Table S1. The circ-Amotl1-AKT1 Distance

N(res No)	atom	chain	AA (res No)	atom	chain	distance	type
U 40	OP1	A	TYR 152	OH	B	2.41	Phil phil
U 40	OP2	A	LEU 155	CD2	B	3.21	Phil phob
G 41	OP2	A	LYS 158	CD	B	2.44	Phil phil
A 42	OP1	A	LYS 182	NZ	B	3.45	Phil phil
A 45	O2′	A	GLU 314	OE1	B	3.17	Phil phil
A 45	N7	A	PHE 358	CZ	B	2.69	Phil phob
A 45	C2	A	LEU 357	CD2	B	1.46	Phil phob
A 45	O2′	A	PRO 313	CG	B	1.94	Phil phob
A 45	N6	A	HIS 354	CB	B	1.71	Phil phil
A 45	OP2	A	LYS 297	CE	B	1.79	Phil phil
U 46	O4	A	TYR 315	CE1	B	2.86	Phil phil
U 46	N3	A	GLU 278	OE1	B	2.09	Phil phil
U 77	O2′	A	HIS 220	ND1	B	2.06	Phil phil
U 77	C5′	A	ASP 221	OD2	B	2.42	Phil phil
G 78	OP2	A	ARG 222	CG	B	2.95	Phil phil
G 78	OP1	A	ASP 221	CG	B	0.8	Phil phil
G 78	OP2	A	THR 219	OG1	B	3.38	Phil phil
C 79	OP1	A	MET 147	CE	B	2.43	Phil phob
G 80	OP1	A	PHE 150	O	B	3.32	Phil phob
G 80	OP2	A	MET 147	O	B	3.09	Phil phob
G 80	O5′	A	ASN 148	ND2	B	2.23	Phil phil
G 81	O6	A	THR 146	OG1	B	3.43	Phil phil
G 81	OP2	A	ASN 148	OD1	B	1.91	Phil phil
G 81	OP1	A	LYS 170	NZ	B	2.86	Phil phil
C 82	OP2	A	LYS 170	CD	B	2.51	Phil phil
C 82	N4	A	ASN 148	O	B	1.17	Phil phil
C 82	N4	A	GLU 149	N	B	2.26	Phil phil
A 83	OP2	A	LYS 170	O	B	3.01	Phil phil
A 83	N6	A	VAL 145	CA	B	3.09	Phil phob
A 83	N6	A	GLU 149	OE1	B	0.81	Phil phil
A 83	C5′	A	ALA 171	CB	B	2.88	Phil phob
C 85	O2	A	ARG 200	NH2	B	3.23	Phil phil
U 86	O2	A	GLN 203	NE2	B	3.16	Phil phil
U 86	O2	A	ARG 200	NH2	B	2.86	Phil phil
G 87	C1′	A	GLN 203	NE2	B	3.06	Phil phil
A 90	O3′	A	GLU 418	O	B	2.21	Phil phil
C 91	OP1	A	LYS 420	CG	B	3.14	Phil phil
C 91	P	A	GLU 418	O	B	3.21	Phil phil
U 97	O2′	A	LYS 284	CE	B	1.87	Phil phil
C 99	C4′	A	GLU 228	OE1	B	1.54	Phil phil
C 99	O3′	A	ALA 212	CB	B	2.44	Phil phob
C 99	O2′	A	ARG 206	NH1	B	2.11	Phil phil
C 99	OP2	A	ARG 174	CD	B	3.41	Phil phil
A 100	OP2	A	LYS 214	CB	B	2.24	Phil phil
A 100	O4′	A	ARG 206	CD	B	3.33	Phil phil
A 100	OP1	A	GLU 228	N	B	2.4	Phil phil
A 100	O2′	A	LEU 202	O	B	1.26	Phil phob
A 100	OP1	A	ALA 212	O	B	1.22	Phil phob
A 100	OP1	A	MET 227	C	B	3.16	Phil phob
A 100	N3	A	GLN 203	CG	B	2.35	Phil phil
A 100	O3′	A	LEU 213	O	B	0.81	Phil phob
G 101	OP2	A	TYR 215	N	B	2.18	Phil phil
G 101	OP1	A	LEU 213	CG	B	0.92	Phil phob
G 101	O3′	A	ASN 199	O	B	2.76	Phil phil
G 101	O3′	A	SER 216	OG	B	2.97	Phil phil
G 101	OP2	A	LYS 214	N	B	1.34	Phil phil
G 101	C4′	A	LEU 202	CD2	B	0.6	Phil phob
G 101	C2	A	ARG 200	NH1	B	0.6	Phil phil
G 101	OP2	A	VAL 226	O	B	3.17	Phil phob
C 102	N4	A	TYR 215	CE1	B	2.23	Phil phil
C 102	C5′	A	ASN 199	N	B	3.43	Phil phil
C 102	OP2	A	SER 216	O	B	2.07	Phil phil
C 102	O4′	A	ARG 200	CG	B	2.84	Phil phil
G 103	O6	A	VAL 145	N	B	1.13	Phil phob
G 104	O6	A	THR 146	OG1	B	1.37	Phil phil
G 104	O6	A	GLU 149	OE2	B	2.14	Phil phil
G 104	N7	A	VAL 145	C	B	3.08	Phil phob
C 105	N4	A	THR 146	CG2	B	3.16	Phil phil

The table reporting a list of atoms “in contact” (within the distance cutoff) with relative distances less than 3.5Å.

Table S2. The circ-Amotl1-PDK1 Distance

N(res No)	atom	chain	AA (res No)	atom	chain	distance	type
G 3	N2	A	GLY 285	CA	B	2.77	Phil phob
A 4	O2′	A	GLY 285	N	B	3.35	Phil phob
A 4	O2′	A	LEU 289	CD2	B	2.69	Phil phob
A 4	C2	A	ASN 286	ND2	B	2.42	Phil phil
A 5	C4	A	LEU 289	CD1	B	0.82	Phil phob
A 5	C2	A	TYR 288	CD2	B	2.32	Phil phil
A 5	C2′	A	GLN 292	OE1	B	2.12	Phil phil
G 6	O4′	A	GLN 292	OE1	B	2.6	Phil phil
U 14	O2	A	ASN 286	ND2	B	2.33	Phil phil
U 15	O4′	A	ASN 286	CB	B	1.67	Phil phil
U 15	C4′	A	GLU 287	N	B	3.07	Phil phil
U 15	O2′	A	GLY 285	O	B	1.53	Phil phob
U 17	N3	A	GLN 247	NE2	B	2.49	Phil phil
U 17	O4	A	THR 245	CG2	B	2.97	Phil phil
A 18	C8	A	GLY 285	O	B	2.91	Phil phob
C 28	O3′	A	ILE 87	CD1	B	2.89	Phil phob
C 28	C4′	A	GLU 90	OE2	B	2.25	Phil phil
C 29	C5′	A	ILE 87	CD1	B	2.94	Phil phob
G 54	OP2	A	GLU 80	CB	B	2.62	Phil phil
G 56	OP1	A	LYS 83	CD	B	2.93	Phil phil
U 68	O3′	A	LYS 77	CE	B	2.37	Phil phil
U 68	C5	A	PRO 74	CG	B	1.54	Phil phob
U 69	O4	A	PRO 72	O	B	3.43	Phil phob
U 69	OP1	A	PHE 147	CB	B	2.17	Phil phob
U 69	C5	A	PRO 74	CD	B	2.75	Phil phob
U 69	C4′	A	TYR 146	O	B	0.99	Phil phil
U 69	O4	A	GLN 73	CB	B	1.36	Phil phil
U 69	OP1	A	LYS 77	CE	B	2.59	Phil phil
C 70	OP1	A	THR 148	CG2	B	2.98	Phil phil
C 70	N4	A	GLN 73	NE2	B	1.29	Phil phil
C 70	P	A	PHE 147	CA	B	3.25	Phil phob
C 71	OP2	A	ARG 131	NH2	B	2.72	Phil phil
C 71	N4	A	GLN 73	NE2	B	2.71	Phil phil
G 107	O2′	A	ILE 119	CD1	B	2.85	Phil phob
A 108	O3′	A	GLN 150	OE1	B	2	Phil phil
A 108	O3′	A	LYS 115	NZ	B	2.69	Phil phil
U 109	OP2	A	LYS 115	NZ	B	3.26	Phil phil
U 109	OP2	A	LEU 155	CD2	B	3.3	Phil phob
U 109	OP2	A	GLN 150	CD	B	0.78	Phil phil
A 115	N6	A	GLN 73	CB	B	3.18	Phil phil
A 115	N6	A	PRO 72	O	B	2.13	Phil phob
C 146	O3′	A	SER 105	N	B	1.2	Phil phil
C 146	O2′	A	ARG 106	CG	B	2.62	Phil phil
C 146	O3′	A	THR 104	C	B	0.4	Phil phil
C 146	O3′	A	ALA 103	C	B	3.27	Phil phob
C 147	O5′	A	ALA 103	C	B	0.89	Phil phob
C 147	OP1	A	GLU 101	O	B	2.08	Phil phil
C 147	P	A	SER 105	N	B	1.81	Phil phil
C 147	C5′	A	THR 104	N	B	0.81	Phil phil
C 147	OP1	A	LEU 102	O	B	2.08	Phil phob
A 148	OP2	A	ALA 103	CB	B	1.79	Phil phob
A 148	OP2	A	LEU 102	C	B	3.35	Phil phob
G 149	OP1	A	ARG 78	NH2	B	3.29	Phil phil
A 171	N1	A	GLU 166	OE2	B	2.74	Phil phil

