

Supplementary Figure Legends

Figure S1. Unsupervised hierarchical clustering of the 23 HCC cell lines (horizontal axis) and phosphorylation status of the mTOR and MAPK signaling nodes (vertical axis). Red, white and blue colors indicate high, intermediate and low levels of signaling node phosphorylation. Light green and yellow represent signaling components of the MAPK pathway and mTOR pathway, respectively. Signaling components of the MAPK and mTOR pathways highly related to HCC cell line subtypes are labeled C1 and C2, respectively. Clustering revealed formation of 2 major groups, A and B, in the cell lines. The 10 cell lines that showed the highest IC50 for sorafenib are highlighted in orange.

Figure S2. Unsupervised hierarchical clustering of the 95 HCC cell lines (horizontal axis) and phosphorylation status of the mTOR and MAPK signaling nodes (vertical axis). Red, white and blue colors indicate high, intermediate and low levels of signaling node phosphorylation. Light green and yellow represent signaling components of the MAPK pathway and mTOR pathway, respectively. Signaling components related to HCC cell line subtypes are labeled C1 and C2, respectively. Clustering revealed formation of 2 major groups, A and B, in the cell lines. The 23 HCC cell lines are highlighted in purple.

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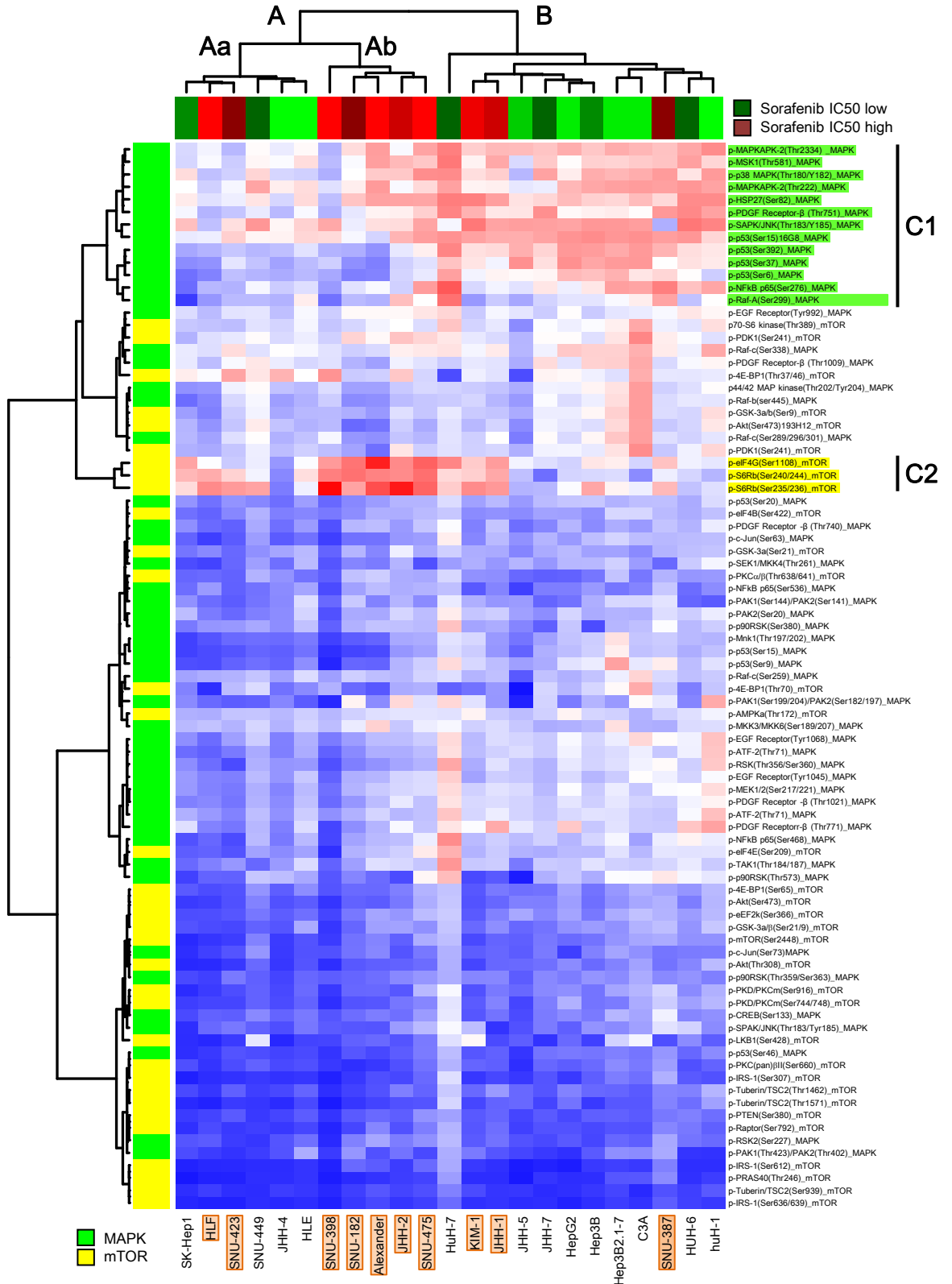
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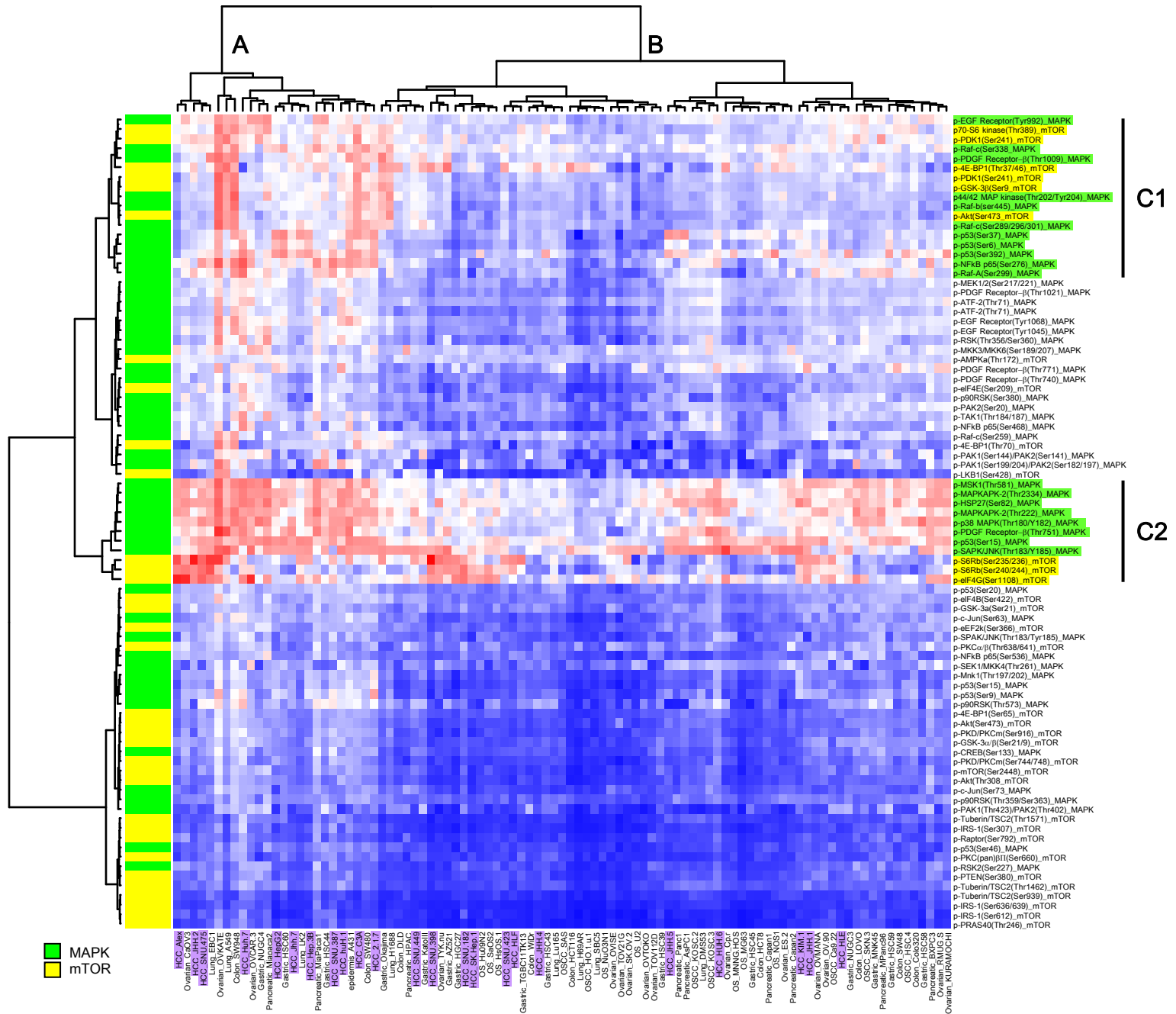
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Supplementary Figure S1.



Supplementary Figure S2.

