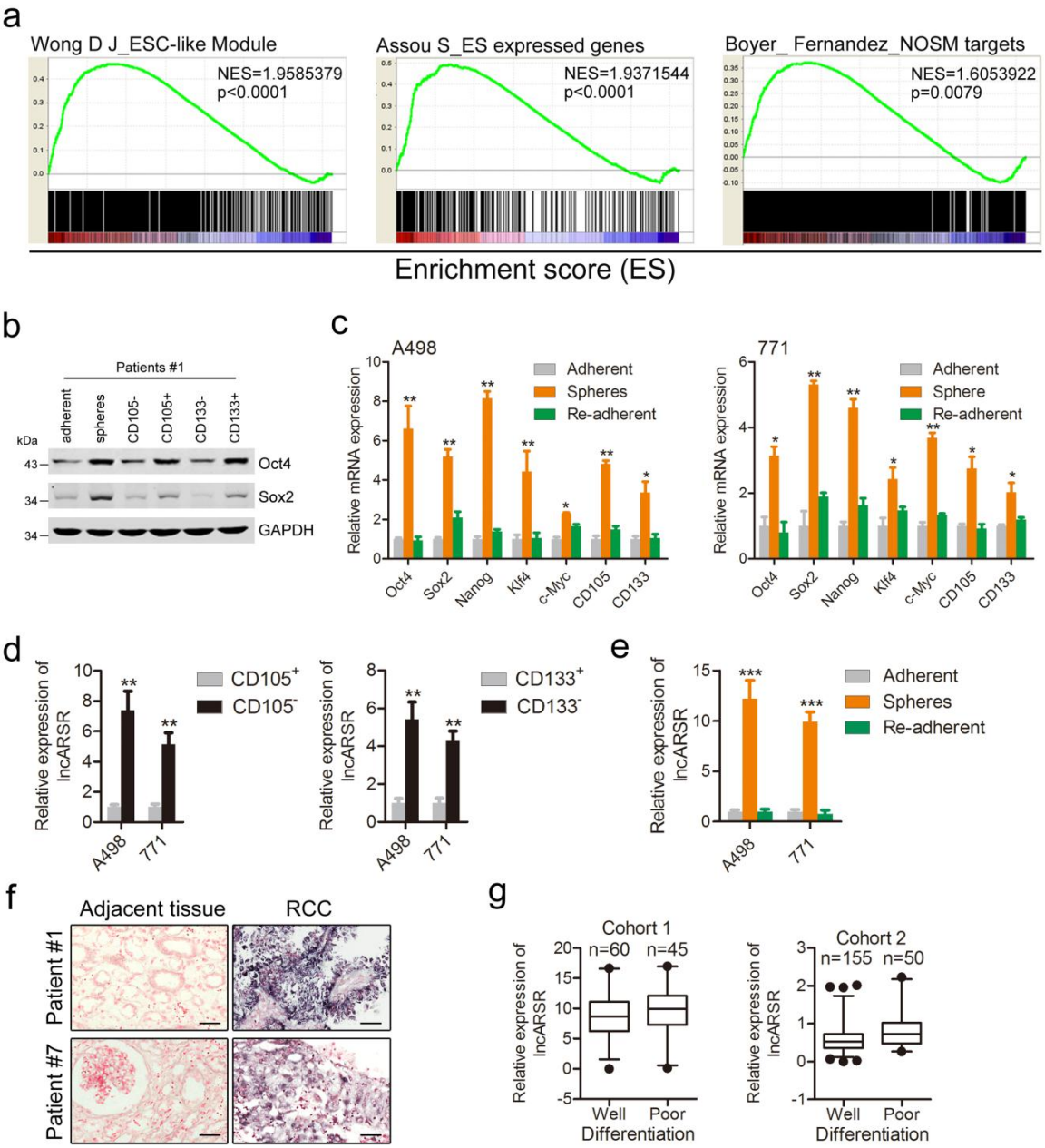
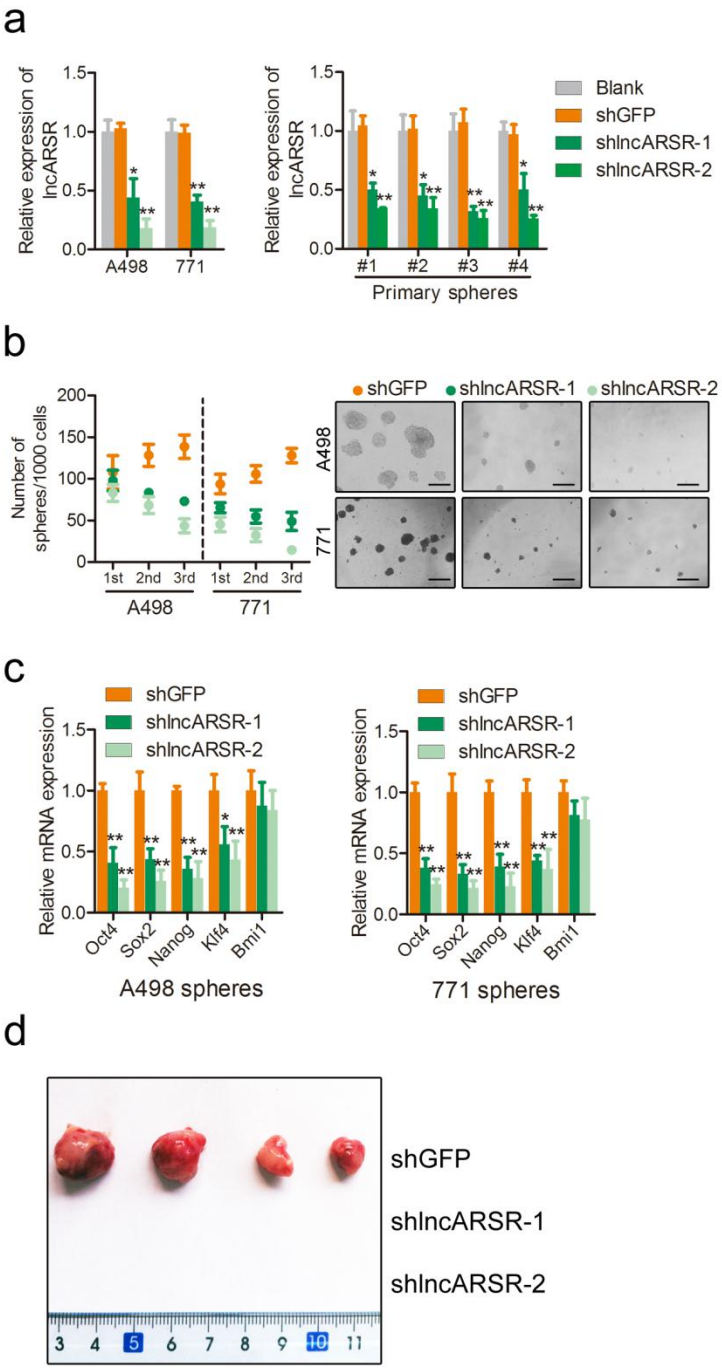

a
Wong D J_ESC-like Module
NES=1.9585379
p<0.0001
Assou S_ES expressed genes
NES=1.9371544
p<0.0001
Boyer_ Fernandez_NOSM targets
NES=1.6053922
p=0.0079
Enrichment score (ES)
b
Patients #1
adherent
spheres
CD105-
CD105+
CD133-
CD133+
kDa
Oct4
Sox2
GAPDH
c
A498
771
Adherent
Spheres
Sphere
Re-adherent
Relative mRNA expression
Oct4
Sox2
Nanog
Klf4
c-Myc
CD105
CD133
d
Relative expression of lncARSR
CD105+
CD105-
CD133+
CD133-
A498
771
e
Adherent
Spheres
Re-adherent
f
Adjacent tissue
RCC
Patient #1
Patient #7
g
Cohort 1
n=60
n=45
Cohort 2
n=155
n=50
Well
Poor
Differentiation

