Supplementary Data

Figure S1: No difference in the methylation degree (%) of CpGisland1 in untreated (DMSO) and 5aza treated follicular carcinoma cells (FTC236, FTC238 and WRO) and melanoma cells (NPA) (mean ±SEM). Black bar: DMSO samples; gray bar: 5aza samples.

Figure S2 No difference in the methylation degree (%) of CpGisland1 between T and NT samples.

Figure S3: TCGA data analysis of the expression of FOXE1 target genes. Downregulation in T compared to NT of PAX8 TG, TPO, NIS and ZEB1, and upregulation T compared to NT of NKX2.1 and PDGFA * p<0.0001, no difference was observed for DUOX2 expression.

Figure S4: Patients' samples analysis of the expression of *TG* and *PAX8.* Low expression in T compared to NT samples without significance ($P > 0.05$).
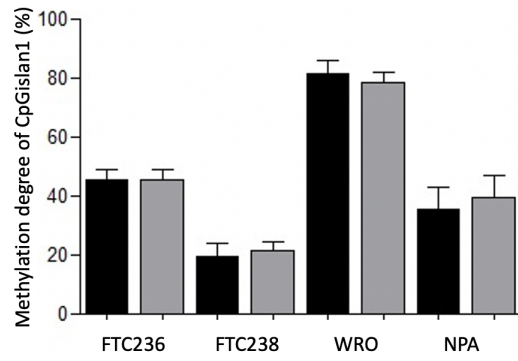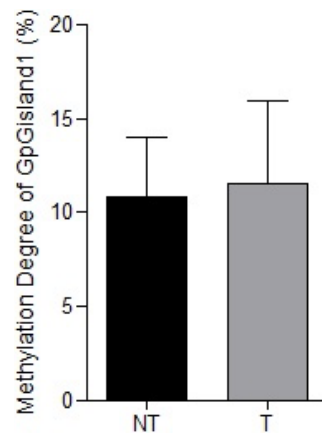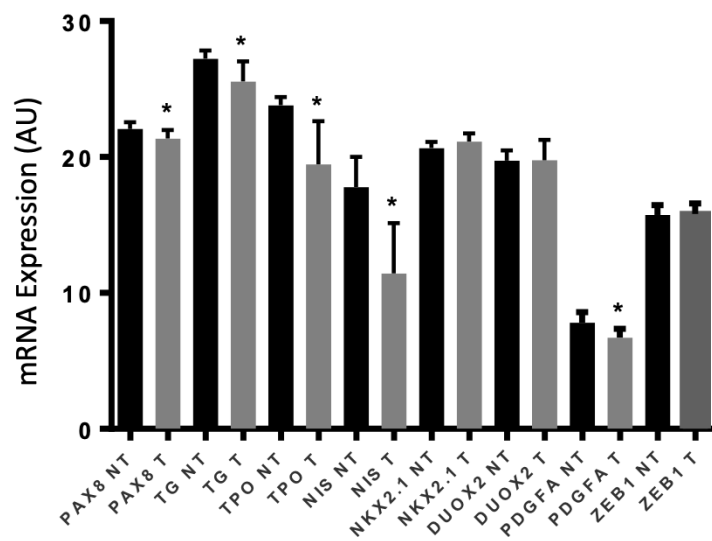
Figure S1

Figure S2
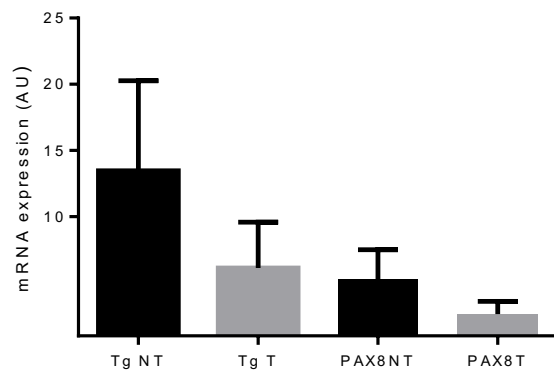

Figure S3

Figure S4

Table S1: Clinical data of the patients.

ID	Age (Y)	Gender	Histology Variant		Ultrasound Focality	Lymph Node Involvement	T N M staging		
1	45	M	PTC	Classical	Unifocal	Reactive	T1a	N0	M0
2	30	F	PTC	Classical	Unifocal	Reactive	T1b	N0	M0
3	49	M	PTC	Classical	Unifocal	Pathological	T1a	N1a	M1
4	49	F	PTC	Classical	-	-	-	-	-
5	57	F	PTC	Classical	Multifocal	Reactive	T3	N0	M1
6	38	F	PTC	Classical	Unifocal	Reactive	T3	N0	M0
7	54	M	PTC	Classical	Multifocal	Reactive	T1a	N1a	M1
8	30	F	PTC	Classical	Multifocal	Pathological	T3	N1b	M0
9	64	F	PTC	Classical/ Follicular	Absent	Absent	-	-	-
10	27	F	PTC	Classical	Multifocal	Reactive	T1b	N0	M0
11	55	F	PTC	Follicular	Multifocal	Pathological	T1a	N0	M0
12	27	F	PTC	Classical	Multifocal	Reactive	T1a	N1a	M0
13	-	F	PTC	Classical	Absent	Absent	-	-	-
14	22	F	PTC	Classical	Absent	Absent	-	-	-
15	24	F	PTC	Classical	-	-	-	-	-
16	32	F	PTC	Solid	Unifocal	Pathological	T3	N1a	M0
17	42	F	PTC	Classical	Multifocal	Reactive	T3	N0	M0
18	48	M	PTC	Classical	Multifocal	-	T1a	N0	M0
19	49	F	PTC	Classical	Multifocal	Reactive	T1a	N0	M0
20	31	F	PTC	Tall cell	Absent	Absent	-	-	-
21	40	F	PTC	Diffuse Sclerosing	-	-	-	-	-
22	-	F	PTC	Classical	Absent	Absent	-	-	-
23	59	F	PTC	Clear cell	Absent	Absent	-	-	-
24	-	M	PTC	Oncocytic	Absent	Absent	-	-	-
25	-	F	PTC	Classical	Absent	Absent	-	-	-
26	31	M	PTC	Classical	Absent	Pathological	-	-	-
27	44	F	PTC	Classical	Unifocal	Reactive	T1a	N0	M0
28	-	F	PTC	Classical	Absent	Absent	-	-	-
29	-	F	PTC	Classical	Absent	Absent	-	-	-
30	47	F	PTC	Classical	-	-	-	-	-
31	49	F	PTC	Classical	Absent	Absent	-	-	-
32	44	F	PTC	Classical	-	-	-	-	-
33	-	F	PTC	Follicular	-	-	-	-	-

