LEGENDS TO SUPPLEMENTARY FIGURES

Supplementary Figure S1. Expression of Hippo pathway components in a series of human melanoma cell lines. A, Quantitative real-time RT-PCR analysis of *Merlin*, *MST1, MST2, LATS1* and *LATS2* expression in a panel of 12 human melanoma cell lines. mRNA expression was normalized against that of *GAPDH*. B, Western analysis of MERLIN, MST2 and phospho-MST1/2, LATS1 and P-LATS1 protein levels in 1205Lu, WM852, SKmel28 and 501mel human melanoma cell lines. An anti-UKHC antibody was used as a loading control. C, Immunofluorescent staining of YAP, P-YAP, TAZ and P-TAZ in 1205Lu human melanoma cell lines. Dapi staining was used to visualize nuclei. For this purpose, cells in 24-well plates were washed with PBS, fixed with 4% paraformaldehyde, permeabilized with 0.2% Triton X-100 in PBS, and blocked with 1% SVF-PBS prior to addition of primary antibodies for 1h: rabbit anti-YAP (sc-15407, 1:200), rabbit anti-phospho-YAP (Cell Signaling Technology Inc. #4911, 1:200), rabbit anti-TAZ (BD Biosciences #560235; 1:200), rabbit anti-phospho-TAZ (sc-17610, 1:200). Then cells were washed with 0.1% Tween-PBS, incubated with donkey anti-rabbit or mouse Alexa Fluor 568 for 1h (1:1000 in 2% BSA-PBS), and washed with 0.1% Tween-PBS. Cell nuclei were visualized by DAPI staining. Images were captured using a spinning disk confocal scanner (CSU10, Yokogawa) on Leica DMIRE2 or Zeiss Axiovert 200M and analyzed with ImageJ software (NIH).

Supplementary Figure S2. YAP or TAZ knockdown in human melanoma cell lines does not alter their proliferative potential and morphology.

. Melanoma cell lines were infected with lentiviruses expressing either YAP1/2 or TAZ shRNA. A, Q-PCR analysis of *YAP1*, *YAP2* and *TAZ* transcript levels in shCTL-, shYAP-, and shTAZ-transduced 1205Lu, WM852, SKmel28 and 501mel melanoma cell lines. B, Western analysis of YAP and TAZ protein levels in shCTL-, shYAP-, and shTAZ-transduced 1205Lu, WM852, SKmel28 and 501mel melanoma cell lines (note that for manuscript clarity, the same 1205Lu and SKmel28 data are shown in Fig. 2A). C, Representative images of shCTL-, shYAP-, and shTAZ-transduced 1205Lu, WM852, SKmel28 and 501mel melanoma cell lines in culture using phase contrast microscopy. D, 4-day growth curve shCTL-, shYAP-, and shTAZ-transduced 1205Lu, WM852, SKmel28 and 501mel melanoma cell lines in culture.

Supplementary Figure S3. siRNA-mediated YAP and TAZ knockdown in 1205Lu and SKmel28 melanoma cell lines inhibits invasiveness in Matrigel™ without affecting cell proliferation. Melanoma cell lines were transfected with two distinct siRNAs targeting either YAP or TAZ, either alone or in combination. A, Q-PCR analysis of *YAP1*, *YAP2* and *TAZ* transcript levels in siCTL-, siYAP-, siTAZ- and siYAP/TAZ-transfected 1205Lu and SKmel28 melanoma cell lines. B, Western analysis of YAP and TAZ protein levels in siCTL-, siYAP-, siTAZ- and siYAP+siTAZ-transfected 1205Lu (upper panel) and SKmel28 (lower panel) melanoma cell lines. C, 4-day growth curve of siCTL-, siYAP-, siTAZ- and siYAP/TAZ-transfected 1205Lu (upper panels) and SKmel28 (lower panels) melanoma cell lines in culture. D, Matrigel invasion assay. siCTL-, siYAP-, siTAZ- and siYAP/TAZ-transfected 1205Lu (upper panels) and SKmel28 (lower panels) melanoma cell lines were added to the upper well of Matrigel invasion chambers in serum-free RPMI medium. The number of invading cells was counted using bright field microscopy after staining colonies

with crystal violet, 24h (1205Lu) or 48h (SKmel28) later. Results are expressed as mean +/- s.e.m. of 3 independent experiments. ** P<0.001, ***P<0.0001.

