SUPPLEMENTARY DATA

Isolation of compounds from Cimicifuga

The EtOAc-soluble fraction (308 g) of the rhizomes of *C. yunnanensis* was subjected to silica gel column chromatography (cc) and eluted with CHCl₃-MeOH (100:0, 50:1, 20:1, 10:1, 0:100) to afford fractions A (68.3 g), B (13.2 g), C (92.5 g) and D (42.7 g). Fraction C was successive subjected to silica gel cc and eluted with CHCl₃-MeOH (30:1 to 10:1) to afford four fractions (C.1-C.4). Fraction C.3 (24.6 g) was further resolved into five fractions (C.3.1-C.3.5) by eluting on a RP-18 column (MeOH-H₂O, gradient from 50:50 to 100:0). Fraction C.3.3 (9.6 g) was further subjected to repeated silica gel cc, eluted with CHCl₃-Me₂CO (gradient from 20:1 to 10:1) to yield **KCY03** (120.6 mg), **04** (80.2 mg), **05** (4.3 mg), **06** (20.1 mg), **14** (58.7 mg), **31** (7.6 mg), **44** (12.3 mg), and **49** (13.4 mg). **KCY08** (135.4 mg) and **37** (10.2 mg) were isolated from fraction C.3.2 (4.2 g) by conducting silica gel cc, eluting with CHCl₃-Me₂CO (gradient from 15:1 to 8:1). The EtOAc-soluble fraction (158 g) of the roots of *C. foetida* was

The EtOAc-soluble fraction (158 g) of the roots of C. *Toetida* was chromatographed over a silica gel column and eluted with CHCl₃-MeOH (100:0, 50:1, 20:1, 10:1, 0:100) to afford fractions A (13.4 g), B (8.7 g), C (34.5 g), and D (37.2 g). Fraction B (8.7 g) was subjected to cc on silica gel. Gradient elution with CHCl₃-MeOH (60:1 to 40:1) gave fractions B.1, B.2 and B.3. Fraction B.2 (3.8 g) was chromatographed on an RP-18 column (MeOH-H₂O, gradient from 70:30 to 100:0) and then purified on Sephadex LH-20 (MeOH) to afford **KHF06** (13.1 mg), **07** (21.5 mg), **08** (11.4 mg), **13** (9.7 mg), **21** (17.2 mg), **22** (14.3 mg), **27**(8.4 mg) and **30** (7.6 mg). Fraction C (34.5 g) was subjected to cc on silica gel and eluted

with CHCl₃-MeOH (gradient from 40:1 to 20:1) to yield fractions C.1, C.2 and C.3. Fraction C.2 (2.6 g) was subjected to silica gel cc (CHCl₃-Me₂CO, 4:1), then RP-18 (MeOH-H₂O, 60:40) to yield **KHF17** (11.2 mg), **24** (4.3 mg), **29** (3.7 mg), **41** (5.6 mg), and **51** (3.8 mg). Fraction C.3 (16.3 g) was chromatographed on silica gel cc (CHCl₃-Me₂CO, gradient from 10:1 to 5:1); then RP-18 (MeOH-H₂O, 60:40) to afford fractions C.3.1-C.3.4. Fraction C.3.2 (2.5 g) was subjected to cc on an RP-18 column (MeOH-H₂O, 60:40), then purified on a Sephadex LH-20 column (MeOH) to afford **KHF16** (45.3 mg), **18** (11.5 mg) and **38** (23.5 mg).