Supplementary Table S1. List of cell lines used for RPPA construction

#	Cell line	Source	#	Cell line	Source
Hepatocellular carcinoma (HCC): 23 cell lines			Colon cancer: 9 cell lines		
1	HepG2	JCRB-HSRRB	1	DLD1	JCRB-HSRRB
2	HLE	JCRB-HSRRB	2	HCT-116	ATCC
3	huH-1	JCRB-HSRRB	3	WiDr	JCRB-HSRRB
4	HUH-6 clone 5	JCRB-HSRRB	4	SW1116	ATCC
5	HuH-7	JCRB-HSRRB	5	SW48	ATCC
6	JHH-7	JCRB-HSRRB	6	SW948	ATCC
7	HLF	JCRB-HSRRB	7	SW480	ATCC
8	C3A(HepG2/C3A)	ATCC	8	COLO-320	RBCCB
9	Hep 3B2.1-7	ATCC	9	Lovo	JCRB-HSRRB
10	JHH-1	JCRB-HSRRB	Pancreatic cancer: 9 cell lines		
11	JHH-2	JCRB-HSRRB	1	MIAPaCa-1	ATCC
12	JHH-4	JCRB-HSRRB	2	MIAPaCa-2	ATCC
13	JHH-5	JCRB-HSRRB	3	MPanc-96	ATCC
14	Alexander	ATCC	4	PANC-1	ATCC
15	Hep-3B	JCRB-HSRRB	5	AsPC-1	ATCC
16	KIM-1	JCRB-HSRRB	6	BxPC-3	ATCC
17	SK-Hep-1	ATCC	7	Capan-1	ATCC
18	SNU-182	ATCC	8	Capan-2	ATCC
19	SNU-387	ATCC	9	HPAC	ATCC
20	SNU-398	ATCC	Lung cancer: 8 cell lines		
21	SNU-423	ATCC	1	A549	JCRB-HSRRB
22	SNU-449	ATCC	2	EBC1	JCRB-HSRRB
23	SNU-475	ATCC	3	LK-2	RBCCB
Ovarian cancer: 16 cell lines			4	Lu-165	RBCCB
1	CaOV-3	ATCC	5	NCI-H1688	ATCC
2	TYK-nu	JCRB-HSRRB	6	H69AR	ATCC
3	TYK-nu.CP-r	JCRB-HSRRB	7	SBC5	JCRB-HSRRB
4	RMUG-S	JCRB-HSRRB	8	DMS53	ATCC
5	ES-2	ATCC	Osteosarcoma: 8 cell lines		
6	SK-OV-3	ATCC	1	U-2	ATCC
7	OV-90	ATCC	2	SaOS2	ATCC
8	TOV-112D	ATCC	3	NOS1	RBCCB
9	TOV-21G	ATCC	4	HuO 9N2	RBCCB
10	KURAMOCHI	JCRB-HSRRB	5	HuO-3N1	RBCCB
11	OVCAR-3	ATCC	6	MNNG/HOS	ATCC
12	OVISE	JCRB-HSRRB	7	MG-63	RBCCB
13	OVKATE	JCRB-HSRRB	8	Hs-OS-1	RBCCB
14	OVMANA	JCRB-HSRRB	Oral cancer: 7 cell lines		
15	OVSAGO	JCRB-HSRRB	1	SAS	JCRB-HSRRB
16	OVTOKO	JCRB-HSRRB	2	Ca9-22	RBCCB
Gastric cancer: 15 cell lines			3	Ho-1-u-1	JCRB-HSRRB
1	HSC-39	Suppl. Ref [1]	4	HSC-4	RBCCB
2	HSC-43	Suppl. Ref [1]	5	KOSC-2	JCRB-HSRRB
3	HSC-44	Suppl. Ref [1]	6	KOSC-3	JCRB-HSRRB
4	HSC-45	Suppl. Ref [1]	7	SKN-3	JCRB-HSRRB
5	HSC-58	Suppl. Ref [1]	Epidermoid carcinoma: 1 cell line†		
6	HSC-60	Suppl. Ref [1]	1	A431	RBCCB
7	HSC-59	Suppl. Ref [1]			
8	MKN-45	JCRB-HSRRB	Abbreviations: JCRB-HSRPB, Japanese Collection of Research		
9	Okajima	Suppl. Ref [2]	Bioresources-Human Science Research Resources Bank (Osaka,		
10	AZ521	RBCCB	Japan); ATCC, American Type Culture Collection (Manassas,		
11	Kato-III	RBCCB	VA); RBCCB, RIKEN BioResource Center Cell Bank (Tsukuba,		
12	NUGC-3	JCRB-HSRRB	Japan).		
13	NUGC-4	JCRB-HSRRB	†EGF treated A431 cells were included as a control.		
14	HGC27	RBCCB			
15	TGBC11TKB	RBCCB			

SUPPLEMENTARY REFERENCES

1. Yanagihara K, Tanaka H, Takigahira M, Ino Y, Tamaguchi Y, Toge T, et al. Establishment of two cell lines from human gastric scirrhous carcinoma that possess the potential to metastasize spontaneously in nude mice. *Cancer Sci.* 2004;95:575-582.
2. Yamada Y, Yoshida T, Hayashi K, Sekiya T, Yokota J, Hirohashi S, et.al. p53 gene mutations in gastric cancer metastases and in gastric cancer cell lines derived from metastases. *Cancer Res.* 1991 Nov 1;51(21):5800-5.

Supplementary Table S2. List of 180 phosphorylation site-specific antibodies

Supplier	Cat. #	Ab name	Pathway	Dilution	Ab type
CST	9570	p-eNOS (Ser1177) C9C3	Angiogenesis	1:1000	Ra mAb
CST	9296	p-Bad(Ser112)	Apoptosis	1:2000	Mo mAb
CST	5286	p-Bad(Ser136) 185D10	Apoptosis	1:500	Ra mAb
CST	9297	p-Bad(Ser155)	Apoptosis	1:1000	Ra pAb
CST	2827	p-Bcl-2(Ser70) 5H2	Apoptosis	1:1000	Ra mAb
CST	2875	p-Bcl-2 (Thr56) Antibody (Human Specific)	Apoptosis	1:1000	Ra pAb
CST	4585	p-Bim (Ser69) D7E11	Apoptosis	1:1000	Ra mAb
CST	3079	p-Aurora A (Thr288) C39D8	Cell cycle	1:1000	Ra mAb
CST	2914	p-Aurora A (Thr288)/Aurora B (Thr232)/Aurora C (Thr198) D13A11	Cell cycle	1:2000	Ra mAb
CST	3300	p-Cyclin D1 (Thr286) D29B3	Cell cycle	1:1000	Ra mAb
CST	9307	p-Rb (Ser780)	Cell cycle	1:1000	Ra pAb
CST	9301	p-Rb (Ser795)	Cell cycle	1:1000	Ra pAb
CST	9308	p-Rb (Ser807/811)	Cell cycle	1:1000	Ra pAb
CST	4910	p-Wee1 (Ser642) D47G5	Cell Cycle	1:1000	Ra mAb
CST	3843	p-AP2M1	Cytoskelton	1:1000	Ra pAb
CST	3313	p-Cofilin(Ser3) 77G2	Cytoskelton	1:1000	Ra mAb
CST	3149	p-Ezrin(Thr567)/Radixin(Thr564)/Moesin(thr558) 41A3	Cytoskelton	1:1000	Ra mAb
CST	3040	p-MYPT(Ser507)	Cytoskelton	1:1000	Ra pAb
CST	3048	p-MYPT(Ser668)	Cytoskelton	1:1000	Ra pAb
CST	4563	p-MYPT(Thr853)	Cytoskelton	1:1000	Ra pAb
CST	3111	p-VASP(Ser157)	Cytoskelton	1:1000	Ra pAb
CST	3114	p-VASP(Ser239)	Cytoskelton	1:1000	Ra pAb
CST	4526	p-ATM(Ser1981) 10H11.E12	DNA damage	1:1000	Mo mAb
CST	2853	p-ATR(Ser428)	DNA damage	1:1000	Ra pAb
CST	9373	P-BAP1 (Ser592)	DNA damage	1:1000	Ra pAb
CST	9009	p-BRCA1(Ser1524)	DNA damage	1:1000	Ra pAb
CST	2349	p-Chk1 (Ser296)	DNA damage	1:1000	Ra pAb
CST	2344	p-Chk1 (Ser317)	DNA damage	1:1000	Ra pAb
CST	2341	p-Chk1 (Ser345)	DNA damage	1:1000	Ra pAb
CST	2348	p-Chk1 (Ser345) 133D3	DNA damage	1:1000	Ra mAb
CST	2666	p-Chk2 (Ser19)	DNA damage	1:1000	Ra pAb
CST	2665	p-Chk2 (Ser33/35)	DNA damage	1:1000	Ra pAb
CST	2668	p-Chk2 (Thr387)	DNA damage	1:1000	Ra pAb
CST	2661	p-Chk2 (Thr68)	DNA damage	1:1000	Ra pAb
CST	9284	p-p53(Ser15)	DNA damage	1:1000	Ra pAb
CST	9286	p-p53(Ser15) 16G8	DNA damage	1:1000	Mo mAb
CST	9287	p-p53(Ser20)	DNA damage	1:2000	Ra pAb
CST	9289	p-p53(Ser37)	DNA damage	1:1000	Ra pAb
CST	9281	p-p53(Ser392)	DNA damage	1:1000	Ra pAb
CST	2521	p-p53(Ser46)	DNA damage	1:750	Ra pAb
CST	9285	p-p53(Ser6)	DNA damage	1:1000	Ra pAb
CST	9288	p-p53(Ser9)	DNA damage	1:1000	Ra pAb
CST	9461	p-FoxO1 (Ser256)	Forkhead	1:750	Ra pAb
CST	2487	p-FoxO1 (Ser319)/FoxO4(Ser262)	Forkhead	1:1000	Ra pAb
CST	9464	p-FoxO1 (Thr24)/FoxO3a (Thr32)	Forkhead	1:750	Ra pAb
CST	2599	p-FoxO1 (Thr24)/FoxO3a (Thr32)/FoxO4 (Thr28) 4G6	Forkhead	1:1000	Ra mAb
CST	9466	p-FoxO3a (Ser253)	Forkhead	1:1000	Ra pAb
CST	9465	p-FoxO3a (Ser318/321)	Forkhead	1:750	Ra pAb
CST	3661	p-Acetyl-CoA carboxylase(Ser79)	Glucose metabolism	1:1000	Ra pAb
CST	2535	p-AMPKa(Thr172)	Glucose metabolism	1:1000	Ra pAb
CST	4181	p-AMPKb(Ser108)	Glucose metabolism	1:1000	Ra pAb
CST	3482	p-LKB1 (Ser428) C67A3	Glucose metabolism	1:1000	Ra mAb
CST	2381	p-IRS-1(Ser307)	Glucose metabolism	1:1000	Ra pAb
CST	3203	p-IRS-1(Ser612) C15H5	Glucose metabolism	1:1000	Ra mAb
CST	2388	p-IRS-1(Ser636/639)	Glucose metabolism	1:1000	Ra pAb

