

**Supplemental 1:** Transcripts from top inflammatory pathways differentially expressed in colonic  $\rho^0$  and TNF treated (control and  $\rho^0$ ) cells relative to control cells (>|1.5|-fold change compared to control untreated cells, FDR < 0.05, Ebsseq).

<b>Dendritic Cell Maturation</b>	$\rho^0$	TNF	$\rho^0$ TNF	<b>TREM1 Signaling</b>	$\rho^0$	TNF	$\rho^0$ TNF
ICAM-1	1.50	6.70	21.47	IL-8	8.33	189.61	754.67
COL3A1	18.50	N/A	9.49	CD54	1.50	6.70	21.47
AKT3	12.56	N/A	14.78	AKT3	12.56	N/A	14.78
TLR3	2.87	2.79	8.75	TLR3	2.87	2.79	8.75
IL-15	2.45	2.50	8.85	TLR1	2.44	N/A	1.57
PIK3R3	5.63	N/A	4.62	JAK2	1.58	N/A	1.58
CREB5	3.16	N/A	5.67	CD29	1.60	N/A	1.51
STAT4	2.48	N/A	1.99	NLRP2	-1.66	N/A	-1.56
CD58	2.32	N/A	2.08	NLRP5	-18.98	N/A	-44.58
DDR2	1.80	N/A	2.28				
IRS2	1.91	N/A	1.72	<b>NF-<math>\kappa</math>B Signaling</b>	$\rho^0$	TNF	$\rho^0$ TNF
PLCD4	1.53	N/A	2.08	BMPR1B	43.12	N/A	16.37
TNFRSF1A	1.61	N/A	1.60	AKT3	12.56	N/A	14.78
JAK2	1.58	N/A	1.58	MAP3K8	2.56	5.02	9.16
TRAF6	1.50	N/A	1.61	EGF	9.13	N/A	6.80
HLA-DRB1	-1.74	N/A	N/A	TLR3	2.87	2.79	8.75
HLA-DQB1	-1.75	N/A	N/A	PIK3R3	5.63	N/A	4.62
IRS1	-1.61	N/A	-1.88	TGFA	2.02	1.56	2.49
				TLR1	2.44	N/A	1.57
<b>IL-8 Signaling</b>	$\rho^0$	TNF	$\rho^0$ TNF	MAP3K1	1.66	N/A	2.27
IL-8	8.33	189.61	754.67	IRS2	1.91	N/A	1.72
ICAM1	1.50	6.70	21.47	BMPR2	1.85	N/A	1.64
AKT3	12.56	N/A	14.78	MRAS	1.60	N/A	1.64
IRAK2	2.73	8.00	15.70	TNFRSF1A	1.61	N/A	1.60
EGF	9.13	N/A	6.80	TRAF6	1.50	N/A	1.61
ITGB3	7.03	N/A	7.03	TNFSF13B	2.00	N/A	N/A
PIK3R3	5.63	N/A	4.62	BIMP1	-2.18	N/A	N/A
JUN	1.82	2.40	4.06	TRAF2	-2.46	N/A	N/A
RND3	2.07	1.83	3.30	IRS1	-1.61	N/A	-1.88
HMOX1	1.81	1.70	2.80				
HBEGF	2.44	N/A	3.68	<b>Acute Phase Response Signaling</b>	$\rho^0$	TNF	$\rho^0$ TNF
IRS2	1.91	N/A	1.72	SERPINA1	6.21	2.78	25.56
MRAS	1.60	N/A	1.64	NFKBIA	1.26	14.88	17.01
ANGPT2	1.61	N/A	1.61	AKT3	12.56	N/A	14.78
TRAF6	1.50	N/A	1.61	FN1	6.14	N/A	5.46
PRKCE	1.52	N/A	1.57	PIK3R3	5.63	N/A	4.62
FIGF	2.56	N/A	N/A	c-Jun	1.82	2.40	4.06
DIRAS3	-2.52	N/A	N/A	FGG	7.33	N/A	N/A
IRS1	-1.61	N/A	-1.88	HMOX1	1.81	1.70	2.80
GNB3	-2.12	N/A	-1.67	IL1RAP	2.32	N/A	2.34
GNAI1	-1.90	N/A	-2.21	Ferritin	1.98	N/A	2.50
GNG5	-2.19	N/A	-2.21	NR3C1	2.03	N/A	2.10
CR2	-2.41	N/A	-2.57	MAP3K1	1.66	N/A	2.27
RHOU	-3.40	-2.22	-6.72	MRAS	1.60	N/A	1.64
				TNFRSF1A	1.61	N/A	1.60
<b>IL-6 Signaling</b>	$\rho^0$	TNF	$\rho^0$ TNF	JAK2	1.58	N/A	1.58
CXCL8	8.33	189.61	754.67	TRAF6	1.50	N/A	1.61
AKT3	12.56	N/A	14.78	TRAF2	-2.46	N/A	N/A
MDR1	5.96	N/A	6.11				
PIK3R3	5.63	N/A	4.62	<b>NRF2-mediated Oxidative Stress Response</b>	$\rho^0$	TNF	$\rho^0$ TNF
JUN	1.82	2.40	4.06	SQSTM1	2.11	3.02	5.25
IL1RAP	2.32	N/A	2.34	PIK3R3	5.63	N/A	4.62
IRS2	1.91	N/A	1.72	TXNRD1	1.98	1.98	4.46
MRAS	1.60	N/A	1.64	JUN	1.82	2.40	4.06
TNFRSF1A	1.61	N/A	1.60	HMOX1	1.81	1.70	2.80
JAK2	1.58	N/A	1.58	HSPB8	3.01	N/A	2.84
TRAF6	1.50	N/A	1.61	FTL	1.98	N/A	2.50
TRAF2	-2.46	N/A	N/A	DNAJB5	1.83	N/A	2.46
IRS1	-1.61	N/A	-1.88	EPHX1	2.00	N/A	2.11
				MAP3K1	1.66	N/A	2.27
<b>Leukocyte Extravasation Signaling</b>	$\rho^0$	TNF	$\rho^0$ TNF	IRS2	1.91	N/A	1.72
MMP13	42.80	N/A	54.66	GCLC	1.65	N/A	1.94
ICAM1	1.50	6.70	21.47	MRAS	1.60	N/A	1.64
MMP7	3.02	10.25	14.51	PRKCE	1.52	N/A	1.57