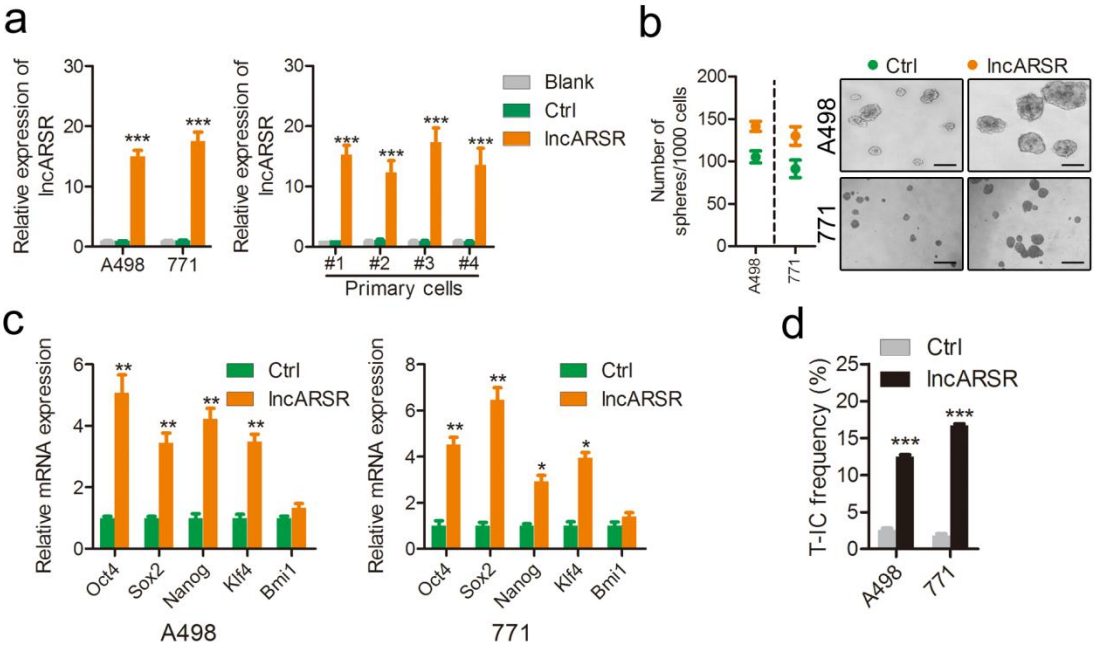
Supplementary Figure 1. lncARSR is upregulated in T-ICs and predicts poor prognosis

(a) Gene set enrichment analysis using three stem cell-like gene signatures. NES, normalized enrichment score. (b) Western blot analysis of indicated proteins in enriched T-Ics from primary RCC cells. (c) qRT-PCR analysis of indicated mRNAs in RCC adherent, spheres and re-adherent cells (n = 3). (d) qRT-PCR analysis of lncARSR in MACS sorted $CD105^+$ (left) or $CD133^+$ (right) RCC cells relative to negative cells (n = 3). (e) qRT-PCR analysis of lncARSR in RCC adherent, spheres and re-adherent cells (n = 3). (c-e) Data are represented as mean ± s.d.; *p < 0. 05, **p < 0. 01 and ***p < 0. 001; two-tailed Student's t-test. (f) Representative images of lncARSR expression detected by RNA ISH (in situ hybridization) in cohort 2. Scale bar = 50 μm. (g) Comparison of lncARSR levels in well or poorly differentiated RCC tissues in cohorts 1 (left, p = 0.013, Mann–Whitney U-test) and cohort 2 (right, p < 0.001, Mann–Whitney U-test). The horizontal lines in the box plots represent the median, the boxes represent the interquartile range, and the whiskers represent the 2.5th and 97.5th percentiles.


a
Relative expression of lncARSR
1.5
1.0
0.5
0.0
A498
771
#1
#2
#3
#4
Primary spheres
Blank
shGFP
shlncARSR-1
shlncARSR-2
b
Number of spheres/1000 cells
200
150
100
50
0
1st
2nd
3rd
A498
771
shGFP
shlncARSR-1
shlncARSR-2
c
Relative mRNA expression
Oct4
Sox2
Nanog
Klf4
Bmi1
A498 spheres
771 spheres
d
shGFP
shlncARSR-1
shlncARSR-2

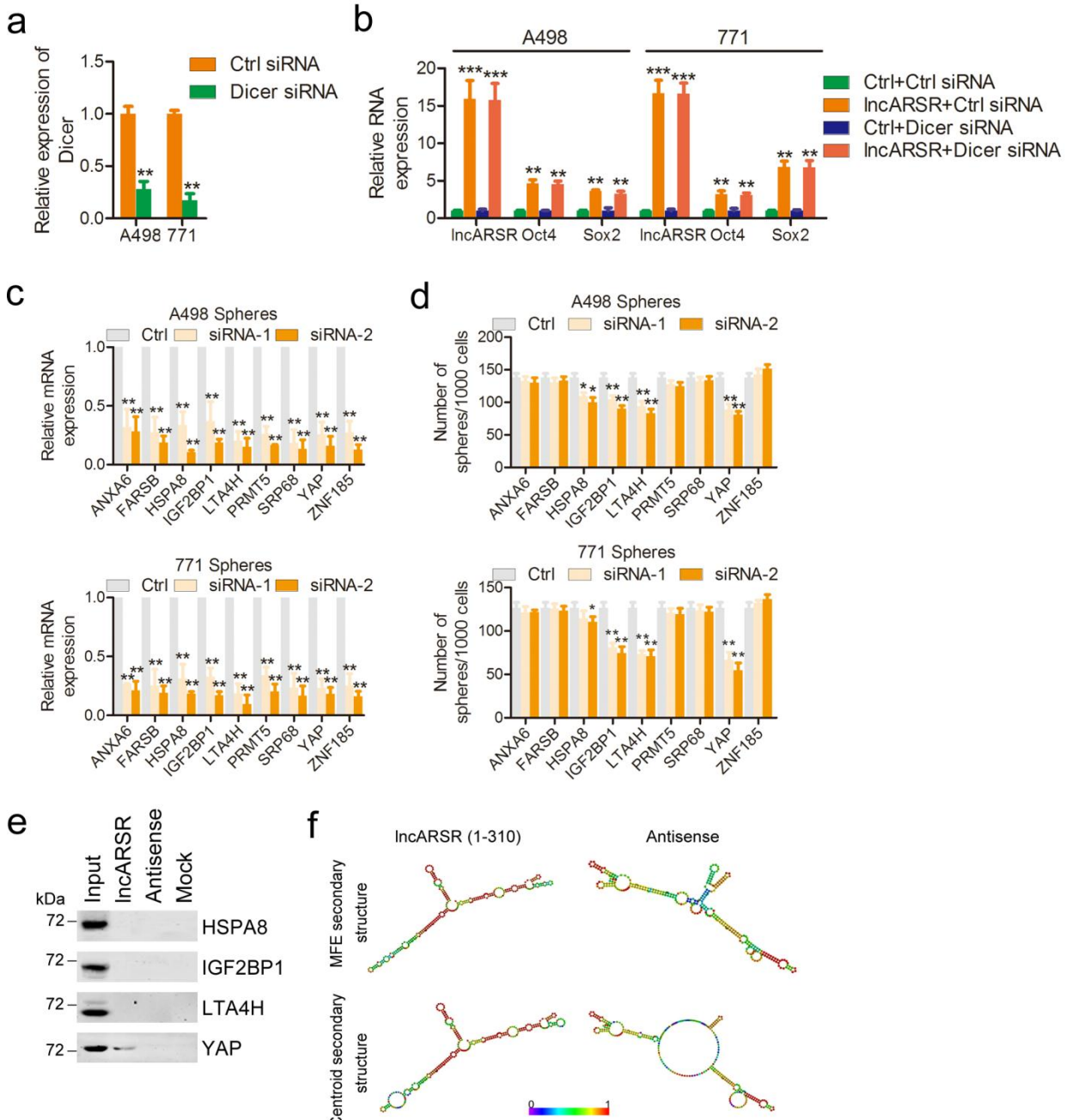
Supplementary Figure 2. lncARSR is required for the maintenance of renal T-ICs

