

ORIGINAL RESEARCH ARTICLE

Reduced FOXO1 expression is associated with tumor progression through metabolic and immune dysregulation in kidney renal clear cell carcinoma

Supplementary Files

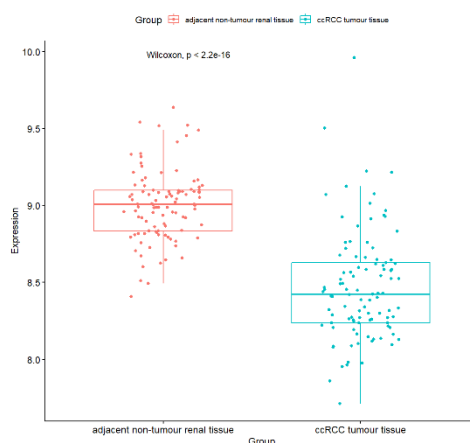


Figure S1. Differences in *FOXO1* expression in KIRC tumor tissues and adjacent non-tumorous renal tissues based on the Gene Expression Omnibus dataset (GSE40435)

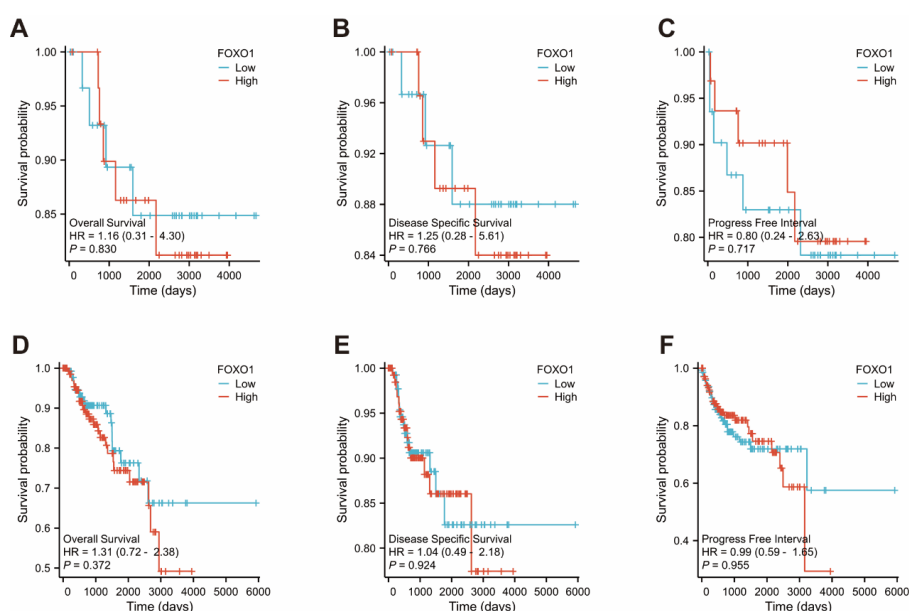


Figure S2. Kaplan–Meier survival curves showing survival probabilities for overall survival, disease-specific survival, and progression-free interval in patients with low- and high-FOXO1 expression in the KIRC (A, B, C) and KIRP (D, E, F)
Abbreviations: KIRC: Kidney chromophobe renal cell carcinoma; KIRP: Kidney renal papillary cell carcinoma.

