

Supplementary Information

Table S1 Sequences of siRNAs and shRNAs used in this study

Definition	sequences
si-circIGF1R	5'-ATGCCTGGCCCGCAGATTTTC-3'
si-NC	5'-GAAAATCTGCGGG CCAGGCAT-3'
sh-RBFOX3	5'CCGGGTCGTGTATCAGGATGGATTCTCGAGAAA TCCATCCTGATACACGACTTTTTTG-3'
sh-NC	5'CCGGCAACAAGATGAAGAGCACCAACTCGAGTT GGTGCTCTTCATCTTGTTGTTTTTG -3'

Table S2 Primer sequences used in RT-qPCR and PCR analysis

Gene	Primer Sequence (5'→3')	
circIGF1R	Forward	CAAACCGCTGCCAGAAAATCT
	Reverse	GCTGCTGATAGTCGTTGCGGA
IGF1R	Forward	TCGACATCCGCAACGACTATC
	Reverse	CCAGGGCGTAGTTGTAGAAGAG
YBX1	Forward	CTGGTTTTTCTCAATACGCC
	Reverse	TATTAACAGGTGCTTGCACT
HNRNPM	Forward	AGAAAAAGGGATGTGCTGTT
	Reverse	CATGTTCACCATCAGGATCT
HNRNPH1	Forward	TGGAAGAGACCTCAATTACTG
	Reverse	GTTGTGCTCTGGAAAGTAGA
HNRNPF	Forward	TCCTCAAGGTTGAGAACAAA
	Reverse	TAATGAAATGTCCACGGAGG
RBFOX3	Forward	GAAATGTTCTTGGCTGTAGG
	Reverse	CACAGGAAGACTGTTAGCTT
FUS	Forward	ACATGGCCTCAAACGATTAT
	Reverse	GCTCTGGCCATAAGAAGAAT
GAPDH	Reverse	GCACCGTCAAGGCTGAGAAC
	Reverse	TGGTGAAGACGCCAGTGGA
a (RIP assay)	Forward	CGTGATGAGTCACTCCTATGA
	Reverse	TGGCACACTGGCCTTCAATTC
b (RIP assay)	Forward	CGGTTCTCCAGTGTAGAGTAG
	Reverse	CAGTGCCAACACTGGACCAGA
c (RIP assay)	Forward	CAAACCGCTGCCAGAAAATCT
	Reverse	GCTGCTGATAGTCGTTGCGGA
d (RIP assay)	Forward	CTTCTCTTCTGAGTGACGAG
	Reverse	GAAGGTCAGCAAGTGTCTAGC
e (RIP assay)	Forward	TCTCTCTCTACCATTGCTGTC
	Reverse	GGCACCTTTAAGATTCACTGC

Table S3 Antibodies and dilution

Antibodies	Dilution (application)
RBFOX3	1:1000 (WB)
VANGL2	1:2000 (WB)
WNT1	1:1000 (WB)
CTNNB1	1:1000 (WB)
GAPDH	1:10000 (WB)
Goat Anti-Rabbit IgG H&L(HRP)	1:10000 (WB)
Rabbit Anti-Mouse IgG H&L(HRP)	1:10000 (WB)

Table S4 Mass Spectrometry Experiment Protein List

Protein number	Protein access number	Protein Descriptions
1	sp P67809 YBOX1_HUMAN	Y-box-binding protein 1 OS=Homo sapiens OX=9606 GN=YBX1 PE=1 SV=3
2	sp P02768 ALBU_HUMAN	Serum albumin OS=Homo sapiens OX=9606 GN=ALB PE=1 SV=2
3	sp P13645 K1C10_HUMAN	Keratin, type I cytoskeletal 10 OS=Homo sapiens OX=9606 GN=KRT10 PE=1 SV=6
4	sp P04264 K2C1_HUMAN	Keratin, type II cytoskeletal 1 OS=Homo sapiens OX=9606 GN=KRT1 PE=1 SV=6
5	sp P35908 K22E_HUMAN	Keratin, type II cytoskeletal 2 epidermal OS=Homo sapiens OX=9606 GN=KRT2 PE=1 SV=2
6	sp P60709 ACTB_HUMAN	Actin, cytoplasmic 1 OS=Homo sapiens OX=9606 GN=ACTB PE=1 SV=1
7	sp P35579 MYH9_HUMAN	Myosin-9 OS=Homo sapiens OX=9606 GN=MYH9 PE=1 SV=4
8	sp P08670 VIME_HUMAN	Vimentin OS=Homo sapiens OX=9606 GN=VIM PE=1 SV=4
9	sp P62753 RS6_HUMAN	40S ribosomal protein S6 OS=Homo sapiens OX=9606 GN=RPS6 PE=1 SV=1
10	sp P52272 HNRPM_HUMAN	Heterogeneous nuclear ribonucleoprotein M OS=Homo sapiens OX=9606 GN=HNRNPM PE=1 SV=3
11	sp P15927 RFAX2_HUMAN	Replication protein A 32 kDa subunit OS=Homo sapiens OX=9606 GN=RPA2 PE=1 SV=1
12	sp P31943 HNRH1_HUMAN	Heterogeneous nuclear ribonucleoprotein H OS=Homo sapiens OX=9606 GN=HNRNPH1 PE=1 SV=4
13	sp P13647 K2C5_HUMAN	Keratin, type II cytoskeletal 5 OS=Homo sapiens OX=9606 GN=KRT5 PE=1 SV=3
14	sp P52597 HNRPF_HUMAN	Heterogeneous nuclear ribonucleoprotein F OS=Homo sapiens OX=9606 GN=HNRNPF PE=1 SV=3
15	sp P25705 ATPA_HUMAN	ATP synthase subunit alpha, mitochondrial OS=Homo sapiens OX=9606 GN=ATP5F1A PE=1 SV=1

