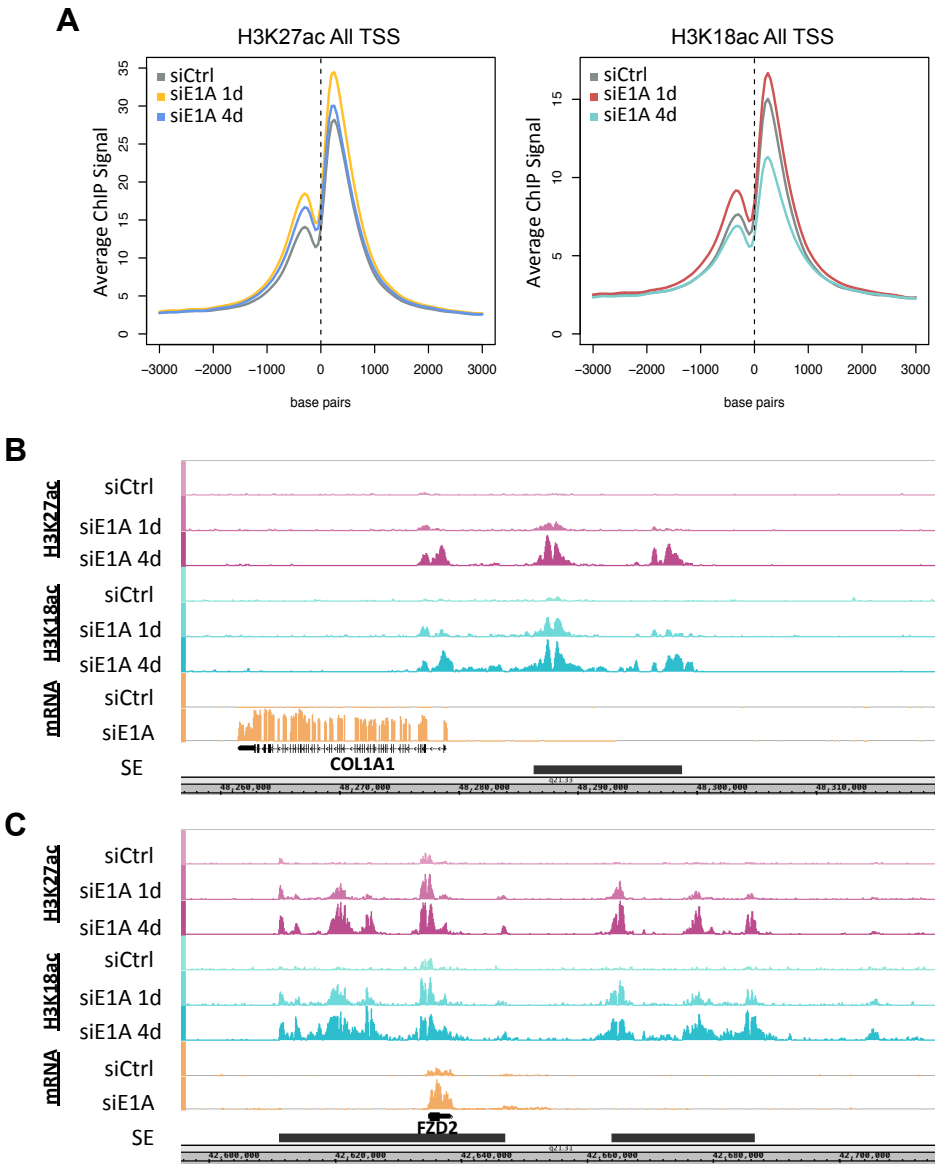


Figure S1: E1AKD establishes super-enhancers. Related to Fig 1.

(A) Average normalized ChIP-seq signal after transfection with the indicated siRNAs for 1 or 4 days centered at all TSSs. **(B)** Genome browser plots displaying normalized H3K27ac and H3K18ac ChIP-seq and RNA-seq reads at *COL1A1* and **(C)** *FZD2*. Super-enhancers (SE) indicated by black bars.

