Supporting Information for

New Cytotoxic Salinosporamides from the Marine Actinomycete

Salinispora tropica.

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General methods. Melting points were determined on a melting point block and are corrected. Optical rotations were measured at the sodium line (589 nm). IR bands were measured as a thin film on a NaCl disc. NMR spectra were acquired in C₆D₆ or C₅D₅N as indicated, while ¹³C NMR spectra were recorded on at 100 MHz using the residual solvent signals as an internal reference (C₆D₆, δ_{H} 7.16 ppm, δ_{C} 128.1 ppm; C₅D₅N, δ_{H} 7.22 ppm, δ_{C} 128.9 ppm). High-resolution mass spectral data were measured on a MALDI-FTMS using the ES mode.

Experimental Procedures

Cultivation of Strain CNB-392. Strain CNB-392 was isolated from a sample of sediment collected at a depth of approximately 1 m in June 1989 from a mangrove environment in Chub Cay, Bahamas. The strain was cultured in 2.8L Fernbach flasks (20 x 1L) in a seawater-based medium (chitosan 0.2%, kelp powder 0.2%, menhaden meal 0.2%, fish solubles 0.2%, starch 0.5%) and shaken at 230 rpm at 27 °C. After nine days of cultivation, 20 g of sterilized Amberlite XAD-16 resin was added to each flask and the slurry shaken for 24h.

Isolation of Compounds 5 and 6. XAD-16 resin was added to the 1L fermentations and the slurry left to shake for 24h before it was filtered off from the bacterial cells and washed with water. The resin was then extracted overnight with DCM-methanol (1:1) and the aqueous organic extract concentrated *in vacuo* to afford 349 mg of a dark brown gum. The gum was then subjected to purification by flash column chromatography using C-18 silica gel. Elution of the column with increasing concentrations of methanol in water gave nine fractions. The fractions eluting with 25 and 50% methanol in water were combined (115.6 mg) and subjected to further purification by normal phase HPLC using a mixture of hexane and ethyl acetate as the mobile phase.

Isolation of Compounds 1, 3, 4, 7-9. Strain CNB-392 was recultivated as described above, then the XAD-16 resin was then collected by filtration and washed with DI-water. After overnight extraction with a 1:1 mixture of DCM-acetone, the organic extract was concentrated *in vacuo* to afford 4.18 g of material. This material was then purified by silica flash column chromatography using increasing concentrations of acetone in dichloromethane. The fractions eluting with 10:1 and 5:1 DCM-acetone were combined and rotovaped to dryness. Recrystallization of this fraction from ethyl acetate-isooctane (3:1) afforded pure salinosporamide A (**1**, 150 mg, 3.6% yield based on the crude extract). Further purification by NP-HPLC [Dynamax, 250 x 10mm, flow rate 2.5 mL/min, RI detection] using a combination of hexane and ethyl acetate as the eluant yielded **1** and **3-9**.

Salinosporamide B (3, 6.3 mg, 0.15% yield): amorphous crystals, mp 143-145 °C; $[\alpha]_D -54.5^\circ$ (*c* 0.286, MeOH); UV (MeOH) $\lambda_{\max}$ (log ϵ) 256 (3.7) nm; IR (NaCl) $\nu_{\max}$ 3362, 2926, 1820, 1700 cm^{-1} ; ^1H and ^{13}C NMR see Table 1 and 2; ESIMS m/z 280.1 ($\text{M}+\text{H}$) $^+$; HRMALDI-FTMS m/z 279.1471 [calcd for $\text{C}_{15}\text{H}_{21}\text{NO}_4\text{M}^+$, 279.1471].

Salinosporamide C (4, 6.0 mg, 0.14% yield): colorless oil, $[\alpha]_D -33.6^\circ$ (*c* 0.268, MeOH); UV (MeOH) $\lambda_{\max}$ (log ϵ) 222 (3.9) nm; IR (NaCl) $\nu_{\max}$ 3366, 2919, 1702, 1662, 1392, 1318, 1100 cm^{-1} ; ^1H and ^{13}C NMR see Table 2; ESIMS m/z 284.1 ($\text{M}+\text{H}$) $^+$; HRMALDI-FTMS m/z 284.1059 [calcd for $\text{C}_{14}\text{H}_{19}\text{ClNO}_3(\text{M}+\text{H})^+$, 284.1053].

