

Supplementary Table S4: Statistics and source data for the quantitative results.

Figure 3A

Representative experiment			Control	2,5µM 5-Itu	5µM 5-Itu	10µM 5-Itu	2,5µM 5-Itu+TNF	5µM 5-Itu+TNF	10µM 5-Itu+TNF			
	MK2 KO+ MK2	Biol. Replicate 1	95,31	95,28	89,41	87,18	74,77	75,59	65,72			
		Biol. Replicate 2	100,43	93,30	85,11	81,32	75,72	71,80	66,56			
		Biol. Replicate 3	104,27	89,22	84,78	78,88	78,21	73,54	70,75			
	MK2 KO+ vector	Biol. Replicate 1	97,67	88,17	76,83	84,11	43,05	32,26	24,38			
		Biol. Replicate 2	100,72	85,12	80,51	82,65	43,87	30,85	24,77			
		Biol. Replicate 3	101,61	87,83	79,65	76,90	44,21	28,17	24,67			
	p-values (MK2KO+ MK2 vs MK2KO+vector)		1,000000	0,069401	0,018783	0,727071	0,000334	0,000013	0,001233	Statistically Significant values (p<0.01) shaded		
	Experiment 2											
		MK2 KO+ MK2	Biol. Replicate 1	Control	2,5µM 5-Itu	5µM 5-Itu	10µM 5-Itu	2,5µM 5-Itu+TNF	5µM 5-Itu+TNF	10µM 5-Itu+TNF		
Biol. Replicate 2			99,44	91,69	94,81	96,41	84,48	91,94	90,16			
Biol. Replicate 3			104,33	88,06	93,80	86,47	82,12	91,00	99,56			
MK2 KO+ vector		Biol. Replicate 1	96,24	94,17	93,33	84,48	84,88	88,73	89,64			
		Biol. Replicate 2	96,20	84,99	79,72	82,84	72,62	49,99	49,96			
		Biol. Replicate 3	101,36	88,30	78,64	81,84	70,92	55,40	52,67			
p-values (MK2KO+ MK2 vs MK2KO+vector)		1,000000	0,098197	0,000412	0,130062	0,000720	0,000157	0,002180	Statistically Significant values (p<0.01) shaded			
Experiment 3												
		MK2 KO+ MK2	Biol. Replicate 1	Control	2,5µM 5-Itu	5µM 5-Itu	10µM 5-Itu	2,5µM 5-Itu+TNF	5µM 5-Itu+TNF	10µM 5-Itu+TNF		
	Biol. Replicate 2		99,08	86,80	88,95	87,46	88,56	81,40	82,14			
	Biol. Replicate 3		101,06	88,55	88,59	89,94	90,19	80,62	80,16			
	MK2 KO+ vector	Biol. Replicate 1	99,86	88,48	89,10	87,59	88,19	83,16	83,09			
		Biol. Replicate 2	92,65	73,70	74,54	72,67	71,57	33,35	32,36			
		Biol. Replicate 3	90,89	73,65	73,32	72,72	65,77	33,63	30,19			
	p-values (MK2KO+ MK2 vs MK2KO+vector)		0,002495	0,000553	0,000299	0,008789	0,006894	0,000049	0,000009	Statistically Significant values (p<0.01) shaded		

Figure 3B

Representative experiment			Control-6h	5-Itu-6h	Control-24h	5-Itu-24h	
	MK2 KO+ MK2	Biol. Replicate 1	95,67	87,18	95,88	37,04	
		Biol. Replicate 2	100,98	81,32	98,66	39,33	
		Biol. Replicate 3	103,35	78,88	105,46	38,92	
	MK2 KO+ vector	Biol. Replicate 1	98,03	84,11	99,36	33,73	
		Biol. Replicate 2	101,84	82,65	101,01	33,16	
Biol. Replicate 3		100,13	76,90	99,63	32,28		
p-values (MK2KO+ MK2 vs MK2KO+vector)		1,000000	0,727071	1,000000	0,005602	Statistically Significant values (p<0.01) shaded	
Experiment 2			Control-6h	5-Itu-6h	Control-24h	5-Itu-24h	
	MK2 KO+ MK2	Biol. Replicate 1	95,67	94,07	100,24	26,41	
		Biol. Replicate 2	100,98	91,61	99,54	26,83	
		Biol. Replicate 3	103,35	90,52	100,22	27,03	
	MK2 KO+ vector	Biol. Replicate 1	98,03	78,14	100,38	27,08	
		Biol. Replicate 2	101,84	79,32	100,83	26,11	
Biol. Replicate 3		100,13	80,60	98,78	26,64		
p-values (MK2KO+ MK2 vs MK2KO+vector)		1,000000	0,001038	1,000000	0,695566	Statistically Significant values (p<0.01) shaded	
Experiment 3			Control-6h	5-Itu-6h	Control-24h	5-Itu-24h	
	MK2 KO+ MK2	Biol. Replicate 1	99,08	87,46	96,09	33,69	
		Biol. Replicate 2	101,06	89,94	100,88	34,61	
		Biol. Replicate 3	99,86	87,59	103,03	34,19	
	MK2 KO+ vector	Biol. Replicate 1	92,65	72,67	86,44	26,08	
		Biol. Replicate 2	90,89	72,72	84,08	25,32	
Biol. Replicate 3		89,44	65,99	84,45	20,76		
p-values (MK2KO+ MK2 vs MK2KO+vector)		0,002495	0,008789	0,010939	0,023616	Statistically Significant values (p<0.01) shaded	

