	2.176	1.49E-03
IL17F	cytokine	Activated	2.41	2.52E-03
Ccl2	cytokine	Activated	2.611	3.35E-03
IL36A	cytokine	Activated	2.234	5.73E-03
IFNE	cytokine	Activated	2.219	1.37E-02
LTA	cytokine	Activated	2.219	4.09E-02
JAG1	growth factor	Activated	2.2	9.60E-02

* IPA analysis of upstream regulators ranked by z-score and filtered by cytokine or growth factor as Molecule type, and by Activated as Predicted Activation state. Also included are TLRs and TFEB

LPS-regulated gene showing increased expression by SPP1 macrophages

ID	Genes in dataset	Prediction (based on measurement)		
		direction)	Expr Log Ratio	Findings
SPP1	SPP1	Activated	4.66	Upregulates (7)
CCL2	CCL2	Activated	4.341	Upregulates (97)
TIMP1	TIMP1	Activated	2.213	Upregulates (11)
CCL3	CCL3	Activated	1.573	Upregulates (45)
CCL7	CCL7	Activated	1.568	Upregulates (9)
CTSL	CTSL	Activated	1.55	Upregulates (1)
G0S2	G0S2	Activated	1.481	Upregulates (4)
PLA2G7	PLA2G7	Activated	1.337	Upregulates (10)
S100A8	S100A8	Activated	1.298	Upregulates (54)
CXCL8	CXCL8	Activated	1.277	Upregulates (288)
IL1RN	IL1RN	Activated	1.104	Upregulates (71)
S100A9	S100A9	Activated	1.083	Upregulates (7)
MARCKS	MARCKS	Activated	1.08	Upregulates (6)
SOD2	SOD2	Activated	1.06	Upregulates (19)
GPR183	GPR183	Activated	1.06	Upregulates (2)
CTSB	CTSB	Activated	1.01	Upregulates (7)
SLC2A3	SLC2A3	Affected	0.941	Regulates (1)
CALM3	CALM1 (includes of	Inhibited	0.94	Downregulates (1)
CXCL2	CXCL2	Activated	0.933	Upregulates (123)
LGALS1	LGALS1	Activated	0.922	Upregulates (1)
RGS1	RGS1	Activated	0.897	Upregulates (12)
CD36	CD36	Inhibited	0.883	Downregulates (4)
ISG15	ISG15	Activated	0.872	Upregulates (16)
PLAUR	PLAUR	Activated	0.866	Upregulates (6)
LILRB4	LILRB4	Activated	0.84	Upregulates (4)
CD48	CD48	Activated	0.832	Upregulates (1)
TYMP	TYMP	Affected	0.816	Regulates (1)
IER3	IER3	Activated	0.8	Upregulates (4)
AREG	AREG	Activated	0.799	Upregulates (4)
LIMS1	LIMS1	Activated	0.776	Upregulates (2)
HAMP	HAMP	Activated	0.771	Upregulates (1)
RGS2	RGS2	Inhibited	0.756	Downregulates (7)
CD63	CD63	Activated	0.749	Upregulates (1)
CD14	CD14	Activated	0.747	Upregulates (49)
HIF1A	HIF1A	Activated	0.737	Upregulates (38)
HM13	HM13	Activated	0.717	Upregulates (2)
MIF	MIF	Activated	0.698	Upregulates (6)
CREM	CREM	Activated	0.694	Upregulates (4)
PDIA6	PDIA6	Activated	0.675	Upregulates (1)
EREG	EREG	Activated	0.669	Upregulates (5)
SOCS3	SOCS3	Activated	0.644	Upregulates (57)
CSTB	CSTB	Activated	0.643	Upregulates (1)
CORO1A	CORO1A	Inhibited	0.638	Downregulates (1)
HMGA1	HMGA1	Activated	0.637	Upregulates (4)
ENO1	ENO1	Activated	0.63	Upregulates (4)
CLEC5A	CLEC5A	Activated	0.63	Upregulates (2)
DUSP2	DUSP2	Activated	0.617	Upregulates (6)
FABP5	FABP5	Activated	0.605	Upregulates (2)
HSPA5	HSPA5	Activated	0.596	Upregulates (16)
CCL20	CCL20	Activated	0.586	Upregulates (24)