The EtOAc extract (313.6 g) of the aerial parts of *C. foetida* was subjected to silica gel cc, eluted with CHCl₃-MeOH (100:0, 50:1, 20:1, 10:1) to afford fractions A (43.2 g), B (23.4 g), C (78.5 g) and D (91.3 g). Fraction B (23.4 g) was divided into four sub-fractions (B.1-B.4) after performing silica gel cc, eluted with CHCl₃-MeOH (gradient from 60:1 to 40:1). **KYY11** (8.9 mg), **14** (5.6 mg), and **27** (12.3 mg) were purified from fraction **B.2** (8.1 g) by conducting cc on RP-18 (MeOH-H₂O, 70:30) and then Sephadex LH-20 (MeOH). Fraction **C** (78.5 g) was fractionated into three sub-fractions (**C.1-C.3**) by performing silica gel, eluted with CHCl₃-MeOH (gradient from 40:1 to 20:1). Fraction **C.2** (16.6 g) was subjected to silica gel cc (CHCl₃-Me₂CO, 10:1), then RP-18 (MeOH-H₂O, 60:40) to yield **KYY04** (21.4 mg), **08** (16.4 mg), **15** (14.3 mg), **18** (8.9 mg), **20** (45.3 mg), **33** (7.6 mg), **41** (23.1 mg) and **56** (18.3 mg).

The EtOAc extract (13.1 g) of the roots of *C. dahurica* was subjected to silica gel cc, eluted with CHCl₃-MeOH (100:0, 50:1, 20:1, 10:1) to afford fractions A (0.4 g), B (2.8 g), C (5.5 g) and D (3.3 g). Fraction B was subjected to repeated silica gel

cc, eluted with $CHCl_3-Me_2CO$ (gradient from 20:1 to 10:1) and then repeated semi-preparative HPLC (eluted with CH_3CN-H_2O , gradient from 60:40 to 85:15) to yield **KXG42** (3.5 mg). **KXG106** (2.8 mg), **113** (3.2 mg), and **115** (3.5 mg), were purified from fraction C by conducting silica gel cc, eluting with $CHCl_3-Me_2CO$ (10:1), followed by repeated semi-preparative HPLC (eluted with CH_3CN-H_2O , gradient from 50:50 to 80:20).

The EtOAc extract (12.8 g) of the roots of *C. heracleifolia* was subjected to silica gel cc, eluted with CHCl₃-MeOH (100:0, 50:1, 20:1, 10:1) to afford fractions A (0.5 g), B (2.3 g), C (4.9 g) and D (2.8 g). Fraction C was subjected to repeated silica gel cc, eluted with CHCl₃-Me₂CO (10:1) and then repeated semi-preparative HPLC (eluted with CH₃CN-H₂O, gradient from 50:50 to 80:20) to yield **KSY38** (2.7 mg).

Serial number	Name	Structure
КСҮ03	Actein	HO OH HO OH
KCY04	23- <i>epi</i> -26-deoxyactein	HO OH HO OH
KCY05	26-methylacteinol	HO LINE COLLAR

The names and chemical structures of compounds isolated from Cimicifuga

КСҮОб	24- <i>O</i> -acetyl-25-anhydroshengman ol-3- <i>O-в</i> -D-xylopyranoside	
KCY08	cimigenol-3- <i>O-8</i> -D-xylopyranoside	HO OH HO OH
KCY14	25- <i>О</i> -acetylcimigenol-3- <i>О-в</i> -D-xyl opyranoside	HO OAC
KCY31	Cimicifugoside H1	
KCY37	15α-hydrofoetidol-3- <i>Ο-ϐ</i> -D-xylopy ranoside	HO HO OH HO OH HO OH
KCY44	12 <i>в-О</i> -acetyl-25-anhydrocimigeno l-3- <i>О-в</i> -D-xylopyranoside	
KCY49	25-chlorodeoxycimigenol-3- <i>O-6</i> -D -xylopyranoside	
KHF06	24-O-acetylhydroshengmanol-3-O -β-D-xylopyranoside	
KHF07	23-O-acetylshengmanol-3-O-B-D-x ylopyranoside	

