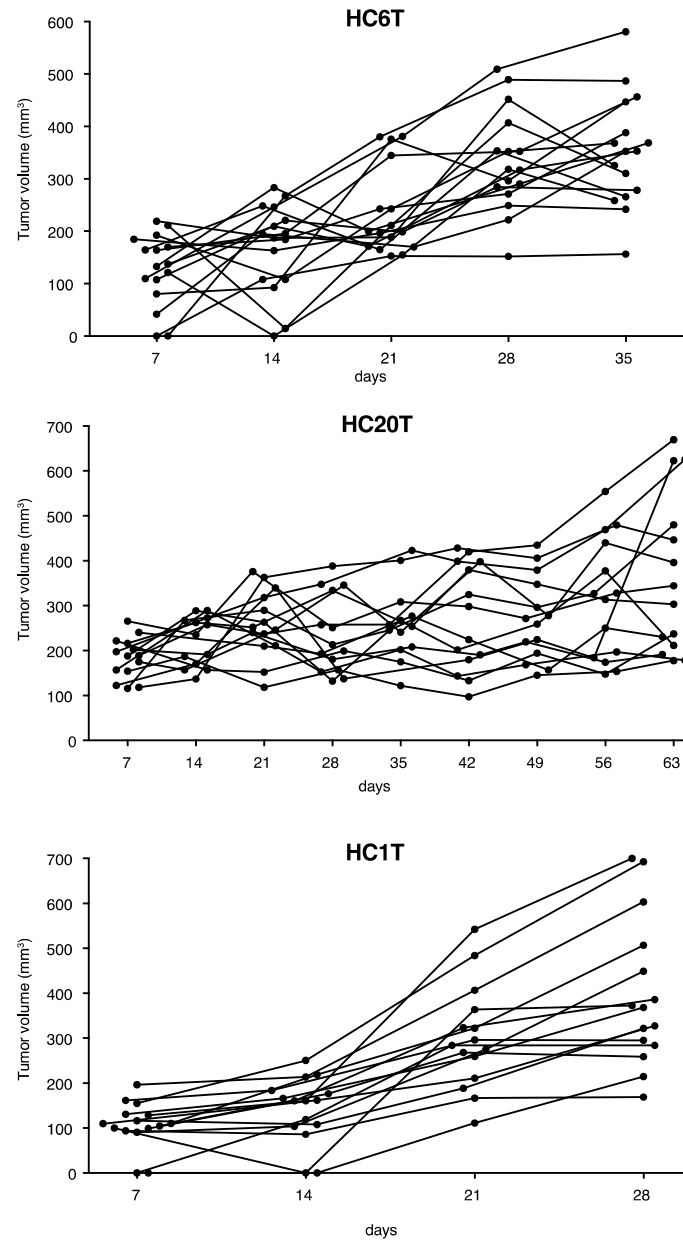
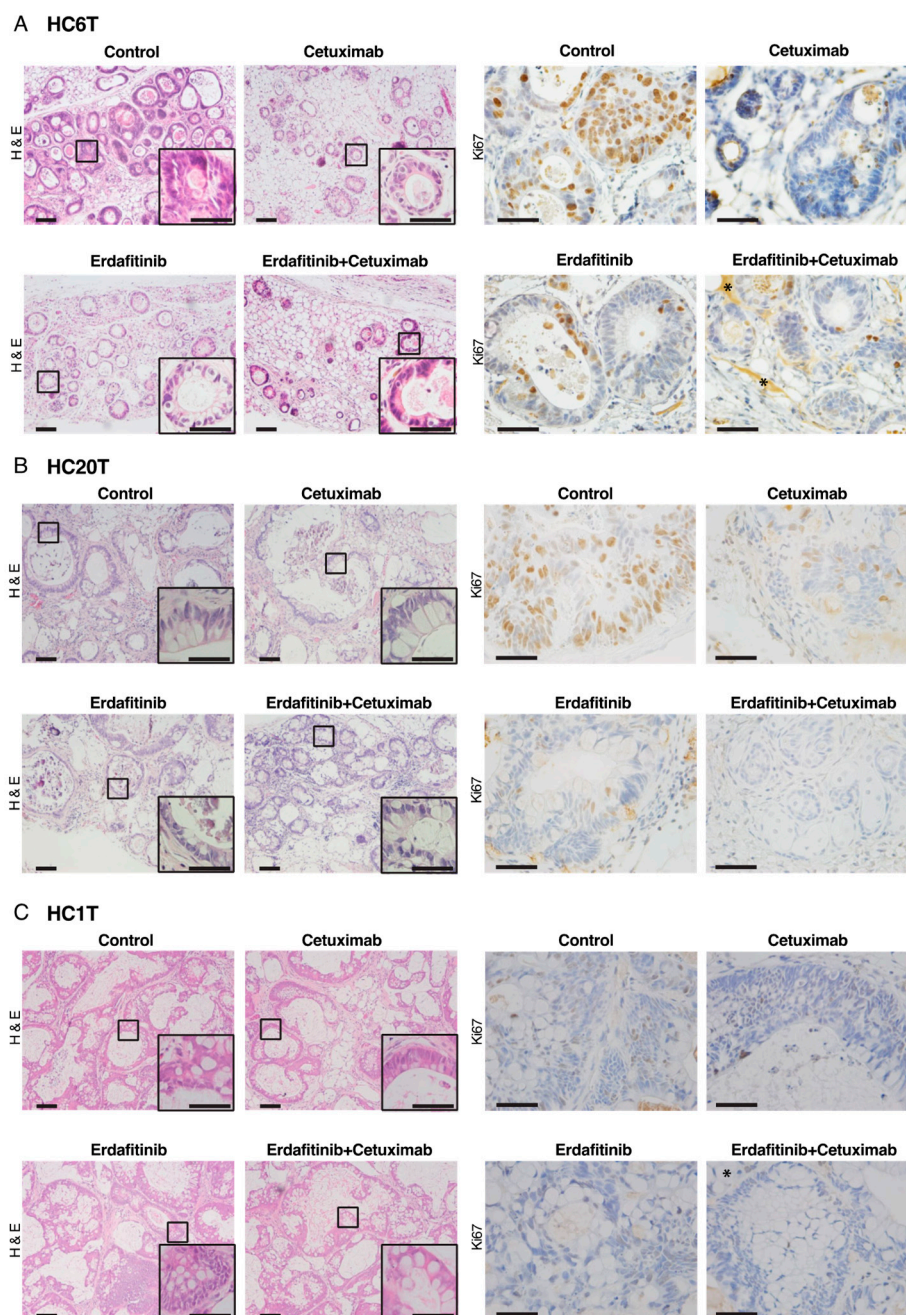


**Figure S1.** Effects of erlotinib (A. left) or cetuximab (A. right) on the growth of three colon cancer spheroid lines, HC6T, HC9T, and HC20T. Dose-dependent growth inhibition was observed by erlotinib but not by cetuximab on all three spheroid lines in vitro likely because of its poor permeability to the culture medium that contained Matrigel. GEI ~0.7, efficacy threshold, dashed lines; clinical doses,  $10^{-6}$  M in erlotinib and ~80  $\mu\text{g}/\text{mL}$  in cetuximab, dotted lines. Effects of erdafitinib (0.1  $\mu\text{M}$ ), erlotinib (1  $\mu\text{M}$ ), or erdafitinib (0.1  $\mu\text{M}$ )/erlotinib (1  $\mu\text{M}$ ) combination on the in vitro growth of 15 RAS/RAF-wild type colorectal cancer TIC spheroid lines and two normal colorectal epithelial stem cell spheroid lines (HC6N, HC10N) (B). The mean values of four replicates are shown as bars with raw data points as dots. The cut-off value of GEI that classifies spheroids as “responsive” or “non-responsive” was assigned at 0.7 (broken line).



