SUPPORTING INFORMATION

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An Approach to Investigate Intracellular Protein Network Responses

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Figure S1. Normalized radiality dose-response curves for AKT, HSP27, IKBa, p53, and p90RSK. Radiality parameters are normalized to the sum of radiality parameters for all measured proteins.

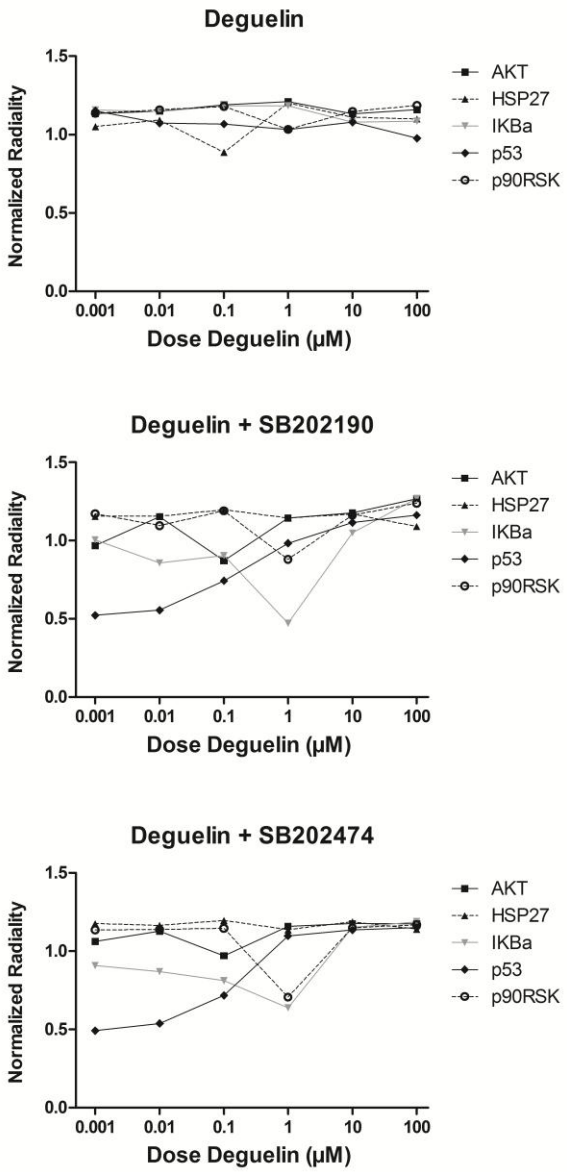

Table S1. Euclidean distances between all possible protein pairs calculated from the phosphorylation responses of cells exposed to increasing doses of deguelin.

