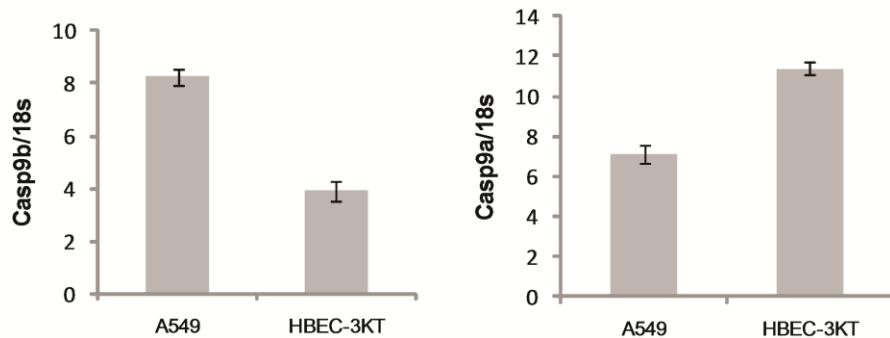


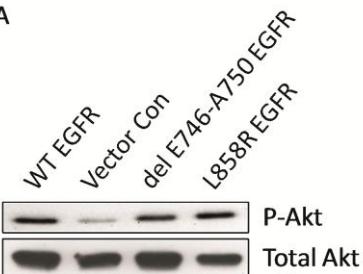
**Shultz et al.**  
**Supplemental Figure 1.**