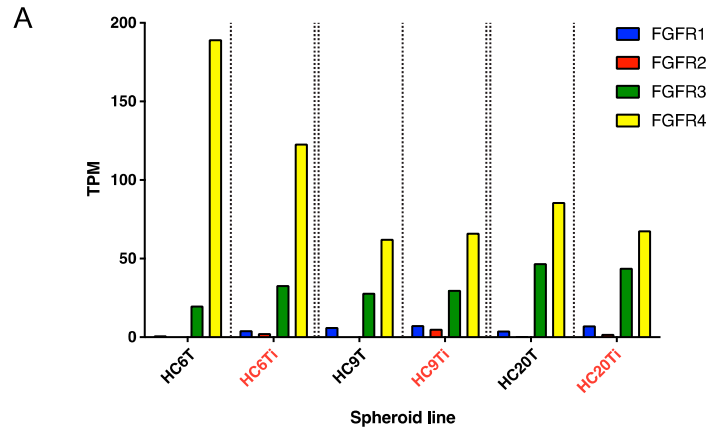
**Figure S2.** Growth of PDSX tumors derived from colorectal cancer TIC spheroid lines (top, HC6T; middle, HC20T; and bottom, HC1T) before drug treatments. Mice with xenografts of the following characteristics were excluded from the dosing tests; too small (<100 mm<sup>3</sup>), spontaneously shrinking, remaining unchanged in size for more than two weeks, or deeply implanted and difficult to be measured.



**Figure S3.** Histological specimens of xenograft tumors derived from HC6T (A), HC20T (B), and HC1T (C) spheroid lines on day 21 stained with H&E (left two columns) or immunostained for a proliferation marker, Ki67 (right two columns). Magnification bars, 100  $\mu$ m or 50  $\mu$ m (insets).

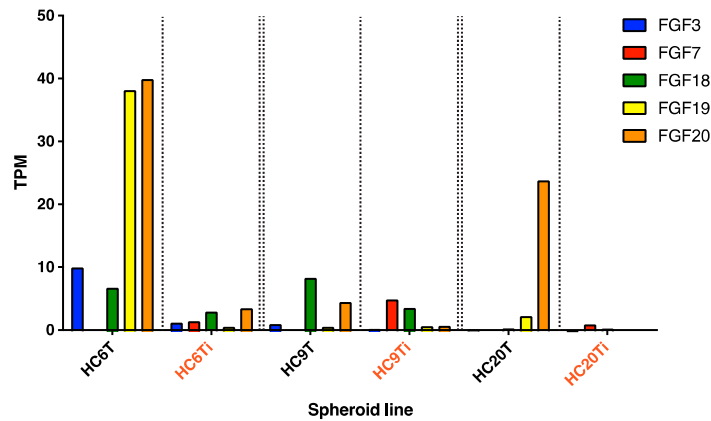
	FGF1	FGF2	FGF3	FGF4	FGF5	FGF6	FGF7	FGF8	FGF9	FGF10	FGF11	FGF12	FGF13	FGF14	FGF16	FGF17	FGF18	FGF19	FGF20	FGF21	FGF22	FGF23	Erda	Erlo	Erda/Erlo
HC6N	0.00	0.90	0.00	0.00	0.00	0.00	0.00	0.19	0.00	0.00	0.95	0.00	0.03	0.00	0.00	0.22	0.00	0.29	0.00	3.78	0.00	0.03			
HC9N	0.00	3.32	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	9.35	0.00	0.00	0.00	0.00	0.00	0.22	0.82	0.00	0.00	0.00	0.00			
HC20N	0.00	1.31	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	4.02	0.00	0.00	0.00	0.00	0.00	0.04	0.11	0.00	0.00	0.18	0.00			
HC6T	0.00	0.02	10.12	0.36	0.00	0.00	0.00	0.00	0.39	0.00	1.80	0.00	0.25	0.00	0.00	0.37	6.87	38.30	40.06	0.00	0.23	0.05	R	NR	R
HC9T	0.03	0.00	1.09	0.00	0.00	0.00	0.00	0.00	0.09	0.00	1.41	0.06	0.04	0.00	0.00	0.19	8.44	0.67	4.60	0.00	0.81	0.00	R	NR	R
HC20T	0.05	0.00	0.25	0.00	0.00	0.00	0.00	0.23	0.20	0.00	1.88	0.00	0.04	0.00	0.00	0.00	0.39	2.34	23.96	0.00	0.80	0.13	R	NR	R
HC28T	0.05	3.48	51.10	0.00	0.00	0.00	0.00	0.89	6.64	0.00	0.70	0.00	0.14	0.00	0.00	0.89	6.64	52.02	7.39	0.14	0.57	0.00	R	NR	R
HC67T	0.06	0.00	0.20	0.00	0.00	0.00	0.04	0.00	2.55	0.00	1.90	0.00	0.18	0.00	0.00	0.00	3.35	1.04	29.25	0.36	0.00	0.16	R	NR	R
HC80T	0.02	0.00	9.23	0.00	0.00	0.00	0.00	1.58	0.49	0.00	2.27	0.02	0.03	0.00	0.00	0.25	2.01	176.46	15.79	0.13	0.36	0.47	R	NR	R
HC93T	0.06	0.00	1.12	1.42	0.00	0.00	0.00	0.52	10.19	0.00	0.51	0.00	0.13	0.00	0.00	0.31	5.24	17.01	5.54	0.00	1.79	0.05	R	NR	R
HC7T	0.06	0.00	0.21	0.00	0.00	0.00	0.00	0.00	0.43	0.00	1.17	0.02	0.22	0.00	0.00	0.08	9.25	2.78	35.70	0.12	0.00	0.40	NR	R	R
HC10T	0.00	0.30	0.00	0.00	0.00	0.00	0.00	0.13	0.00	0.00	0.71	0.00	0.00	0.00	0.00	0.00	0.36	0.74	0.00	0.65	0.00	0.00	NR	R	R
HC73T	0.00	0.00	0.13	0.00	0.00	0.00	0.00	0.09	0.00	0.00	21.13	0.02	0.39	0.00	0.00	0.30	0.42	0.87	0.10	0.23	0.00	0.00	NR	R	R
HC108T	0.00	0.00	1.97	0.00	0.00	0.00	0.00	0.00	1.51	0.00	1.90	0.02	0.08	0.00	0.00	0.00	10.09	11.31	34.46	1.57	0.00	1.01	NR	R	R
HC117T	0.00	1.50	0.10	0.00	0.00	0.00	0.00	0.27	0.07	0.00	0.54	0.05	0.00	0.05	0.00	0.11	1.19	0.31	0.15	0.00	0.23	0.00	NR	R	R
HC1T	0.00	0.16	0.00	0.00	0.00	0.18	0.00	0.00	0.18	0.00	2.35	0.00	0.00	0.00	0.00	0.10	0.14	0.00	0.13	0.00	0.21	0.04	NR	NR	R
HC8T	0.00	2.24	0.00	0.00	0.00	0.00	0.00	0.88	0.25	0.00	1.01	0.09	0.04	0.05	0.00	0.10	2.30	3.41	35.60	0.00	1.09	0.09	NR	NR	R
HC11T	0.00	0.04	0.09	0.00	0.00	0.00	0.00	0.12	0.00	0.00	2.07	0.02	0.16	0.00	0.00	0.10	0.21	0.51	0.00	0.00	0.21	0.00	NR	NR	R
HC16T	0.00	0.09	0.56	0.00	0.00	0.00	0.00	0.00	0.29	0.00	0.89	0.00	0.21	0.00	0.00	0.00	1.39	2.10	0.57	0.00	0.11	0.19	NR	NR	R
HC21T	0.00	0.29	0.09	0.00	0.00	0.00	0.00	0.00	0.32	0.00	1.08	0.02	0.12	0.00	0.00	0.00	2.69	5.87	10.64	0.00	0.00	0.00	NR	NR	R
HC22T	0.06	0.02	27.24	7.73	0.03	0.00	0.00	33.85	38.32	0.00	1.73	0.55	0.16	0.00	0.00	1.05	10.76	21.14	82.64	0.00	1.67	0.00	NR	NR	R
HC74T	0.00	0.04	1.12	0.00	0.00	0.14	0.00	0.09	4.09	0.00	0.46	0.00	0.18	0.00	0.00	0.07	1.10	1.16	0.25	0.23	0.08	0.00	NR	NR	R
HC142T	0.11	1.00	0.06	0.00	0.09	0.00	0.50	0.08	0.18	0.00	1.46	0.01	0.49	0.09	0.00	0.13	13.32	1.14	27.79	0.15	0.21	0.22	NR	NR	R
HC146T	0.00	0.04	1.51	0.00	0.00	0.00	0.00	0.12	0.09	0.00	1.07	0.00	0.41	0.00	0.00	0.66	0.13	3.77	0.00	0.00	0.09	0.09	NR	NR	R
HC40T	0.00	0.04	7.28	0.00	0.00	0.00	0.00	0.00	5.21	0.00	0.95	0.00	0.28	0.00	0.00	0.09	7.07	6.84	11.08	0.00	0.56	0.00	NR	NR	NR
HC106T	0.00	0.35	1.72	0.00	0.00	0.00	0.00	0.27	5.58	0.00	1.82	0.02	0.00	0.24	0.00	0.21	7.09	49.62	2.91	0.00	0.00	0.00	NR	NR	NR
HC120T	0.00	0.00	0.27	0.00	0.00	0.00	0.00	0.12	0.18	0.00	0.57	0.02	0.00	0.00	0.00	0.00	5.74	3.45	0.20	0.00	0.43	0.00	NR	NR	NR
HC129T	0.06	0.40	0.85	0.09	0.00	0.00	0.00	0.00	0.21	0.00	3.49	0.05	0.23	0.00	0.00	0.12	2.41	2.61	2.24	0.13	0.18	0.53	NR	NR	NR
r value	-0.16	0.19	-0.20	-0.05	0.23	0.15	0.22	0.01	0.00		0.05	0.08	0.12	0.40		-0.17	0.02	-0.35	-0.18	0.04	-0.29	-0.03			