Supplementary Figure S4. **YAP2 overexpression in 1205Lu and SKmel28 melanoma cell lines**. 1205Lu (left) or SKmel28 (right) melanoma cells were stably transfected with either empty pEGFP or YAP2 expression vectors. YAP2 expression was verified by Q-PCR. Results are expressed as mean +/- s.e.m. of 3 independent measurements. ***P<0.0001. B, Representative images of the appearance of pEGFP and YAP2 clones under a phase contrast microscope. C, 4-day growth curves from two distinct mock and YAP-overexpressing clones from 1205Lu (left) and SKmel28 (right) melanoma cell lines in culture.

Supplementary Figure S5. ***CCN2*** **expression and TEAD-dependent transcriptional activity are proportional to YAP and TAZ levels in SKmel28 melanoma cells.** A, Quantitative real-time RT-PCR analysis of *CCN2* expression in SKmel28 melanoma cells in response to either stable knockdown (left panel) of YAP or TAZ or overexpression of YAP (right panel). *CCN2* transcript levels were normalized against *GAPDH*. B, *CCN2* promoter activity in SKmel28 melanoma cells following either stable knockdown of YAP or TAZ (left panel) or overexpression of YAP (right panel). Cells were co-transfected with *CCN2*-luc and pRL-TK-luc. Luciferase activity was determined 18h later. C, TEAD-specific transcription in SKmel28 melanoma cells following either stable knockdown of YAP or TAZ (left panel) or overexpression of YAP (right panel). Cells were transfected with 8XGTII-luc and pRL-TK-luc. Luciferase activity was determined 18h later. D, TEAD-specific transcription in SKmel28 melanoma cells following overexpression of nuclear YAP

and TAZ mutants (YAP5SA and TAZS89A), a YAP mutant incapable of binding TEADs (YAPS94A), or an exclusively cytoplasmic TAZ mutant (TAZΔ393). In panels B-D, Renilla was used as a control for transfection efficiency. Results are mean ± s.e.m. of three independent experiments using triplicate dishes. ***P<0.0001.

Supplementary Figure S6. Modulation of *CCN2* expression in 1205Lu and SKmel28 melanoma cell lines upon siRNA-mediated YAP and TAZ knockdown. 1205Lu (A) and SKmel28 (B) melanoma cell lines were transfected with two distinct siRNAs targeting either YAP or TAZ, either alone or in combination. A non-targeting siRNA (siCTL) was used as control. Fourty-eight hours later, RNA was extracted and *CCN2* expression was measured in duplicate by Q-PCR. *GAPDH* levels were used as internal standard. ** P<0.001, ***P<0.0001.