Figure 3C

Representative experiment			-TNF	+TNF	5-Itu	5-Itu+TNF	ABT702	ABT702+TNF	Gemcitabine	Gemcitabine+TNF	Etoposide	Etoposide+TNF	Doxorubicin	Doxorubicin+TNF	Staurosporine	Staurosporine+TNF
	MK2 KO+ MK2	Biol. Replicate 1	99,50	92,75	91,17	80,92	96,80	90,14	97,80	77,33	94,05	76,83	79,56	66,06	45,46	20,79
		Biol. Replicate 2	107,65	89,41	92,62	81,14	92,38	85,12	103,49	102,29	83,23	80,17	70,31	66,12	45,17	21,50
		Biol. Replicate 3	92,85	97,70	90,21	87,34	98,47	86,75	103,27	90,30	88,31	78,01	74,00	65,76	40,21	20,01
	MK2 KO+ vector	Biol. Replicate 1	88,84	88,93	71,37	56,00	95,29	80,87	98,33	78,31	92,55	67,37	72,80	65,69	45,19	19,98
		Biol. Replicate 2	101,64	91,58	73,63	55,47	92,51	81,46	95,33	75,90	90,90	67,71	77,31	64,11	40,34	18,22
		Biol. Replicate 3	90,15	81,59	85,78	53,25	94,80	87,39	85,13	80,12	86,54	62,61	72,54	55,60	40,56	18,31
p-values (MK2KO+ MK2 vs MK2KO+vector)		0,335681	0,200678	0,081022	0,002099	0,467410	0,191509	0,151841	0,239448	0,710128	0,005753	0,902943	0,313862	0,533718	0,058568	
Experiment 2																
	MK2 KO+ MK2	Biol. Replicate 1	-TNF	+TNF	5-Itu	5-Itu+TNF	ABT702	ABT702+TNF	Gemcitabine	Gemcitabine+TNF	Etoposide	Etoposide+TNF	Doxorubicin	Doxorubicin+TNF	Staurosporine	Staurosporine+TNF
		Biol. Replicate 2	97,79	95,09	94,63	80,55	84,23	102,86	90,78	85,10	93,94	88,81	83,78	50,67	25,20	
		Biol. Replicate 3	100,13	93,34	98,32	80,89	85,19	86,25	104,49	93,66	99,65	89,26	86,32	81,65	55,39	24,93
	MK2 KO+ vector	Biol. Replicate 1	102,08	94,99	91,05	79,06	96,22	84,47	101,61	91,02	91,10	88,88	89,03	87,02	52,13	24,93
		Biol. Replicate 2	97,42	84,49	91,79	42,10	88,20	82,18	95,94	86,50	83,05	85,51	79,07	78,08	47,92	22,60
		Biol. Replicate 3	102,40	88,88	90,94	44,24	90,00	82,49	96,83	84,18	91,45	88,65	86,52	77,90	49,50	21,89
p-values (MK2KO+ MK2 vs MK2KO+vector)		1,000000	0,050503	0,157617	0,000002	0,883674	0,429904	0,032325	0,010766	0,402570	0,138098	0,158803	0,076159	0,102864	0,012610	
Experiment 3																
	MK2 KO+ MK2	Biol. Replicate 1	-TNF	+TNF	5-Itu	5-Itu+TNF	ABT702	ABT702+TNF	Gemcitabine	Gemcitabine+TNF	Etoposide	Etoposide+TNF	Doxorubicin	Doxorubicin+TNF	Staurosporine	Staurosporine+TNF
		Biol. Replicate 2	100,12	101,98	88,83	91,92	97,00	102,86	98,78	106,61	70,58	71,01	88,65	88,36	40,63	20,67
		Biol. Replicate 3	98,36	102,38	92,47	92,13	96,67	94,85	99,31	98,38	68,96	73,56	86,95	85,12	38,66	21,24
	MK2 KO+ vector	Biol. Replicate 1	101,53	102,64	92,11	90,16	94,85	94,34	97,96	97,99	71,64	71,34	88,65	84,76	40,30	20,63
		Biol. Replicate 2	100,24	96,44	81,34	57,16	90,26	94,76	92,47	92,21	60,18	60,39	79,69	86,27	40,45	22,35
		Biol. Replicate 3	99,90	96,20	82,39	56,09	91,59	93,16	94,36	94,43	62,77	62,44	80,33	83,21	39,67	21,76
p-values (MK2KO+ MK2 vs MK2KO+vector)		1,000000	0,000163	0,011139	0,000006	0,005123	0,226766	0,020225	0,097913	0,003904	0,008306	0,002422	0,253213	0,997864	0,019770	
Experiment 4																
	MK2 KO+ MK2	Biol. Replicate 1	-TNF	+TNF	5-Itu	5-Itu+TNF	ABT702	ABT702+TNF	Gemcitabine	Gemcitabine+TNF	Etoposide	Etoposide+TNF	Doxorubicin	Doxorubicin+TNF	Staurosporine	Staurosporine+TNF
		Biol. Replicate 2	100,52	97,75	83,30	82,26	92,01	90,49	94,01	94,71	80,97	86,28	76,68	76,20	44,93	23,06
		99,34	94,54	81,45	81,59	94,36	91,67	94,28	92,41	86,19	85,91	82,65	79,33	47,76	23,13	

