

Supplementary

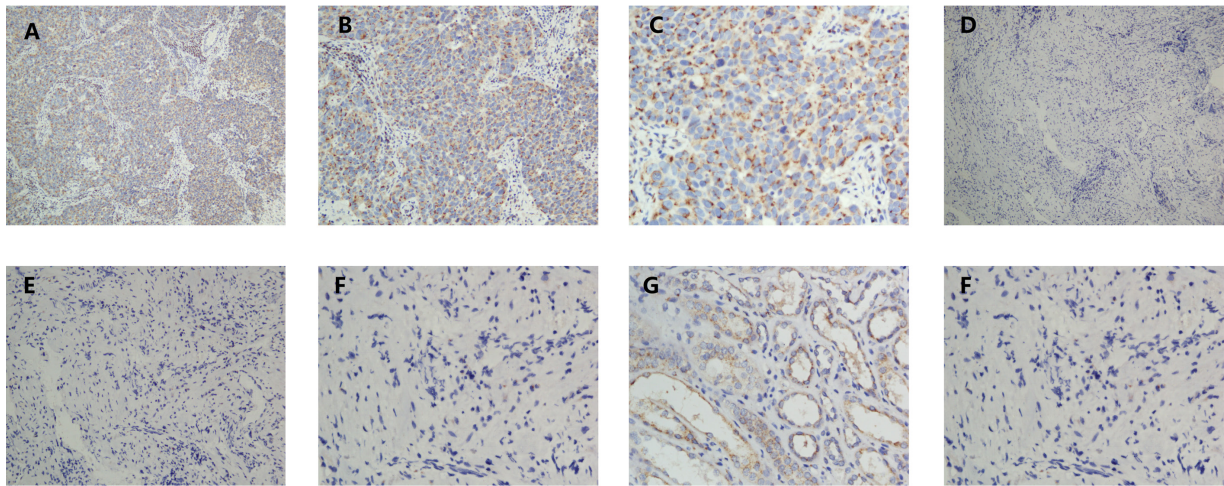


Figure S1 IHC staining of Expression of FGFR3 in different control tissues. (A) Positive expression of FGFR3 in bladder cancer tissue (Original Magnification $\times 100$). (B) Positive expression of FGFR3 in bladder cancer tissue (Original Magnification $\times 200$). (C) Positive expression of FGFR3 in bladder cancer tissue (Original Magnification $\times 400$). (D) Negative expression of FGFR3 in bladder cancer tissue (Original Magnification $\times 100$). (E) Negative expression of FGFR3 in bladder cancer tissue (Original Magnification $\times 200$). (F) Negative staining of FGFR3 in bladder cancer tissue (Original Magnification $\times 400$). (G) Positive expression of FGFR3 in bladder cancer tissue (Original Magnification $\times 400$).

Table S1 Basic information for FGFR3 expression and mutation

ID	Histology	FGFR3 expression	FGFR3 mutation		
			Exon 7	Exon 10	Exon 15
2	AC	2+	p.N294N; c.882; AAT>AAC	WT	WT
20	AC	2+	WT	p.S455S; c.1365; C > T	WT
23	AC	2+	WT	p.L457L; c.1371; C > T	WT
27	AC	2+	p.N294N; c.882; AAT>AAC	p.T450M; c.1349; C > T	WT
29	AC	1+	p.N294N; c.882; AAT>AAC	WT	WT
51	SCC	2+	WT	p.L457L; c.1371; C > T	WT
74	SCC	1+	p.N294N; c.882; AAT>AAC	p.T450M; c.1349C > T	WT
82	SCC	0	p.N294N; c.882; AAT>AAC	WT	WT

AC, adenocarcinoma; FGFR3, fibroblast growth factor receptor 3; SCC, squamous cell carcinoma; WT, wild type.

Table S2 List of the FGFR3 antibodies used for immunohistochemistry and the scoring criteria in bladder cancer

Antibody	Clone	Dilution	Approach	Source	Percentage (%)	Intensity	Categories	Localization
FGFR3 (37)	B9	1:100	TMA	Santa Cruz	ND	0 = (-) 1 = (+) 2 = (++) 3 = (+++)	0 – 1 = L 2 – 3 = H	C/M
FGFR3 (41)	Rabbit monoclonal immunoglobulin G clone aa 359–372 (E10234)	1:50	TMA	Spring Bioscience	ND	ND	N or P*	ND
FGFR3 (38)	B9 monoclonal antibody	ND	TMA	Santa Cruz	ND	0 = (-) 1 = (+) 2 = (++) 3 = (+++)	0 – 1 = L 2–3 = H	ND
FGFR3 (42)	B9	1:50	TMA	Santa Cruz	ND	0 = (-) 1 = (+) 2 = (++) 3 = (+++)	0 – 1 = N 2 – 3 = P	C/M

*, focal (partly positive stained urothelial tissue on the TMA section) or weak FGFR3 (positive but with reduced intensity) immunoreactivity was also considered to be positive. C, cytoplasm; H, high; L, low; M, membrane; N, negative; ND, not determined; P, positive; TMA, tissue microarray.

Table S3 Overview of FGFR3 protein expression studies in NSCLC

Country	Techniques	Cases	Sample types	Frequencies of expression (%) in NSCLC	FGFR3 antibody	Scoring criteria
The Netherlands (40)	IHC	612	FFPE	20 (3.3%)	B-9, sc-13121, Santa Cruz Biotechnology, Dallas, TX, dilution 1/50	Intensity: 0 (negative, N), 1+ (low, L), 2+ (high, H). The percentage of cells was not scored, as it was homogenous among all tumors (i.e., it was 100% in all tumors).
Spain (39)	IHC	275	FFPE	5/275 (2%) (only in SCC)	B-9, Santa Cruz Biotechnology, 1:25	Percentage (%): ND; Intensity: 0 = (-); 1 = (+); Categories: 0 = N, 1 = P
China (33)	IHC	103 (all SCC)	FFPE	22.3% (23/103) (all SCC)	polyclonal antibody, 1:50; Abcam,	
China (33)	IHC	103 (all SCC)	FFPE	11.7% (12/103) (all SCC)	clone: C51F2, 1:50; Cell Signaling Technology	

C, cytoplasm; FFPE, formalin-fixed, paraffin-embedded; FGFR3, fibroblast growth factor receptor 3; H, high; IHC, immunohistochemistry; L, low; M, membrane; N, negative; ND, not determined; NSCLC, non-small cell lung cancer; P, positive; SCC, squamous cell carcinoma; TMA, tissue microarray.

Table S4 Overview of FGFR3 mutation status studies in NSCLC

Country	Techniques	Cases	Sample types	Frequencies of mutations (%) in NSCLC	Frequencies of mutations (%) in SCC	Frequencies of mutations (%) in AC	Mutations
Japan (29)	Sequencing	214	FFPE	2/214 (0.9%)	2/63 (3.2%)	0	Exon 7; p.R248H
The Netherlands (40)	Sequencing	612	FFPE	6/200 (3.0%)	4/76 (5.3%)	2/111 (1.8%)	FGFR3 fusion
Spain (39)	Sequencing	50	FFPE	0	0	0	
China (33)	Sequencing	1328	Surgically frozen tumor tissue	15/1328 (1.1%)	9/312 (2.9%)	6/1016 (0.6%)	FGFR3 fusion

FGFR3, fibroblast growth factor receptor 3; NSCLC, non-small cell lung cancer.