Compound 5 (4.4 mg): amorphous crystals, mp 158-160 °C, $[\alpha]_D -1.5^\circ$ (*c* 1.0, MeOH); UV (MeOH) $\lambda_{\max}$ (log ϵ) 256 (3.5), 204 (3.7) nm; IR (NaCl) $\nu_{\max}$ 3437, 3272, 2923, 2931, 1719, 1684, 1431, 1384, 1278, 1167, 1020 cm^{-1} ; ^1H and ^{13}C NMR see Table S1 and S2; ESIMS m/z 346.1 ($\text{M}+\text{H}$) $^+$; HRMALDI-FTMS m/z 346.1413 [calcd for $\text{C}_{16}\text{H}_{25}\text{ClNO}_5(\text{M}+\text{H})^+$, 346.1421].

Compound 6 (6.0 mg): amorphous crystals, mp 180-181 °C, $[\alpha]_D -3.2^\circ$ (c 1.0, MeOH); UV (MeOH) $\lambda_{\max}$ (log ϵ) 256 (0.4), 208 (0.8) nm; IR (NaCl) $\nu_{\max}$ 3293, 2938, 1734, 1694, 1442, 1264, 1092 cm^{-1} ; ^1H and ^{13}C NMR see Table S1 and S2; ESIMS m/z 310.1 (M+H) $^+$; HRMALDI-FTMS m/z 310.1637 [calcd for $\text{C}_{16}\text{H}_{24}\text{NO}_5$ (M+H) $^+$, 310.1655].

Compound 7 (2.0 mg): colorless cubes, mp 144-145 °C, $[\alpha]_D -131.7^\circ$ (c 0.315, MeOH); UV (MeOH) $\lambda_{\max}$ (log ϵ) 282 (4.4) nm; IR (NaCl) $\nu_{\max}$ 3166, 3025, 2860, 1684 cm^{-1} ; ^1H and ^{13}C NMR see Table S1 and S2; ESIMS m/z 251.1 (M) $^+$; HRMALDI-FTMS m/z 252.1147 [calcd for $\text{C}_{14}\text{H}_{19}\text{ClNO}$ (M+H) $^+$, 251.1155].

Compound 8 (2.9 mg): colorless oil, $[\alpha]_D -50.3^\circ$ (c 0.165, MeOH); UV (MeOH) $\lambda_{\max}$ (log ϵ) 234 (3.5) nm; IR (NaCl) $\nu_{\max}$ 3283, 2931, 2860, 1678, 1184, 1143, 1055 cm^{-1} ; ^1H and ^{13}C NMR see Table S1 and S2; ESIMS m/z 270.1 (M+H) $^+$; HRMALDI-FTMS m/z 270.1271 [calcd for $\text{C}_{14}\text{H}_{21}\text{ClNO}_2$ (M+H) $^+$, 270.1261].

Compound 9 (2.6 mg): colorless oil, $[\alpha]_D -8.8^\circ$ (c 0.295, MeOH); UV (MeOH) $\lambda_{\max}$ (log ϵ) 219 (4.4) nm; IR (NaCl) $\nu_{\max}$ 3319, 2923, 2849, 1672 cm^{-1} ; ^1H and ^{13}C NMR see Table S1 and S2; ESIMS m/z 270.1 (M+H) $^+$; HRMALDI-FTMS m/z 270.1253 [calcd for $\text{C}_{14}\text{H}_{21}\text{ClNO}_2$ (M+H) $^+$, 270.1260].

Table S1. Spectral Data for Salinosporamide B (**3**).

C/H#	3 $\delta_{\text{H}}^{\text{a}}$ multiplicity (<i>J</i> in Hz)	3 $\delta_{\text{C}}^{\text{b}}$	COSY
1		176.9, C	
2	2.72, dd (8.8, 5.8)	49.8, CH	12a, 12b
3		86.3, C	
4		79.3, C	
5	4.24, t (8.8)	70.4, CH	5, OH
6	2.90, m	38.7, CH	5, 7, 11a, 11b
7	6.44, d (10.3)	128.2, CH	6, 8
8	5.88, m	128.4, CH	7, 9
9	1.92, m	24.7, CH ₂	8, 10
10a	1.39, m	21.1, CH ₂	9, 10b, 11a, 11b
10b	1.72, m		10a
11a	1.72, m	25.9, CH ₂	
11b	2.32, m		10a, 12a, 12b
12a	1.90, m	18.5, CH ₂	12b, 13a, 13b
12b	2.14, m		12a
13a	1.21, t (7.3)	12.3, CH ₂	12a, 12b, 13b
14	2.05, s	20.2, CH ₃	
15		169.1, C	
NH	10.42, br s		
OH	7.49, d (8.8)		

Table S2. ^1H NMR Spectral Data for **5-9** at 300 MHz.

