

ADVANCED HEALTHCARE MATERIALS

Supporting Information

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Engineering Inflammation-Resistant Cartilage: Bridging Gene Therapy and Tissue Engineering

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Supporting Information

Supplementary figures

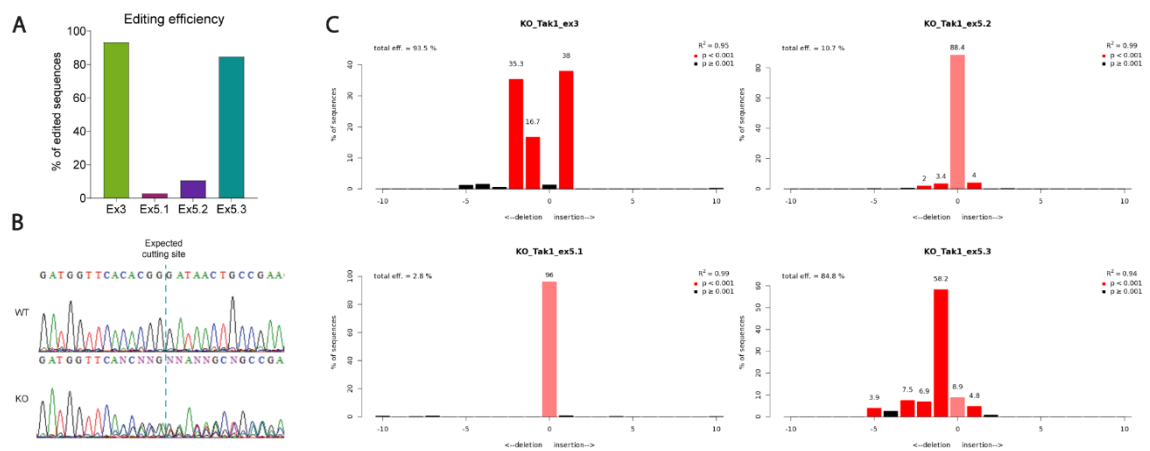


Figure S1. Sanger sequencing of KO performed with different guide RNAs. (A) Indels analysis of 4 different guide RNAs, **(B)** Sanger sequencing of a representative WT and KO sequence, with marking on expected cutting site. **(C)** Indel analysis performed with Tide.

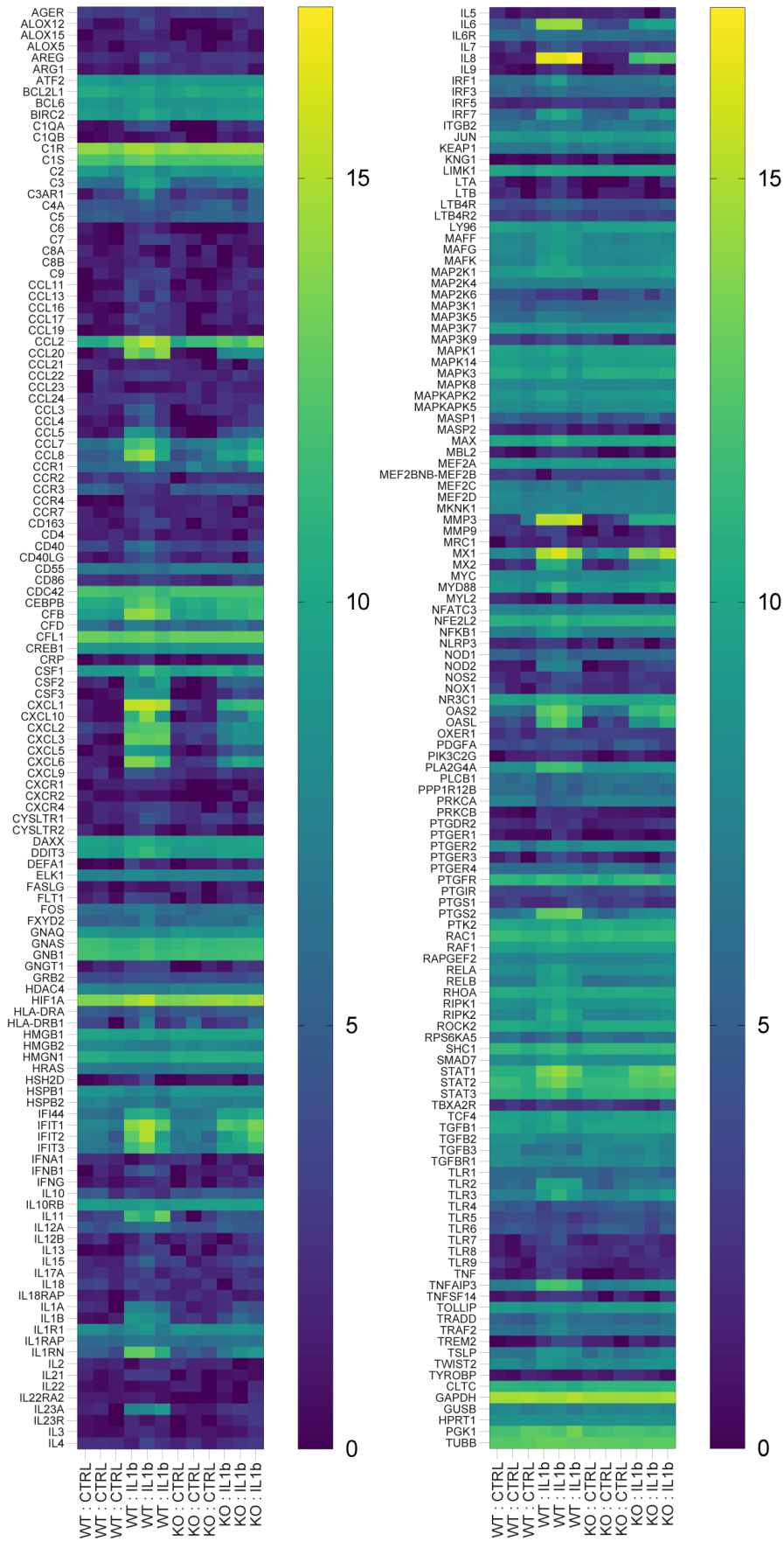


Figure S2. Heatmap of expressed genes by WT and KO samples, with or without IL-1 β treatment (n=3).

