The Lysosome and HER3 (ErbB3) Selective Anticancer

Agent Kahalalide F: Semisynthetic Modifications and

Antifungal Lead-Exploration Studies

Supporting Information

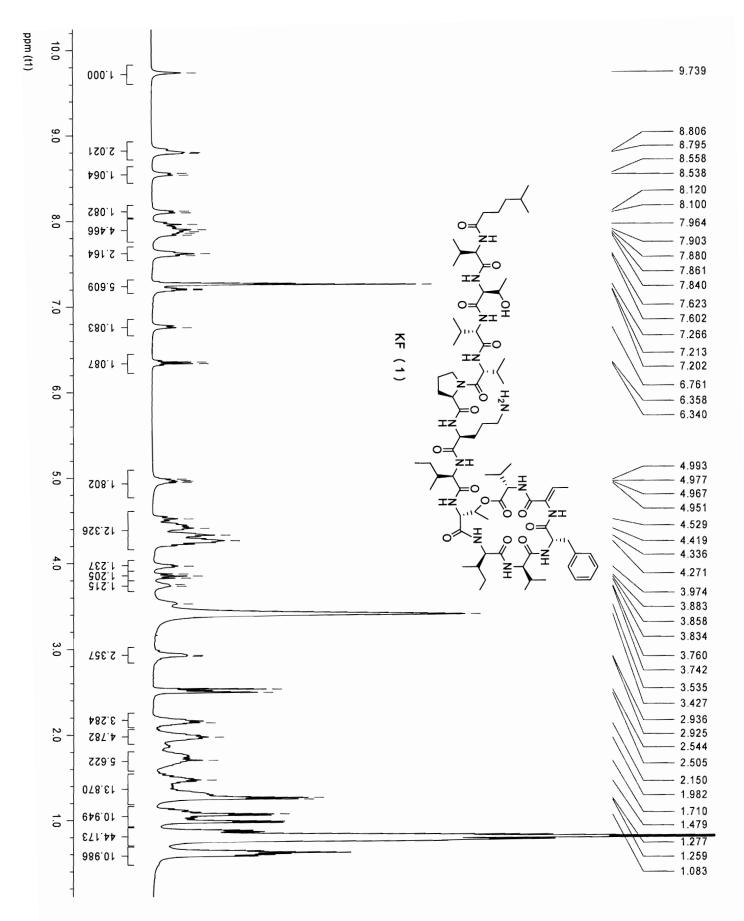
Abbas Gholipour Shilabin, Noer Kasanah, David E. Wedge² and Mark T. Hamann 1**

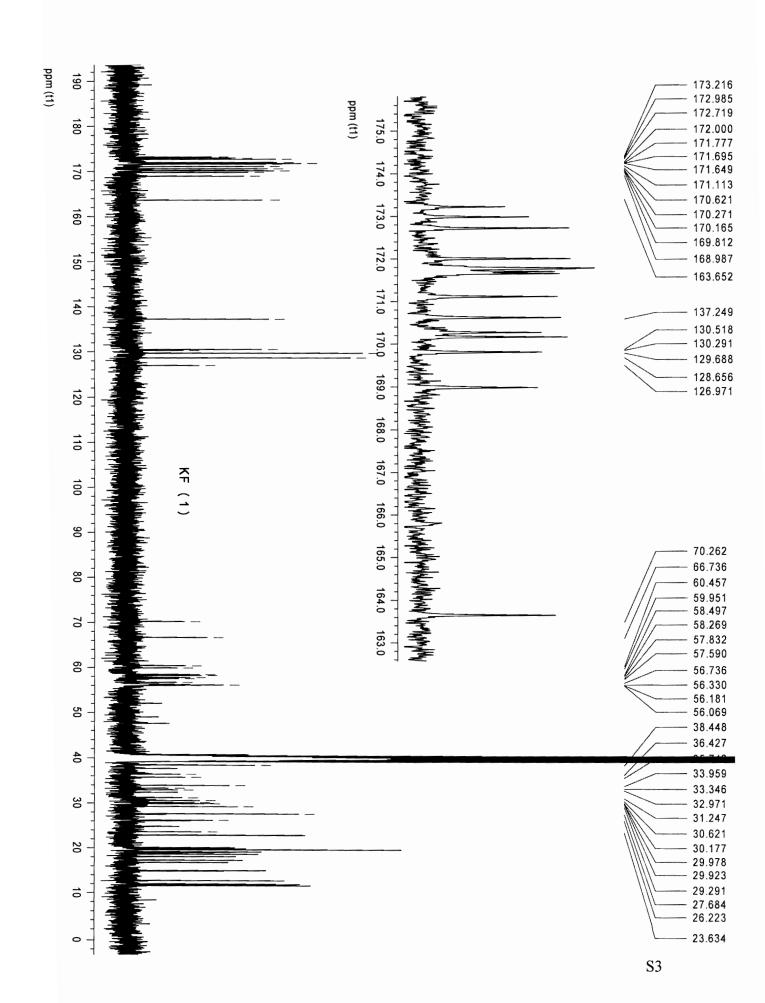
¹Dept of Pharmacognosy, School of Pharmacy, the University of Mississippi, University, MS 38677

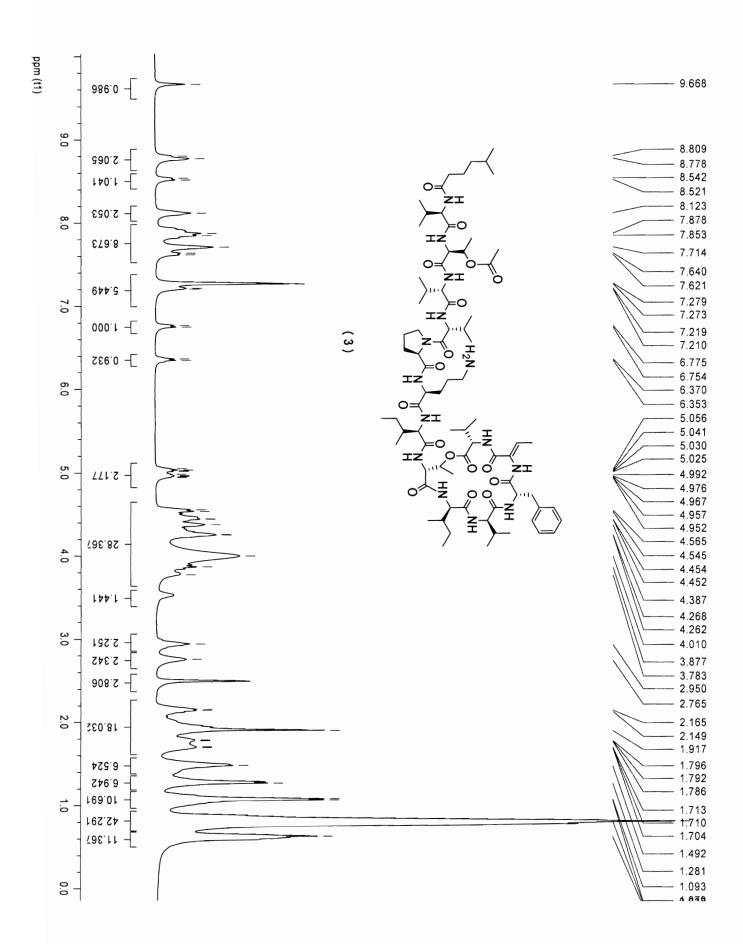
²ARS, Natural Product Utilization Research Unit, National Center for Natural Products Research, University of Mississippi, University, MS 38677