(a) Left: qRT-PCR analysis of lncARSR expression in lncARSR-knockdown and control RCC cells (n = 3). Right: qRT-PCR analysis of lncARSR expression in lncARSR-knockdown and control primary RCC cells (n = 3). Data are represented as mean ± s.d.; *p < 0. 05 and **p < 0. 01; two-tailed Student's t-test. (b) Spheres formation assay of lncARSR-knockdown and control RCC cells (n = 3). The number of primary, secondary and tertiary passaged spheres was counted after 7 days (left). Representative images of spheres are shown (right). Scale bar = 200 μm. (c) qRT-PCR analysis of indicated mRNAs in lncARSR-knockdown and control RCC spheres (n = 3). Data are represented as mean ± s.d.; *p < 0. 05 and **p < 0. 01; two-tailed Student's t-test. (d) Subcutaneous xenograft assay of 1×10^4 RCC cells derived from lncARSR-knockdown and control xenografts for 2 months (n = 4 per group).



Supplementary Figure 3. lncARSR promotes renal T-ICs expansion

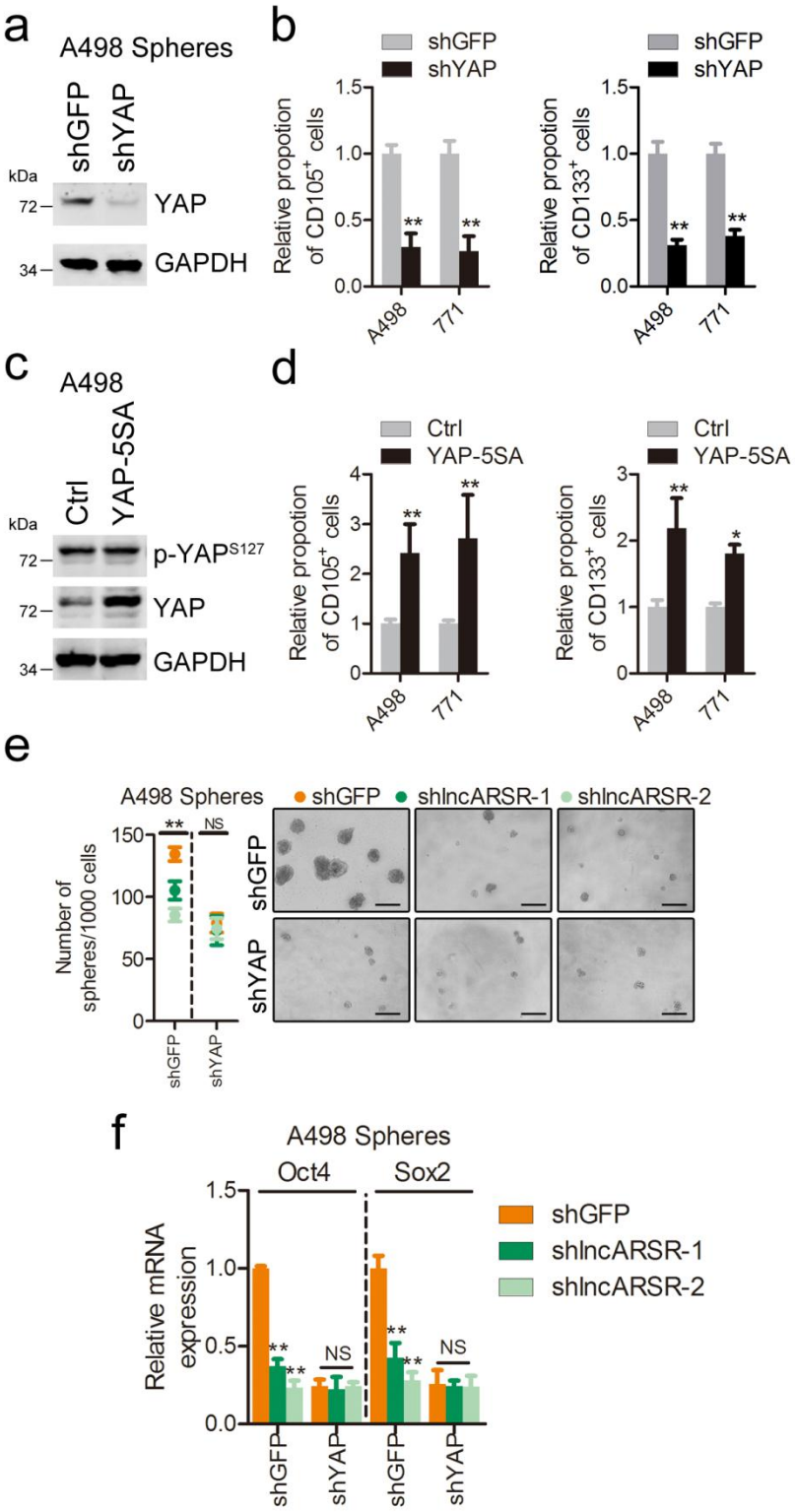
(a) Left: qRT-PCR analysis of lncARSR expression in lncARSR-overexpressing and control RCC cells (n = 3). Right: qRT-PCR analysis of lncARSR expression in lncARSR-overexpressing and control primary RCC cells (n = 3). (b) Spheres formation assay of lncARSR-overexpressing and control RCC cells (n = 3). The number of spheres was counted after 7 days (left). Representative images of spheres are shown (right). Scale bar = 200 μm. (c) qRT-PCR analysis of indicated mRNAs in lncARSR-overexpressing and control RCC cells (n = 3). (d) In vitro limiting dilution assay of lncARSR-overexpressing and control RCC cells. The results were shown as natural logarithm of the proportion of T-ICs. (a, c and d) Data are represented as mean ± s.d.; *p < 0. 05, **p < 0. 01 and ***p < 0. 001; two-tailed Student's t-test.