H# ^a	5 ^b	6 ^b	7 ^c	8 ^c	9 ^c
1					
2	3.65, dd (8.8, 4.4)	3.29, d (7.3)			
3					
4				3.70, br s	3.70, d (5.2)
5	4.54, d (6.4)	4.31, s	4.89, d (9.2)	3.27, d (10.0)	3.28, t (4.4)
6	2.71, m	2.72, m	2.95, m	2.42, m	2.16, m
7	6.50, d (10.7)	6.46, d (10.3)	5.66, m	6.22, d (10.4)	5.66, dd (10.4, 2.4)
8	5.78, br d (10.7)	5.78, br d (10.3)	5.48, d (9.2)	5.81, dm (10.4)	5.76, dq (10.4, 3.2)
9	1.93, m	1.93, m	1.83, m	1.94, m	1.78, m
10a	1.33, m	1.22, m	1.55-1.70, m	1.63, m	1.24, m
10b	1.68, m	1.62, m		1.73, m	
11a	1.62, m	1.83, m	1.55-1.70, m	1.71, m	1.30, m
11b	1.87, m			1.74, m	2.07, m
12a	2.39, m	2.49, m	2.50, t (6.9)	2.54, m	2.41, m
12b	2.65, m	2.69, m		2.64, m	2.51, m
13	4.18, t (7.3)	3.80, m 3.87, m	3.53, t (6.8)	3.60, m 3.73, m	3.60, m
14	2.10, s	1.65, s	1.50, s	1.55, s	1.58, s
15					
16	3.69, s	3.79, s			
NH	9.80, br s	9.98, br s		8.55, br s	7.23, br s
OH	6.85, br s	6.85, br s			

^a Numbering consistent with Salinosporamide A (**1**). ^b NMR spectra recorded in C₅D₅N.^c NMR spectra recorded in C₆D₆.

Table S3. ^{13}C NMR Spectral Data for **5-9** at 100 MHz.

Carbon # ^a	5 ^b	6 ^b	7 ^c	8 ^c	9 ^c
C-1	178.6, C	177.8, C	171.6, C	176.3, C	173.9, C
C-2	49.6, CH	53.6, CH	128.4, C	129.6, C	130.0, C
C-3	82.1, C	91.0, C	143.3, C	155.7, C	154.6, C
C-4	78.1, C	76.4, C	138.2, C	63.2, CH	63.0, CH
C-5	77.0, CH	76.3, CH	114.7, CH	73.8, CH	76.0, CH
C-6	40.5, CH	39.5, CH	38.4, CH	40.9, CH	38.4, CH
C-7	129.1, CH	128.8, CH	129.1, CH	129.1, CH	131.2, CH
C-8	129.2, CH	129.4, CH	127.3, CH	128.2, CH	126.6, CH
C-9	25.6, CH ₂	25.6, CH ₂	25.2, CH ₂	25.6, CH ₂	25.5, CH ₂
C-10	22.6, CH ₂	22.5, CH ₂	21.3, CH ₂	22.2, CH ₂	22.0, CH ₂
C-11	27.4, CH ₂	26.7, CH ₂	29.7, CH ₂	26.7, CH ₂	27.5, CH ₂
C-12	29.5, CH ₂	28.7, CH ₂	27.8, CH ₂	27.7, CH ₂	27.7, CH ₂
C-13	45.4, CH ₂	67.4, CH ₂	43.2, CH ₂	43.4, CH ₂	43.5, CH ₂
C-14	21.3, CH ₃	20.4, CH ₃	9.6, CH ₃	12.4, CH ₃	13.6, CH ₃
C-15	172.2, C	171.5, C			
C-16	51.8, CH ₃	52.0, CH ₃			

^a Numbering consistent with Salinosporamide A (**1**). ^b NMR spectra recorded in C₅D₅N.

^c NMR spectra recorded in C₆D₆.

Table S4. Spectral Data for **6** in CDCl₃.

C/H #	δ_{H} multiplicity (J in Hz)	δ_{C}	COSY	HMBC	ROESY
1		177.3, C			
2	2.91, d (8.0)	52.4, CH	12b	1, 3, 12, 13	12a, 12b, 14
3		89.9, C			
4		52.4, C			
5	4.00, br s	75.2, CH	6	4, 7, 15	14
6	2.20, m	38.2, CH	5		
7	5.61, br d (9.0)	123.7, CH		5, 6, 8, 9, 11	
8	6.02, br d (10.0)	134.4, CH		6, 7, 9, 10	
9a	1.75, m	28.3, CH ₂			
9b	1.50, m				
10	1.60, m	20.8, CH ₂			
11	1.98, m	25.0, CH ₂			
12a	2.35, dd (12.5, 5.0)	28.0, CH ₂	12b, 13a, 13b		
12b	2.00, m		12a, 13a, 13b		
13a	3.90, td (8.5, 1.5)	67.2, CH ₂	13b		
13b	3.70, m		13a		
14	1.55, s	19.8, CH ₃		2, 3, 4	2, 5, 13a
15		169.7, C			
16	3.79, s	52.5, CH ₃		15	

Table S5. Spectral Data for **8** in C₆D₆.