**Shultz et al.**

**Supplemental Figure 2.**

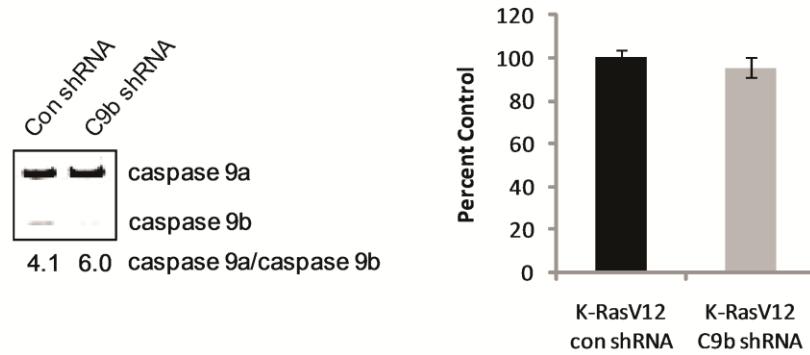
**A**



**B**

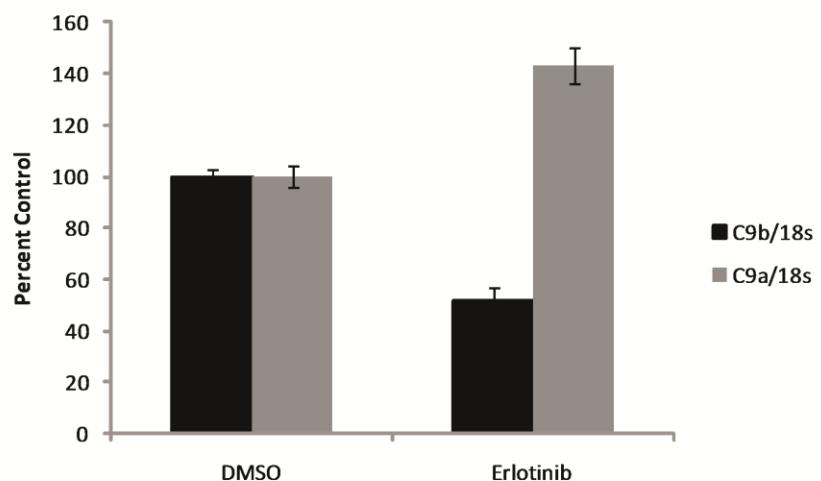


**Shultz et al.**  
**Supplemental Figure 3.**

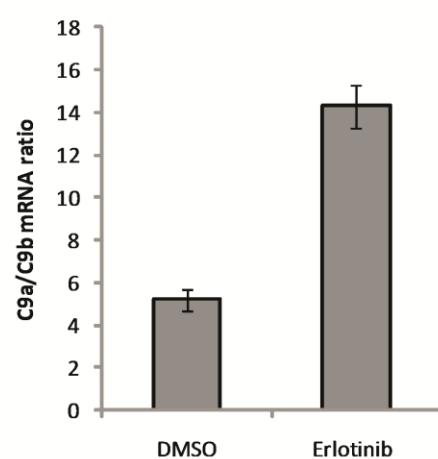


**Shultz et al.**  
**Supplemental Figure 4.**

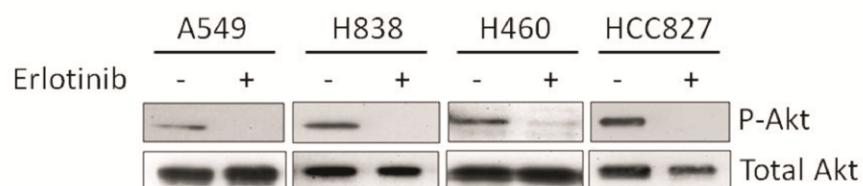
**A**



**B**

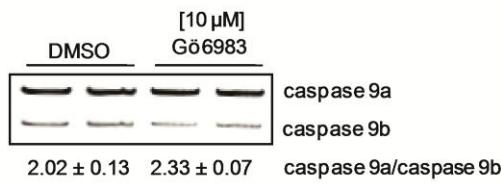


**C**

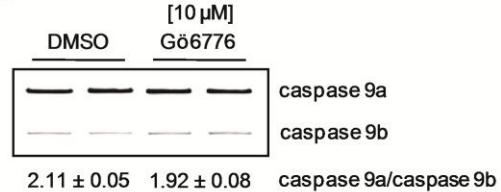


