

Supplementary Table 1. Effect of inhibition of SMS1 by D609 treatment on lipid levels. Reported are the levels of individual species of ceramide (**A**), DAG (**B**) and SM (**C**) as measured by mass spectrometry during treatment with D609 (50 $\mu\text{g/ml}$) after 24 and 48 hours. Since basal levels of lipids were variable among the different experiments whereas the pattern of changes between experimental conditions was similar (Figure 4A and B), reported are the absolute values of one representative experiment. In bold are the values that were significantly different compared to the time-matched control once the fold change versus the appropriate control was calculated among three independent experiments ($p < 0.05$ versus CT). CT: Control cells.

A Ceramide species (pmoles/nmole of Pi)

Samples	C14-Cer	C16-Cer	C18-Cer	C18:1-Cer	C20-Cer	C20:1-Cer	C22-Cer	C22:1-Cer	C24-Cer	C24:1-Cer	C26-Cer	C26:1-Cer	Tot Cer
CT 24h	0.018	0.117	0.020	0.007	0.014	0.003	0.082	0.030	1.13	0.445	0.015	0.035	1.92
D609 24h	0.097	0.323	0.073	0.025	0.082	0.008	0.213	0.073	1.15	0.502	0.042	0.053	2.64
CT 48h	0.012	0.063	0.012	0.003	0.010	0.002	0.047	0.018	0.73	0.300	0.013	0.015	1.23
D609 48h	0.093	0.277	0.053	0.020	0.080	0.012	0.158	0.082	0.90	0.420	0.020	0.023	2.14

B DAG species (pmoles/nmole of Pi)

Samples	C14:0/16:0-DAG	C14:0/18:0-DAG	C14:0/18:1-DAG	C16:0/18:0-DAG	C16:0/18:1-DAG	C16:0/20:0-DAG	C16:0/24:1-DAG	C16:1/18:0-DAG	C16:1/18:1-DAG
CT 24h	0.620	0.225	0.127	3.82	5.39	0.182	0.217	0.072	0.393
D609 24h	0.177	0.050	0.080	0.84	1.32	0.005	0.008	0.115	0.602
CT 48h	0.497	0.298	0.142	3.59	3.14	0.275	0.267	0.022	0.285
D609 48h	0.068	0.050	0.075	0.69	0.78	0.020	0.020	0.003	0.237

B continued DAG species (pmoles/nmole of Pi)

Samples	C18:0/18:1-DAG	C18:0/18:2-DAG	C18:0/20:4-DAG	Di-C14:0-DAG	Di-C16:0-DAG	Di-C18:0-DAG	Di-C18:1-DAG	Total DAG
CT 24h	0.92	0.28	1.08	0.080	2.54	0.207	0.121	16.27
D609 24h	0.65	0.48	0.66	0.060	0.45	0.178	0.225	5.89
CT 48h	2.05	0.16	0.58	0.068	2.01	0.093	0.288	13.77
D609 48h	0.61	0.14	0.90	0.022	0.23	0.197	0.195	4.24

C**SM species (pmoles/nmole of Pi)**

Samples	C14-SM	C16-SM	C18-SM	C18:1-SM	C20-SM	C20:1-SM	C22-SM	C22:1-SM	C24-SM	C24:1-SM	C26-SM	C26:1-SM	Tot SM
CT 24h	0.505	21.25	3.16	2.23	1.07	0.28	6.67	2.86	7.59	16.59	0.09	0.37	62.67
D609 24h	0.735	22.23	2.71	1.62	0.98	0.22	3.93	1.80	4.56	8.37	0.25	0.41	47.82
CT 48h	0.725	27.02	3.31	3.09	0.81	0.14	7.14	2.40	7.68	17.01	0.07	0.20	69.60
D609 48h	0.885	23.19	2.97	2.85	0.87	0.13	7.67	2.44	9.41	16.80	0.28	0.40	67.90