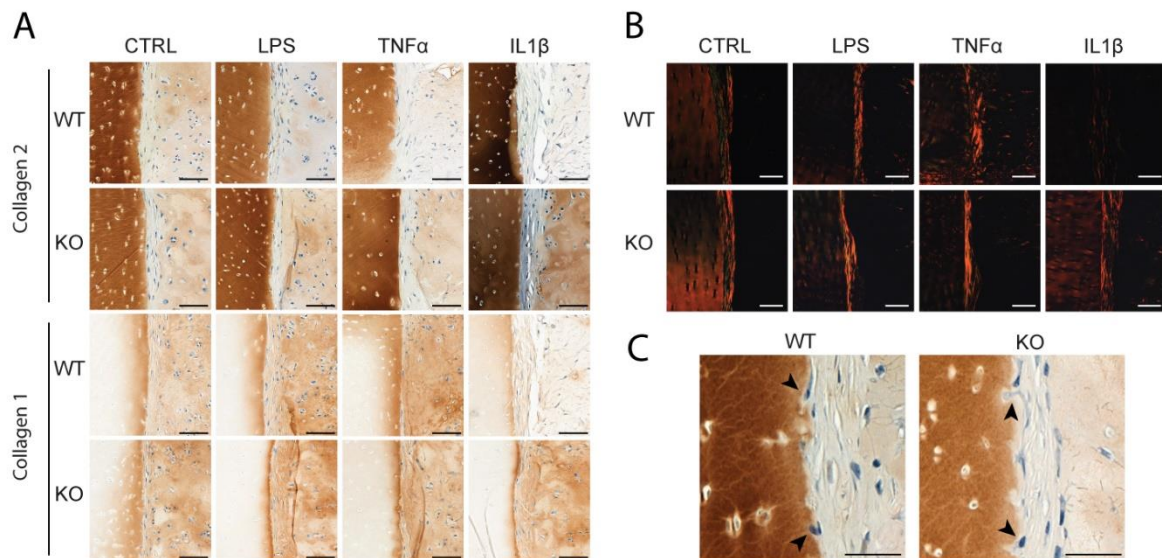


Figure S3. TAK1-KO cells produce highly aligned collagen 1 fibers at the interface with bovine rings in inflamed conditions and actively migrate into the mature bovine cartilage. (A) Closeup of the interface between the mature cartilage bovine rings (left) and the neocartilage (right) from WT or KO cells. Scale bar, 100 µm. (B) Polarized light microscopy of the collagen fibers deposited from WT or KO cells at the interface between the bovine rings (left) and the newly formed cartilage (right). Scale bar, 100 µm. (C) High magnification of interface between bovine cartilage (left) and WT or KO cells (right); representative image of control conditions, human cells are indicated with black arrows. Scale bar, 50 µm.

Supplementary Tables

Table S1. Sequences of possible analyzed off-targets. Mismatches are marked in bold.

Off target								
Identifier	gRNA sequence	PAM	Score	Mismatches	Gene	Locus	Primer Fw	Primer Rv
TAK1 KO	AATATTAGGATGGTT CACAC	GG G	N/A		MAP3 K7	chr6:+90568 587		
OT 1	AATAGTA A TATGGTT CACAC	TG G	23	3		chr4:+11545 6560	CAAGGTGACACCAGA GTGGG	TTGGGGTGCGCATGTA AGTA
OT 2	CA A ATTAGGATGGT TCACTC	TG G	24	3		chr16:+8495 8643	ACTAGTCTGAGGTCCC CCAC	GCCAACAGACAACAGT GCAG
OT 3	AGTATTA A GGAGGT TCACAC	CG G	24	4		chr7:- 67608135	TGAGAGAGATGGGAG CGTGT	ACACGCAAAGAGTCCCT GAG
OT 4	AACAT C AGGATGAT TCACAC	CA G	30	3		chr3:- 9036920	GAGGGAAGACCCTGA GACCT	CAAATGCTTTCCAGTGG CCC
OT 5	ATTCTTAGGATG- TTCACAC	AG G	33	3		chr5:- 128930785	ATTAAGGCTGGGCTG CCTAC	ACCATGCCTAAATAAGG TAGCAC
OT 6	AGTTTTATGATGGTT TACAC	TG G	36	4		chr13:+7134 2904	TGGACAGGTGCACAT TTTTGTC	TAGAGGATGTCGTTGTC ATGC

OT 7	AACATTAAGATG- TTCACAC	AA G	38	3		chr4:- 31998396	TCACAATTCAGGGG GCCAA	ACTAACCATTATTTTGT CA
OT 8	GTTATTAGGAAGTTT CACAC	GA G	44	4		chr15:+6066 8518	AGCGACATAATCAGC CGGAG	GGCATTTCATTGGCTG CGT

Table S2. Multiplex inflammatory genes expression in WT and *TAK1*-KO cells, in control or IL-1 β treated conditions.