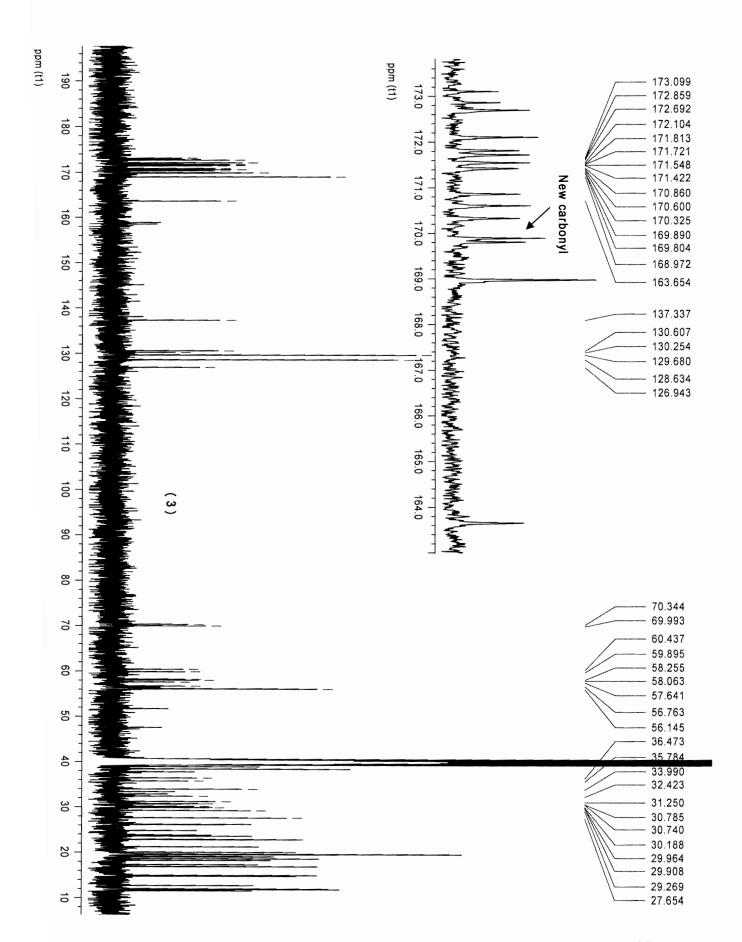
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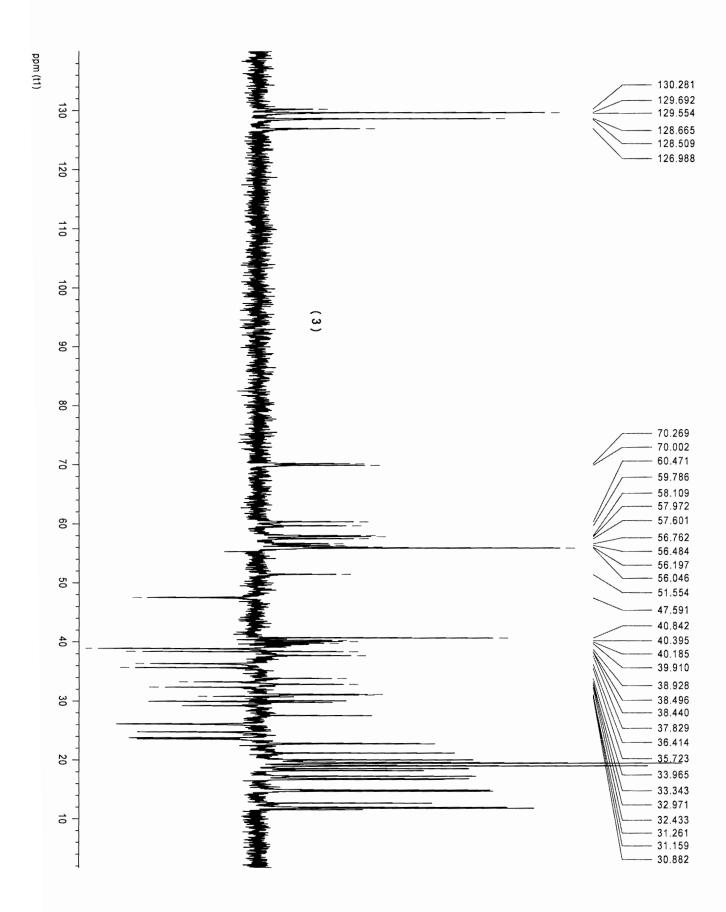
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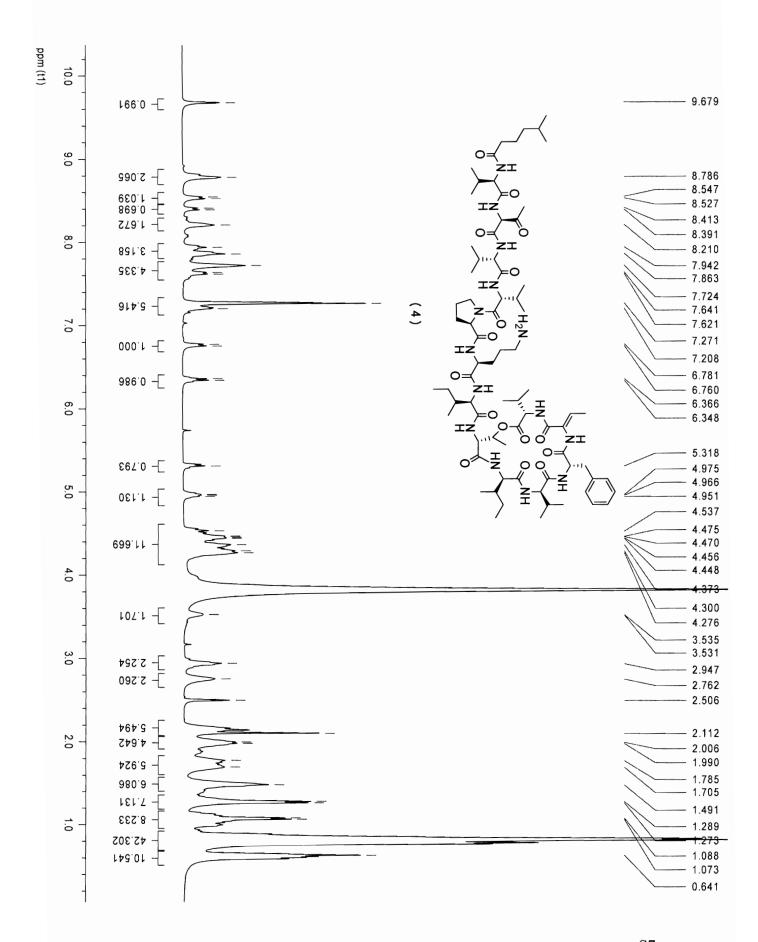