		•
KHF08	Cimiaceroside B	HO OH
KHF13	12 <i>6</i> -hydroxycimigenol-3- <i>О-6</i> -D-xyl opyranoside	
KHF16	24- <i>O</i> -acetylisodahurinol-3- <i>О-в</i> -D- xylopyranoside	
KHF17	12 <i>в</i> ,25- <i>О</i> -diacetylcimigenol-3- <i>О-в</i> -D-xylopyranoside	
KHF18	Asiaticoside A	HO OH HO OH
KHF21	26-deoxyacteinol	HO HO
KHF22	Acteinol	HO TO OH
KHF24	4′,25- <i>O</i> -diacetylcimigenol-3- <i>O</i> -β-D -xylopyranoside	
KHF27	12 <i>в-О</i> -acetylcimigenol	

KHF29	2'-O-(E)-2-butenoyl-25-O-acetylcim igenol-3-O-β-D-xylopyanoside	
KHF30	3'-O-acetylactein	HO O OH ACO OH
KHF38	cimigenol-3- <i>Ο-α</i> -L-arabinoside	
KHF41	3'-O-acetyl-23- <i>epi</i> -26-deoxyactein	HO CO CH
KHF51	2′,25- <i>O</i> -diacetylcimigenol-3- <i>O-в</i> -D-x ylopyranosid	
КҮҮО4	2'-O-acetylcimigenol-3-O-α-L-arabi noside	
КҮҮО8	2',24- <i>O</i> -diacetylisodahurinol-3- <i>O</i> - α -L-arabinoside	
КҮҮ11	12 <i>6</i> -hydroxy-25-anhydrocimigeno	HO OH

КҮҮ14	Isodahurinol	HO TO H
KYY18	25-anhydrocimigenol-3- <i>Ο-α</i> -L-ara binopyranoside	
КҮҮ20	25- <i>O</i> -acetylcimigenol-3- <i>O</i> -α-L-ara binoside	
KYY27	Cimiracemonol B	HO TO THE REPORT OF
КҮҮЗЗ	2',24- <i>O</i> -diacetoxy-25-anhydroshe ngmanol-3- <i>O</i> -α-L-arabinopyranosi de	HO OH HO OH OH
КҮҮ41	4',23- <i>O</i> -diacetylshengmanol-3- <i>O</i> - α-L-arabinopyranoside	
KYY15	24- <i>O</i> -acetylisodahurinol-3- <i>O</i> -α-L-a rabinoside	

KYY56	23- <i>O</i> -acetylshengmanol-3- <i>O</i> -α-L-a rabinopyranoside	H H H H H
KXG42	Acerinol	О ОН
KXG106	2'-O-(E)-2-butenoylcimigenol-3-O- α-L-arabinopyranoside	
KXG113	3',25- <i>O</i> -diacetylcimigenol-3- <i>O</i> -α-L-a rabinopyranoside	H H H H H H H H H H H H H H H H H H H
KXG115	4',25- <i>O</i> -diacetylcimigenol-3-O-α-L-a rabinopyranoside	
KSY38	2',4'-O-diacetylcimigenol-3-O-α-L-a rabinopyranoside	

SUPPLEMENTARY Figure Legend

Figure S1. KHF16 decreases the protein expression levels of multiple cell

cycle and apoptosis regulators in MDA-MB-468 and SW527

The legend is same with Figure 5. The quantification data is listed below each band.

Figure S2.. KHF16 blocks the TNF α -induced NF- κ B signaling pathway and

anti-apoptosis protein expression in MDA-MB-468 and SW527

The legend is same with Figure 6. The quantification data is listed below each band.