**Figure S4.** The levels of mRNA for all 22 FGF ligands in the 25 spheroid lines. The association (*r*-value) between FGFR inhibitor sensitivity (GEI) and mRNA levels (TPM) is shown at the bottom column. The background color shows the level of expression ranging from blue (for the highest) to red (for the lowest). There was a correlation of the sensitivity to erdafitinib with the mRNA level of *FGF19* (*r* = -0.35), but not with those of other *FGF* ligands. Abbreviations R and NR stand for “responsive” and “non-responsive”, respectively, to erdafitinib, erlotinib, and the erdafitinib/erlotinib combination. Note that no human *FGF15* is assigned whereas *Fgf15* is the mouse ortholog of human *FGF19*.



B

	FGF1	FGF2	FGF3	FGF4	FGF5	FGF6	FGF7	FGF8	FGF9	FGF10	FGF11	FGF12	FGF13	FGF14	FGF16	FGF17	FGF18	FGF19	FGF20	FGF21	FGF22	FGF23
HC6T	0.00	0.02	10.12	0.36	0.00	0.00	0.00	0.00	0.39	0.00	1.80	0.00	0.25	0.00	0.00	0.37	6.87	38.30	40.06	0.00	0.23	0.05
HC6Ti	0.27	0.47	1.32	0.00	0.00	0.00	1.54	0.00	0.09	0.22	2.05	0.03	2.30	0.04	0.00	0.29	3.08	0.67	3.61	0.00	0.00	0.00
HC9T	0.03	0.00	1.09	0.00	0.00	0.00	0.00	0.00	0.09	0.00	1.41	0.06	0.04	0.00	0.00	0.19	8.44	0.67	4.60	0.00	0.81	0.00
HC9Ti	0.42	2.34	0.32	0.00	0.00	0.00	5.02	0.00	0.77	0.52	1.31	0.08	1.16	0.05	0.00	0.00	3.65	0.76	0.80	0.00	0.00	1.19
HC20T	0.05	0.00	0.25	0.00	0.00	0.00	0.00	0.23	0.20	0.00	1.88	0.00	0.04	0.00	0.00	0.00	0.39	2.34	23.96	0.00	0.80	0.13
HC20Ti	0.09	0.15	0.09	0.00	0.00	0.00	1.02	0.00	0.42	0.44	0.58	0.00	0.06	0.00	0.00	0.00	0.38	0.00	0.00	0.00	0.00	0.00



**Figure S5.** The mRNA levels for *FGF* receptors (A) and the ligands (B) in frozen whole tumor tissues for HC6T, HC9T, and HC20T determined by RNA-seq analysis (in transcripts per million; TPM). Note that the *FGFR* mRNA levels were similar between the tumor tissues (HC6Ti, HC9Ti, and HC20Ti) and corresponding spheroid lines (HC6T, HC9T, and HC20T) (A), whereas the ligand mRNA levels were relatively low in all the three tested whole tissues to the corresponding spheroid lines (B).