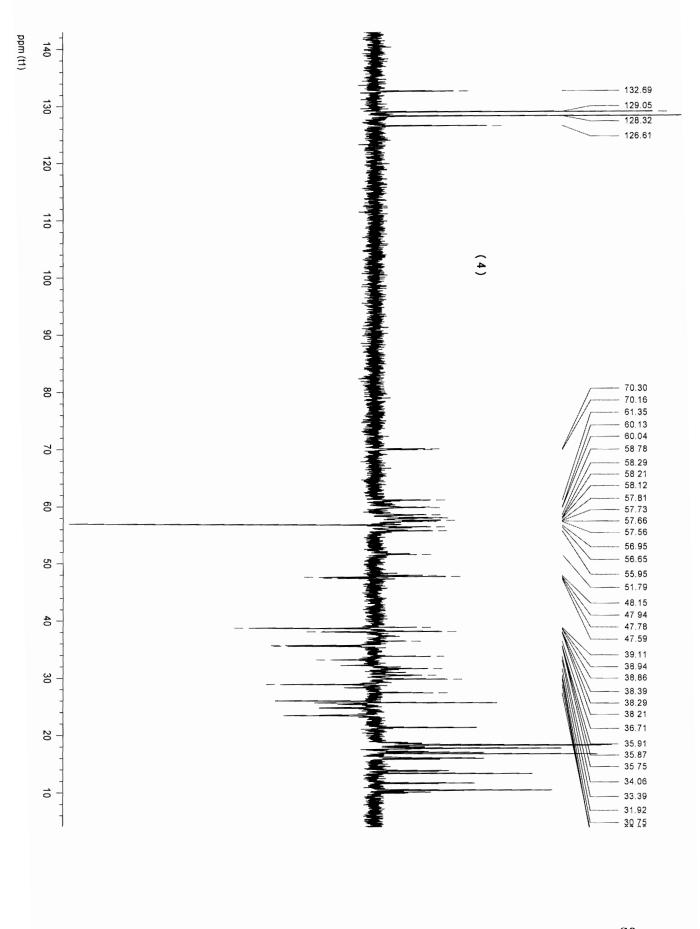


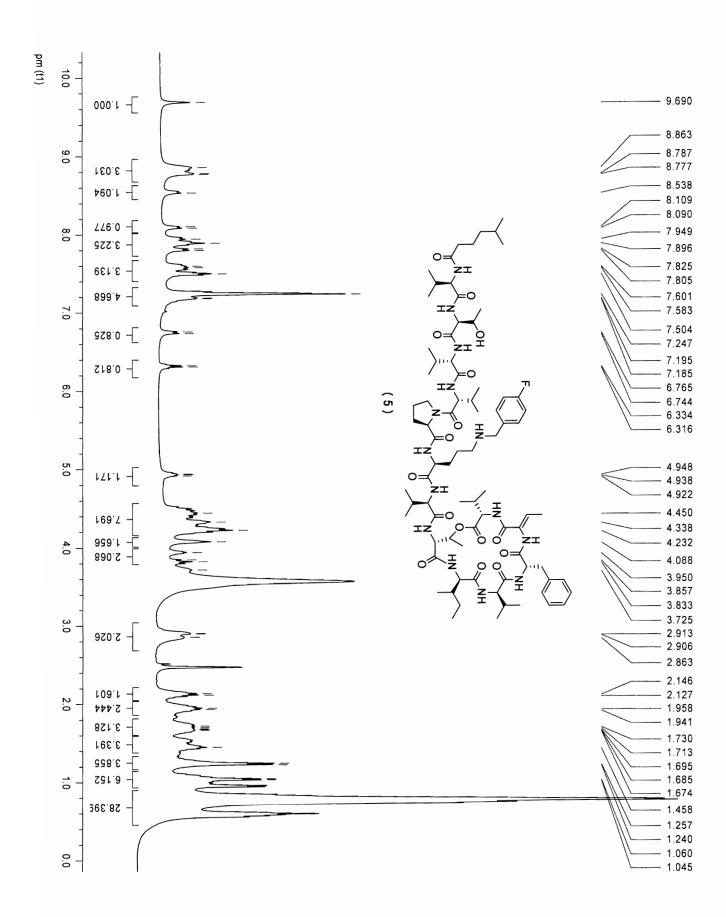


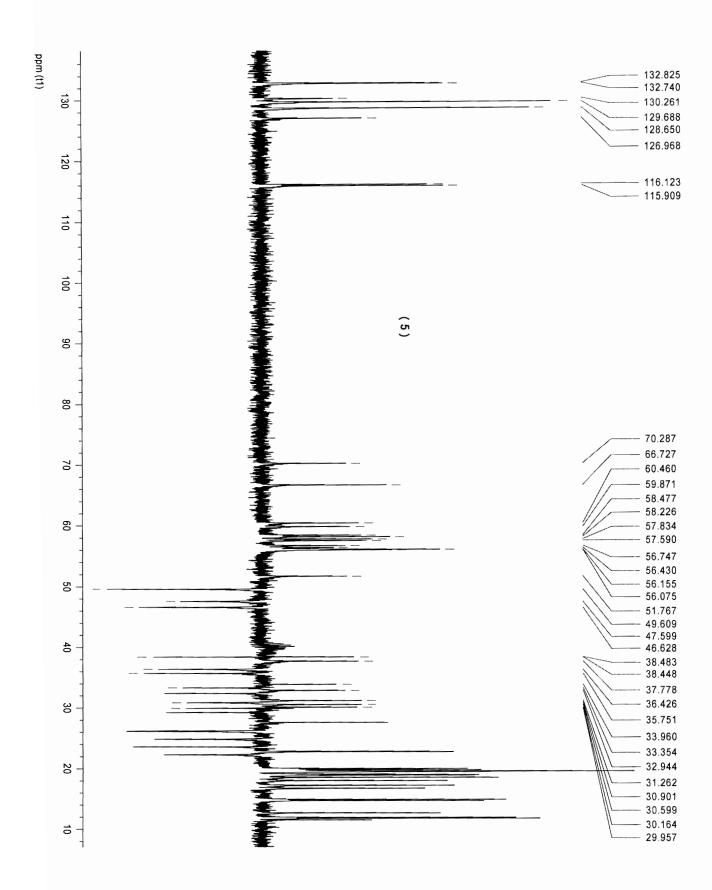


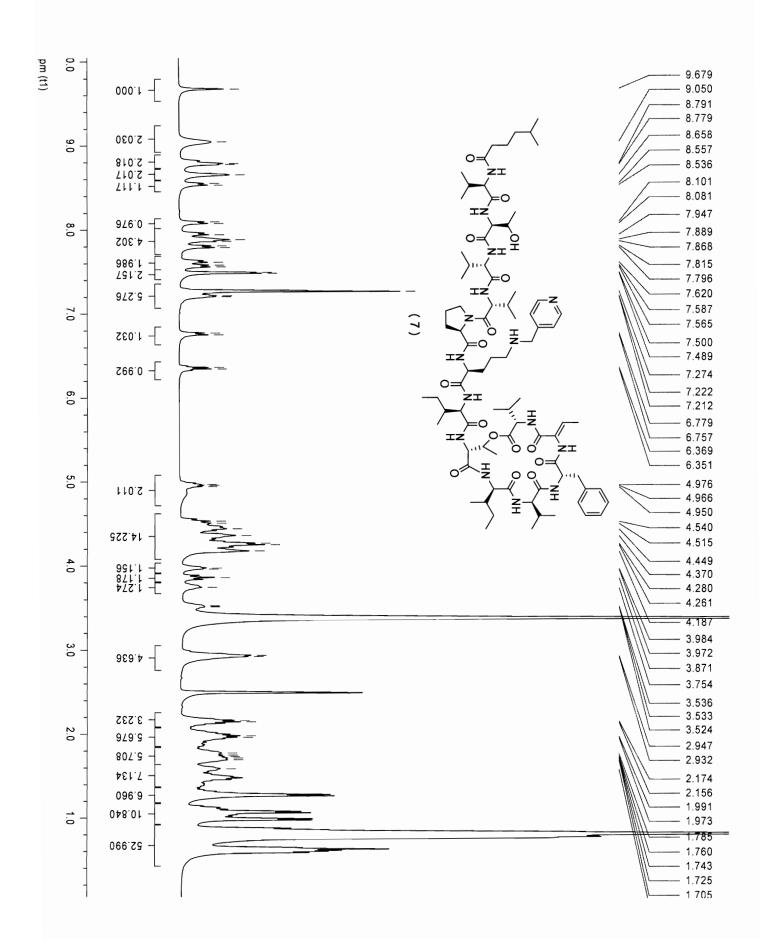


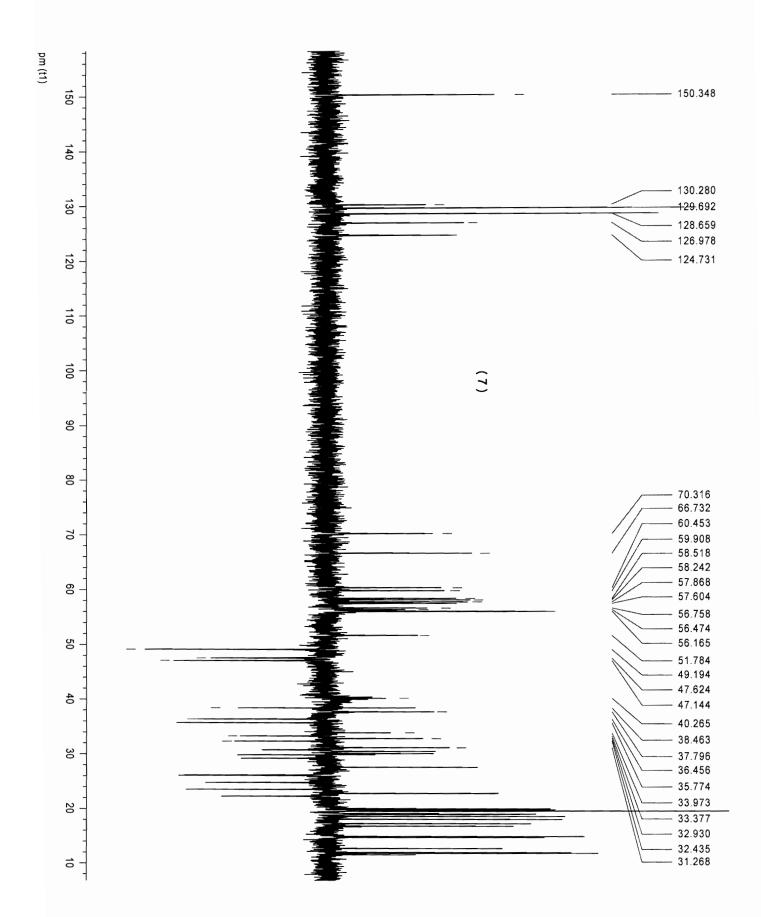


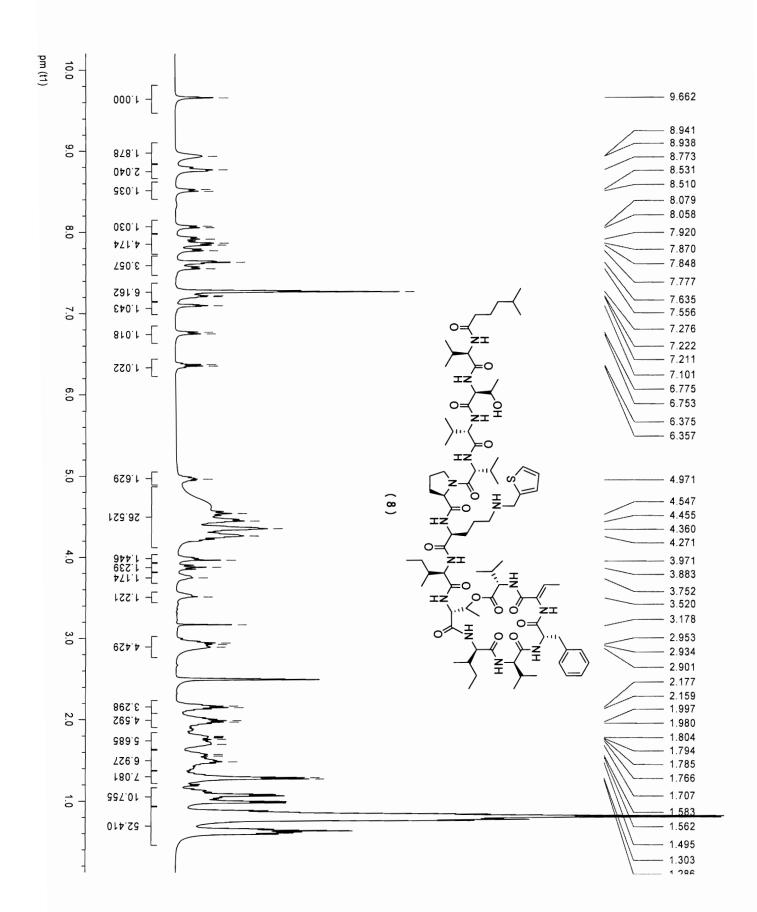


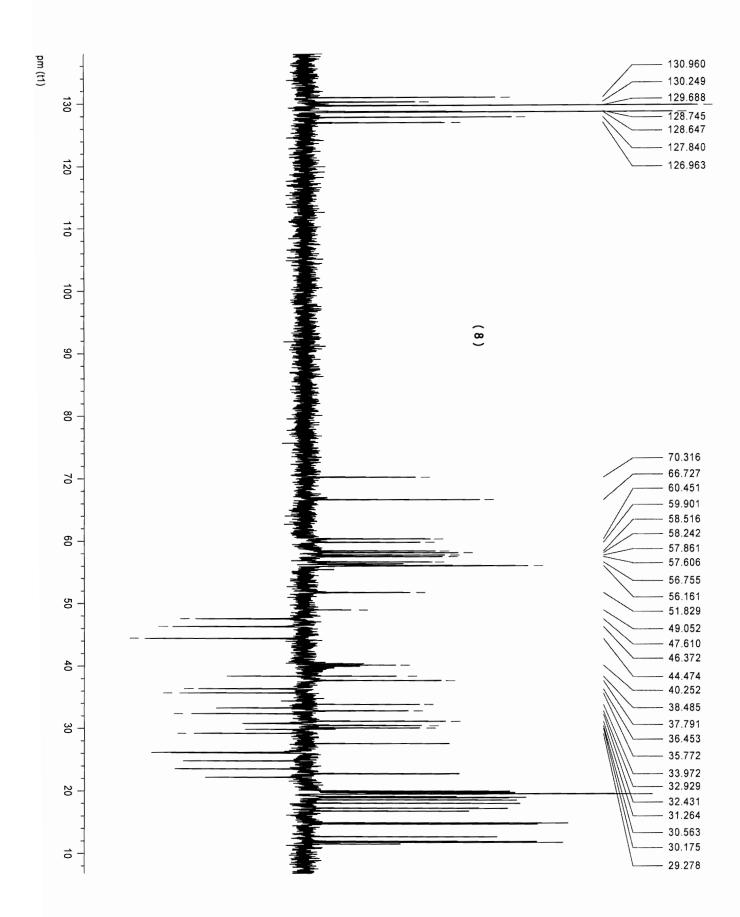


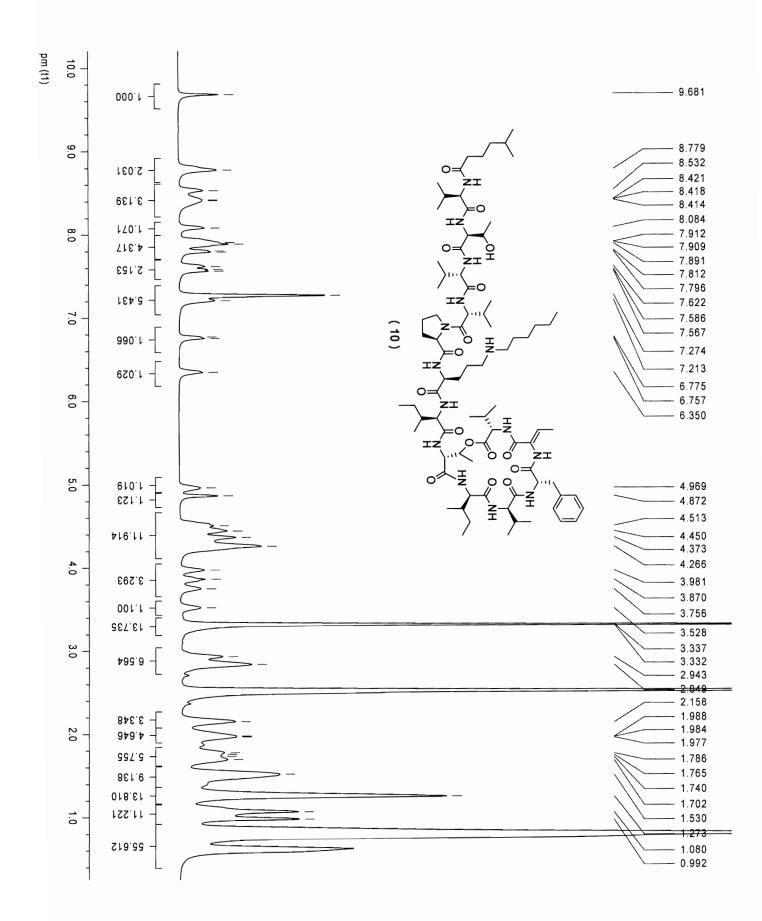


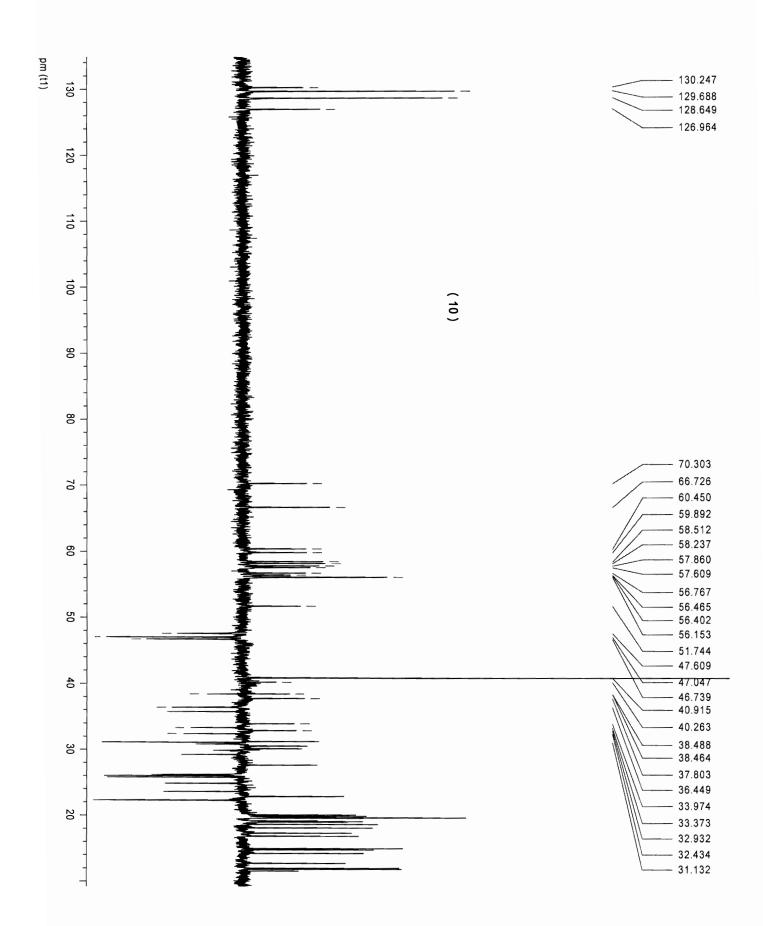


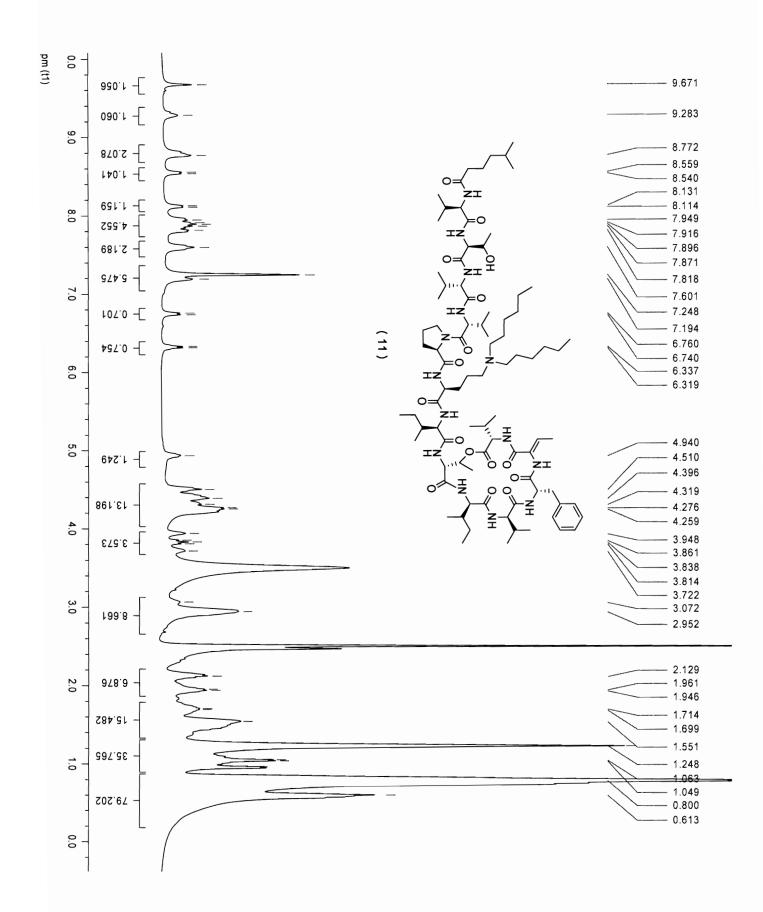


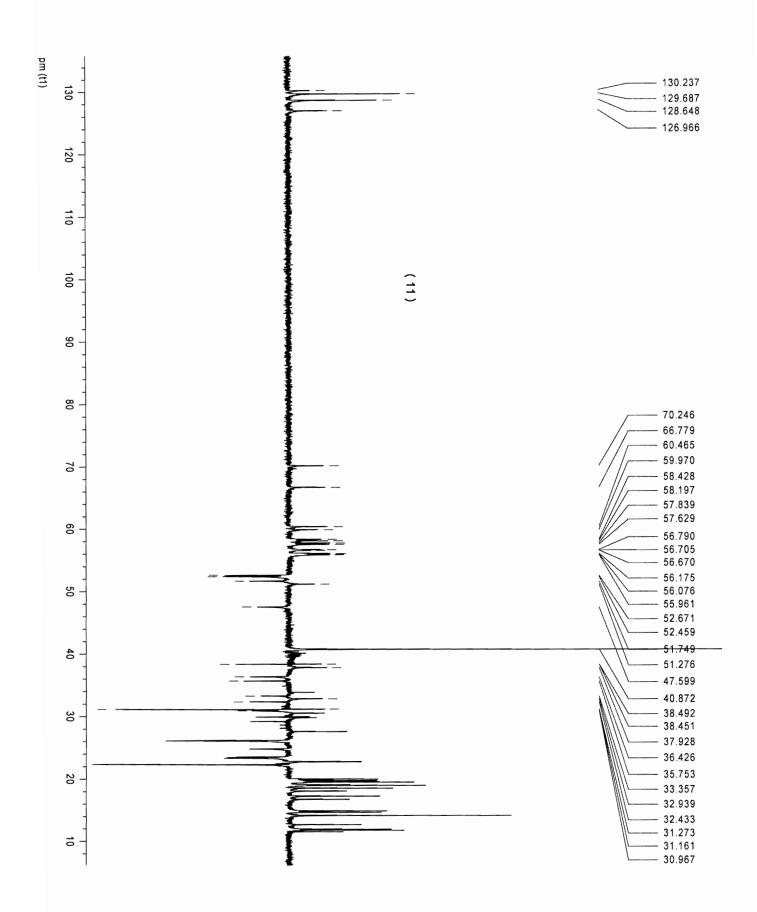


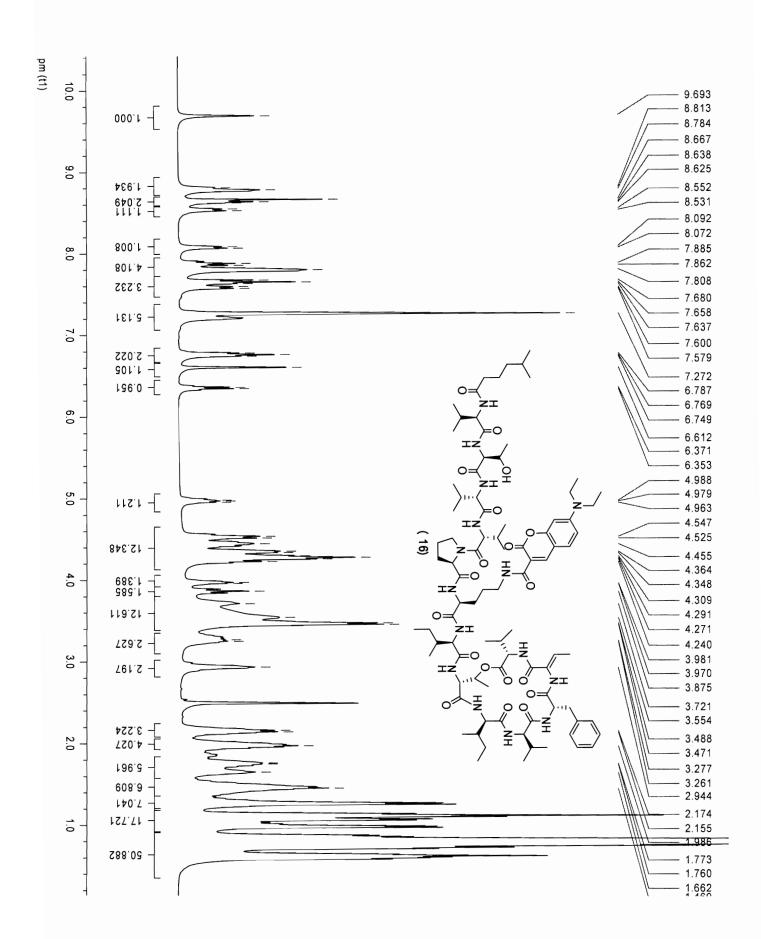


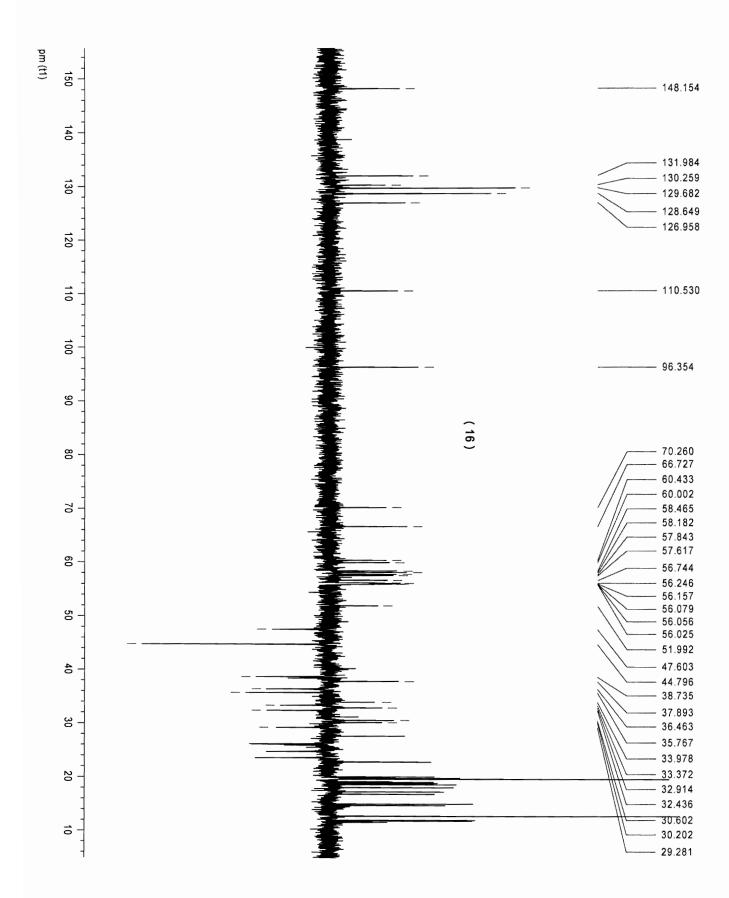


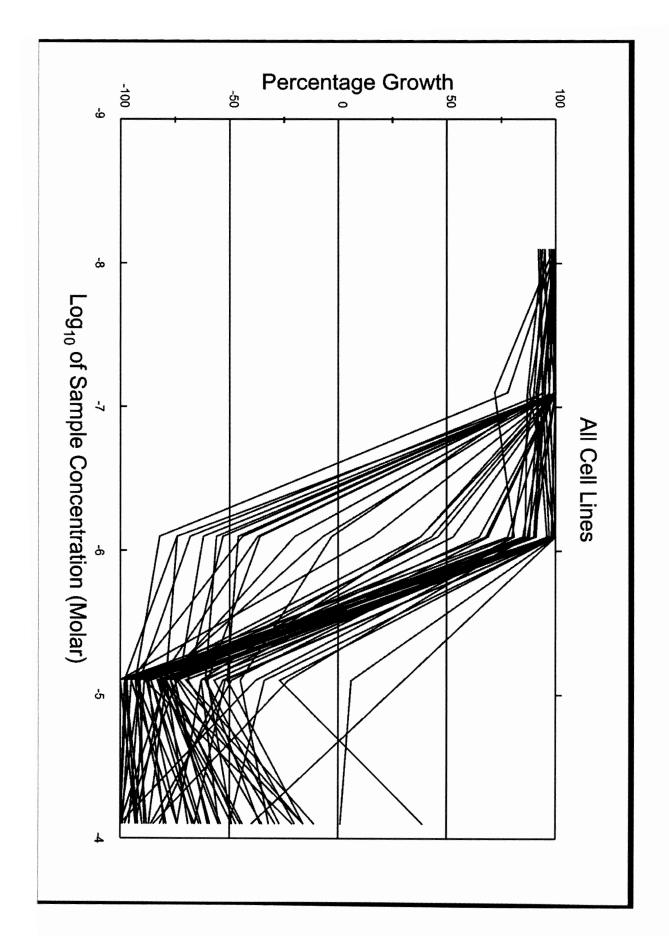


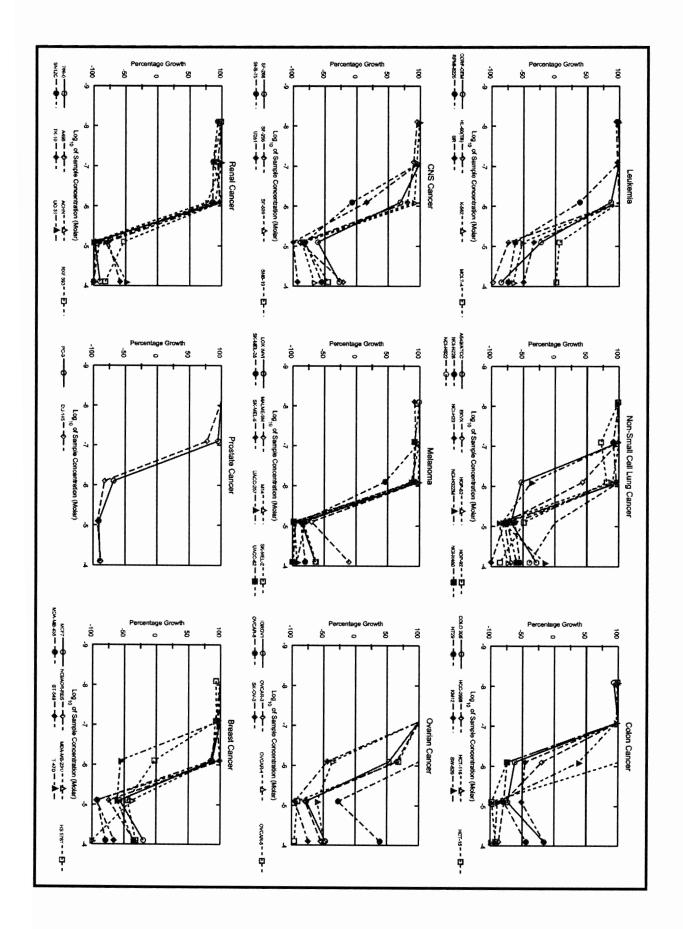




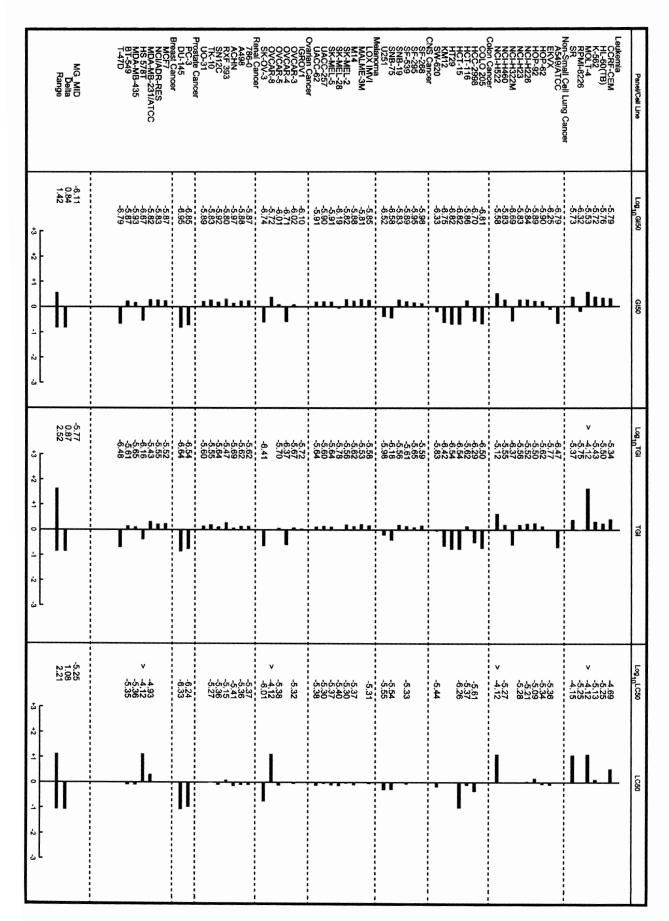


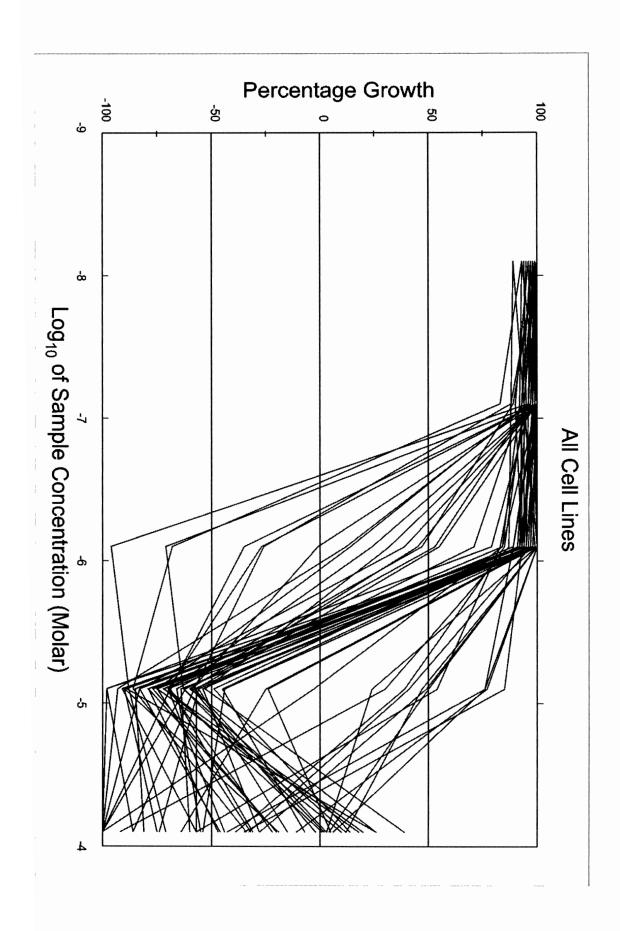


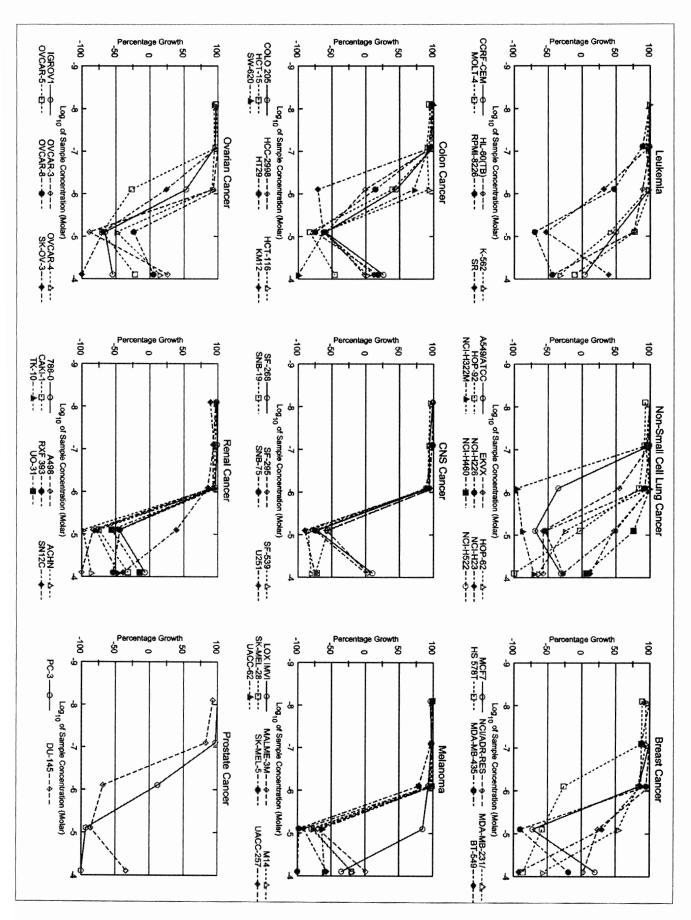




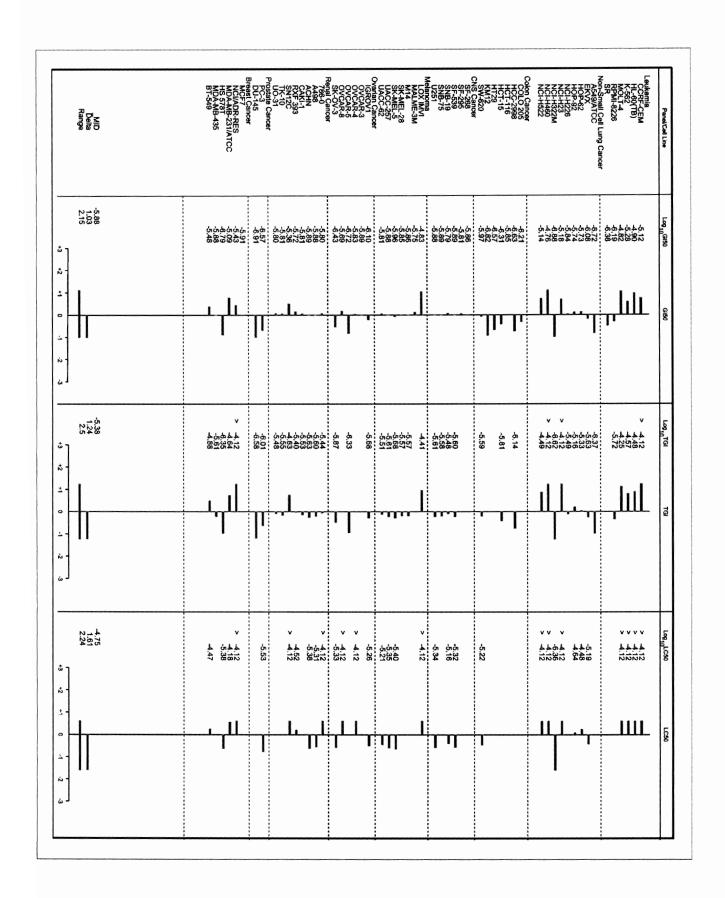
MCF7 NCI/ADR-RES MIDA-MB-231/ATCC MS 7/81 MDA-MB-435 B1-549 T-47D	Prostate Cancer PC-3 DU-145	Renal Cancer 788-0 788-0 A498 ACHN RXF 393 SN12C TK-10 UO-31	Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 SK-OV-3	Melanome LOX IMM/ MALME-3M M14 SK-MEL-2 SK-MEL-2 SK-MEL-2 UACC-62 UACC-62	CNS Cancer SF-268 SF-255 SF-539 SF-539 SNB-19 SNB-75 U251	Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-145 