cancers

MDPI

Targeting IGF2BP2 Promotes Differentiation of Radioiodine Refractory Papillary Thyroid Cancer via Destabilizing RUNX2 mRNA

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Table S1. The primer sequences.

gene	sequences
SLC5A5-S	CTGCCCCAGACCAGTACATGCC
SLC5A5-A	TGACGGTGAAGGAGCCCTGAAG
IGF2BP2-S	AACCCCAAAGAAGAAGTGAAGC
IGF2BP2-A	TTTGGTCACGAGGCACGAT
β-actin-S	TCTACAATGAGCTGCGTGTG
β-actin-A	TAGATGGGCACAGTGTGGGT

Table S2. Expression of m6A key regulators and iodide-handling genes in normal thyroid tissues and thyroid cancer based on TCGA database.

gene	normal thyroid tissues Mean	thyroid cancer Mean	logFC	*p* Value
YTHDC1	16.475244	12.36228568	-0.414354322	4.86E-19
TSHR	145.5524059	100.3074123	-0.537110468	3.21E-14
TG	7096.331946	3053.501668	-1.216608863	2.48E-21
FTO	5.22394037	3.930772179	-0.410325679	6.69E-16
ALKBH5	38.92788526	34.64486202	-0.168162563	4.24E-08
METTL14	5.241399729	3.951812242	-0.407437735	1.92E-19
SLC5A5	20.99236121	3.699198362	-2.50457988	1.04E-26
HNRNPC	44.56087334	48.77368184	0.130325375	5.79E-05
TPO	666.2346093	185.7948459	-1.84231982	4.61E-23
YTHDF1	22.62329119	20.68445037	-0.129262202	2.20E-06
RBM15B	11.01082181	11.68894403	0.086222454	0.003823026
YTHDF3	12.07129406	10.18577346	-0.245024808	3.18E-08
YTHDC2	3.200695013	2.698269876	-0.246350561	1.78E-06
YTHDF2	16.99331941	16.93274625	-0.005151714	0.904226929
HNRNPA2B1	93.17716572	79.5028424	-0.228970006	1.03E-09
IGF2BP1	0.014391499	0.033158128	1.20414574	2.35E-07
RBM15	2.681661904	1.841058101	-0.542592201	8.64E-24
KIAA1429	5.489612952	4.709760701	-0.221050675	3.87E-08
IGF2BP3	0.139347652	0.252216971	0.855976661	1.57E-10
METTL3	7.094790945	6.137485522	-0.209112458	8.14E-05
WTAP	17.36785137	14.499494	-0.26041673	1.74E-09
IGF2BP2	3.42588301	12.25571513	1.838906878	1.78E-24
ZC3H13	10.76703674	8.151836341	-0.401424259	2.10E-13

Table S3. Pearson correlation between SLC5A5 and top 30 genes from RNA-seq associated with cell differentiation of malignant cancers.

	R	*p*Value
CCND1	-0.086	0.051
THRB	-0.017	0.7
NOTCH3	0.013	0.77
PLCG2	0.065	0.14
MMP14	-0.027	0.55

GPX1	-0.052	0.24
HLA-B	-0.054	0.22
SLC9A1	0.25	7.60E-09
RUNX2	-0.099	0.041
EGR1	-0.022	0.62
GNA12	-0.0028	0.95
PPARG	0.0086	0.85
MAPK3	0.17	0.00015
ITGB3	0.092	0.037
TCF7	-0.047	0.29
SIN3A	-0.009	0.84
FOXO1	-0.023	0.61
MEF2C	0.051	0.25
THRA	0.071	0.11
PIK3R1	-0.027	0.54
HDAC1	-0.011	0.8
MAPK1	-0.029	0.51
NOTCH1	0.11	0.01
SRC	-0.011	0.014
RCAN1	0.0019	0.97
GNA13	-0.0011	0.98
TCF7L2	-0.036	0.41
KAT2A	-0.073	0.099
GATA3	-0.027	0.55
RXRA	0.14	0.0013