**Leukocyte Extravasation Signaling (continued)**

MMP19	3.10	2.89	9.18
ITGB3	7.03	N/A	7.03
CXCR4	2.38	5.32	5.23
PIK3R3	5.63	N/A	4.62
MMP1	9.25	N/A	N/A
MMP16	5.82	N/A	N/A
SELPLG	2.57	N/A	2.58
RASSF5	1.73	N/A	2.11
IRS2	1.91	N/A	1.72
ITGA2	1.51	N/A	1.77
ITGB1	1.60	N/A	1.51
PRKCE	1.52	N/A	1.57
MMP28	2.68	N/A	N/A
ACTA2	1.52	N/A	N/A
VAV2	-1.71	N/A	N/A
IRS1	-1.61	N/A	-1.88
CLDN7	-1.85	N/A	-1.79
GNAI1	-1.90	N/A	-2.21
CLDN22	-57.60	N/A	N/A

**Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses**

	$\rho^0$	TNF	$\rho^0$ TNF
CXCL8	8.33	189.61	754.67
MDA-5	1.44	4.56	14.67
TLR3	2.87	2.79	8.75
PIK3R3	5.63	N/A	4.62
RIG-1	1.67	2.44	5.36
MYD88	1.28	1.17	1.94
TLR1	2.44	N/A	1.57
IRS2	1.91	N/A	1.72
TRAF6	1.50	N/A	1.61
PRKCE	1.52	N/A	1.57
TGFB3	2.81	N/A	N/A
TGFB2	2.28	N/A	N/A
IRS1	-1.61	N/A	-1.88
IL17D	-1.85	N/A	-2.11
SYK	-3.92	N/A	-3.59