C/H #	δ_{H} multiplicity (<i>J</i> in Hz)	δ_{C}	COSY	HMBC	ROESY
1		176.3, C			
2		129.6, C			
3		155.7, C			
4	3.70, br s	63.2, CH	5, 6, NH	1, 2, 3	4, 5, 10b, 12b, NH
5	3.27, d (10.0)	73.8, CH	4, 6		
6	2.42, m	40.9, CH	5, 10		7, 10b, NH
7	6.22, d (10.4)	129.1, CH	6, 8, 9		6, 8
8	5.81, dm (10.4)	128.2, CH	7, 9		7, 9
9	1.94, m	25.6, CH ₂	6, 8		8, 10b
10a	1.63, m	22.2, CH ₂	9, 10		
10b	1.73, m		6, 10		4, 5, 6
11a	1.71, m	26.7, CH ₂			
11a	1.74, m		6, 10		4, 5, 6
12a	2.54, m	27.7, CH ₂	13	1, 2, 3, 13	12b
12b	2.64, m		13	1, 2, 3, 13	12a
13a	3.60, m	43.4, CH ₂	12, 13	2, 12	12b, 13b
13b	3.73, m		12, 13	2, 12	12b, 13a
14	1.55, s	12.4, CH ₃		1, 2, 3, 4, 13	4, 5, 12b
NH	8.55, br s		4	3, 4, 7	4, 6

Table S6. Spectral Data for **9** in C₆D₆.

C/H #	δ_{H} multiplicity (<i>J</i> in Hz)	δ_{C}	COSY	HMBC	ROESY
1		173.9, C			
2		130.0, C			
3		154.6, C			
4	3.70, d (5.2)	63.0, CH		2, 3, 5, 6	NH, 8, 7, 5, 14
5	3.28, t (4.4)	76.0, CH	4, 6	2, 6, 8	4, 6, 14
6	2.16, m	38.4, CH	5		NH, 8, 7, 5, 10
7	5.66, dd (10.4, 2.4)	131.2, CH		9	4, 8, 6, 9
8	5.76, dq (10.4, 3.2)	126.6, CH	9	6	6, 7, 6, 9
9	1.78, m	25.5, CH ₂	8		7, 10
10a	1.24, m	22.0, CH ₂	6		
10b	1.30, m				
11	2.07, m	27.5, CH ₂			
12a	2.41, m	27.7, CH ₂	13	1, 2, 3, 13	
12b	2.51, m		13	1, 2, 3, 13	
13	3.60, m	43.5, CH ₂		2	12a, 12b
14	1.58, s	13.6, CH ₃		1, 2, 3, 4, 13	4, 5
NH	7.23, br s				4, 6

Figure S1. ^1H NMR Spectrum (300 MHz) of Salinosporamide B (**3**) in pyridine- d_5

Figure S2. ^{13}C NMR Spectrum (100 MHz) of Salinosporamide B (**3**) in pyridine- d_5

Figure S3. COSY NMR Spectrum (300 MHz) of Salinosporamide B (**3**) in pyridine- d_5

Figure S4. HSQC NMR Spectrum (300 MHz) of Salinosporamide B (**3**) in pyridine- d_5

Figure S6. NOESY NMR Spectrum (300 MHz) of Salinosporamide B (**3**) in pyridine- d_5

Figure S7. ^1H NMR Spectrum (300 MHz) of Salinosporamide C (**4**) in pyridine- d_5

Figure S8. ^{13}C NMR Spectrum (100 MHz) of Salinosporamide C (**4**) in pyridine- d_5

Figure S9. COSY NMR Spectrum (300 MHz) of Salinosporamide C (**4**) in pyridine-*d*₅

Figure S10. HMQC NMR Spectrum (300 MHz) of Salinosporamide C (**4**) in pyridine-*d*₅

Figure S11. HMBC NMR Spectrum (300 MHz) of Salinosporamide C (**4**) in pyridine-*d*₅

Figure S12. NOESY NMR Spectrum (300 MHz) of Salinosporamide C (**4**) in pyridine- d_5