The table reporting a list of atoms “in contact” (within the distance cutoff) with relative distances less than 3.5Å.

Table S3. Accessible Surface Area table of circ-Amolt1-Akt1 complex

Buried area upon the complex formation (A^2) 4527.2
Buried area upon the complex formation (%) 9.08
Interface area (A^2) 2263.6
Interface area circ-AMOTL1 (%) 7.24
Interface area AKT1 (%) 12.17
POLAR Buried area upon the complex formation (A^2) 1888.0
POLAR Interface (%) 41.70
POLAR Interface area (A^2) 944.0
NON POLAR Buried area upon the complex formation (A^2) 2639.2
NON POLAR Interface (%) 58.30
NON POLAR Interface area (A^2) 1319.6
Residues at the interface_total (n) 93
Residues at the interface_circ-AMOTL1 34
Residues at the interface_AKT1 59

Table S4. Accessible Surface Area table of circ-Amolt1-PDK1 complex

Buried area upon the complex formation (A^2) 3920.5
Buried area upon the complex formation (%) 8.94
Interface area (A^2) 1960.25
Interface area circ-AMOTL1 (%) 6.56
Interface area PDK1 (%) 14.00
POLAR Buried area upon the complex formation (A^2) 1730.3
POLAR Interface (%) 44.13
POLAR Interface area (A^2) 865.15
NON POLAR Buried area upon the complex formation (A^2) 2190.1
NON POLAR Interface (%) 55.86
NON POLAR Interface area (A^2) 1095.05
Residues at the interface_total (n) 101
Residues at the interface_circ-AMOTL1 42
Residues at the interface_PDK1 59

Table S5. circ-Amolt1-AKT1 interaction overview

Number of interacting residues circ-AMOTL1	**25**
Number of interacting residues AKT1	**41**
Number of hydrophilic-hydrophobic interaction	**19**
Number of hydrophilic-hydrophilic interaction	**49**
Number of hydrophobic-hydrophobic interaction	**0**

Table S6. circ-Amolt1-PDK1 interaction overview

Number of interacting residues circ-AMOTL1	**25**
Number of interacting residues PDK1	**32**
Number of hydrophilic-hydrophobic interaction	**21**
Number of hydrophilic-hydrophilic interaction	**33**
Number of hydrophobic-hydrophobic interaction	**0**

a

1. circ-FAM21C, circ-MTHFD1L, circ-NRIP3, circ-METTL25, circ-WWC2, circ-KANK1, circ-MAP3K4, circ-PARL, circ-WDFY2, circ-DHX34
11. circ-TGFBR1, circ-MRRF, circ-CARKD, circ-LINC-PINT, circ-PICALM, circ-PRIM2, circ-SLC25A26, circ-CLK1, circ-VRK1, circ-L3MBTL2
21. circ-DUSP3, circ-VLDLR-AS1, circ-PRPF4B, circ-BIRC6, circ-SMU1, circ-SUN1, circ-RANGAP1, circ-MCM7, circ-TSPAN14, circ-ZNF250
31. circ-BBS7, circ-COMMD1, circ-MAN1B1, circ-SLC9A7, circ-WIPI1, circ-CAMK1, circ-POLR3H, circ-TM2D1, circ-TCF4, circ-TRIM37
41. circ-NCEH1, circ-PPM1D, circ-BCAT1, circ-SLC31A1, circ-GCLM, circ-LPGAT1, circ-C6orf106, circ-TMTC3, circ-PSMD5, circ-SLC30A5
51. circ-MTX2, circ-ELP6, circ-SLC25A17, circ-NR4A3, circ-LRR1, circ-MATR3, circ-POLR2E, circ-CNOT2, circ-ANKRD13C, circ-ERCC6
61. circ-PEX1, circ-VPS37B, circ-RNF38, circ-NR2F6, circ-PARP2, circ-PSAP, circ-DYRK1A, circ-RHEB, circ-ZNF292, circ-HAUS6
71. circ-MCCC2, circ-LRBA, circ-FNTA, circ-TBC1D14, circ-COPA, circ-HPS5, circ-ZDHHC5, circ-MRPL30, circ-LRCH3, circ-MED13L
81. circ-RPS12, circ-VPS13C, circ-INTS1, circ-GRAMD4, circ-LINC01031, circ-TUBGCP4, circ-OTUD4, circ-CHD7, circ-ZNF462, circ-FAM192A
91. circ-EPS15, circ-CHFR, circ-LINC01473, circ-ASCC3, circ-SLC30A6, circ-VPS41, circ-CCNB1IP1, circ-LRP11, circ-PHIP, circ-EP400
101. circ-NRF1, circ-LILRA5, circ-PPIA, circ-USP54, circ-FIRRE, circ- CRIM1, circ-PHF8, circ-TERF2IP, circ-XPO1, circ-ATG3
111. circ-MPHOSPH8, circ-ABL2, circ-WARS2, circ-RPS6KC1, circ-CCNY, circ-RNF13, circ-HN1, circ-AK308944, circ-ZBTB40, circ-MTSS1
121. circ-TRAM1, circ-CAPZB, circ-CCT6B, circ-GIT2, circ-RERE, circ- FMN2, circ-CHD2, circ-PDE7B, circ-CCDC6, circ-NPTN
131. circ-DEK, circ-KIF20B, circ-KIF16B, circ-GINS1, circ-FAM196A, circ-RHOBTB3, circ-UGP2, circ-SMPD2, circ-HECTD1, circ-AHI1
141. circ-ST3GAL5, circ-KDM1A, circ-CSRP2BP, circ-TFF1, circ-TAB2, circ-SMARCA5, circ-DPP8, circ-SEPT10, circ-BIRC2, circ-LINC00669
151. circ-PPM1B, circ-OSBPL10, circ-UBXN7, circ-AGO1, circ-SYNCRIP, circ-ZNF483, circ-YTHDC2, circ-DCP2, circ-ZNF639, circ-VPRBP
161. circ-ATAD2B, circ-PMAIP1, circ-RNF217, circ-RPS29, circ-VAV2, circ-SNRNP40, circ-LRP6, circ-CTPS1, circ-TYW1B, circ-ZFYVE26
171. circ-RBBP8, circ-WWC3, circ-EXOC4, circ-STAT2, circ-NDUFS1, circ-LARGE, circ-GPC1, circ-GIGYF2, circ-EMC1, circ-ARHGEF9
181. circ-TMCC2, circ-ARL6IP1, circ-ACLY, circ-AMOTL1, circ-EZH2, circ-ITGA3, circ-REXO4, circ-ZNF66, circ-TOPBP1, circ-EIF2B3
191. circ-TBCD, circ-TBC1D1, circ-CCDC57, circ-SPG11, circ-GPS2, circ-ZRANB1, circ-FOXN3, circ-STXBP5, circ-CDK8, circ-ATP13A1