Probe Name	WT : CTR L	WT : CTR L	WT : CTR L	WT : IL- 1 β	WT : IL- 1 β	WT : IL- 1 β	KO : CTR L	KO : CTR L	KO : CTR L	KO : IL- 1 β	KO : IL- 1 β	KO : IL- 1 β
AGER	3.16	2.75	2.64	3.47	3.04	2.08	2.95	3.16	2.87	3.73	3.24	2.52
ALOX12	2.03	0.43	0.47	1.88	3.88	2.08	0	0	0.06	0.73	1.51	2.52
ALOX15	0	1.43	1.47	2.3	2.3	1.34	0	0.99	0.06	0	2.24	0.52
ALOX5	0.7	1.43	0	1.3	1.71	1.76	2.28	0.99	0.06	1.32	1.51	0.52
AREG	2.03	2.43	1.79	1.3	4.52	3.22	1.95	1.99	2.87	2.73	2.92	2.52
ARG1	0.7	1.43	1.06	0.3	2.71	2.08	2.54	1.99	2.38	2.32	2.73	0.52
ATF2	9.29	9.19	8.41	8.93	9.32	8.46	9.11	9.12	9.02	9.01	9.04	9.03
BCL2L1	10.4	10.4 2	9.83	9.53	10.1 8	9.13	9.8	10.4	9.95	9.99	9.92	10.6 5
BCL6	8.85	8.93	8.34	9.37	9.73	8.56	8.7	8.7	8.78	9.1	8.97	9.33
BIRC2	9.53	9.37	8.79	9.18	10.5 9	9.56	8.79	9.52	8.83	9.49	9.69	9.83
C1QA	0.7	0.43	1.06	3.47	4.62	3.76	0	0	0.06	2.73	1.92	3.32
C1QB	0	0.43	1.06	0.3	0.71	1.34	1.95	0	0.06	1.73	0.92	1.52
C1R	14.2 2	14.2	13.4	14.5 6	14.7 6	13.7 6	14.3 6	13.9 9	14.2 4	14.3 2	14.5 1	14.3 3
C1S	12.1 4	12.1 2	11.5	12.6 8	13.1 9	12.0 5	12.0 8	12.1 7	12.1 3	12.2 6	12.3 4	12.5
C2	9.32	9.22	7.8	9.23	9.43	7.9	9.28	9.06	8.68	8.76	9.25	9.3
C3	6.27	5.75	5.74	9.54	10.3 8	9	4.95	5.58	5.58	7.23	6.86	7.41
C3AR1	0.7	3.02	3.17	5.91	8.49	4.22	1.95	3.8	3.38	2.9	1.92	5.42
C4A	4.29	4.75	4.28	4.3	5.41	4.34	3.86	4.45	5.55	5.94	3.73	5.6

C5	4.87	5.24	4.96	4.1	4.52	3.76	5.24	5.69	5.45	5.62	5.09	5.8
C6	1.29	0.43	0	1.88	2.71	1.34	0	0	0.06	0	0	1.52
C7	0.7	0.43	0	2.3	3.71	3.56	2.28	1.58	0.06	1.73	0.92	1.52
C8A	2.03	0.43	1.06	2.3	0.71	0	2.28	0	2.06	0	0.92	0.52
C8B	1.29	1.43	1.06	1.88	2.71	0.76	2.28	0.99	1.64	0	1.92	0.52
C9	0	2.02	1.06	2.88	3.3	3.66	1.54	0	0.06	0.73	2.24	2.84
CCL11	0	0.43	0.47	4	2.71	3.22	0	1.58	0.06	1.32	2.51	1.52
CCL13	0	1.43	1.79	4	1.71	4.08	0.95	1.58	1.06	2.73	1.51	2.52
CCL16	0.7	0.43	0	2.3	4.04	2.76	1.95	0	0.06	2.06	1.51	2.1
CCL17	2.29	0.43	1.06	4	2.71	2.76	1.95	0	1.64	2.32	0.92	2.52
CCL19	0	0.43	0.47	1.88	3.52	2.34	1.95	0	0.06	0.73	0.92	0.52
CCL2	10.2	10.1	11.5	14.0	15.4	14.4	9.98	11.6	11.6	12.7	11.8	13.6
	7	4	7	8	9	2		1	6	1	5	2
CCL20	0	1.43	2.06	13.5	12.3	14.0	0.95	0	0.06	7.81	8.68	8.5
					3	8						
CCL21	2.29	2.02	0.47	2.3	1.71	2.08	1.95	1.58	0.06	2.06	0	3.1
CCL22	0	3.02	2.06	2.88	3.52	3.22	1.95	1.99	2.06	1.32	3.09	2.1
CCL23	0	2.43	1.79	0.3	0.71	0.76	0.95	2.58	1.06	2.32	1.51	1.52
CCL24	1.7	2.43	2.64	2.88	3.52	2.34	2.28	2.58	1.06	2.54	2.24	2.1
CCL3	2.03	2.02	1.06	4.76	5.76	2.56	0	1.58	2.38	2.54	1.92	3.32
CCL4	0.7	1.43	0.47	2.88	4.88	2.56	0	0	0.06	1.32	2.24	3.32
CCL5	1.29	0.43	1.47	9.07	8.92	5.56	0.95	0	0.06	3.82	5.38	5.98
CCL7	6.16	5.82	7.23	11.6	12.4	9.94	5.79	6.76	7.01	8.78	7.89	10.0
				4	7							9
CCL8	4.61	4.75	5.72	13.6	14.5	10.1	3.66	4.74	6.66	9.8	9.46	11.4
				3	4	6						3
CCR1	5.68	5.56	6	6.4	8.95	5	5	7.76	6.01	6.72	5.17	8.93
CCR2	2.29	3.43	2.28	3.76	4.04	3.66	0	1.99	2.87	2.32	2.51	2.52
CCR3	5.4	5.75	4.72	2.88	3.04	1.76	5.28	4.45	4.97	5.64	5.31	4.6
CCR4	0	0.43	0	2.62	2.3	1.76	1.54	1.58	2.38	1.32	2.24	0.52
CCR7	1.7	0.43	1.06	2.88	3.52	1.34	1.54	1.99	2.06	1.73	0	2.1