16	sp P05787 K2C8_HUMAN	Keratin, type II cytoskeletal 8 OS=Homo sapiens OX=9606 GN=KRT8 PE=1 SV=7
17	sp P16989 YBOX3_HUMAN	Y-box-binding protein 3 OS=Homo sapiens OX=9606 GN=YBX3 PE=1 SV=4
18	sp Q9NSU2 TREX1_HUMAN	Three-prime repair exonuclease 1 OS=Homo sapiens OX=9606 GN=TREX1 PE=1 SV=2
19	sp P02533 K14_HUMAN	Keratin, type I cytoskeletal 14 OS=Homo sapiens OX=9606 GN=KRT14 PE=1 SV=4
20	sp P07437 TUBB5_HUMAN	Tubulin beta chain OS=Homo sapiens OX=9606 GN=TUBB PE=1 SV=2
21	sp Q9UL12 SARDH_HUMAN	Sarcosine dehydrogenase, mitochondrial OS=Homo sapiens OX=9606 GN=SARDH PE=1 SV=1
22	sp P21333 FLNA_HUMAN	Filamin-A OS=Homo sapiens OX=9606 GN=FLNA PE=1 SV=4
23	sp O43795 MYO1B_HUMAN	Unconventional myosin-Ib OS=Homo sapiens OX=9606 GN=MYO1B PE=1 SV=3
24	sp Q5VZL5 ZMYM4_HUMAN	Zinc finger MYM-type protein 4 OS=Homo sapiens OX=9606 GN=ZMYM4 PE=1 SV=1
25	sp Q765P7 MTSS2_HUMAN	Protein MTSS 2 OS=Homo sapiens OX=9606 GN=MTSS2 PE=1 SV=1
26	sp Q9Y6N5 SQOR_HUMAN	Sulfide:quinone oxidoreductase, mitochondrial OS=Homo sapiens OX=9606 GN=SQOR PE=1 SV=1
27	sp A3KN83 SBNO1_HUMAN	Protein strawberry notch homolog 1 OS=Homo sapiens OX=9606 GN=SBNO1 PE=1 SV=1
28	sp Q13126 MTAP_HUMAN	S-methyl-5~-thioadenosine phosphorylase OS=Homo sapiens OX=9606 GN=MTAP PE=1 SV=2
29	sp P0DMR3 ATXN8OS_HUMAN	Putative protein ATXN8OS OS=Homo sapiens OX=9606 GN=ATXN8OS PE=5 SV=1
30	sp Q2NKJ3 CTC1_HUMAN	CST complex subunit CTC1 OS=Homo sapiens OX=9606 GN=CTC1 PE=1 SV=2
31	sp Q5R372 RABGAP1L_HUMAN	Rab GTPase-activating protein 1-like OS=Homo sapiens OX=9606 GN=RABGAP1L PE=1 SV=1
32	sp Q00536 CDK16_HUMAN	Cyclin-dependent kinase 16 OS=Homo sapiens OX=9606 GN=CDK16 PE=1 SV=1
33	sp Q9BQI9 NRIP2_HUMAN	Nuclear receptor-interacting protein 2 OS=Homo sapiens OX=9606 GN=NRIP2 PE=1 SV=3
34	sp P20700 LMNB1_HUMAN	Lamin-B1 OS=Homo sapiens OX=9606 GN=LMNB1 PE=1 SV=2
35	sp A6NNC1 POM121L_HUMAN	Putative POM121-like protein 1-like OS=Homo sapiens OX=9606 PE=5 SV=3
36	sp Q14527 HLTF_HUMAN	Helicase-like transcription factor OS=Homo sapiens OX=9606 GN=HLTF PE=1 SV=2
37	sp Q15583 TGIF1_HUMAN	Homeobox protein TGIF1 OS=Homo sapiens OX=9606 GN=TGIF1 PE=1 SV=3

38	sp P08779 K1C16_HUMAN	Keratin, type I cytoskeletal 16 OS=Homo sapiens OX=9606 GN=KRT16 PE=1 SV=4
39	sp P27144 KAD4_HUMAN	Adenylate kinase 4, mitochondrial OS=Homo sapiens OX=9606 GN=AK4 PE=1 SV=1
40	sp Q9NZU0 FLRT3_HUMAN	Leucine-rich repeat transmembrane protein FLRT3 OS=Homo sapiens OX=9606 GN=FLRT3 PE=1 SV=1
41	sp Q2UY09 COLSA1_HUMAN	Collagen alpha-1(XXVIII) chain OS=Homo sapiens OX=9606 GN=COL28A1 PE=2 SV=2
42	sp Q5H9R4 ARMX4_HUMAN	Armadillo repeat-containing X-linked protein 4 OS=Homo sapiens OX=9606 GN=ARMCX4 PE=2 SV=3
43	sp Q2WGI9 FER1L6_HUMAN	Fer-1-like protein 6 OS=Homo sapiens OX=9606 GN=FER1L6 PE=2 SV=2
44	sp P36406 TRIM23_HUMAN	E3 ubiquitin-protein ligase TRIM23 OS=Homo sapiens OX=9606 GN=TRIM23 PE=1 SV=1
45	sp Q8WY64 MYLIP_HUMAN	E3 ubiquitin-protein ligase MYLIP OS=Homo sapiens OX=9606 GN=MYLIP PE=1 SV=2
46	sp Q96I15 SCLY_HUMAN	Selenocysteine lyase OS=Homo sapiens OX=9606 GN=SCLY PE=1 SV=4
47	sp Q10588 BST1_HUMAN	ADP-ribosyl cyclase/cyclic ADP-ribose hydrolase 2 OS=Homo sapiens OX=9606 GN=BST1 PE=1 SV=2
48	sp O75764 TCEA3_HUMAN	Transcription elongation factor A protein 3 OS=Homo sapiens OX=9606 GN=TCEA3 PE=1 SV=2
49	sp P27694 RPA1_HUMAN	Replication protein A 70 kDa DNA-binding subunit OS=Homo sapiens OX=9606 GN=RPA1 PE=1 SV=2
50	sp Q9H1I8 ASCC2_HUMAN	Activating signal cointegrator 1 complex subunit 2 OS=Homo sapiens OX=9606 GN=ASCC2 PE=1 SV=3
51	sp Q96DU9 PABPC5_HUMAN	Polyadenylate-binding protein 5 OS=Homo sapiens OX=9606 GN=PABPC5 PE=2 SV=1
52	sp Q9BRU9 UTP23_HUMAN	rRNA-processing protein UTP23 homolog OS=Homo sapiens OX=9606 GN=UTP23 PE=1 SV=2
53	sp Q14894 CRYM_HUMAN	Ketimine reductase mu-crystallin OS=Homo sapiens OX=9606 GN=CRYM PE=1 SV=1
54	sp Q8WXD9 CASKIN1_HUMAN	Caskin-1 OS=Homo sapiens OX=9606 GN=CASKIN1 PE=1 SV=1
55	sp P0C874 SPATA31D3_HUMAN	Spermatogenesis-associated protein 31D3 OS=Homo sapiens OX=9606 GN=SPATA31D3 PE=2 SV=1
56	sp Q13368 MPP3_HUMAN	MAGUK p55 subfamily member 3 OS=Homo sapiens OX=9606 GN=MPP3 PE=1 SV=2
57	sp P26374 CHML2_HUMAN	Rab proteins geranylgeranyltransferase component A 2 OS=Homo sapiens OX=9606 GN=CHML2 PE=1 SV=2
58	sp Q7Z5P9 MUC19_HUMAN	Mucin-19 OS=Homo sapiens OX=9606 GN=MUC19 PE=1 SV=3
59	sp P30414 NKT	NK-tumor recognition protein OS=Homo sapiens