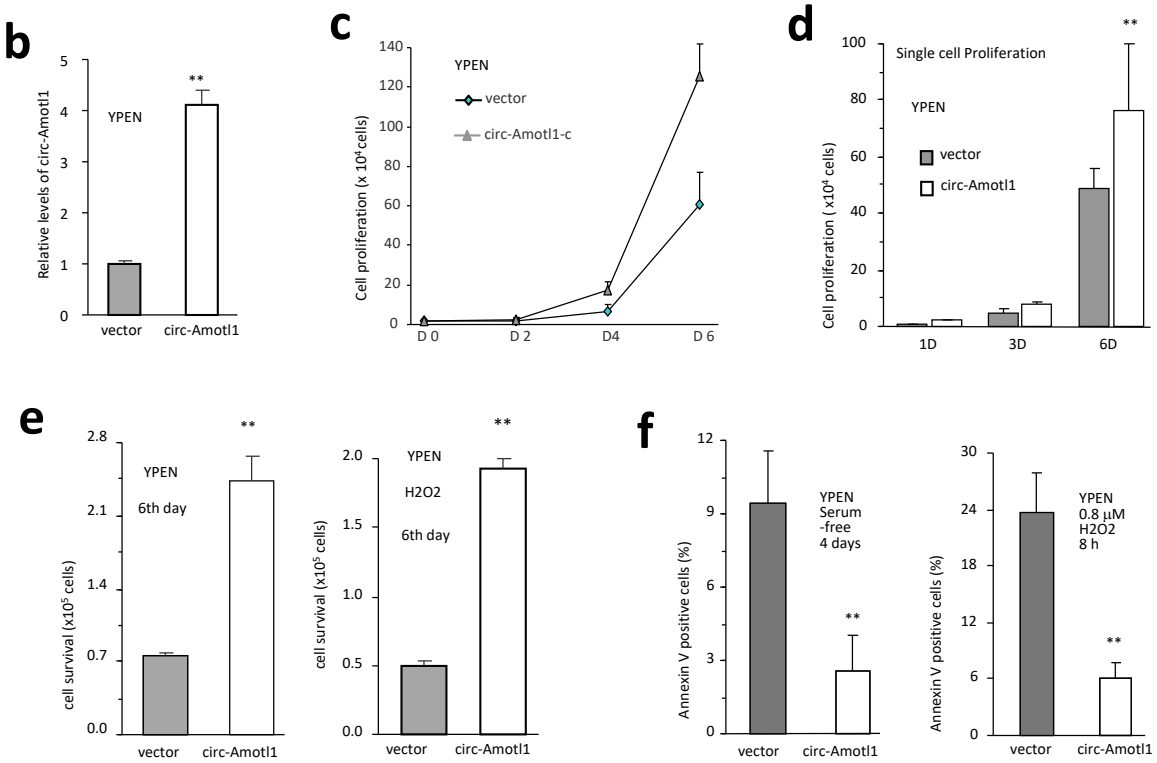


Fig S1. Expression of circ-Amotl1 decreased cell apoptosis

(a) Names of circular RNAs in Fig 1a.

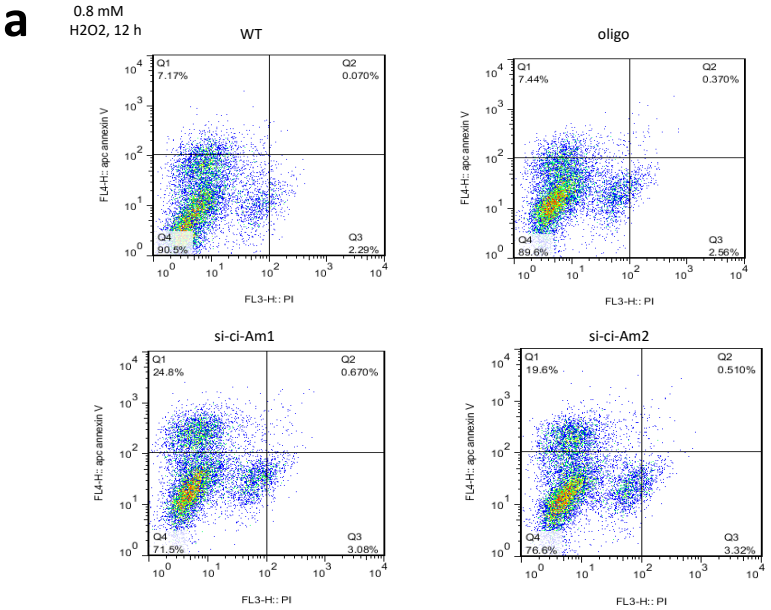
(b) Transfection with circ-Amotl1 increased expression of circ-Amotl1 in Ypen cells.

(c) Proliferation assays were performed in Ypen cells transfected with circ-Amotl1 or the control vector. Circ-Amotl1 expression enhanced cell proliferation (n=3).

(d) Single cell proliferation was determined. Over-expression of circ-Amotl1 increased proliferation of YPEN cells (n=20).

(e) Circ-Amotl1- and vector-transfected YPEN cells were subject to cell survival assay. Transfection with circ-Amotl1 enhanced cell survival.

(f) YPEN cells transfected with circ-Amtol1 expression construct or the control vector were cultured in different conditions and subject to apoptotic assays. Expression of circ-Amotl1 decreased levels of apoptosis (*n=4*).



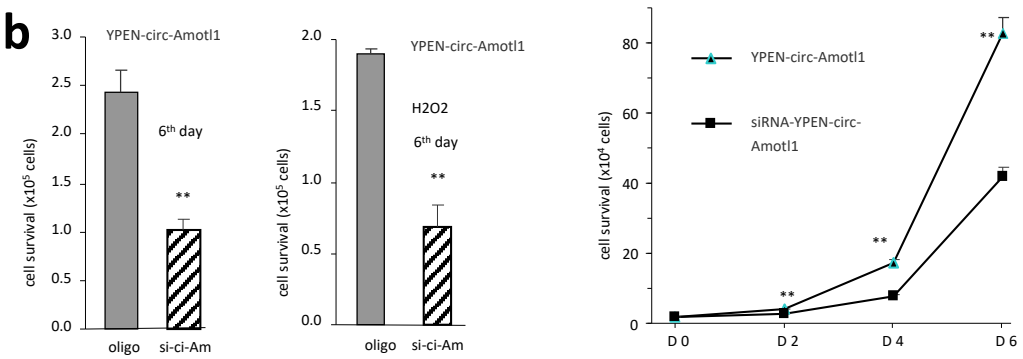


Fig S2. Effects of endogenous circ-Amotl1 on cell activities

(a) MCF-7 cells transfected with circ-Amotl1 siRNAs or a control oligo were cultured in H2O2 for 12 h. Typical pictures showed silencing circ-Amotl1 increased Annexin V positive cells (*n=4*).

(b) Ypen cells transiently transfected with siRNA against circ-Amotl1 decreased cell survival (n=4).