CD163	1.7	1.43	0.47	1.88	3.71	3.46	1.54	0	2.06	1.73	1.92	1.52
CD4	1.29	1.43	2.28	1.3	2.71	0.76	1.54	1.58	1.06	1.32	0	2.52
CD40	3.61	3.89	2.28	5.72	6.92	4.28	3.41	3.69	2.64	3.43	3.38	4.32
CD40LG	1.29	0.43	1.47	3.62	4.8	3.34	1.54	0.99	2.06	2.32	0	3.32
CD55	6.91	7.03	6.52	6.15	6.74	5.8	7.15	7.21	7.29	6.78	6.73	6.96
CD86	2.51	2.43	1.79	2.3	3.71	3.34	2.28	1.99	1.06	1.73	3.51	3.1
CDC42	12.1	12.1	11.7	11.7	12.2	11.2	12.1	12.0	12.0	12.0	12.1	12.1
	6		3	7	8	3	1	9	2	1	2	4
CEBPB	10.4	10.4	9.99	11.9	12.8	11.8	10.0	10.5	10.2	11.3	11.1	11.5
	4	7		6	9	5	3	5	1	9	7	6
CFB	9.4	9.45	8.88	14.1	14.4	12.9	9.38	10.1	9.74	10.8	10.8	11.8
				4	6	4		5		9	9	1
CFD	6.42	6.31	4.28	7.36	7.14	5.25	6.14	4.99	5.58	5.76	6.61	5.04
CFL1	13.1	13.1	12.6	12.9	13.2	12.2	13.0	12.9	12.9	12.8	13.0	13.0
	9	9		8	8	9	8	6	8	9	6	6
CREB1	8.99	8.87	8.48	8.8	9.17	8.44	8.98	8.74	8.73	8.83	8.85	8.95
CRP	0	1.43	0.47	1.3	2.3	0	0.95	0	1.06	0.73	0.92	2.84
CSF1	8.95	8.98	9.28	9.27	11.6	10.2	9.12	9.62	10.0	10.6	9.52	10.6
					8	2			9	2		1
CSF2	1.7	2.43	0	8.4	7.22	9.74	0.95	0	1.06	5.02	5.85	5.1
CSF3	0	0.43	1.06	8.91	8.71	8.62	0	0	1.06	2.06	4.01	3.32
CXCL1	1.7	0.43	0.47	15.3	15.5	14.9	3.54	2.58	1.06	10.4	11.3	11.5
				1	9	7				4	3	3
CXCL10	1.29	0.43	0.47	10.9	14.1	8.6	0	1.58	1.06	6.18	5.97	9.65
				3								
CXCL2	3.61	2.43	2.06	12.0	12.3	12.5	3.12	3.16	3.76	7.33	8.93	8.25
				7	7	2						
CXCL3	2.51	0.43	0	13.0	12.7	13.1	1.95	3.31	2.38	7.07	8.46	8.4
				8	8	5						
CXCL5	0	1.43	1.06	9.38	8.8	8.29	0.95	0	1.06	3.64	5.38	4.98

CXCL6	1.7	1.43	0	13.8	13.7 9	11.7 8	2.28	2.8	3.23	8.12	10.2 7	9.62
CXCL9	1.7	2.75	0.47	4.69	4.62	3.22	2.54	1.58	1.64	3.19	1.92	2.1
CXCR1	0	1.43	1.47	2.3	2.3	2.08	0.95	0	0.06	0.73	0	1.52
CXCR2	1.7	0.43	0.47	1.3	0.71	0.76	0	0	0.06	0	2.24	0.52
CXCR4	0.7	2.02	1.79	3.1	3.52	3.84	2.28	1.99	0.06	2.32	0	2.84
CYSLTR 1	0.7	2.02	1.47	2.3	4.62	3.93	2.28	1.99	3.38	3.32	1.92	3.84
CYSLTR 2	2.03	0.43	0	2.3	2.71	0.76	0	1.58	2.06	0.73	0	0.52
DAXX	9.74	9.67	9.13	10.2 5	10.6 1	9.57	9.41	9.57	9.36	9.5	9.59	9.85
DDIT3	9.37	9.39	8.74	10.3 5	11.3 1	10.2 8	9.02	9.02	9.04	9.57	9.54	9.73
DEFA1	0	0.43	0	3.62	1.71	2.08	0	0.99	1.06	2.32	0.92	2.52
ELK1	7.58	7.58	7.08	8.13	8.17	7.29	7.42	7.52	7.57	7.47	7.36	7.53
FASLG	0.7	1.43	0	1.3	0.71	0.76	1.95	2.31	0.06	1.73	1.92	0.52
FLT1	1.29	2.43	0.47	3.76	3.3	3.08	0	1.99	0.06	1.32	2.24	1.52
FOS	6.24	5.89	5.86	6.71	7.36	5.95	6.29	5.42	6.04	6.45	6.59	6.07
FXD2	5.06	4.95	5.49	5.1	7.12	5	5.41	6.37	6.34	6.36	5.7	7.52
GNAQ	9.01	8.88	8.17	8.07	8.6	7.87	9.11	8.92	8.65	8.61	8.98	8.92
GNAS	11.8 5	11.7 3	11.1	11.0 2	11.7 7	10.9 3	11.2 5	11.5 2	11.2	11.5 1	11.5 4	11.5 7
GNB1	11.9	11.8 5	11.4 3	11.5 2	12.1 3	11.3 8	11.6 6	11.8 4	11.5 8	11.7 3	11.8 4	11.9 8
GNGT1	0.7	2.02	1.47	3.3	3.52	3.56	0	0	1.64	0.73	2.92	2.52
GRB2	3.87	3.75	3.56	4.1	4.3	4.22	3.66	4.08	4.15	3.82	3.83	4.52
HDAC4	7.75	7.55	6.81	7.06	7.11	6.8	7.71	7.35	7.59	7.7	7.67	7.46
HIF1A	13.7 8	13.7	13.5 9	14.4 5	15.3 8	13.4 6	13.6 8	13.8 9	14.2	14.4 4	14.0 4	14.6 3