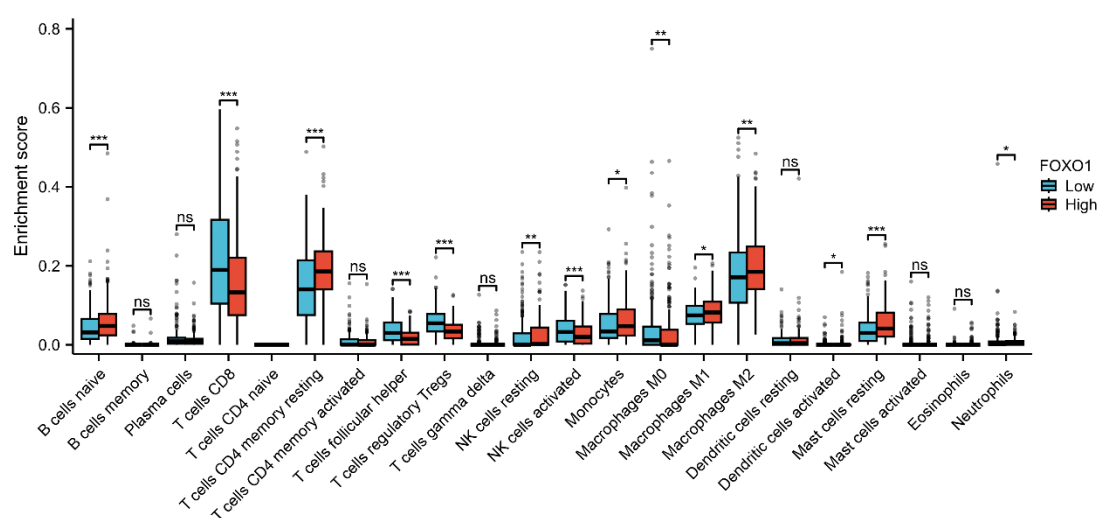


Figure S3. Validation of immune infiltration analysis using the Cell-type Identification by Estimating Relative Subsets of RNA Transcripts (CIBERSORT) algorithm. Box plots showing the correlation between *FOXO1* expression and the estimated abundance of immune cell populations inferred by CIBERSORT.

Table S1. Differences in *FOXO1* expression in tumor and normal samples

Group	Sample size (<i>n</i>)		Log ₂ Fold change	<i>p</i> -value
	Normal	Tumor		
KICH	25	65	0.0262	0.8614
KIRC	72	541	-0.6653	2.72e ⁻¹⁶
KIRP	32	291	-1.2024	3.56e ⁻²⁵

Abbreviations: KICH: Kidney chromophobe renal cell carcinoma; KIRC: Kidney renal clear cell carcinoma; KIRP: Kidney renal papillary cell carcinoma.

Table S2. Differences in *FOXO1* expression in tumor and paired normal samples

Group	Sample size (<i>n</i>)		Log ₂ Fold change	<i>p</i> -value
	Normal	Tumor		
KICH	24	24	0.0281	0.9087
KIRC	72	72	-0.5200	1.84e ⁻⁷
KIRP	32	32	-1.0314	1.44e ⁻⁹

Abbreviations: KICH: Kidney chromophobe renal cell carcinoma; KIRC: Kidney renal clear cell carcinoma; KIRP: Kidney renal papillary cell carcinoma.

Table S3. Clinical information of the KIRC cohort in terms of *FOXO1* expression

Parameter	Sub-category	Number of events	Median follow-up time (day)
OS	Low	112	2,190
	High	63	-
DSS	Low	75	3,554
	High	34	-
PFI	Low	97	2,352
	High	63	3,766

Abbreviations: DSS: Disease-specific survival; KIRC: Kidney renal clear cell carcinoma; OS: Overall survival; PFI: Progression-free interval.

Table S4. Statistical summary of correlations between FOXO1 expression and ssGSEA-derived immune cell signatures in the TCGA-KIRC cohort

Immune cell	<i>p</i> -value	FDR (BH adjusted <i>p</i>)
aDC	0.06741172	0.10111758
B cells	0.526590033	0.549485252
CD8 T cells	0.125196559	0.143081782
Cytotoxic cells	3.98×10^{-6}	1.06×10^{-5}
DC	0.008646791	0.013834866
Eosinophils	0.001617445	0.002986052
iDC	2.90×10^{-5}	6.05×10^{-5}
Macrophages	0.097222299	0.120069048
Mast cells	2.43×10^{-21}	2.91×10^{-20}
Neutrophils	3.03×10^{-5}	6.05×10^{-5}
NK CD56bright cells	1.82×10^{-23}	4.37×10^{-22}
NK CD56dim cells	0.74987883	0.74987883
NK cells	1.51×10^{-8}	5.17×10^{-8}
pDC	2.15×10^{-5}	5.16×10^{-5}
T cells	0.005918154	0.010145407
T helper cells	4.49×10^{-7}	1.35×10^{-6}
Tcm	2.67×10^{-16}	2.14×10^{-15}
Tem	1.98×10^{-11}	1.19×10^{-10}
TFH	0.301210417	0.328593182
Tgd	1.02×10^{-9}	4.07×10^{-9}
Th1 cells	0.095519026	0.120069048
Th17 cells	0.100057540	0.120069048
Th2 cells	0.080468617	0.113602753
Treg	9.59×10^{-11}	4.60×10^{-10}

Abbreviations: aDC: Activated dendritic cells; BH: Benjamini–Hochberg; DC: Dendritic cells; FDR: False discovery rate; iDC: Immature dendritic cells; NK cells: Natural killer cells; pDC: Plasmacytoid dendritic cells; Tcm: Central memory T cells; Tem: Effector memory T cells; TFH: T follicular helper cells; Tgd: $\gamma\delta$ T cells; Th cells: T helper cells; Treg: Regulatory T cells.