CST	3827	p-PKM2 (Tyr105)	Glucose metabolism	1:1000	Ra pAb
CST	3776	p-Jak2 (Tyr1007/1008) C80C3	JAK/STAT	1:1000	Ra mAb
CST	9171	p-Stat 1(Y701)	JAK/STAT	1:1000	Ra pAb
CST	4441	p-Stat 2(Y690)	JAK/STAT	1:1000	Ra pAb
CST	9134	p-Stat 3(Ser727)	JAK/STAT	1:1000	Ra pAb
CST	9145	p-Stat 3(Y705) D3A7	JAK/STAT	1:3000	Ra mAb
CST	9359	p-Stat 5(Y694) C11C5	JAK/STAT	1:1000	Ra mAb
CST	9361	p-Stat 6(Y641)	JAK/STAT	1:1000	Ra pAb
CST	9321	p-Tyk2 (Tyr1054/1055)	JAK/STAT	1:1000	Ra pAb
CST	2577	p-Histone H2A.X(Ser139)	Mitosis marker	1:1000	Ra pAb
CST	9701	p-Histone H3(Ser10)	Mitosis marker	1:1000	Ra pAb
CST	9713	p-Histone H3(Ser28)	Mitosis marker	1:1000	Ra pAb
CST	9764	p-Histone H3(Thr11)	Mitosis marker	1:1000	Ra pAb
CST	9714	p-Histone H3(Thr3)	Mitosis marker	1:1000	Ra pAb
CST	2681	p-IKK α (Ser180)/IKK β (Ser181)	NFkB	1:1000	Ra pAb
CST	9246	p-I κ B- α (Ser32/36) 5A5	NFkB	1:1000	Mo mAb
CST	3037	p-NFkB p65(Ser276)	NFkB	1:1000	Ra pAb
CST	3039	p-NFkB p65(Ser468)	NFkB	1:1000	Ra pAb
CST	3033	p-NFkB p65(Ser536)93H1	NFkB	1:1000	Ra mAb
CST	5112	p-ATF-2(Thr71)11G2	p38 MAPK	1:1000	Ra mAb
CST	2401	p-HSP27(Ser82)	p38 MAPK	1:1000	Ra pAb
CST	3316	p-MAPKAPK-2(Thr222) 9A7	p38 MAPK	1:1000	Ra mAb
CST	3007	p-MAPKAPK-2(Thr2334)27B7	p38 MAPK	1:1000	Ra mAb
CST	9236	p-MKK3/MKK6(Ser189/207) 22A8	p38 MAPK	1:1000	Ra mAb
CST	9595	p-MSK1(Thr581)	p38 MAPK	1:1000	Ra pAb
CST	4511	p-p38 MAPK(Thr180/Y182) D3F9	p38 MAPK	1:1000	Ra mAb
CST	9371	p-PKC(pan) β II (Ser660)	Phospholipase	1:1000	Ra pAb
CST	9375	p-PKC α / β (Thr638/641)	Phospholipase	1:1000	Ra pAb
CST	9374	p-PKC Δ (Thr505)	Phospholipase	1:1000	Ra pAb
CST	9376	p-PKC Δ / θ (Ser643/676)	Phospholipase	1:750	Ra pAb
CST	9378	p-PKCZ/ λ (Thr410/403)	Phospholipase	1:750	Ra pAb
CST	9377	p-PKC θ (Thr538)	Phospholipase	1:750	Ra pAb
CST	3871	p-PLCg(Y1217)	Phospholipase	1:1000	Ra pAb
CST	3874	p-PLCg(Y759)	Phospholipase	1:1000	Ra pAb
CST	2821	p-PLCg(Y783)	Phospholipase	1:1000	Ra pAb
CST	4923	Non-p-4E-BP1(Thr46) 87D12	PI3K-AKT-mTOR	1:1000	Ra mAb
CST	9451	p-4E-BP1 (Ser65)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	2855	p-4E-BP1 (Thr37/46)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	9455	p-4E-BP1 (Thr70)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	9234	p70-S6 kinase(Thr389)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	4058	Phospho-Akt (Ser473) 193H12	PI3K-AKT-mTOR	1:2000	Ra mAb
CST	2965	p-Akt(Thr308)C31E5	PI3K-AKT-mTOR	1:1000	Ra mAb
CST	3691	p-eEF2k(Ser366)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	3591	p-eIF4B(Ser422)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	9741	p-eIF4E(Ser209)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	2441	p-eIF4G(Ser1108)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	9316	p-GSK-3 α (Ser21)36E9	PI3K-AKT-mTOR	1:1000	Ra mAb
CST	9327	p-GSK-3 α / β (Ser21/9)37F11 (GSK-3 α preferred)	PI3K-AKT-mTOR	1:1000	Ra mAb
CST	9323	p-GSK-3 β (Ser9)5B3	PI3K-AKT-mTOR	1:1000	Ra mAb
CST	2971	p-mTOR(Ser2448)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	3061	p-PDK1(Ser241)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	2054	p-PKD/PKCm(Ser744/748)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	2051	p-PKD/PKCm(Ser916)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	2997	p-PRAS40(Thr246) C77D7	PI3K-AKT-mTOR	1:1000	Ra mAb
CST	9551	p-PTEN(Ser380)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	2083	p-Raptor(Ser792)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	3556	p-RSK2 (Ser227) D53A11	PI3K-AKT-mTOR	1:1000	Ra mAb
CST	4858	p-S6Rb(Ser235/236) D57.2.2e	PI3K-AKT-mTOR	1:2000	Ra mAb
CST	4838	p-S6Rb(Ser240/244)	PI3K-AKT-mTOR	1:1000	Ra pAb

CST	3615	p-Tuberin/TSC2 (Ser939)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	3617	p-Tuberin/TSC2 (Thr1462) 5B12	PI3K-AKT-mTOR	1:1000	Ra mAb
CST	3614	p-Tuberin/TSC2 (Thr1571)	PI3K-AKT-mTOR	1:1000	Ra pAb
CST	9101	p44/42 MAP kinase(Thr202/Tyr204)	Ras-Raf	1:1000	Ra pAb
CST	9198	p-CREB (Ser133) 87G3	Ras-Raf	1:1000	Ra mAb
CST	9154	p-MEK1/2 (Ser217/221) 41G9	Ras-Raf	1:1000	Ra mAb
CST	2111	p-Mnk1 (Thr197/202)	Ras-Raf	1:1000	Ra pAb
CST	9335	p-p90RSK(Ser380) 9D9	Ras-Raf	1:1000	Ra mAb
CST	9344	p-p90RSK(Thr359/Ser363)	Ras-Raf	1:1000	Ra pAb
CST	9346	p-p90RSK(Thr573)	Ras-Raf	1:1000	Ra pAb
CST	2606	p-PAK1(Ser144)/PAK2(Ser141)	Ras-Raf	1:1000	Ra pAb
CST	2605	p-PAK1(Ser199/204)/PAK2(Ser182/197)	Ras-Raf	1:1000	Ra pAb
CST	2601	p-PAK1(Thr423)/PAK2(Thr402)	Ras-Raf	1:1000	Ra pAb
CST	2607	p-PAK2(Ser20)	Ras-Raf	1:1000	Ra pAb
CST	4431	p-Raf-A (Ser299)	Ras-Raf	1:1000	Ra pAb
CST	2696	p-Raf-b(ser445)	Ras-Raf	1:1000	Ra pAb
CST	9421	p-Raf-c (Ser259)	Ras-Raf	1:1000	Ra pAb
CST	9431	p-Raf-c(Ser289/296/301)	Ras-Raf	1:1000	Ra pAb
CST	9427	p-Raf-c(Ser338)56A6	Ras-Raf	1:1000	Ra mAb
CST	9348	p-RSK(Thr356/Ser360)	Ras-Raf	1:1001	Ra pAb
CST	2102	Non-p-Src(Y416)7G9	RTK/TK	1:1000	Mo mAb
CST	2107	Non-p-Src(Y527)	RTK/TK	1:1000	Ra pAb
CST	3714	pALK (Tyr1282/1283)	RTK/TK	1:1000	Ra pAb
CST	3073	p-c-Kit(Y703)D12E12	RTK/TK	1:1000	Ra mAb
CST	2237	p-EGF Receptor (Tyr1045)	RTK/TK	1:1000	Ra pAb
CST	3777	p-EGF Receptor (Tyr1068) D7A5	RTK/TK	1:1000	Ra mAb
CST	2235	p-EGF Receptor (Tyr992)	RTK/TK	1:1000	Ra pAb
CST	3474	p-FLT3(Y591) 33G6	RTK/TK	1:1000	Ra mAb
CST	3233	p-Gab1 (Tyr627) C32H2	RTK/TK	1:1000	Ra mAb
CST	3882	p-Gab2 (Tyr452) C33G1	RTK/TK	1:1000	Ra mAb
CST	2243	p-HER2/ErbB2 (Tyr1221/1222) 6B12	RTK/TK	1:1000	Ra mAb
CST	2247	p-HER2/ErbB2 (Tyr1248)	RTK/TK	1:1000	Ra pAb
CST	3790	p-HER4/ErbB4 (Tyr984)	RTK/TK	1:1000	Ra pAb
CST	3021	p-IGF-I Receptor (Tyr1131)/Insulin Receptor (Tyr1146)	RTK/TK	1:1000	Ra pAb
CST	3024	p-IGF-I Receptor (Tyr1135/1136)	RTK/TK	1:1000	Ra pAb
CST	4568	p-IGF-I Receptor (Tyr980)	RTK/TK	1:1000	Ra pAb
CST	3077	p-Met(Thr1234/1235) D26	RTK/TK	1:1000	Ra mAb
CST	3124	p-PDGF Receptor-β(Thr1009) 42F9	RTK/TK	1:1000	Ra mAb
CST	2227	p-PDGF Receptor-β(Thr1021) 6F10	RTK/TK	1:1000	Ra mAb
CST	3168	p-PDGF Receptor-β(Thr740) 32A9	RTK/TK	1:1000	Ra mAb
CST	4549	p-PDGF Receptor-β(Thr751) C63G6	RTK/TK	1:1000	Ra mAb
CST	3173	p-PDGF Receptor-β(Thr771)	RTK/TK	1:1000	Ra mAb
CST	3221	p-Ret (Tyr905)	RTK/TK	1:1000	Ra pAb
Upstate	209	p-SHC(Y239)	RTK/TK	1:1000	Ra pAb
Upstate	206	p-SHC(Y317)	RTK/TK	1:1000	Ra pAb
CST	2007	p-SHIP2(Tyr1135)	RTK/TK	1:1000	Ra pAb
CST	2101	p-Src Family (Y416)	RTK/TK	1:1000	Ra pAb
CST	2105	p-Src(Y527)	RTK/TK	1:1000	Ra pAb
CST	2715	p-Syk (Tyr323)	RTK/TK	1:1000	Ra pAb
CST	2711	p-Syk (Tyr525/526)	RTK/TK	1:1000	Ra pAb
CST	3817	p-VEGF Receptor 2 (Tyr1059) D5A6	RTK/TK	1:1000	Ra mAb
CST	3770	p-VEGF Receptor 2 (Tyr1175) D5B11	RTK/TK	1:1000	Ra mAb
CST	4991	p-VEGF Receptor 2 (Tyr951) 15D2	RTK/TK	1:1000	Ra mAb
CST	2701	p-Zap-70 (Tyr319)/Syk (Tyr352)	RTK/TK	1:1000	Ra pAb
CST	9221	p-ATF-2(Thr71)	SAPK/JNK	1:1000	Ra pAb
CST	9261	p-c-Jun (Ser63) II	SAPK/JNK	1:1000	Ra pAb
CST	3270	p-c-Jun (Ser73) D47G9	SAPK/JNK	1:1000	Ra mAb
CST	4671	p-SAPK/JNK(Thr183/Y185) 98F2	SAPK/JNK	1:1000	Ra mAb
CST	9151	p-SEK1/MKK4(Thr261)	SAPK/JNK	1:1000	Ra pAb

CST	4668	p-SPAK/JNK(Thr183/Tyr185) 81E11	SAPK/JNK	1:1000	Ra mAb
CST	9516	p-Smad1/5(Ser463/465) 41D10	TGF- β	1:1000	Ra mAb
CST	3108	p-Smad2(Ser465/467) 138D4	TGF- β	1:1000	Ra mAb
CST	4508	p-TAK1 (Thr184/187) 90C7	TGF- β	1:1000	Ra mAb
CST	2568	p-LRP6 (Ser1490)	Wnt	1:1000	Ra pAb
CST	9561	p- β -catenin(Ser33/37/Thr41)	Wnt	1:750	Ra pAb
CST	9564	p- β -catenin(Ser45)	Wnt	1:1000	Ra pAb
Sigma	T6557	γ -Tublin	For normalization	1:2000	Mo mAb

Abbreviations: CST, Cell Signaling Technology, Inc. (Danvers, MA); Upstate, Upstate Biotechnology, Inc. (Lake Placid, NY); Sigma, Sigma-Aldrich, Co. (St. Louis, MO); RTK/TK, Rreceptor tyrosine kinase/tyrosine kinase; Mo, mouse; Ra, rabbit; mAb, monoclonal antibody; pAb, polyconal antibody.

Supplementary Table S3.