HLA-DRA	5.03	4.82	3.79	4.54	6.11	3.66	4.76	4.63	4.15	4.94	4.88	5.1
HLA-DRB1	3.79	3.6	0	3.62	7.56	2.08	3.28	6.42	2.06	3.06	3.24	6.04
HMGB1	9.88	9.96	9.44	9.48	9.89	9.2	9.93	9.91	9.72	9.89	9.94	9.82
HMGB2	8.06	7.89	7.92	7.19	6.74	6.74	8.14	7.55	8.07	7.94	7.71	7.16
HMGNI	10.58	10.51	9.93	9.94	9.97	9.46	10.55	10.47	10.55	10.48	10.43	10.42
HRAS	7.02	6.77	6.58	6.51	6.57	6.02	6.81	7.01	6.83	6.83	6.84	7.01
HSH2D	0	0.43	1.47	1.88	4.3	0	0	0.99	1.06	1.32	0	2.1
HSPB1	8.92	8.8	8.54	7.67	8.09	7.08	9.05	8.68	8.78	8.72	8.74	8.66
HSPB2	7.55	7.76	6.55	6.53	7.4	5.86	7.55	7.62	7.05	6.84	7.28	7.23
IFI44	6.35	6.08	5.58	10.29	10.86	9.5	6.54	6.4	6.81	9.86	9.66	10.63
IFIT1	7.85	7.75	6.85	14.04	15.13	12.88	7.19	7.19	7.53	12.36	11.77	13.59
IFIT2	7.05	6.92	4.28	12.67	15.01	9.5	6.54	7.29	5.15	8.97	10.45	12.78
IFIT3	6.81	6.66	5.68	11.57	12.89	10.18	6.71	6.26	6.45	9.88	9.82	11.29
IFNA1	2.29	2.43	1.79	0.3	1.71	2.34	2.54	2.8	0.06	2.06	0.92	1.52
IFNB1	0	2.02	1.06	3.88	5.3	3.76	0	1.58	1.06	1.32	2.24	0.52
IFNG	0.7	1.43	0.47	1.3	1.71	2.56	0	1.99	0.06	2.06	1.51	2.84
IL10	4.79	4.95	2.06	3.76	3.04	2.08	4.66	4.16	5.45	5.54	4.92	4.98
IL10RB	9.24	9.29	9.06	8.97	9.75	8.7	9.27	9.52	9.49	9.42	9.37	9.42
IL11	2.7	3.6	3.72	11.71	10.7	13.12	3.12	0	2.87	4.86	4.73	4.32
IL12A	4.79	3.89	4.83	5.51	6.55	6.02	4.6	4.08	3.97	5.49	4.78	4.76
IL12B	1.7	2.75	0.47	1.3	3.71	0.76	1.54	2.58	1.06	0	2.24	3.32
IL13	0	0.43	0	1.88	3.04	3.22	0	2.31	0.06	2.32	1.51	2.84
IL15	2.03	1.43	1.47	3.76	5.57	3.08	3.28	0.99	2.06	2.9	3.92	4.1

IL17A	2.03	2.43	1.79	2.62	3.52	1.34	2.54	2.8	1.64	1.73	2.92	2.1
IL18	3.29	3.6	1.79	3.62	2.71	3.34	1.54	1.58	2.64	0	2.73	3.1
IL18RAP	1.29	1.43	0	1.3	3.04	1.76	1.54	2.58	1.64	2.32	0.92	1.52
IL1A	2.29	2.02	0	7.53	7.31	5.82	2.54	0.99	1.64	2.32	4.68	3.98
IL1B	0.7	0.43	1.47	9.04	8.38	7.73	2.28	2.8	1.64	4.06	6.13	4.84
IL1R1	8.3	8.34	7.02	8.25	9.11	6.77	8.65	8.52	8.34	8.33	8.61	8.46
IL1RAP	5.7	5.79	5.56	6.49	6.88	6.28	6.38	5.82	6.12	6.35	6.55	6.32
IL1RN	5.23	5.13	3.72	12.7 6	12.9 5	10.7 2	4.35	5.31	3.97	6.72	8.42	9.13
IL2	2.03	1.43	1.79	0.3	2.3	2.08	2.95	1.58	1.64	2.06	0	0.52
IL21	1.7	0.43	1.06	2.88	3.04	2.76	0	1.58	0.06	0.73	0.92	0.52
IL22	0.7	0.43	1.06	0.3	0.71	0.76	1.54	1.58	0.06	1.32	0	2.1
IL22RA2	1.29	1.43	1.06	1.3	1.71	0.76	0	0	0.06	0.73	0	2.52
IL23A	1.7	2.02	0	7.58	7.77	9.27	1.54	0.99	1.06	2.54	3.09	2.84
IL23R	0.7	0.43	0	1.88	0.71	1.76	0	0.99	0.06	1.32	1.92	2.84
IL3	0.7	0.43	0.47	1.88	2.3	1.34	0	0.99	1.06	0.73	0.92	2.1
IL4	2.29	2.43	2.28	1.3	3.71	2.34	1.54	2.58	1.06	2.06	2.51	2.84
IL5	2.29	0.43	1.47	1.3	1.71	1.34	1.54	1.58	2.06	1.73	0	2.52
IL6	4.7	4.24	5.86	14.2 3	14.4 6	14.4 1	4.28	3.45	3.64	8.77	9.62	9.69
IL6R	6.38	6.08	5.2	6.54	6.44	5.71	6	6.65	6.21	5.8	6.07	5.87
IL7	1.7	3.24	1.06	3.88	5.04	4.08	2.54	2.58	2.87	3.64	2.92	3.32
IL8	0.7	1.43	1.47	16.4	16.3 4	17.0 2	0.95	1.58	1.64	11.6 2	12.6 1	12.3 9
IL9	1.29	0.43	0	1.88	3.04	1.76	0	0	1.64	2.32	2.51	0.52
IRF1	6.21	6.19	6.03	7.76	9.51	6.77	6.35	6.43	6.45	6.57	6.73	7.64
IRF3	5.59	6.05	5	5.76	6.64	5.54	5.71	5.97	6.31	6.14	5.97	6.32
IRF5	2.03	1.43	2.06	1.88	2.71	2.93	2.54	2.58	2.87	2.06	2.92	1.52
IRF7	5.38	5.43	4.38	9.21	10.2 6	8.79	5.51	5.31	4.87	8.43	8.17	9.41
ITGB2	6.5	6.31	7.23	6.47	7.12	6.99	5.86	6.63	7.3	7.08	5.92	6.56