	R_HUMAN	OX=9606 GN=NKTR PE=1 SV=2
60	sp P27816 MAP4_HUMAN	Microtubule-associated protein 4 OS=Homo sapiens OX=9606 GN=MAP4 PE=1 SV=3
61	sp A8MTQ0 NOTO_HUMAN	Homeobox protein notochord OS=Homo sapiens OX=9606 GN=NOTO PE=2 SV=2
62	sp Q9NQL2 RRAGD_HUMAN	Ras-related GTP-binding protein D OS=Homo sapiens OX=9606 GN=RRAGD PE=1 SV=1
63	sp Q7Z6B7 SRGP1_HUMAN	SLIT-ROBO Rho GTPase-activating protein 1 OS=Homo sapiens OX=9606 GN=SRGAP1 PE=1 SV=1
64	sp Q14166 TTL12_HUMAN	Tubulin--tyrosine ligase-like protein 12 OS=Homo sapiens OX=9606 GN=TTLL12 PE=1 SV=2
65	sp Q99518 FMO2_HUMAN	Dimethylaniline monooxygenase [N-oxide-forming] 2 OS=Homo sapiens OX=9606 GN=FMO2 PE=1 SV=5
66	sp O94986 CEP52_HUMAN	Centrosomal protein of 152 kDa OS=Homo sapiens OX=9606 GN=CEP152 PE=1 SV=4
67	sp O14734 ACOT8_HUMAN	Acyl-coenzyme A thioesterase 8 OS=Homo sapiens OX=9606 GN=ACOT8 PE=1 SV=1
68	sp Q9HCM7 FBSL_HUMAN	Fibrosin-1-like protein OS=Homo sapiens OX=9606 GN=FBRSL1 PE=1 SV=4
69	sp Q9NQ79 CRAC1_HUMAN	Cartilage acidic protein 1 OS=Homo sapiens OX=9606 GN=CRTAC1 PE=1 SV=2
70	sp O15379 HDAC3_HUMAN	Histone deacetylase 3 OS=Homo sapiens OX=9606 GN=HDAC3 PE=1 SV=2
71	sp Q9ULN7 PNM8B_HUMAN	Paraneoplastic antigen-like protein 8B OS=Homo sapiens OX=9606 GN=PNMA8B PE=2 SV=4
72	sp Q16798 ME3ON_HUMAN	NADP-dependent malic enzyme, mitochondrial OS=Homo sapiens OX=9606 GN=ME3 PE=2 SV=2
73	sp Q0VG73 YC023_HUMAN	Putative uncharacterized protein LOC152225 OS=Homo sapiens OX=9606 PE=5 SV=1
74	sp Q8WVM7 STAG1_HUMAN	Cohesin subunit SA-1 OS=Homo sapiens OX=9606 GN=STAG1 PE=1 SV=3
75	sp A6NFN3 RBFOX3_HUMAN	RNA binding protein fox-1 homolog 3 OS=Homo sapiens OX=9606 GN=RBFOX3 PE=2 SV=4
76	sp Q14865 ARID5B_HUMAN	AT-rich interactive domain-containing protein 5B OS=Homo sapiens OX=9606 GN=ARID5B PE=1 SV=3
77	sp Q9BWT6 MND1_HUMAN	Meiotic nuclear division protein 1 homolog OS=Homo sapiens OX=9606 GN=MND1 PE=1 SV=1
78	sp Q2TAM9 TUSC1_HUMAN	Tumor suppressor candidate gene 1 protein OS=Homo sapiens OX=9606 GN=TUSC1 PE=1 SV=3
79	sp P08922 ROS1_HUMAN	Proto-oncogene tyrosine-protein kinase ROS OS=Homo sapiens OX=9606 GN=ROS1 PE=1 SV=3
80	sp P05120 SERPINB2_HUMAN	Plasminogen activator inhibitor 2 OS=Homo sapiens OX=9606 GN=SERPINB2 PE=1 SV=2

81	sp P19883 FST_HUMAN	Follistatin OS=Homo sapiens OX=9606 GN=FST PE=1 SV=2
82	sp P49895 IOD1_HUMAN	Type I iodothyronine deiodinase OS=Homo sapiens OX=9606 GN=DIO1 PE=2 SV=3
83	sp Q04721 NOTC2_HUMAN	Neurogenic locus notch homolog protein 2 OS=Homo sapiens OX=9606 GN=NOTCH2 PE=1 SV=3
84	sp P13569 CFTR_HUMAN	Cystic fibrosis transmembrane conductance regulator OS=Homo sapiens OX=9606 GN=CFTR PE=1 SV=3
85	sp Q5T1A1 DCST2_HUMAN	DC-STAMP domain-containing protein 2 OS=Homo sapiens OX=9606 GN=DCST2 PE=2 SV=2
86	sp Q15784 NDF2_HUMAN	Neurogenic differentiation factor 2 OS=Homo sapiens OX=9606 GN=NEUROD2 PE=1 SV=2
87	sp Q9UL68 MYT1L_HUMAN	Myelin transcription factor 1-like protein OS=Homo sapiens OX=9606 GN=MYT1L PE=2 SV=3

Figure S1. circIGF1R binding protein and expression levels. (a) Metascape analysis of functional categories enriched in the circIGF1R binding proteins. (b-f) The relative expression levels of YBX1, FUS, HNRNPH1, HNRNPF and HNRNPM mRNAs in NSCLC and lung normal cell lines. (g-h) HNRNPH1 and HNRNPF mRNA levels in 15 paired NSCLC and para-cancerous tissues.

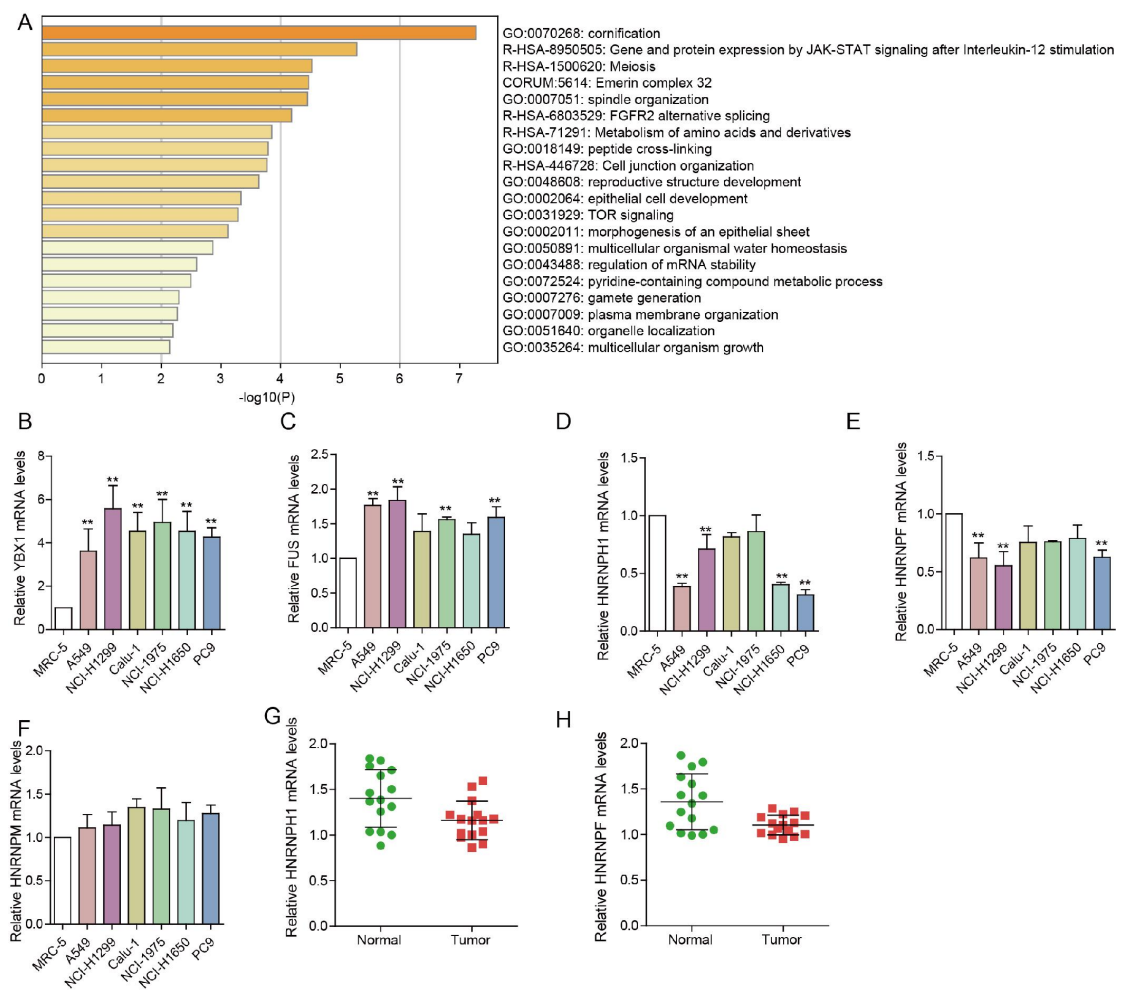


Figure S2. Analysis of transfection efficiency. (a-f) the protein and mRNA levels of RBFOX3 were significantly overexpressed in A549 and PC9 cells following transfection with the ov-RBFOX3 overexpression plasmid. (g-l) After transfection of A549 and PC9 cells with sh-RBFOX3 interference plasmid, the protein and mRNA levels of RBFOX3 were significantly low expressed.