Correlation between sensitivity to sorafenib and the phosphorylation of 180 signaling nodes

Rank	Antibody	Spearman CC	<i>P</i> value	Rank	Antibody	Spearman CC	<i>P</i> value
1	p-S6Rb(Ser235/236) D57.2.2e	0.5791	0.0044	60	p-p53(Ser46)	-0.0504	0.8196
2	p-S6Rb(Ser240/244)	0.5524	0.0070	61	p-Ret (Tyr905)	-0.0534	0.8091
3	p-RSK2 (Ser227) D53A11	0.3370	0.1156	62	p-Stat 1(Y701)	-0.0613	0.7812
4	p-eIF4G(Ser1108)	0.3320	0.1213	63	p-MSK1(Thr581)	-0.0632	0.7742
5	p-NFkB p65(Ser536) 93H1	0.3281	0.1260	64	p-Raf-c (Ser259)	-0.0642	0.7708
6	p-IRS-1(Ser612) C15H5	0.3093	0.1502	65	p-β-catenin(Ser33/37/Thr41)	-0.0692	0.7535
7	p-c-Kit(Y703) D12E12	0.2688	0.2133	66	p-ATR(Ser428)	-0.0702	0.7501
8	p-Chk1 (Ser317)	0.2609	0.2274	67	p-Smad2(Ser465/467) 138D4	-0.0731	0.7398
9	p-Tuberin/TSC2 (Ser939)	0.2470	0.2537	68	p-Tuberin/TSC2 (Thr1571)	-0.0800	0.7160
10	p-Bad(Ser136)185D10	0.2322	0.2839	69	p-Rb (Ser807/811)	-0.0860	0.6958
11	p-90RSK(Ser380) 9D9	0.2292	0.2902	70	p-PRAS40(Thr246) C77D7	-0.0870	0.6925
12	p-Bim (Ser69) D7E11	0.2233	0.3031	71	P-BAP1 (Ser592)	-0.0968	0.6593
13	p-PAK1(Thr423)/PAK2(Thr402)	0.2134	0.3254	72	p-Met(Thr1234/1235) D26	-0.1077	0.6236
14	Non-p-Src(Y527)	0.1937	0.3730	73	p-Stat 5(Y694) C11C5	-0.1087	0.6203
15	p-Cyclin D1 (Thr286) D29B3	0.1897	0.3829	74	p-Stat 3(Ser727)	-0.1097	0.6171
16	p-Chk1 (Ser345)	0.1729	0.4270	75	p-p90RSK(Thr359/Ser363)	-0.1126	0.6076
17	p-PAK1(Ser199/204)/PAK2(Ser182/197)	0.1670	0.4432	76	p-Rb (Ser795)	-0.1166	0.5949
18	p-PKCZ/λ(Thr410/403)	0.1611	0.4597	77	p-Acetyl-CoA carboxylase(Ser79)	-0.1206	0.5824
19	p-PTEN(Ser380)	0.1512	0.4879	78	p-Bcl-2(Thr56)	-0.1245	0.5699
20	p-PAK1(Ser144)/PAK2(Ser141)	0.1344	0.5379	79	p-LRP6 (Ser1490)	-0.1255	0.5669
21	p-ATM(Ser1981) 10H11.E12	0.1324	0.5440	80	p-Bad(Ser155)	-0.1275	0.5607
22	p-PKCa/β(Thr638/641)	0.1166	0.5933	81	p-MEK1/2 (Ser217/221) 41G9	-0.1314	0.5485
23	p-HER2/ErbB2 (Tyr1221/1222) 6B12	0.1136	0.6028	82	p-MYPT(Ser668)	-0.1364	0.5334
24	p-PKCθ(Thr538)	0.1136	0.6028	83	p-Histone H3(Ser28)	-0.1374	0.5304
25	p-AMPKα(Thr172)	0.1117	0.6119	84	p-p53(Ser20)	-0.1443	0.5097
26	p-Raptor(Ser792)	0.1107	0.6123	85	p-Src(Y527)	-0.1443	0.5097
27	p-HER2/ErbB2 (Tyr1248)	0.0988	0.6511	86	p-Src Family (Y416)	-0.1443	0.5097
28	p-Chk2 (Ser19)	0.0879	0.6874	87	p-eEF2k(Ser366)	-0.1462	0.5039
29	p-eNOS (Ser1177) C9C3	0.0800	0.7143	88	p-PKD/PKCm(Ser744/748)	-0.1462	0.5039
30	p-Ezrin(Thr567)/Radixin(Thr564)/Moesin(thr558)	0.0771	0.7245	89	p-EGF Receptor (Tyr1045)	-0.1482	0.4980
31	p-FLT3(Y591) 33G6	0.0731	0.7381	90	p-Gab2 (Tyr452) C33G1	-0.1571	0.4723
32	p-Wee1 (Ser642) D47G5	0.0573	0.7933	91	p-p38 MAPK(Thr180/Y182) D3F9	-0.1581	0.4695
33	p-EGF Receptor (Tyr992)	0.0553	0.8003	92	p-eIF4B(Ser422)	-0.1611	0.4611
34	p-IRS-1(Ser636/639)	0.0455	0.8354	93	p-PKD/PKCm(Ser916)	-0.1611	0.4611
35	p-Tuberin/TSC2 (Thr1462) 5B12	0.0336	0.8780	94	p-PKCA(Thr505)	-0.1640	0.4528
36	p-eIF4E(Ser209)	0.0296	0.8923	95	p-BRCA1(Ser1524)	-0.1650	0.4500
37	p-GSK-3α(Ser21) 36E9	0.0267	0.9030	96	p-Chk2 (Thr68)	-0.1680	0.4418
38	p-PAK2(Ser20)	0.0257	0.9066	97	p-LKB1 (Ser428) (C67A3)	-0.1680	0.4418
39	p-Smad1/5(Ser463/465) 41D10	0.0227	0.9173	98	p-FoxO3a (Ser318/321)	-0.1700	0.4364
40	p-PDGF Receptor-β(Thr740)	0.0198	0.9281	99	p-p53(Ser9)	-0.1709	0.4337
41	p-MKK3/MKK6(Ser189/207) 22A8	0.0168	0.9388	100	p-4E-BP1 (Thr70)	-0.1779	0.4151
42	p-PKCAΔ/θ(Ser643/676)	0.0148	0.9460	101	p-IGF-I Receptor (Tyr1135/1136)	-0.1789	0.4124
43	p-Raf-A (Ser299)	0.0030	0.9892	102	p-CREB (Ser133) 87G3	-0.1818	0.4046
44	p-HSP27(Ser82)	0.0020	0.9928	103	p-PLCg(Y759)	-0.1828	0.4020
45	p-Raf-c(Ser338) 56A6	0.0010	0.9964	104	p-IRS-1(Ser307)	-0.1877	0.3892
46	p-Chk1 (Ser296)	-0.0079	0.9730	105	p-mTOR(Ser2448)	-0.1927	0.3767
47	p-AP2M1	-0.0089	0.9694	106	p-Mnk1 (Thr197/202)	-0.1927	0.3767
48	p-4E-BP1 (Thr37/46)	-0.0109	0.9622	107	p-VASP(Ser157)	-0.1996	0.3595
49	p-Aurora A (T288)/Aurora B (T232)/Aurora C (T198)	-0.0119	0.9586	108	p-Chk2 (Ser33/35)	-0.2016	0.3547
50	p-PLCg(Y783)	-0.0178	0.9370	109	p-IkB-α (Ser32/36) 5A5	-0.2036	0.3499
51	p-SPAK/JNK(Thr183/Tyr185) 81E11	-0.0287	0.8976	110	p-Zap-70 (Tyr319)/Syk (Tyr352)	-0.2036	0.3499
52	p-TAK1 (Thr184/187) 90C7	-0.0356	0.8727	111	p-Chk2 (Thr387)	-0.2065	0.3428
53	p-IGF-I R(Tyr1131)/Insulin R (Tyr1146)	-0.0366	0.8691	112	Non-p-Src(Y416) 7G9	-0.2085	0.3381
54	p-Cofilin(Ser3) 77G2	-0.0425	0.8478	113	p-Tyk2 (Tyr1054/1055)	-0.2125	0.3289
55	p-Rb (Ser780)	-0.0435	0.8443	114	p-PKC(pan)βII (Ser660)	-0.2144	0.3243
56	p-FoxO1 (Ser319)/FoxO4(Ser262)	-0.0445	0.8407	115	p-VEGF Receptor 2 (Tyr1175)	-0.2164	0.3198
57	p-VASP(Ser239)	-0.0494	0.8231	116	p-PDGF Receptor-β(Thr751)	-0.2174	0.3175
58	p-GSK-3α/β(Ser21/9) 37F11	-0.0494	0.8231	117	p-PKM2 (Tyr105)	-0.2174	0.3175
59	p-VEGF Receptor 2 (Tyr1059)D5A6	-0.0494	0.8231	118	p-MAPKAPK-2(Thr2334)27B7	-0.2194	0.3131

Rank	Antibody	Spearman CC	<i>P</i> value
119	p-PDGF Receptor-β(Thr1021)	-0.2204	0.3108
120	p-PLCg(Y1217)	-0.2223	0.3064
121	p70-S6 kinase(Thr389)	-0.2233	0.3042
122	p-IGF-I Receptor (Tyr980)	-0.2253	0.2999
123	p-Bad(Ser112)	-0.2253	0.2999
124	p-MAPKAPK-2(Thr222) 9A7	-0.2273	0.2956
125	p-SHIP2(Tyr1135)	-0.2312	0.2871
126	p-p53(Ser15)	-0.2332	0.2829
127	p-Syk (Tyr323)	-0.2372	0.2746
128	p-VEGF Receptor 2 (Tyr951) 15D2	-0.2372	0.2746
129	p-p53(Ser6)	-0.2460	0.2566
130	p-NFκB p65(Ser276)	-0.2470	0.2546
131	p-IKKα (Ser180)/IKKβ (Ser181)	-0.2500	0.2488
132	p-Histone H3(Ser10)	-0.2500	0.2488
133	p-PDGF Receptor-β(Thr771)	-0.2540	0.2412
134	p-FoxO1 (Thr24)/FoxO3a (Thr32)	-0.2579	0.2338
135	p-p53(Ser15) 16G8	-0.2609	0.2283
136	p-p90RSK(Thr573)	-0.2619	0.2265
137	p-Histone H3(Thr11)	-0.2638	0.2229
138	p-FoxO1 (Thr24)/FoxO3a (Thr32)/FoxO4 (Thr28) 4C	-0.2717	0.2090
139	p-Histone H2A.X(Ser139)	-0.2737	0.2056
140	p-NFκB p65(Ser468)	-0.2757	0.2022
141	p-Syk (Tyr525/526)	-0.2866	0.1844
142	p-EGF Receptor (Tyr1068) D7A5	-0.2885	0.1813
143	p-4E-BP1 (Ser65)	-0.2895	0.1798
144	p-Chk1 (Ser345) 133D3	-0.2945	0.1722
145	p-FoxO3a (Ser253)	-0.2994	0.1649
146	p-MYPT(Thr853)	-0.3024	0.1606
147	p-Jak2 (Tyr1007/1008) C80C3	-0.3103	0.1495
148	p-ATF-2(Thr71)11G2	-0.3123	0.1468
149	p-p53(Ser392)	-0.3142	0.1442
150	p-RSK(Thr356/Ser360)	-0.3172	0.1403
151	p-Gab1 (Tyr627) C32H2	-0.3221	0.1339
152	p-Raf-c(Ser289/296/301)	-0.3271	0.1278
153	p-MYPT(Ser507)	-0.3271	0.1278
154	p-c-Jun (Ser73) D47G9	-0.3291	0.1254
155	p-GSK-3β(Ser9) 5B3	-0.3419	0.1107
156	p-FoxO1 (Ser256)	-0.3458	0.1064
157	p-AMPKb(Ser108)	-0.3518	0.1003
158	p-SHC(Y239)	-0.3557	0.0963
159	p-Histone H3(Thr3)	-0.3577	0.0944
160	p-Akt(Thr308) C31E5	-0.3597	0.0925
161	p-PDK1(Ser241)	-0.3656	0.0869
162	p-p53(Ser37)	-0.3656	0.0869
163	p44/42 MAP kinase(Thr202/Tyr204)	-0.3666	0.0860
164	p-ATF-2(Thr71)	-0.3686	0.0843
165	Non-p-4E-BP1(Thr46) 87D12	-0.3745	0.0791
166	p-Stat 2(Y690)	-0.3745	0.0791
167	p-SEK1/MKK4(Thr261)	-0.3765	0.0774
168	p-ALK (Tyr1282/1283)	-0.3844	0.0711
169	p-Raf-b(ser445)	-0.3864	0.0695
170	p-Stat 6(Y641)	-0.3962	0.0622
171	p-PDGF Receptor-β(Thr1009)	-0.3982	0.0609
172	p-Aurora A (Thr288) C39D8	-0.4051	0.0562
173	p-Bcl-2(Ser70) 5H2	-0.4101	0.0531
174	p-c-Jun (Ser63) II	-0.4111	0.0525
175	p-HER4/ErbB4 (Tyr984)	-0.4160	0.0495
176	p-β-catenin(Ser45)	-0.4298	0.0418
177	p-Akt(Ser473) 193H12	-0.4684	0.0254
178	p-Stat 3(Y705) D3A7	-0.4713	0.0244
179	p-SAPK/JNK(Thr183/Y185) 98F2	-0.5188	0.0122
180	p-SHC(Y317)	-0.5623	0.0060