Dose Deguelin																	
0.001 μM			0.01 μM			0.1 μM			1 μM			10 μM			100 μM		
Node 1	Node 2	Distance	Node 1	Node 2	Distance	Node 1	Node 2	Distance	Node 1	Node 2	Distance	Node 1	Node 2	Distance	Node 1	Node 2	Distance
p90RSK	ERK1/2	4.5	p53	HSP27	10.9	IKBa	AKT	18.2	HSP27	JNK	1.5	p53	IKBa	4.0	p90RSK	AKT	26.6
p53	AKT	12.8	p90RSK	AKT	11.2	p90RSK	IKBa	20.0	IKBa	HSP27	13.3	HSP27	ERK1/2	11.2	IKBa	AKT	28.2
p53	IKBa	15.7	p90RSK	IKBa	11.4	p90RSK	AKT	22.6	IKBa	JNK	13.4	p90RSK	AKT	19.7	p53	IKBa	30.2
IKBa	ERK1/2	23.3	IKBa	AKT	19.7	p90RSK	ERK1/2	48.4	p38	ERK1/2	14.8	IKBa	AKT	27.4	p90RSK	IKBa	53.6
p90RSK	IKBa	27.8	ERK1/2	AKT	19.8	IKBa	ERK1/2	61.2	JNK	AKT	30.3	p53	AKT	27.6	p53	AKT	56.6
IKBa	AKT	28.5	p90RSK	ERK1/2	30.9	p53	HSP27	66.2	HSP27	AKT	31.8	JNK	ERK1/2	37.4	p90RSK	p53	79.2
p53	ERK1/2	37.7	IKBa	ERK1/2	39.0	ERK1/2	AKT	70.9	IKBa	AKT	35.6	HSP27	JNK	37.7	p38	ERK1/2	82.6
p90RSK	p53	42.1	p53	p38	61.6	p53	p38	79.8	p53	IKBa	36.2	p90RSK	IKBa	46.3	HSP27	JNK	92.2
ERK1/2	AKT	50.1	HSP27	p38	72.4	p53	AKT	97.8	p53	HSP27	45.4	p90RSK	p53	47.0	p90RSK	JNK	92.8
p90RSK	AKT	54.4	p90RSK	HSP27	83.0	HSP27	p38	112.3	p53	JNK	46.4	p90RSK	JNK	55.5	JNK	AKT	107.1
p53	HSP27	75.5	IKBa	HSP27	84.3	p53	IKBa	112.5	p53	AKT	71.6	p90RSK	ERK1/2	66.4	HSP27	ERK1/2	111.8
HSP27	AKT	76.7	HSP27	AKT	92.4	p90RSK	p53	119.5	p90RSK	AKT	120.6	JNK	AKT	67.8	p90RSK	HSP27	124.5
IKBa	HSP27	77.0	p90RSK	p53	93.1	p38	AKT	129.0	p90RSK	ERK1/2	144.7	p90RSK	HSP27	75.2	IKBa	JNK	132.7
HSP27	p38	93.0	p53	IKBa	94.0	IKBa	p38	134.2	p90RSK	JNK	150.4	ERK1/2	AKT	84.7	HSP27	AKT	150.1