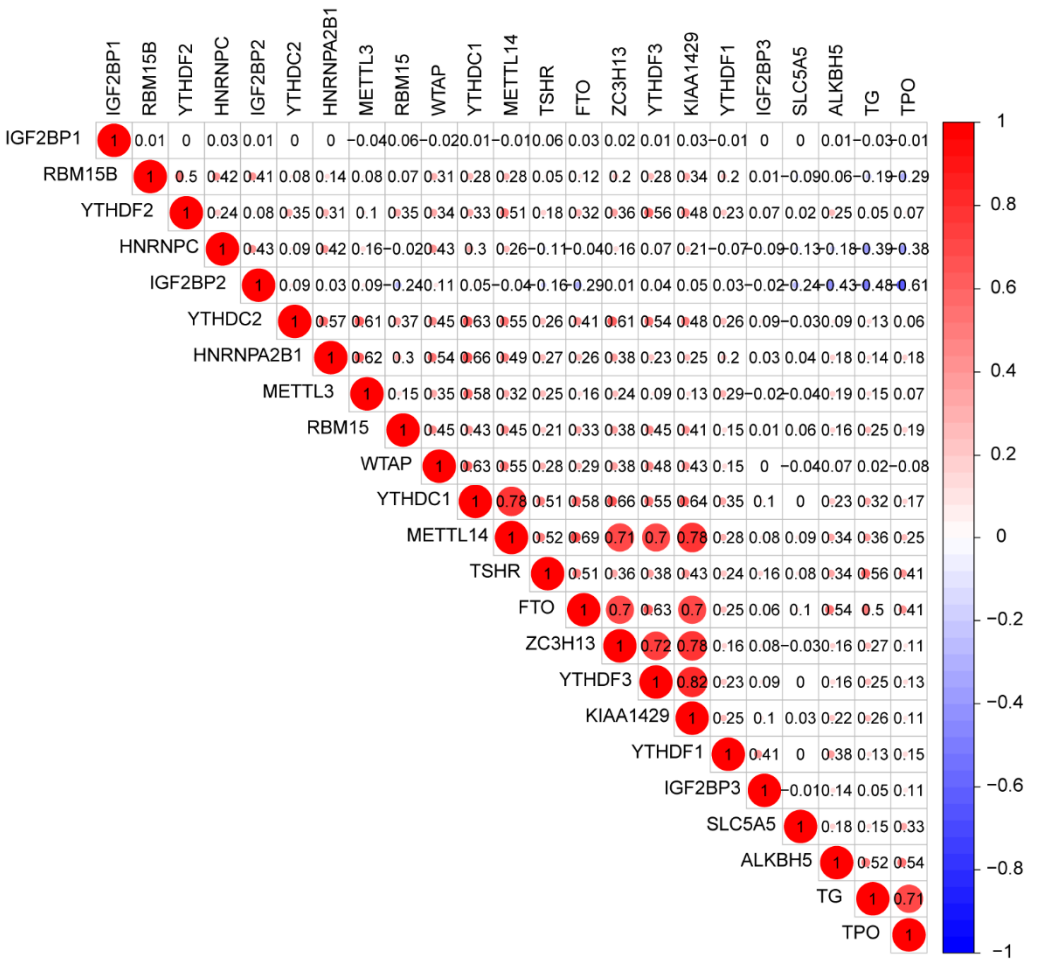

Figure S1. Negative association between the expression of IGF2BP2 and iodide-handling genes with correlation coefficient.