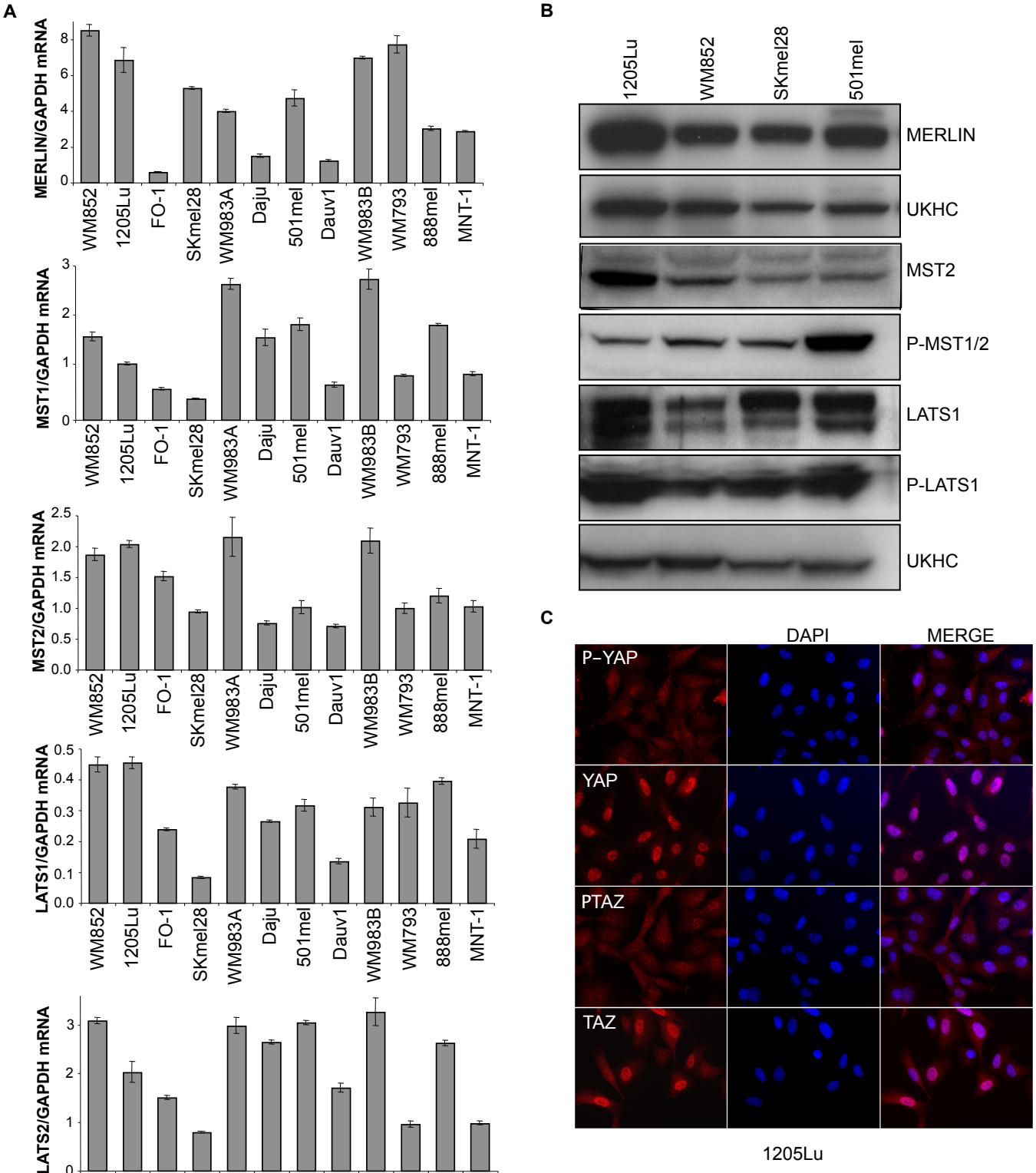
A
MERLIN/GAPDH mRNA
MST1/GAPDH mRNA
MST2/GAPDH mRNA
LATS1/GAPDH mRNA
LATS2/GAPDH mRNA
WM852
1205Lu
FO-1
SKmel28
WM983A
Daju
501mel
Dauv1
WM983B
WM793
888mel
MNT-1
B
1205Lu
WM852
SKmel28
501mel
MERLIN
UKHC
MST2
P-MST1/2
LATS1
P-LATS1
UKHC
C
DAPI
MERGE
P-YAP
YAP
PTAZ
TAZ
1205Lu