Abbreviation: Spearman CC, Spearman correlation coefficient.

Supplementary Table S4. Clinical characteristics of patients

Patient	Age	Gender	Viral infection	Stage ^a	TNM ^a	Duration of Nexavar treatment (mo)	OS (mo)	AFP (ng/ml) before treatment ^b	AFP (ng/ml) after treatment ^b	Response ^c	Positivity ^d	Intensity ^e
1	62	Male	(-)	IV	cT4N0M1	24.0	27.0	1,621	816	PR	1	1
2	67	Male	HBV	IV	cT3NxM1	2.4	2.4	1,786	–	PD	4	3
3	59	Male	HBV	IV	cT3NxM1	2.4	2.4	154,470	182780	PD	3	3
4	69	Female	HCV	IV	cT3NxM1	1.2	4.0	29	412	PD	3	3
5	75	Female	(-)	IIIC	cT3NxM0	1.0	1.0	3	–	PD	4	3
6	78	Male	(-)	IIIB	cT3bN0M0	1.7	–	–	–	PD	2	3
7	60	Male	HBV	IIIA	cT3aN0M0	2.3	14.4	–	–	PD	4	3
8	51	Female	HCV	IV	cT3bN1M0	0.5	2.0	4,359	–	PD	2	3
9	90	Male	(-)	II	cT2N0M0	1.8	3.0	166	–	PD	2	3

^aAccording to the International Union Against Cancer (UICC) TNM Classification of Malignant Tumours, 7th edition (2009).

^bMeasured before and a month after sorafenib treatments.

^cAccording to the Response Evaluation Criteria for Solid Tumors (RECIST) guidelines.

^dPercentage of p-RPS6 Ser235/236-positive cells (0 = 0%, 1 = 1-25%, 2 = 26-50%, 3 = 51-75% and 4 = 76-100%).

^eIntensity of p-RPS6 Ser235/236 staining (0, absent; 1, weak; 2, moderate; and 3, strong).

Abbreviations: mo, month; OS, overall survival; AFP, α -fetoprotein; PR, partial response; PD, progressive disease

Supplementary Table S5.**List of the 511 Kinase Genes Sequenced**

#	Name	Entrez_Symbol	#	Name	Entrez_Symbol	#	Name	Entrez_Symbol
1	AAK1	AAK1	57	CaMK1g	CAMK1G	113	DCLK2	DCAMKL2
2	LMR1	AATK	58	CaMK2a	CAMK2A	114	DCLK3	DCAMKL3
3	ABL1	ABL1	59	CaMK2b	CAMK2B	115	DDR1	DDR1
4	ABL2	ABL2	60	CaMK2d	CAMK2D	116	DDR2	DDR2
5	ALK2	ACVR1	61	CaMK2g	CAMK2G	117	SgK223	DKFZp761P0423
6	ALK4	ACVR1B	62	CaMK4	CAMK4	118	DMPK1	DMPK
7	ALK7	ACVR1C	63	CaMKK1	CAMKK1	119	DYRK1A	DYRK1A
8	ACTR2	ACVR2A	64	CaMKK2	CAMKK2	120	DYRK1B	DYRK1B
9	ACTR2B	ACVR2B	65	VACAMKL	CAMKV	121	DYRK2	DYRK2
10	ALK1	ACVRL1	66	CASK	CASK	122	DYRK3	DYRK3
11	ADCK1	ADCK1	67	CCRK	CCRK	123	DYRK4	DYRK4
12	ADCK2	ADCK2	68	CDC2	CDC2	124	eEF2K	EEF2K
13	ADCK4	ADCK4	69	CHED	CDC2L5	125	EGFR	EGFR
14	ADCK5	ADCK5	70	CDK11	CDC2L6	126	HRI	EIF2AK1
15	BARK1	ADRBK1	71	MRCKa	CDC42BPA	127	PKR	EIF2AK2
16	BARK2	ADRBK2	72	MRCKb	CDC42BPB	128	PEK	EIF2AK3
17	AKT1	AKT1	73	DMPK2	CDC42BPG	129	GCN2	EIF2AK4
18	AKT2	AKT2	74	CDC7	CDC7	130	EphA1	EPHA1
19	AKT3	AKT3	75	CDK10	CDK10	131	EphA10	EPHA10
20	ALK	ALK	76	CDK2	CDK2	132	EphA2	EPHA2
21	AlphaK3	ALPK1	77	CDK3	CDK3	133	EphA3	EPHA3
22	AlphaK2	ALPK2	78	CDK4	CDK4	134	EphA4	EPHA4
23	AlphaK1	ALPK3	79	CDK5	CDK5	135	EphA5	EPHA5
24	STLK6	ALS2CR2	80	CDK6	CDK6	136	EphA6	EPHA6
25	PFTAIRE2	ALS2CR7	81	CDK7	CDK7	137	EphA7	EPHA7
26	MISR2	AMHR2	82	CDK8	CDK8	138	EphA8	EPHA8
27	SgK288	ANKK1	83	CDK9	CDK9	139	EphB1	EPHB1
28	ARAF	ARAF	84	CDKL1	CDKL1	140	EphB2	EPHB2
29	ATM	ATM	85	CDKL2	CDKL2	141	EphB3	EPHB3
30	ATR	ATR	86	CDKL3	CDKL3	142	EphB4	EPHB4
31	AurA	AURKA	87	CDKL4	CDKL4	143	EphB6	EPHB6
32	AurB	AURKB	88	CDKL5	CDKL5	144	ErbB2	ERBB2
33	AurC	AURKC	89	CHK1	CHEK1	145	ErbB3	ERBB3
34	AXL	AXL	90	CHK2	CHEK2	146	ErbB4	ERBB4
35	BCKDK	BCKDK	91	IKKa	CHUK	147	IRE1	ERN1
36	BCR	BCR	92	CRIK	CIT	148	IRE2	ERN2
37	BLK	BLK	93	CLK1	CLK1	149	FASTK	FASTK
38	BIKE	BMP2K	94	CLK2	CLK2	150	FER	FER
39	BMPR1A	BMPR1A	95	CLK3	CLK3	151	FES	FES
40	BMPR1B	BMPR1B	96	CLK4	CLK4	152	FGFR1	FGFR1
41	BMPR2	BMPR2	97	CRK7	CRKRS	153	FGFR2	FGFR2
42	BMX	BMX	98	FMS	CSF1R	154	FGFR3	FGFR3
43	BRAF	BRAF	99	CSK	CSK	155	FGFR4	FGFR4
44	BRD2	BRD2	100	CK1a	CSNK1A1	156	FGR	FGR
45	BRD3	BRD3	101	CK1a2	CSNK1A1L	157	SgK196	FLJ23356
46	BRD4	BRD4	102	CK1d	CSNK1D	158	SgK494	FLJ25006
47	BRDT	BRDT	103	CK1e	CSNK1E	159	FLT1	FLT1
48	BRSK1	BRSK1	104	CK1g1	CSNK1G1	160	FLT3	FLT3
49	BRSK2	BRSK2	105	CK1g2	CSNK1G2	161	FLT4	FLT4
50	BTK	BTK	106	CK1g3	CSNK1G3	162	FRAP	FRAP1
51	BUB1	BUB1	107	CK2a1	CSNK2A1	163	FRK	FRK
52	BUBR1	BUB1B	108	CK2a2	CSNK2A2	164	FYN	FYN
53	SgK071	C9orf96	109	DAPK1	DAPK1	165	GAK	GAK
54	ADCK3	CABC1	110	DAPK2	DAPK2	166	RHOK	GRK1
55	CaMK1a	CAMK1	111	DAPK3	DAPK3	167	GPRK4	GRK4
56	CaMK1d	CAMK1D	112	DCLK1	DCAMKL1	168	GPRK5	GRK5