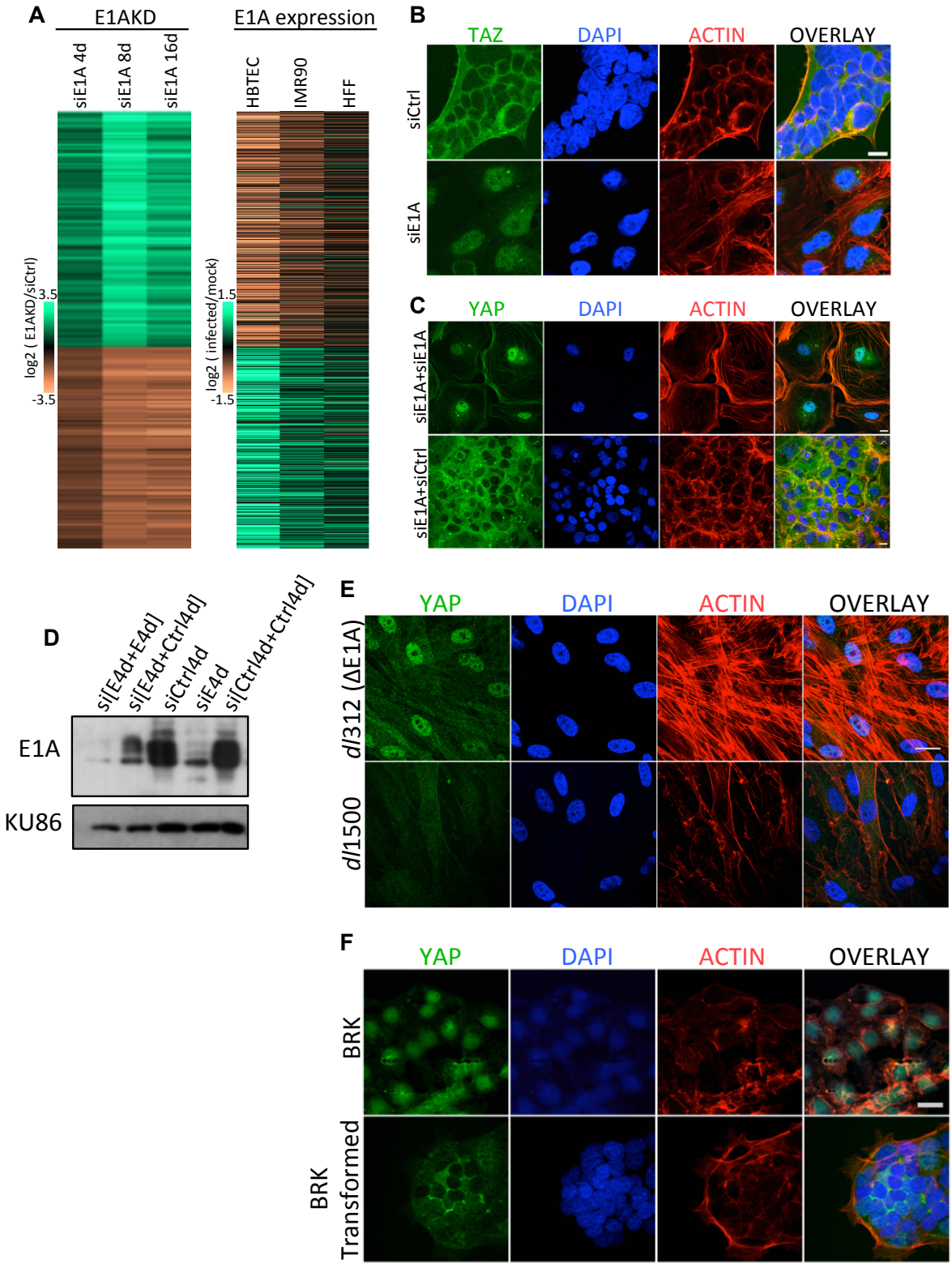

A
E1AKD
siE1A 4d
siE1A 8d
siE1A 16d
log2 (E1AKD/siCtrl)
3.5
-3.5
E1A expression
HBTEC
IMR90
HFF
log2 (infected/mock)
1.5
-1.5
B
TAZ
DAPI
ACTIN
OVERLAY
siCtrl
siE1A
C
YAP
DAPI
ACTIN
OVERLAY
siE1A+siE1A
siE1A+siCtrl
D
si[E4d+E4d]
si[E4d+Ctrl4d]
siCtrl4d
siE4d
si[Ctrl4d+Ctrl4d]
E1A
KU86
E
YAP
DAPI
ACTIN
OVERLAY
dl312 (ΔE1A)
dl1500
F
YAP
DAPI
ACTIN
OVERLAY
BRK
BRK Transformed

Figure S2: E1A regulates localization of YAP/TAZ in different cells. Related to Fig 3.