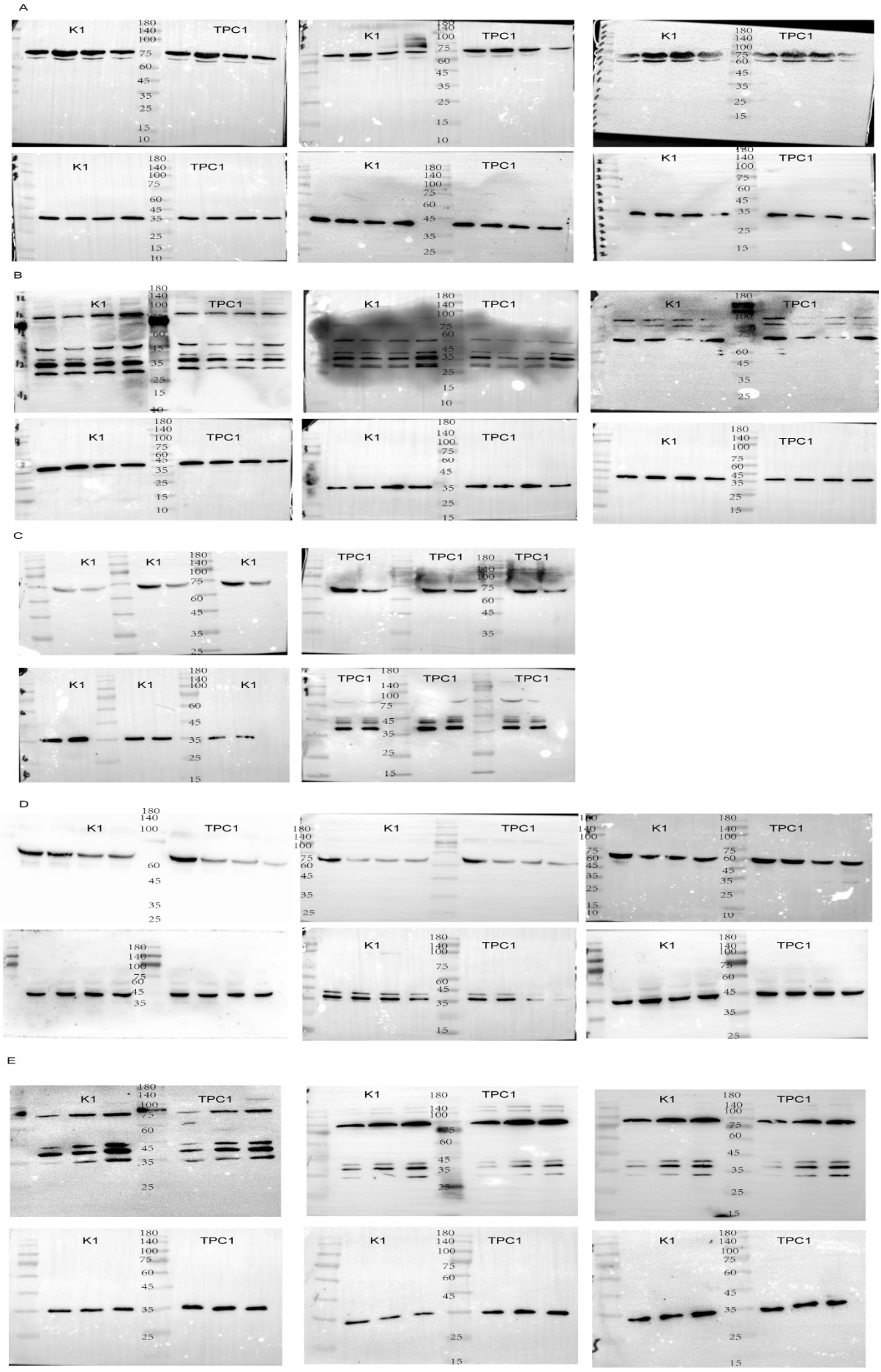
A
K1
TPC1
B
K1
TPC1
C
K1
TPC1
D
K1
TPC1
E
K1
TPC1

Figure S2. The uncropped Western blot figures for Figure 3A (A), Figure 3E (B), Figure 4B (C), Figure 5A (D), supplementary Figure 4C (E).