**Shultz et al.**  
**Supplemental Figure 5.**

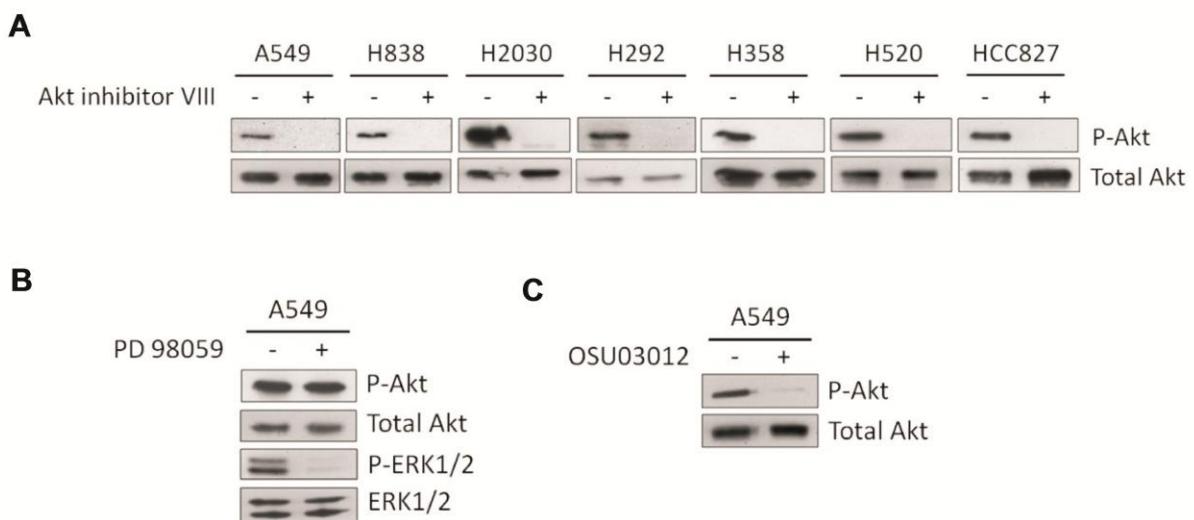
**A**



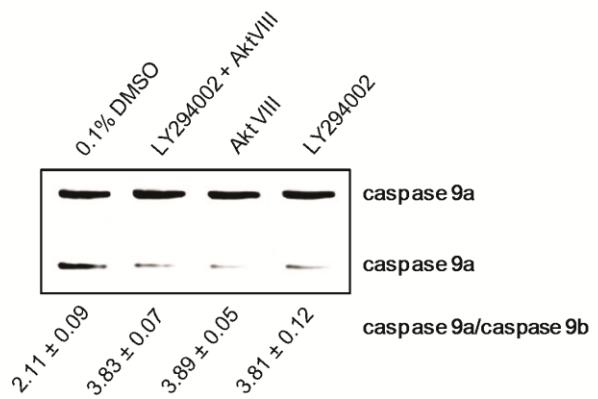
**B**



**Shultz et al.**  
**Supplemental Figure 6.**

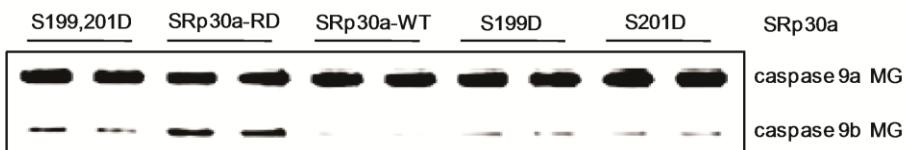


**Shultz et al.**  
**Supplemental Figure 7.**

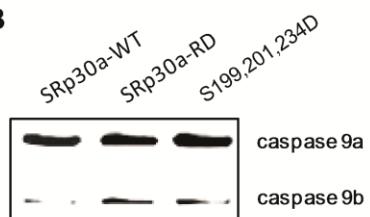


**Shultz et al.**  
**Supplemental Figure 8.**

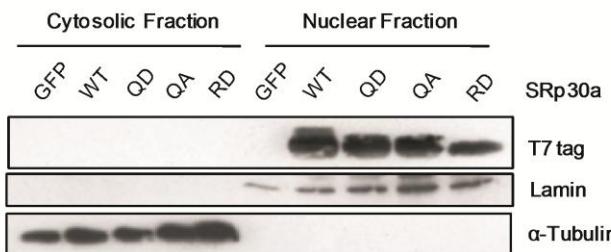
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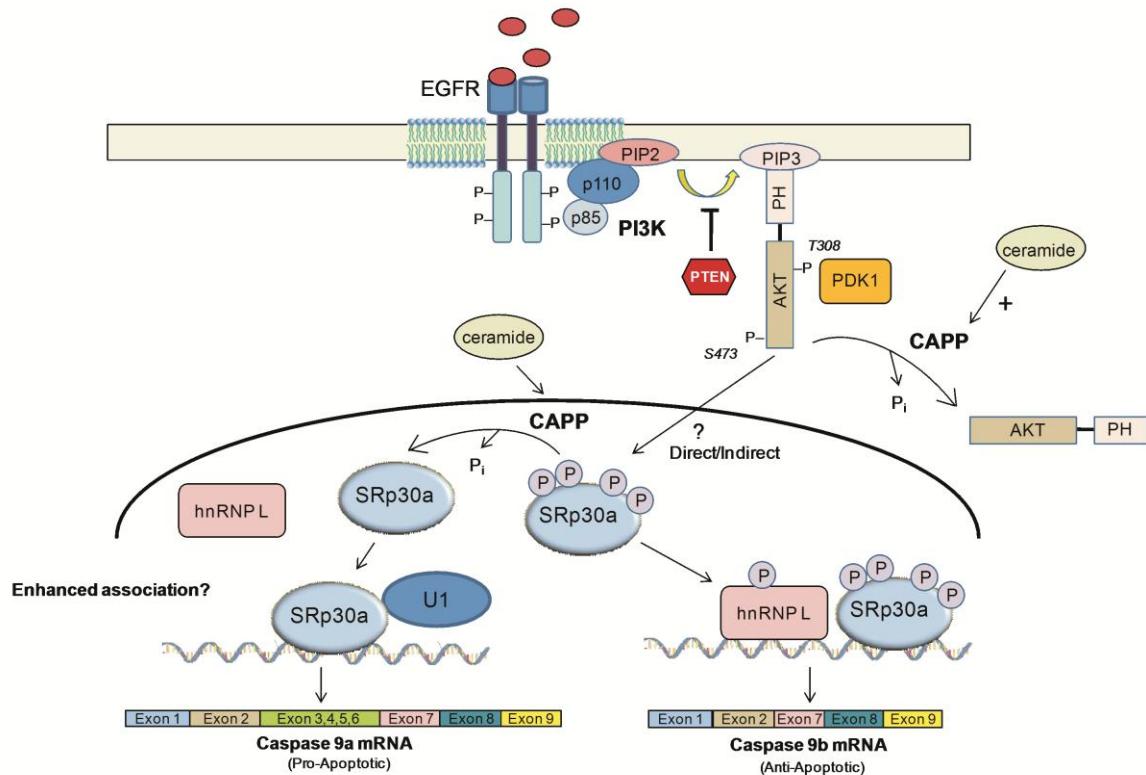
**B**