Figure S1

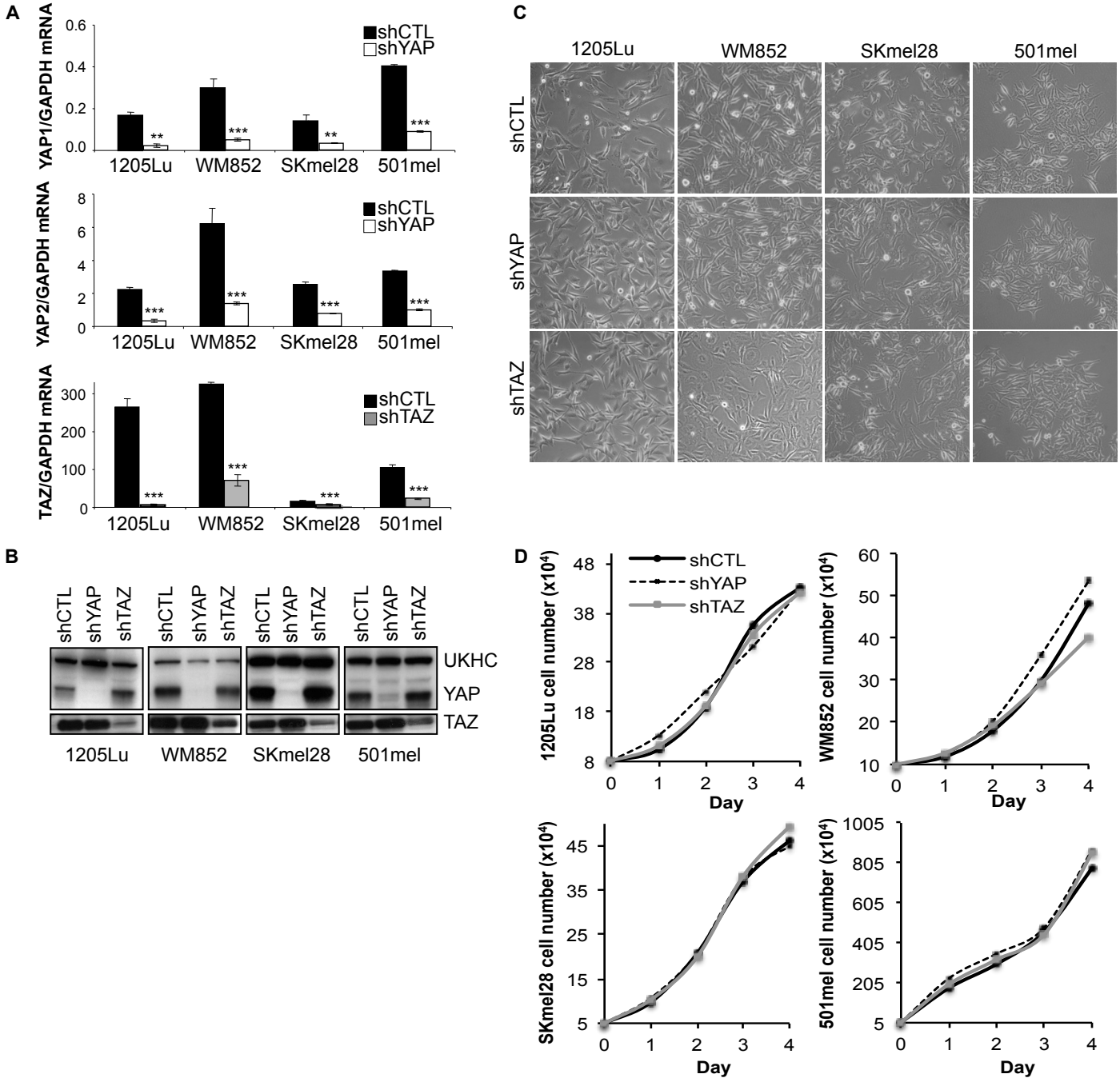
A
YAP1/GAPDH mRNA
shCTL
shYAP
1205Lu
WM852
SKmel28
501mel
YAP2/GAPDH mRNA
TAZ/GAPDH mRNA
shTAZ
B
shCTL
shYAP
shTAZ
UKHC
YAP
TAZ
C
shCTL
shYAP
shTAZ
D
1205Lu cell number (x10⁴)
WM852 cell number (x10⁴)
SKmel28 cell number (x10⁴)
501mel cell number (x10⁴)
Day