HSP27	ERK1/2	94.0	p53	AKT	102.8	p90RSK	p38	150.5	p90RSK	HSP27	151.9	p53	JNK	92.5	p53	JNK	162.7
p90RSK	HSP27	97.7	HSP27	ERK1/2	108.1	HSP27	AKT	163.1	p90RSK	IKBa	155.7	HSP27	AKT	92.8	IKBa	HSP27	178.0
IKBa	p38	162.4	p53	ERK1/2	118.8	p53	ERK1/2	167.7	p90RSK	p38	159.3	IKBa	JNK	93.6	JNK	ERK1/2	179.4
p53	p38	165.2	IKBa	p38	150.8	IKBa	HSP27	178.5	p90RSK	p53	190.5	IKBa	ERK1/2	112.1	HSP27	p38	186.6
p38	AKT	168.6	p90RSK	p38	152.0	p90RSK	HSP27	184.0	ERK1/2	AKT	265.0	p53	ERK1/2	112.2	p53	HSP27	203.0
p38	ERK1/2	172.6	p38	AKT	162.3	p38	ERK1/2	195.3	p38	AKT	279.5	p53	HSP27	120.0	p38	JNK	233.6
p90RSK	p38	175.1	p38	ERK1/2	179.3	JNK	ERK1/2	214.5	JNK	ERK1/2	294.6	IKBa	HSP27	120.2	p90RSK	ERK1/2	235.5
p90RSK	JNK	314.8	JNK	ERK1/2	289.6	HSP27	ERK1/2	231.7	HSP27	ERK1/2	296.0	HSP27	p38	312.6	ERK1/2	AKT	260.5
JNK	ERK1/2	316.9	JNK	AKT	307.9	p90RSK	JNK	262.8	IKBa	ERK1/2	300.3	p38	ERK1/2	320.2	IKBa	ERK1/2	288.6
p53	JNK	327.0	p90RSK	JNK	318.9	IKBa	JNK	274.8	p38	JNK	309.0	p38	JNK	345.1	p90RSK	p38	305.1
IKBa	JNK	327.2	IKBa	JNK	323.1	JNK	AKT	285.3	HSP27	p38	310.4	p90RSK	p38	386.2	p53	ERK1/2	314.5
JNK	AKT	327.4	HSP27	JNK	396.1	p53	JNK	381.0	IKBa	p38	314.9	p38	AKT	404.8	p38	AKT	328.2
HSP27	JNK	402.4	p53	JNK	407.0	p38	JNK	406.5	p53	ERK1/2	335.2	IKBa	p38	432.2	IKBa	p38	356.4
p38	JNK	489.0	p38	JNK	468.3	HSP27	JNK	442.6	p53	p38	349.8	p53	p38	432.3	p53	p38	384.1

Table S2. Euclidean distances between all possible protein pairs calculated from the phosphorylation responses of cells exposed to increasing doses of deguelin in combination with 350 nM SB202190.

