

Supporting information

Yes-associated protein (YAP) and transcriptional co-activator with PDZ-binding motif (TAZ) mediate cell density–dependent proinflammatory responses

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This Supporting Information contains Table S1-S3 and Figure S1-S6.

Table S1 Related to Figure S7E List of genes regulated by YAP/TAZ in top 15 pathways analyzed by KEGG pathway enrichment.

YAP-5SA/GFP (vehicle)

Influenza A; Q-value: 5.17886E-02			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
IRF9	10379	-1.67191	0.001889
DDX58	23586	-1.05802	0.029097
PYCARD	29108	NA	NA
HLA-DMB	3109	-3.87203	2.55E-05
HSPA1A	3303	-1.17356	0.011811
IL6	3569	3.402643	0.006632
CXCL8	3576	-2.17607	0.000657
CXCL10	3627	2.263607	0.01033
IRF7	3665	-2.06141	0.000337
MX1	4599	-2.82545	6.14E-05
MYD88	4615	-1.68169	0.002626
OAS1	4938	-2.896	2.5E-05
OAS2	4939	-2.08107	0.002389
OAS3	4940	-1.57935	0.00223
MAP2K3	5606	1.410369	0.024206
MAP2K6	5608	-1.98641	0.016837
CCL2	6347	-1.93681	0.000553
CCL5	6352	3.862631	4.64E-06
STAT1	6772	-2.58406	5.73E-05
TLR3	7098	-1.61819	0.013925
TNFSF10	8743	-2.76945	0.002639
TNFRSF10D	8793	1.936941	0.002414
RSAD2	91543	-1.71655	0.003356
Toll-like receptor signaling pathway; Q-value: 2.20246E-01			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
MAP3K8	1326	-1.48992	0.047178
IL6	3569	3.402643	0.006632
CXCL8	3576	-2.17607	0.000657
CXCL10	3627	2.263607	0.01033
IRF7	3665	-2.06141	0.000337
MYD88	4615	-1.68169	0.002626

MAP2K3	5606	1.410369	0.024206
MAP2K6	5608	-1.98641	0.016837
CCL5	6352	3.862631	4.64E-06
CXCL11	6373	2.387413	0.005897
SPP1	6696	-4.47849	3.62E-06
STAT1	6772	-2.58406	5.73E-05
TLR3	7098	-1.61819	0.013925
CD14	929	-1.77312	0.003001
CD40	958	-2.86863	0.008529

Complement and coagulation cascades; Q-value: 3.07939E-01

Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
CFD	1675	-1.15359	0.022094
F2R	2149	-2.4617	0.001469
FGA	2243	-4.03717	0.000318
FGB	2244	-2.96963	0.000816
FGG	2266	-2.70874	0.023063
CFH	3075	-3.70774	0.000623
SERPINE1	5054	1.188989	0.012013
PLAUR	5329	1.801838	0.001339
PROS1	5627	1.03167	0.028207
C3	718	-1.77336	0.001041
C5	727	-1.60811	0.003599

TNF signaling pathway; Q-value: 2.90287E-01

Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
MAP3K8	1326	-1.48992	0.047178
EDN1	1906	-1.47144	0.003642
CXCL1	2919	-1.44412	0.009717
IL6	3569	3.402643	0.006632
CXCL10	3627	2.263607	0.01033
MMP9	4318	1.500338	0.014066
MAP2K3	5606	1.410369	0.024206
MAP2K6	5608	-1.98641	0.016837
PTGS2	5743	-4.46222	2.3E-06
CCL2	6347	-1.93681	0.000553
CCL5	6352	3.862631	4.64E-06
VCAM1	7412	-2.47053	0.035259

CASP10	843	-2.56502	0.004974
RPS6KA4	8986	1.420474	0.011852
Herpes simplex infection; Q-value: 2.51256E-01			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
IRF9	10379	-1.67191	0.001889
DDX58	23586	-1.05802	0.029097
HLA-DMB	3109	-3.87203	2.55E-05
HLA-F	3134	-1.2429	0.009888
IFIT1	3434	-1.22194	0.008995
IL6	3569	3.402643	0.006632
IRF7	3665	-2.06141	0.000337
MYD88	4615	-1.68169	0.002626
OAS1	4938	-2.896	2.5E-05
OAS2	4939	-2.08107	0.002389
OAS3	4940	-1.57935	0.00223
CCL2	6347	-1.93681	0.000553
CCL5	6352	3.862631	4.64E-06
SKP2	6502	1.268765	0.007955
STAT1	6772	-2.58406	5.73E-05
TLR3	7098	-1.61819	0.013925
TP53	7157	1.056805	0.02835
C3	718	-1.77336	0.001041
C5	727	-1.60811	0.003599
PER2	8864	-2.25016	0.005003
Measles; Q-value: 2.0727E-01			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
IRF9	10379	-1.67191	0.001889
DDX58	23586	-1.05802	0.029097
FYN	2534	3.680725	0.003164
HSPA1A	3303	-1.17356	0.011811
IL6	3569	3.402643	0.006632
IRF7	3665	-2.06141	0.000337
JAK3	3718	-1.12363	0.026577
MX1	4599	-2.82545	6.14E-05
MYD88	4615	-1.68169	0.002626
OAS1	4938	-2.896	2.5E-05

OAS2	4939	-2.08107	0.002389
OAS3	4940	-1.57935	0.00223
STAT1	6772	-2.58406	5.73E-05
TP53	7157	1.056805	0.02835
TNFSF10	8743	-2.76945	0.002639
TNFRSF10D	8793	1.936941	0.002414

Legionellosis; Q-value: 2.27865E-01

Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
PYCARD	29108	NA	NA
CXCL1	2919	-1.44412	0.009717
HSPA1A	3303	-1.17356	0.011811
IL6	3569	3.402643	0.006632
CXCL8	3576	-2.17607	0.000657
ITGB2	3689	2.243522	0.0167
MYD88	4615	-1.68169	0.002626
C3	718	-1.77336	0.001041
CD14	929	-1.77312	0.003001

Malaria; Q-value: 3.34329E-01

Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
IL6	3569	3.402643	0.006632
CXCL8	3576	-2.17607	0.000657
ITGB2	3689	2.243522	0.0167
MYD88	4615	-1.68169	0.002626
CCL2	6347	-1.93681	0.000553
SDC2	6383	3.683773	0.000184
VCAM1	7412	-2.47053	0.035259
CD40	958	-2.86863	0.008529

YAP-5SA/GFP (IL-1 β)

Influenza A; Q-value: 9.1536E-03

Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
IRF9	10379	-1.54769	0.002933
IVNS1ABP	10625	1.279452	0.010992
DDX58	23586	-1.15498	0.019203
HLA-DMB	3109	-4.15021	2.11E-05