TGFB1-regulated gene showing increased expression by SPP1 macrophages

ID	Genes in dataset	Prediction (based on measurement		Findings
		direction)	Expr Log Ratio	
SPP1	SPP1	Activated	4.66	Upregulates (6)
CCL2	CCL2	Activated	4.341	Upregulates (13)
TIMP1	TIMP1	Activated	2.213	Upregulates (28)
CCL3	CCL3	Activated	1.573	Upregulates (1)
CTSL	CTSL	Activated	1.55	Upregulates (1)
CXCL8	CXCL8	Inhibited	1.277	Downregulates (9)
IL1RN	IL1RN	Activated	1.104	Upregulates (4)
SOD2	SOD2	Inhibited	1.06	Downregulates (1)
SDC2	SDC2	Activated	1.02	Upregulates (2)
CTSB	CTSB	Activated	1.01	Upregulates (5)
SLC2A3	SLC2A3	Affected	0.941	Regulates (4)
CALM3	CALM1 (includes othe	Activated	0.94	Upregulates (1)
CXCL2	CXCL2	Activated	0.933	Upregulates (1)
CD36	CD36	Inhibited	0.883	Downregulates (6)
PLAUR	PLAUR	Activated	0.866	Upregulates (8)
TYMP	TYMP	Activated	0.816	Upregulates (2)
IER3	IER3	Activated	0.8	Upregulates (11)
AREG	AREG	Activated	0.799	Upregulates (11)
LIMS1	LIMS1	Activated	0.776	Upregulates (1)
HAMP	HAMP	Activated	0.771	Upregulates (2)
SGK1	SGK1	Activated	0.755	Upregulates (10)
CD14	CD14	Activated	0.747	Upregulates (5)
HIF1A	HIF1A	Activated	0.737	Upregulates (15)
PDXK	PDXK	Activated	0.691	Upregulates (1)
BCAT1	BCAT1	Inhibited	0.688	Downregulates (1)
EREG	EREG	Activated	0.669	Upregulates (6)
SOCS3	SOCS3	Activated	0.644	Upregulates (11)
ATP13A3	ATP13A3	Affected	0.643	Regulates (2)
HMGA1	HMGA1	Inhibited	0.637	Downregulates (11)
ENO1	ENO1	Affected	0.63	Regulates (2)
AQP9	AQP9	Inhibited	0.629	Downregulates (1)
FABP5	FABP5	Activated	0.605	Upregulates (1)
HSPA5	HSPA5	Activated	0.596	Upregulates (1)
CCL20	CCL20	Activated	0.586	Upregulates (4)
HCST	HCST	Inhibited	0.572	Downregulates (4)
DUSP4	DUSP4	Activated	0.57	Upregulates (8)
INSIG1	INSIG1	Affected	0.558	Regulates (2)
CCR1	CCR1	Activated	0.555	Upregulates (4)
FOSB	FOSB	Activated	0.554	Upregulates (6)
NR4A2	NR4A2	Affected	0.553	Regulates (2)
NAMPT	NAMPT	Affected	0.528	Regulates (1)
ABCA1	ABCA1	Activated	0.524	Upregulates (3)
CEBPD	CEBPD	Activated	0.521	Upregulates (1)
NFKBIA	NFKBIA	Activated	0.518	Upregulates (11)
VEGFA	VEGFA	Activated	0.508	Upregulates (51)
NME1	NME1	Activated	0.505	Upregulates (2)
TGFB1	TGFB1	Activated	0.489	Upregulates (5)
HMOX1	HMOX1	Activated	0.483	Upregulates (19)
CHST11	CHST11	Activated	0.481	Upregulates (1)
FOSL2	FOSL2	Activated	0.459	Upregulates (6)

IL33-regulated gene showing increased expression by SPP1 macrophages

ID	Genes in dataset	Prediction (based on measurement)		Findings
		direction	Expr Log Ratio	
CCL2	CCL2	Activated	4.341	Upregulates (1)
TIMP1	TIMP1	Activated	2.213	Upregulates (1)
CCL3	CCL3	Activated	1.573	Upregulates (1)
G0S2	G0S2	Affected	1.481	Regulates (1)
S100A8	S100A8	Affected	1.298	Regulates (2)
CXCL8	CXCL8	Activated	1.277	Upregulates (12)
IL1RN	IL1RN	Activated	1.104	Upregulates (1)
S100A9	S100A9	Activated	1.083	Upregulates (1)
SOD2	SOD2	Activated	1.06	Upregulates (1)
CXCL2	CXCL2	Activated	0.933	Upregulates (4)
LGALS1	LGALS1	Affected	0.922	Regulates (1)
RGS1	RGS1	Activated	0.897	Upregulates (1)
CD36	CD36	Inhibited	0.883	Downregulates (4)
LILRB4	LILRB4	Inhibited	0.84	Downregulates (1)
IER3	IER3	Affected	0.8	Regulates (1)
AREG	AREG	Activated	0.799	Upregulates (1)
HIF1A	HIF1A	Inhibited	0.737	Downregulates (2)
MIF	MIF	Activated	0.698	Upregulates (2)
CREM	CREM	Affected	0.694	Regulates (1)
SCGB3A1	SCGB3A1	Inhibited	0.653	Downregulates (1)
SOCS3	SOCS3	Activated	0.644	Upregulates (1)
CSTB	CSTB	Activated	0.643	Upregulates (2)
DUSP2	DUSP2	Activated	0.617	Upregulates (1)
CCR1	CCR1	Activated	0.555	Upregulates (1)
ABCA1	ABCA1	Activated	0.524	Upregulates (4)
NFKBIA	NFKBIA	Inhibited	0.518	Downregulates (8)
POLR2L	POLR2L	Activated	0.509	Upregulates (2)
TNFRSF1B	TNFRSF1B	Activated	0.508	Upregulates (2)
VEGFA	VEGFA	Inhibited	0.508	Downregulates (1)
NME1	NME1	Activated	0.505	Upregulates (2)
HMOX1	HMOX1	Activated	0.483	Upregulates (1)
CHST11	CHST11	Activated	0.481	Upregulates (1)
PEA15	PEA15	Activated	0.477	Upregulates (1)
BCL2A1	BCL2A1	Activated	0.461	Upregulates (6)
FOSL2	FOSL2	Affected	0.459	Regulates (1)
ZEB2	ZEB2	Activated	0.434	Upregulates (1)
TPI1	TPI1	Activated	0.424	Upregulates (2)
GNA13	GNA13	Activated	0.419	Upregulates (1)
APOE	APOE	Activated	0.416	Upregulates (4)
ITGAM	ITGAM	Activated	0.41	Upregulates (2)
ITGAX	ITGAX	Activated	0.403	Upregulates (2)
JUNB	JUNB	Activated	0.395	Upregulates (2)
IL4I1	IL4I1	Affected	0.392	Regulates (2)
PAPSS2	PAPSS2	Affected	0.389	Regulates (1)
ICAM1	ICAM1	Activated	0.374	Upregulates (2)
HSPE1	HSPE1	Activated	0.333	Upregulates (2)
CD83	CD83	Affected	0.329	Regulates (2)
TLR2	TLR2	Activated	0.311	Upregulates (1)
ATP5MPL	ATP5MJ	Activated	0.31	Upregulates (2)
NFKB1	NFKB1	Activated	0.299	Upregulates (2)