Figure S3. ReIA knockdown reduces the efficacy of KHF16 in MDA-MB-468 and SW527

- A. RelA was knocked down in MDA-MB-468 as measured by WB. RelA siRNA pool contains two target sequences: #1:
 5'-GCCCUAUCCCUUUACGUCAdTdT-3', #2:
 5'-UCCAGUGUGUGAAGAAGCGdTdT-3'.
- B. ReIA was silenced in MDA-MB-468 for 24 h. The cells were treated with KHF16 (10 or 20 μ M) for 24 h. The cell viability was measured by the Sulforhodamine B (SRB) assay. *P < 0.05 (Student's t-test).
- C. RelA was silenced in MDA-MB-468 for 24 h. The cell viability was measured after the cells were treated with KHF16 KHF16 (10 μ M) for 8 or 24 h.
- D. RelA was knocked down in SW527 as measured by WB.
- E. RelA was silenced in SW527 for 24 h. The cell viability was measured after the cells were treated with KHF16 (10 or 20 μ M) for 24 h.
- F. RelA was silenced in SW527 for 24 h. The cell viability was measured after the cells were treated with KHF16 (10 μ M) for 8 or 24 h.

Figure S4. KHF16 is not toxic to mouse splenocytes but inhibits the NF- κ B pathway dependent immune response

A. KHF16 is not toxic to mouse splenocytes. Cell viability of mouse splenocytes were performed with the Cell Counting Kit-8 (Dojindo) according to the manufacturer's guidelines after the cells were treated with KHF16 (5-20 μM for 4-24 h). FVB mice were maintained in a specific pathogen–free facility, and all animal experiments were conducted in accordance with protocols approved by the Institutional Animal Care and Use Committee of Kunming Institute of Zoology. Primary splenocytes were isolated from the spleen of

8-week female mice using the mouse 1× Lymphocyte Separation Medium (DKW33-R0100). Blood red cells were deleted using the 1× RBC Lysis Buffer Solution (eBioscience). Splenocytes were cultured in RPMI-1640 medium (Gibco) supplemented with 10% (vol/vol) FBS and 100 U/ml penicillin and 0.1 mg/mL streptomycin (Biological Industries).

B. KHF16 completely blocked the induction of IFN γ by PMA/Ionomycin in mouse splenocytes. SYBR Select Master Mix (Life technologies) and a 7900HT Fast Real-time PCR System (Life Technologies) were used for quantitative RT-PCR. Total RNA was prepared for mouse splenocytes and subjected to qRT-PCR using gene-specific primers: mouse IFN γ forward primer, 5'-GCGTCATTGAATCACACCTG -3'; reverse primer, 5'-TGAGCTCATTGAATGCTTGG -3'); mouse β -actin (forward primer, 5'-AGGTCATTGAATGCTTGG-3'); mouse β -actin (forward primer, 5'-AGGTCATCACTATTGGCAACGA-3'; reverse primer, 5'-CACTTCATGATGGAATTGAATGTAGTT-3'). Mouse splenocytes were treated with or without KHF16 (10 µM) for 4 h. The cells were treated with or without PMA (20 nM) plus ionomycin (1 µM) along with KHF16 (10µM) for 4 h. Total RNA was extracted for qRT-PCR. *P < 0.05 (Student's t-test).