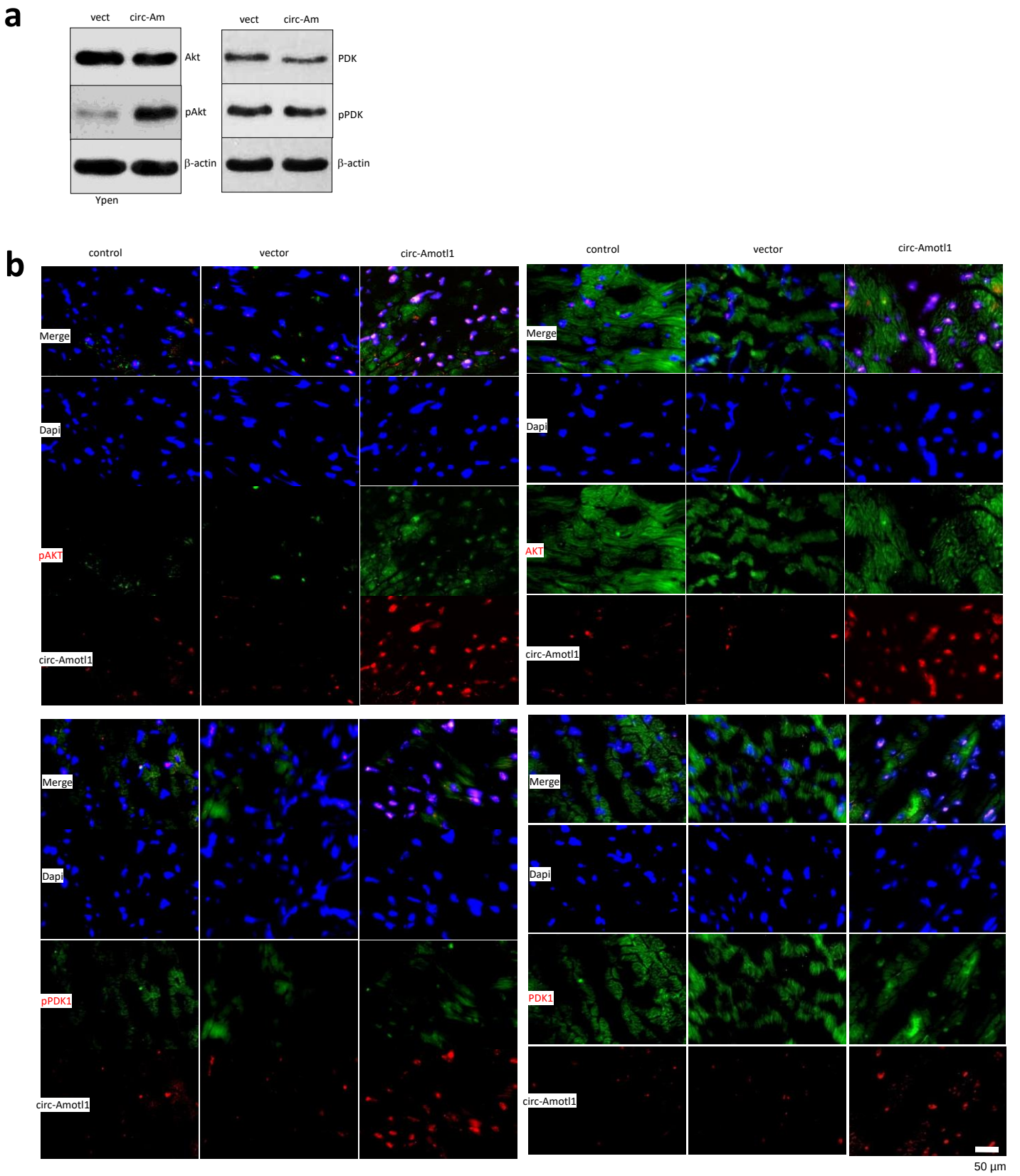


Fig S3. Circ-Amotl1 expression induced Akt activation.

(a) Western blot analysis revealed that ectopic expression of circ-Amotl1 had no effect on levels of Akt, PDK1, and pPDK1, but induced activation of Akt.

(b) Heart tissues were stained with DAPI (blue), circ-AMOTL1 (red) and green fluorescence showing expression of pAKT, AKT, pPDK1 and PDK1. Delivery of circ-Amotl1 enhanced pAKT expression, and pAKT, AKT, pPDK1 and PDK1 nuclear translocation.

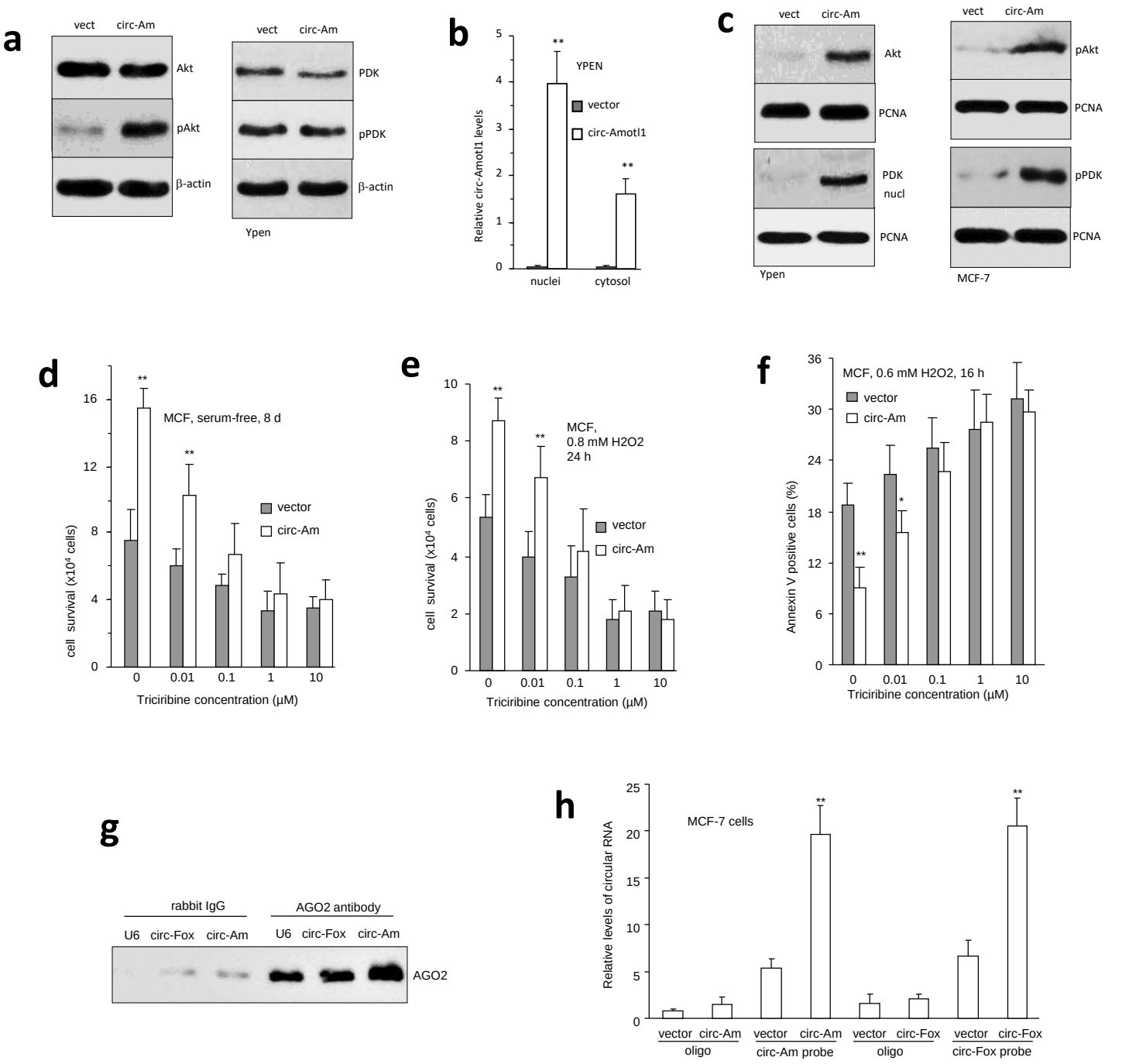


Fig S4. Effect of circ-Amotl1 expression on Akt signalling.