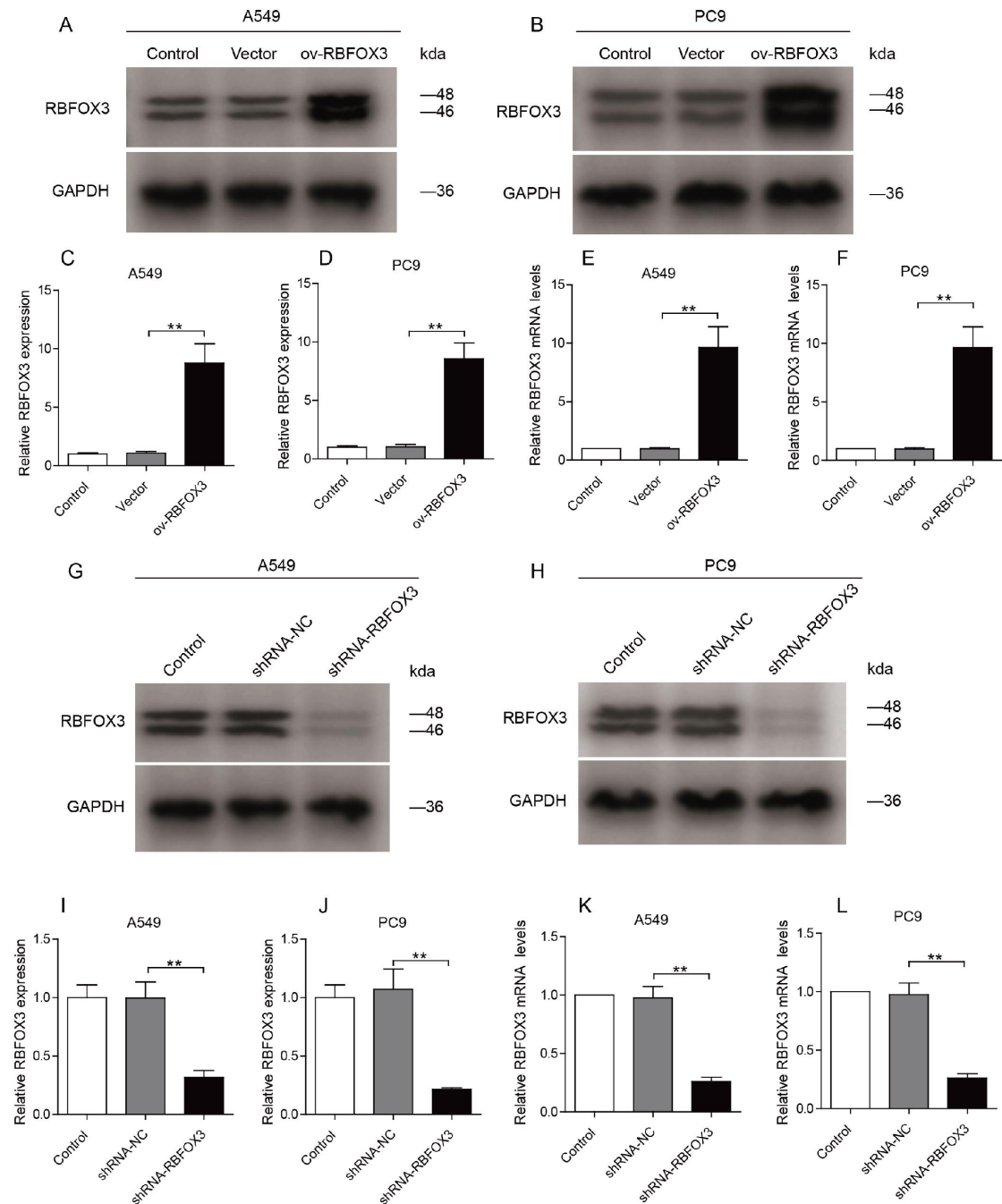
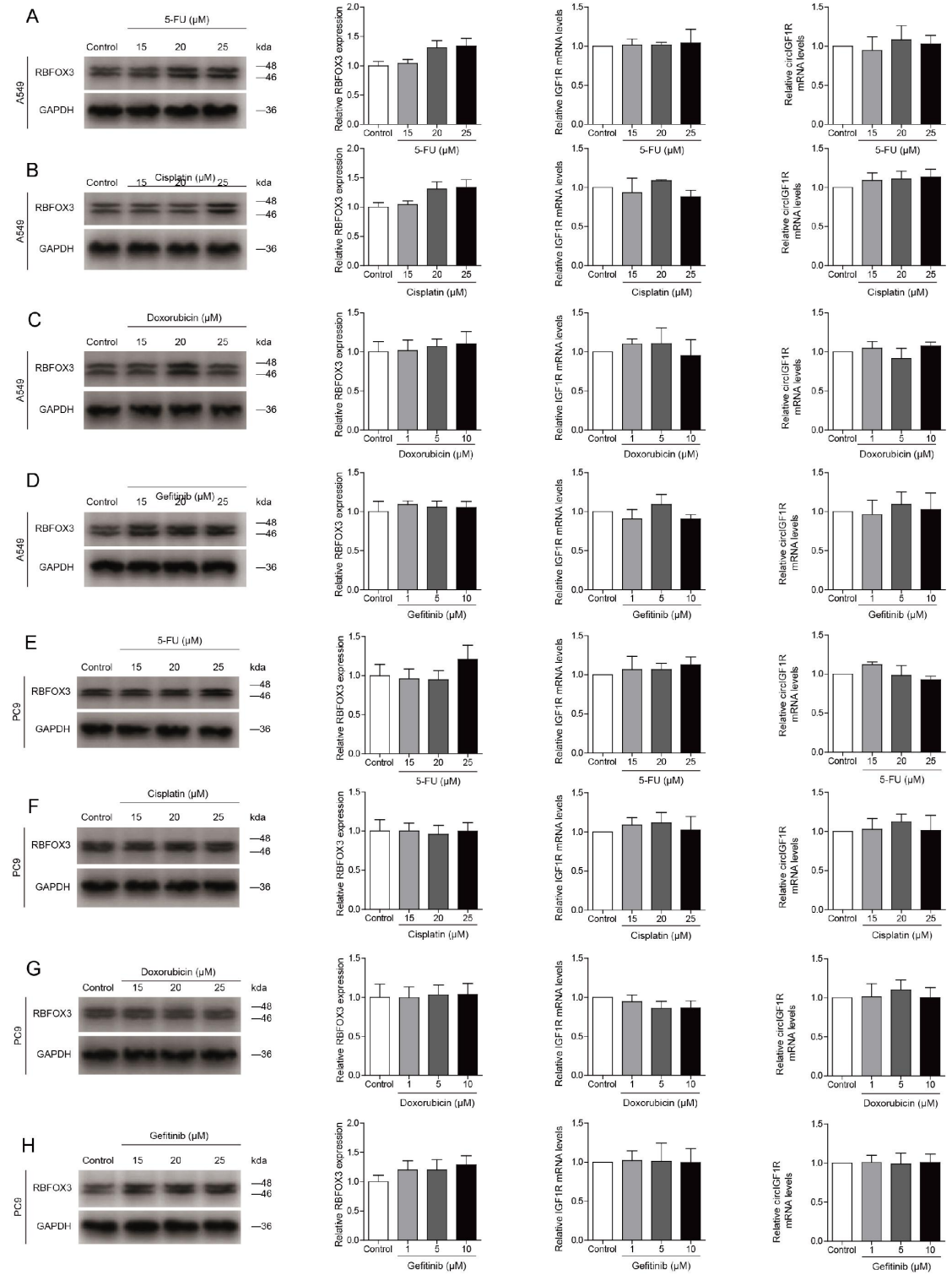


Figure S3. Effect of different drug treatments on A549 and PC9 cells. (a-h) RBFOX3 protein, IGF1R and circIGF1R mRNA levels in A549 and PC9 cells treated with different concentrations of 5-fluorouracil, cisplatin, doxorubicin, gefitinib.