Supplementary Table 2. Effect of inhibition of *SMS1* by siRNA treatment on lipid levels. Reported are the levels of individual species of ceramide (**A**), DAG (**B**) and SM (**C**) as measured by mass spectrometry during down-regulation of *SMS1* (SMS1-) with siRNA as compared to a scrambled control sequence (SCR) after 24 and 48 hours. Since basal levels of lipids were variable among the different experiments whereas the pattern of changes between experimental conditions was similar (Figure 4C and D), reported are the absolute values of one representative experiment. In bold are the values that were significantly different compared to the time-matched control once the fold change versus the appropriate control was calculated among three independent experiments ($p < 0.05$ versus SCR).

A

Ceramide species (pmoles/nmole of Pi)

Samples	C14-Cer	C16-Cer	C18-Cer	C18:1-Cer	C20-Cer	C20:1-Cer	C22-Cer	C22:1-Cer	C24-Cer	C24:1-Cer	C26-Cer	C26:1-Cer	Tot Cer
SCR 24h	0.008	0.140	0.155	0.012	0.021	0.001	0.072	0.042	1.137	0.907	0.038	0.026	2.56
SMS1- 24h	0.001	0.118	0.160	0.004	0.014	0.001	0.070	0.039	0.802	0.904	0.015	0.021	2.15
SCR 48h	0.036	0.307	0.124	0.021	0.026	0.004	0.112	0.069	1.532	1.427	0.053	0.067	3.77
SMS1- 48h	0.044	0.463	0.204	0.046	0.065	0.011	0.127	0.105	1.246	1.555	0.029	0.053	3.95

B

DAG species (pmoles/nmole of Pi)

Samples	C14:0/16:0-DAG	C14:0/18:0-DAG	C14:0/18:1-DAG	C16:0/18:0-DAG	C16:0/18:1-DAG	C16:0/20:0-DAG	C16:0/24:1-DAG	C16:1/18:0-DAG	C16:1/18:1-DAG
SCR 24h	0.774	0.399	0.062	7.208	2.132	0.288	0.090	0.087	0.060
SMS1- 24h	0.559	0.146	0.036	3.172	1.695	0.095	0.077	0.051	0.045
SCR 48h	0.277	0.122	0.053	2.908	1.766	0.105	0.061	0.060	0.048
SMS1- 48h	0.178	0.062	0.037	1.856	1.499	0.080	0.058	0.044	0.052

B continued

DAG species (pmoles/nmole of Pi)

Samples	C18:0/18:1-DAG	C18:0/18:2-DAG	C18:0/20:4-DAG	Di-C14:0-DAG	Di-C16:0-DAG	Di-C18:0-DAG	Di-C18:1-DAG	Total DAG
SCR 24h	1.102	0.034	0.072	0.041	2.534	0.106	0.103	15.09
SMS1- 24h	0.567	0.019	0.037	0.028	1.637	0.028	0.086	8.28
SCR 48h	1.413	0.082	0.432	0.019	0.667	0.064	0.120	8.20
SMS1- 48h	1.262	0.103	0.351	0.014	0.452	0.029	0.134	6.21

C**SM species (pmoles/nmole of Pi)**

Samples	C14-SM	C16-SM	C18-SM	C18:1-SM	C20-SM	C20:1-SM	C22-SM	C22:1-SM	C24-SM	C24:1-SM	C26-SM	C26:1-SM	Total SM
SCR 24h	1.17	22.0	2.96	0.301	0.687	0.195	2.94	1.50	3.98	8.38	0.035	0.204	44.35
SMS1- 24h	1.06	19.0	2.69	0.305	0.702	0.224	2.64	1.46	3.04	7.39	0.042	0.174	38.73
SCR 48h	1.22	22.5	2.77	0.260	0.681	0.186	2.34	1.31	3.77	7.18	0.077	0.197	42.49
SMS1- 48h	0.96	13.0	1.84	0.249	0.663	0.172	2.28	1.31	2.86	6.21	0.027	0.118	29.69