Figure S2

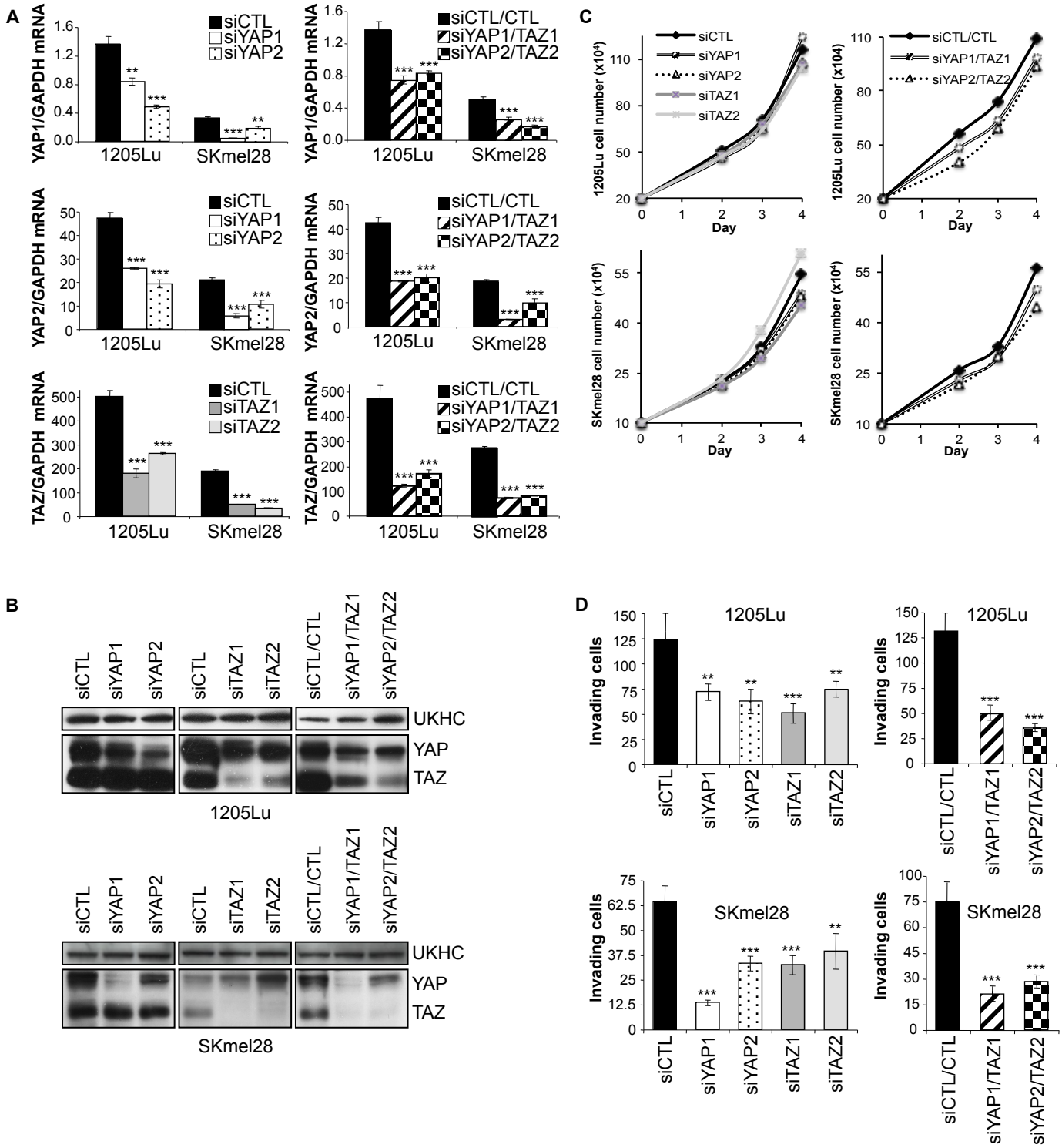
A
YAP1/GAPDH mRNA
siCTL
siYAP1
siYAP2
siCTL/CTL
siYAP1/TAZ1
siYAP2/TAZ2
1205Lu
SKmel28
YAP2/GAPDH mRNA
TAZ/GAPDH mRNA
siTAZ1
siTAZ2
B
UKHC
YAP
TAZ
C
1205Lu cell number (x10⁴)
SKmel28 cell number (x10⁴)
Day
D
Invading cells