Figure S13. ^1H NMR Spectrum (300 MHz) of **5** in pyridine- d_5

Figure S14. ^{13}C NMR Spectrum (100 MHz) of **5** in pyridine- d_5

Figure S15. ^1H NMR Spectrum (300 MHz) of **6** in pyridine- d_5

Figure S16. ^{13}C NMR Spectrum (100 MHz) of **6** in pyridine- d_5

Figure S17. ^1H NMR Spectrum (300 MHz) of **6** in CDCl_3

Figure S18. ^{13}C NMR Spectrum (100 MHz) of **6** in CDCl_3

Figure S19. HMQC NMR Spectrum (300 MHz) of **6** in CDCl₃

Figure S20. COSY NMR Spectrum (300 MHz) of **6** in CDCl₃

Figure S21. HMBC NMR Spectrum (300 MHz) of **6** in CDCl₃

Figure S22. NOESY NMR Spectrum (300 MHz) of **6** in CDCl₃

Figure S23. ^1H NMR Spectrum (300 MHz) of **7** in CDCl_3

Figure S24. ^{13}C NMR Spectrum (100 MHz) of **7** in CDCl_3

Figure S25. ^1H NMR Spectrum (300 MHz) of **8** in benzene- d_6

Figure S26. ^{13}C NMR Spectrum (100 MHz) of **8** in benzene- d_6

Figure S27. .HSQC NMR Spectrum (300 MHz) of **8** in benzene- d_6

Figure S28. COSY NMR Spectrum (300 MHz) of **8** in benzene- d_6

Figure S29. HMBC NMR Spectrum (300 MHz) of **8** in benzene- d_6

Figure S30. NOESY NMR Spectrum (300 MHz) of **8** in benzene- d_6

Figure S31. ^1H NMR Spectrum (300 MHz) of **9** in benzene- d_6

Figure S32. ^{13}C NMR Spectrum (100 MHz) of **9** in benzene- d_6

Figure S33. .HSQC NMR Spectrum (300 MHz) of **9** in benzene- d_6

Figure S34. COSY NMR Spectrum (300 MHz) of **9** in benzene- d_6

Figure 35. HMBC NMR Spectrum (300 MHz) of **9** in benzene- d_6

Figure S36. .NOESY NMR Spectrum (300 MHz) of **9** in benzene- d_6

Table S7. Results from Salinosporamide A NCI In-Vitro Testing

National Cancer Institute Developmental Therapeutics Program																		
In-Vitro Testing Results																		
NSC: D-721267 / 1				Experiment ID: 0106NS98-75						Test Type: 08				Units: Molar				
Report Date: August 1, 2001				Test Date: June 25, 2001						QNS:				MC:				
COMI: CNB932.313 (8348)				Stain Reagent: SRB Dual-Pass						SSPL: 075T								
		Log10 Concentration																
Panel/Cell Line	Time	Mean Optical Densities										Percent Growth				GI50	TGI	LC50
	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-3.0	-2.0	-1.0	-0.5	-0.25	-0.125	-0.0625	-0.03125	-0.015625		
Leukemia																		
CCRF-CEM	0.119	0.656	0.205	0.228	0.207	0.195	0.208	16	20	16	14	16	<1.00E-08	>1.00E-04	>1.00E-04	>1.00E-04		
HL-60(TB)	0.902	1.969	1.009	1.040	0.930	0.985	0.924	10	13	3	8	2	<1.00E-08	>1.00E-04	>1.00E-04	>1.00E-04		
K-562	0.221	0.869	0.413	0.354	0.255	0.197	0.166	30	20	5	-11	-25	<1.00E-08	2.12E-06	>1.00E-04	>1.00E-04		
MOLT-4	0.138	0.657	0.424	0.399	0.169	0.189	0.178	55	50	6	10	8	1.01E-07	<1.00E-04	>1.00E-04	>1.00E-04		
RFMI-8226	0.395	1.013	0.325	0.323	0.306	0.304	0.318	-18	-18	-23	-23	-20	<1.00E-08	<1.00E-08	>1.00E-04	>1.00E-04		