Supplementary Table 3. Effect of overexpression of *BCR-ABL* in HL-60 cells on lipid levels. Reported are the levels of individual species of ceramide (**A**), DAG (**B**), and SM (**C**) extracted from HL-60/neo and HL-60/Bcr-abl cells as measured by mass spectrometry. Cells from each experimental condition were harvested after the same amount of time in culture and during the logarithmic stage of growth. Since basal levels of lipids were variable among the different experiments whereas the pattern of changes between experimental conditions were similar (Figure 5), reported are the absolute values of one representative experiment. In bold are the values that were significantly different compared to the time-matched control once the fold change versus the appropriate control was calculated among two independent experiments ($p < 0.05$ versus HL-60/neo). BDL: below detection limit.

A Ceramide species (pmoles/nmole of Pi)

Samples	C14-Cer	C16-Cer	C18-Cer	C18:1-Cer	C20-Cer	C20:1-Cer	C22-Cer	C22:1-Cer	C24-Cer	C24:1-Cer	C26-Cer	C26:1-Cer	Total Cer
HL-60/neo	0.08	0.83	0.07	0.03	0.02	BDL	0.08	0.02	1.81	1.39	0.07	0.16	4.56
HL-60/Bcr-abl	0.09	0.97	0.10	0.05	0.04	0.01	0.25	0.10	3.68	3.71	0.13	0.28	9.41

B DAG species (pmoles/nmole of Pi)

Samples	C14:0/16:0-DAG	C14:0/18:0-DAG	C14:0/18:1-DAG	C16:0/18:0-DAG	C16:0/18:1-DAG	C16:0/20:0-DAG	C16:1/18:0-DAG	C16:1/18:1-DAG	C18:0/18:1-DAG
HL-60/neo	0.55	0.11	0.49	0.83	3.22	0.02	0.08	1.60	1.03
HL-60/Bcr-abl	1.53	0.52	0.26	5.95	8.53	0.32	0.25	0.45	2.87

B continued DAG species (pmoles/nmole of Pi)

Samples	C18:0/18:2-DAG	C18:0/20:4-DAG	Di-C14:0-DAG	Di-C16:0-DAG	Di-C16:1-DAG	Di-18:0-DAG	Di-18:1-DAG	Total DAG
HL-60/neo	0.08	0.09	0.06	1.55	0.17	0.08	0.51	10.47
HL-60/Bcr-abl	0.17	0.35	0.15	8.59	0.05	0.13	0.48	30.60

C**SM species (pmoles/nmole of Pi)**

Samples	C14-SM	C16-SM	C18-SM	C18:1-SM	C20-SM	C20:1-SM	C22-SM	C22:1-SM	C24-SM	C24:1-SM	Total SM
HL-60/neo	0.16	69.34	1.33	0.17	0.21	0.01	2.41	0.89	2.03	23.95	100.5
HL-60/Bcr-abl	0.23	59.52	4.89	3.69	1.36	0.28	6.72	3.55	6.82	18.24	105.3

Supplementary Table 4. Effect of down-regulation of *BCR-ABL* on lipid levels of HL-60/Bcr-abl cells. Reported are the levels of individual species of ceramide (**A**), DAG, (**B**), and SM (**C**) from HL-60/Bcr-abl cells after down-regulation of *BCR-ABL*. HL-60/Bcr-abl cells were treated with either *BCR-ABL* targeting siRNA [HL-60/Bcr-abl/Bcr-abl(-)] or scrambled Allstar RNAi control [HL-60/Bcr-abl/SCR] and cells from each condition were collected after 36 hours and lipids were extracted for analysis. Since basal levels of lipids were variable among the different experiments whereas the pattern of changes between experimental conditions was similar (Figure 6A and B), reported are the absolute values of one representative experiment. In bold are the values that were significantly different compared to the time-matched control once the fold change versus the appropriate control was calculated among three independent experiments ($p < 0.05$ versus HL-60/Bcr-abl/SCR). BDL: below detection limit.