FAS	355	1.623256	0.032451
IL1A	3552	-2.23937	0.010361
IL6	3569	3.520328	1.66E-05
CXCL8	3576	-1.5937	0.001615
IRF7	3665	-2.32224	0.000138
MX1	4599	-3.07184	3.47E-05
MYD88	4615	-1.2105	0.017233
OAS1	4938	-2.62675	5E-05
OAS2	4939	-2.22045	0.001688
OAS3	4940	-1.40111	0.004743
MAP2K6	5608	-1.74665	0.022416
CCL2	6347	-2.73544	3.11E-05
CCL5	6352	3.10744	1.56E-05
STAT1	6772	-2.1867	0.000192
STAT2	6773	-1.09412	0.024919
TLR3	7098	-1.32125	0.03906
TNF	7124	-1.2369	0.013186
TNFSF10	8743	-2.68104	0.003074
TNFRSF10D	8793	1.835328	0.005753
RSAD2	91543	-1.55062	0.008391

Herpes simplex infection; Q-value: 2.77656E-02

Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
IRF9	10379	-1.54769	0.002933
DDX58	23586	-1.15498	0.019203
HLA-DMB	3109	-4.15021	2.11E-05
HLA-F	3134	-1.7526	0.019705
IFIT1	3434	-2.12936	0.000183
FAS	355	1.623256	0.032451
IL6	3569	3.520328	1.66E-05
IRF7	3665	-2.32224	0.000138
MYD88	4615	-1.2105	0.017233
OAS1	4938	-2.62675	5E-05
OAS2	4939	-2.22045	0.001688
OAS3	4940	-1.40111	0.004743
CCL2	6347	-2.73544	3.11E-05
CCL5	6352	3.10744	1.56E-05
SKP2	6502	1.705008	0.001136
STAT1	6772	-2.1867	0.000192

STAT2	6773	-1.09412	0.024919
TAP1	6890	-1.03275	0.023139
TLR3	7098	-1.32125	0.03906
TNF	7124	-1.2369	0.013186
C3	718	-1.32662	0.007367
C5	727	-1.84659	0.001583
PER2	8864	-1.82877	0.025115

Measles; Q-value: 4.66089E-02

Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
IRF9	10379	-1.54769	0.002933
DDX58	23586	-1.15498	0.019203
FYN	2534	4.229881	0.003173
FAS	355	1.623256	0.032451
IL1A	3552	-2.23937	0.010361
IL6	3569	3.520328	1.66E-05
IRF7	3665	-2.32224	0.000138
MX1	4599	-3.07184	3.47E-05
MYD88	4615	-1.2105	0.017233
OAS1	4938	-2.62675	5E-05
OAS2	4939	-2.22045	0.001688
OAS3	4940	-1.40111	0.004743
STAT1	6772	-2.1867	0.000192
STAT2	6773	-1.09412	0.024919
STAT5A	6776	-2.16035	0.000436
TNFSF10	8743	-2.68104	0.003074
TNFRSF10D	8793	1.835328	0.005753
CCND3	896	-1.31981	0.006268

Malaria; Q-value: 5.49832E-02

Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
CSF3	1440	-1.09374	0.016929
IL6	3569	3.520328	1.66E-05
CXCL8	3576	-1.5937	0.001615
ITGB2	3689	2.61115	0.002915
MYD88	4615	-1.2105	0.017233
CCL2	6347	-2.73544	3.11E-05
SDC2	6383	2.875647	0.008918

TNF	7124	-1.2369	0.013186
VCAM1	7412	-3.30666	0.000981
CD40	958	-3.84823	0.001653
TNF signaling pathway; Q-value: 6.09995E-02			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
MAP3K8	1326	-1.61687	0.005157
EDN1	1906	-1.41679	0.004536
CXCL3	2921	-1.30031	0.007155
BIRC3	330	-1.35607	0.005095
FAS	355	1.623256	0.032451
IL6	3569	3.520328	1.66E-05
MMP9	4318	1.324193	0.026184
MAP2K6	5608	-1.74665	0.022416
PTGS2	5743	-3.67815	4.61E-06
BCL3	602	-2.05559	0.00029
CCL2	6347	-2.73544	3.11E-05
CCL5	6352	3.10744	1.56E-05
TNF	7124	-1.2369	0.013186
VCAM1	7412	-3.30666	0.000981
CASP10	843	-2.37489	0.005197
Pertussis; Q-value: 7.10365E-02			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
GNAI1	2770	-1.05252	0.03876
IL1A	3552	-2.23937	0.010361
IL6	3569	3.520328	1.66E-05
CXCL8	3576	-1.5937	0.001615
IRF1	3659	-1.81035	0.000775
ITGB2	3689	2.61115	0.002915
MYD88	4615	-1.2105	0.017233
CXCL5	6374	-1.63301	0.001905
TNF	7124	-1.2369	0.013186
C3	718	-1.32662	0.007367
C5	727	-1.84659	0.001583
CD14	929	-1.70038	0.004159
Toll-like receptor signaling pathway; Q-value: 1.21805E-01			

Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
MAP3K8	1326	-1.61687	0.005157
IL6	3569	3.520328	1.66E-05
CXCL8	3576	-1.5937	0.001615
IRF7	3665	-2.32224	0.000138
MYD88	4615	-1.2105	0.017233
MAP2K6	5608	-1.74665	0.022416
CCL3	6348	3.422669	0.035243
CCL5	6352	3.10744	1.56E-05
SPP1	6696	-4.79375	2.78E-06
STAT1	6772	-2.1867	0.000192
TLR3	7098	-1.32125	0.03906
TNF	7124	-1.2369	0.013186
CD14	929	-1.70038	0.004159
CD40	958	-3.84823	0.001653
African trypanosomiasis; Q-value: 1.75409E-01			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
F2RL1	2150	-4.20107	2.08E-05
FAS	355	1.623256	0.032451
IL6	3569	3.520328	1.66E-05
IDO1	3620	-3.38948	0.011629
MYD88	4615	-1.2105	0.017233
TNF	7124	-1.2369	0.013186
VCAM1	7412	-3.30666	0.000981
Complement and coagulation cascades; Q-value: 2.20432E-01			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
CFD	1675	-2.12549	0.000741
F2R	2149	-2.37275	0.002536
FGA	2243	-4.35858	0.000237
FGB	2244	-2.91212	0.000848
CFH	3075	-3.24738	0.001673
PLAUR	5329	1.14676	0.023365
PROS1	5627	1.329701	0.006905
BDKRB2	624	-2.17556	0.034946
C3	718	-1.32662	0.007367