**Shultz et al.**  
**Supplemental Figure 9.**



**Shultz et al.**  
**Supplemental Figure 10.**



**Supplemental Table I.**

Pathology-verified patient tumor samples.							
Sample	Diagnosis	Group	Caspase 9a/9b ratio	Sample	Diagnosis	Group	Caspase 9a/9b ratio
1-I	Normal	Normal	4.0	37-II	Squamous cell carcinoma	High	1.3
2-I	Normal	Normal	4.0	38-II	Large cell carcinoma	High	1.7
3-I	Normal	Normal	3.5	3-III	Normal	Normal	3.9
5-I	Normal	Normal	4.0	7-III	Normal	Normal	3.8
6-I	Normal	Normal	3.9	9-III	Squamous cell carcinoma	Normal	3.6
7-I	Normal	Normal	4.0	10-III	Large cell carcinoma	High	2.0
9-I	Squamous cell carcinoma	High	2.0	12-III	Bronchioloalveolar carcinoma	Normal	3.7
11-I	Squamous cell carcinoma	Moderate	3.0	15-III	Squamous cell carcinoma	Normal	4.5
13-I	Squamous cell carcinoma	High	2.0	16-III	Squamous cell carcinoma	Moderate	2.3
14-I	Large cell carcinoma	Moderate	2.3	19-III	Large cell carcinoma	High	1.0
17-I	Non-small cell carcinoma	High	2.0	20-III	Non-small cell carcinoma	High	2.0
19-I	Large cell carcinoma	Moderate	2.5	23-III	Squamous cell carcinoma	Moderate	3.2
20-I	Squamous cell carcinoma	High	1.0	25-III	Squamous cell carcinoma	Moderate	2.7
21-I	Squamous cell carcinoma	Normal	4.0	27-III	Squamous cell carcinoma	High	1.8
24-I	Squamous cell carcinoma	Normal	3.7	30-III	Squamous cell carcinoma	Normal	4.0
26-I	Squamous cell carcinoma	Moderate	3.2	31-III	Squamous cell carcinoma	High	1.1
28-I	Large cell carcinoma	Normal	3.4	32-III	Squamous cell carcinoma	Normal	3.5
30-I	Squamous cell carcinoma	High	1.8	33-III	Adenosquamous carcinoma	High	1.7
31-I	Non-small cell carcinoma	Moderate	3.0	34-III	Large cell carcinoma	High	0.9
32-I	Squamous cell carcinoma	Moderate	3.0	39-III	Adenosquamous carcinoma	Normal	3.7
38-I	Squamous cell carcinoma	High	1.0	43-III	Non-small cell carcinoma	Normal	3.9
40-I	Squamous cell carcinoma	Normal	4.0	44-III	Non-small cell carcinoma	High	1.6
41-I	Large cell carcinoma	Normal	3.5	45-III	Squamous cell carcinoma	High	1.0
43-I	Squamous cell carcinoma	Moderate	2.3	<b>Matched-pair Analysis (Normal tissue vs. Tumor tissue)</b>			
44-I	Squamous cell carcinoma	Moderate	2.6	1-IV	Normal 1	Normal	4.0
46-I	Adenocarcinoma	High	1.2	2-IV	Squamous cell carcinoma 1	High	0.9
47-I	Squamous cell carcinoma	Moderate	2.8	5-IV	Normal 2	Moderate	2.8
48-I	Non-small cell carcinoma	Moderate	2.3	6-IV	Large cell carcinoma 2	High	1.8
2-II	Large cell carcinoma	High	1.5	9-IV	Normal 3	Normal	4.7
6-II	Squamous cell carcinoma	High	2.0	10-IV	Large cell carcinoma 3	High	1.7
10-II	Large cell carcinoma	Moderate	2.6	11-IV	Normal 4	Normal	3.7
11-II	Squamous cell carcinoma	Moderate	3.0	12-IV	Large cell carcinoma 4	Normal	3.7
14-II	Squamous cell carcinoma	Moderate	2.7	17-IV	Normal 5	Normal	4.5
17-II	Squamous cell carcinoma	High	2.0	18-IV	Squamous cell carcinoma 5	High	1.0
18-II	Squamous cell carcinoma	High	1.1	21-IV	Normal 6	Normal	4.0
21-II	Squamous cell carcinoma	Moderate	2.3	22-IV	Non-small cell carcinoma 6	High	2.1
23-II	Non-small cell carcinoma	Moderate	2.3	23-IV	Normal 7	Normal	3.8
24-II	Squamous cell carcinoma	Moderate	2.4	24-IV	Squamous cell carcinoma 7	Normal	3.5
27-II	Squamous cell carcinoma	High	2.0	25-IV	Normal 8	Normal	3.5
31-II	Squamous cell carcinoma	Normal	4.5	26-IV	Squamous cell carcinoma 8	Moderate	2.9
32-II	Squamous cell carcinoma	Normal	3.6	31-IV	Normal 9	Normal	3.6
35-II	Squamous cell carcinoma	High	1.0	32-IV	Squamous cell carcinoma 9	Moderate	2.4