(a) Lysates prepared from MCF-7 cells transfected with circ-Amotl1 siRNA or an control oligo, were mixed with the DNA probe or an control oligo. Silencing circ-Amotl1 with siRNA decreased circ-Amotl1 expression in the input (*n=6*).

(b) Silencing circ-Amotl1 resulted in pulling down decreased levels of Akt and PDK1 with the probe complementary to circ-Amotl1.

(c) Ectopic expression of circ-Amotl1 induced nuclear translocation of Akt and PDK1 in Ypen (left) and MCF-7 (right) cells.

(d-e) Treatment with Akt inhibitor Triciribine abolished the effects of circ-Amotl1 on cell survival when the cells were cultured in serum-free medium (d) or treated with H2O2 (e).

(f) Treatment with Akt inhibitor Triciribine abolished the effects of circ-Amotl1 on cell apoptosis.

(g) The anti-Ago2 antibody was able to precipitate Ago2 protein.

(h) The probes of both circ-Foxo3 and circ-Amotl1 could pull down circ-Foxo3 and circ-Amotl1 respectively (n=4).

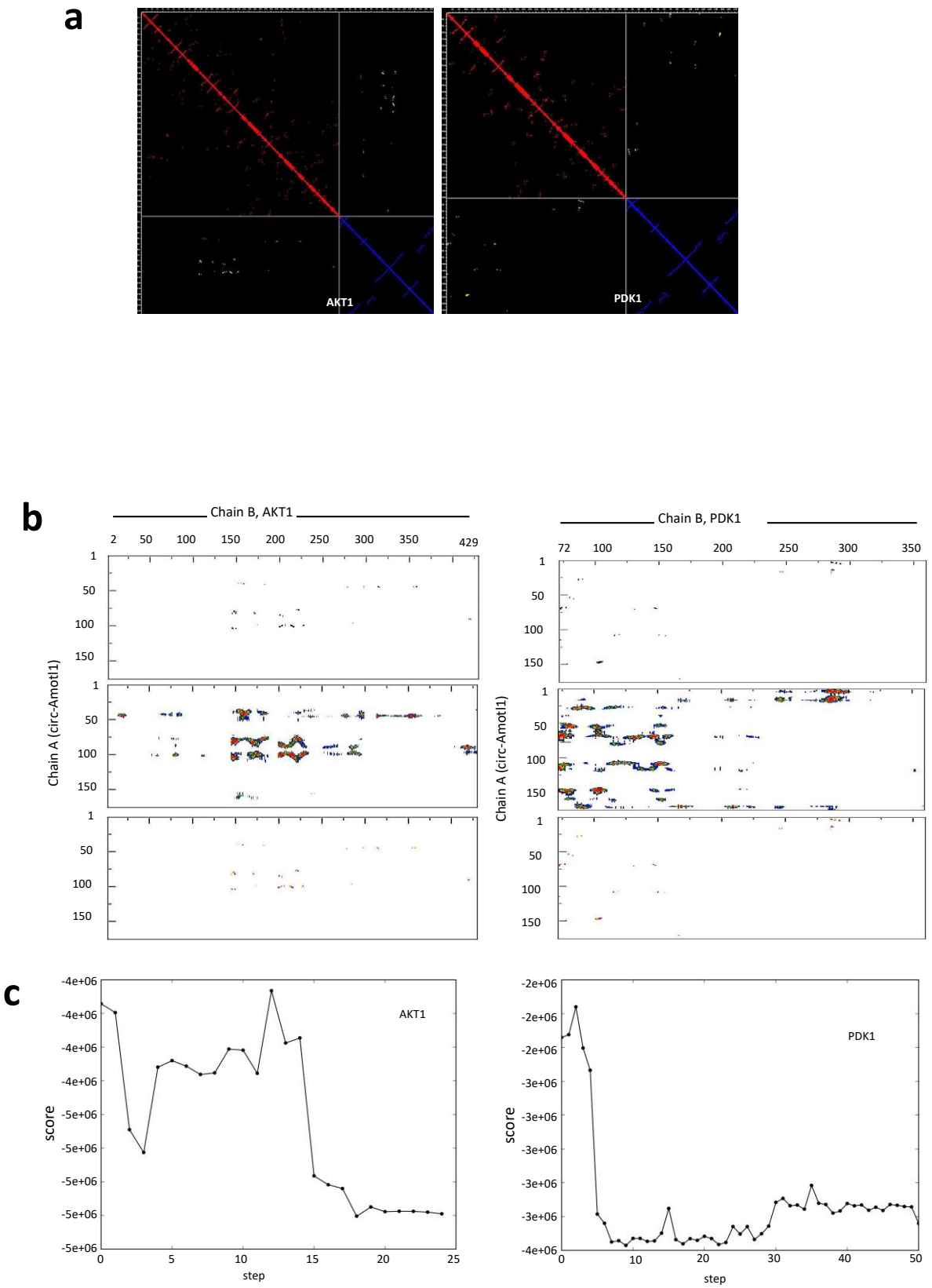


Fig S5. Computational analysis of circ-Amotl1 interacting with Akt and PDK1.
(a) The contact map in the binding residues between circ-Amotl1 and Akt or PDK1.
(b) The residue-level resolution contact maps in the binding residues between circ-Amotl1 and Akt or PDK1.
(c) Refinement of the best docked circ-Amotl1-Akt model and circ-Amotl1-PDK1 model showing MC score vs. steps of simulation.