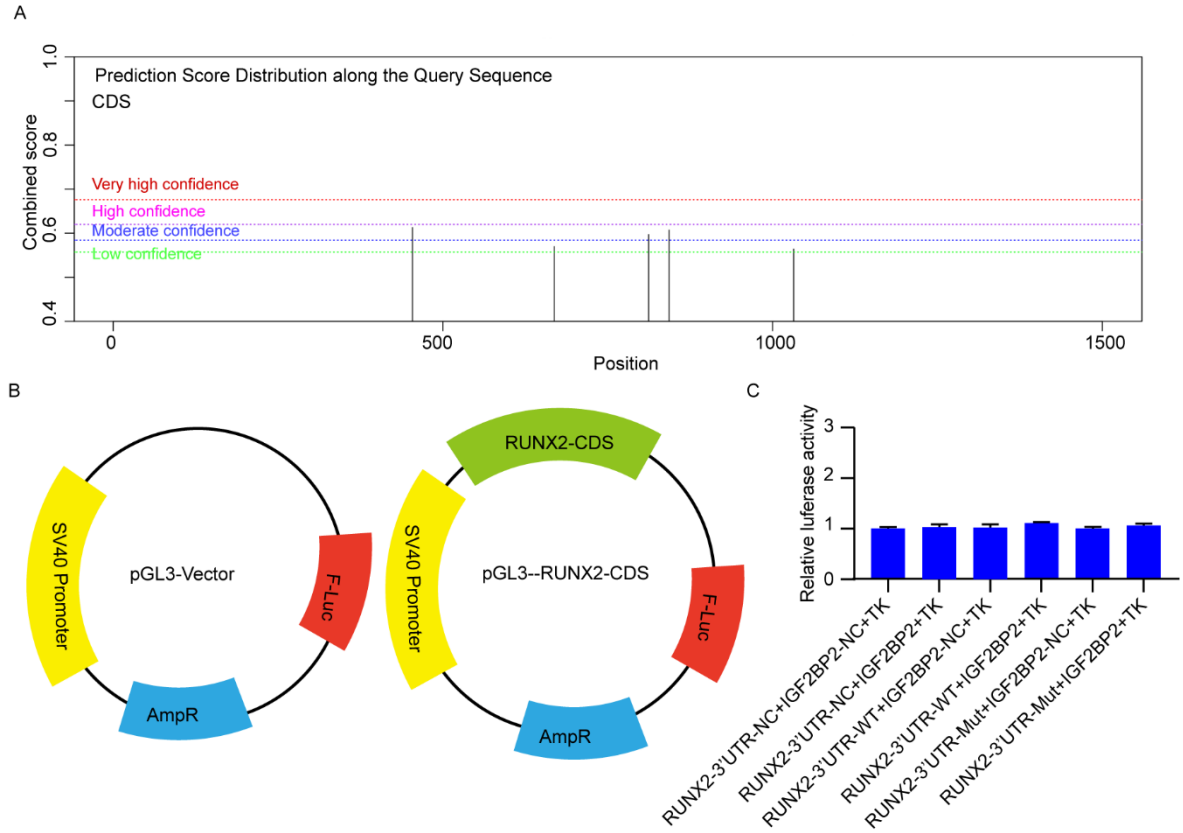

Figure S3. IGF2BP2 does not bind to the CDS of RUNX2. (A) Prediction of potential m6A binding sites in CDS of RUNX2 mRNA. (B) Graphical explanation for construction of luciferase reporters with wild-type or mutant (m6A motif mutated) sequence of RUNX2–CDS inserting into a pGL3 vector. (C) Relative luciferase activities in TPC1 cells with stably expressing IGF2BP2 or vector co-transfected with RUNX2–CDS wild-type or mutant luciferase reporters.