a
Relative expression of Dicer
Ctrl siRNA
Dicer siRNA
A498 771
b
A498
771
Relative RNA expression
Ctrl+Ctrl siRNA
lncARSR+Ctrl siRNA
Ctrl+Dicer siRNA
lncARSR+Dicer siRNA
lncARSR Oct4 Sox2 lncARSR Oct4 Sox2
c
A498 Spheres
Ctrl siRNA-1 siRNA-2
Relative mRNA expression
ANXA6 FARSB HSPA8 IGF2BP1 LTA4H PRMT5 SRP68 YAP ZNF185
771 Spheres
d
A498 Spheres
Number of spheres/1000 cells
771 Spheres
e
kDa
Input lncARSR Antisense Mock
72
HSPA8
IGF2BP1
LTA4H
YAP
f
lncARSR (1-310)
Antisense
MFE secondary structure
Centroid secondary structure

Supplementary Figure 4. lncARSR physically interacts with YAP

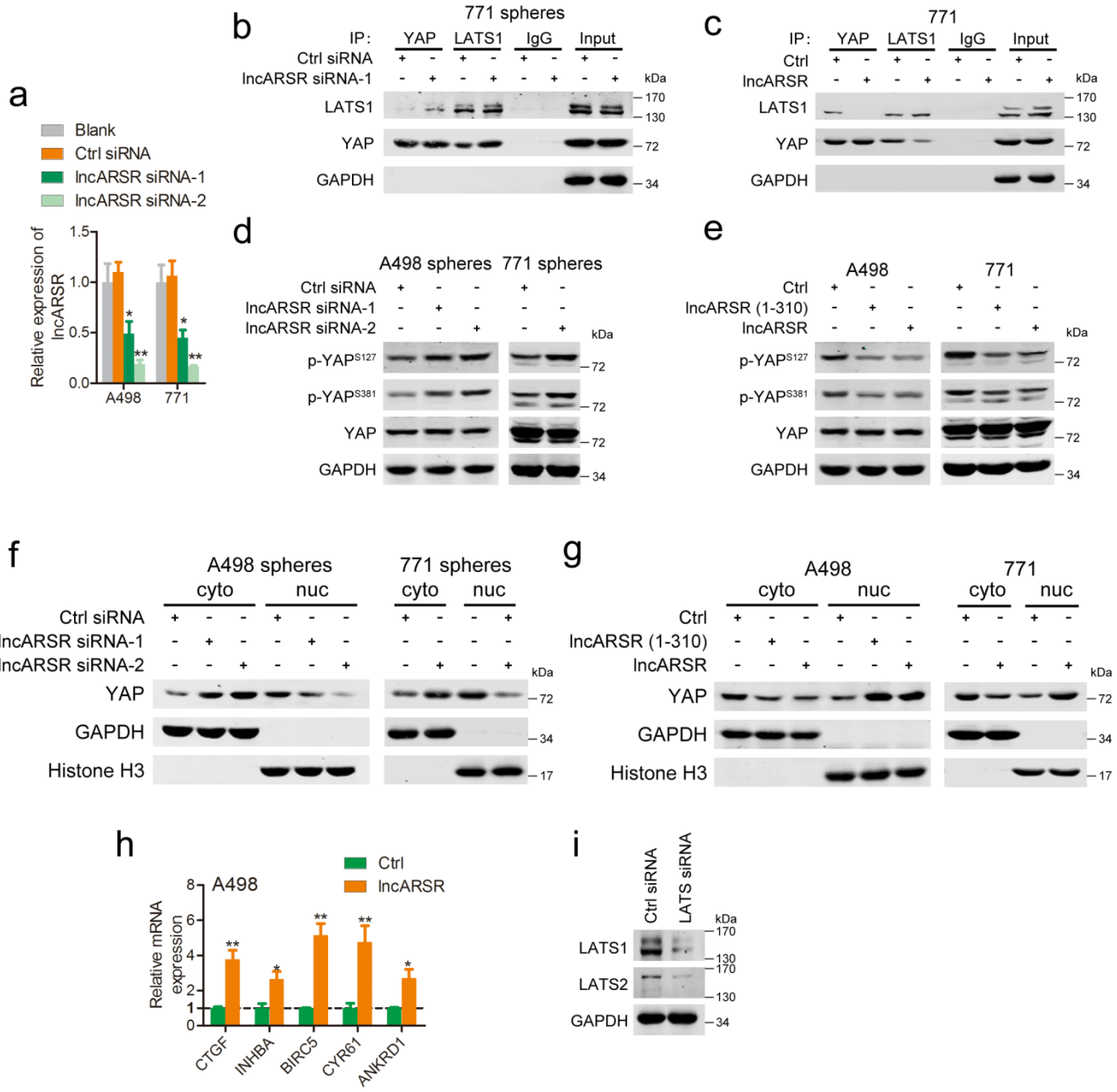
(a) qRT-PCR analysis of Dicer expression in RCC cells transfected with Dicer siRNA after 48h (n = 3). (b) qRT-PCR analysis of indicated RNAs in RCC cells transfected with lncARSR plasmid and Dicer siRNA (n = 3). (c) Verification of interference efficiency of siRNA for indicated mRNAs in RCC spheres by qRT-PCR (n = 3). (d) Spheres formation assay of RCC spheres transfected with indicated siRNAs (n = 3). The number of spheres was counted after 7 days (left). Representative images of spheres are shown (right). Scale bar = 200 μm. (a-d) Data are represented as mean ± s.d.; *p < 0. 05, **p < 0. 01 and ***p < 0. 001; two-tailed Student's t-test. (e) Western blot analysis of indicated proteins in RNA pull-down precipitates retrieved by biotin-labeled lncARSR or antisense RNA from the cytoplasmic lysates of A498 spheres. (f) Secondary structure prediction of 5' segment of lncARSR and its antisense sequence based on minimum free energy (MFE) and partition function (http://rna.tbi.univie.ac.at/). Color scale indicates the prediction confidence for each base with red indicating strong confidence.

Data are shown as means ± s.d. *p < 0. 05; **p < 0. 01; and ***p < 0. 001.


a
A498 Spheres
shGFP
shYAP
kDa
72
YAP
34
GAPDH
b
shGFP
shYAP
Relative propotion of CD105+ cells
1.5
1.0
0.5
0.0
**
**
A498
771
shGFP
shYAP
Relative propotion of CD133+ cells
1.5
1.0
0.5
0.0
**
**
A498
771
c
A498
Ctrl
YAP-5SA
kDa
72
p-YAPS127
72
YAP
34
GAPDH
d
Ctrl
YAP-5SA
Relative propotion of CD105+ cells
4
3
2
1
0
**
**
A498
771
Ctrl
YAP-5SA
Relative propotion of CD133+ cells
3
2
1
0
**
*
A498
771
e
A498 Spheres
shGFP
shlncARSR-1
shlncARSR-2
Number of spheres/1000 cells
150
100
50
0
**
NS
shGFP
shYAP
shGFP
shYAP
f
A498 Spheres
Oct4
Sox2
Relative mRNA expression
1.5
1.0
0.5
0.0
**
**
NS
**
**
NS
shGFP
shlncARSR-1
shlncARSR-2
shGFP
shYAP
shGFP
shYAP