#	Name	Entrez_Symbol	#	Name	Entrez_Symbol	#	Name	Entrez_Symbol
169	GPRK6	GRK6	226	MAP2K4	MAP2K4	283	caMLCK	MLCK
170	GPRK7	GRK7	227	MAP2K5	MAP2K5	284	MLKL	MLKL
171	Haspin	GSG2	228	MAP2K6	MAP2K6	285	MOS	MOS
172	GSK3A	GSK3A	229	MAP2K7	MAP2K7	286	RON	MST1R
173	GSK3B	GSK3B	230	MAP3K1	MAP3K1	287	MUSK	MUSK
174	HSER	GUCY2C	231	MLK2	MAP3K10	288	smMLCK	MYLK
175	CYGD	GUCY2D	232	MLK3	MAP3K11	289	skMLCK	MYLK2
176	CYGF	GUCY2F	233	DLK	MAP3K12	290	MYO3A	MYO3A
177	HCK	HCK	234	LZK	MAP3K13	291	MYO3B	MYO3B
178	HIPK1	HIPK1	235	NIK	MAP3K14	292	NEK1	NEK1
179	HIPK2	HIPK2	236	MAP3K7	MAP3K15	293	NEK10	NEK10
180	HIPK3	HIPK3	237	MAP3K2	MAP3K2	294	NEK11	NEK11
181	HIPK4	HIPK4	238	MAP3K3	MAP3K3	295	NEK2	NEK2
182	H11	HSPB8	239	MAP3K4	MAP3K4	296	NEK3	NEK3
183	HUNK	HUNK	240	MAP3K5	MAP3K5	297	NEK4	NEK4
184	ICK	ICK	241	MAP3K6	MAP3K6	298	NEK5	NEK5
185	IGF1R	IGF1R	242	TAK1	MAP3K7	299	NEK6	NEK6
186	IKKb	IKBKB	243	COT	MAP3K8	300	NEK7	NEK7
187	IKKe	IKBKE	244	MLK1	MAP3K9	301	NEK8	NEK8
188	ILK	ILK	245	HPK1	MAP4K1	302	NEK9	NEK9
189	INSR	INSR	246	GCK	MAP4K2	303	NLK	NLK
190	IRR	INSRR	247	KHS2	MAP4K3	304	ANPa	NPR1
191	IRAK1	IRAK1	248	HGK	MAP4K4	305	ANPb	NPR2
192	IRAK2	IRAK2	249	KHS1	MAP4K5	306	NRBP1	NRBP1
193	IRAK3	IRAK3	250	Erk2	MAPK1	307	NRBP2	NRBP2
194	IRAK4	IRAK4	251	JNK3	MAPK10	308	NRK	NRK
195	ITK	ITK	252	p38b	MAPK11	309	TRKA	NTRK1
196	JAK1	JAK1	253	p38g	MAPK12	310	TRKB	NTRK2
197	JAK2	JAK2	254	p38d	MAPK13	311	TRKC	NTRK3
198	JAK3	JAK3	255	p38a	MAPK14	312	NuaK1	NUAK1
199	Trad	KALRN	256	Erk7	MAPK15	313	NuaK2	NUAK2
200	KDR	KDR	257	Erk1	MAPK3	314	Obscn	OBSCN
201	QSK	KIAA0999	258	Erk4	MAPK4	315	OSR1	OXSR1
202	MLK4	KIAA1804	259	Erk3	MAPK6	316	PAK1	PAK1
203	SgK269	KIAA2002	260	Erk5	MAPK7	317	PAK2	PAK2
204	KIT	KIT	261	JNK1	MAPK8	318	PAK3	PAK3
205	KSR1	KSR1	262	JNK2	MAPK9	319	PAK4	PAK4
206	KSR2	KSR2	263	MAPKAPK2	MAPKAPK2	320	PAK6	PAK6
207	LATS1	LATS1	264	MAPKAPK3	MAPKAPK3	321	PAK5	PAK7
208	LATS2	LATS2	265	MAPKAPK5	MAPKAPK5	322	PASK	PASK
209	LCK	LCK	266	MARK1	MARK1	323	PBK	PBK
210	LIMK1	LIMK1	267	MARK2	MARK2	324	PCTAIRE1	PCTK1
211	LIMK2	LIMK2	268	MARK3	MARK3	325	PCTAIRE2	PCTK2
212	LMR2	LMTK2	269	MARK4	MARK4	326	PCTAIRE3	PCTK3
213	MAST4	LOC375449	270	MAST1	MAST1	327	PDGFRa	PDGFRA
214	SgK069	LOC646643	271	MAST2	MAST2	328	PDGFRb	PDGFRB
215	SPEG	LOC729871	272	MAST3	MAST3	329	CLIK1L	PDIK1L
216	SgK493	LOC91461	273	MASTL	MASTL	330	PDHK1	PDK1
217	LRRK1	LRRK1	274	CTK	MATK	331	PDHK2	PDK2
218	LRRK2	LRRK2	275	MELK	MELK	332	PDHK3	PDK3
219	LTK	LTK	276	MER	MERTK	333	PDHK4	PDK4
220	STLK5	LYK5	277	MET	MET	334	PDK1	PDPK1
221	LYN	LYN	278	TBCK	MGC16169	335	PFTAIRE1	PFTK1
222	MAK	MAK	279	NIM1	MGC42105	336	PHKg1	PHKG1
223	MAP2K1	MAP2K1	280	MINK	MINK1	337	PHKg2	PHKG2
224	MAP2K2	MAP2K2	281	MNK1	MKNK1	338	PIK3R4	PIK3R4
225	MAP2K3	MAP2K3	282	MNK2	MKNK2	339	PIM1	PIM1

#	Name	Entrez_Symbol	#	Name	Entrez_Symbol	#	Name	Entrez_Symbol
340	PIM2	PIM2	397	ROR2	ROR2	454	TAO1	TAOK1
341	PIM3	PIM3	398	ROS	ROS1	455	TAO2	TAOK2
342	PINK1	PINK1	399	SgK085	RP11-145H9.1	456	TAO3	TAOK3
343	MYT1	PKMYT1	400	MST4	RP6-213H19.1	457	TBK1	TBK1
344	PKN1	PKN1	401	RSK3	RPS6KA1	458	TEC	TEC
345	PKN2	PKN2	402	RSK1	RPS6KA2	459	TIE2	TEK
346	PKN3	PKN3	403	RSK2	RPS6KA3	460	TESK1	TESK1
347	PLK1	PLK1	404	MSK2	RPS6KA4	461	TESK2	TESK2
348	PLK2	PLK2	405	MSK1	RPS6KA5	462	SgK307	TEX14
349	PLK3	PLK3	406	RSK4	RPS6KA6	463	TGFbR1	TGFBR1
350	PLK4	PLK4	407	p70S6K	RPS6KB1	464	TGFbR2	TGFBR2
351	CaMK1b	PNCK	408	p70S6Kb	RPS6KB2	465	TIE1	TIE1
352	AMPKa1	PRKAA1	409	RSKL1	RPS6KC1	466	TLK1	TLK1
353	AMPKa2	PRKAA2	410	RSKL2	RPS6KL1	467	TLK2	TLK2
354	PKACa	PRKACA	411	RYK	RYK	468	TNIK	TNIK
355	PKACb	PRKACB	412	SBK	SBK1	469	TNK1	TNK1
356	PKACg	PRKACG	413	SCYL1	SCYL1	470	ACK	TNK2
357	PKCa	PRKCA	414	SCYL2	SCYL2	471	HH498	TNNI3K
358	PKCb	PRKCB1	415	SCYL3	SCYL3	472	PRPK	TP53RK
359	PKCd	PRKCD	416	SGK1	SGK	473	Trb1	TRIB1
360	PKCe	PRKCE	417	SGK2	SGK2	474	Trb2	TRIB2
361	PKCg	PRKCG	418	SGK3	SGK3	475	Trb3	TRIB3
362	PKCh	PRKCH	419	SLK	SLK	476	TIF1a	TRIM24
363	PKCi	PRKCI	420	SMG1	SMG1	477	TIF1b	TRIM28
364	PKCt	PRKCCQ	421	SIK	SNF1LK	478	TIF1g	TRIM33
365	PKCz	PRKCCZ	422	QIK	SNF1LK2	479	Trio	TRIO
366	PKD1	PRKD1	423	SNRK	SNRK	480	ChaK2	TRPM6
367	PKD2	PRKD2	424	SRC	SRC	481	ChaK1	TRPM7
368	PKD3	PRKD3	425	SRM	SRMS	482	TRRAP	TRRAP
369	DNAPK	PRKDC	426	SRPK1	SRPK1	483	TSSK1	TSSK1B
370	PKG1	PRKG1	427	SRPK2	SRPK2	484	TSSK2	TSSK2
371	PKG2	PRKG2	428	MSSK1	SRPK3	485	TSSK3	TSSK3
372	PRKX	PRKX	429	LOK	STK10	486	TSSK4	TSSK4
373	PRKY	PRKY	430	LKB1	STK11	487	SSTK	TSSK6
374	PRP4	PRPF4B	431	MPSK1	STK16	488	TTBK1	TTBK1
375	PSKH1	PSKH1	432	DRAK1	STK17A	489	TTBK2	TTBK2
376	PSKH2	PSKH2	433	DRAK2	STK17B	490	TTK	TTK
377	FAK	PTK2	434	G11	STK19	491	TTN	TTN
378	PYK2	PTK2B	435	MST3	STK24	492	TXK	TXK
379	BRK	PTK6	436	YSK1	STK25	493	TYK2	TYK2
380	CCK4	PTK7	437	MST2	STK3	494	TYRO3	TYRO3
381	Slob	PXK	438	SgK396	STK31	495	KIS	UHMK1
382	RAF1	RAF1	439	YANK1	STK32A	496	ULK1	ULK1
383	MOK	RAGE	440	YANK2	STK32B	497	ULK2	ULK2
384	RET	RET	441	YANK3	STK32C	498	ULK3	ULK3
385	RIOK1	RIOK1	442	STK33	STK33	499	ULK4	ULK4
386	RIOK2	RIOK2	443	CLIK1	STK35	500	VRK1	VRK1
387	RIOK3	RIOK3	444	Fused	STK36	501	VRK2	VRK2
388	RIPK1	RIPK1	445	NDR1	STK38	502	VRK3	VRK3
389	RIPK2	RIPK2	446	NDR2	STK38L	503	Wee1	WEE1
390	RIPK3	RIPK3	447	STLK3	STK39	504	Wnk1	WNK1
391	ANKRD3	RIPK4	448	MST1	STK4	505	Wnk2	WNK2
392	SgK496	RIPK5	449	SgK495	STK40	506	Wnk3	WNK3
393	RNAsel	RNASEL	450	SuRTK106	STYK1	507	Wnk4	WNK4
394	ROCK1	ROCK1	451	SYK	SYK	508	YES	YES1
395	ROCK2	ROCK2	452	TAF1	TAF1	509	MAP3K8	YSK4
396	ROR1	ROR1	453	TAF1L	TAF1L	510	ZAK	ZAK
						511	ZAP70	ZAP70

Supplementary Table S6.