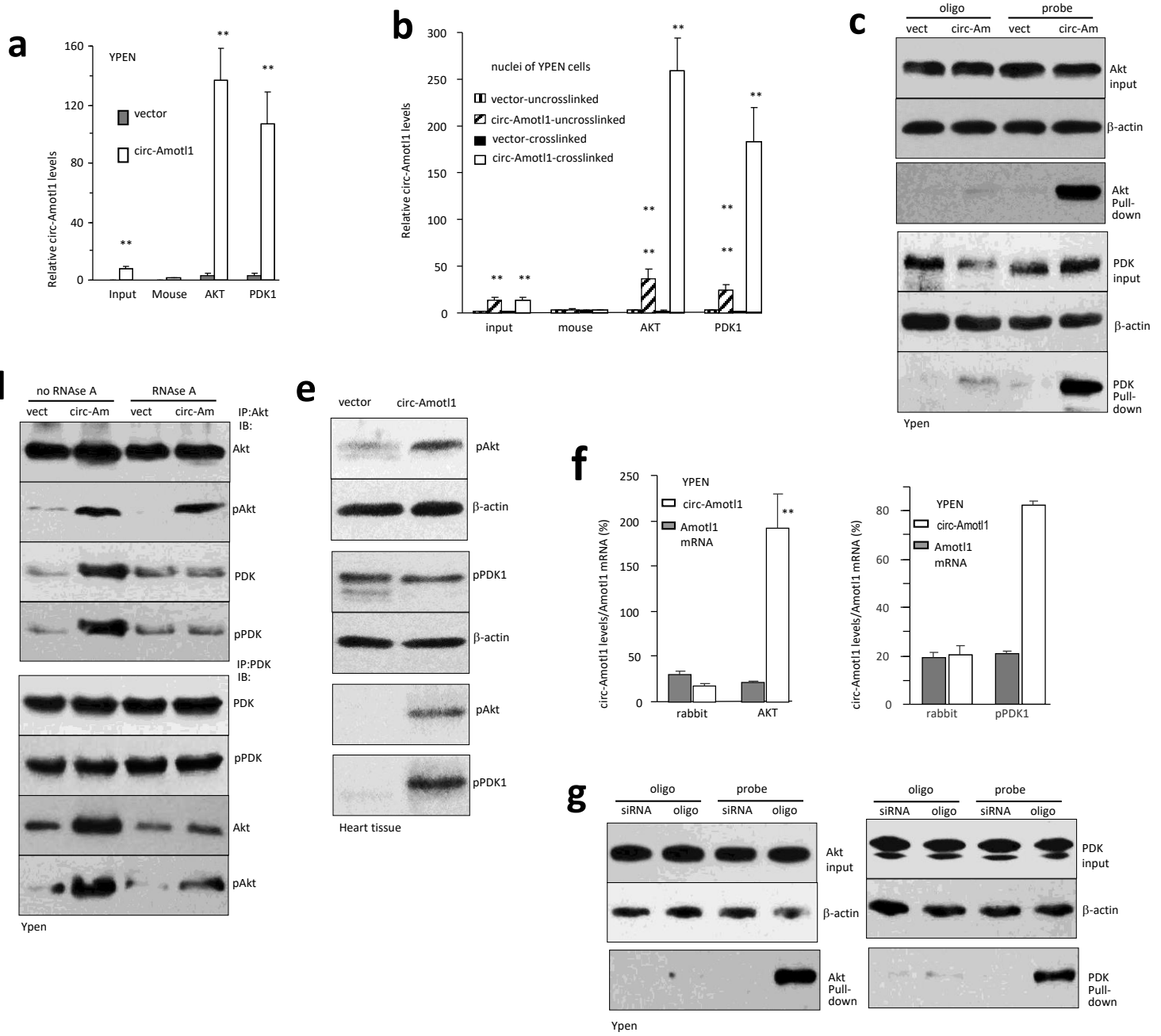


Fig S6. Circ-Amotl1 interacted with Akt and PDK1

(a) Lysates prepared from YPEN cells transfected with vector control or circ-Amotl1, were subject to immuno-precipitation, followed by real-time PCR amplifying circ-Amotl1. Anti-AKT and anti-PDK1 antibodies precipitated more circ-Amotl1 from cells transfected with circ-Amotl1 than from control (*n*=*6*).

(b) To confirm the interaction of circ-Amotl1 with AKT and PDK1 in nuclei, we performed the precipitation assay, after cross-linking and nuclear isolation. Cross-linking significantly increased precipitation of circ-Amotl1 by AKT and PDK1. RIP assays indicated that anti-Akt and anti-PDK1 antibodies precipitated more circ-Amotl1 from cells transfected with circ-Amotl1 than from control. In uncross-linked samples, the antibodies precipitated less circ-Amotl1 compared to cross-linked samples (*n*=*6*).

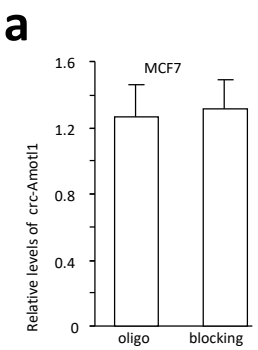
(c) The circ-Amotl1 probe precipitating circ-Amotl1 could pull-down Akt and PDK1.

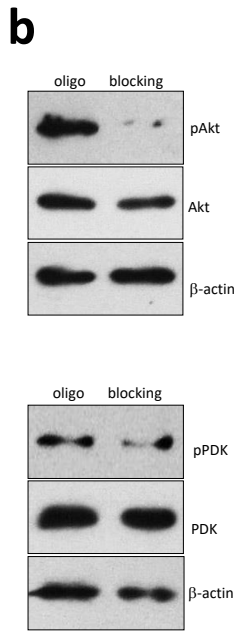
(d) In the lysate prepared from circ-Amotl1-transfected Ypen cells, anti-Akt antibody precipitated increased levels of PDK1 and pPDK1, while anti-PDK1 antibody precipitated more Akt and pAkt relative to controls, suggesting both Akt and PDK1 bound to the same circ-Amotl1. Treatment with RNAse A abolished the interaction.

(e) In heart tissues, circ-Amotl1 precipitation pulled down pAkt and pPDK1.

(f) Antibodies against Akt and pPDK1 precipitated circ-Amotl1 but not the linear Amotl1 mRNA.

(g) Lysates prepared from Ypen cells transfected with circ-Amotl1 siRNA or an control oligo, were mixed with the DNA probe or an control oligo. Silencing circ-Amotl1 resulted in pulling down decreased levels of Akt and PDK1 with the probe complementary to circ-Amotl1.





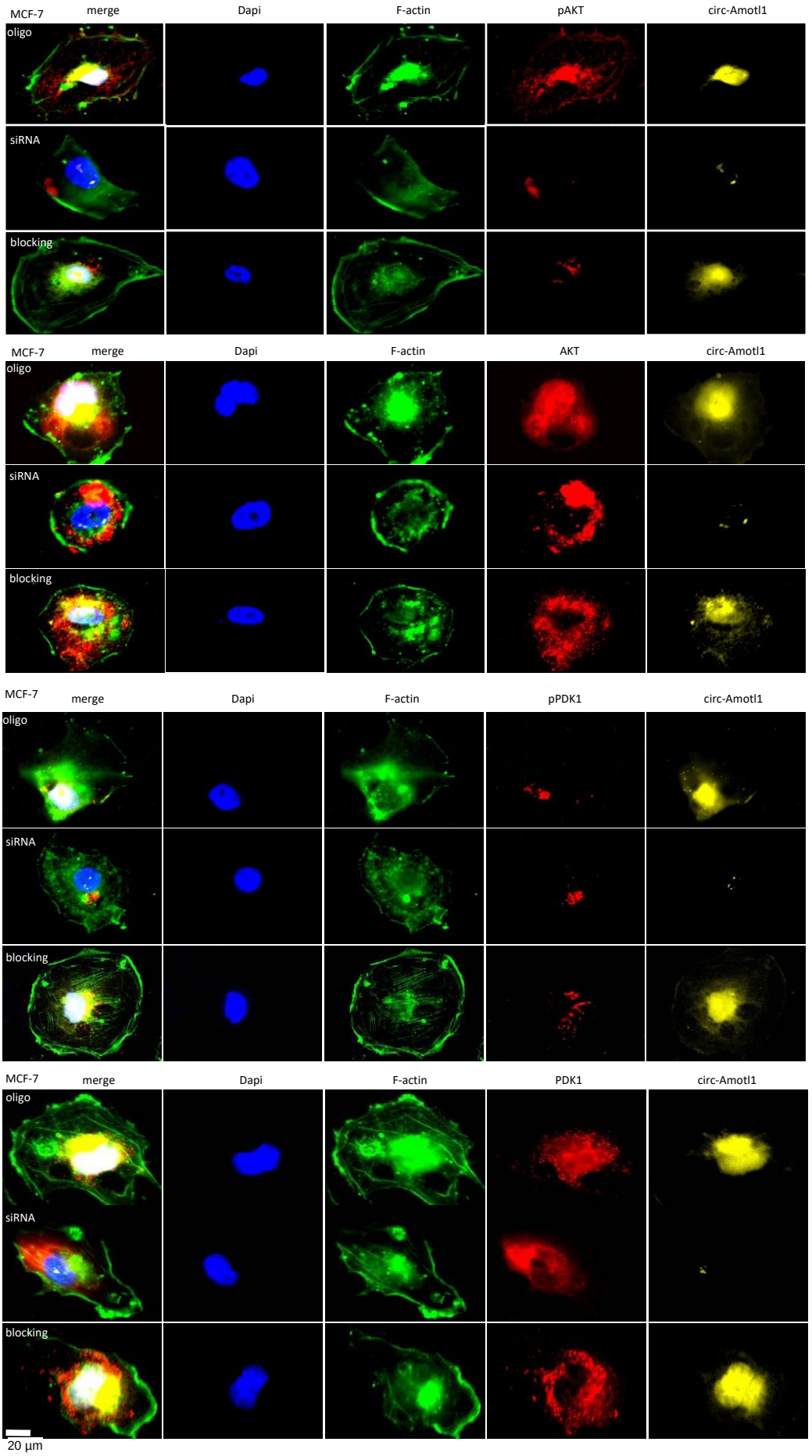
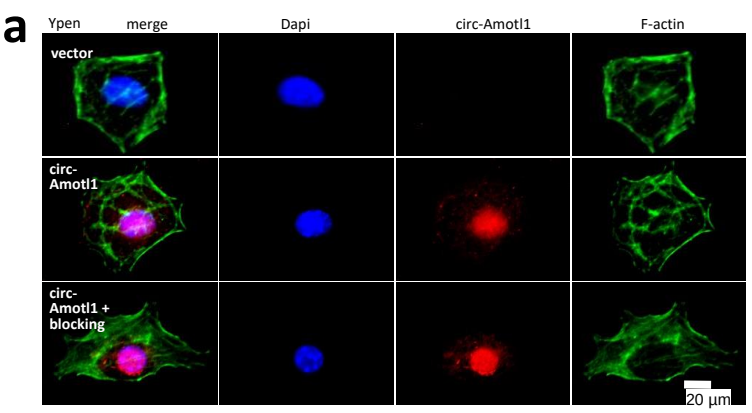