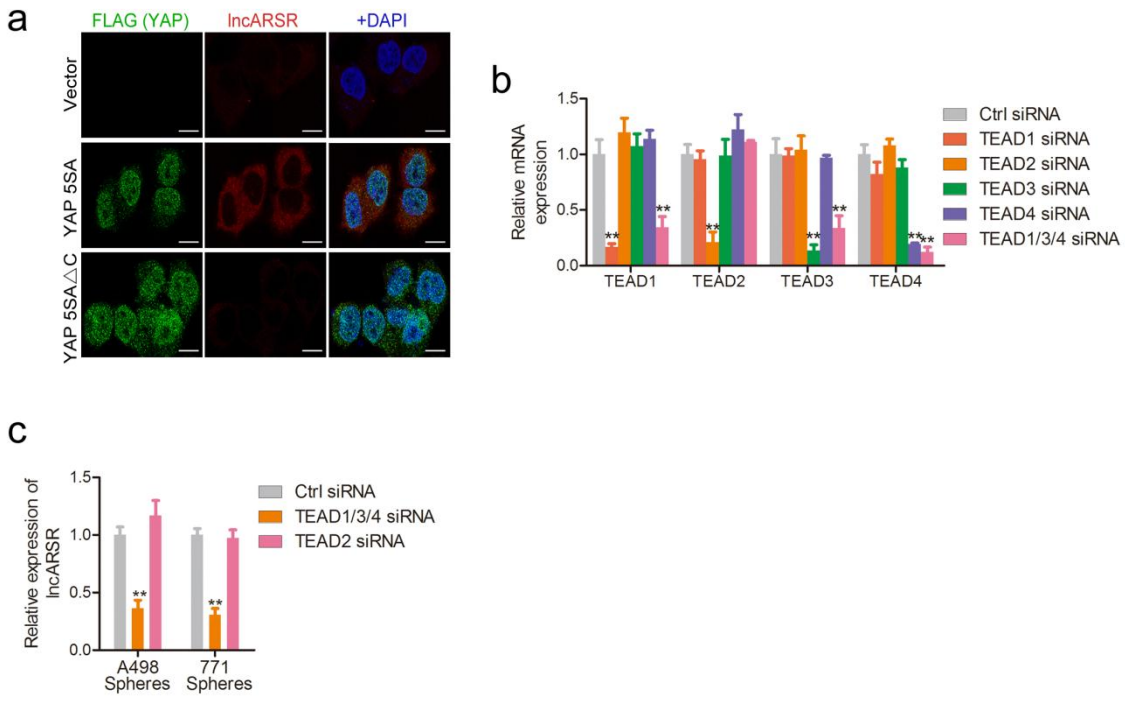
Supplementary Figure 5. YAP is responsible for lncARSR-mediated T-IC properties

(a) Western blot analysis of YAP in YAP-knockdown and control A498 spheres. (b) Flow cytometric analysis of the proportion of CD105+ (left) or CD133+ (right) cells in YAP-knockdown and control RCC cells (n = 3). (c) Western blot analysis of YAP in YAP-5SA-overexpressing and control A498 cells. (d) Flow cytometric analysis of the proportion of CD105+ (left) or CD133+ (right) cells in YAP-5SA-overexpressing and control RCC cells (n = 3). (e) Spheres formation assay of A498 spheres transfected with indicated plasmids (n = 3). The number of spheres was counted after 7 days (left). Representative images of spheres are shown (right). Scale bar = 200 μm. (f) qRT-PCR analysis of Oct4 and Sox2 in A498 spheres transfected with indicated plasmids after 48h (n = 3). (b, d-f) Data are represented as mean ± s.d.; *p < 0. 05 and **p < 0. 01; two-tailed Student's t-test.


a
Blank
Ctrl siRNA
lncARSR siRNA-1
lncARSR siRNA-2
Relative expression of lncARSR
1.5
1.0
0.5
0.0
A498
771
b
771 spheres
IP:
YAP
LATS1
IgG
Input
Ctrl siRNA
lncARSR siRNA-1
kDa
LATS1
YAP
GAPDH
170
130
72
34
c
771
IP:
YAP
LATS1
IgG
Input
Ctrl
lncARSR
kDa
LATS1
YAP
GAPDH
170
130
72
34
d
A498 spheres
771 spheres
Ctrl siRNA
lncARSR siRNA-1
lncARSR siRNA-2
kDa
p-YAPS127
p-YAPS381
YAP
GAPDH
72
72
72
34
e
A498
771
Ctrl
lncARSR (1-310)
lncARSR
kDa
p-YAPS127
p-YAPS381
YAP
GAPDH
72
72
72
34
f
A498 spheres
771 spheres
cyto
nuc
Ctrl siRNA
lncARSR siRNA-1
lncARSR siRNA-2
kDa
YAP
GAPDH
Histone H3
72
34
17
g
A498
771
cyto
nuc
Ctrl
lncARSR (1-310)
lncARSR
kDa
YAP
GAPDH
Histone H3
72
34
17
h
A498
Ctrl
lncARSR
Relative mRNA expression
8
6
4
2
1
0
CTGF
INHBA
BIRC5
CYR61
ANKRD1
i
Ctrl siRNA
LATS siRNA
kDa
LATS1
LATS2
GAPDH
170
130
170
130
34

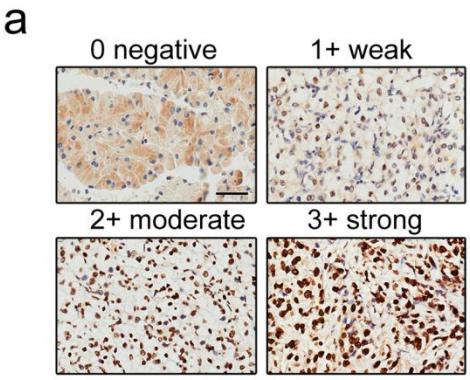
Supplementary Figure 6. lncARSR blocks LATS1-mediated YAP phosphorylation

(a) qRT-PCR analysis of lncARSR expression in lncARSR-knockdown and control RCC cells (n = 3). Data are represented as mean ± s.d.; *p < 0. 05 and **p < 0. 01; two-tailed Student's t-test. (b) Coimmunoprecipitation of YAP and LATS1 in lysates of lncARSR-knockdown and control 771 spheres. GAPDH acted as a loading control. (c) Coimmunoprecipitation of YAP and LATS1 in lysates of lncARSR-overexpressing and control 771 cells. GAPDH acted as a loading control. (d) Western blot analysis of YAP in lncARSR-knockdown and control RCC spheres. (e) Western blot analysis of YAP in RCC cells with lncARSR overexpression or 5′ segment (nucleotides 1-310) overexpression. (f) Western blot analysis of YAP in subcellular fractions of lncARSR-knockdown and control RCC spheres. GAPDH and Histone H3 acted as cytoplasm and nucleus marker respectively. (g) Western blot analysis of YAP in subcellular fractions of RCC cells with lncARSR overexpression or 5′ segment (nucleotides 1-310) overexpression. GAPDH and Histone H3 acted as cytoplasm and nucleus marker respectively. (h) qRT-PCR analysis of indicated mRNAs in lncARSR-overexpressing and control A498 cells (n = 3). Data are represented as mean ± s.d.; *p < 0. 05 and **p < 0. 01; two-tailed Student's t-test. (i) Western blot analysis of LATS1 and LATS2 in A498 cells transfected with LATS siRNA mix after 48h.