Representative Experiment	Control	300 nM	300 nM + 100 nM
Biol. Replicate 1	99.44	90.16	90.22

Representative experiment	Control	BE26/44022	IRS4-VAD	IRS4-VAD+BE26/44022	IRS4-5 (T ₁)	IRS4-5 (T ₁)+BE26/44022
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Condition	F13044022	LP3127ND	LP3127ND7F13044022	LP313110	LP3131107F13044022
Replicate 1	105.14	77.54	100.58	51.66	14.94

Representative experiment	Control	5-ITu	5-ITu+PF3644022	5-ITu+PF3644022+Nec1s	SM+5-ITu	SM+5-ITu+PF3644022	SM+5-ITu+PF3644022+Nec1s
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Biol. Replicate 1	98.34	80.21	74.90	72.62	68.80	50.47	75.43
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p-value (SM+5-ITu+PF3644022 vsSM+5-ITu+PF3644022+Nec1s)										0,0000112		
Experiment 4	RAW 264,7 macrophages	Biol. Replicate 1	Control	5-ITu	5-ITu+ PF3644022	5-ITu+ PF3644022+Nec1s	SM+5-ITu	SM+5-ITu+PF3644022	4H5-ITu+PF3644022+Nec1s			
			101,64	66,13	27,82	40,97	54,14	9,83	34,04			
		Biol. Replicate 2	96,38	62,10	27,18	48,37	52,79	8,15	34,34			
		Biol. Replicate 3	101,98	65,40	33,35	50,21	53,93	8,43	36,09			
p-value (SM+5-ITu vs SM+5-ITu+PF3644022)										0,0000000		Statistically Significant values (p<0.01) shaded
p-value (SM+5-ITu+PF3644022 vsSM+5-ITu+PF3644022+Nec1s)										0,0000090		