C5	727	-1.84659	0.001583
Hepatitis B; Q-value: 3.27804E-01			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
DDX58	23586	-1.15498	0.019203
FAS	355	1.623256	0.032451
IL6	3569	3.520328	1.66E-05
CXCL8	3576	-1.5937	0.001615
IRF7	3665	-2.32224	0.000138
MMP9	4318	1.324193	0.026184
MYD88	4615	-1.2105	0.017233
SRC	6714	-1.2605	0.013069
STAT1	6772	-2.1867	0.000192
STAT2	6773	-1.09412	0.024919
STAT4	6775	-2.64139	0.000525
STAT5A	6776	-2.16035	0.000436
TLR3	7098	-1.32125	0.03906
TNF	7124	-1.2369	0.013186
CASP10	843	-2.37489	0.005197
Legionellosis; Q-value: 3.3643E-01			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
CXCL3	2921	-1.30031	0.007155
IL6	3569	3.520328	1.66E-05
CXCL8	3576	-1.5937	0.001615
ITGB2	3689	2.61115	0.002915
MYD88	4615	-1.2105	0.017233
TNF	7124	-1.2369	0.013186
C3	718	-1.32662	0.007367
CD14	929	-1.70038	0.004159

YAP-5SA/GFP (TNF α)

Influenza A; Q-value: 1.7375E-01			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
IRF9	10379	-1.06426	0.03467
IVNS1ABP	10625	1.708614	0.002088
EIF2AK1	27102	-1.27248	0.019058

PYCARD	29108	NA	NA
HLA-DMB	3109	-4.7543	1.63E-05
HSPA2	3306	-1.52657	0.002519
ICAM1	3383	-1.69794	0.038916
IFNAR2	3455	-1.33355	0.020802
IFNGR1	3459	-1.21821	0.016418
IL6	3569	2.764161	0.000186
CXCL8	3576	-2.28294	0.000109
IRF7	3665	-1.8443	0.000922
EIF2AK4	440275	1.214541	0.023646
MX1	4599	-2.90645	5.87E-05
OAS1	4938	-2.51262	8.09E-05
OAS2	4939	-2.0704	0.00329
OAS3	4940	-1.24662	0.010581
CCL2	6347	-2.5755	4.61E-05
CCL5	6352	3.241986	1.16E-05
STAT1	6772	-1.85648	0.000771
TNF	7124	-1.38582	0.010494
TNFSF10	8743	-3.13985	0.002389
RSAD2	91543	-1.21691	0.032577
Complement and coagulation cascades; Q-value: 9.55349E-02			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
CFD	1675	-1.8051	0.001534
F2R	2149	-2.6669	0.001819
FGA	2243	-4.94364	7.41E-05
FGB	2244	-2.84381	0.002551
FGG	2266	-3.97925	0.008753
CFH	3075	-3.89436	0.001124
SERPINE1	5054	1.05809	0.022043
PLAUR	5329	1.266832	0.018217
PROS1	5627	1.914723	0.000588
BDKRB2	624	-2.53174	0.040739
C3	718	-1.67141	0.001766
C5	727	-2.36857	0.000232
CD59	966	1.07774	0.018749
Herpes simplex infection; Q-value: 1.17698E-01			

Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
IRF9	10379	-1.06426	0.03467
EIF2AK1	27102	-1.27248	0.019058
HLA-DMB	3109	-4.7543	1.63E-05
HLA-F	3134	-1.38961	0.045378
IFIT1	3434	-1.64557	0.001255
IFNAR2	3455	-1.33355	0.020802
IFNGR1	3459	-1.21821	0.016418
IL6	3569	2.764161	0.000186
IRF7	3665	-1.8443	0.000922
EIF2AK4	440275	1.214541	0.023646
OAS1	4938	-2.51262	8.09E-05
OAS2	4939	-2.0704	0.00329
OAS3	4940	-1.24662	0.010581
CCL2	6347	-2.5755	4.61E-05
CCL5	6352	3.241986	1.16E-05
SKP2	6502	1.763521	0.000876
STAT1	6772	-1.85648	0.000771
TNF	7124	-1.38582	0.010494
C3	718	-1.67141	0.001766
C5	727	-2.36857	0.000232
CUL1	8454	-1.27412	0.014971
TNFSF14	8740	-2.74894	0.022745
PER2	8864	-2.53657	0.005645
TNF signaling pathway; Q-value: 1.02053E-01			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
MAP3K8	1326	-1.41688	0.014597
EDN1	1906	-1.96767	0.000435
CXCL3	2921	-1.99073	0.000456
BIRC2	329	-1.16874	0.013764
BIRC3	330	-1.63126	0.001474
ICAM1	3383	-1.69794	0.038916
IL6	3569	2.764161	0.000186
MMP9	4318	1.543945	0.011919
PTGS2	5743	-4.20504	2.5E-06
BCL3	602	-1.37595	0.00628
CCL2	6347	-2.5755	4.61E-05

CCL5	6352	3.241986	1.16E-05
CCL20	6364	-1.35706	0.004692
TNF	7124	-1.38582	0.010494
VCAM1	7412	-2.85812	0.004471
CASP10	843	-2.44446	0.008366
NF-kappa B signaling pathway; Q-value: 1.00301E-01			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
BIRC2	329	-1.16874	0.013764
BIRC3	330	-1.63126	0.001474
XIAP	331	-1.31205	0.006982
ICAM1	3383	-1.69794	0.038916
IL1R1	3554	-1.35075	0.030884
CXCL8	3576	-2.28294	0.000109
PTGS2	5743	-4.20504	2.5E-06
TNF	7124	-1.38582	0.010494
UBE2I	7329	-1.06252	0.019886
VCAM1	7412	-2.85812	0.004471
TNFSF14	8740	-2.74894	0.022745
TNFRSF11A	8792	1.202901	0.037273
CD14	929	-1.35677	0.017607
CD40	958	-4.28264	0.000581
Legionellosis; Q-value: 1.41693E-01			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
PYCARD	29108	NA	NA
CXCL3	2921	-1.99073	0.000456
HSPA2	3306	-1.52657	0.002519
IL6	3569	2.764161	0.000186
CXCL8	3576	-2.28294	0.000109
ITGB2	3689	2.701684	0.006417
ARF1	375	-1.10332	0.02624
TNF	7124	-1.38582	0.010494
C3	718	-1.67141	0.001766
CD14	929	-1.35677	0.017607
Measles; Q-value: 1.64856E-01			

Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
IRF9	10379	-1.06426	0.03467
FYN	2534	3.603977	0.00386
EIF2AK1	27102	-1.27248	0.019058
HSPA2	3306	-1.52657	0.002519
IFNAR2	3455	-1.33355	0.020802
IFNGR1	3459	-1.21821	0.016418
IL6	3569	2.764161	0.000186
IRF7	3665	-1.8443	0.000922
EIF2AK4	440275	1.214541	0.023646
MX1	4599	-2.90645	5.87E-05
OAS1	4938	-2.51262	8.09E-05
OAS2	4939	-2.0704	0.00329
OAS3	4940	-1.24662	0.010581
STAT1	6772	-1.85648	0.000771
STAT5A	6776	-2.05106	0.000754
TNFSF10	8743	-3.13985	0.002389
CCND3	896	-1.47854	0.002828
Malaria; Q-value: 2.00611E-01			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
ICAM1	3383	-1.69794	0.038916
IL6	3569	2.764161	0.000186
CXCL8	3576	-2.28294	0.000109
ITGB2	3689	2.701684	0.006417
CCL2	6347	-2.5755	4.61E-05
SDC2	6383	2.882383	0.001258
TNF	7124	-1.38582	0.010494
VCAM1	7412	-2.85812	0.004471
CD40	958	-4.28264	0.000581
Pertussis; Q-value: 2.5183E-01			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
GNAI1	2770	-1.20037	0.020327
PYCARD	29108	NA	NA
IL6	3569	2.764161	0.000186
CXCL8	3576	-2.28294	0.000109

IRF1	3659	-1.41752	0.003868
ITGB2	3689	2.701684	0.006417
CXCL5	6374	-1.87641	0.000835
TNF	7124	-1.38582	0.010494
C3	718	-1.67141	0.001766
C5	727	-2.36857	0.000232
CD14	929	-1.35677	0.017607
Rheumatoid arthritis; Q-value: 2.67507E-01			
Gene_symbol	Entrez_gene_id	log2 (Ratio)	P-value (Differentially expressed)
HLA-DMB	3109	-4.7543	1.63E-05
ICAM1	3383	-1.69794	0.038916
IL6	3569	2.764161	0.000186
CXCL8	3576	-2.28294	0.000109
ITGB2	3689	2.701684	0.006417
CCL2	6347	-2.5755	4.61E-05
CCL5	6352	3.241986	1.16E-05
CCL20	6364	-1.35706	0.004692
CXCL5	6374	-1.87641	0.000835
TNF	7124	-1.38582	0.010494
TNFRSF11A	8792	1.202901	0.037273
ATP6V1F	9296	-1.04461	0.023304

Table S2 Related to Materials and Methods List of oligos used in this study.

RNAi	Sequence	Species
LATS1	CCUCCAUAACGAGUCAAAUCAdTdT	Human
LATS2	CAAGCAUCCUGAGCACGCAdTdT	Human
YAP	CCACCAAGCUAGAUAAGAdTdT	Human
TAZ	CCGCAGGGCTCATGAGTATdTdT	Human
TEAD1/3/4	GAUCAACUUCAUCCACAAGCUdTdT	Human
HDAC4	CGACAGGCCUCGUGUAUGAdTdT	Human
HDAC6	CUGCAAGGGAUGGAUCUGAdTdT	Human
HDAC7	GGACAAGAGCAAGCGAAGUdTdT	Human
HDAC11	GGGCUACCAUCAUUGAUCUdTdT	Human
MST1	CAAGCGAAAACAGUGAUdTdT	Human
MST2	CAGCACUGAAGGGCUUUAUdTdT	Human

qPCR Primers	Sequence	Species
COX-2 forward primer	CGGTGAAACTCTGGCTAGACAG	Human
COX-2 reverse primer	GCAAACCGTAGATGCTCAGGGA	Human
GAPDH forward primer	GTCTCCTCTGACTTCAACAGCG	Human
GAPDH reverse primer	ACCACCCTGTTGCTGTAGCCAA	Human
COX-1 forward primer	GATGAGCAGCTTTTCCAGACGAC	Human
COX-1 reverse primer	AACTGGACACCGAACAGCAGCT	Human
I κ B α forward primer	TCCACTCCATCCTGAAGGCTAC	Human
I κ B α reverse primer	CAAGGACACCAAAAGCTCCACG	Human
A20 forward primer	CTCAACTGGTGTGCGAGAAGTCC	Human
A20 reverse primer	TTCCTTGAGCGTGCTGAACAGC	Human
CTGF forward primer	CTTGCGAAGCTGACCTGGAAGA	Human
CTGF reverse primer	CCGTCGGTACATACTCCACAGA	Human
TEAD1 forward primer	CCTGGCTATCTATCCACCATGTG	Human
TEAD1 reverse primer	TTCTGGTCCTCGTCTTGCCCTGT	Human
LATS1 forward primer	CACTGGCTTCAGATGGACACAC	Human
LATS1 reverse primer	GGCTTCAGTCTGTCTCCACATC	Human
HDAC4 forward primer	AGGTGAAGCAGGAGCCCATTGA	Human
HDAC4 reverse primer	GGTAGTTCCTCAGCTGGTGGAT	Human
HDAC6 forward primer	GCCTCAATCACTGAGACCATCC	Human
HDAC6 reverse primer	GGTGCCTTCTTGGTGACCAACT	Human
HDAC7 forward primer	TCCTGGCACAGCGGATGTTTGT	Human
HDAC7 reverse primer	TGAAGGCGAGGTCAGTGACACT	Human
HDAC11 forward primer	CTTCTGTGCCTATGCGGACATC	Human
HDAC11 reverse primer	GAAGTCTCGCTCATGCCCATTG	Human
IL6 forward primer	AGACAGCCACTCACCTCTTCAG	Human
IL6 reverse primer	TTCTGCCAGTGCCTCTTTGCTG	Human

TRAF1 forward primer	CGATGGCACTTTCCTGTGGAAG	Human
TRAF1 reverse primer	TACAGCCGCAGGCACAACCTTGT	Human
ChIP-qPCR Primers	Sequence	Species
COX-2 (-0.6kb) promoter forward primer	GGGTGAAGGTACGGAGAACAGT	Human
COX-2 (-0.6kb) promoter reverse primer	TGTTTTATGTTTTAGTGACGACGC	Human
COX-2 (-1.5kb) promoter forward primer	TTCAGTAGATGCAACCTACTCCTTTA	Human
COX-2 (-1.5kb) promoter reverse primer	TTCCATCTCATCTAGGAAGCCTT	Human
guide RNA	sequence	Species
HDAC7	accgcctgcagcagcagcgcctcgg	Human

Table S3 Related to Materials and Methods List of antibodies used in this study.