Supplementary Figure 7. YAP/TEAD complex transactivates lncARSR

(a) RNA FISH analysis of lncARSR and immunofluorescence detection of YAP in A498 cells transfected with Flag-YAP-5SA plasmid or Flag-YAP-5SAΔC plasmid after 48h. Scale bars = 10 μm. (b) Verification of interference efficiency of TEADs siRNA for indicated mRNAs in RCC spheres by qRT-PCR (n = 3). (c) qRT-PCR analysis of lncARSR in RCC spheres transfected with indicated siRNA after 48h (n = 3). (b and c) Data are represented as mean ± s.d.; $^{**}p < 0.01$; two-tailed Student's t-test.



Supplementary Figure 8. Combining lncARSR and YAP exhibits improved prognostic value

(a) Representative images of different nuclear YAP staining intensity in RCC tissues in Cohort 2. Scale bar = 50 μm.

Supplementary Table 1. Clinical Characteristics of RCC Patients

Variables	Cohort 1 (*n* = 105)	Cohort 2 (*n* = 205)
Gender (%)		
Male	65 (61.9)	139 (67.8)
Female	40 (38.1)	66 (32.2)
Age (%)		
≤60	69 (65.7)	133 (64.9)
＞60	36 (34.3)	72 (35.1)
Tumor size (%)		
≤4 cm	45 (42.9)	86 (41.9)
＞4 cm	60 (57.1)	119 (58.1)
Furman grade (%)		
Ⅰ and Ⅱ	60 (57.1)	155 (75.6)
Ⅲ and Ⅳ	45 (42.9)	50 (24.4)
TNM stage (%)		
Ⅰ and Ⅱ	62 (87.6)	142 (69.3)
Ⅲ and Ⅳ	43 (12.4)	63 (30.7)
Tumor thrombus (%)		
No	95 (90.5)	186 (90.7)
Yes	10 (9.5)	19 (9.3)
Distant metastasis (%)		
No	92 (87.6)	173 (84.4)
Yes	13 (12.4)	32 (15.6)

Supplementary Table 2. Correlation of lncARSR Levels and Clinical Characteristics in Cohort 1

Variables	Low lncARSR (*n* = 53)	High lncARSR (*n* = 52)	*p*-value
Gender			1.000
Male	30	30	
Female	23	22	
Age			0.838
≤60	34	35	
＞60	19	17	
Tumor size			0.238
≤4cm	26	19	
＞4cm	27	33	
Furman grade			0.031
Ⅰ/Ⅱ	36	24	
Ⅲ/Ⅵ	17	28	
TNM stage			0.010
Ⅰ/Ⅱ	38	24	
Ⅲ/Ⅵ	15	28	
Tumor thrombus			0.052
No	51	44	
Yes	2	8	
Distant metastasis			0.042
No	50	42	
Yes	3	10	

Supplementary Table 3. Correlation of lncARSR Levels and Clinical Characteristics in Cohort 2

Variables	Low lncARSR (*n* = 103)	High lncARSR (*n* = 102)	*p*-value
Gender			0.296
Male	66	73	
Female	37	29	
Age			0.661
≤60	65	68	
＞60	38	34	
Tumor size			0.888
≤4cm	44	42	
＞4cm	59	60	
Furman grade			0.023
Ⅰ/Ⅱ	85	70	
Ⅲ/Ⅵ	18	32	
TNM stage			0.010
Ⅰ/Ⅱ	80	62	
Ⅲ/Ⅵ	23	40	
Tumor thrombus			0.008
No	99	87	
Yes	4	15	
Distant metastasis			0.002
No	95	78	
Yes	8	24	

Supplementary Table 4. Univariate and Multivariate Analyses of Factors Associated with Overall Survival in Cohort 1

Variable	Univariate	Multivariate		
		Hazard Ratio	95% CI	*p*-value
lncARSR expression				
High vs Low	0.004	3.215	1.269-8.145	0.014*
Furman grade				
Ⅲ/Ⅵvs Ⅰ/Ⅱ	0.040	1.236	0.489-3.125	0.655
TNM				
Ⅲ/Ⅵvs Ⅰ/Ⅱ	0.006	2.015	0.771-5.265	0.153
Tumor thrombus				
Yes vs No	0.047	1.222	0.419-3.565	0.713
Distant metastasis				
Yes vs No	0.003	2.052	0.756-5.570	0.158

Supplementary Table 5. Univariate and Multivariate Analyses of Factors Associated with Recurrence in Cohort 1

Variable	Univariate	Multivariate		
		Hazard Ratio	95% CI	*p*-value
lncARSR expression				
High vs Low	0.001	3.073	1.476-6.400	0.003*
TNM				
Ⅲ/Ⅵvs Ⅰ/Ⅱ	0.043	1.242	0.574-2.688	0.583
Distant metastasis				
Yes vs No	0.003	2.736	1.279-5.851	0.009*

Supplementary Table 6. Univariate and Multivariate Analyses of Factors Associated with Overall Survival in Cohort 2

Variable	Univariate	Multivariate		
		Hazard Ratio	95% CI	*p*-value
lncARSR expression				
High vs Low	0.008	2.173	1.230-3.837	0.007*
TNM				
Ⅲ/Ⅵvs Ⅰ/Ⅱ	0.009	2.186	1.079-4.428	0.030*
Distant metastasis				
Yes vs No	0.005	2.451	1.187-5.061	0.015*

Supplementary Table 7. Univariate and Multivariate Analyses of Factors Associated with Recurrence in Cohort 2

Variable	Univariate	Multivariate		
		Hazard Ratio	95% CI	*p*-value
lncARSR expression				
High vs Low	0.002	2.023	1.213-3.375	0.007*
TNM				
Ⅲ/Ⅵvs Ⅰ/Ⅱ	0.048	1.751	0.911-3.369	0.093
Tumor thrombus				
Yes vs No	0.138	0.992	0.510-1.932	0.982
Distant metastasis				
Yes vs No	0.004	2.793	1.393-5.597	0.004*

Supplementary Table 8. Frequency of T-ICs in lncARSR-knockdown and control sphere-derived RCC cells

Cell type inoculated	T-ICs Frequency		*p*-value
	Estimate	Upper and Lower Limits	Ratio of prop.'s=1
A498 Sphere			
shGFP	1/3181	1/8043-1/1258	
shlncARSR-1	1/38490	1/94240-1/15720	<0.0001
shlncARSR-2	1/84598	1/214144-1/33421	<0.0001
771 Sphere			
shGFP	1/7908	1/19790-1/3160	
shlncARSR-1	1/84598	1/214144-1/33421	0.0002
shlncARSR-2	1/280334	1/1115137-1/70473	<0.0001

Supplementary Table 9. Frequency of T-ICs in lncARSR-overexpressing and control RCC cells

Cell type inoculated	T-ICs Frequency		*p*-value
	Estimate	Upper and Lower Limits	Ratio of prop.'s=1
A498			
Ctrl	1/460139	1/1110523-1/190656	
lncARSR	1/57086	1/138002-1/23614	0.0007
771			
Ctrl	1/1228510	1/3410211-1/442564	
lncARSR	1/122257	1/333981-1/44753	0.0009

Supplementary Table 10. Frequency of T-ICs in indicated RCC cells

Cell type inoculated	T-ICs Frequency		*p*-value
	Estimate	Upper and Lower Limits	Ratio of prop.'s=1
A498			
Ctrl shGFP	1/376880	1/925194-1/153523	
lncARSR shGFP	1/31801	1/80421-1/12575	<0.0001
Ctrl shYAP	1/681902	1/1670761-1/278311	0.318
lncARSR shYAP	1/384893	1/942399-1/157197	0.971