		MD	A-ME	8-468		SW527									
	0	4	8	12	24	0		4	8	12	24	hrs			
PARP	-	-	-	-		-	-	=	=	=	-	-116			
cl-PARP	1.00	1.38	1.92	1.98	3.72	1.0	00	1.51	2.13	2.01	2.48	10000			
cl-Caspase3		Sec.	and the	-	-			-	-	-	-	-19			
	1.00	1.58	1.97	1.80	4.87	1.00)	1.38	1.20	1.11	2.61				
XIAP	-	-	-	-	-	-	-	-	-	-	-	-53			
	1.00	1.59	1.41	1.13	0.96	1.0	0	1.08	0.60	0.51	0.57				
McI-1	-			- 70		_	_			0.50	0.50	-40			
	1.00	0.99	0.96	0.73	0.66	1.0	0	1.08	0.70	0.56	0.50				
Survivin	-	•	-	0.50	0.40				0.00		0.44	-17			
	1.00	0.96	0.66	0.59	0.42	1.00		0.57	0.38	0.32	0.14				
Bcl-XL	-	-	-	-		-	-	-	-	-	-	-30			
	1.00	1.10	1.02	0.89	0.97	1.0	00	1.20	0.96	0.87	0.87				
Cyclin B1	-	**	100	-	-	-	-		-	-	-	-48			
	1.00	0.66	0.81	0.82	1.00	1.0	0	1.17	0.98	1.00	0.90				
Cyclin D1	-	-	-	-	-	-	-	-	-	-		-36			
	1.00	0.94	1.01	0.92	1.03	1.0	0	0.89	0.60	0.60	0.46				
Cyclin E1	-	-	-	-	-	-			-	-	-	-50			
	1.00	1.32	0.99	0.97	1.45	1.0	0	0.85	0.85	0.70	0.58				
p27		-	-		-						-	-27			
	1.00	1.13	1.43	0.94	1.34	1.0	0	1.14	0.97	0.88	1.26				
p21		-	-	-		-	-	-				-21			
-14.000	1.00	1.49	1.08	1.56	2.10	1.0	00	2.59	1.71	1.46	0.83				
p15	_	_	_	_	_	-	_	_	_	_	_	-17			
	1.00	1.17	1.18	1.04	1.37	1.	00	1.24	1.05	1.01	1.15				
												1			
p53	-	-			-	-	_	-	-	-	-	-53			
	1.00	0.99	0.54	0.49 (0.58	1.0	00	1.08	0.97	0.69	0.53				
β-actin	-	-	-	-	1	-	_		_	-	_	-43			

	MD	DA-N	1B-4	68		SW2	257	
5	0	5	10	20	0	5	10	20
PARP	-	-	-	See .	-	-		-
cl-PARP	1.00	1.43	1.61	2.17	1.00	1.33	1.38	2.95
Caspase3	-	-	-	-	-	-	-	
-Caspase3	4.00	4.40			1.00	1.07	-	-
Casnase7	1.00	1.49	1.71	2.93	1.00	1.27	5.03	6.45
-Caspase7				-10250				
easpass, 1	1.00	1.18	1.98	2.20	1.00	1.03	1.03	1.73
Caspase8	-	-	-	-	-	-	-	-
-Caspase8	1.00	1.19	2.81	4.66	1.00	0.96	0.98	2.79
XIAP	-							
7 (0 U I	1.00	1.23	1.01	0.90	1.00	1.16	0.80	0.83
Mol 1			Christe	22240405				
	1.00	1.34	0.99	1.01	1.00	1.36	0.93	0.85
Cumulation	1.00	1.01	0.00	1.01	1.00	1.00	0.00	0.00
Survivin	1.00	1.29	1.08	1.05	1.00	0.90	0.72	0.60
Bal V.						10000		
DCI-XL	1.00	1 14	1 16	1.18	1.00	1.01	1.01	1.06
Quella D4	1.00			1.10		1.01		1.00
Cyclin B1	1.00	0.93	0.93	0.87	1.00	0.97	0.49	0.45
10 0 0210		0.010.00	0.00					
Cyclin D1					-			
	1.00	1.37	1.21	1.17	1.00	0.53	0.28	0.26
Cyclin E1	-	-	-	-	-	-		
	1.00	1.31	1.21	1.10	1.00	0.96	0.65	5 0.55
07								
p27	1.00	1.49	1 1 2	1.04	1.00	1 10	1 30	1.06
	1.00	1.40	1.15	1.04	1.00	1.10	1.55	1.00
p21	-	-	-	-	-	-		
	1.00	1.42	1.61	2.13	1.00	1.08	0.75	0.64
n15						02020		
pro	-	-	-	-	-	_	_	
	1.00	1.21	1.24	1.20	1.00	0.96	0.81	0.84
n52	-	_	_	_	-			
h22	4.00	4.42	4.00	0.00	4.00	0.00	0.70	0.50
	7 1111	1 1 3	1 119	0.98	1.00	0.96	U 12	0.58