A

FG FR 4

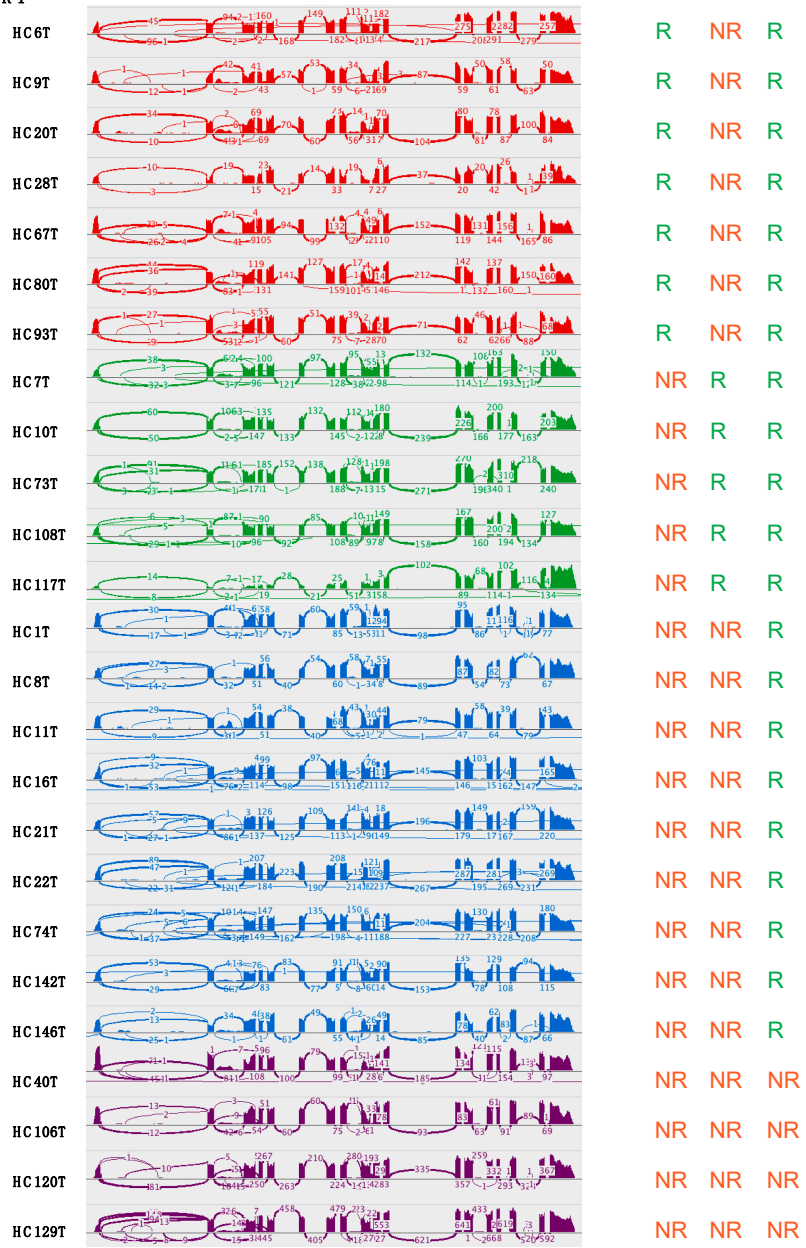
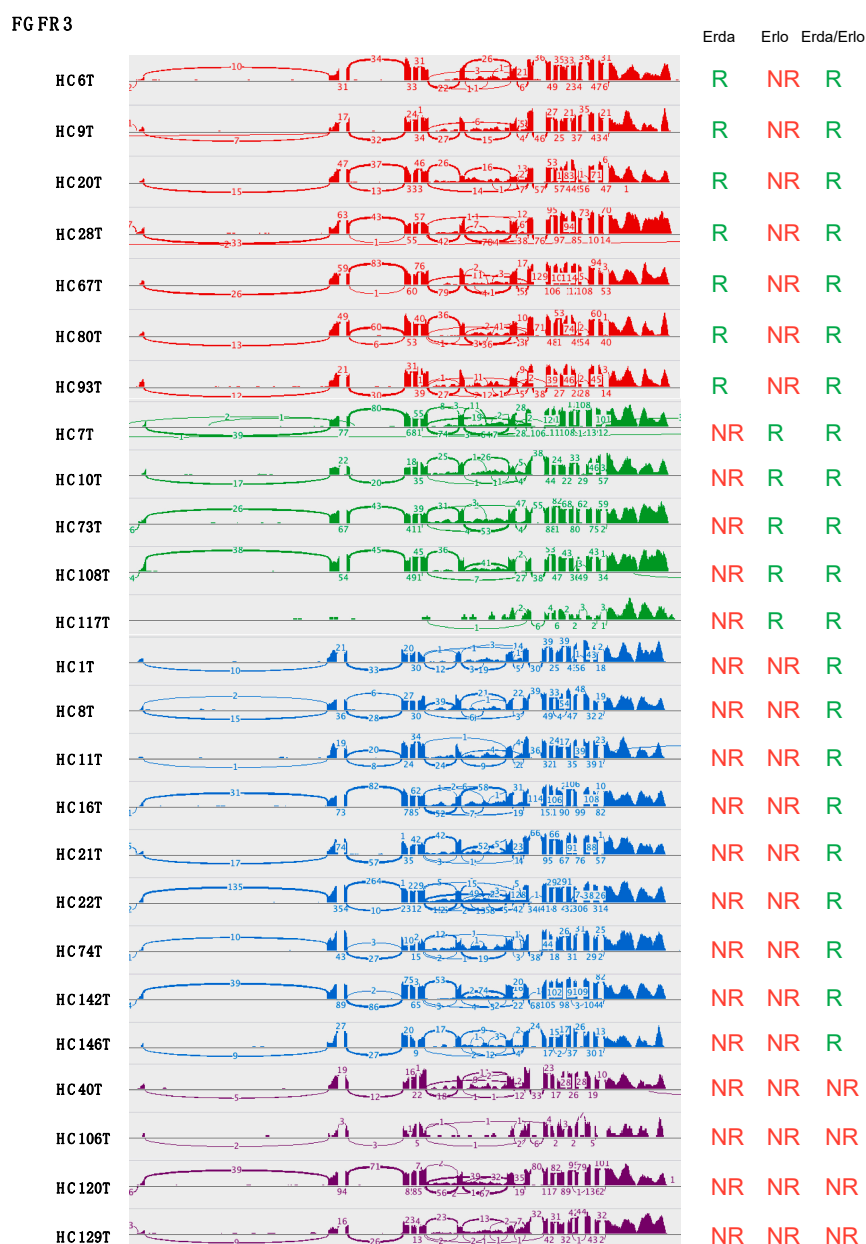


Figure 6. Cont.