Dose Deguelin																	
0.001 μM			0.01 μM			0.1 μM			1 μM			10 μM			100 μM		
Node 1	Node 2	Distance	Node 1	Node 2	Distance	Node 1	Node 2	Distance	Node 1	Node 2	Distance	Node 1	Node 2	Distance	Node 1	Node 2	Distance
p90RSK	JNK	6.3	p90RSK	AKT	27.5	p90RSK	HSP27	27.0	JNK	AKT	18.3	p90RSK	HSP27	26.6	p90RSK	IKBa	16.5
IKBa	p38	39.2	JNK	AKT	27.7	IKBa	p38	32.9	HSP27	JNK	26.6	p53	IKBa	27.8	p90RSK	p53	29.4
IKBa	ERK1/2	53.2	HSP27	JNK	33.8	p53	AKT	49.9	HSP27	AKT	42.8	HSP27	AKT	38.6	p53	IKBa	35.7
HSP27	JNK	66.4	IKBa	p38	40.4	p90RSK	JNK	52.4	HSP27	p38	60.4	p90RSK	AKT	50.8	IKBa	AKT	38.2
p90RSK	HSP27	67.2	p38	ERK1/2	51.6	HSP27	JNK	53.3	p38	JNK	69.7	p53	AKT	50.8	p38	ERK1/2	45.0
HSP27	ERK1/2	67.4	p90RSK	JNK	55.1	IKBa	ERK1/2	61.1	p90RSK	ERK1/2	70.8	p90RSK	p38	59.9	p90RSK	AKT	53.1
p38	ERK1/2	91.8	HSP27	AKT	60.0	p38	ERK1/2	80.1	p38	AKT	70.9	IKBa	JNK	71.8	p53	AKT	72.3
p90RSK	AKT	95.5	IKBa	ERK1/2	78.3	JNK	ERK1/2	109.2	p53	ERK1/2	81.5	HSP27	p38	74.6	HSP27	AKT	78.2
JNK	AKT	99.8	p90RSK	HSP27	86.2	p90RSK	AKT	113.7	p90RSK	p53	87.2	IKBa	AKT	78.2	p90RSK	JNK	86.4
JNK	ERK1/2	104.3	HSP27	ERK1/2	119.4	HSP27	AKT	129.0	p38	ERK1/2	93.6	p53	JNK	83.0	IKBa	HSP27	97.2
p90RSK	ERK1/2	108.8	JNK	ERK1/2	134.8	HSP27	ERK1/2	138.5	p53	p38	111.0	p53	HSP27	86.5	IKBa	JNK	100.7
IKBa	HSP27	112.3	ERK1/2	AKT	159.2	p90RSK	p53	144.9	ERK1/2	AKT	143.9	p90RSK	p53	101.6	p53	JNK	102.1
p53	AKT	137.3	p90RSK	p53	163.8	p90RSK	ERK1/2	153.9	HSP27	ERK1/2	151.4	p38	AKT	109.3	p53	HSP27	112.5
HSP27	p38	145.5	HSP27	p38	170.9	IKBa	JNK	163.8	JNK	ERK1/2	151.8	JNK	AKT	111.9	p90RSK	HSP27	112.9
HSP27	AKT	156.3	p90RSK	ERK1/2	185.5	JNK	AKT	164.7	p90RSK	p38	158.1	IKBa	HSP27	114.2	JNK	AKT	125.1
IKBa	JNK	157.4	p38	JNK	185.5	p53	HSP27	165.6	p53	HSP27	167.8	p90RSK	IKBa	128.8	HSP27	JNK	197.3
p90RSK	IKBa	161.7	p53	AKT	190.9	p38	JNK	188.5	p53	JNK	180.6	HSP27	JNK	149.6	HSP27	p38	221.7
p38	JNK	195.4	IKBa	HSP27	191.5	p53	JNK	190.9	p53	AKT	180.8	p90RSK	JNK	152.0	p38	AKT	236.3
p90RSK	p38	199.4	p38	AKT	209.1	IKBa	HSP27	198.6	p90RSK	AKT	214.4	p53	p38	159.7	HSP27	ERK1/2	246.0
ERK1/2	AKT	204.1	IKBa	JNK	211.2	p90RSK	IKBa	212.1	p90RSK	HSP27	218.1	IKBa	p38	187.3	ERK1/2	AKT	246.9
p90RSK	p53	232.4	p53	JNK	217.9	HSP27	p38	217.8	p90RSK	JNK	221.3	p38	JNK	210.8	IKBa	p38	274.5
p53	JNK	237.0	p90RSK	p38	234.7	p90RSK	p38	234.0	IKBa	JNK	222.9	p38	ERK1/2	231.8	IKBa	ERK1/2	284.8
IKBa	AKT	257.1	IKBa	AKT	236.6	ERK1/2	AKT	266.6	IKBa	AKT	227.2	p90RSK	ERK1/2	289.9	p90RSK	p38	289.0
p53	HSP27	289.2	p53	HSP27	245.3	p53	ERK1/2	298.2	IKBa	HSP27	234.8	HSP27	ERK1/2	306.3	p90RSK	ERK1/2	298.0
p38	AKT	294.8	p90RSK	IKBa	263.3	IKBa	AKT	325.5	IKBa	p38	292.1	ERK1/2	AKT	340.4	p53	p38	307.0
p53	ERK1/2	341.2	p53	ERK1/2	348.6	p38	AKT	346.4	IKBa	ERK1/2	370.6	p53	ERK1/2	391.1	p53	ERK1/2	319.2
p53	IKBa	394.0	p53	p38	396.6	p53	IKBa	354.6	p53	IKBa	402.3	IKBa	ERK1/2	418.6	JNK	ERK1/2	339.2
p53	p38	431.2	p53	IKBa	426.7	p53	p38	378.2	p90RSK	IKBa	441.3	JNK	ERK1/2	431.9	p38	JNK	340.6