Kinase gene alterations in HCC Cell Lines^a

No.	Gene	Chr	RefSeq ^b	cDNA	Amino acid	Type	SNU449	HUH6	JHH7	HuH7	SKHep1	JHH5	C3A	HepG2	JHH4	huH1	HLE	SNU398	SNU475	HLF	Alex	KIM1	JHH1	SNU182	SNU423	SNU378	
1	TTN	2	NM_133432	c.G77113A	p.D25705N	nonsynonymous SNV	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.T71588C	p.L23863P	nonsynonymous SNV	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.G70443A	p.W23481X	stopgain SNV	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.G66505T	p.V22169L	nonsynonymous SNV	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.62007_62008insG	p.R20669fs	frameshift insertion	-	-	-	-	○	-	-	-	-	-	-	○	-	○	-	-	-	-	○	-	
	TTN	2	NM_133432	c.60574_60576del	p.20192_20192del	nonframeshift deletion	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.G60069T	p.W20023C	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	
	TTN	2	NM_133432	c.C58586G	p.S19529C	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	
	TTN	2	NM_133432	c.C45917T	p.P15306L	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	
	TTN	2	NM_133432	c.A40264G	p.T13422A	nonsynonymous SNV	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.T40097C	p.I13366T	nonsynonymous SNV	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.A39550G	p.T13184A	nonsynonymous SNV	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.A32462G	p.N10821S	nonsynonymous SNV	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.C27845G	p.T9282S	nonsynonymous SNV	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.G23632A	p.E7878K	nonsynonymous SNV	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.A18388G	p.I6130V	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.G16597C	p.D5533H	nonsynonymous SNV	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.A9128G	p.Q3043R	nonsynonymous SNV	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.T8795C	p.I2932T	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	
	TTN	2	NM_133432	c.C7931T	p.T2644I	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.A6339C	p.E2113D	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.A3590C	p.Q1197P	nonsynonymous SNV	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	TTN	2	NM_133432	c.A665T	p.E222V	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	
2	OBSCN	1	NM_001098623	c.C959T	p.T320I	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
	OBSCN	1	NM_001098623	c.G1408T	p.A470S	nonsynonymous SNV	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	OBSCN	1	NM_001098623	c.G2539A	p.E847K	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	
	OBSCN	1	NM_001098623	c.C5078T	p.A1693V	nonsynonymous SNV	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	
	OBSCN	1	NM_001098623	c.G5272C	p.E1758Q	nonsynonymous SNV	-	-	-	-	-	○	-	-	-	-	-	-	-	○	-	-	-	-	-	-	
	OBSCN	1	NM_001098623	c.T6816G	p.F2272L	nonsynonymous SNV	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	OBSCN	1	NM_001098623	c.C7882T	p.R2628C	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	
	OBSCN	1	NM_001098623	c.C9473T	p.T3158I	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
	OBSCN	1	NM_001098623	c.C10936T	p.R3646W	nonsynonymous SNV	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	OBSCN	1	NM_001098623	c.T12574G	p.W4192G	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	
	OBSCN	1	NM_001098623	c.C13820T	p.P4607L	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	
	OBSCN	1	NM_001098623	c.G14003A	p.R4668Q	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	
	OBSCN	1	NM_001098623	c.C17573A	p.A5858E	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
	OBSCN	1	NM_052843	c.19093_19094insC	p.T6365fs	frameshift insertion	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	
3	EPHA1	7	NM_005232	c.T2743C	p.Y915H	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	
	EPHA1	7	NM_005232	c.G2155T	p.D719Y	nonsynonymous SNV	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	EPHA1	7	NM_005232	c.C772G	p.P258A	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	
	EPHA1	7	NM_005232	c.T770G	p.V257G	nonsynonymous SNV	-	○	○	○	○	○	○	○	○	-	○	○	-	○	○	○	○	○	○	-	○
	EPHA1	7	NM_005232	c.A701C	p.H234P	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
	EPHA1	7	NM_005232	c.A688G	p.T230A	nonsynonymous SNV	-	-	○	○	○	○	○	-	-	○	-	-	-	○	○	○	○	-	○	-	-
4	ROS1	6	NM_002944	c.G6878A	p.G2293D	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	

	ROS1	6	NM_002944	c.C6847A	p.Q2283K	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	
	ROS1	6	NM_002944	c.A5689G	p.T1897A	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	
	ROS1	6	NM_002944	c.T3325G	p.S1109A	nonsynonymous SNV	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	ROS1	6	NM_002944	c.C848A	p.S283Y	nonsynonymous SNV	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	ROS1	6	NM_002944	c.T397C	p.W133R	nonsynonymous SNV	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
5	KSR2	12	NM_173598	c.C2350A	p.L784M	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	
	KSR2	12	NM_173598	c.C479T	p.P160L	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
	KSR2	12	NM_173598	c.C353A	p.S118Y	nonsynonymous SNV	-	-	-	-	-	-	-	-	○	-	-	○	-	-	-	-	-	-	-	-	
	KSR2	12	NM_173598	c.G262T	p.E88X	stopgain SNV	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	
	KSR2	12	NM_173598	c.G166C	p.E56Q	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	
6	MAP3K4	6	NM_005922	c.C533T	p.S178L	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	
	MAP3K4	6	NM_005922	c.G2719A	p.G907S	nonsynonymous SNV	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	
	MAP3K4	6	NM_005922	c.A2996G	p.N999S	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	
	MAP3K4	6	NM_005922	c.3566_3568del	p.1189_1190del	nonframeshift deletion	○	○	○	○	-	○	○	○	○	-	○	○	○	○	○	○	○	○	○	○	○
	MAP3K4	6	NM_005922	c.G3656A	p.S1219N	nonsynonymous SNV	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	
7	NTRK1	1	NM_002529	c.A748C	p.T250P	nonsynonymous SNV	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	NTRK1	1	NM_002529	c.T902C	p.I301T	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	
	NTRK1	1	NM_002529	c.T2048G	p.V683G	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
	NTRK1	1	NM_002529	c.G2212A	p.D738N	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	
	NTRK1	1	NM_002529	c.A2378C	p.D793A	nonsynonymous SNV	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
8	ALK	2	NM_004304	c.G3630T	p.E1210D	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	
	ALK	2	NM_004304	c.A3089C	p.H1030P	nonsynonymous SNV	-	○	○	○	○	-	○	○	○	○	○	○	-	○	○	○	○	○	○	○	○
	ALK	2	NM_004304	c.T1508G	p.V503G	nonsynonymous SNV	-	-	-	-	○	-	-	-	-	○	-	-	○	-	-	-	-	○	-	-	-
	ALK	2	NM_004304	c.T843A	p.H281Q	nonsynonymous SNV	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
9	EPHA2	1	NM_004431	c.G2845C	p.V949L	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
	EPHA2	1	NM_004431	c.A769C	p.I257L	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	
	EPHA2	1	NM_004431	c.766_767insG	p.P256fs	frameshift insertion	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	
	EPHA2	1	NM_004431	c.T764G	p.V255G	nonsynonymous SNV	-	○	○	○	○	○	○	○	○	○	○	○	○	-	○	○	○	○	-	○	○
10	INSR	19	NM_000208	c.T3661G	p.S1221A	nonsynonymous SNV	○	○	-	○	-	-	○	-	○	○	-	-	○	○	-	-	○	-	-	-	
	INSR	19	NM_000208	c.G3143A	p.G1048D	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	
	INSR	19	NM_000208	c.C1988G	p.A663G	nonsynonymous SNV	-	○	-	-	-	-	-	-	-	-	-	-	-	-	○	-	○	-	-	-	
	INSR	19	NM_000208	c.C806T	p.P269L	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	
11	MYLK	3	NM_053031	c.89_89del	p.30_30del	frameshift deletion	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	MYLK	3	NM_053026	c.G2161C	p.G721R	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	
	MYLK	3	NM_053026	c.G617A	p.R206H	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	
	MYLK	3	NM_053026	c.G455A	p.R152H	nonsynonymous SNV	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
12	PRKDC	8	NM_006904	c.G11221A	p.V3741M	nonsynonymous SNV	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	PRKDC	8	NM_006904	c.C10466T	p.P3489L	nonsynonymous SNV	-	-	-	-	-	-	○	○	-	-	-	-	-	-	-	-	-	-	-	-	
	PRKDC	8	NM_006904	c.6337_6339del	p.2113_2113del	nonframeshift deletion	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	PRKDC	8	NM_006904	c.419_430del	p.140_144del	nonframeshift deletion	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
13	SPEG	2	NM_005876	c.C2282A	p.A761E	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	
	SPEG	2	NM_005876	c.G2971A	p.V991M	nonsynonymous SNV	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	SPEG	2	NM_005876	c.A3992G	p.Q1331R	nonsynonymous SNV	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	
	SPEG	2	NM_005876	c.C8926A	p.R2976S	nonsynonymous SNV	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
14	ACVR2A	2	NM_001616	c.T234A	p.C78X	stopgain SNV	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	
	ACVR2A	2	NM_001616	c.C452T	p.A151V	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	
	ACVR2A	2	NM_001616	c.A945C	p.K315N	nonsynonymous SNV	-	○	○	○	-	-	○	○	○	-	-	-	-	○	-	○	-	-	-	○	

144	PRKACB	1	NM_001242858	c.C738G	p.F246L	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
145	PRKACG	9	NM_002732	c.G565A	p.A189T	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
146	PRKCQ	10	NM_006257	c.A428G	p.H143R	nonsynonymous SNV	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	
147	PRKCZ	1	NM_002744	c.A295C	p.T99P	nonsynonymous SNV	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	○	-	-	
148	PTK2	8	NM_153831	c.3127_3131del	p.1043_1044del	frameshift deletion	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	
149	RET	10	NM_020630	c.G1588A	p.E530K	nonsynonymous SNV	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
150	RIPK4	21	NM_020639	c.C2296G	p.L766V	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
151	RNASEL	1	NM_021133	c.G1823A	p.R608Q	nonsynonymous SNV	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
152	RPS6KA1	1	NM_002953	c.T214G	p.S72A	nonsynonymous SNV	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
153	RPS6KB2	11	NM_003952	c.G1264A	p.V422I	nonsynonymous SNV	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
154	RPS6KC1	1	NM_001136138	c.A2204G	p.K735R	nonsynonymous SNV	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	
155	SCYL1	11	NM_001048218	c.G163A	p.E55K	nonsynonymous SNV	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
156	SCYL2	12	NM_017988	c.T767C	p.M256T	nonsynonymous SNV	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	
157	SGK2	20	NM_016276	c.A923C	p.H308P	nonsynonymous SNV	-	○	-	-	-	○	○	○	-	○	○	-	-	○	○	○	-	-	-	○
158	SIK1	21	NM_173354	c.G1888A	p.A630T	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
159	SRPK1	6	NM_003137	c.G1427A	p.G476E	nonsynonymous SNV	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
160	STK10	5	NM_005990	c.G2753A	p.R918Q	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	
161	STK17B	2	NM_004226	c.A304T	p.N102Y	nonsynonymous SNV	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
162	STK24	13	NM_003576	c.G310A	p.D104N	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	
163	STK4	20	NM_006282	c.G350A	p.R117Q	nonsynonymous SNV	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	
164	STK40	1	NM_032017	c.769_770del	p.257_257del	frameshift deletion	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
165	STYK1	12	NM_018423	c.A91G	p.T31A	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
166	TBCK	4	NM_001163435	c.G19A	p.A7T	nonsynonymous SNV	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
167	TEK	9	NM_000459	c.A880G	p.K294E	nonsynonymous SNV	○	○	○	○	○	○	○	-	○	-	-	○	-	-	-	-	○	○	○	-
168	TEX14	17	NM_031272	c.G3570C	p.Q1190H	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	
169	TGFBR1	9	NM_001130916	c.G856C	p.D286H	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	
170	TNK2	3	NM_001010938	c.C1814T	p.P605L	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	
171	TRIB2	2	NM_021643	c.A494C	p.H165P	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
172	TRIM28	19	NM_005762	c.C2441T	p.P814L	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	
173	TRIO	5	NM_007118	c.T7775C	p.F2592S	nonsynonymous SNV	-	-	○	-	○	-	-	-	-	-	-	-	-	-	-	-	○	-	○	
174	TRPM6	9	NM_001177310	c.C3733A	p.P1245T	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	
175	TSSK4	14	NM_174944	c.T311A	p.L104Q	nonsynonymous SNV	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	
176	TTBK1	6	NM_032538	c.A295G	p.N99D	nonsynonymous SNV	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	○	-	-	
177	TYK2	19	NM_003331	c.1036_1037insG	p.N346fs	frameshift insertion	○	○	-	○	○	-	-	○	-	-	-	○	○	○	-	○	-	○	○	
178	TYRO3	15	NM_006293	c.G1135A	p.A379T	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	
179	UHMK1	1	NM_175866	c.C29T	p.A10V	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	
180	ULK2	17	NM_014683	c.2621delA	p.Q874fs	frameshift deletion	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	
181	ULK4	3	NM_017886	c.G3746A	p.R1249Q	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	
182	VRK2	2	NM_001130481	c.G775A	p.A259T	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	-	
183	WNK1	12	NM_014823	c.C4468G	p.P1490A	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	
184	WNK2	9	NM_006648	c.G5350A	p.V1784M	nonsynonymous SNV	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	
185	WNK4	17	NM_032387	c.G2167A	p.E723K	nonsynonymous SNV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	○	-	
186	YES1	18	NM_005433	c.G271C	p.G91R	nonsynonymous SNV	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

^aThe 20 HCC cell lines analyzed were SNU-449, HUH-6, JHH-7, SK-Hep1, JHH-5, C3A, HepG2, JHH-4, huH-1, HLE, SNU-398, SNU-475, HLF, Alexander, KIM-1, JHH-1, JHh-2, SNU-182, SNU-423 and SNU-387.