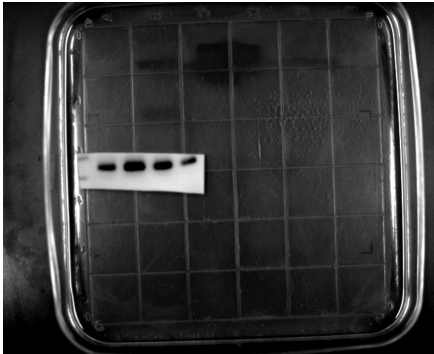
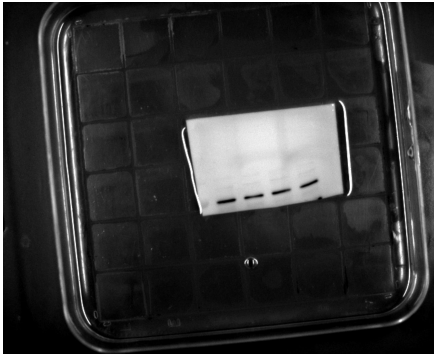


Fig 2i-CTNNB1



2i-GAPDH

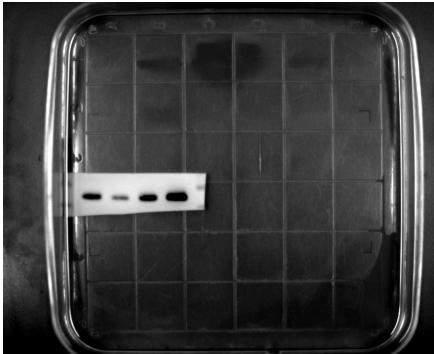


Fig 2i-VANGL2

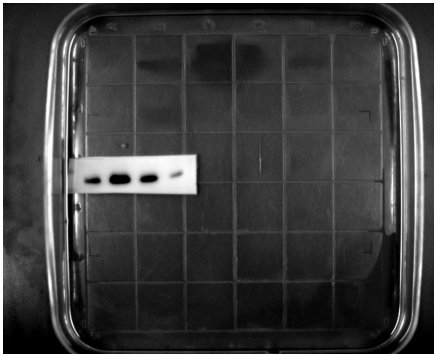


Fig 2i-WNT1

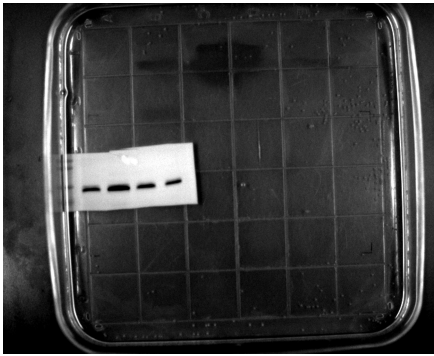


Fig 2m-CTNNB1

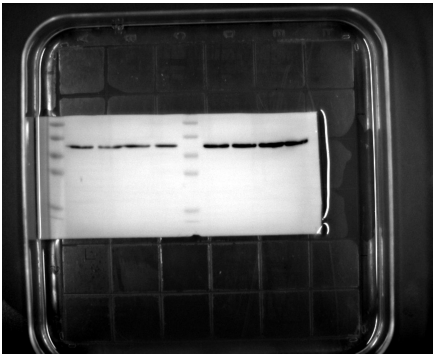


Fig 2m-GAPDH

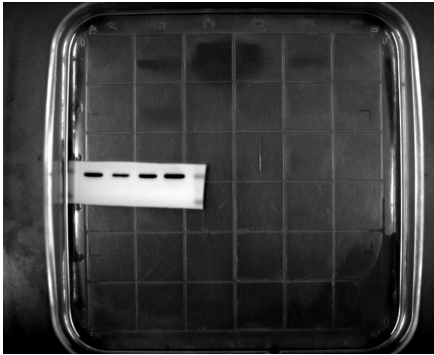


Fig 2m-VANGL2

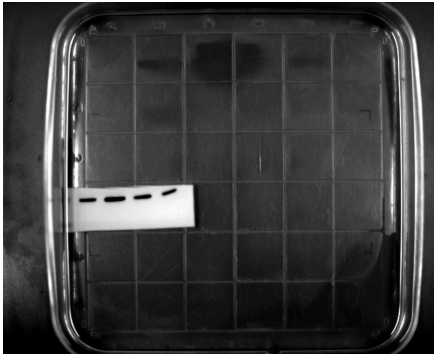


Fig 2m-WNT1

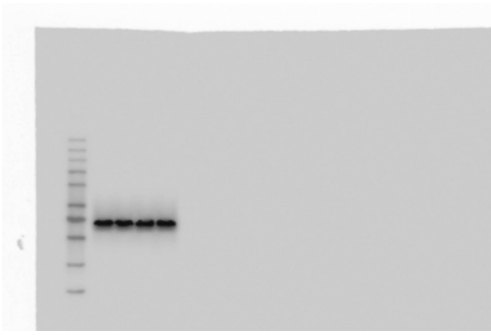


Fig 5f-GAPDH

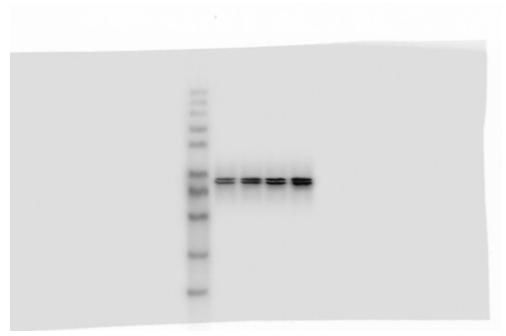


Fig 5f-RBFOX3



5j-GAPDH

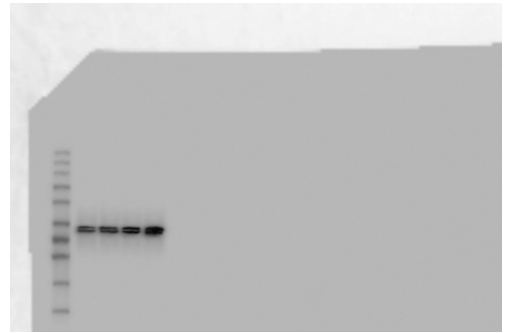