HT29 KM12 SW-620	Non-Small Ceil Lung Ca AS48/ATCC EKVX HOP-62 HOP-92 NCH-123 NCH-123 NCH-1322M NCH-1522M NCH-1522 NCH-1522M	CCRF-CEM HL-80(TB) K-582 MOLT4 RPMI-8226 SR	Panel/Cell Line	
0.287 0.406 0.377 0.426 0.475 0.377 0.627	0.356 0.220	0.322 1.109 0.204 0.768 0.613 0.656 0.525	0.818 0.406 0.443 0.366 0.099 0.651	0.193 0.484 0.350 0.662 0.254 0.234 1.047 0.620	0.364 0.476 0.385 0.501 0.725 0.247	0.211 0.549 0.124 0.223 0.168 0.388 0.388	Cancer 0.311 0.469 0.185 0.918 0.473 0.491 0.554 0.236 0.854	0.872 0.495 0.612 0.355 0.889 0.315	Time Zero	ı
1.754 1.311 1.002 0.895 1.555 0.755	1.134 0.917	1.311 1.739 0.793 1.197 2.358 1.300 1.402	1.930 0.741 1.019 0.800 0.439 1.447	1.198 0.744 1.112 1.156 0.728 1.399 2.028 2.141	1.194 1.096 1.325 1.326 1.124 1.178	0.953 1.588 1.053 1.298 1.129 1.483 0.668	1.434 1.267 0.557 1.462 1.064 1.306 1.249 1.991 2.079	2.997 1.178 1.981 1.292 3.044 1.365	ă. Ĉ	
1.777 1.356 1.005 0.863 1.578 0.771 1.352	1.139 0.920	1.301 1.746 0.801 1.192 2.251 1.340 1.472	1.980 0.801 1.057 0.832 0.460 1.585	1.189 0.777 1.159 1.206 0.727 1.306 2.070 2.134	1.215 1.068 1.319 1.392 1.145 1.219	0.898 1.687 1.075 1.292 1.153 1.492 0.661	1.512 1.324 0.547 1.458 1.112 1.383 1.279 2.101 2.112	3.290 1.248 1.956 1.332 3.008 1.317	<u>6</u> .2	