Figure S3

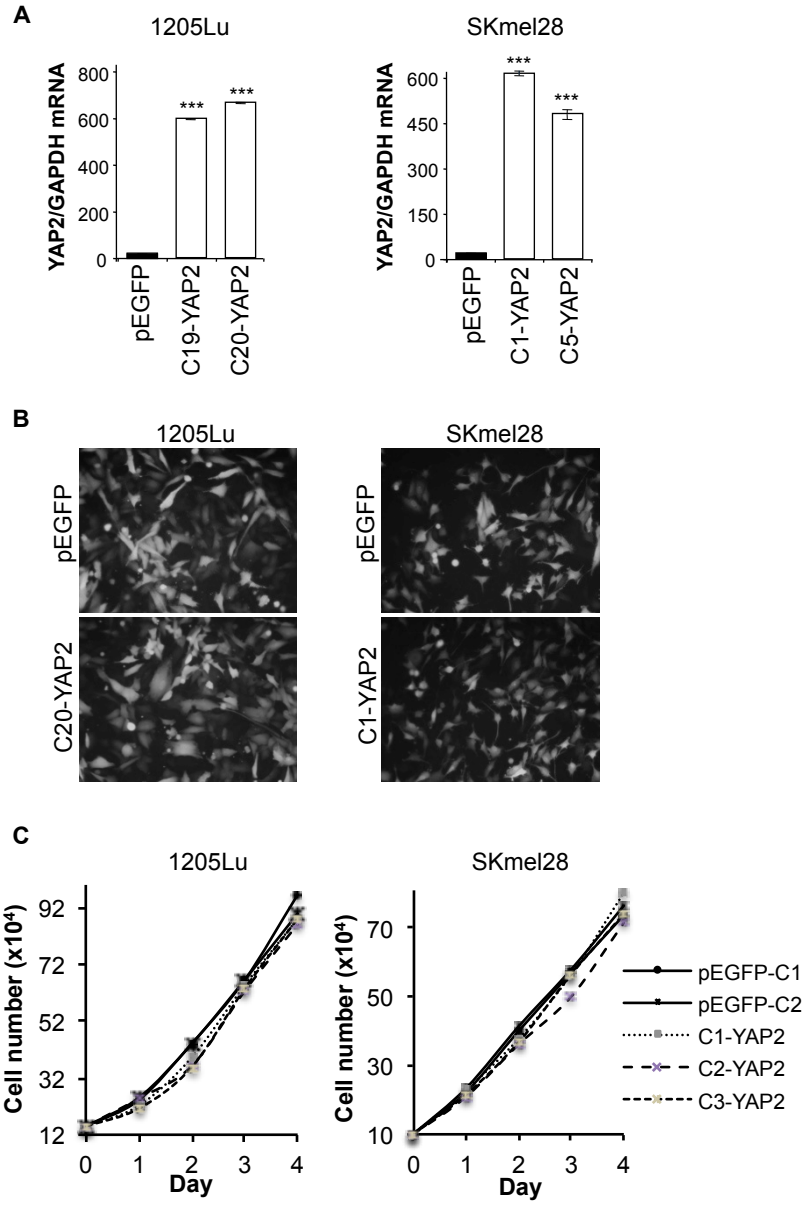
A
1205Lu
SKmel28
YAP2/GAPDH mRNA
800
600
400
200
0
***
pEGFP
C19-YAP2
C20-YAP2
600
450
300
150
C1-YAP2
C5-YAP2
B
pEGFP
C20-YAP2
C1-YAP2
C
Cell number (x10⁴)
92
72
52
32
12
70
50
30
10
0
1
2
3
4
Day
pEGFP-C1
pEGFP-C2
C1-YAP2
C2-YAP2
C3-YAP2

Figure S4

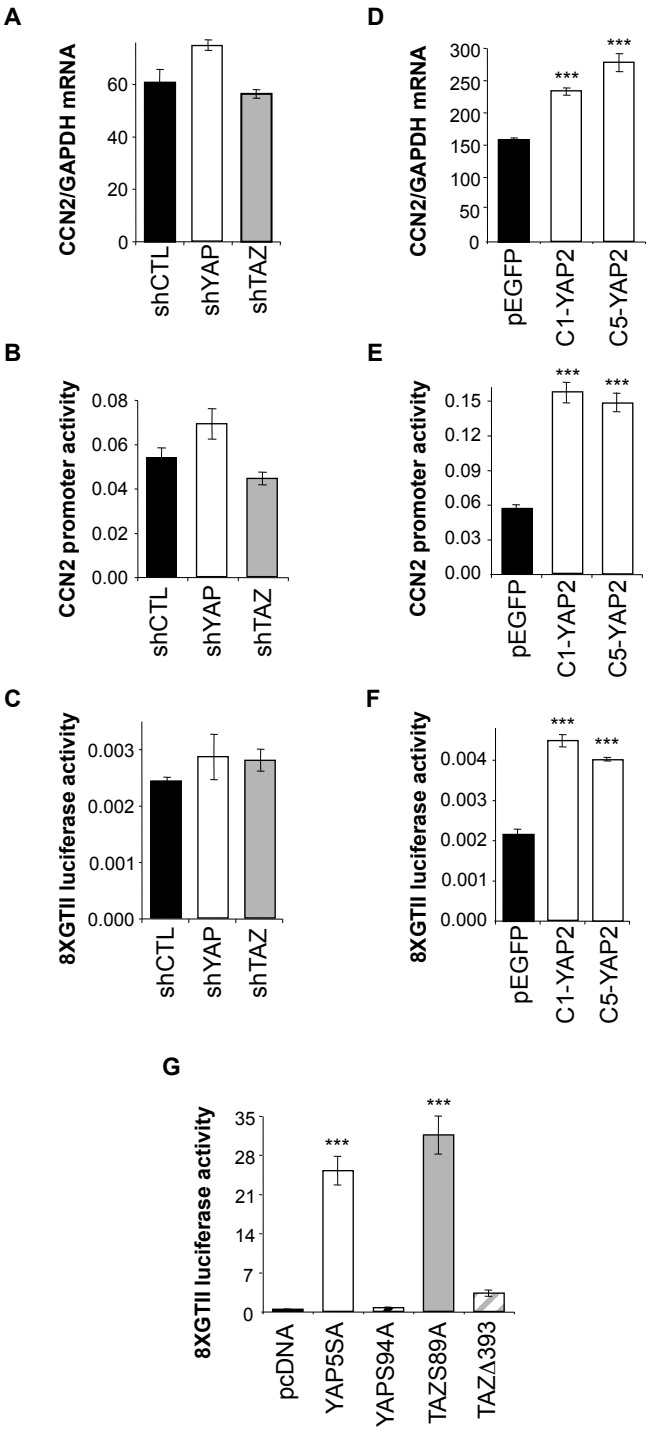
A
CCN2/GAPDH mRNA
0
20
40
60
shCTL
shYAP
shTAZ
D
CCN2/GAPDH mRNA
0
50
100
150
200
250
300
***
***
pEGFP
C1-YAP2
C5-YAP2
B
CCN2 promoter activity
0.00
0.02
0.04
0.06
0.08
shCTL
shYAP
shTAZ
E
CCN2 promoter activity
0.00
0.03
0.06
0.09
0.12
0.15
***
***
pEGFP
C1-YAP2
C5-YAP2
C
8XGTII luciferase activity
0.000
0.001
0.002
0.003
shCTL
shYAP
shTAZ
F
8XGTII luciferase activity
0.000
0.001
0.002
0.003
0.004
***
***
pEGFP
C1-YAP2
C5-YAP2
G
8XGTII luciferase activity
0
7
14
21
28
35
***
***
pcDNA
YAP5SA
YAPS94A
TAZS89A
TAZΔ393