Fig 5j-RBFOX3

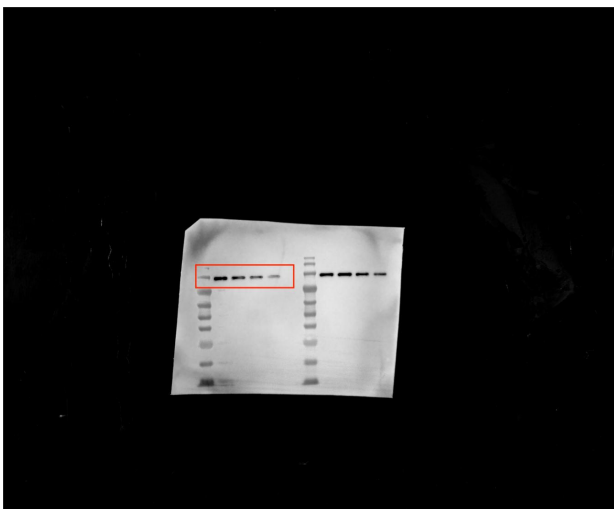


Fig 5q-CTNNB1

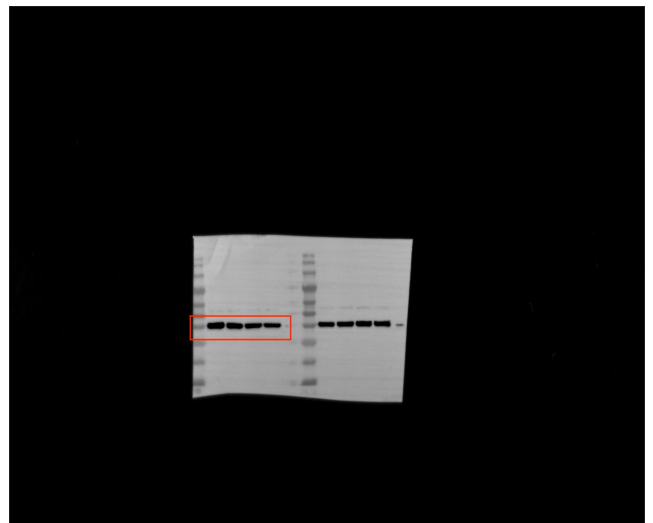


Fig 5q-GAPDH

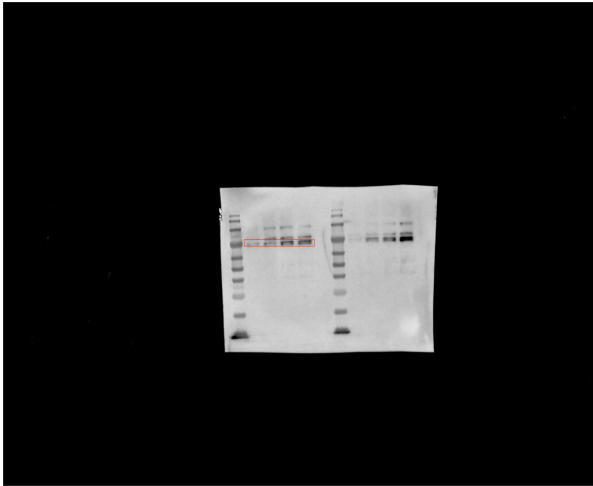


Fig 5q-VANGL2

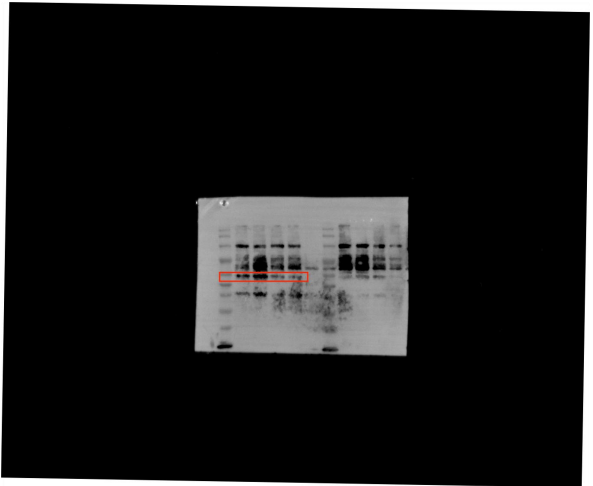


Fig 5q-WNT1

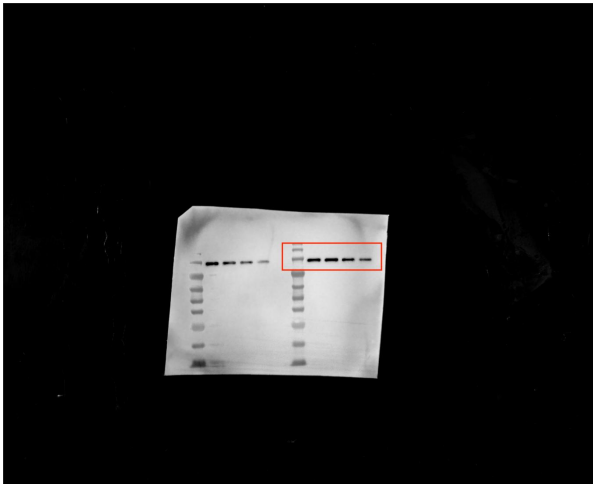


Fig 5u-CTNNB1

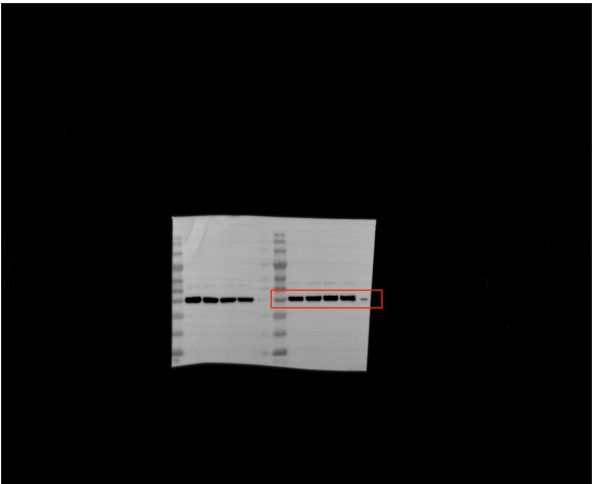


Fig 5u-GAPDH

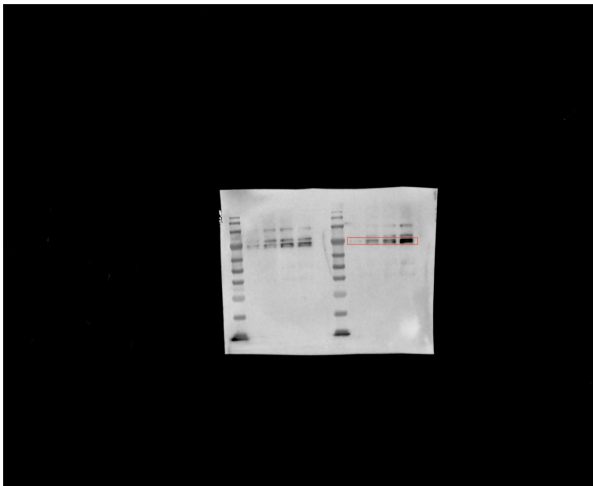


Fig 5u-VANGL2

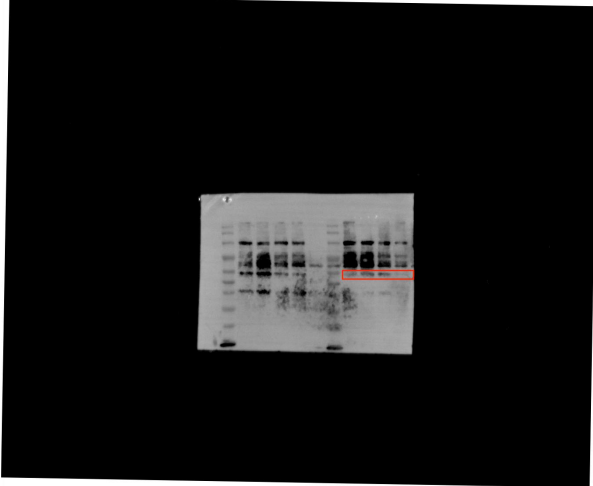


Fig 5u-WNT1

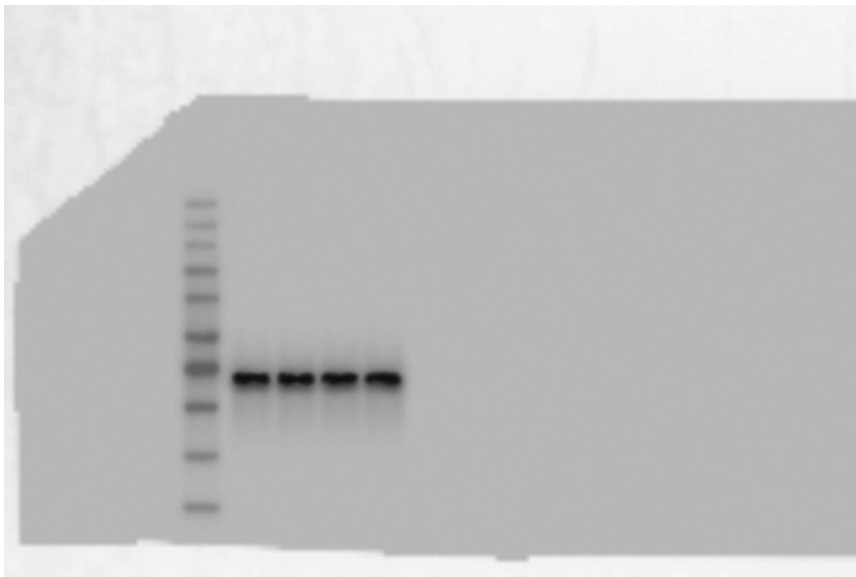


Fig 6k-GAPDH

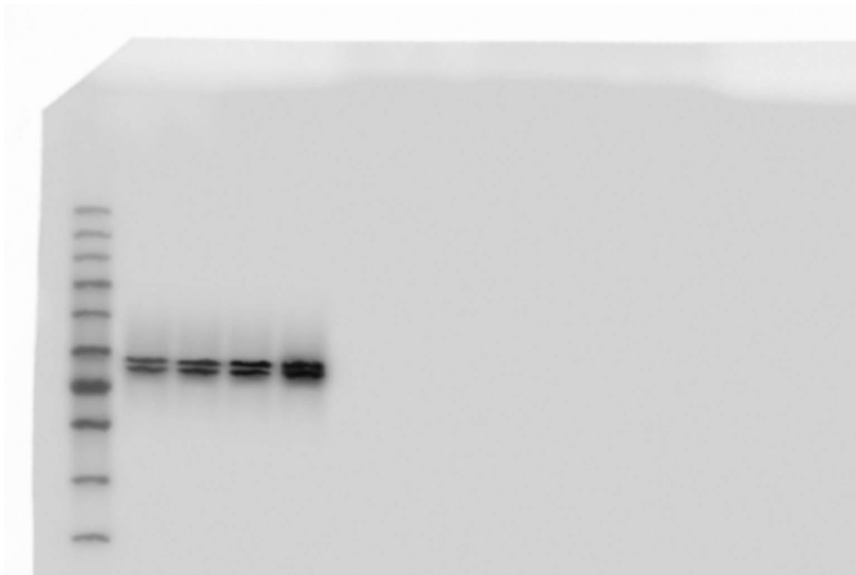


Fig 6k-RBFOX3