1.850 1.399 0.953 0.865 1.526 0.738 1.290	1.099 0.764	1.346 1.701 0.790 1.145 2.128 1.304	2.033 0.799 1.076 0.845 0.447 1.525	1.213 0.819 1.151 1.220 0.734 1.326 2.070 2.075	1,233 1,031 1,282 1,368 1,202 1,192	0.969 1.610 1.091 1.339 1.168 1.575 0.653	1.444 1.257 0.588 1.309 1.010 1.408 1.366 2.063 2.253	3.242 1.341 2.183 1.432 3.064 1.333	4.1	
1.569 1.328 0.928 0.413 1.389 0.750 0.278	0.114 0.039	1.324 1.723 0.664 1.199 2.114 1.311 1.316	1,404 0.626 0.284 0.662 0.449 0.363	1.223 0.754 1.097 1.197 1.497 0.474 1.277 1.902 2.004	0.939 0.975 1.240 1.402 0.671 0.401	0.081 0.441 1.085 0.059 0.044 0.211 0.310	0.147 0.814 0.519 1.357 1.040 1.328 0.347 2.017 2.208	2.729 1.323 2.228 1.430 1.700 1.422	Mean Optical Densities -6.1 -5.1	· ·
0.123 0.106 0.235 0.236 0.036 0.028 0.246	0.032 0.015	0.005 0.039 -0.004 0.358 0.054 0.154 0.094	0.188 0.087 0.177 0.034 0.072 0.030	0.028 0.147 0.011 0.116 0.034 0.012 0.209 0.011	0.141 0.052 0.054 0.087 0.141	0.057 0.115 -0.006 0.006 0.036 0.192 0.192	0.096 0.098 0.023 0.472 0.176 0.105 0.099 0.085	0.668 0.128 0.296 0.412 0.330 0.209	al Densitie	i