A Ceramide species (pmoles/nmole of Pi)

Samples	C14-Cer	C16-Cer	C18-Cer	C18:1-Cer	C20-Cer	C20:1-Cer	C22-Cer	C22:1-Cer	C24-Cer	C24:1-Cer	C26-Cer	C26:1-Cer	Total Cer
HL-60/Bcr-abl/SCR	0.10	0.72	0.07	0.03	0.07	0.01	0.24	0.11	2.42	2.27	0.08	0.13	6.25
HL-60/Bcr-abl/Bcr-abl(-)	0.15	0.53	0.11	0.07	0.07	0.03	0.18	0.15	1.12	1.78	0.03	0.06	4.28

B DAG species (pmoles/nmole of Pi)

Samples	C14:0/16:0 DAG	C14:0/18:0 DAG	C14:0/18:1 DAG	C16:0/18:0 DAG	C16:0/18:1 DAG	C16:0/20:0 DAG	C16:1/18:0 DAG	C16:1/18:1 DAG	C18:0/18:1 DAG
HL-60/Bcr-abl/SCR	1.24	0.56	0.20	7.09	4.48	0.26	0.06	0.40	0.61
HL-60/Bcr-abl/Bcr-abl (-)	0.05	0.02	0.01	0.58	0.57	0.23	0.48	0.50	0.32

B continued DAG species (pmoles/nmole of Pi)

Samples	C18:0/18:2-DAG	C18:0/20:4-DAG	Di-C14:0-DAG	Di-C16:0-DAG	Di-C16:1-DAG	Di-C18:0-DAG	Di-C18:1-DAG	Total DAG
HL-60/Bcr-abl/SCR	0.02	0.06	0.08	3.11	0.01	0.06	0.12	18.36
HL-60/Bcr-abl/Bcr-abl (-)	0.03	0.22	BDL	0.09	BDL	0.03	0.06	3.19

C**SM species (pmoles/nmole of Pi)**

Samples	C14-SM	C16-SM	C18-SM	C18:1-SM	C20-SM	C20:1-SM	C22-SM	C22:1-SM	C24-SM	C24:1-SM	C26-SM	C26:1-SM	Total SM
HL-60/Bcr-abl/SCR	0.72	55.52	3.56	1.27	1.16	0.33	5.87	3.28	4.97	16.00	0.01	0.33	93.02
HL-60/Bcr-abl/Bcr-abl(-)	0.70	39.47	2.92	1.15	0.83	0.24	4.33	2.70	3.25	12.80	0.02	0.22	68.63

Supplementary Table 5. Effect of inhibition of Bcr-abl activity with Imatinib on lipid levels in K562 cells. Reported are the levels of individual species of ceramide (**A**), DAG (**B**) and SM (**C**) as measured by mass spectrometry during pharmacological inhibition of Bcr-abl in K562 cells with different concentrations of Imatinib (0.4 and 1 μ M, Im) after 24 and 30 hours of incubation. Since basal levels of lipids were variable among the different experiments whereas the pattern of changes between experimental conditions was similar (Figure 6C and D), reported are the values of one representative experiment. In bold are the values that were significantly different compared to the time-matched control once the fold change versus the appropriate control was calculated among three independent experiments ($p < 0.05$ versus CT). BDL: below detection limit.