Figure S5

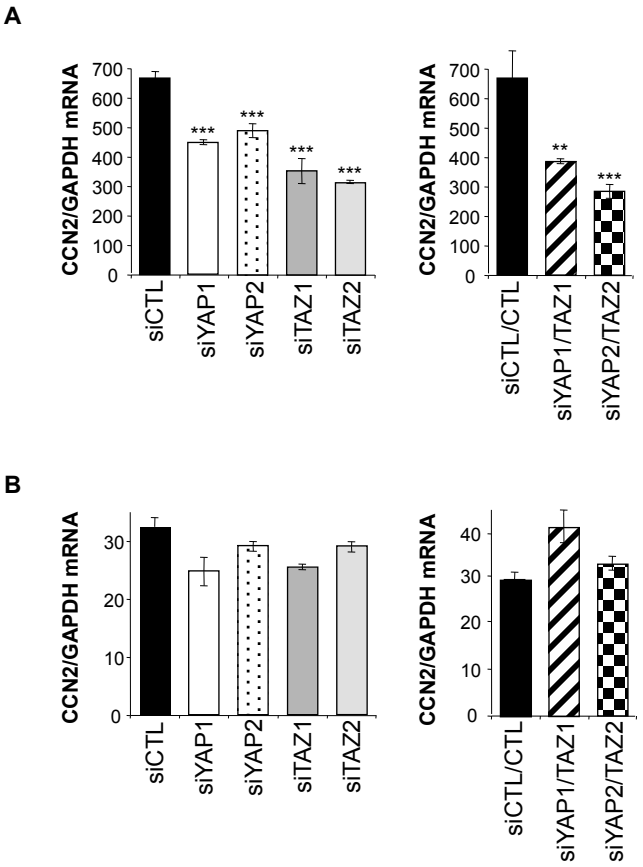
A
CCN2/GAPDH mRNA
700
600
500
400
300
200
100
0
***
***
***
***
siCTL
siYAP1
siYAP2
siTAZ1
siTAZ2
CCN2/GAPDH mRNA
**
***
siCTL/CTL
siYAP1/TAZ1
siYAP2/TAZ2
B
CCN2/GAPDH mRNA
30
20
10
0
siCTL
siYAP1
siYAP2
siTAZ1
siTAZ2
CCN2/GAPDH mRNA
40
30
20
10
0
siCTL/CTL
siYAP1/TAZ1
siYAP2/TAZ2

Figure S6