Antibody	Company	Catalog #	Species	Clone	Dilution		
					WB	IF	CHIP
Primary antibodies							
anti-COX-2	CST	12282	Rabbit	Monoclonal	1:1000	1:500	
anti-YAP/TAZ	CST	8418	Rabbit	Monoclonal	1:1000		
anti-I κ B α	CST	9242	Rabbit	Polyclonal	1:1000		
anti-Lats1	CST	9153	Rabbit	Monoclonal	1:1000		
anti-TEAD1	CST	12292	Rabbit	Monoclonal	1:1000		
anti-A20	CST	5630	Rabbit	Monoclonal	1:1000		
anti-CYLD	CST	8462	Rabbit	Monoclonal	1:1000		
anti-CYR61	CST	14479	Rabbit	Monoclonal	1:1000		

anti-CTGF	Santa Cruz	sc-14939	Mouse	Polyclonal	1:1000		
anti-YAP	CST	14074	Rabbit	Monoclonal			1:100
anti-HDAC7	abcam	ab50212	Mouse	Monoclonal	1:2000		1:200
anti-YAP1	abcam	ab56701	Mouse	Monoclonal		1:200	
anti-GAPDH	HuaAn	M1211-1	Rabbit	Polyclonal	1:2000		
anti-MST1	abcam	ab124787,	Rabbit	Monoclonal	1:1000		
anti-MST2	abcam	ab52641	Rabbit	Monoclonal	1:1000		
anti-Flag	abmart	M20008	Mouse	Monoclonal	1:5000		
anti-HA	abmart	M20003	Mouse	Monoclonal	1:5000		
anti-Myc	abmart	M20002	Mouse	Monoclonal	1:5000		
Secondary antibodies							
anti-rabbit IgG-conjugated alkaline phosphatase conjugate	Promega	S373B			1:10000		
anti-mouse IgG-conjugated alkaline phosphatase conjugate	Promega	S372B			1:10000		
anti-Rabbit IgG secondary Antibody, Alexa Fluor 488	Thermo Fisher Scientific	R37118			1:2000		
anti-mouse IgG secondary Antibody, Alexa Fluor 594	Thermo Fisher Scientific	R37115			1:2000		

Supplementary Figure S1. Cell density regulates COX-2 induction without affecting NF- κ B activation. Related to Figure 1.

(A) Cell density does not affect the activation of NF- κ B induced by IL-1 β . H358 cells (about 2×10^5 cells) were seeded onto 10, 6 and 3.5 cm plates for low, medium or high cell densities, respectively, and treated with 10 ng/ml IL-1 β . Cells were then harvested and analyzed by immunoblotting with the indicated antibodies.

(B) Cell density does not affect the induction of A20 and I κ B α by IL-1 β and the transcription of COX-1. H358 cells (about 2×10^5 cells) were seeded onto 10, 6 and 3.5 cm plates for different cell confluences and treated with IL-1 β for the indicated time. The mRNA levels of the indicated target genes were measured by qRT-PCR. n=3 independent experiments. Data are presented as mean \pm S.D.. n.s., not significant, $P > 0.05$ (compared with low density group at the same induction time point), by unpaired, two-tailed Student's t-test.

(C, D) High cell density enhances the induction of COX-2 by DFO and serum starvation. H358 cells (about 2×10^5 cells) were seeded onto 10, 6 and 3.5 cm plates for low, medium or high cell densities, respectively, and treated with 100 μ M DFO for the indicated time (C) or starved in serum-free media for 6 hours (D). Cells were then harvested and analyzed by immunoblotting with the indicated antibodies.

Abbreviations used: DFO, Deferoxamine mesylate salt.

Supplementary Figure S2. YAP and TAZ inhibit the induction of COX-2. Related to Figure 2.

(A) Hippo pathway does not affect the ERK1/2 or NF- κ B signaling pathways. H358 cells were transfected with the indicated siRNAs and treated with IL-1 β for the indicated duration of time. Cells were then lysed and analyzed by immunoblotting with the indicated antibodies.

(B, C) Hippo signaling regulates COX-2 induction by hypoxia and serum starvation. H358 cells were transfected with siRNAs against YAP/TAZ or LATS1/2 and treated with DFO (B) or starved in serum-free medium (C). Cell lysates were analyzed by immunoblotting with the indicated antibodies.

(D) The expression of COX-2 is repressed in the active YAP-induced liver tumors. Murine liver tumors induced by overexpression of constitutively active YAP(5SA) were subjected to immunohistochemistry staining for COX-2 and YAP. Positive staining for the antibodies is shown in brown. Nuclei were counterstained with hematoxylin shown in blue.

(E) New protein synthesis is not required for YAP/TAZ- inhibited COX-2 induction. H358 cells were transfected with control siRNA or siRNAs against LATS1/2 for 48 hours, treated with CHX for 6 hours and stimulated with IL-1 β as indicated. Total RNAs were extracted and subjected to qRT-PCR for COX-2 (upper panel) and CTGF mRNA expression (lower panel). n=3 independent experiments. Data are presented as mean \pm S.D.. * $P < 0.05$; ** $P < 0.01$ and *** $P < 0.001$ (compared with siNC group untreated or treated with CHX respectively at the same induction time point), by unpaired, two-tailed Student's t-test.

(F) YAP and TAZ do not repress the COX-2 induction through inducing miRNA. H358 cells were transfected with siRNAs against LATS1/2, DICER or both for 48 hours and treated with IL-1 β for

2 hours. Cells were harvested and immunoblotted using the indicated antibodies.
NC, Negative Control; DFO, Deferoxamine mesylate salt.

Supplementary Figure S3. TEADs are indispensable for the suppression function of YAP/TAZ. Related to Figure 3.

(A, B) TEADs are essential for the regulation of COX-2 induction by Hippo pathway. H358 cells were transfected with the indicated siRNAs for 48 hours and then starved in serum-free media (A) or treated with DFO for 6 or 12 hours (B) before harvesting for immunoblotting using the indicated antibodies.

(C) The efficiencies of TEAD1 and LATS1/2 knockdown. H358 cells were transfected with the indicated siRNAs and treated with IL-1 β for the indicated time. Total RNAs were isolated and mRNA levels of COX-1, TEAD1, CTGF and LATS1 were measured by qRT-PCR. Quantification of COX-1 indicates its expression is not affected by the Hippo signaling. n=3 independent experiments. Data are presented as mean \pm S.D.. *P < 0.05; ***P < 0.001 and n.s., not significant (P > 0.05), by unpaired, two-tailed Student's t-test.

(D) DNA-binding of TEAD1 is indispensable for the inhibition of COX-2 induction. Schematic representation of structure of TEAD1, which contains an N-terminal DNA-binding domain (DBD) and a C-terminal transcriptional activation domain (TAD). Residues 88 aa -101 aa refer to its DNA binding surface (upper panel). HeLa cells were transfected with Flag tagged TEAD1 or its DNA-binding domain-deficient mutant, stimulated with IL-1 β for 2 hours and then collected for immunoblotting using the indicated antibodies (lower panel).

NC, Negative Control; DFO, Deferoxamine mesylate salt; aa, amino acid; DBD, DNA-Binding Domain; TAD, Transcriptional Activation Domain.

Supplementary Figure S4. HDAC inhibitors reverse the suppression of COX-2 induction by YAP/TAZ. Related to Figure 4.

(A) NaB rescues inhibition of COX-2 induction by LATS1/2 knockdown. H358 cells were transfected with the indicated siRNAs, followed by starved in serum-free media for 6 hours and treated with NaB for 6 more hours before cell harvesting. COX-2 induction was analyzed by immunoblotting.