A Ceramide species (pmoles/nmole of Pi)

Samples	C14-Cer	C16-Cer	C18-Cer	C18:1-Cer	C20-Cer	C20:1-Cer	C22-Cer	C22:1-Cer	C24-Cer	C24:1-Cer	C26-Cer	C26:1-Cer	Total Cer
CT 24h	0.051	0.56	0.038	0.02	0.043	0.004	0.19	0.062	2.63	2.18	0.049	0.111	5.94
Im (0.4 μ M) 24h	0.089	0.57	0.051	0.087	0.061	0.008	0.24	0.107	2.36	2.83	0.038	0.1	6.54
Im (1 μ M) 24h	0.107	0.65	0.061	0.073	0.071	0.009	0.20	0.102	2.24	2.80	0.033	0.067	6.41
CT 30h	0.068	0.99	0.031	0.026	0.053	0.003	0.26	0.080	3.15	2.73	0.058	0.115	7.56
Im (0.4 μ M) 30h	0.170	1.02	0.109	0.119	0.106	0.017	0.34	0.202	2.85	3.89	0.045	0.120	8.99
Im (1 μ M) 30h	0.181	0.92	0.109	0.118	0.089	0.019	0.27	0.163	2.53	3.75	0.038	0.092	8.28

B DAG species (pmoles/nmole of Pi)

Samples	C14:0/16:0-DAG	C14:0/18:0-DAG	C14:0/18:1-DAG	C16:0/18:0-DAG	C16:0/18:1-DAG	C16:0/20:0-DAG	C16:1/18:0-DAG	C16:1/18:1-DAG
CT 24h	0.29	0.23	0.024	4.15	1.60	0.19	0.12	0.07
Im (0.4 μ M) 24h	0.03	0.04	0.015	1.49	0.83	0.03	0.03	0.02
Im (1 μ M) 24h	0.02	0.03	0.01	1.14	0.62	BDL	0.02	0.02
CT 30h	0.69	0.65	0.073	10.61	3.03	0.57	0.30	0.19
Im (0.4 μ M) 30h	0.07	0.20	0.015	3.73	1.12	0.12	0.06	0.05
Im (1 μ M) 30h	0.02	0.06	0.013	1.45	0.97	0.03	0.04	0.03

B continued**DAG species (pmoles/nmole of Pi)**

Samples	C18:0/18:1-DAG	C18:0/18:2-DAG	C18:0/20:4-DAG	Di-C14:0-DAG	Di-C16:0-DAG	Di-C18:0-DAG	Di-C18:1-DAG	Total DAG
CT 24h	0.72	0.08	0.35	0.007	1.07	0.16	0.24	9.30
Im (0.4uM) 24h	0.53	0.04	0.84	0.002	0.21	0.08	0.19	4.38
Im (1uM) 24h	0.73	0.20	2.01	0.001	0.10	0.13	0.26	5.29
CT 30h	1.75	0.21	0.74	0.013	2.36	0.39	0.47	22.05
Im (0.4uM) 30h	1.09	0.36	1.96	0.003	0.35	0.23	0.36	9.72
Im (1uM) 30h	1.15	0.45	3.07	0.002	0.13	0.13	0.49	8.04

C**SM species (pmoles/nmole of Pi)**

Samples	C14-SM	C16-SM	C18-SM	C18:1-SM	C20-SM	C20:1-SM	C22-SM	C22:1-SM	C24-SM	C24:1-SM	C26-SM	C26:1-SM	Total SM
CT 24h	0.056	15.7	3.42	0.33	0.67	0.063	4.75	2.38	4.34	12.8	0.009	0.043	44.56
Im (0.4uM) 24h	0.059	11.9	1.95	0.16	0.14	0.040	2.47	1.42	2.36	9.0	0.002	0.027	29.53
Im (1uM) 24h	0.075	14.5	2.35	0.23	0.17	0.052	3.25	1.90	3.15	11.3	0.001	0.034	37.01
CT 30h	0.074	21.5	4.18	0.39	0.80	0.071	6.02	2.85	5.47	15.9	0.012	0.055	57.32
Im (0.4uM) 30h	0.093	19.7	3.04	0.32	0.29	0.067	4.22	2.58	4.07	14.8	0.005	0.047	49.23
Im (1uM) 30h	0.091	19.2	3.00	0.28	0.21	0.060	3.95	2.29	4.13	14.1	0.001	0.043	47.36