MAPK3	10.4	10.4	9.68	9.58	10.4 2	8.9	10.4 3	10.7 3	10.4 9	10.3	10.3 4	10.8 6
MAPK8	8.05	7.95	7.54	8.15	8.32	7.95	7.68	7.81	7.81	7.95	8.11	7.64
MAPKA PK2	8.83	8.83	8.35	9.55	9.84	8.41	8.91	8.85	8.83	8.92	8.95	9.3
MAPKA PK5	8.17	8.19	7.7	8.33	8.66	7.6	8.08	8.28	8.26	8.16	8.33	8.46
MASP1	4.91	5.48	4.23	4.54	4.71	3.93	5.71	3.8	4.52	4.32	5.9	3.84
MASP2	2.03	1.43	1.06	1.88	2.71	0.76	1.54	0.99	2.06	0.73	0	1.52
MAX 3	10.0	9.98	9.48	10.1 7	11.2	9.82	9.93	9.91	9.93	10.1	10.1 1	10.3 5
MBL2	1.29	0.43	0	1.88	2.71	2.56	1.54	0	0.06	1.32	0	0.52
MEF2A	9.17	9.22	8.79	8.59	9.39	9	9.14	9.38	9.05	9.11	9.21	9.58
MEF2B NB- MEF2B	2.7	3.02	2.64	0.3	3.3	3.34	3.12	3.16	3.06	3.43	2.24	3.98
MEF2C	7.63	7.51	6.28	6.85	7.51	5.82	7.58	7.1	7.43	7.35	7.55	7.52
MEF2D	8.09	8.03	7.23	7.55	7.3	7.47	7.73	7.74	7.57	7.55	7.9	7.55
MKNK1	7.84	7.68	7.34	7.73	8.07	7.25	7.78	7.73	7.79	7.71	7.87	7.67
MMP3	2.87	2.43	7.14	15.2 1	15.0 5	15.5 5	1.54	2.58	3.97	10.2 6	10.3 7	10.5 9
MMP9	2.51	3.02	1.79	3.47	3.52	0.76	0	2.31	0.06	1.32	2.24	1.52
MRC1	0	2.02	1.47	1.3	3.52	1.34	2.54	1.58	1.64	1.73	2.51	1.52
MX1	7.83	8.03	6.97	14.9	16.0 9	14.0 3	7	8.89	8.04	13.9 3	13.3 8	15.1 7
MX2	1.29	2.75	1.79	10.2 6	10.7 7	8.13	1.95	0.99	2.87	6.99	7.36	8.64
MYC	8.22	8.03	7.76	8.12	8.11	7.72	8.33	8.13	7.89	8.23	8.57	8.56
MYD88	9.04	8.82	7.89	10.1 6	11.3 7	9.34	8.96	8.88	8.85	9.77	9.67	10.6
MYL2	2.29	2.02	1.06	0.3	2.71	0.76	2.28	1.99	0.06	0	1.51	0.52

NFATC3	7.62	7.6	7.09	7.68	8.1	7.13	7.76	7.77	7.77	7.69	7.75	7.86
NFE2L2	10.7	10.6	10.2	10.3	11.4	10.1	10.6	10.7	10.9	11.0	10.8	11
	7	7	2	7		6	8	7	1	1	7	
NFKB1	7	6.89	6.56	8.8	9.7	8.1	6.78	6.68	6.74	6.84	7.19	7.37
NLRP3	1.7	1.43	1.79	3.1	3.04	0.76	2.28	0	2.64	2.06	0	2.1
NOD1	5.29	5.34	4.12	5.91	6.69	4.8	5.35	5.38	5.73	5.66	5.68	6.04
NOD2	1.29	1.43	0.47	7.09	7.68	6.72	0	0.99	1.06	3.06	3.83	3.98
NOS2	2.29	1.43	2.93	2.3	4.17	4.4	2.28	2.58	1.64	3.32	2.51	2.52
NOX1	3.61	1.43	0.47	3.1	4.04	3.08	1.95	1.99	1.64	2.9	3.24	2.1
NR3C1	9.82	9.8	9.41	10.5	11.0	10.2	10.0	10.0	9.93	9.86	10.1	10.1
				2	6	6	4	3			2	7
OAS2	6.39	6.16	5.28	12.5	13.3	11.6	6.22	5.63	6.36	11.3	11.0	12.2
				3	8	9				6	5	3
OASL	3.51	4.43	2.47	11.3	12.9	10.3	1.54	4.16	2.64	8.73	8.22	10.9
				1	2	4						4
OXER1	2.29	3.24	1.79	3.62	3.88	2.93	3.28	3.31	3.38	3.19	2.92	2.84
PDGFA	3.79	3.43	4.23	3.62	4.41	4.71	4.12	2.99	5.1	5.19	4.44	2.84
PIK3C2	0	1.43	1.47	2.3	2.71	2.08	0.95	0	1.06	2.32	0.92	0.52
G												
PLA2G4	8.24	8.49	8.05	11.6	11.9	11.2	8.4	8.04	8.39	8.93	9.11	9.24
A				6	3	9						
PLCB1	6.11	5.48	6.52	4.38	6.11	5.22	6.14	6.42	6.73	6.63	5.99	6.8
PPP1R1	6.03	6.19	5.78	4.62	5.88	4.71	5.98	6.43	5.67	6.02	6.01	5.56
2B												
PRKCA	7.48	7.58	7.33	4.88	5.84	6.08	7.49	7.45	7.63	7.38	7.11	7.26
PRKCB	0.7	0.43	0	2.62	2.3	2.34	1.95	0.99	1.06	0.73	0.92	0.52
PTGDR2	2.29	2.02	1.47	3.1	2.3	2.93	0.95	1.58	1.64	1.73	2.51	3.1
PTGER1	1.29	0.43	0.47	0.3	2.71	1.34	0	0	1.06	0.73	0	0.52
PTGER2	8.06	7.95	5.85	8.26	8.53	7.6	8.61	8.73	8.35	8.1	8.75	8.72
PTGER3	1.29	2.75	0	2.88	4.17	2.76	1.54	2.58	1.06	0.73	0	2.84
PTGER4	5.97	5.64	5.62	5.79	5.88	6.34	5.28	7.01	6.76	6.3	4.44	5.84