SR	0.260	0.696	0.149	0.173	0.161	0.148	0.153	-43	-34	-38	-43	-41	<1.00E-08	<1.00E-08	>1.00E-04	>1.00E-04		
Non-Small Cell Lung Cancer																		
A549/ATCC	0.203	1.051	0.467	0.426	0.340	0.210	0.108	31	26	16	1	-47	<1.00E-08	1.04E-05	>1.00E-04	>1.00E-04		
ERVK	0.483	1.026	0.688	0.601	0.548	0.497	0.545	38	22	12	2	11	<1.00E-08	>1.00E-04	>1.00E-04	>1.00E-04		
HOP-62	0.399	0.873	0.434	0.459	0.331	0.268	0.224	7	13	-17	-33	-44	<1.00E-08	2.66E-07	>1.00E-04	>1.00E-04		
NCI-H226	0.789	1.012	0.457	0.452	0.481	0.395	0.280	-42	-43	-39	-50	-65	<1.00E-08	<1.00E-08	1.01E-05	>1.00E-04		
NCI-H23	0.268	0.627	0.217	0.182	0.104	0.089	0.096	-19	-32	-61	-67	-64	<1.00E-08	<1.00E-08	4.09E-07	>1.00E-04		
NCI-H322M	0.725	1.201	0.793	0.654	0.583	0.363	0.389	14	-10	-20	-50	-46	<1.00E-08	3.89E-08	>1.00E-04	>1.00E-04		
NCI-H460	0.113	1.247	0.359	0.263	0.228	0.119	0.146	22	13	10	1	3	<1.00E-08	>1.00E-04	>1.00E-04	>1.00E-04		
NCI-H522	0.652	1.289	0.246	0.139	0.109	0.135	0.091	-62	79	-83	-79	-86	<1.00E-08	<1.00E-08	<1.00E-08	>1.00E-04		
Colon Cancer																		
COLO 205	0.415	1.401	0.622	0.559	0.401	0.196	0.084	21	15	-3	-53	-80	<1.00E-08	6.40E-07	8.74E-06	>1.00E-04		
HCC-2998	0.227	0.470	0.130	0.085	0.025	0.010	0.018	-43	-63	-89	-96	-92	<1.00E-08	<1.00E-08	2.33E-08	>1.00E-04		
HCT-116	0.098	0.513	0.096	0.088	0.038	0.014	0.016	2	-1	-57	-84	-82	<1.00E-08	5.71E-08	7.41E-07	>1.00E-04		
HCT-15	0.237	0.973	0.404	0.419	0.323	0.281	0.184	23	25	12	6	-22	<1.00E-08	1.63E-05	>1.00E-04	>1.00E-04		
KM12	0.415	1.266	0.512	0.495	0.337	0.301	0.358	11	9	-19	-27	-14	<1.00E-08	2.14E-07	>1.00E-04	>1.00E-04		
SW-620	0.266	0.955	0.353	0.309	0.272	0.243	0.214	13	6	1	-9	-20	<1.00E-08	1.21E-06	>1.00E-04	>1.00E-04		
CNS Cancer																		
SP-268	0.293	1.040	0.451	0.407	0.427	0.308	0.261	21	15	18	2	-11	<1.00E-08	1.42E-05	>1.00E-04	>1.00E-04		
SP-295	0.376	1.131	0.298	0.208	0.093	0.042	0.101	-21	-45	-75	-89	-73	<1.00E-08	<1.00E-08	1.49E-07	>1.00E-04		
SP-539	0.814	1.619	0.702	0.660	0.534	0.540	0.522	-14	-19	-34	-34	-36	<1.00E-08	<1.00E-08	>1.00E-04	>1.00E-04		
SNB-19	0.463	0.934	0.517	0.488	0.474	0.475	0.413	11	5	2	3	-11	<1.00E-08	1.55E-05	>1.00E-04	>1.00E-04		
U251	0.304	1.252	0.299	0.283	0.268	0.148	0.081	-2	-7	-12	-51	-74	<1.00E-08	<1.00E-08	9.26E-06	>1.00E-04		
Melanoma																		
LOX IMVI	0.202	0.976	0.158	0.131	0.046	0.020	0.019	-22	-35	-77	-90	-91	<1.00E-08	<1.00E-08	2.24E-07	>1.00E-04		
MALME-3M	0.810	1.376	0.683	0.750	0.675	0.615	0.815	-16	-7	-17	-24	1	<1.00E-08	.	>1.00E-04	>1.00E-04		
M14	0.186	0.544	0.238	0.205	0.140	0.095	0.137	14	5	-25	-49	-27	<1.00E-08	1.50E-07	>1.00E-04	>1.00E-04		
SK-MEL-2	0.853	1.733	0.333	0.354	0.198	0.209	0.159	-61	-58	-77	-75	-81	<1.00E-08	<1.00E-08	<1.00E-08	>1.00E-04		
SK-MEL-28	0.717	0.985	0.321	0.296	0.310	0.289	0.210	-55	-59	-57	-60	-71	<1.00E-08	<1.00E-08	<1.00E-08	>1.00E-04		