0.231 0.263 -0.020 0.288 0.098 0.130 0.403	0.040	0.031 -0.027 0.001 0.141 -0.022 0.271 0.268	0.435 0.185 0.227 0.014 0.233 0.170	0.070 0.430 0.024 0.244 0.052 0.003 0.078	0.265 0.376 0.128 0.277 0.323 0.017	0.177 0.074 -0.026 0.018 0.094 0.325 0.007	0.222 0.146 0.049 0.133 0.213 0.002 0.465 0.095	0.131 0.008 0.206 0.368 0.231 0.156	<u>+</u> .	
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107 110 92 94 95 96	95 78	104 94 98 88 88 101	110 110 110 110	92 10 10 10 10 10 10 10 10 10 10 10 10 10	12 12 13 15 12 15 15 15 15 15 15 15 15 15 15 15 15 15	102 102 104 104 108 97	101 99 103 97 72 72 113 114 114	112 124 115 115 101 97	-7.1	ation
នំខន ិន	& &	90 90 90 90 90 90 90	± 53 88 88 88	91 8 8 8 8 8 9 10 2 9 1	105 91 86 86 105 91 86 86	-62 -20 -74 -74 -38	11 11 11 11 11 11 11 11 11 11 11 11 11	87 121 118 115 38	-6.1	
5 2 2 4 3 4 5 5	-94 93	577 ± 538	95 17 95 17 95 17 95 17 95 17	***	106 4 3 8 8 4 6	-73 -79 -98 -51	. 78 78 78	ដូវជន្ង	Percent Growth	
នុងខ្លួន	8 8	\$ \$ \$ \$ \$ \$ \$ \$	£2&&&\$	2 2 8 8 8 8 2 2 2 2 2 2 2 2 2 2 2 2 2 2	8 8 6 6 2 2	-16 -100 -100 -15 -15	4.50 6.50 6.50 6.50 6.50 6.50 6.50 6.50 6	\$ 2 1 2 2	ï F	