Supplementary Figure 2a

Representative experiment	DKO+ MK2	Biol. Replicate 1	Control	2,5µM 5-ITu	5µM 5-ITu	10µM 5-ITu	2,5µM 5-ITu+TNF	5µM 5-ITu+TNF	10µM 5-ITu+TNF								
		Biol. Replicate 2	91,80	101,02	93,42	103,22	108,61	81,87	93,73								
		Biol. Replicate 3	105,41	104,40	102,93	102,65	109,30	94,44	91,81								
		Biol. Replicate 1	102,79	102,13	104,38	102,34	117,12	96,84	92,31								
		Biol. Replicate 2	106,27	104,20	112,23	103,69	83,35	46,61	46,72								
		Biol. Replicate 3	105,50	105,50	105,36	101,72	82,02	46,24	42,46								
	DKO+ vector	Biol. Replicate 1	107,10	102,24	115,95	96,34	77,28	50,04	40,81								
		p-values (DKO+ MK2 vs DKO+vector)	0,269567	0,346878	0,078200	0,430599	0,001327	0,007939	0,000475	Statistically Significant values (p<0.01) shaded							
Experiment 2	DKO+ MK2	Biol. Replicate 1	Control	2,5µM 5-ITu	5µM 5-ITu	10µM 5-ITu	2,5µM 5-ITu+TNF	5µM 5-ITu+TNF	10µM 5-ITu+TNF								
		Biol. Replicate 2	95,74	101,57	96,20	94,02	100,28	92,60	85,81								
		Biol. Replicate 3	99,82	97,48	96,40	95,21	98,72	96,26	86,82								
		Biol. Replicate 1	104,44	94,80	95,64	93,91	96,69	90,06	85,38								
		Biol. Replicate 2	99,60	94,43	97,58	94,09	94,05	76,33	62,97								
		Biol. Replicate 3	101,49	96,48	96,96	89,10	83,76	75,66	61,16								
	DKO+ vector	Biol. Replicate 1	98,91	99,01	96,48	91,99	82,24	72,73	56,12								
		p-values (DKO+ MK2 vs DKO+vector)	1,000000	0,614365	0,084126	0,202432	0,075665	0,002257	0,004688	Statistically Significant values (p<0.01) shaded							
Experiment 3	DKO+ MK2	Biol. Replicate 1	Control	2,5µM 5-ITu	5µM 5-ITu	10µM 5-ITu	2,5µM 5-ITu+TNF	5µM 5-ITu+TNF	10µM 5-ITu+TNF								
		Biol. Replicate 2	102,17	91,95	97,16	87,27	96,08	88,39	80,06								
		Biol. Replicate 3	98,12	94,12	99,64	85,89	91,39	86,19	75,40								
		Biol. Replicate 1	99,71	92,77	101,07	86,46	91,18	88,06	75,38								
		Biol. Replicate 2	96,00	91,35	100,27	84,31	79,04	60,13	51,25								
		Biol. Replicate 3	104,09	94,25	94,07	85,34	78,55	64,11	52,00								
	DKO+ vector	Biol. Replicate 1	99,92	88,77	92,78	82,11	77,74	62,31	52,82								
		p-values (DKO+ MK2 vs DKO+vector)	1,000000	0,454594	0,260824	0,094940	0,009095	0,000192	0,002114	Statistically Significant values (p<0.01) shaded							

Supplementary Figure 2b

Representative experiment											
Experiment 1	DKO+ MK2	Biol. Replicate 1	Control-6h	5-ITu-6h	Control-24h	5-ITu-24h					
			91,80	103,22	94,92	21,85					
			105,41	102,65	103,20	20,88					
			102,79	102,34	101,87	20,68					
	DKO+ vector	Biol. Replicate 1	106,27	103,69	102,66	20,43					
			105,50	101,72	98,83	21,21					
			107,10	96,34	98,51	19,81					
			p-values (DKO+ MK2 vs DKO+vector)		0,269567	0,430599	1,000000	0,296533	Statistically Significant values (p<0.01) shaded		
Experiment 2	DKO+ MK2	Biol. Replicate 1	Control-6h	5-ITu-6h	Control-24h	5-ITu-24h					
			102,17	87,27	97,66	19,72					
			98,12	85,89	100,30	19,18					
			99,71	86,46	102,04	18,49					
	DKO+ vector	Biol. Replicate 1	96,00	84,31	98,77	27,27					
			104,09	85,34	102,62	26,68					
			99,92	82,11	98,61	26,79					
			p-values (DKO+ MK2 vs DKO+vector)		1,000000	0,094940	1,000000	0,000310	Statistically Significant values (p<0.01) shaded		