(A) Heatmap of expression changes for all genes repressed and de-repressed >2-fold q<0.05 by E1A siRNA 8 days post transfection. E1AKD at 4, 8, and 16 days post siRNA in HEK293 cells (left), and the same genes in HBTEC, IMR90, or HFF 24 h post infection with Ad5 *dl*1500 expressing small E1A (right). **(B)** Confocal microscopy of 4 day siRNA transfected HEK293 cells fixed and immuno-stained with anti-TAZ (CL0371) and stained with phalloidin-iFluor and DAPI. Scale bars = 20 μM. **(C)** HEK293 cells were transfected with siE1A RNA. Four days later, the media was changed to media with siE1A RNA (top row, siE1A+siE1A), or media with siCtrl RNA (siE1A+siCtrl). 4 days later cells were fixed and stained with anti-YAP antibody (DH81X), phalloidin-iFluor and DAPI and confocal micrographs were prepared. **(D)** Western blot for E1A protein (M58 antibody) from cell extract transfected with indicated siRNAs for indicated time, + indicates following first transfection. KU86 serves as loading control. **(E)** Confocal microscopy of IMR90 cells infected for 4 days with Ad5 *dl*312 (ΔE1A) or *dl*1500 (expressing small E1A) at MOI 10. Fixed and immuno-stained with anti-YAP (DH81X) phalloidin-iFluor and DAPI. **(F)** Confocal microscopy of normal BRK cells or BRK transformed with Ad2 E1A and E1B. Fixed and immuno-stained with anti-YAP (DH81X) and stained with phalloidin-iFluor and DAPI.

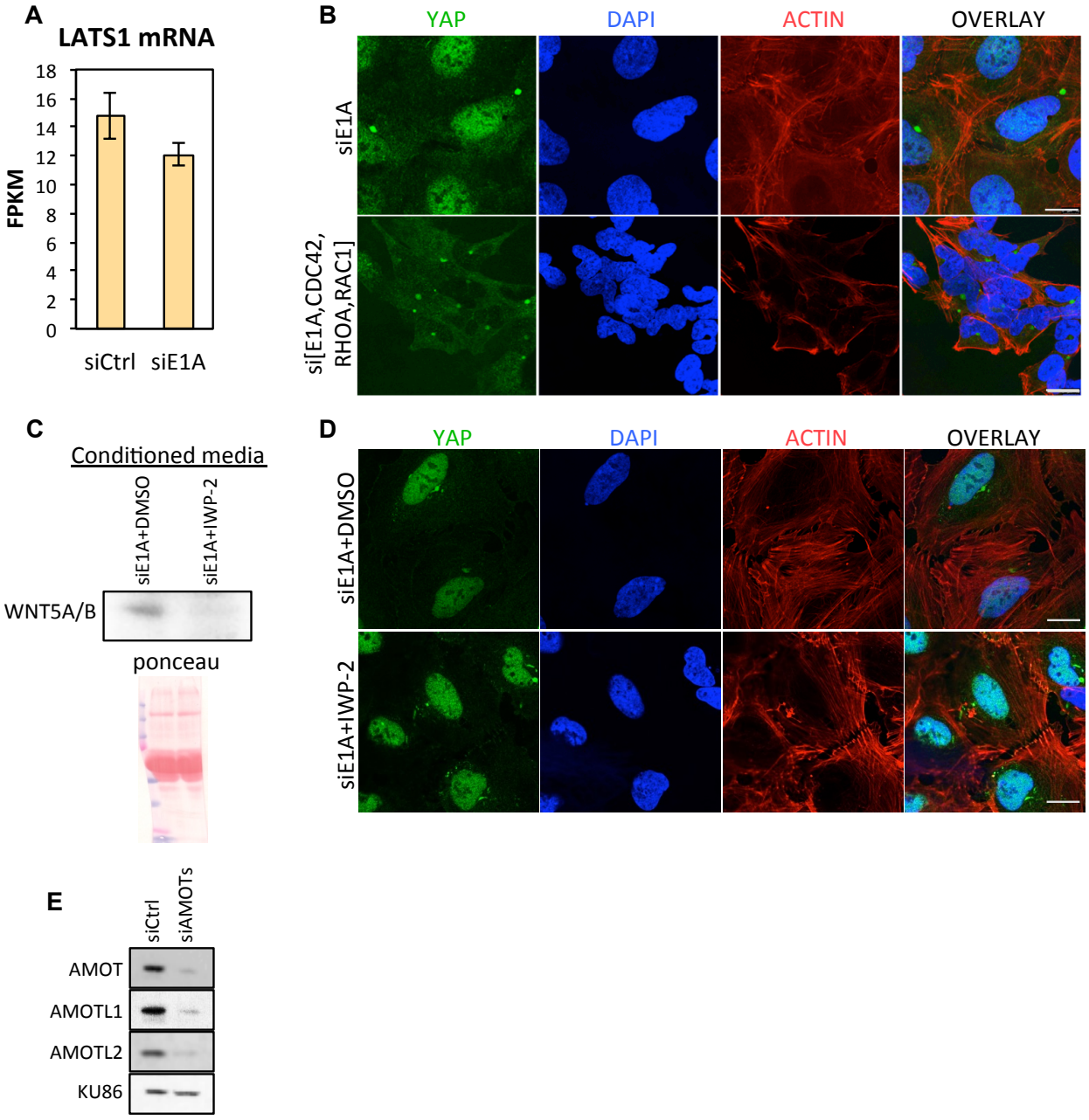
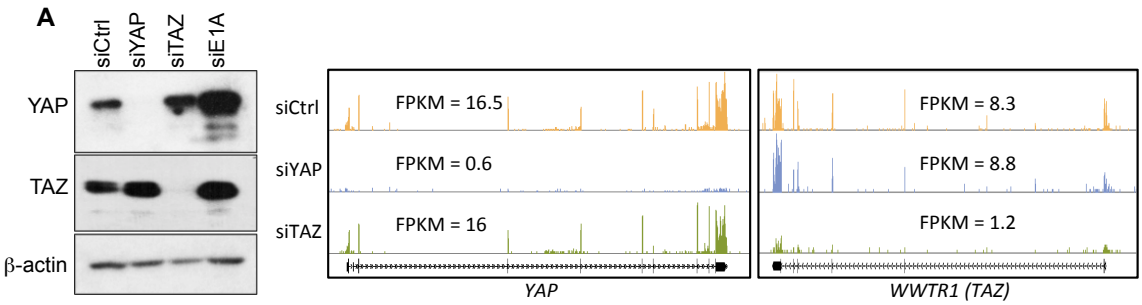