Figure S1

В

	MDA-MB-468							SW527																		
KHF16(10µM)	_		-				_		4	ŀ			_									-	ŀ			
TNF-α(10ng/ml)	0	5	15	30	60	120	0	5	15	30	60	120	()	5	15	30	60	120	0	5	15	30	60	120	min
p-IKKa(ser176)	and the second s				-	-		1		-	-	-				-		-	-		-	-	-		-	-85
/IKKp(sel 177)	1.00	1.97	3.40	3.04	1.78	1.80	1.39	1.20	1.12	1.25	0.97	1.38	1.00) 1	.23	3.74	2.54	2.49	2.01	1.74	1.29	1.80	1.90	1.38	1.56	
ΙΚΚα	_	_	_	_	_	_	_	_	_	_	_	-	-		_	_	_	_	_	_	_	_	_	_	_	-85
l	1.00	1.14	1.11	1.24	1.40	1.28	1.51	1.43	1.47	1.40	1.3	9 1.43	1.0	0 0	.95	1.04	0.99	1.13	0.96	0.99	1.01	0.96	1.18	1.00	1.00	,
ικκβ	_	_	_	_	_	_	_	_	_	-	_		-		_	_	-	_	_	_	_	-	_	_	_	-87
· · · ·	1.00	1.05	1.01	1.08	1.20	1.03	1.21	1.10	1.15	1.15	1.08	1.14	1.	00 0	.93	1.07	7 0.95	5 1.09	0.87	0.96	0.94	0.91	1.09	0.87	1.02	1
p-lkBa	-	-	-	-	-	-	1	-	-	-	_	-]. [_		-	-		1000					-39
	1.00	1.54	3.07	2.14	2.98	3.49	1.50	1.76	2.24	1.75	5 1.8	3 2.41	1.0	0 1	.15	1.61	1.19	3.2	2.65	1.09	0.96	0.95	0.98	3 0.99	1.02]
lkBα	-	-	-	_	-	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-]
	1.00	1.05	0.90	0.55	0.56	1.07	0.87	0.85	0.78	0.60	0.5	5 0.99	1	00	0.93	0.59	0.49	0.7	4 0.9	5 0.90	0.89	9 0.81	0.75	5 0.72	0.99	
XIAP	-	_	_	_	_	_	_	_	_	_	_		-			-	-	-			-				-	-54
, , , , ,	1.00	1.23	1.21	1.35	1.48	1.42	1.37	1.37	1.19	1.29	1.04	0.79	1.	00 '	1.53	1.81	1.30	1.3	1.21	1.16	1.30	1.56	1.34	0.98	0.90	1
McI-1	_	-	_	_	_	-	_	_	_	_	_	_	-		_	-	-	-	-	-	-	_	_	_	-	-40
	1.00	1.04	1.03	1.17	1.38	1.20	0.83	0.84	0.79	0.93	0.89	0.74	1.	00	1.06	1.14	0.91	1.18	1.10	0.94	0.75	0.86	0.95	0.84	0.91	1
Survivin	-	-	-	-	-	-	_	_		-				_	_	-	-	-	-	-	-	-	_	-	-	l-17
	1.00	1.40	1.35	1.53	1.97	1.78	1.42	1.15	0.78	0.82	0.39	0.39	1	00	1.20	0.95	5 0.98	3 1.26	1.21	0.95	0.98	0.88	1.07	1.06	0.74	1
Bel-2	-	_	_	_	-	=	_	_	_	_	_	_					-		-	-						-26
2012	1.00	1.35	1.48	1.37	1.41	2.24	2.08	1.78	1.49	2.07	1.46	1.08	1.0	00 1	.06	1.00	1.61	1.39	1.39	1.10	0.91	1.11	0.97	0.86	0.57	20
																										_
RelB	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-		-	-	-	-70
	1.00	1.11	1.23	1.26	1.31	1.44	1.25	1.30	1.32	1.24	1.21	1.46	1	00	0.94	1.03	3 1.00) 1.1	1.16	1.05	5 1.12	2 1.14	1.2	3 1.1	5 1.03	
p-65	-	-	-	-	-	-	-	-	-	-	-	-	-		_	-	-	-	-	-	-	-	_	-	-	-65
, l	1.00	1.09	1.18	1.16	1.16	1.20	1.13	1.16	1.19	1.16	1.07	1.23	1.0	0 1	.02	1.02	0.92	0.96	0.94	0.85	0.92	2 0.9	3 1.05	5 1.01	0.88	1
A20	-	-	-		-	-			-				-		-	_	_	_	-	-	_	_	_	-	-	-85
	1.00	0.95	1.04	1.01	1.58	3 2.89	1.53	0.85	0.83	3 1.0	8 0.8	5 0.60	1.0	0 0	.98	0.83	3 0.98	3 1.28	1.68	1.01	1.10	1.05	1.15	1.02	1.23	1
GAPDH	_	_	_	_	_	_	_	_	_	_	_	_	-	_	_	_	_	_		_	_	_	_	_	_	-39