^bRefSeq Accession number registered in the National Center for Biotechnology Information (NCBI) database (<http://www.ncbi.nlm.nih.gov/sites/entrez?db=gene>).

Abbreviation: Chr, chromosome

Supplementary Table S7.
mTOR and MAPK pathway gene alterations in the HCC cell lines

Gene symbol	Alternative name	rsID ^a	RefSeq ID ^b	Chr	Genome position	cDNA	Amino acid	Cell lines																				
								SNU44	HUH6	JHH7	HuH7	SKHep1	JHH5	C3A	HepG2	JHH4	huH1	HLE	SNU39	SNU47	HLF	Alex	KIM1	JHH1	SNU18	SNU42	SNU378	
BRAF		rs113488022	NM_004333	7	140453136	c.T1799A	p.V600E	-	-	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
RPS6KA1	RSK1		NM_002953	1	26873463	c.T214G	p.S72A	-	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
RPS6KA1	RSK1	rs2229712	NM_002953	1	26883511	c.A1004C	p.K335T	-	-	-	-	-	-	-	-	-	○	-	-	○	-	-	-	-	○	-	-	
RPS6KA6	RSK4	rs6616890	NM_014496	X	83320017	c.G2074A	p.D692N	○	-	-	-	-	-	-	-	-	-	-	○	○	-	-	○	-	-	-	-	
RPS6KB2	S6K2		NM_003952	11	67202161	c.G1264A	p.V422I	-	○	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
RPS6KB2	S6K2	rs55987642	NM_003952	11	67200812	c.C800T	p.P267L	-	-	-	-	○	-	-	-	○	-	-	-	-	-	-	-	○	○	-	-	
RPS6KB2	S6K2	rs13859	NM_003952	11	67202156	c.C1259T	p.A420V	○	○	○	○	○	-	-	-	○	○	-	-	-	-	○	○	○	○	-	-	
STK11	LKB1	rs59912467	NM_000455	19	1223125	c.C1062G	p.F354L	-	-	○	-	-	-	-	-	-	-	-	-	○	-	-	-	-	-	-	-	

^aReference Cluster ID registered in the dbSNP (<http://www.ncbi.nlm.nih.gov/projects/SNP/>) database (as of March 2013).

^bRefSeq accession number registered in the NCBI database.

Shaded rows indicate DNA variations not registered as genetic polymorphisms in the dbSNP database.

Supplementary Table S8. Chou-Talalay median dose effect analysis

	1	2	3	4	5
AZD8055 (nM)	12.5	25	50	100	200
CI-1040 (μM)	3.75	7.5	15	30	60
Drug Combination Ratio	1:300	1:300	1:300	1:300	1:300
CI^a	0.893	0.766	0.711	0.709	0.835

^aCI value was calculated using the CompuSyn software package (ComboSyn, Inc, <http://www.combosyn.com>). CI = 1, additive effect; CI <1, synergistic effect; CI >1, antagonistic effect.
Abbreviations: CI, combination index.

Supplementary Table S9. List of the MAPK and mTOR signaling components for unsupervised hierarchical clustering analyses

#	Signaling Components	Phosphorylation site(s)	KEGG Pathway ^a	CST Antibody Category
1	p-p53	Ser20	MAPK	DNA damage
2	p-p53	Ser46	MAPK	DNA damage
3	p-p53	Ser15 16G8	MAPK	DNA damage
4	p-p53	Ser37	MAPK	DNA damage
5	p-p53	Ser392	MAPK	DNA damage
6	p-p53	Ser6	MAPK	DNA damage
7	p-p53	Ser9	MAPK	DNA damage
8	p-p53	Ser15	MAPK	DNA damage
9	p-NFκB p65	Ser536	MAPK	NFκB
10	p-NFκB p65	Ser276	MAPK	NFκB
11	p-NFκB p65	Ser468	MAPK	NFκB
12	p-ATF-2	Thr71 11G2	MAPK	p38 MAPK
13	p-HSP27	Ser82	MAPK	p38 MAPK
14	p-MAPKAPK-2	Thr222	MAPK	p38 MAPK
15	p-MAPKAPK-2	Thr2334	MAPK	p38 MAPK
16	p-MKK3/MKK6	Ser189/207	MAPK	p38 MAPK
17	p-MSK1	Thr581	MAPK	p38 MAPK
18	p-p38 MAPK	Thr180/Y182	MAPK	p38 MAPK
19	p44/42 MAP kinase	Thr202/Tyr204	MAPK	Ras-Raf
20	p-CREB	Ser133	MAPK	Ras-Raf
21	p-MEK1/2	Ser217/221	MAPK	Ras-Raf
22	p-Mnk1	Thr197/202	MAPK	Ras-Raf
23	p-p90RSK	Thr359/Ser363	MAPK	Ras-Raf
24	p-p90RSK	Ser380	MAPK	Ras-Raf
25	p-p90RSK	Thr573	MAPK	Ras-Raf
26	p-PAK1	Ser144	MAPK	Ras-Raf
27	p-PAK1	Ser199/204	MAPK	Ras-Raf
28	p-PAK1	Thr423	MAPK	Ras-Raf
29	p-PAK2	Ser20	MAPK	Ras-Raf
30	p-Raf-A	Ser299	MAPK	Ras-Raf
31	p-Raf-b	ser445	MAPK	Ras-Raf
32	p-Raf-c	Ser338	MAPK	Ras-Raf
33	p-Raf-c	Ser289/296/301	MAPK	Ras-Raf
34	p-Raf-c	Ser259	MAPK	Ras-Raf
35	p-RSK	Thr356/Ser360	MAPK	Ras-Raf
36	p-RSK2	Ser227	MAPK	PI3K-AKT-mTOR
37	p-EGF Receptor	Tyr1045	MAPK	RTK/TK
38	p-EGF Receptor	Tyr1068	MAPK	RTK/TK
39	p-EGF Receptor	Tyr992	MAPK	RTK/TK
40	p-PDGF Receptor-β	Thr1009	MAPK	RTK/TK
41	p-PDGF Receptor-β	Thr740	MAPK	RTK/TK
42	p-PDGF Receptor-β	Thr751	MAPK	RTK/TK
43	p-PDGF Receptor-β	Thr771	MAPK	RTK/TK
44	p-PDGF Receptor-β	Thr1021	MAPK	RTK/TK
45	p-ATF-2	Thr71	MAPK	SAPK/JNK
46	p-c-Jun	Ser63	MAPK	SAPK/JNK

47	p-c-Jun	Ser73	MAPK	SAPK/JNK
48	p-SAPK/JNK	Thr183/Y185	MAPK	SAPK/JNK
49	p-SAPK/JNK	Thr183/Tyr185	MAPK	SAPK/JNK
50	p-SEK1/MKK4	Thr261	MAPK	SAPK/JNK
51	p-TAK1	Thr184/187	MAPK	TGF- β
52	p-AMPK α	Thr172	mTOR	Glucose metabolism
53	p-IRS-1	Ser307	mTOR	Glucose metabolism
54	p-IRS-1	Ser612	mTOR	Glucose metabolism
55	p-IRS-1	Ser636/639	mTOR	Glucose metabolism
56	p-LKB1	Ser428	mTOR	Glucose metabolism
57	p-PKC(pan) β II	Ser660	mTOR	Phospholipase
58	p-PKC α/β	Thr638/641	mTOR	Phospholipase
59	p-4E-BP1	Thr70	mTOR	PI3K-AKT-mTOR
60	p-4E-BP1	Thr37/46	mTOR	PI3K-AKT-mTOR
61	p-4E-BP1	Ser65	mTOR	PI3K-AKT-mTOR
62	p70-S6 kinase	Thr389	mTOR	PI3K-AKT-mTOR
63	p-Akt	Thr308	mTOR	PI3K-AKT-mTOR
64	p-eEF2k	Ser366	mTOR	PI3K-AKT-mTOR
65	p-eIF4B	Ser422	mTOR	PI3K-AKT-mTOR
66	p-eIF4E	Ser209	mTOR	PI3K-AKT-mTOR
67	p-eIF4G	Ser1108	mTOR	PI3K-AKT-mTOR
68	p-GSK-3 α	Ser21	mTOR	PI3K-AKT-mTOR
69	p-GSK-3 α/β	Ser21/9	mTOR	PI3K-AKT-mTOR
70	p-GSK-3 β	Ser9	mTOR	PI3K-AKT-mTOR
71	Phospho-Akt	Ser473	mTOR	PI3K-AKT-mTOR
72	p-mTOR	Ser2448	mTOR	PI3K-AKT-mTOR
73	p-PDK1	Ser241	mTOR	PI3K-AKT-mTOR
74	p-PKD/PKCm	Ser744/748	mTOR	PI3K-AKT-mTOR
75	p-PKD/PKCm	Ser916	mTOR	PI3K-AKT-mTOR
76	p-PRAS40	Thr246	mTOR	PI3K-AKT-mTOR
77	p-PTEN	Ser380	mTOR	PI3K-AKT-mTOR
78	p-Raptor	Ser792	mTOR	PI3K-AKT-mTOR
79	p-S6Rb	Ser235/236	mTOR	PI3K-AKT-mTOR
80	p-S6Rb	Ser240/244	mTOR	PI3K-AKT-mTOR
81	p-Tuberin/TSC2	Ser939	mTOR	PI3K-AKT-mTOR
82	p-Tuberin/TSC2	Thr1462	mTOR	PI3K-AKT-mTOR
83	p-Tuberin/TSC2	Thr1571	mTOR	PI3K-AKT-mTOR

Abbreviations: CST, Cell Signaling Technology, Inc. (Danvers, MA)

^aThe MAPK and mTOR signaling components were selected based on KEGG pathway maps (<http://www.genome.jp/kegg/kegg3a.html>) and used for unsupervised hierarchical clustering analyses.

Supplementary Table S10. Fisher's exact test: Association of cancer types with activation status of the MAPK and mTOR signaling

	A ^a	B ^b	<i>P</i> value (fisher's exact test)
HCC	11	12	0.011
Ovarian Cancer	3	12	0.753
Gastric Cancer	3	12	0.753
Colon Cancer	2	7	1.000
Pancreatic Cancer	2	7	1.000
Osteosarcoma	0	8	0.109
Lung Cancer	3	5	0.416
Oral Cancer	0	7	0.185

^{a,b} A and B indicate the subgroups shown in Supplementary Fig.2.