Figure S3: E1AKD-activation of YAP depends on F-actin and Rho-family GTPases but not Alternative Wnt signaling. Related to Fig 5.

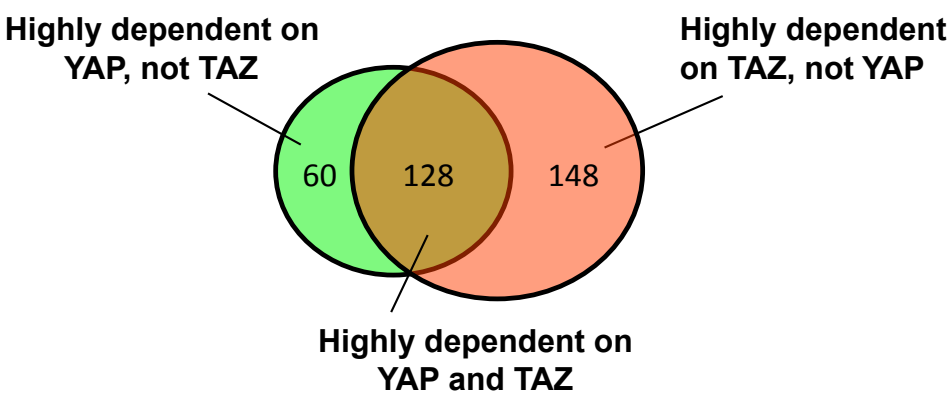
(A) Average expression level (FPKM) of LATS1 from 3 replicates of siRNA transfected HEK293 cells. **(B)** Confocal microscopy of 4 day siRNA transfected HEK293 cells fixed and immuno-stained with anti-YAP (DH81X), phalloidin-iFluor

and DAPI. Scale bars = 20μM. **(C)** Western blot for WNT5A/B using supernatant of E1AKD293 cell culture conditioned media following 4 days of transfection and DMSO or IWP-2 (2μM) treatment. Ponceau red of membrane serves as a loading control. **(D)** Confocal microscopy of HEK293 cells 4days after siRNA transfection and addition of either DMSO or IWP-2 in DMSO (2 μM final media concentration). Cells were fixed and immuno-stained with anti-YAP (DH81X) and stained with phalloidin-iFluor and DAPI. **(E)** Western blots of AMOT, AMOTL1, and AMOTL2 in cells treated for 3 days with siCtrl or siAMOT, siAMOTL1, and siAMOTL2 (siAMOTs). KU86 serves as loading control.