PTGFR	11.1 2	11.0 9	10.4 3	11.4 9	11.1 7	10.5 6	11.2 2	10.0 2	11.0 8	11.3 1	11.6 2	10.6 9
PTGIR	3.51	3.24	3.28	3.3	4.8	3.93	3.12	3.58	3.52	4.26	3.24	4.1
PTGS1	2.51	3.43	2.06	1.88	2.3	4.08	3.41	2.58	3.23	3.19	1.92	2.1
PTGS2	6.15	6.24	7.71	12.7 4	12.8 7	13.2	6.46	5.12	6.15	7.86	8.44	8.39
PTK2	10.1 9	10.1 6	9.58	9.82	10.4 2	9.67	10.2 3	10.5 3	10.1 8	10.1 6	10.3 3	10.6 7
RAC1	11.4 9	11.4 3	10.9 6	10.9 1	11.6 1	10.6 8	11.1 4	11.3 5	11.0 4	11.2 7	11.4 2	11.3 5
RAF1	9.57	9.52	9.15	9.83	10.1 9	9.5	9.4	9.51	9.5	9.55	9.5	9.61
RAPGEF 2	7.63	7.37	7.19	7.87	8.03	7.46	7.45	7.55	7.43	7.55	7.72	7.76
RELA	8.27	8.28	7.91	9.27	10.1 6	8.59	8.24	8.23	8.19	8.27	8.5	8.58
RELB	6.9	6.74	6.75	9.2	9.64	8.53	5.98	6.14	6.23	6.72	6.83	7.12
RHOA	10.4 6	10.3 6	10.2	10.2 4	10.5 4	10.1	10.4 2	10.2 3	10.4 4	10.3 6	10.2 8	10.3 1
RIPK1	8.62	8.47	8	9.27	10.2	8.78	8.64	8.75	8.61	8.99	9.02	9.41
RIPK2	7.68	7.83	7.31	9.99	11.0 1	9.63	7.57	7.49	7.4	7.98	8.14	8.5
ROCK2	10.3	10.3 3	9.9	9.73	10.2	9.21	10.3 4	10.3 7	10.3 6	10.3 6	10.4 1	10.3 8
RPS6KA 5	6.06	6.56	4.72	5.76	6.94	4.56	6.63	6.5	5.76	5.69	6.65	6.32
SHC1	11.1 9	11.1 7	10.4 1	11.1 7	11.5 6	10.3 8	11.1	11.2 4	11.1 7	11.1 6	11.1 4	11.3 9
SMAD7	8.01	8.08	7.72	8.83	9.74	8.71	8.27	8.09	8.26	8.12	8.36	8.48
STAT1	10.7 5	10.7 4	10.6 7	13.4 7	14.4 3	13.0 1	10.6 9	10.7 6	10.9 1	12.8 2	12.5 3	13.4 7

STAT2	11.5 5	11.5 4	10.4 9	12.5 4	13.5 1	12.0 3	11.3 2	11.3 1	11.3 7	12.3	12.2 8	12.6 2
STAT3	10.9 7	10.9 8	10.5 1	10.9 1	11.5 9	9.77	11.0 1	10.9 7	11.2 7	11.3 7	11.1 7	11.3 5
TBXA2R	1.7	2.75	1.79	3.3	2.71	2.34	2.76	3.45	2.38	2.32	1.51	3.84
TCF4	9.68	9.6	9.41	9.53	10.5 2	9.05	9.32	9.26	9.99	10.0 4	9.54	9.75
TGFB1	10.1 2	9.92	9.07	9.68	10.3 1	8.85	9.93	9.97	9.89	9.87	9.91	10.2 7
TGFB2	8.62	8.41	8.51	7.49	7.41	6.97	7.89	7.94	8.51	8.48	8.25	7.52
TGFB3	8.13	8.15	6.01	6.49	6.71	5.48	8.17	7.65	7.34	7.33	8.17	7.28
TGFBR1	8.42	8.34	7.71	7.7	7.43	7.86	8.28	7.86	7.78	7.88	8.45	7.59
TLR1	5.85	5.56	5.54	6.34	5.3	5.43	5.31	4.69	5.81	6	5.9	4.91
TLR2	5.66	6.05	5.35	9.99	9.95	9.69	5.57	4.58	6.27	7.22	6.7	7.12
TLR3	7.08	7.19	7.03	9.29	11.0 1	8.99	7.45	7.64	7.65	8.93	8.5	9.75
TLR4	4.99	4.34	4.96	3.1	4.62	4.51	4.2	4.74	5.55	5.29	4.31	5.16
TLR5	3.7	3.89	4	3.3	3.71	2.56	3.28	4.24	4.45	4.64	3.73	4.42
TLR6	4.16	4.89	4.47	3.88	4.3	3.56	4.66	5.45	5.19	4.86	3.24	5.22
TLR7	1.29	0.43	2.64	3.3	4.41	1.76	0.95	1.99	2.06	2.73	2.24	1.52
TLR8	1.29	0.43	1.47	3.1	3.3	2.76	2.28	1.99	2.87	1.73	2.73	1.52
TLR9	2.51	1.43	0.47	3.3	2.71	2.08	1.95	1.58	1.06	2.06	2.24	2.1
TNF	1.29	0.43	1.06	2.62	3.52	1.34	0	0	1.06	0.73	1.51	2.52
TNFAIP 3	6.77	7.02	7.58	11.8 3	12.1 6	11.3 6	6.43	7.17	6.8	7.76	8.22	8.58
TNFSF1 4	0.7	1.43	1.06	2.62	3.04	2.76	1.95	0	2.38	1.32	0	2.52
TOLLIP	9.18	9.19	8.75	8.75	9.21	8.15	9.12	9.25	9.29	9.32	9.18	9.46
TRADD	5.35	4.75	4.56	6.38	7.31	5.82	6.06	5.94	5.27	5.76	5.28	6.16
TRAF2	6.29	6.34	5.86	7.1	7.99	6.66	6.54	6.6	6.45	6.59	6.51	6.87
TREM2	0	0.43	0.47	2.3	3.88	3.56	1.54	1.58	0.06	2.06	0.92	2.1