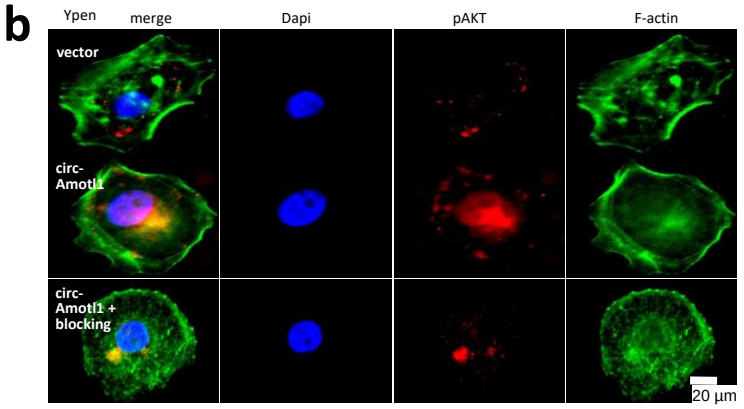
Fig S7. Blocking circ-Amotl1 interacting with Akt and PDK1 decreased nuclear translocation in MCF-7 cells.

(a) PCR showed transfection of blocking oligo did not change circ-Amotl1 expression (*n*=*6*).

(b) Western blot showed that expression of blocking oligo deceased pAkt levels in MCF-7 cells.

(c) circ-Amotl1-siRNA-, blocking oligo- and control oligo-transfected MCF-7 cells were stained with phalloidins (green), DAPI (blue), circ-Amotl1 (yellow) and red fluorescence showing expression of pAKT, Akt, pPDK1 and PDK1. While transfection with the siRNA decreased circ-Amotl1 levels, blocking oligo did not change circ-Amotl1 expression. Both siRNA and blocking oligo decreased nuclear translocation of pAkt, Akt, pPDK1 and PDK1.





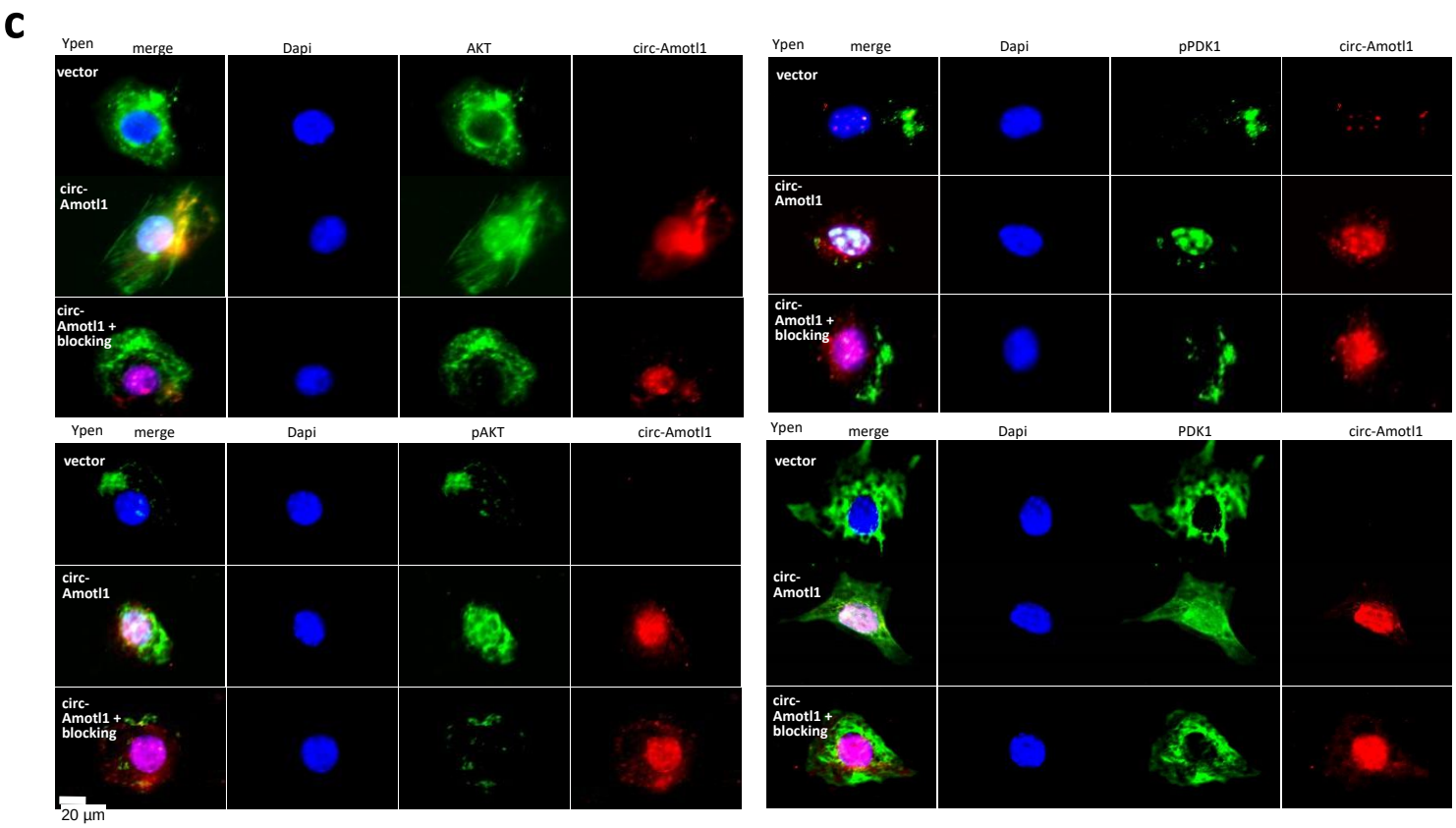
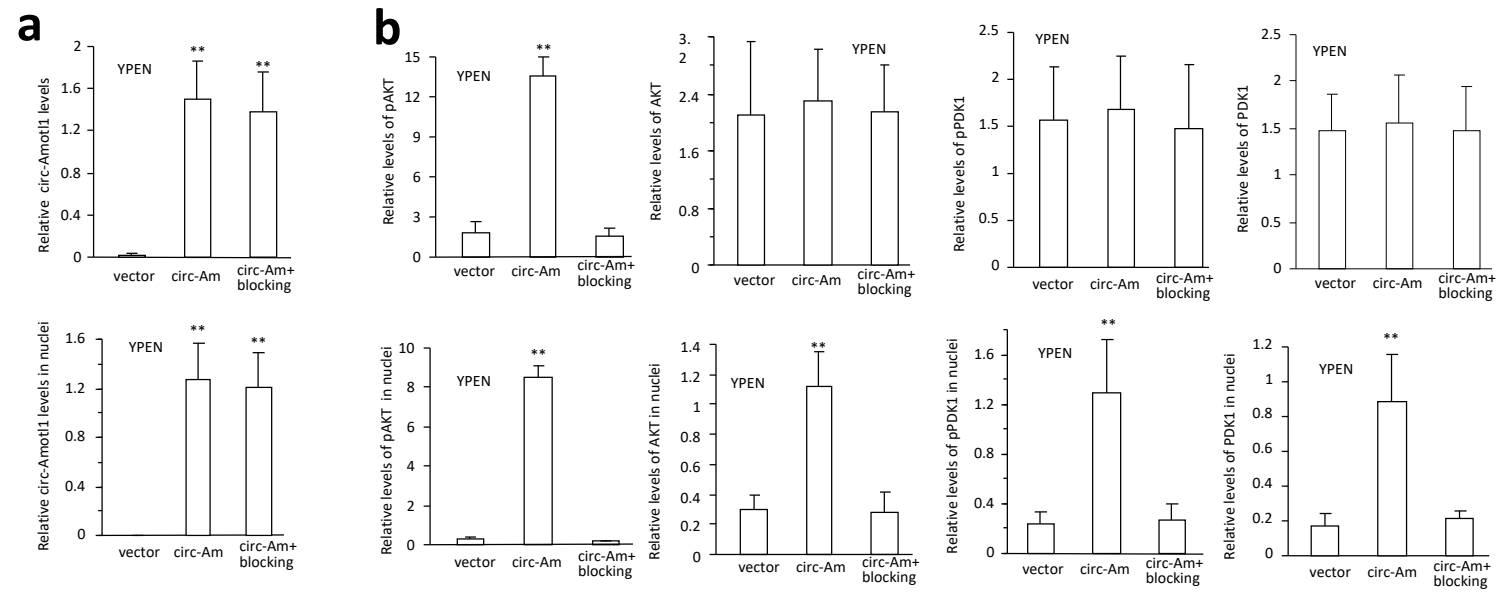