1.36E-6 1.48E-6 1.50E-6 2.12E-7 1.18E-6 1.35E-6 1.61E-7	1.42E-7 1.12E-7	1.36E-6 1.32E-6 1.08E-6 1.59E-6 1.20E-6 1.46E-6 1.26E-6	7.87E-7 9.60E-7 1.93E-7 9.76E-7 1.91E-6 1.83E-7	1.43E-6 1.52E-6 1.32E-6 1.52E-6 1.52E-6 6.46E-7 1.23E-6 1.25E-6	1.05E-6 1.13E-6 1.28E-6 1.48E-6 2.65E-7 3.03E-7	1.56E-7 2.01E-7 1.37E-6 1.51E-7 1.51E-7 1.79E-7 4.65E-7	1.61E-7 5.65E-7 1.26E-6 1.30E-6 1.46E-6 1.46E-6 1.47E-6 2.03E-7 1.47E-6	1.63E-6 1.74E-6 1.89E-6 2.95E-6 4.78E-7 1.88E-6	GI50	
3.02E-6 2.85E-6 3.76E-6 6.95E-7 2.25E-6 2.46E-6 3.33E-7	2.87E-7 2.30E-7	2.41E-6 2.36E-6 2.06E-6 3.37E-6 2.29E-6 2.79E-6 2.50E-6	1.91E-6 2.14E-6 4.25E-7 2.01E-6 3.87E-7	2.63E-6 2.98E-6 2.39E-6 2.77E-6 1.68E-6 2.29E-6 2.49E-6 2.27E-6	2.54E-6 2.24E-6 2.45E-6 2.72E-6 6.55E-7 1.04E-6	3.15E-7 5.17E-7 2.42E-6 2.89E-7 2.88E-7 3.79E-7 1.48E-6	3.40E-7 1.59E-6 2.40E-6 3.16E-6 3.02E-6 2.76E-6 4.29E-7 7.54E-6	4.61E-8 3.13E-6 3.72E-6 > 7.50E-5 1.78E-6 4.30E-8	TGI	
1.18E-5 > 7.50E-5 4.32E-6 4.49E-6	5.81E-7 4.72E-7	4 29E-6 4 32E-6 3.93E-6 7.12E-6 4.39E-6 5.32E-8	4.75E-8 4.16E-6 > 7.50E-5 9.72E-7	4.84E-6 4.31E-6 5.07E-6 3.98E-6 4.28E-6 4.98E-6 4.17E-6	4.69E-6 2.86E-6 2.79E-8	2.43E-6 4.26E-6 5.52E-7	4.34E-6 4.59E-8 8.16E-6 6.23E-6 5.21E-6 5.43E-6 7.50E-5	2.03E-5 5.64E-8 7.34E-8 > 7.50E-5 5.58E-6 7.03E-5	LC50	