**Supplemental Table II. Characterization of NSCLC cell lines**

Cell line	NSCLC Histology	Mutational Status	Caspase 9a/9b ratio	Degree of Dysregulation
A549	AD	WT p53, K-Ras <sup>V12</sup> mutation	1.92 ± 0.16	H
H520	SQ	p53 mutation, WT Ras	2.25 ± 0.15	H
H1703	ADSQ	p53 mutation, WT Ras	3.32 ± 0.08	N
H292	SQ	WT p53, WT Ras	1.72 ± 0.20	H
H2030	AD	WT p53, K-Ras <sup>V12</sup> mutation	2.06 ± 0.11	H
H838	AD	p53 mutation, WT Ras	1.42 ± 0.18	H
H596	ADSQ	p53 mutation, WT Ras	2.73 ± 0.09	M
H2170	SQ	p53 mutation, WT Ras	3.65 ± 0.09	N
H2347	AD	WT p53, N-Ras mutation	3.68 ± 0.10	N
H226	SQ	WT p53, WT Ras	2.15 ± 0.12	H
H358	BA	WT p53, K-Ras <sup>V12</sup> mutation	3.02 ± 0.16	M

AD, adenocarcinoma; SQ, squamous cell carcinoma; ADSQ, adenosquamous cell carcinoma; BA, bronchioalveolar carcinoma; H, highly dysregulated; M, moderately dysregulated; N, normal.

**Supplemental Table III. Mitogen signaling pathways demonstrating no involvement in the alternative splicing of caspase 9 as analyzed by small molecule inhibitors.**

Mitogenic Pathways Investigated	Inhibitor	Concentration
Mitogen Activated Protein Kinase (MAPK)	U0126	10 µM
	PD98059	10 µM
	SB202190	10 µM
Rho Kinase (ROCK)	Y-27632	10 µM
Casein Kinase (CK)	DMAT	10 µM
Src Family Tyrosine Kinases	Src Kinase Inhibitor I	25 µM
Protein Kinase C	Gö6983	10 µM
	Gö6976	10 µM
mTOR	Rapamycin	10 µM
Glycogen Synthase Kinase (GSK)	SB216763	10 µM
c-Jun-N-Terminal Kinase (JNK/SAP Kinase)	JNK Inhibitor II	10 µM

**Supplemental Table IV.** Potential phosphorylation sites in SRp30a involved in regulating the alternative splicing of caspase 9.

Possible phosphosite	Determination	ESI-LC-MS/MS confirmed	Affect on C9a/C9b ratio
S199	Mass Spectrometry	Yes	Yes
S201	Mass Spectrometry	Yes	Yes
S205	Mass Spectrometry	Yes	No
S221	Kinase site prediction	No	No
S225	Mass Spectrometry	Yes	No
S227	Mass Spectrometry	Yes	Yes
S231	Mass Spectrometry	Yes	No
S234	Mass Spectrometry	Yes	Yes
S238	Mass Spectrometry	Yes	No
S242	Mass Spectrometry	Yes	No
S244	Mass Spectrometry	Yes	No
S246	Kinase site prediction	No	No
T248	Kinase site prediction	No	No