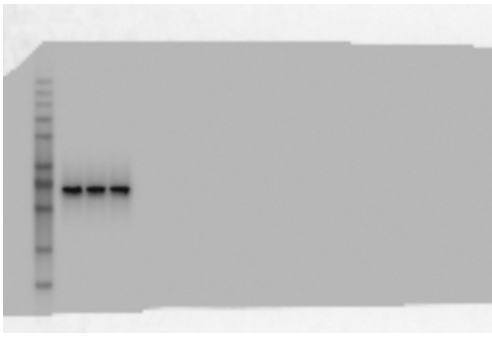


Fig S2a-GAPDH

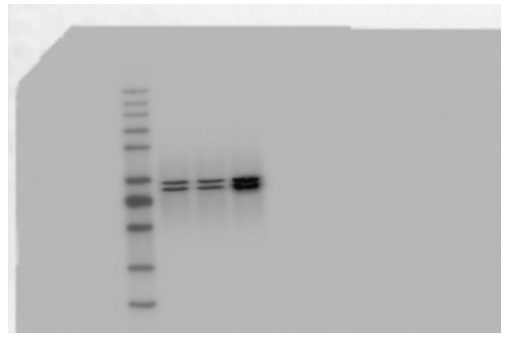


Fig S2a-RBFOX3

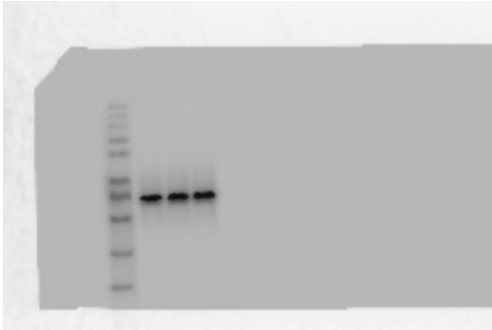


Fig S2b-GAPDH

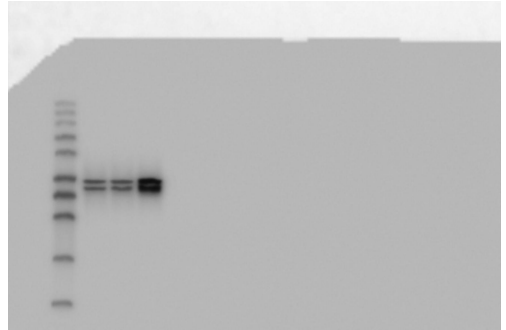


Fig S2b-RBFOX3

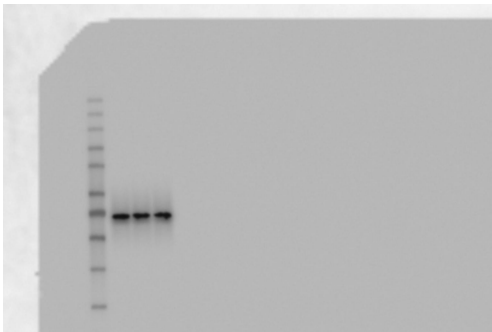


Fig S2g-GAPDH

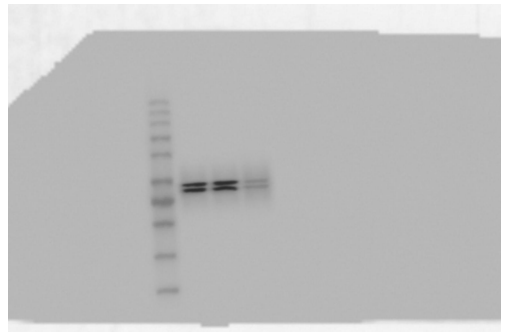


Fig S2g-RBFOX3

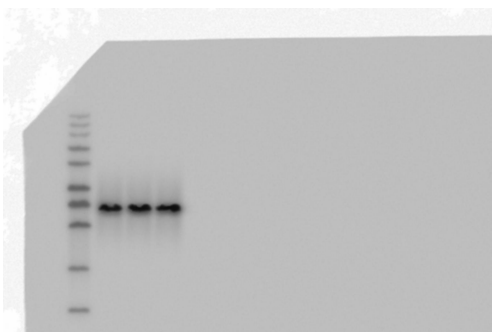


Fig S2h-GAPDH



Fig S2h-RBFOX3

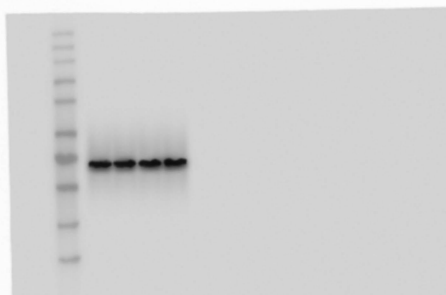


Fig S3a-GAPDH

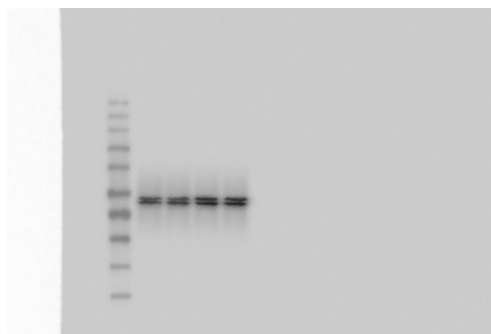


Fig S3a-RBFOX3

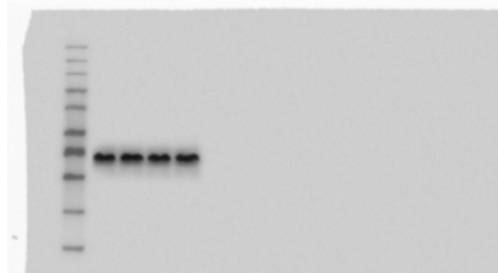


Fig S3b-GAPDH

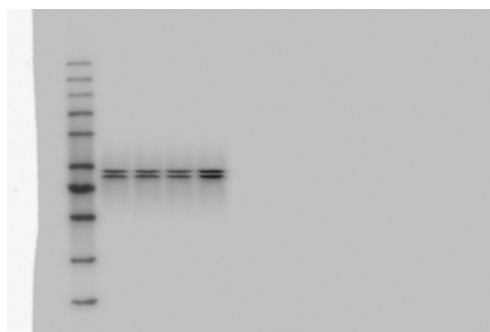