A



B



Highly dependent on YAP, not TAZ

	P-value	Benjamini
focal adhesion	3.2E-07	4.5E-05
positive regulation of cell proliferation	1.4E-06	1.1E-03
angiogenesis	5.3E-06	1.5E-03
extracellular region	2.2E-05	1.6E-03
cell growth	2.7E-05	5.5E-03

Highly dependent on TAZ, not YAP

extracellular space	1.3E-15	1.4E-13
proteinaceous extracellular matrix	3.1E-12	1.4E-14
extracellular matrix	3.8E-05	1.3E-03
heparin binding	1.3E-04	1.7E-02
calcium ion binding	4.0E-04	2.6E-02

Highly dependent on both YAP and TAZ

extracellular space	2.0E-13	2.0E-11
proteinaceious extracellular matrix	2.8E-10	1.4E-08
extracellular matrix structural constituent	3.7E-07	4.4E-05
collagen fibril organization	2.4E-06	1.5E-03
extracellular matrix	9.5E-06	3.2E-04

Figure S4: Genes highly dependent on YAP but not TAZ are enriched for cell proliferation. Related to Fig 6.

(A) Left: protein levels (western blots) of YAP and TAZ following indicated siRNA transfections for 2 days. β-actin serves as a loading control. Right: Genome browser plots (IGB) displaying mRNA-seq signal of *YAP* and *WWTR1* (*TAZ*) following indicated siRNA treatment. **(B)** Venn diagram and gene ontology (DAVID) enrichment terms for E1AKD de-repressed genes (siE1A/siCtrl > 2X, q<0.05) that are highly dependent on YAP, not TAZ (si[E1A+YAP]/siE1A < 0.2), highly dependent on TAZ, not YAP (si[E1A+TAZ]/siE1A < 0.2), or highly dependent on YAP and TAZ (si[E1A+YAP]/siE1A < 0.2 and si[E1A+TAZ]/siE1A < 0.2).