Table S3. Euclidean distances between all possible protein pairs calculated from the phosphorylation responses of cells exposed to increasing doses of deguelin in combination with 34 nM SB202474.

Dose Deguelin																	
0.001 μM			0.01 μM			0.1 μM			1 μM			10 μM			100 μM		
Node 1	Node 2	Distance	Node 1	Node 2	Distance	Node 1	Node 2	Distance	Node 1	Node 2	Distance	Node 1	Node 2	Distance	Node 1	Node 2	Distance
p90RSK	AKT	36.5	p90RSK	AKT	16.6	IKBa	p38	33.3	JNK	AKT	20.0	p53	IKBa	4.9	p53	HSP27	11.4
p90RSK	JNK	36.9	IKBa	p38	28.4	p38	ERK1/2	58.5	p38	JNK	39.1	IKBa	AKT	14.5	IKBa	AKT	19.0
HSP27	JNK	37.0	JNK	AKT	32.1	p90RSK	HSP27	62.6	p38	AKT	48.1	p53	AKT	18.7	p90RSK	p53	21.8
p38	ERK1/2	52.0	p90RSK	JNK	41.9	HSP27	JNK	67.3	HSP27	AKT	50.7	JNK	AKT	25.6	p90RSK	IKBa	26.7
IKBa	p38	54.9	p38	ERK1/2	57.0	p90RSK	AKT	68.1	p53	ERK1/2	63.1	IKBa	JNK	27.0	p38	AKT	28.1
IKBa	ERK1/2	58.5	p90RSK	HSP27	73.7	p90RSK	JNK	79.0	HSP27	JNK	70.7	HSP27	AKT	27.8	p90RSK	HSP27	31.7
JNK	AKT	70.4	HSP27	JNK	78.0	p53	AKT	80.5	p53	HSP27	84.7	HSP27	JNK	30.0	p53	IKBa	45.2
p90RSK	HSP27	72.5	HSP27	ERK1/2	81.2	IKBa	ERK1/2	91.8	HSP27	p38	89.0	p53	JNK	31.1	p90RSK	AKT	45.5
HSP27	ERK1/2	91.3	IKBa	ERK1/2	82.0	HSP27	ERK1/2	107.1	p90RSK	ERK1/2	106.3	p90RSK	HSP27	36.4	IKBa	p38	47.0
HSP27	AKT	107.3	HSP27	AKT	84.0	HSP27	AKT	128.9	p53	AKT	117.2	IKBa	HSP27	40.8	IKBa	HSP27	51.9
HSP27	p38	121.4	HSP27	p38	136.6	JNK	ERK1/2	136.3	p53	p38	125.6	p53	HSP27	45.6	p53	AKT	63.9
JNK	ERK1/2	127.8	p90RSK	ERK1/2	153.8	p90RSK	p53	136.7	p53	JNK	133.2	p90RSK	AKT	62.3	HSP27	AKT	69.9
IKBa	HSP27	149.5	JNK	ERK1/2	157.1	JNK	AKT	139.9	HSP27	ERK1/2	144.8	p90RSK	JNK	65.0	p90RSK	p38	73.2
p38	JNK	157.7	IKBa	HSP27	162.9	HSP27	p38	164.7	p38	ERK1/2	160.1	p90RSK	IKBa	76.3	p53	p38	92.0
p90RSK	ERK1/2	160.9	ERK1/2	AKT	165.1	p90RSK	ERK1/2	169.6	p90RSK	p53	164.6	p90RSK	p53	80.9	HSP27	p38	97.8
p53	AKT	178.2	p53	AKT	187.7	p38	JNK	184.0	ERK1/2	AKT	167.4	p90RSK	p38	147.4	HSP27	JNK	120.3
IKBa	JNK	186.2	p53	JNK	189.7	p53	JNK	188.0	JNK	ERK1/2	179.6	p38	ERK1/2	168.4	p53	JNK	129.9
p90RSK	p38	193.9	p90RSK	p53	203.0	IKBa	HSP27	197.9	IKBa	JNK	184.2	HSP27	p38	183.5	IKBa	JNK	137.3
ERK1/2	AKT	197.0	p90RSK	p38	207.2	p53	HSP27	199.1	IKBa	AKT	193.4	p38	AKT	209.6	p90RSK	JNK	140.0
p90RSK	p53	214.4	p38	JNK	213.6	IKBa	JNK	214.7	IKBa	p38	216.0	p38	JNK	209.9	JNK	AKT	141.3
p90RSK	IKBa	219.4	p38	AKT	219.6	p90RSK	p38	226.7	IKBa	HSP27	222.9	IKBa	p38	223.7	p38	JNK	154.5
p38	AKT	228.1	p90RSK	IKBa	234.5	ERK1/2	AKT	235.7	p90RSK	HSP27	249.0	p53	p38	228.3	JNK	ERK1/2	328.7
p53	JNK	244.3	IKBa	JNK	239.1	p90RSK	IKBa	259.8	p90RSK	p38	263.0	p90RSK	ERK1/2	315.1	p38	ERK1/2	336.1
IKBa	AKT	255.5	IKBa	AKT	246.5	p38	AKT	293.5	p90RSK	AKT	273.6	HSP27	ERK1/2	350.8	ERK1/2	AKT	355.1
p53	HSP27	280.7	p53	HSP27	267.0	p53	ERK1/2	305.4	p90RSK	JNK	285.4	JNK	ERK1/2	375.7	IKBa	ERK1/2	370.2
p53	ERK1/2	371.9	p53	ERK1/2	346.8	IKBa	AKT	326.8	p53	IKBa	305.9	ERK1/2	AKT	377.5	p90RSK	ERK1/2	394.0
p53	p38	395.7	p53	p38	403.3	p53	p38	361.2	IKBa	ERK1/2	360.5	IKBa	ERK1/2	391.3	HSP27	ERK1/2	400.3
p53	IKBa	430.1	p53	IKBa	428.8	p53	IKBa	394.0	p90RSK	IKBa	466.8	p53	ERK1/2	396.0	p53	ERK1/2	402.4