TSLP	6.47	6.36	6.38	9.04	8.84	8.26	5.81	7.38	6.1	6.8	7.45	8.33
TWIST2	8.1	8.1	7.07	9.07	8.66	7.51	8.21	8.13	7.92	8.47	8.66	8.59
TYROBP	0.7	0.43	1.79	1.3	0.71	0.76	1.54	0.99	2.38	2.06	1.51	0.52
CLTC	11.0	11.0	10.7	10.6	10.8	10.3	11.0	11.3	11.1	11.0	11.0	11.2
	8	1	1	1	8	3	2	2	9	5	3	2
GAPDH	14.8	14.7	14.9	14.6	14.5	15.1	14.5	14.6	14.5	14.6	14.5	14.7
		4	2	4	9			4	5	3	1	3
GUSB	7.86	8.02	6.99	7.55	7.78	6.79	7.82	7.6	7.4	7.69	7.97	7.56
HPRT1	8.58	8.64	8.77	8.35	8.23	8.37	8.78	8.55	8.71	8.67	8.73	8.52
PGK1	11.9	11.8	12.7	12.6	12.1	13.4	11.8	11.9	12.2	12.1	11.8	12.0
	1	5	3	1	9	3	1	1	1	6	1	1
TUBB	12.6	12.5	12.7	13.0	13.1	12.7	12.9	12.8	12.7	12.6	12.7	12.7
		6		6	4	9			6	1	7	8
NEG_A	0	1.58	2	0	1	1	2	1	1	2.81	1	1.58
NEG_B	1	2	1	1.58	2.32	3.32	1	0	1	1.58	1	0
NEG_C	2.32	0	2	3	0	1	2.58	2	2	3.17	1.58	1
NEG_D	2	1	2	1.58	0	1.58	2	2	1	1	2	1
NEG_E	2.58	2.32	2	1	2	2.32	2.81	2	2	2	1.58	2
NEG_F	2.81	2.58	2.58	1.58	2	2	2	1.58	0	1.58	2	1
NEG_G	0	0	1.58	1	0	1.58	2	1	1.58	0	2	1
NEG_H	1.58	1	1	0	1.58	1	2.58	2	2	1	0	0
POS_A	15.6	14.8	15.2	14.8	15.1	15.0	15.2	15.1	15.0	15.5	15.3	15
	1		8	7		9	2	3	8	4	2	
POS_B	13.3	12.5	13.1	12.8	12.9	12.9	13.1	12.9	12.9	13.3	13.1	12.7
	8	9		2		3	1	2	8	3	7	8
POS_C	12.0	11.2	11.6	11.2	11.4	11.4	11.6	11.5	11.5	11.9	11.7	11.3
	1	1	9	9	1		5	7	7	5	6	8
POS_D	9.83	9.06	9.5	9.12	9.29	9.31	9.5	9.36	9.38	9.74	9.59	9.09
POS_E	7.77	6.94	7.67	7.13	7.25	7.27	7.52	7.5	7.42	7.57	7.45	7.27
POS_F	5.81	5.32	5.39	4.39	5.52	4.7	5.29	5.29	5.64	5.86	5.52	4.95

Table S3. List of upregulated genes based on adjusted P value on WT and *TAK1*-KO cells treated with IL-1 β

WT IL-1 β			KO IL-1 β		
Gene name	Log2 change	Adjusted P value	Gene name	Log2 change	Adjusted P value
IL8	15.38	0.99232	IL8	11	0.71038
TNFAIP3	4.66	0.26389	CXCL1	10.23	0.68180
CXCL6	12.08	0.31767	OAS2	5.61	0.96867
PLA2G4A	3.37	0.31403	CXCL6	8.29	0.70850
CXCL1	14.42	0.57524	IFI44	4.05	0.25877
CXCL5	7.99	0.62398	CXCL2	5.47	0.62877
IL1B	7.52	0.94249	MX1	6.55	0.92409
CCL20	12.14	0.33368	MX2	5.72	0.96362
TLR2	4.19	0.44544			
OAS2	6.59	0.50047			
CSF3	8.25	0.03063			
NOD2	6.1	0.67769			
CXCL2	9.62	0.52820			
IL23A	6.97	0.30641			
MX1	7.4	0.95689			
MAP2K1	1.11	0.03408			
OASL	8.05	0.17733			
IRF7	4.36	0.71755			
IL1RN	7.45	0.12335			
CSF2	7.07	0.17118			
IL6	9.43	0.06578			
IL11	8.5	0.93572			
IFI44	4.22	0.60764			
PRKCB	2.04	0.14217			
MX2	7.77	0.05012			
CXCL3	12.02	0.21715			

C1QA	3.22	0.09298			
IFIT1	6.53	0.15728			
MAFF	1.23	0.11469			
CCL2	4	0.03094			
IL1A	5.45	0.01077			
CFB	4.6	0.67201			
PTGS2	6.24	0.39072			
C3	3.71	0.53666			
TNFSF14	1.74	0.37886			
CCR4	2.08	0.22216			
CCR3	-2.73	0.15813			