Supplementary Table 11. Correlation of Nuclear YAP and lncARSR Levels in Cohort 2

	Low lncARSR	**High lncARSR**	***p*-value**
cyto-YAP	79	38	$p < 0.001$
nuc-YAP	24	64	

Supplementary Table 12. Sequences of Primers Used for Plasmid Construction

pcDNA3.1 -lncARSR	Forward (5’-3’)	GGGGTACCACCCCCGGAGGCACTCG
	Reverse (5’-3’)	CCGCTCGAGTTTTTTTTTTGTTTTATCAAA GGAATTTA
pSPT19 -lncARSR	Forward (5’-3’)	GCTCTAGAACCCCCGGAGGCACTCG
	Reverse (5’-3’)	CCCAAGCTTTTTTTTTTTTGTTTTATCAAAG GAATTTA
pSPT19 -lncARS R -5’ (1-310)	Reverse (5’-3’)	CCGCTCGAG TGAGACCAGCCAGTTGAGTTGG
pSPT19 -lncARSR -3’(282-591)	Forward (5’-3’)	GCCC AAGCTT CTATACCCCAACTCAACTGGCTGG
shlncARSR-1	Sense (5’-3’)	CCGGGAGCATGAAGAACTCCAACTTCTCG AGAAGTTGGAGTTCTTCATGCTCTTTTT
	Antisense (5’-3’)	AATTAAAAAGAGCATGAAGAACTCCAACT TCTCGAGAAGTTGGAGTTCTTCATGCTC
shlncARSR-2	Sense (5’-3’)	CCGGGCATGAAGAACTCCAACTTCACTCG AGTGAAGTTGGAGTTCTTCATGCTTTTT
	Antisense (5’-3’)	AATTAAAAAGCATGAAGAACTCCAACTTC ACTCGAGTGAAGTTGGAGTTCTTCATGC
shGFP	Sense (5’-3’)	5'-CCGGGCAAGCTGACCCTGAAGTTCATCT CGAGATGAACTTCAGGGTCAGCTTGCTTT TTG-3'
	Antisense (5’-3’)	5'-AATTCAAAAAGCAAGCTGACCCTGAAG TTCATCTCGAGATGAACTTCAGGGTCAGCT TGC-3'
YAP(1M) -(EcoRI)	Forward (5’-3’)	CCGGAATTCGCCACCATGGATCCCGGGCA GCAGC
YAP(154T) -(SalI)	Reverse (5’-3’)	GGACCGTCGACTGTAGCTGCTGGGCCAGA GACTACTCC
YAP(155P) -(EcoRI)	Forward (5’-3’)	CCGGAATTCGCCACCATGGATCCCACAGC TCAGCATCTTCGACA
YAP(504L) -(SalI)	Reverse (5’-3’)	GGACCGTCGACTAACCATGTAAGAAAGCT TTCTTTATCTAGCTTGG
YAP(263L) -(SalI)	Reverse (5’-3’)	GGACCGTCGACAAGCCTTGGGTCTAGCCA AGAGG
YAP(264D) -(EcoRI)	Forward (5’-3’)	CCGGAATTCGCCACCATGGACCCTCGTTTT GCCATGAACC
YAP(287P) -(SalI)	Reverse (5’-3’)	GGACCGTCGACGGGAGCCAGGGGTGGTG G
YAP(288Q) -(EcoRI)	Forward (5’-3’)	CCGGAATTCGCCACCATGGATCAGAGCCC ACAGGGAGGCG
YAP(499S) -(SalI)	Reverse (5’-3’)	GGACCGTCGACGCTTTCTTTATCTAGCTTG GTGGCAGCC

Supplementary Table 13. Sequences of siRNA Used in This Study

lncARSR siRNA	Sense (5’-3’)	CAACCCUGGAUCCAAAGUATT
	Antisense (5’-3’)	UACUUUGGAUCCAGGGUUGTT
YAP siRNA-1	Sense (5’-3’)	GGUGAUACUAUCAACCAAATT
	Antisense (5’-3’)	UUUGGUUGAUAGUAUCACCTT
YAP siRNA-2	Sense (5’-3’)	CUGCCACCAAGCUAGAUAATT
	Antisense (5’-3’)	UUAUCUAGCUUGGUGGCAGTT
TEAD1 siRNA	Sense (5’-3’)	CUGCCAUUCAUAACAAGCUTT
	Antisense (5’-3’)	AGCUUGUUAUGAAUGGCAGTT
TEAD2 siRNA	Sense (5’-3’)	GCCAGAUGCAGUUGAUUCUTT
	Antisense (5’-3’)	AGAAUCAACUGCAUCUGGCTT
TEAD3 siRNA	Sense (5’-3’)	CCAGUGUCCUGCAGAACAATT
	Antisense (5’-3’)	UUGUUCUGCAGGACACUGGTT
TEAD4 siRNA	Sense (5’-3’)	GAACGUCCCAUGAUGUGAATT
	Antisense (5’-3’)	UUCACAUCAUGGGACGUUCTT
TEAD1/3/4 siRNA	Sense (5’-3’)	UGAUCAACUUCAUCCACAATT
	Antisense (5’-3’)	UUGUGGAUGAAGUUGAUCATT
LATS1 siRNA	Sense (5’-3’)	GCAGCGUCUACAUCGUAAATT
	Antisense (5’-3’)	UUUACGAUGUAGACGCUGCTT
LATS2 siRNA	Sense (5’-3’)	CUACCAGAAAGAGUCUAAUTT
	Antisense (5’-3’)	AUUAGACUCUUUCUGGUAGTT
Dicer siRNA	Sense (5’-3’)	GGGCACCCAUCUCUAAUUATT
	Antisense (5’-3’)	UAAUUAGAGAUGGGUGCCCTT
ANXA6 siRNA-1	Sense (5’-3’)	GGGACUUUGAGAAGCUAAUTT
	Antisense (5’-3’)	AUUAGCUUCUCAAAGUCCCTT
ANXA6 siRNA-2	Sense (5’-3’)	CUCGGACCAAUGCUGAAAUTT
	Antisense (5’-3’)	AUUUCAGCAUUGGUCCGAGTT
FARSB siRNA-1	Sense (5’-3’)	CACCUACACUGACGAAGAATT
	Antisense (5’-3’)	UUCUUCGUCAGUGUAGGUGTT
FARSB siRNA-2	Sense (5’-3’)	CCUGUAUCCAGUUAUCUAUTT
	Antisense (5’-3’)	AUAGAUAACUGGAUACAGGTT
HSPA8 siRNA-1	Sense (5’-3’)	GUCCUCAUCAAGCGUAAUATT
	Antisense (5’-3’)	UAUUACGCUUGAUGAGGACTT
HSPA8 siRNA-2	Sense (5’-3’)	GCUGGUCUCAAUGUACUUATT
	Antisense (5’-3’)	UAAGUACAUUGAGACCAGCTT
IGF2BP1 siRNA-1	Sense (5’-3’)	GGCCCAUAAUAACUUUGUATT
	Antisense (5’-3’)	UACAAAGUUAUUAUGGGCCTT
IGF2BP1 siRNA-2	Sense (5’-3’)	GCUCCCUAUAGCUCCUUUATT
	Antisense (5’-3’)	UAAAGGAGCUAUAGGGAGCTT
LTA4H siRNA-1	Sense (5’-3’)	CAAAGGACCUUACAAUAGATT
	Antisense (5’-3’)	UCUAUUGUAAGGUCCUUUGTT
LTA4H siRNA-2	Sense (5’-3’)	CAUGAAAUAUCUCAUAGCUTT
	Antisense (5’-3’)	AGCUAUGAGAUAUUUCAUGTT
PRMT5 siRNA-1	Sense (5’-3’)	CCGGACUUUGUGUGACUAUTT
	Antisense (5’-3’)	AUAGUCACACAAAGUCCGGTT
PRMT5 siRNA-2	Sense (5’-3’)	GGUGAACACAGUACUACAUTT
	Antisense (5’-3’)	AUGUAGUACUGUGUUCACCTT
SRP68 siRNA-1	Sense (5’-3’)	GAGCUUCUGACCGAUAAUATT
	Antisense (5’-3’)	UAUUAUCGGUCAGAAGCUCTT
SRP68 siRNA-2	Sense (5’-3’)	CAGCUACCAUGAGUGAAGUTT
	Antisense (5’-3’)	ACUUCACUCAUGGUAGCUGTT
ZNF185 siRNA-1	Sense (5’-3’)	CCACUGAGGAUUACAAGAATT
	Antisense (5’-3’)	UUCUUGUAAUCCUCAGUGGTT
ZNF185 siRNA-2	Sense (5’-3’)	CAACUUGUCAGACGAGAGATT
	Antisense (5’-3’)	UCUCUCGUCUGACAAGUUGTT
Ctrl siRNA	Sense (5’-3’)	UUCUCCGAACGUGUCACGUTT
	Antisense (5’-3’)	ACGUGACACGUUCGGAGAATT