(B) TSA reverses the inhibition of COX-2 induction by LATS1/2 knockdown. H358 cells were transfected with the indicated siRNAs, then starved in serum-free media for 6 hours and treated with TSA for another 6 hours before cell harvesting. Harvested cells were lysed and immunoblotted using the indicated antibodies.

(C) HDACs suppress the expression of COX-2. HeLa cells were transfected with Flag tagged HDACs as indicated. Cells were lysed and analyzed by western blots after treatment with IL-1 β for 2 hours. The dotted black line indicates a splicing site on the PVDF membrane from the same gel.

(D) The siRNA-based knockdown efficiencies of HDACs and YAP/TAZ were measured by qRT-PCR. The expression of CTGF was used to indicate the knockdown efficiencies of YAP/TAZ. n=3 independent experiments. Data are presented as mean \pm S.D.. ***P < 0.001 (compared with siNC group), by unpaired, two-tailed Student's t-test.

NC, Negative Control; NaB, Sodium Butyrate; TSA, Trichostatin A.

Supplementary Figure S5. The viability of H358 cells is not affected by stable expression of COX-2 and YAP(5SA). Related to Figure 6.

(A) Generation of H358 cell lines expressing GFP, YAP(5SA), COX-2 or both YAP(5SA) and COX-2. H358 cell lines stably expressing EGFP, YAP(5SA), COX-2 or YAP(5SA) and COX-2 were generated by infection with recombinant lentiviruses and puromycin selection. The four cell lines were treated with IL-1 β for the indicated time and then harvested for immunoblotting using the indicated antibodies.

(B) Comparable viability and proliferation among the H358 stable cell lines. Proliferation analysis was conducted by MTT assay with or without IL-1 β treatment. n=3 independent experiments. Data are presented as mean \pm S.D.. n.s., not significant ($P > 0.05$), by unpaired, two-tailed Student's t-test.

Supplementary Figure S6. Numbers of genes suppressed by active YAP are related to cell migration, angiogenesis or inflammatory responses. Related to Figure 7.

(A, B) The typical target genes of NF- κ B signaling are upregulated or not regulated by YAP(5SA). A list of target genes of NF- κ B that are not regulated or upregulated by YAP(5SA) was presented. Gene selection criteria: upregulated: log₂ ratio ≥ 1 , unregulated: log₂ ratio between -1 and 1 (A). GFP-expressing or YAP(5SA)-expressing H358 cells were treated with vehicle, IL-1 β or TNF α . RNAs were extracted for qRT-PCR analysis. n=3 independent experiments. Data are presented as mean \pm S.D.. *** $P < 0.001$ and n.s., not significant ($P > 0.05$), by unpaired, two-tailed Student's t-test (B).

(C, D) YAP(5SA) also regulates the expression of non-NF- κ B target genes. The heatmap represents the intensity of genes, which are downregulated (C) or upregulated (D) by YAP(5SA), but not proinflammatory factors. The values on the right are fold changes in log₂ of corresponding genes among compared groups.

(E) KEGG pathway analysis shows the anti-microbial responses-related pathways are significantly regulated by activated YAP. H358 cells stably expressing EGFP, or YAP(5SA) were treated with TNF- α , IL-1 β or vehicle for 1 hour and used for RNA extraction for whole-genome expression microarray analysis. The 15 most significant enriched KEGG pathways by differentially expressed genes between YAP(5SA)-expressing and GFP-expressing cells enriched were listed. The differentially expressed genes were listed in Table S1. Gene selection criteria: log₂ ratio ≥ 1 or ≤ -1 . $P < 0.05$.

(F) Suppressed genes by YAP(5SA) related to cell migration, angiogenesis or inflammatory responses through GO analysis in all three compared groups (vehicle, IL-1 β and TNF- α) are listed. $P < 0.05$.