Β

Α

MDA-MB-468 SW527 KHF16(10µM) + TNF-α(10ng/ml) 0 5 15 30 60 120 0 5 15 30 60 120 0 5 15 30 60 120 0 5 15 30 60 120 min р-ЛК 1.00 0.85 0.72 0.80 1.17 1.45 3.00 3.27 3.08 2.90 3.16 2.96 1.00 1.25 1.36 2.21 1.46 1.44 2.32 2.23 2.02 1.71 2.20 2.46 JNK 🔚 1.00 0.88 0.88 1.11 1.16 0.84 0.82 0.90 0.99 0.99 0.88 0.78 1.00 1.13 1.03 1.02 1.05 1.00 1.11 1.01 1.05 0.96 0.89 0.96 1.00 1.07 1.25 1.34 1.34 1.54 1.53 1.69 1.63 1.69 1.54 1.67 1.00 1.11 1.11 1.27 1.26 1.32 1.24 1.14 1.11 1.12 1.10 0.96 STAT3 _____ 1.00 0.96 0.99 1.05 1.12 0.96 0.86 1.00 0.95 1.04 1.02 0.97 1.00 1.18 1.16 1.25 1.23 1.17 1.27 1.08 1.13 1.12 1.21 1.07 p-AKT ______ -60 1.00 1.02 1.23 1.29 1.17 0.99 0.97 1.13 1.13 1.25 1.02 0.91 AKT -----1.00 1.02 1.16 1.23 1.41 1.29 1.13 1.13 1.22 1.28 1.57 1.20 1.00 1.14 1.03 1.13 1.03 1.00 1.00 0.97 0.97 0.96 0.95 0.97 1.00 0.91 1.03 1.07 1.08 0.84 0.79 0.92 0.93 1.02 0.86 0.83 1.00 1.17 1.31 1.65 1.50 1.31 1.16 1.05 1.37 1.36 1.71 1.35 1.00 0.58 0.69 0.97 1.00 0.89 0.77 0.84 0.84 0.97 0.80 0.88 1.00 0.93 0.95 1.15 1.02 1.04 1.00 0.94 1.05 1.12 1.35 1.19 1.00 0.87 1.06 1.03 1.00 0.77 0.82 1.04 1.08 1.23 0.97 0.96 1.00 1.15 1.50 1.80 1.54 1.31 1.19 1.42 1.70 1.73 1.80 1.31 1.00 0.92 0.98 1.00 0.96 0.87 0.77 0.86 0.90 0.96 0.86 0.85 1.00 1.01 0.86 1.02 0.95 0.97 1.02 0.93 1.21 1.03 1.16 1.00

Figure S2





Figure S4