**B**



**Figure S6.** (A) Sashimi plots across RNA-seq samples of *FGFR4* mRNA in all 25 colorectal cancer TIC-spheroid lines. Read densities across exons are quantified in RPKM (read per kilobase/million) and junction reads are shown as arcs, annotated with read numbers. Abbreviations R and NR stand for “responsive” and “non-responsive”, respectively, to erdafitinib, erlotinib, and the erdafitinib/erlotinib combination. (B) Sashimi plots across RNA-seq samples of *FGFR3* mRNA in all 25 colorectal cancer TIC-spheroid lines. Read densities across exons are quantified in RPKM (read per kilobase/million) and junction reads are shown as arcs, annotated with read numbers. Abbreviations R and NR stand for “responsive” and “non-responsive”, respectively, to erdafitinib, erlotinib, and the erdafitinib/erlotinib combination.

**Table S1.** Mutational status detected by targeted next-generation sequencing of 409 cancer-related genes in each spheroid sample.

Chrom	Position	Ref	Variant	Frequency	Type	Allele Name	Gene ID	AChange.refGene
<b>HC1T</b>								
chr2	5833842	C	T	54.4	SNP	---	SOX11	NM_003108:exon1:c.989C>T;p.A330V
chr3	178936091	G	A	47.8	SNP	COSM763	PIK3CA	NM_006218:exon10:c.1633G>A;p.E545K
chr5	112175513	G	T	46.3	SNP	COSM18822	APC	NM_000038:exon16:c.4222G>T;p.E1408X
chr7	50367288	C	T	44.4	SNP	---	IKZF1	NM_006060:exon3:c.95C>T;p.P32L
chr8	71037056	G	A	51.5	SNP	---	NCOA2	NM_006540:exon20:c.3961C>T;p.P1321S
chr18	48604788	A	G	100	SNP	---	SMAD4	NM_005359:exon12:c.1610A>G;p.D537G
chr22	36689877	G	T	43.4	SNP	---	MYH9	NM_002473:exon29:c.3870C>A;p.S1290R
<b>HC6T</b>								
chr5	112174920	AT	-	53.3	DEL	---	APC	NM_000038:exon16:c.3629_3630del;p.H1210fs
chr5	112175466	C	A	34.4	SNP	---	APC	NM_000038:exon16:c.4175C>A;p.S1392X
chr9	8340383	G	T	29.5	SNP	---	PTPRD	NM_130391:exon27:c.3992C>A;p.T1331N
chr17	7577121	G	A	99.9	SNP	COSM10659	TP53	NM_000546:exon8:c.817C>T;p.R273C
chrX	41031129	G	C	20.5	SNP	---	USP9X	NM_001039590:exon21:c.3066G>C;p.W1022C
<b>HC7T</b>								
chr2	5833373	G	A	50.4	SNP	---	SOX11	NM_003108:exon1:c.520G>A;p.A174T
chr4	88047313	C	T	100	SNP	---	AFF1	NM_005935:exon13:c.2615C>T;p.S872X
chr6	56483001	G	A	27.6	SNP	---	DST	NM_001723:exon23:c.5831C>T;p.A1944V
chr11	44129747	A	G	34.1	SNP	---	EXT2	NM_000401:exon2:c.584A>G;p.Q195R
chr11	118375555	G	A	69	SNP	---	MLL	NM_005933:exon27:c.8939G>A;p.G2980E
chr17	7577498	C	T	100	SNP	COSM43571	TP53	Splicing
chr17	12032474	C	T	100	SNP	---	MAP2K4	NM_003010:exon9:c.910C>T;p.R304X
chr17	29483091	T	-	33.5	DEL	---	NF1	NM_000267:exon2:c.151delT;p.F51fs
chr19	1615470	G	A	35.6	SNP	---	TCF3	NM_003200:exon18:c.1636C>T;p.R546W
chrX	63411291	G	A	52.9	SNP	---	FAM123B	NM_152424:exon2:c.1876C>T;p.R626X
<b>HC9T</b>								
chr3	10191645	A	G	67.3	SNP	---	VHL	NM_000551:exon3:c.638A>G;p.D213G
chr5	112164664	A	-	100	DEL	---	APC	NM_000038:exon14:c.1742delA;p.K581fs
chr17	7578247	-	A	100	INS	---	TP53	NM_000546:exon6:c.601dupT;p.L201fs
chr17	7579714	C	T	100	SNP	---	TP53	NM_000546:exon3:c.82G>A;p.E28K
<b>HC10T</b>								
chr3	37860464	T	C	49.3	SNP	---	ITGA9	NM_002207:exon28:c.3092T>C;p.V1031A
chr3	70014040	C	G	51	SNP	---	MITF	NM_000248:exon9:c.901C>G;p.P301A
chr3	89391088	G	A	48.5	SNP	---	EPHA3	NM_005233:exon5:c.1154G>A;p.R385Q
chr5	112162891	C	T	49.5	SNP	COSM29364	APC	NM_000038:exon12:c.1495C>T;p.R499X
chr5	11215639	C	T	49.2	SNP	COSM13127	APC	NM_000038:exon16:c.4348C>T;p.R1450X
chr11	106558429	A	C	51.1	SNP	---	GUCY1A2	NM_000855:exon8:c.2045T>G;p.L682R
chr12	49420286	C	A	38.8	SNP	---	MLL2	NM_003482:exon48:c.15463G>T;p.V5155F
chr16	68867358	T	C	48.6	SNP	---	CDH1	NM_004360:exon16:c.2605T>C;p.F869L
chr17	7577138	C	T	50.9	SNP	COSM43923	TP53	NM_000546:exon8:c.800G>A;p.R267Q
<b>HC11T</b>								
chr1	115053393	-	GCTGGA	45.5	INS	---	TRIM33	NM_015906:exon1:c.305_306insTCCAGC;p.A102delinsAPA
chr5	112175897	G	T	98.4	SNP	COSM19056	APC	NM_000038:exon16:c.4606G>T;p.E1536X
chr7	106509426	C	G	70.4	SNP	---	PIK3CG	NM_002649:exon2:c.1420C>G;p.L474V
chr10	96522463	A	G	49.9	SNP	---	CYP2C19	NM_000769:exon1:c.1A>G;p.M1V
chr11	95826309	C	A	52.9	SNP	---	MAML2	NM_032427:exon2:c.886G>T;p.D296Y
chr12	4398151	G	A	45.3	SNP	---	CCND2	NM_001759:exon4:c.715G>A;p.D239N
chr13	41240075	G	A	35.7	SNP	---	FOXO1	NM_002015:exon1:c.275C>T;p.A92V
chr17	5462049	G	A	100	SNP	---	NLRP1	NM_014922:exon4:c.1967C>T;p.T656M
chr17	7578398	G	-	100	DEL	COSM44659	TP53	NM_000546:exon5:c.532delC;p.H178fs
chr18	45368213	G	T	100	SNP	---	SMAD2	NM_005901:exon11:c.1389C>A;p.C463X
chrX	48650332	C	T	99.1	SNP	---	GATA1	NM_002049:exon3:c.302C>T;p.T101M
<b>HC16T</b>								
chr1	27088788	-	G	74.9	INS	---	ARID1A	NM_006015:exon7:c.2397dupG;p.Q799fs
chr4	153249384	C	T	20.6	SNP	COSM117308	FBXW7	NM_018315:exon10:c.1505C>T;p.S502L
chr4	153245446	G	A	79.2	SNP	COSM22979	FBXW7	NM_018315:exon8:c.1154G>A;p.R385H
chr5	112128191	C	T	100	SNP	COSM13130	APC	NM_000038:exon7:c.694C>T;p.R232X
chr8	145740393	G	A	79.5	SNP	---	RECQL4	NM_004260:exon9:c.1547C>T;p.A516V
chr12	49424728	C	T	35.5	SNP	---	MLL2	NM_003482:exon40:c.13619G>A;p.R4540Q
chr14	99640652	G	A	72.8	SNP	---	BCL11B	NM_022898:exon3:c.2308C>T;p.R770C
chr17	7577082	C	T	98.7	SNP	COSM99924	TP53	NM_000546:exon8:c.856G>A;p.E286K
<b>HC20T</b>								
chr6	51751973	G	A	50.3	SNP	---	PKHD1	NM_138694:exon44:c.7067C>T;p.P2356L
chr8	113569067	G	C	21.8	SNP	---	CSMD3	NM_052900:exon24:c.3847C>G;p.L1283V
chr8	113569114	T	C	31.2	SNP	---	CSMD3	NM_052900:exon24:c.3800A>G;p.H1267R
chr10	114920414	G	A	50.4	SNP	---	TCF7L2	NM_001146274:exon13:c.1355G>A;p.G452E
chr16	2124279	A	T	20.1	SNP	---	TSC2	NM_000548:exon22:c.2434A>T;p.S812C
chr17	7579389	G	A	100	SNP	---	TP53	NM_000546:exon4:c.298C>T;p.Q100X
chr18	48593504	G	T	100	SNP	---	SMAD4	NM_005359:exon10:c.1255G>T;p.G419W
<b>HC21T</b>								
chr4	153251894	T	C	52.6	SNP	---	FBXW7	NM_018315:exon6:c.872A>G;p.K291R
chr5	112175068	A	-	72.3	DEL	---	APC	NM_000038:exon16:c.3777_3778del;p.L1259fs
chr7	138252340	C	A	24.8	SNP	---	TRIM24	NM_003852:exon10:c.1543C>A;p.Q515K
chr8	113317138	G	T	20	SNP	---	CSMD3	NM_198123:exon52:c.8078C>A;p.T2693K