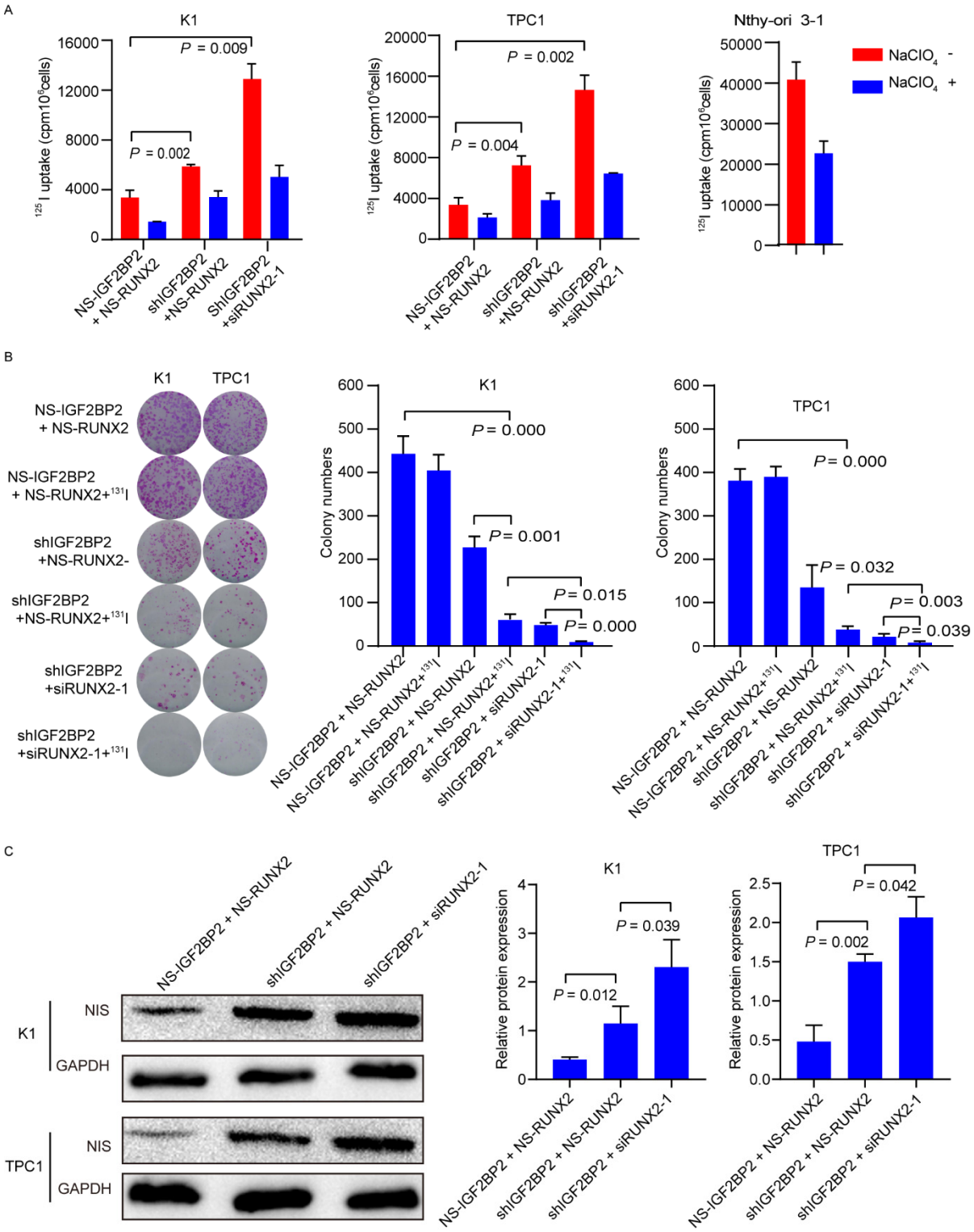

Figure S4. Targeting IGF2BP2 and RUNX2 have robust cell differentiation effect in PTC. (A) ^{125}I uptake in K1 and TPC1 cells with or without co-transfection with shIGF2BP2 and siRUNX2-1. (B) ^{131}I clonogenic assay in K1 and TPC1 cells with or without co-transfection with shIGF2BP2 and siRUNX2-1. (C) NIS protein expression in K1 and TPC1 cells with or without co-transfection with shIGF2BP2 and siRUNX2-1.