SK-MEL-5	0.455	1.573	0.253	0.169	0.098	0.126	0.104	-44	-63	-78	-72	-77	<1.00E-08	<1.00E-08	2.01E-08	>1.00E-04		
UACC-257	0.342	1.203	0.308	0.428	0.225	0.341	0.365	-10	10	-34	.	3	<1.00E-08	.	>1.00E-04	>1.00E-04		
UACC-62	0.812	1.804	0.610	0.480	0.374	0.114	0.137	-25	-41	-54	-86	-83	<1.00E-08	<1.00E-08	4.94E-07	>1.00E-04		
Ovarian Cancer																		
IGROV1	0.681	1.489	0.849	0.917	0.707	0.416	0.153	21	29	3	-39	-78	<1.00E-08	1.19E-06	1.93E-05	>1.00E-04		
OVCAR-3	0.510	1.427	0.583	0.601	0.418	0.280	0.271	8	10	-18	-45	-47	<1.00E-08	2.26E-07	>1.00E-04	>1.00E-04		
OVCAR-5	0.376	0.851	0.440	0.406	0.337	0.284	0.301	13	6	-10	-24	-20	<1.00E-08	2.37E-07	>1.00E-04	>1.00E-04		
OVCAR-8	0.200	1.075	0.387	0.322	0.174	0.172	0.108	21	14	-13	-14	-46	<1.00E-08	3.25E-07	>1.00E-04	>1.00E-04		
SK-OV-3	0.822	1.408	0.811	0.789	0.725	0.630	0.454	-1	-4	-12	-23	-45	<1.00E-08	<1.00E-08	>1.00E-04	>1.00E-04		
Renal Cancer																		
786-0	0.353	0.958	0.431	0.427	0.340	0.215	0.138	13	12	-4	-39	-61	<1.00E-08	5.76E-07	3.12E-05	>1.00E-04		
A498	0.964	1.451	0.384	0.241	0.223	0.275	0.286	-60	-75	-77	-71	-70	<1.00E-08	<1.00E-08	<1.00E-08	>1.00E-04		
ACHN	0.295	1.059	0.418	0.408	0.345	0.280	0.131	16	15	7	-5	-56	<1.00E-08	3.65E-06	7.70E-05	>1.00E-04		
CAKI-1	0.566	1.847	0.664	0.638	0.545	0.456	0.315	8	6	-4	-19	-44	<1.00E-08	3.94E-07	>1.00E-04	>1.00E-04		
RFX 393	0.194	0.723	0.289	0.228	0.177	0.184	0.112	18	6	-9	-5	-43	<1.00E-08	2.59E-07	>1.00E-04	>1.00E-04		
SN12C	0.368	0.975	0.363	0.290	0.230	0.072	0.055	-1	-21	-38	-81	-85	<1.00E-08	<1.00E-08	1.95E-06	>1.00E-04		
TK-10	0.428	0.961	0.515	0.490	0.370	0.324	0.350	16	12	-14	-24	-18	<1.00E-08	2.87E-07	>1.00E-04	>1.00E-04		
UO-31	0.416	1.227	0.732	0.679	0.449	0.324	0.127	39	32	4	-22	-70	<1.00E-08	1.42E-06	3.86E-05	>1.00E-04		
Prostate Cancer																		
PC-3	0.288	0.648	0.362	0.351	0.287	0.248	0.207	20	18	.	-14	-28	<1.00E-08	9.56E-07	>1.00E-04	>1.00E-04		
DU-145	0.149	0.627	0.338	0.338	0.331	0.307	0.239	40	39	38	33	19	<1.00E-08	>1.00E-04	>1.00E-04	>1.00E-04		
Breast Cancer																		
MCF7	0.099	1.137	0.550	0.502	0.420	0.399	0.299	43	39	31	29	19	<1.00E-08	>1.00E-04	>1.00E-04	>1.00E-04		
NCI/ADR-RES	0.658	1.347	0.673	0.600	0.573	0.604	0.389	2	-9	-13	-8	-41	<1.00E-08	1.57E-08	>1.00E-04	>1.00E-04		
MDA-MB 231/ATCC	0.441	0.903	0.397	0.344	0.300	0.254	0.198	-10	-22	-32	-43	-55	<1.00E-08	<1.00E-08	2.93E-05	>1.00E-04		
HS 578T	1.020	1.418	0.739	0.787	0.785	0.763	0.692	-28	-23	-23	-25	-32	<1.00E-08	<1.00E-08	>1.00E-04	>1.00E-04		
MDA-MB-435	0.465	1.621	0.159	0.177	0.131	0.080	0.081	-66	-62	-72	-83	-80	<1.00E-08	<1.00E-08	<1.00E-08	>1.00E-04		
TDA-N	0.703	1.893	0.320	0.354	0.369	0.417	0.411	-54	-50	-48	-41	-42	<1.00E-08	<1.00E-08	.	>1.00E-04		
T-47D	0.284	0.652	0.285	0.222	0.168	0.168	0.113	.	-22	-41	-41	-60	<1.00E-08	1.01E-08	2.94E-05	>1.00E-04		