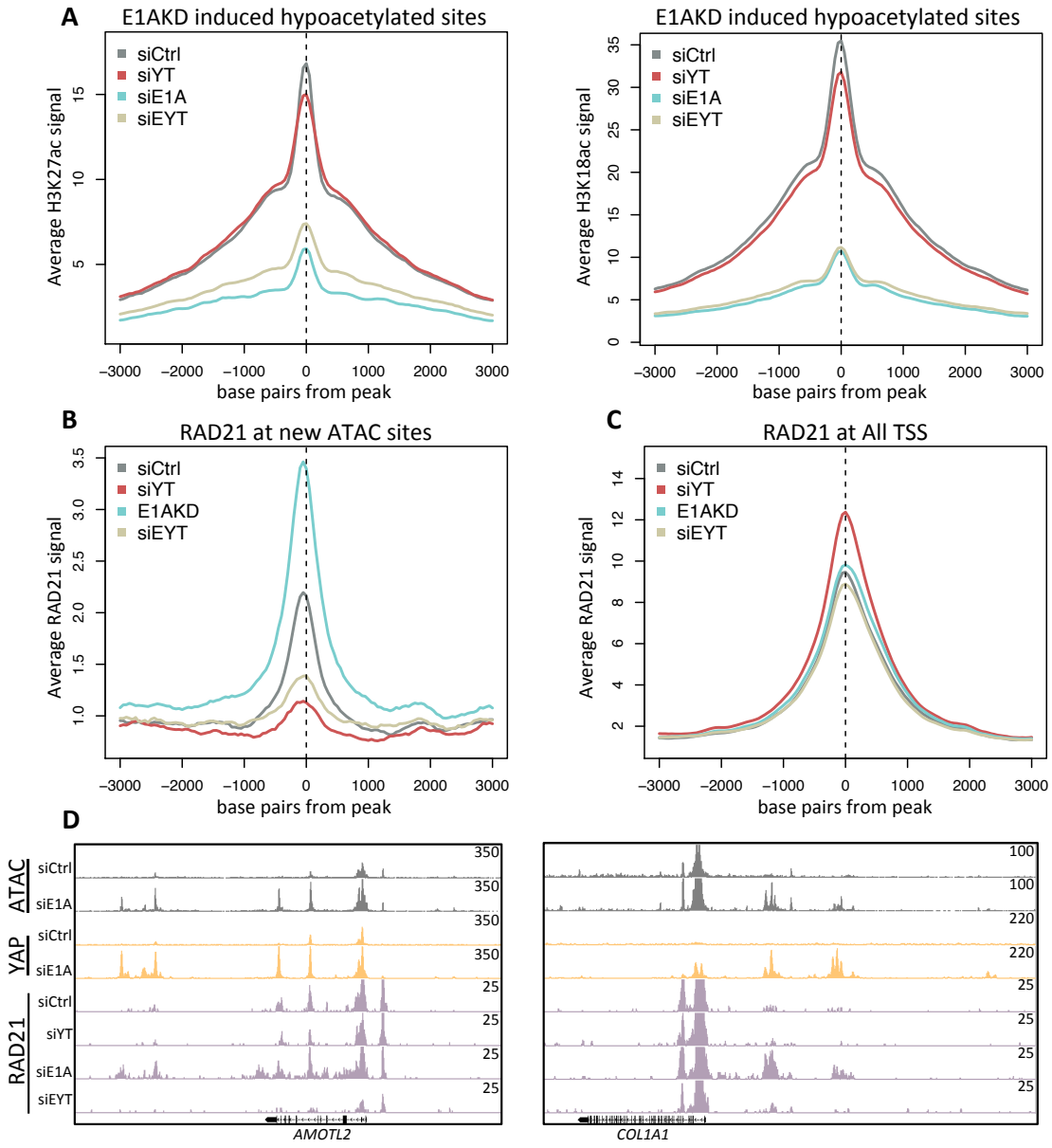

A
E1AKD induced hypoacetylated sites
siCtrl
siYT
siE1A
siEYT
Average H3K27ac signal
base pairs from peak
E1AKD induced hypoacetylated sites
Average H3K18ac signal
base pairs from peak
B
RAD21 at new ATAC sites
siCtrl
siYT
E1AKD
siEYT
Average RAD21 signal
base pairs from peak
C
RAD21 at All TSS
Average RAD21 signal
base pairs from peak
D
ATAC
YAP
RAD21
siCtrl
siE1A
siYT
siEYT
AMOTL2
COL1A1

Figure S5: YAP/TAZ are necessary for cohesin loading at enhancers. Related to Fig 6.

(A) Average ChIP-seq signal after transfection with the indicated siRNAs for 4 days centered at H3K27ac peaks that decreased >2X following 4 days of E1AKD. **(B)** Average RAD21 ChIP-seq signal after transfection with the indicated siRNAs for 4 days centered at ATAC-seq peaks that increased >5X (new ATAC sites) following 4 days of E1AKD. **(C)** Average RAD21 ChIP-seq signal after transfection with the indicated siRNAs for 4 days centered at all TSSs. **(D)** Genome browser plots (IGB) displaying indicated ATAC- and ChIP-seq signal at super-enhancers near E1AKD de-repressed genes *AMOTL2* and *COL1A1*.

