

## SUPPLEMENTARY TABLES

**Supplementary Table 1. Top 10 enriched KEGG pathways of sorafenib in HCC.**

Category	Term	Count	P Value
KEGG	hsa00830:Retinol metabolism	7	8.55E-07
KEGG	hsa00982:Drug metabolism - cytochrome P450	7	1.12E-06
KEGG	hsa05204:Chemical carcinogenesis	7	2.94E-06
KEGG	hsa00591:Linoleic acid metabolism	5	1.34E-05
KEGG	hsa00980:Metabolism of xenobiotics by cytochrome P450	5	5.51E-04
KEGG	hsa00140:Steroid hormone biosynthesis	4	3.29E-03
KEGG	hsa00590:Arachidonic acid metabolism	4	3.98E-03
KEGG	hsa00983:Drug metabolism - other enzymes	3	2.37E-02
KEGG	hsa00232:Caffeine metabolism	2	2.58E-02
KEGG	hsa01100:Metabolic pathways	12	4.29E-02

**Supplementary Table 2. Top 10 enriched KEGG pathways of regorafenib in HCC.**

Category	Term	Count	P Value
KEGG	hsa04151:PI3K-Akt signaling pathway	15	4.72E-08
KEGG	hsa00982:Drug metabolism - cytochrome P450	8	3.49E-07
KEGG	hsa00830:Retinol metabolism	7	4.93E-06
KEGG	hsa05204:Chemical carcinogenesis	6	2.13E-04
KEGG	hsa04512:ECM-receptor interaction	6	3.15E-04
KEGG	hsa00591:Linoleic acid metabolism	4	1.01E-03
KEGG	hsa00980:Metabolism of xenobiotics by cytochrome P450	5	1.65E-03
KEGG	hsa04510:Focal adhesion	7	2.82E-03
KEGG	hsa04015:Rap1 signaling pathway	7	3.10E-03
KEGG	hsa00590:Arachidonic acid metabolism	4	8.93E-03

**Supplementary Table 3. The genes related to the survival of HCC patients in PPI network.**

Gene	Logrank p value	Gene	Logrank p value	Gene	Logrank p value	Gene	Logrank p value
<b>KIF2C</b>	0.000011	MELK	0.0015	KIF14	0.0052	SHCBP1	0.018
<b>EXO1</b>	0.00034	DNA2	0.0015	TEK	0.0052	CYP3A4	0.019
<b>ASPM</b>	0.00061	PDE2A	0.0017	CYP2C8	0.0064	CDC6	0.02
<b>CYP2C9</b>	0.0007	PLK4	0.0028	KNTC1	0.0072	NCAPH	0.02
<b>ECT2</b>	0.00076	BUB1B	0.0028	CCNE2	0.0072	ITGA2	0.022
<b>ANLN</b>	0.00085	TOP2A	0.0028	ABCA9	0.0075	ESPL1	0.024
<b>TYMS</b>	0.0009	POLQ	0.0033	TCF19	0.01	ZNF692	0.024
<b>KIF4A</b>	0.001	MYBL2	0.0034	TARBP1	0.013	COL15A1	0.037
<b>KIF15</b>	0.0011	TROAP	0.0035	MSH5	0.014		
<b>STMN1</b>	0.0011	DTL	0.0049	XDH	0.015		

Abbreviations: PPI, protein-protein interaction.

**Supplementary Table 4. Top10 highest degree proteins of sorafenib and regorafenib in PPI network.**

SORAFENIB			REGORAFENIB		
Node	Type	Degree	Node	Type	Degree
<b>EXO1</b>	down	14	<b>TOP2A</b>	down	22
<b>TYMS</b>	down	14	<b>CDKN3</b>	down	16
<b>POLQ</b>	down	13	<b>MELK</b>	down	16
<b>PLK4</b>	down	13	<b>KIF2C</b>	down	15
<b>UBE2C</b>	down	12	<b>ASPM</b>	down	15
<b>BUB1B</b>	down	12	<b>KIF4A</b>	down	14
<b>DTL</b>	down	12	<b>KIF14</b>	down	14
<b>KIF15</b>	down	12	<b>LRRK2</b>	up	14
<b>ANLN</b>	down	12	<b>TYMS</b>	down	13
<b>CDC6</b>	down	11	<b>KNTC1</b>	down	13

**Supplementary Table 5. The CDIs of siKIF14 in combination with sorafenib in Huh7-SR cells.**

Sorafenib ( $\mu$ M)	siKIF4-2	siKIF4-3
2.5	0.99	0.98
5	0.69	0.69
10	0.72	0.75

Abbreviations: CDI, coefficient of drug interaction.

**Supplementary Table 6. The CDIs of siKIF14 in combination with sorafenib in HepG2-SR cells.**

<b>Sorafenib (<math>\mu</math>M)</b>	<b>siKIF4-2</b>	<b>siKIF4-3</b>
2.5	0.97	0.95
5	0.67	0.66
10	0.71	0.73

Abbreviations: CDI, coefficient of drug interaction.

**Supplementary Table 7. The primers used for RT-PCR in this study.**

<b>Genes</b>	<b>Gene ID</b>	<b>Primers (5' to 3')</b>
ECT2	1894	Forward: GCAAGAGTGGTTCTGGGGAA Reverse: TTGCGATTGCTGTTAGGGGT
TOP2A	7153	Forward: GAAGTGTCACCATTGCAGCC Reverse: TGTCTGGGCGGAGCAAAATA
MELK	9833	Forward: AGATGTTTGGAGCATGGGCA Reverse: ATGCTACTGGGAGAGAGCCA
KIF4A	24137	Forward: ACGCCATCTGAATGACCTCC Reverse: CCACGCACTTCAGTAAGGGA
ASPM	259266	Forward: ATCATCCTGCAATCTAGGATAAGAA Reverse: AAATAAGCACGCCAATGCCTC