Table S8. Results of Salinosporamide A in NCI 60-cell line panel.

National Cancer Institute Developmental Therapeutics Program				NSC: D- 721267 / 1	Units: Molar	SSPL: 075T	Exp. ID:0108RS09-1
Mean Graphs				Report Date: September 17, 2001		Test Date: August 6, 2001	
Panel/Cell Line	Log ₁₀ GI50	GI50	Log ₁₀ TGI	TGI	Log ₁₀ LC50	LC50	
Leukemia							
CCRF-CEM	< -8.00		< -8.00		> -4.00		
HL-60(TB)	< -8.00		-4.32		> -4.00		
K-562	< -8.00		-5.39		> -4.00		
MOLT-4	< -8.00		< -8.00		> -4.00		
RPMI-8226	< -8.00		< -8.00		> -4.00		
SR	< -8.00		< -8.00		-4.19		
Non-Small Cell Lung Cancer							
AS49(ATCC)	< -8.00		-4.70		> -4.00		
BEVK	< -8.00		-5.67		> -4.00		
HOP-62	< -8.00		-4.89		> -4.00		
HOP-92	< -8.00		-7.77		-5.76		
NCI-H1226	< -8.00		< -8.00		< -8.00		
NCI-H123	< -8.00		-7.85		-6.31		
NCI-H1322M	< -8.00		-5.48		-1.37		
NCI-H460	< -8.00		-6.97		> -4.00		
NCI-H522	< -8.00		< -8.00		-7.37		
Colorectal Cancer							
COLO 205	< -8.00		-6.19		-4.06		
HCC-T2998	< -8.00		< -8.00		-7.75		
HCT-116	< -8.00		-7.84		-4.99		
HCT-15	< -8.00		-6.06		-1.25		
HCT29	< -8.00		-7.37		-4.42		
KM12	< -8.00		-6.00		-4.24		
SW-620	< -8.00		> -4.00		> -4.00		
CNS Cancer							
SP-268	< -8.00		-6.92		> -4.00		
SP-295	< -8.00		< -8.00		-6.63		
SP-539	< -8.00		< -8.00		< -8.00		
SNB-19	< -8.00		> -4.00		> -4.00		
SNB-75	< -8.00		> -8.00		-7.50		
U251	< -8.00		-5.99		> -4.00		
Melanoma							
LOX IMVI	< -8.00		-7.87		> -4.00		
MALME-3M	< -8.00		< -8.00		-4.89		
M14	< -8.00		-7.94		-6.73		
SK-MEL-2	< -8.00		< -8.00		-6.79		
SK-MEL-28	< -8.00		< -8.00		< -8.00		
UACC-257	< -8.00		< -8.00		-4.37		
UACC-62	< -8.00		< -8.00		-7.04		
Ovarian Cancer							
IGROV1	< -8.00		-5.18		> -4.00		
OVCAR-3	< -8.00		-4.88		> -4.00		
OVCAR-4	< -8.00		< -8.00		-5.52		
OVCAR-5	< -8.00		-7.26		> -4.00		
OVCAR-8	< -8.00		-7.70		-6.55		
SK-OV-3	< -8.00		< -8.00		> -4.00		
Renal Cancer							
786-O	< -8.00		-5.37		> -4.00		
A498	< -8.00		< -8.00		> -7.94		
ACHN	< -8.00		-5.27		> -4.00		
CAKI-1	< -8.00		> -4.00		> -4.00		
RXF-393	< -8.00		< -8.00		-7.64		
SN12C	< -8.00		< -8.00		-6.20		
TK-10	< -8.00		-7.13		> -4.00		
UO-31	< -8.00		-5.88		-4.59		
Prostate Cancer							
PC-3	< -8.00		-5.81		-4.95		
DU-145	< -8.00		> -4.00		> -4.00		
Breast Cancer							
MCF7	< -8.00		> -4.00		> -4.00		
NCIHADR-RES	< -8.00		< -8.00		> -6.75		
MDA-MB-231(ATCC)	< -8.00		< -8.00		-6.86		
MDA-MB-435	< -8.00		< -8.00		< -8.00		
MDA-N	< -8.00		< -8.00		> -4.00		
BV-549	< -8.00		< -8.00		-7.22		
T-17D	< -8.00		> -4.00		> -4.00		
SIG And	-8.00		-6.79		-5.20		
Delt	0.00		1.21		2.80		
Range	0.00		4.00		4.00		