IL6-regulated gene showing increased expression by SPP1 macrophages

ID	Genes in dataset	Prediction (based on measurement direction)	Expr Log Ratio	Findings
SPP1	SPP1	Activated	4.66	Upregulates (4)
CCL2	CCL2	Activated	4.341	Upregulates (17)
TIMP1	TIMP1	Activated	2.213	Upregulates (13)
CCL7	CCL7	Activated	1.568	Upregulates (1)
CXCL8	CXCL8	Activated	1.277	Upregulates (5)
IL1RN	IL1RN	Activated	1.104	Upregulates (11)
S100A9	S100A9	Activated	1.083	Upregulates (1)
SOD2	SOD2	Activated	1.06	Upregulates (4)
CTSB	CTSB	Activated	1.01	Upregulates (2)
CXCL2	CXCL2	Affected	0.933	Regulates (5)
LGALS1	LGALS1	Affected	0.922	Regulates (1)
CD36	CD36	Activated	0.883	Upregulates (2)
CD48	CD48	Affected	0.832	Regulates (1)
AREG	AREG	Activated	0.799	Upregulates (2)
HAMP	HAMP	Activated	0.771	Upregulates (27)
IFITM3	IFITM3	Activated	0.757	Upregulates (2)
SGK1	SGK1	Activated	0.755	Upregulates (13)
CD14	CD14	Affected	0.747	Regulates (1)
HIF1A	HIF1A	Activated	0.737	Upregulates (5)
SMIM3	SMIM3	Affected	0.681	Regulates (1)
EREG	EREG	Activated	0.669	Upregulates (12)
SOCS3	SOCS3	Activated	0.644	Upregulates (63)
A2M	A2M	Activated	0.631	Upregulates (11)
HSPA5	HSPA5	Activated	0.596	Upregulates (1)
CCL20	CCL20	Activated	0.586	Upregulates (13)
PLEK	PLEK	Activated	0.585	Upregulates (1)
CCR1	CCR1	Activated	0.555	Upregulates (1)
NAMPT	NAMPT	Activated	0.528	Upregulates (10)
ABCA1	ABCA1	Activated	0.524	Upregulates (2)
CEBPD	CEBPD	Activated	0.521	Upregulates (3)
NFKBIA	NFKBIA	Activated	0.518	Upregulates (1)
TNFRSF1B	TNFRSF1B	Affected	0.508	Regulates (1)
VEGFA	VEGFA	Activated	0.508	Upregulates (31)
HMOX1	HMOX1	Activated	0.483	Upregulates (1)
CYP1B1	CYP1B1	Activated	0.465	Upregulates (1)
CFLAR	CFLAR	Activated	0.424	Upregulates (3)
APOE	APOE	Inhibited	0.416	Downregulates (1)
ADM	ADM	Affected	0.413	Regulates (1)
C5AR1	C5AR1	Activated	0.411	Upregulates (3)
ITGAM	ITGAM	Activated	0.41	Upregulates (10)
ETS2	ETS2	Affected	0.402	Regulates (2)
JUNB	JUNB	Activated	0.395	Upregulates (24)
ICAM1	ICAM1	Activated	0.374	Upregulates (12)
CSF1R	CSF1R	Affected	0.361	Regulates (1)
CDKN1A	CDKN1A	Affected	0.339	Regulates (14)
CD44	CD44	Activated	0.337	Upregulates (1)
MERTK	MERTK	Activated	0.331	Upregulates (1)
CD83	CD83	Activated	0.329	Upregulates (2)
MRAS	MRAS	Affected	0.313	Regulates (1)
TLR2	TLR2	Inhibited	0.311	Downregulates (2)