Supplementary Figure 2c

Representative experiment																			
Experiment 1	DKO+ MK2	Biol. Replicate 1	Control	TNF	5-4Tu	5-4Tu+TNF	ABT702	ABT702+TNF	Gemcitabine	Gemcitabine+TNF	Etoposide	Etoposide+TNF	Doxorubicin	Doxorubicin+TNF	Staurosporine	Staurosporine+TNF			
			97.510	99.41	95.60	91.16	107.13	95.601	106.99	85.81	71.82	57.58	89.93	79.83	49.08	27.42			
			101.036	97.04	95.89	91.70	105.79	95.267	103.27	86.05	69.53	57.27	86.05	82.26	46.23	27.72			
			101.454	99.41	95.05	95.31	101.73	101.425	104.99	86.49	68.92	57.43	86.78	47.84	28.16				
			99.90	96.35	97.76	64.06	90.46	101.99	94.07	84.81	70.41	51.26	89.88	90.60	49.094	32.77			
	DKO+ vector	Biol. Replicate 2	100.85	99.89	96.82	59.86	90.05	98.54	95.87	89.37	69.48	50.99	88.33	91.96	48.536	32.64			
			Biol. Replicate 3	99.25	101.03	97.45	59.91	90.18	96.49	89.00	86.68	68.65	48.82	89.73	87.53	49.580	32.07		
				p-values (DKO+ MK2 vs DKO+vector)		1.000000	0.789499	0.008126	0.000132	0.011695	0.572658	0.013497	0.594908	0.607559	0.010019	0.455449	0.087453	0.237406	0.000100
			Experiment 2	DKO+ MK2	Biol. Replicate 1	Control	TNF	5-4Tu	5-4Tu+TNF	ABT702	ABT702+TNF	Gemcitabine	Gemcitabine+TNF	Etoposide	Etoposide+TNF	Doxorubicin	Doxorubicin+TNF	Staurosporine	Staurosporine+TNF
95.88	93.82	91.80				92.44	92.82	100.34	90.38	81.17	77.37	72.45	81.83	81.39	43.48	26.24			
100.63	93.18	92.68				87.31	104.74	97.34	99.27	94.62	75.91	70.20	81.33	78.69	44.17	25.92			
103.50	94.17	95.79				88.89	105.63	95.78	100.07	85.35	76.90	71.81	83.28	80.71	44.87	25.91			
101.58	99.51	95.61				63.33	96.57	100.41	85.81	88.64	72.16	58.76	81.88	80.06	48.79	29.01			
DKO+ vector	Biol. Replicate 2	100.26		101.79	89.01	62.76	96.40	99.18	88.25	89.53	75.47	58.63	88.08	82.03	48.13	29.59			
		Biol. Replicate 3		98.16	99.77	96.01	57.11	99.63	99.88	92.90	88.30	75.91	59.55	88.20	81.43	49.60	29.47		
				p-values (DKO+ MK2 vs DKO+vector)		1.000000	0.005403	0.965605	0.000484	0.485982	0.270876	0.122257	0.698447	0.193627	0.000757	0.196120	0.421461	0.001361	0.000156

Supplementary Figure 2d

Representative experiment											
Experiment 1				Control	5-ITu+TNF	5-ITu+TNF+Nec1s					
		DKO+ MK2	Biol. Replicate 1	102,17	80,06	86,57					
			Biol. Replicate 2	98,12	75,40	83,05					
			Biol. Replicate 3	99,71	75,38	84,75					
		DKO+ vector	Biol. Replicate 1	96,00	51,25	76,47					
			Biol. Replicate 2	104,09	52,00	74,34					
			Biol. Replicate 3	99,92	52,82	71,27					
			p-values (5-ITu +TNF-DKO+MK2 vs 5-ITu +TNF-DKO+vector)		0,0021143		Statistically Significant values (p<0.01) shaded				
			p-values (5-ITu +TNF-DKO+MK2 vs 5-ITu +TNF+Nec1s-DKO+vector)			0,002542					
Experiment 2				Control	5-ITu+TNF	5-ITu+TNF+Nec1s					
		DKO+ MK2	Biol. Replicate 1	94,05	80,88	95,99					
			Biol. Replicate 2	104,13	88,09	93,14					
			Biol. Replicate 3	101,82	87,39	95,34					

		Biol. Replicate 1	98,15	44,52	83,71				
		Biol. Replicate 2	103,12	42,44	77,81				
		Biol. Replicate 3	98,73	43,03	71,43				
	p-values (S-ITu +TNF-DKO+MK2 vs S-ITu +TNF-DKO+vector)			0,0016968		Statistically Significant values (p<0.01) shaded			
	p-values (S-ITu +TNF-DKO+MK2 vs S-ITu +TNF+Nec1s-DKO+vector)				0,008911				