Table S1. Cont.

chr9	135787745	G	C	55.5	SNP	---		<i>TSC1</i>	NM_000368:exon9:c.837C>G;p.H279Q
chr10	76735968	T	G	37.6	SNP	---		<i>KAT6B</i>	NM_012330:exon8:c.1873T>G;p.F625V
chr11	71715775	T	C	53.2	SNP	---		<i>NUMA1</i>	NM_006185:exon24:c.5917A>G;p.I1973V
chr17	7578275	G	A	99	SNP	COSM10733		<i>TP53</i>	NM_000546:exon6:c.574C>T;p.Q192X
<b>HC22T</b>									
chr4	106156877	A	T	96.4	SNP	---		<i>TET2</i>	NM_017628:exon3:c.1778A>T;p.Q593L
chr5	112162870	CACTACAGTATTA	-	100	DEL	---		<i>APC</i>	NM_000038:exon12:c.1474_1486del;p.H492fs
chr7	91603046	A	G	20.9	SNP	---		<i>AKAP9</i>	NM_005751:exon2:c.70A>G;p.K24E
chr17	7577548	C	T	100	SNP	COSM6932		<i>TP53</i>	NM_000546:exon7:c.733G>A;p.G245S
chr18	50848557	T	G	35.4	SNP	---		<i>DCC</i>	NM_005215:exon17:c.2525C>A;p.T842N
chr22	41553373	C	G	27.5	SNP	---		<i>EP300</i>	NM_001429:exon18:c.3462C>G;p.D1154E
<b>HC28T</b>									
chr3	71026184	C	A	51.4	SNP	---		<i>FOXP1</i>	NM_032682:exon17:c.1438G>T;p.E480X
chr3	178936082	G	A	52.2	SNP	COSM760		<i>PIK3CA</i>	NM_006218:exon10:c.1624G>A;p.E542K
chr5	112151261	C	T	100	SNP	COSM13862		<i>APC</i>	NM_000038:exon9:c.904C>T;p.R302X
chr22	24176338	C	T	54	SNP	---		<i>SMARCB1</i>	NM_003073:exon9:c.1129C>T;p.R377C
<b>HC40T</b>									
chr3	178936091	G	A	67.8	SNP	COSM125370		<i>PIK3CA</i>	NM_006218:exon10:c.1633G>A;p.E545K
chr5	112103086	AG	-	36.6	DEL	COSM25153		<i>APC</i>	NM_000038:exon4:c.417_418del;p.K139fs
chr5	112176398	G	A	60	SNP	---		<i>APC</i>	NM_000038:exon16:c.5107G>A;p.G1703R
chr5	176618907	C	T	65.6	SNP	---		<i>NSD1</i>	NM_022455:exon3:c.950C>T;p.T317M
chr7	55211097	G	A	42.5	SNP	---		<i>EGFR</i>	NM_005228:exon3:c.340G>A;p.E114K
chr10	70332760	G	T	48.4	SNP	---		<i>TET1</i>	NM_030625:exon2:c.665G>T;p.R222L
chr10	90767542	A	C	50.2	SNP	---		<i>FAS</i>	NM_000043:exon3:c.282A>C;p.K94N
chr13	28964142	A	T	31.7	SNP	---		<i>FLT1</i>	NM_002019:exon13:c.1760T>A;p.V587D
chr16	2127724	G	A	44.5	SNP	---		<i>TSC2</i>	NM_000548:exon26:c.2963G>A;p.R988H
chr16	27460579	C	G	28.3	SNP	---		<i>IL21R</i>	NM_021798:exon9:c.1592C>G;p.S531W
chr17	7578406	C	T	100	SNP	COSM99914		<i>TP53</i>	NM_000546:exon5:c.524G>A;p.R175H
chrX	41029432	A	C	45.8	SNP	---		<i>USP9X</i>	NM_001039590:exon19:c.2821A>C;p.I941L
<b>HC67T</b>									
chr5	38481794	C	T	76.2	SNP	---		<i>LIFR</i>	NM_002310:exon20:c.3197G>A;p.R1066Q
chr5	112175958	-	A	100	INS	COSM18561		<i>APC</i>	NM_000038:exon16:c.4662dupA;p.E1554fs
chr6	51524309	T	C	31	SNP	---		<i>PKHD1</i>	NM_138694:exon61:c.10615A>G;p.M3539V
chr6	152599456	C	T	65.6	SNP	---		<i>SYNE1</i>	NM_033071:exon45:c.6726A>C;p.E2242D
chr10	88649927	T	A	95.6	SNP	---		<i>BMPR1A</i>	NM_004329:exon4:c.176T>A;p.L59X
chr17	78360208	A	G	100	SNP	---		<i>RNF213</i>	NM_001256071:exon62:c.14698A>G;p.K4900E
<b>HC73T</b>									
chr5	112162891	C	T	57.8	SNP	COSM29364		<i>APC</i>	NM_000038:exon12:c.1495C>T;p.R499X
chr5	112175510	AG	-	47.2	DEL	COSM19088		<i>APC</i>	NM_000038:exon16:c.4217_4218del;p.Q1406fs
chr8	113564823	C	T	99.3	SNP	---		<i>CSMD3</i>	NM_052900:exon40:c.6069delT;p.F2023fs
chr13	110436398	C	G	68.7	SNP	---		<i>IRS2</i>	NM_003749:exon1:c.2003G>C;p.G668A
chr17	7578190	T	C	100	SNP	COSM99720		<i>TP53</i>	NM_000546:exon6:c.659A>G;p.Y220C
chr17	37881392	A	T	48.9	SNP	---		<i>ERBB2</i>	NM_004448:exon21:c.2584A>T;p.T862S
<b>HC74T</b>									
chr2	30143052	G	-	48.2	DEL	---		<i>ALK</i>	NM_004304:exon1:c.475G>A;p.G159R
chr5	112116592	C	T	51.3	SNP	COSM13134		<i>APC</i>	NM_000038:exon16:c.4185delT;p.S1395fs
chr5	112175476	T	-	50.2	DEL	---		<i>APC</i>	NM_000038:exon6:c.637C>T;p.R213X
chr7	92733555	A	C	30.3	SNP	---		<i>SAMD9</i>	NM_017654:exon3:c.1856T>G;p.L619R
chr13	113975779	G	A	48.3	SNP	---		<i>LAMP1</i>	NM_005561:exon7:c.937G>A;p.A313T
chr17	7577105	G	A	97.7	SNP	COSM10863		<i>TP53</i>	NM_000546:exon8:c.833C>T;p.P278L