Fig S3b-RBFOX3

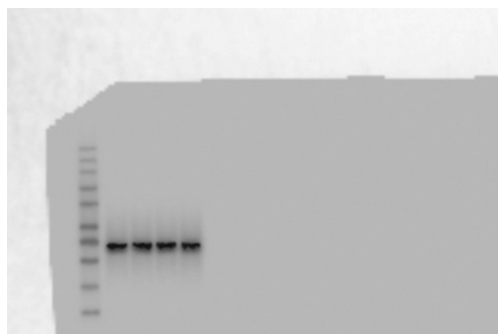


Fig S3c-GAPDH

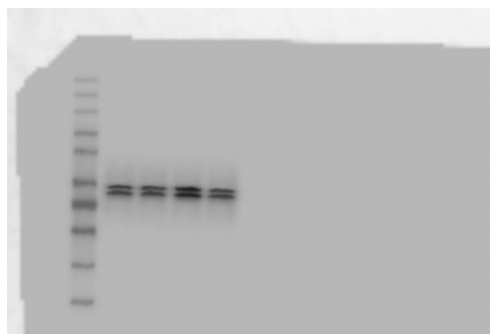


Fig S3c-RBFOX3

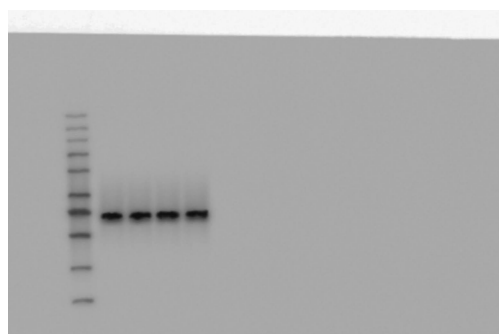


Fig S3d-GAPDH

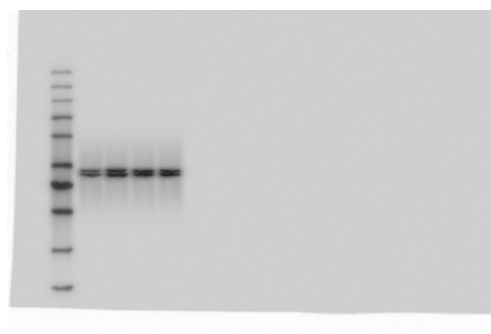


Fig S3d-RBFOX3

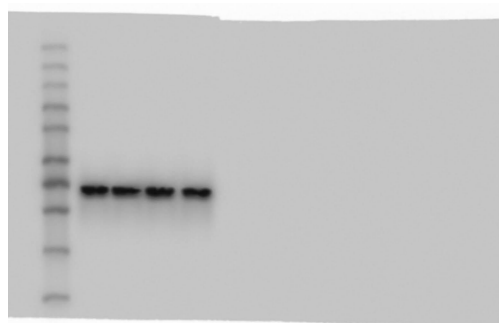


Fig S3e-GAPDH

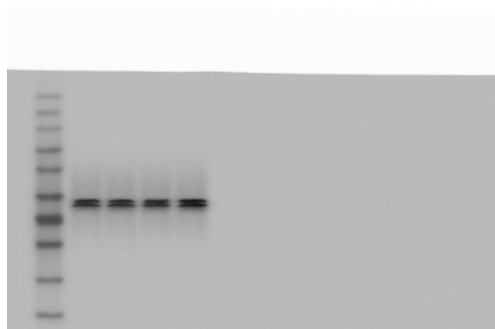


Fig S3e-RBFOX3

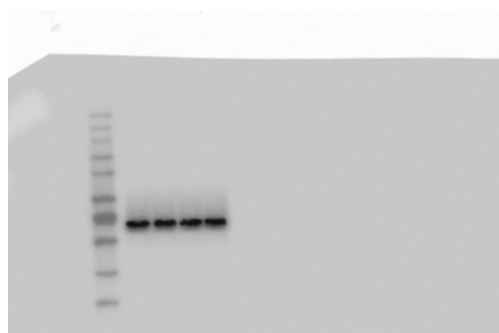


Fig S3f-GAPDH



Fig S3f-RBFOX3



Fig S3g-GAPDH

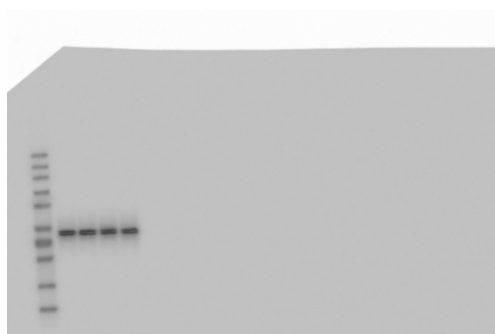


Fig S3g-RBFOX3

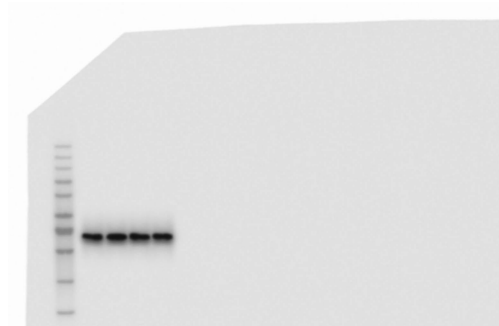


Fig S3h-GAPDH



Fig S3h-RBFOX3