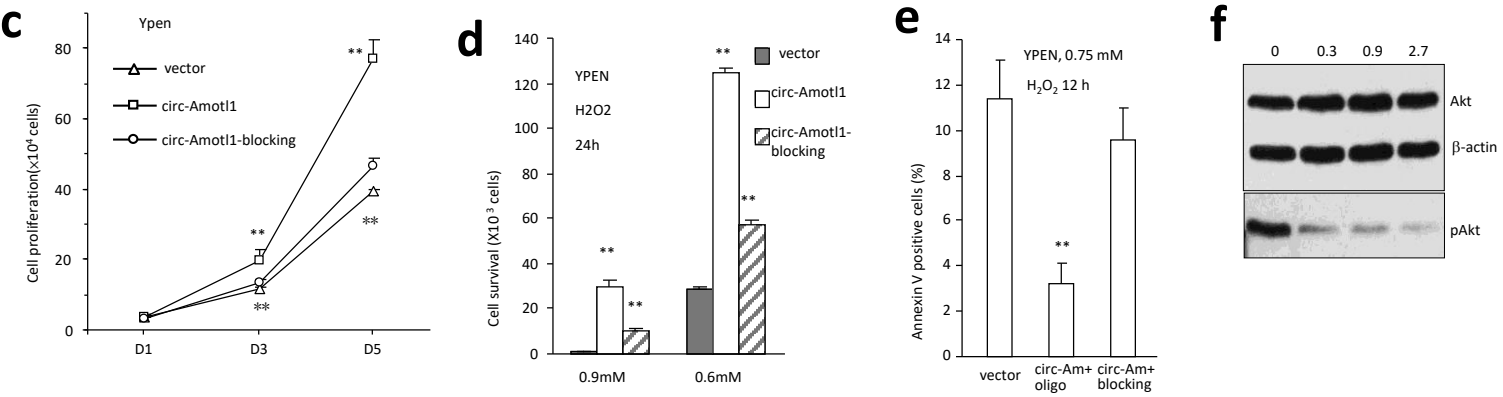
Fig S8. Blocking circ-Amotl1 interacting with Akt and PDK1 decreased nuclear translocation in Ypen cells.

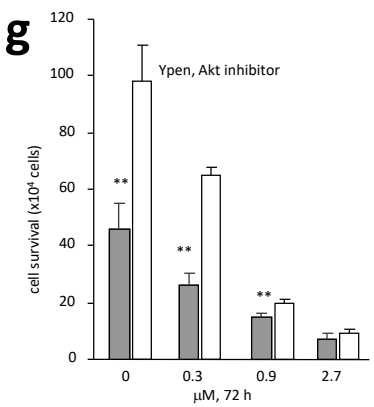
(a) circ-Amotl1-, circ-Amotl1-, blocking oligo-, and control vector-transfected YPEN cells were stained with phalloidins (green), DAPI (blue) and circ-Amotl1 (red). The blocking oligo did not affect circ-Amotl1 expression.

(b) Cells were stained with phalloidins (green), DAPI (blue) and pAkt (red). The blocking oligo decreased pAkt expression.

(c) The cells were stained with DAPI (blue), circ-Amotl1 (red), and red fluorescence showing expression of pAKT, Akt, pPDK1 and PDK1. Transfection of circ-Amotl1 increased circ-Amotl1 and pAKT expression, and promoted circ-Amotl1, pAkt, Akt, pPDK1 and PDK1 nuclear translocation. Transfection with the blocking oligo inhibited these processes.







h

name	sequence
Cir.Amotl1-HindIII	5'ttt ttt aag c ttgaagatcctctttgtaac
Cir.Amotl1-SalI	5' ttt ttt gtcga ctc gtt acccc ata ctc agg
Cir.AMOTL1-R	5' cct gga tca gccgc tgc aata ctg ttcc agc
cir.Amotl1-F	5' agtatGGGGTAACGAG TTGAAGAT
circ-Amotl1 probe	5' caaagaggatcttcaactcgttaccccatact
probe for circ-Amotl1 & linear Amotl1	5' tctcatttccacctctgagatcctcaggaagtttgggg
control oligo	5' tccttcctctctttctctcccttgtga
siRNA-1	5' GGGGUAACGAGUUGAAGAUUU 5' AUCUUCAACUCGUUACCCCUU
siRNA-2	5' GGGUAACGAGUUGAAGAUCUU 5' GAUCUUCAACUCGUUACCCUU

Fig S9. Blocking circ-Amotl1 modulated cellular activities. (a) Image J analyses showed that the blocking oligo did not affected nuclear translocation of circ-Amotl1 (*n=6*). (b) Image J analyses showed that the blocking oligo decreased nuclear translocation of pAkt, Akt, pPDK1 and PDK1 (*n=6*). (c) Ypen cells transfected with the blocking oligo or a control oligo were cultured in H2O2 for 10 h or 12 h. Transfection with the blocking oligo increased Annexin V positive cells (*n=4*). (d) While expression of circ-Amotl1 increased, transfection with the blocking oligo decreased proliferation of Ypen cells. (e) Transfection with the blocking oligo decreased survival of Ypen cells. (f) Treatment with Akt inhibitor did not affect Akt expression, but decreased Akt phosphorylation. (g) Treatment with Akt inhibitor decreased cell survival. (h) Sequences of oligos used in the study. Cloning primers: Cir.Amotl1-HindIII and Cir-.Amotl1-SalI; PCR primers: Cir-.Amotl1-R and Cir.Amotl1-F