chr17	48263150	C	T	53.6	SNP	---		<i>COL1A1</i>	NM_000088:exon50:c.4237G>A;p.D1413N
<b>HC80T</b>									
chr1	27106006	C	-	60	DEL	---		<i>ARID1A</i>	NM_006015:exon20:c.5617delC;p.P1873fs
chr5	112102946	G	A	36.9	SNP	---		<i>APC</i>	NM_000038:exon4:c.281G>A;p.R94H
chr5	112128143	C	T	99.2	SNP	COSM98420		<i>APC</i>	NM_000038:exon7:c.646C>T;p.R216X
chr7	142568063	C	T	27.9	SNP	---		<i>EPHB6</i>	NM_004445:exon15:c.2704C>T;p.R902C
chr12	43925980	G	A	47	SNP	---		<i>ADAMTS20</i>	NM_025003:exon3:c.472C>T;p.Q158X
chr12	56482415	G	C	27.6	SNP	---		<i>ERBB3</i>	NM_001982:exon8:c.963G>C;p.E321D
chr17	7577124	C	T	100	SNP	COSM10891		<i>TP53</i>	NM_000546:exon8:c.814G>A;p.V272M
<b>HC93T</b>									
chr1	27088705	T	-	25	DEL	---		<i>ARID1A</i>	NM_006015:exon7:c.2314delT;p.S772fs
chr3	52713613	AA	-	59.5	DEL	---		<i>PBRM1</i>	NM_018313:exon2:c.114_115del;p.L38fs
chr6	152642901	T	C	63.6	SNP	---		<i>SYNE1</i>	NM_033071:exon54:c.8395C>T;p.R2799C
chr17	7578406	C	T	100	SNP	COSM10648		<i>TP53</i>	NM_000546:exon5:c.524G>A;p.R175H
<b>HC108T</b>									
chr2	141356273	G	T	45.5	SNP	---		<i>LRP1B</i>	NM_018557:exon43:c.7121C>A;p.A2374E
chr3	142241655	T	C	69.6	SNP	---		<i>ATR</i>	NM_001184:exon23:c.4181A>G;p.Y1394C
chr5	112162891	C	T	67.7	SNP	COSM29364		<i>APC</i>	NM_000038:exon12:c.1495C>T;p.R499X
chr5	112175482	-	GAGTCGT	32.2	INS	---		<i>APC</i>	NM_000038:exon16:c.4190_4191insGAGTCGT;p.E1397fs
chr17	7578406	C	T	100	SNP	COSM10648		<i>TP53</i>	NM_000546:exon5:c.524G>A;p.R175H
<b>HC117T</b>									
chr5	112164586	C	T	40.4	SNP	COSM19040		<i>APC</i>	NM_000038:exon14:c.1660C>T;p.R554X
chr5	112175136	C	G	44.6	SNP	---		<i>APC</i>	NM_000038:exon16:c.3845C>G;p.S1282X
chr6	31133815	T	C	46.5	SNP	---		<i>POU5F1</i>	NM_002701:exon2:c.415A>G;p.I139V
chr8	42176918	G	A	23.1	SNP	---		<i>IKBK</i>	NM_001556:exon14:c.1495G>A;p.E499K

Table S1. Cont.

chr11	44129720 T	C	53.2 SNP	---		<i>EXT2</i>	NM_000401:exon2:c.557T>C;p.F186S
chr17	7577121 G	A	97.6 SNP	COSM10659		<i>TP53</i>	NM_000546:exon8:c.817C>T;p.R273C
<b>HC120T</b>							
chr1	186301460 C	G	100 SNP	---		<i>TPR</i>	NM_003292:exon38:c.5471G>C;p.S1824T
chr2	29606678 C	T	25.1 SNP	---		<i>ALK</i>	NM_004304:exon5:c.1202G>A;p.R401Q
chr7	50467988 G	A	45.8 SNP	---		<i>IKZF1</i>	NM_006060:exon8:c.1223G>A;p.R408H
chr17	7578189 -	A	100 INS	---		<i>TP53</i>	NM_000546:exon6:c.660dupT;p.E221_P222delinsX
chr18	22804908 T	A	100 SNP	---		<i>ZNF521</i>	NM_015461:exon4:c.2974A>T;p.I992F
<b>HC129T</b>							
chr2	100627984 G	A	22.7 SNP	---		<i>AFF3</i>	NM_001025108:exon3:c.103C>T;p.Q35X
chr5	112175217 AAAAG	-	100 DEL	COSM18701		<i>APC</i>	NM_000038:exon16:c.3921_3925del;p.I1307fs
chr8	38271150 C	T	30.7 SNP	---		<i>FGFR1</i>	NM_015850:exon18:c.2459G>A;p.R820H
chr14	102551042 G	C	26.5 SNP	---		<i>HSP90AA1</i>	NM_005348:exon5:c.957C>G;p.D319E
chr15	40915657 A	-	24.3 DEL	---		<i>CASC5</i>	NM_144508:exon10:c.3195delA;p.R1065fs
chr17	7578406 C	T	100 SNP	COSM99022		<i>TP53</i>	NM_000546:exon5:c.524G>A;p.R175H
<b>HC142T</b>							
chr1	204403666 C	T	41.2 SNP	---		<i>PIK3C2B</i>	NM_002646:exon25:c.3587G>A;p.R1196Q
chr4	62801716 G	A	46.1 SNP	---		<i>LPHN3</i>	NM_015236:exon14:c.2168G>A;p.S723N
chr6	44219235 AA	-	50 DEL	---		<i>HSP90AB1</i>	NM_007355:exon8:c.1204_1205del;p.K402fs
chr6	152485403 G	T	43.7 SNP	---		<i>SYNE1</i>	NM_033071:exon130:c.23472C>A;p.S7824R
chr9	37002728 G	A	32.3 SNP	---		<i>PAX5</i>	NM_016734:exon5:c.521C>T;p.S174L
chr11	108188143 T	G	86.7 SNP	---		<i>ATM</i>	NM_000051:exon43:c.6242T>G;p.L2081X
<b>HC146T</b>							
chr1	27105520 G	-	47.5 DEL	---		<i>ARID1A</i>	NM_006015:exon20:c.5131delG;p.G1711fs
chr1	186645619 G	A	46.4 SNP	---		<i>PTGS2</i>	NM_000963:exon7:c.950C>T;p.T317I
chr7	13971180 A	G	48.7 SNP	---		<i>ETV1</i>	NM_004956:exon9:c.749T>C;p.F250S
chr17	7578555 C	T	100 SNP	---		<i>TP53</i>	Splicing