**Tec Kinase Signaling**

	$\rho^0$	TNF	$\rho^0$ TNF
PIK3R3	5.63	N/A	4.62
TNFSF10	3.20	N/A	5.00
FAS	2.01	1.90	3.68
RND3	2.07	1.83	3.30
TNFRSF10B	1.50	1.86	2.83
STAT4	2.48	N/A	1.99
IRS2	1.91	N/A	1.72
ITGA2	1.51	N/A	1.77
MRAS	1.60	N/A	1.64
JAK2	1.58	N/A	1.58
ITGB1	1.60	N/A	1.51
PRKCE	1.52	N/A	1.57
ACTA2	1.52	N/A	N/A
PAK6	-1.55	N/A	N/A
VAV2	-1.71	N/A	N/A
DIRAS3	-2.52	N/A	N/A
IRS1	-1.61	N/A	-1.88
GNB3	-2.12	N/A	-1.67
GNAI1	-1.90	N/A	-2.21
GNG5	-2.19	N/A	-2.21
RHOU	-3.40	-2.22	-6.72

**NRF2-mediated Oxidative Stress Response (continued)**

ACTA2	1.52	N/A	N/A
CLPP	-1.61	N/A	N/A
IRS1	-1.61	N/A	-1.88
SCARB1	-2.44	N/A	-2.10

**LPS-stimulated MAPK Signaling**

	$\rho^0$	TNF	$\rho^0$ TNF
PIK3R3	5.63	N/A	4.62
c-Jun	1.82	2.40	4.06
IRS2	1.91	N/A	1.72
MRAS	1.60	N/A	1.64
PRKCE	1.52	N/A	1.57
IRS1	-1.61	N/A	-1.88

**B Cell Receptor Signaling**

	$\rho^0$	TNF	$\rho^0$ TNF
DAPP1	7.08	9.87	48.81
AKT3	12.56	N/A	14.78
ETS1	3.92	3.68	11.26
MAP3K8	2.56	5.02	9.16
PIK3R3	5.63	N/A	4.62
CREB5	3.16	N/A	5.67
JUN	1.82	2.40	4.06
GAB2	2.96	N/A	3.60
PAG1	3.06	N/A	2.31
MAP3K1	1.66	N/A	2.27
RASSF5	1.73	N/A	2.11
IRS2	1.91	N/A	1.72
NFAT5	2.04	N/A	1.54
MRAS	1.60	N/A	1.64
MAP3K2	1.46	N/A	1.71
VAV2	-1.71	N/A	N/A
CARD11	-2.18	N/A	N/A
IRS1	-1.61	N/A	-1.88
EGR1	-2.47	N/A	-3.64
Syk	-3.92	N/A	-3.59
MEF2C	-4.85	-1.89	-6.67
IL1RAP	2.32	N/A	2.34
MAP3K1	1.66	N/A	2.27
TRAF6	1.50	N/A	1.61
ADCY3	-1.77	N/A	N/A
JUN	1.82	2.40	4.06
SYK	-3.92	N/A	-3.59

**Toll-like Receptor Signaling**

	$\rho^0$	TNF	$\rho^0$ TNF
IRAK2	2.73	8.00	15.70
TLR3	2.87	2.79	8.75
JUN	1.82	2.40	4.06
TLR1	2.44	N/A	1.57
MAP3K1	1.66	N/A	2.27
TRAF6	1.50	N/A	1.61

**Barrier Function Signaling**

	$\rho^0$	TNF	$\rho^0$ TNF
AKT3	12.56	N/A	14.78
JUN	1.82	2.40	4.06
PPP2R5B	2.24	N/A	3.23
ARHGEF2	1.69	N/A	1.89
TNFRSF1A	1.61	N/A	1.60
TGFB3	2.81	N/A	N/A
TGFB2	2.28	N/A	N/A
ACTA2	1.52	N/A	N/A
CDK4	-1.76	N/A	-1.60
CLDN7	-1.85	N/A	-1.79
NUDT21	-1.79	N/A	-1.87
PRKAR1B	-2.20	N/A	-1.68
NECTIN3	-1.96	N/A	-2.36
VT11A	-2.10	N/A	-2.36
CLDN22	-57.60	N/A	N/A