Table S2: Primer sequences, PCR conditions and product sizes.

Gene/region	Sequence (5'-3')	Application	Annealing (°C)	Product size (pb)
FOXE1	F: GGAGCCCCCTACTCTTTGAC	Expression	60	100
	R: TTGTCTGGAAGAGCCTGGAT			
S8	F: AACAAGAAATACCGTGCCC	Expression	60	100
	R: GTACGAACCAGCTCGTTATTAG			
CpGIsland1	F: TAGGGTTTTAGAATTTAATTGAAATG	BS	57	200
	R: ATCACTATCACCCAAAAAACAAAATA			
CpGIsland2	F: GTAAGGATTTGGGTTTTGTTT	BS	57	355
	R: AAAACCTCAATATTCTACTCTATTAAA			
CpGIsland2	F: CCG**GGTACC**GTTTAGCGAGTGTAAAGCCCC	Cloning	60	500
	R: CCG**CTCGAG**GCCATTCACTGGGAGATCCA			

BS: Bisulfite sequencing, bold sequences indicate restriction sites (*Kpn*1, *Xho*1)

Table S3: Patients characteristics from The Cancer Genome Atlas (TCGA) database

		Number	**Percentage**
Diagnosis age	<45	235	46.3
	≥45	273	53.7
Gender	Female	369	72.9
	Male	137	27.1
Race	White	333	65.6
	Black or African American	26	5.1
	Asian	51	10
	Not determined	98	19.3
Ethnicity	Hispanic or Latin	38	7.5
	No Hispanic or Latin	359	70.7
	Not determined	111	21.9
Histological type	Classical	362	71.3
	Follicular	102	20.1
	Tall cells	34	6.7
	Others	8	1.6
	Not determined	2	0.4
Pathologic T stage	T1	44	8.7
	T1a	19	3.7
	T1b	80	15.7
	T2	168	33.1
	T3	173	34.1
	T4	9	1.8
	T4a	12	2.4
	Not determined	3	0.6
Pathologic N stage	N0	226	44.5
	N1	59	11.6
	N1a	91	17.9
	N1b	80	15.7
	NX	50	9.8
	Not determined	2	0.4
Pathologic M stage	M0	281	55.3
	M1	9	1.8
	MX	21	42.3
	Not determined	3	0.6
AJCC	I	288	50.9
	II	51	11.4
	III	110	24.6
	IV	2	0.4
	IVa	47	10.5
	IVc	6	1.3
	Not determined	4	0.9
Disease free status	Free	445	87.6
	Recurrent or Progressive	49	9.6
	Not determined	14	2.8
Overall survival	Living	492	97.2
	Diseased	14	2.8
New neoplasm event post initial therapy	Yes	12	2.4
	No	250	49.2
	Not determined	246	48.4
Surgical margins	R0	387	76.2
	R1	53	10.4
	R2	4	0.8
	RX	30	5.9
	Not determined	34	6.7

Table S4: Correlation analysis of FOXE1 mRNA expression and CpGisland2'methylarion degree with the expression of genes regulated by FOXE1.

Gene	FOXE1 mRNA		CpGisland2' methylation	
	r	P	r	P
	Tumor samples			
PAX8	0.34	**< 0.0001**	-0.31	**< 0.0001**
TG	0.29	**< 0.0001**	-0.28	**< 0.0001**
TPO	0.30	**< 0.0001**	-0.04	0.1586
DUOX2	0.21	**< 0.0001**	-0.36	**< 0.0001**
NIS	-0.03	0.5032	-0.24	**< 0.0001**
NKX2.1	0.17	**0.0002**	0.09	**0.0181**
PDGFA	-0.23	**<0.0001**	0.11	**0.001**
ZEB1	0.14	**< 0.0001**	-0.36	**< 0.0001**
	Non tumor Samples			
PAX8	0.60	**< 0.0001**	-0.37	**0.008**
TG	0.63	**< 0.0001**	-0.28	**0.051**
TPO	0.46	**0.0005**	-0.03	0.82
NIS	0.31	**0.024**	-0.49	**0.0003**
NKX2.1	0.27	0.051	0.05	0.73
PDGFA	-0.21	0.10	-0.29	**0.035**
ZEB1	0.03	0.80	-0.21	0.17
DUOX2	0.48	**0.0003**	-0.49	**0.0003**

Bold values indicate statistical significance.