Supplementary Table 14. Sequences of Primers Used for qRT-PCR in This Study

lncARSR	Forward(5’-3’)	TTTGAAATGCTCTTTGAGGGAT
	Reverse(5’-3’)	TGCAGGTTGTCTGAAGTTGGA
Oct4	Forward(5’-3’)	CTTGCTGCAGAAGTGGGTGGAGGAA
	Reverse(5’-3’)	CTGCAGTGTGGGTTTCGGGCA
Sox2	Forward(5’-3’)	AAATGGGAGGGGTGCAAAAGAGGAG
	Reverse(5’-3’)	CAGCTGTCATTTGCTGTGGGTGATG
Nanog	Forward(5’-3’)	AATACCTCAGCCTCCAGCAGATG
	Reverse(5’-3’)	TGCGTCACACCATTGCTATTCTTC
Klf4	Forward(5’-3’)	GCCCCTCGGGCGGCTTCGTGGCCGAGCTC
	Reverse(5’-3’)	CGTACTCGCTGCCAGGGGCG
c-Myc	Forward(5’-3’)	CATCATCATCCAGGACTGTATGTG
	Reverse(5’-3’)	GGCTGCCGCTGTCTTTGC
CD105	Forward(5’-3’)	CACTAGCCAGGTCTCGAAGG
	Reverse(5’-3’)	CTGAGGACCAGAAGCACCTC
CD133	Forward(5’-3’)	GCAGCAGTCTGACCAGCGTGAA
	Reverse(5’-3’)	ACGGGTGGAAGCTGCCTCAGTT
YAP	Forward(5’-3’)	AGCCCAAATCCCACTCCC
	Reverse(5’-3’)	GTATCTCAAAAGAAGACTGTCGAAGA
CTGF	Forward(5’-3’)	GCCCAAGGACCAAACCG
	Reverse(5’-3’)	GTGCAGCCAGAAAGCTCAAA
INHBA	Forward(5’-3’)	TCGGGGAGAACGGGTATG
	Reverse(5’-3’)	TGCTGGAGACAGGGAAGACA
BIRC5	Forward(5’-3’)	TTCTCAAGGACCACCGCATCT
	Reverse(5’-3’)	CGCACTTTCTCCGCAGTTTC
CYR61	Forward(5’-3’)	AGTGCTGCGAGGAGTGGG
	Reverse(5’-3’)	GGTTGTATAGGATGCGAGGCT
ANKRD1	Forward(5’-3’)	GAGGAACTGGTCACTGGAAAGA
	Reverse(5’-3’)	GGGTCACAGGGTGGGCTA
TEAD1	Forward(5’-3’)	CATCTTATCAGACGAAGGCAAAA
	Reverse(5’-3’)	AGGTCGGGCGTGGAATC
TEAD2	Forward(5’-3’)	GTCTGATGAAGGCAAGATGTATGG
	Reverse(5’-3’)	CAAGGTGAACGGTGTCTGTGAG
TEAD3	Forward(5’-3’)	AGGACGGGGAAGACTCGG
	Reverse(5’-3’)	TGGGGTAGGCTGGCTGTG
TEAD4	Forward(5’-3’)	GGGGACCCTCCAATGCCT
	Reverse(5’-3’)	CTCTGTCTCAACTTTCTCCACCA
β-actin	Forward(5’-3’)	AATCGTGCGTGACATTAAGGAG
	Reverse(5’-3’)	ACTGTGTTGGCGTACAGGTCTT

Supplementary Table 15. Primary Antibodies Used in This Study

Antigens	Manufacturer	Application
Sox2	Abcam	1:1000 for WB
Oct4	Abcam	1:1000 for WB
p-YAP ^{S127}	Cell Signaling Technology	1:1000 for WB
p-YAP ^{S381}	Cell Signaling Technology	1:1000 for WB
YAP	Cell Signaling Technology	1:50 for IP, 1:100 for ICC, 1:1000 for WB,1:100 for IHC, 1:50 for RIP, 1:50 for ChIP
LATS1	Cell Signaling Technology	1:50 for IP, 1:1000 for WB
LATS2	Proteintech	1:1000 for WB
TEAD1	Cell Signaling Technology	1:50 for ChIP
FLAG	Merck Millipore	1:50 for RIP, 1:1000 for WB, 1:100 for ICC, 1:50 for ChIP
MYC	Cell Signaling Technology	1:50 for IP
CD105-APC	ebioscience	1:50 for FACS
CD133-FITC	ebioscience	1:50 for FACS
Histone H3	Abcam	1:1000 for WB
HSPA8	Proteintech	1:1000 for WB
IGF2BP1	Proteintech	1:1000 for WB
LTA4H	Proteintech	1:1000 for WB
GAPDH	Abclonal	1:5000 for WB

WB, western blot; IHC, immunohistochemitry; ICC, Immunocytochemistry;
IP, immunoprecipitation; ChIP, chromatin immunoprecipitation;
RIP, RNA immunoprecipitation, FACS, fluorescence activated cell sorter.

Supplementary Table 16. Sequences of Primers Used for ChIP-qPCR in This Study

TB 1	Forward(5’-3’)	TCACTGGGTGTCTGGTCTGC
	Reverse(5’-3’)	GAGCGTTGCCTTGGGAG
TB 2	Forward(5’-3’)	GGAAGAAAGCAGCCAACAACC
	Reverse(5’-3’)	GACGCCTACCGCAACG
Neg	Forward(5’-3’)	ATCTTACTTCGTTCGGTTCACATC
	Reverse(5’-3’)	GCGACTCCATTTCTGGCTCTA