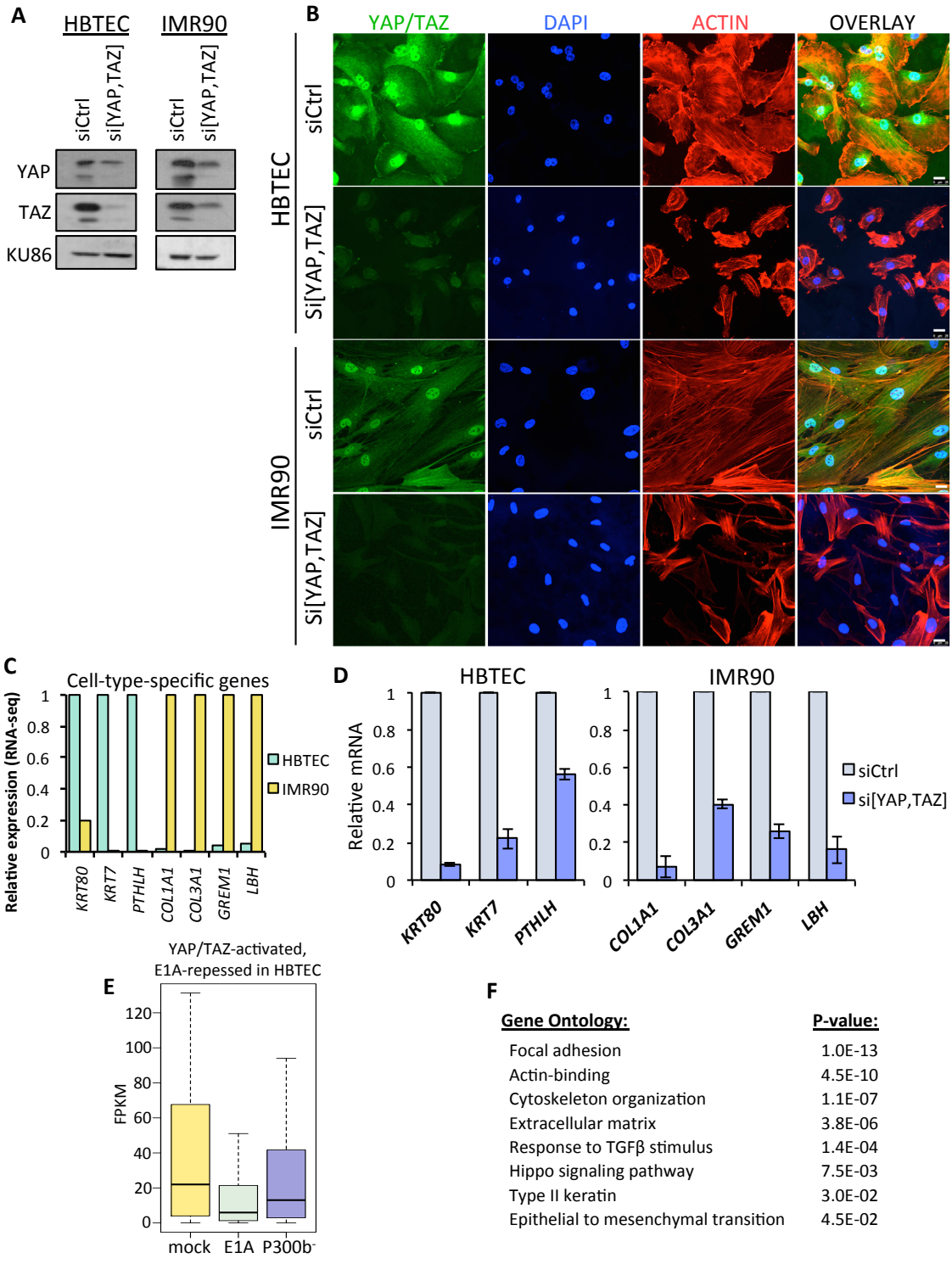


Figure S6: YAP and TAZ are necessary for normal F-actin in primary cells.

Related to Fig 6.

(A) Western blot of YAP or TAZ from HBTEC or IMR90 transfected with indicated siRNAs for 3 days. YAP and TAZ KDs were less efficient than in HEK293 (Fig S4A). KU86 serves as loading control. **(B)** Confocal microscopy of HBTEC or IMR90 cells after 4 day siRNA transfection. Fixed and immuno-stained with anti-YAP (DH81X) and anti-TAZ (CL0371) stained with phalloidin-iFluor and DAPI. Scale bar = 20 μm. **(C)** Relative expression (arbitrary units) from RNA-seq of HBTEC or IMR90 cell type-specific genes. **(D)** qRT-PCR from HBTEC or IMR90 transfected for 3 days with the indicated siRNAs showing averages relative to siCtrl for each gene and standard deviations of three experimental replicates. **(E)** Boxplots representing the distribution of FPKM values of WT small E1A repressed genes (>2-fold repression compared to mock) in HBTEC that are also YAP/TAZ-dependent activated genes (>2-fold defective for activation comparing si[E1A,YAP,TAZ] to si[E1A]) in E1AKD293 cells. E1A = HBTEC infected with an Ad5 vector expressing small E1A. P300b- = HBTEC infected with an Ad5 vector expressing a mutant small E1A unable to bind CBP/p300 (Ferrari et al., 2014). **(F)** Gene ontology terms (DAVID) and p-values for genes analyzed in (E).