Figure S1

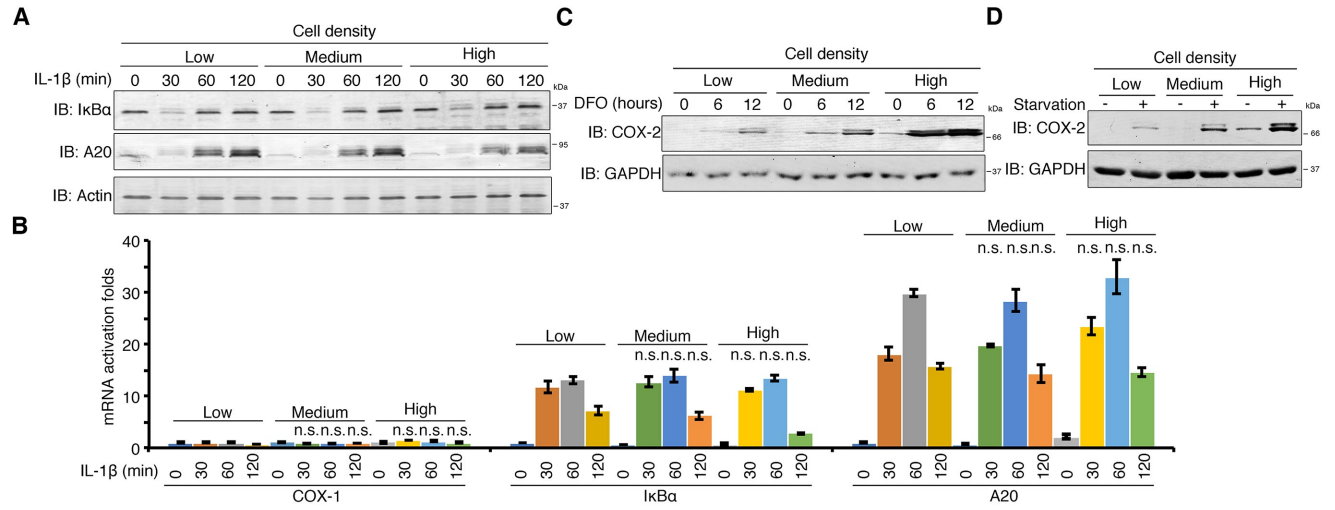


Figure S2

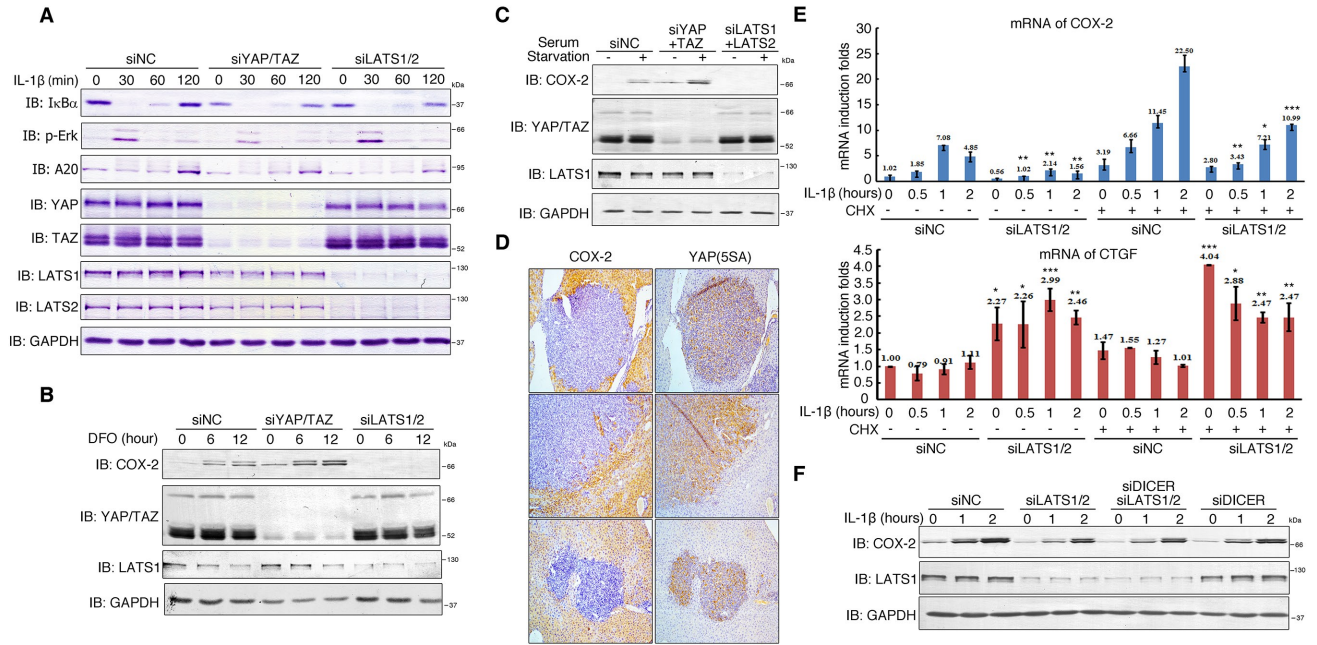


Figure S3

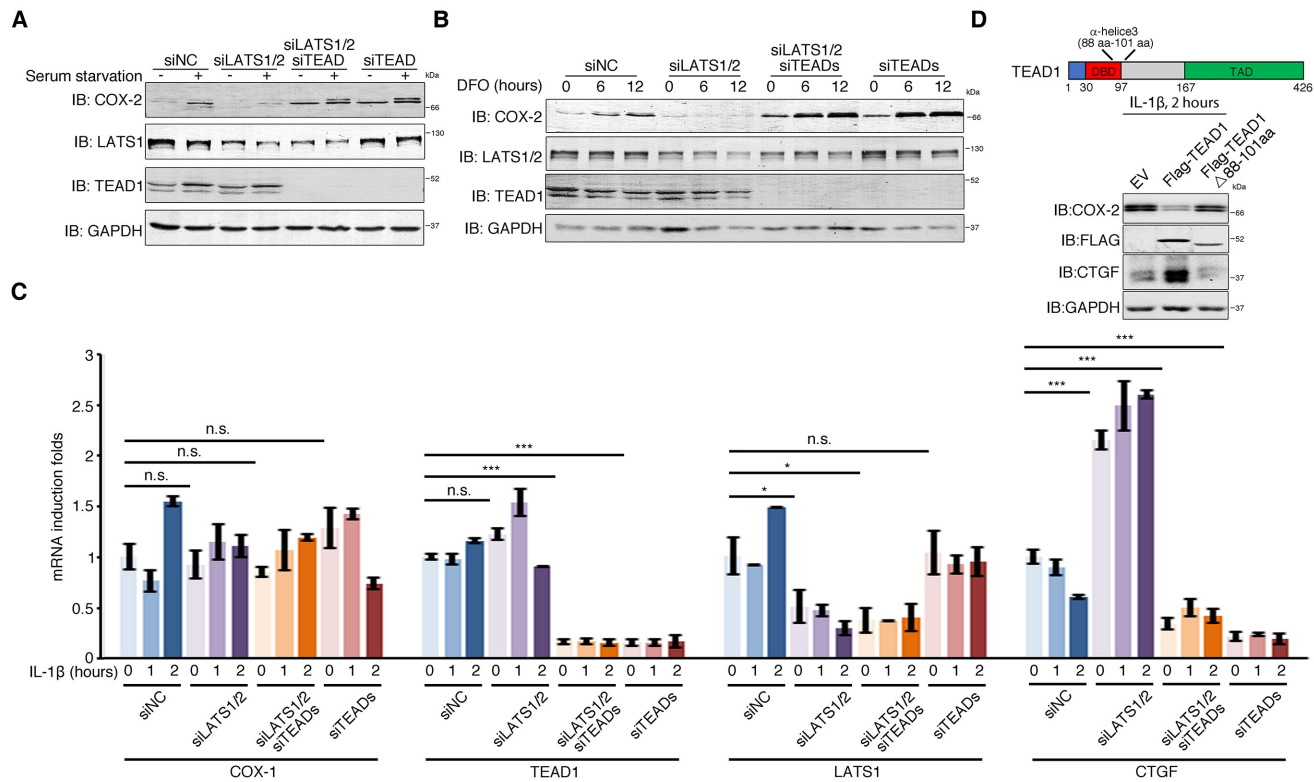
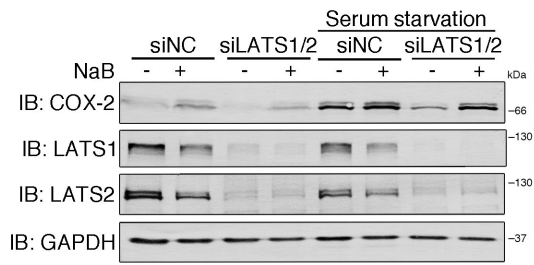
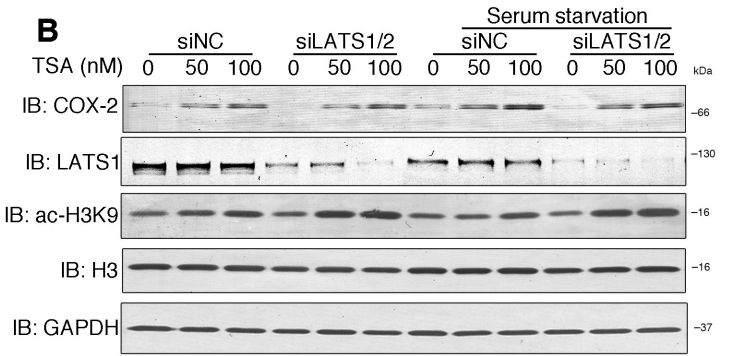