**Table S2.** List of 409 cancer-related genes investigated in the present study.

ABL1	CBL	EP300	GATA2	LAMP1	MYD88	PKHD1	SMARCA4	WHSC1
ABL2	CCND1	EP400	GATA3	LCK	MYH11	PLAG1	SMARCB1	WRN
ACVR2A	CCND2	EPHA3	GDNF	LIFR	MYH9	PLCG1	SMO	WT1
ADAMTS20	CCNE1	EPHA7	GNA11	LPHN3	NBN	PLEKHG5	SMUG1	XPA
AFF1	CD79A	EPHB1	GNAQ	POT1	NCOA1	PML	SOC3	XPC
AFF3	CD79B	EPHB4	GNAS	LPP	NCOA2	PMS1	SOX11	XPO1
AKAP9	CDC73	EPHB6	GPR124	LRP1B	NCOA4	PMS2	SOX2	XRCC2
AKT1	CDH1	ERBB2	GRM8	LTF	NF1	POU5F1	SRC	ZNF384
AKT2	CDH11	ERBB3	GUCY1A2	LTK	NF2	PPARG	SSX1	ZNF521
AKT3	CDH2	ERBB4	HCAR1	MAF	NFE2L2	PPP2R1A	STK11	
ALK	CDH20	ERCC1	HIF1A	MAFB	NFKB1	PRDM1	STK36	
APC	CDH5	ERCC2	HLF	MAGEA1	NFKB2	PRKAR1A	SUFU	
AR	CDK12	ERCC3	HNF1A	MAG1	NIN	PRKDC	SYK	
ARID1A	CDK4	ERCC4	HOOK3	MALT1	NKX2-1	PSIP1	SYNE1	
ARID2	CDK6	ERCC5	HRAS	MAML2	NLRP1	PTCH1	TAF1	
ARNT	CDK8	ERG	HSP90AA1	MAP2K1	NOTCH1	PTEN	TAF1L	
ASXL1	CDKN2A	ESR1	HSP90AB1	MAP2K2	NOTCH2	PTGS2	TAL1	
ATF1	CDKN2B	ETS1	ICK	MAP2K4	NOTCH4	PTPN11	TBX22	
ATM	CDKN2C	ETV1	IDH1	MAP3K7	NPM1	PTPRD	TCF12	
ATR	CEBPA	ETV4	IDH2	MAPK1	NRAS	PTPRT	TCF3	
ATRX	CHEK1	EXT1	IGF1R	MAPK8	NSD1	RAD50	TCF7L1	
AURKA	CHEK2	EXT2	IGF2	MARK1	NTRK1	RAF1	TCF7L2	
AURKB	CIC	EZH2	IGF2R	MARK4	NTRK3	RALGDS	TCL1A	
AURKC	CKS1B	FAM123B	IKBK	MBD1	NUMA1	RARA	TET1	
AXL	CMPK1	FANCA	IKBKE	MCL1	NUP214	RB1	TET2	
BAI3	COL1A1	FANCC	IKZF1	MDM2	NUP98	RECQL4	TFE3	
BAP1	CRBN	FANCD2	IL2	MDM4	PAK3	REL	TGFBF2	
BCL10	CREB1	FANCF	IL21R	MEN1	PALB2	RET	TGM7	
BCL11A	CREBBP	FANCG	IL6ST	MET	PARP1	RHOH	THBS1	
BCL11B	CRKL	FAS	IL7R	MITF	PAX3	RNASEL	TIMP3	
BCL2	CRTC1	FBXW7	ING4	MLH1	PAX5	RNF2	TLR4	
BCL2L1	CSF1R	FGFR1	IRF4	MLL	PAX7	RNF213	TLX1	
BCL2L2	CSMD3	FGFR2	IRS2	MLL2	PAX8	ROS1	TNFAIP3	
BCL3	CTNNA1	FGFR3	ITGA10	MLL3	PBRM1	RPS6KA2	TNFRSF14	
BCL6	CTNNB1	FGFR4	ITGA9	MLLT10	PBX1	RRM1	TNK2	
BCL9	CYLD	FH	ITGB2	MMP2	PDE4DIP	RUNX1	TOP1	
BCR	CYP2C19	FLCN	ITGB3	MN1	PDGFB	RUNX1T1	TP53	
BIRC2	CYP2D6	FLI1	JAK1	MPL	PDGFRA	SAMD9	TPR	
BIRC3	DAXX	FLT1	JAK2	MRE11A	PDGFRB	SBDS	TRIM24	
BIRC5	DCC	FLT3	JAK3	MSH2	PER1	SDHA	TRIM33	
BLM	DDB2	FLT4	JUN	MSH6	PGAP3	SDHB	TRIP11	
BLNK	DDIT3	FN1	KAT6A	MTOR	PHOX2B	SDHC	TRRAP	
BMPR1A	DDR2	FOXL2	KAT6B	MTR	PIK3C2B	SDHD	TSC1	
BRAF	DEK	FOXO1	KDM5C	MTRR	PIK3CA	SEPT9	TSC2	
BRD3	DICER1	FOXO3	KDM6A	MUC1	PIK3CB	SETD2	TSHR	
BRIP1	DNMT3A	FOXP1	KDR	MUTYH	PIK3CD	SF3B1	UBR5	
BTK	DPYD	FOXP4	KEAP1	MYB	PIK3CG	SGK1	UGT1A1	
BUB1B	DST	FZR1	KIT	MYC	PIK3R1	SH2D1A	USP9X	
CARD11	EGFR	G6PD	KLF6	MYCL1	PIK3R2	SMAD2	VHL	
CASC5	EML4	GATA1	KRAS	MYCN	PIM1	SMAD4	WAS	