Figure S4

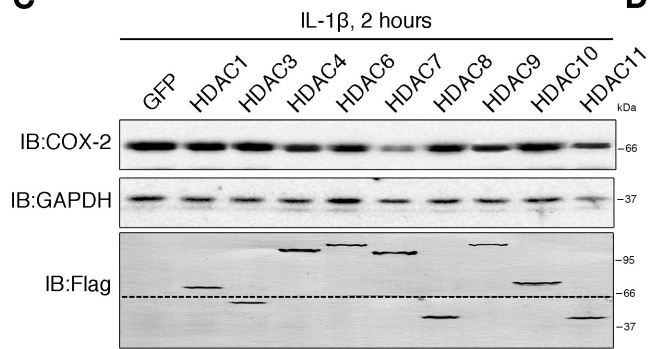
A



B



C



D

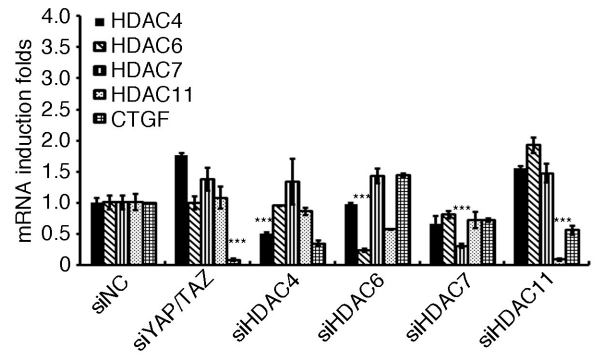
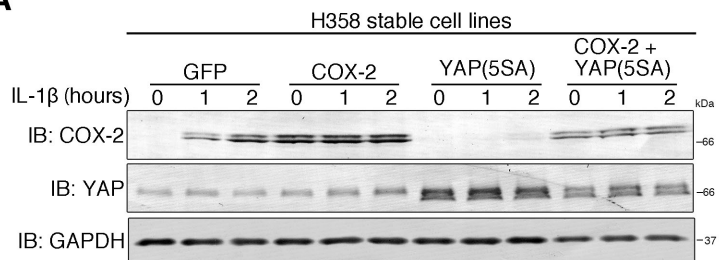


Figure S5

A



B

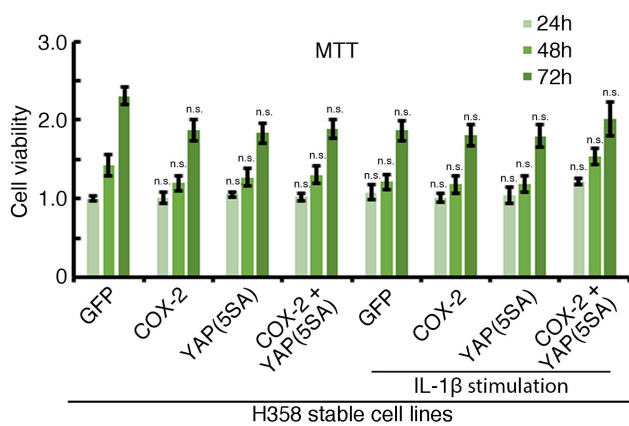
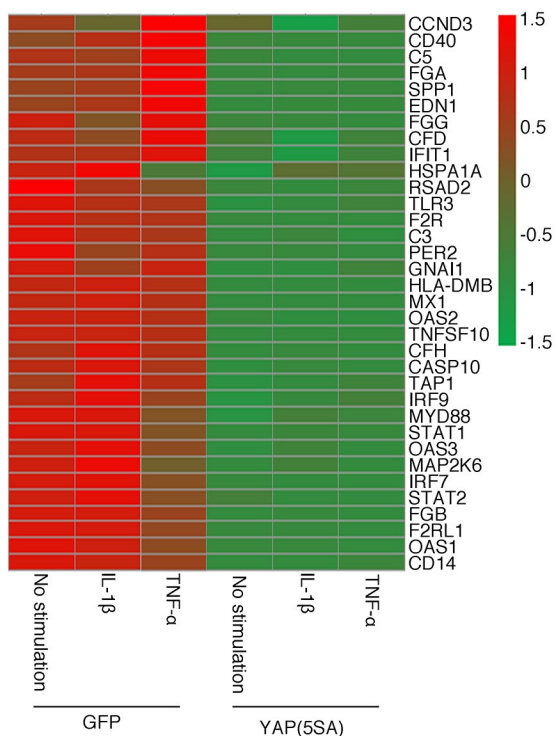


Figure S6

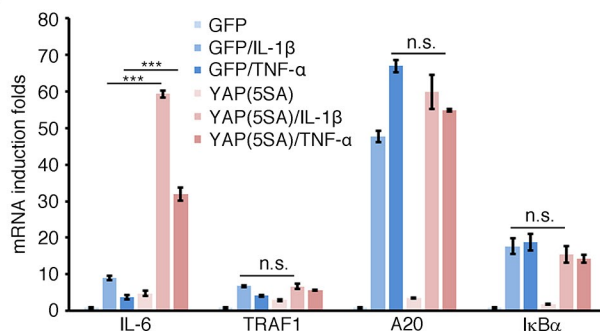
A

	Gene symbol
NF- κ B target genes not regulated by YAP	CCL4L
	TRAF1
	TRAF2
	NFKB2
	RIPK1
	CXCL2
	PLAU
	BCL2A1
	NFKB1
	LTB
	NFKBIA
	TNFAIP3
	IFNGR2
	CXCL1
	IRAK2
	IL32A
ZC3H12A	
NFKBIZ	
NF- κ B target genes upregulated by YAP	PTX3
	IL6

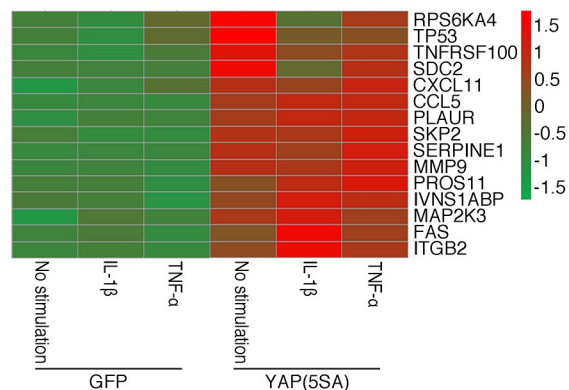
C



B



D



F

Function	Gene symbol
Positive regulation of cell migration	CCL26
	EDN1
	F2R
	F2RL1
	SEMA4G
	BMP4
	PTP4A1
PDGFD	
Positive regulation of substrate adhesion-dependent cell spreading	ADGRG1
	TNF
	VAV3
	FGB
Regulation of angiogenesis	FZD8
	CYP1B1
	JAG1
	TBX1
	NRCAM
PLXND1	
Prostaglandin metabolic process	PTGR1
	HPGD
	AKRIC3
	PTGES

E