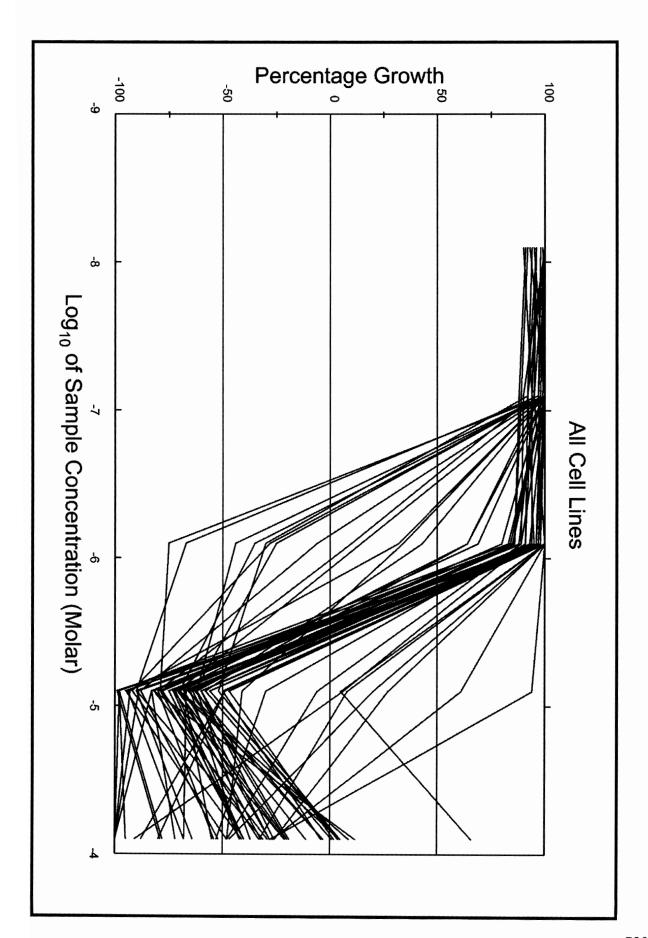


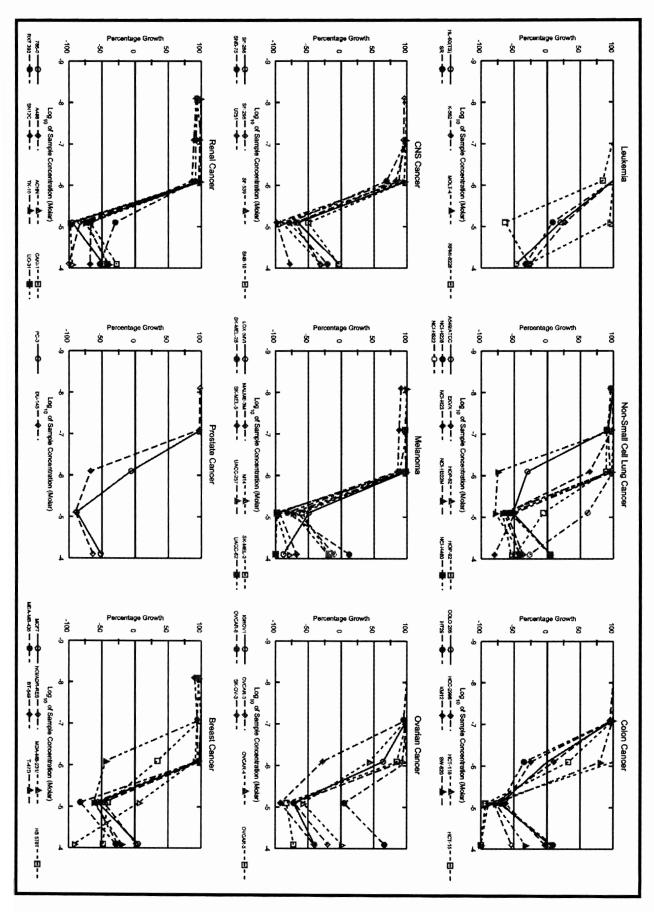




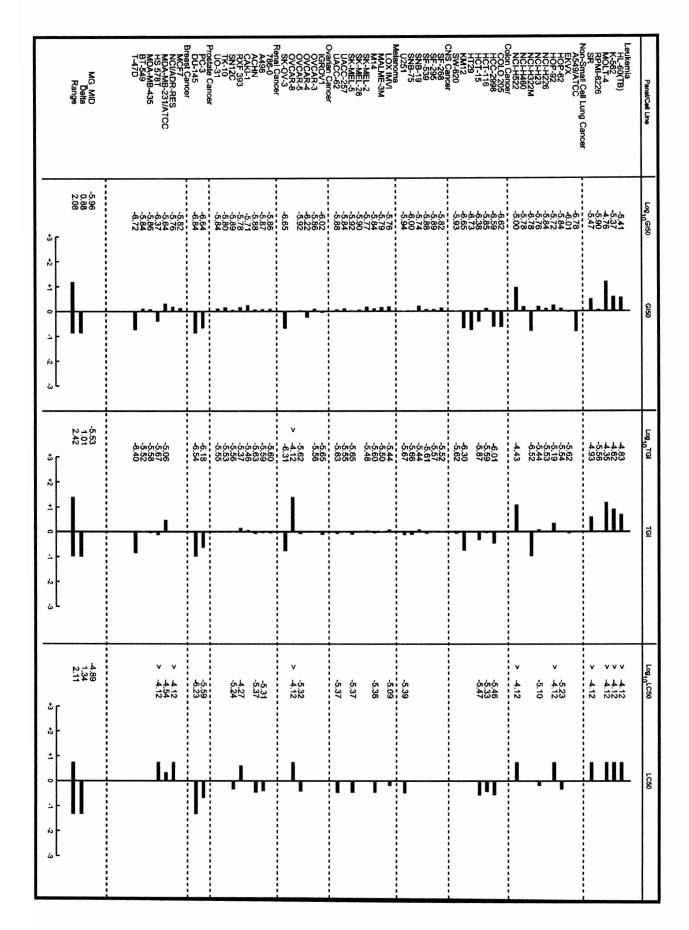
Breast Cancer MCF7 NCI/ADR-RES NDA-MB-231/ATCC HS 578T MDA-MB-435 BT-549	Prostate Cancer PC-3 DU-145	Renal Cancer 788-0 A498 ACHN CAKL-1 CAKL-1 RC-233 SN12C TK10 UO-31	Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-5 OVCAR-8 SK-OV-3	Melanoma LOX IMVI MALME-3M M14 SK-MEL-28 SK-MEL-5 UACC-257 UACC-62	CNS Cancer SF-268 SF-295 SF-539 SNB-19 SNB-75 U251	Colon Cancer COLO 205 HCC-2398 HCT-116 HCT-15 HT29 KM12 SW-620	Non-Small Cell Lung A549/ATCC EK/X HOP-82 HOP-92 NCI-H223 NCI-H23 NCI-H23 NCI-H32M NCI-H320 NCI-H320 NCI-H320	Leukernia CART-CEM HL-60(TB) K-562 MOLT-4 RPMI-8226 SR	Panel/Cell Line
0.226 0.510 0.515 0.432 0.435	0.622 0.170	0.580 0.462 0.367 0.571 0.508 0.537 0.571 0.537	0.241 0.487 0.362 0.583 0.552 0.573	0.260 0.867 0.360 0.685 0.336 0.618 0.435	0.502 0.678 0.738 0.421 0.580 0.226	0.202 0.417 0.185 0.223 0.210 0.458 0.157	Cancer 0.449 0.403 0.372 1.035 0.816 0.816 0.360 0.701 0.241 0.437	0.299 0.414 0.163 0.488 0.713 0.248	Time Zero
0.993 1.563 1.190 0.776 1.584	1.982 0.686	2.208 0.997 1.326 1.098 0.751 1.707 1.169 1.003	0.738 1.286 1.098 1.863 1.798 1.046	1.833 1.244 1.188 1.994 1.150 1.315 1.699	1.748 2.360 1.858 1.384 1.139 1.172	0.821 1.348 1.682 1.282 1.282 1.283 1.530 2.087	1.557 1.148 1.287 1.464 1.760 1.006 1.799 1.845 0.952	1.415 2.157 1.646 2.077 2.224 0.822	Ç
1.080 1.645 1.149 0.737 1.623	2.034 0.651	2.184 0.981 1.296 1.132 0.747 1.577 1.214 1.046	0.724 1.399 1.057 1.826 1.827 1.101	1.776 1.296 1.206 1.976 1.144 1.345 1.705	1.738 2.351 1.807 1.439 1.168 1.180	0.885 1.401 1.624 1.208 1.497 2.053 1.033	1.620 1.259 1.259 1.433 1.860 1.036 1.859 1.903 0.962	1.498 2.309 1.628 2.157 2.333 0.819	2
1.036 1.646 1.155 0.736 1.637	1.939 0.598	2.186 0.958 1.290 1.137 0.785 1.638 1.221	0.717 1.381 1.062 1.902 1.865 1.091	1.799 1.351 1.195 2.011 1.126 1.338 1.793	1.677 2.363 1.778 1.412 1.131 1.149	0.860 1.354 1.536 1.293 1.481 2.146 0.980	1.638 1.199 1.231 1.429 1.856 1.031 1.761 1.808 0.948	1.405 2.162 1.617 1.986 2.051 0.837	Mea -7.1
0.871 1.674 1.078 0.320 1.528	0.783 0.055	2.147 0.960 1.277 1.138 0.785 1.532 1.224 1.014	0.503 1.232 1.030 0.424 1.894 0.688	1.718 1.374 1.163 1.969 0.980 1.282 1.725	1.670 2.370 1.770 1.414 1.077 1.119	0.480 0.413 1.580 0.632 0.390 0.135	0.292 0.811 1.274 1.394 1.688 1.019 0.029 1.838 1.014	1.439 1.966 1.600 2.108 1.425 0.430	n Optica -6,1
0.063 0.762 0.881 0.180 0.044	0.045 0.025	0.319 0.077 0.006 0.144 0.284 0.997 0.119 0.133	0.083 0.056 0.184 0.177 0.422 0.177	1.598 0.202 0.082 0.142 0.07 0.054 0.156	0.139 0.283 0.112 0.185 0.143 0.023	0.081 0.173 0.069 0.038 0.053 0.171	0.139 0.174 0.278 1.000 0.375 0.664 0.086 1.460 0.691	0.859 1.744 0.772 1.707 0.213 0.117	Logi Mean Optical Densities 7.1 -6.1 -5.1 -
0.377 0.538 0.224 0.060 0.353	-0.078 0.113	0.539 0.001 0.051 0.387 0.234 0.326 0.305	0.109 0.695 0.468 0.455 0.617	0.170 0.675 0.288 0.546 -0.065 0.264 0.176	0.621 0.732 0.137 0.108 0.579 0.056	0.365 0.410 0.222 0.120 0.450 0.657	0.310 0.175 0.135 -0.005 -0.591 0.440 0.207 0.332 0.316	0.348 0.238 0.109 0.436 0.398 0.472	sities -8.1
11 8 4 8 8 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	93	106 106 106 107 108	114 94 102 112	86588856	106 88 107 88 107 88	98 98 98 98 98 98 98 98 98 98 98 98 98 9	100 H	107 108 108 107 107	-8.1
35885 3	97 83	107 107 107 108 108 108	103 103 103 103	98 101 101 101 103 103	288588	8585858	98 88 88 88 88	38 2 838	-7.1 p
87 95 25 85 7 84 87 95 26 85 7 84	-68 12	100 8 11 10 8 8 8 8 8 8 8 8 8 8 8 8 8 8	53 93 94 108 24	122 122 102 102 102	2 2 2 3 3 3 3 3 4 3 4 3 3 3 4 3 4 3 3 4 3 4	771 4 3 9 3 4 5	1100 8 2 2 2 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	22 22 23 24 25 25 26 26 26 26 26 26 26 26 26 26 26 26 26	Percent C
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5 - 15 - 5 - 5 - 5 - 5 - 5 - 5 - 5 - 5 -	-100 -34	·100 ·100	-100 -100	65 4 7 6 6 5 7 6 6 6 7 6 6 6 7 6 6 6 7 6 6 6 6	10 3 -74 -75	-100 100 100 100 100 100 100 100 100 100	28 64 71 71 71 71 71 71 71	448±48	<u>4</u>
1.24E-6 3.75E-6 8.19E-6 1.62E-7 1.31E-6	2.67E-7 1.24E-7	1.59E-6 1.31E-8 1.28E-6 1.55E-6 1.90E-6 4.37E-6 1.54E-6 1.59E-6	7.91E-7 1.30E-6 1.47E-6 1.91E-7 2.06E-6 3.74E-7	1,47E-5 1,79E-6 1,39E-6 1,40E-6 1,09E-6 1,31E-6 1,54E-6	1.38E-6 1.56E-6 1.30E-6 1.62E-6 1.29E-6 1.31E-6	6.18E-7 2.36E-7 1.42E-6 4.92E-7 2.72E-7 1.52E-7 1.08E-6	1.89E-7 8.26E-7 1.85E-6 1.82E-6 1.46E-6 6.61E-6 1.31E-7 1.76E-5 7.32E-6	7.56E-6 1.25E-5 5.19E-6 1.51E-5 6.38E-7 4.13E-7	GI50
> 7.50E-5 2.32E-5 4.44E-7 2.45E-6	9.73E-7 2.66E-7	3.60E-6 2.53E-6 2.32E-6 2.92E-6 3.94E-6 2.37E-5 2.85E-6 3.30E-6	2.09E-6 4.63E-7	3.85E-5 2.70E-6 2.68E-6 2.10E-6 2.43E-6 3.08E-6	2.49E-6 3.33E-6 2.44E-6	7.32E-7 1.56E-6	4.25E-7 2.32E-6 4.68E-6 6.86E-6 3.21E-6 > 7.50E-5 2.38E-7 > 7.50E-5 3.27E-5	> 7.50E-5 3.29E-5 2.68E-5 5.65E-5 1.89E-6	TGI
> 7,50E-5 6.55E-5 4.14E-6	2.93E-6	> 7.50E-5 4.85E-6 4.21E-6 2.99E-5 > 7.50E-5	5.54E-6 > 7.50E-5 > 7.50E-5 4.67E-6	> 7.50E-5 4.02E-6 4.50E-6 6.17E-6	4.76E-6 6.87E-6	6.08m.4	6.51E-6 3.29E-5 2.28E-5 2.28E-5 7.50E-5 7.50E-5 7.50E-5	> 7.50E-5 > 7.50E-5 > 7.50E-5 > 7.50E-5	LC50

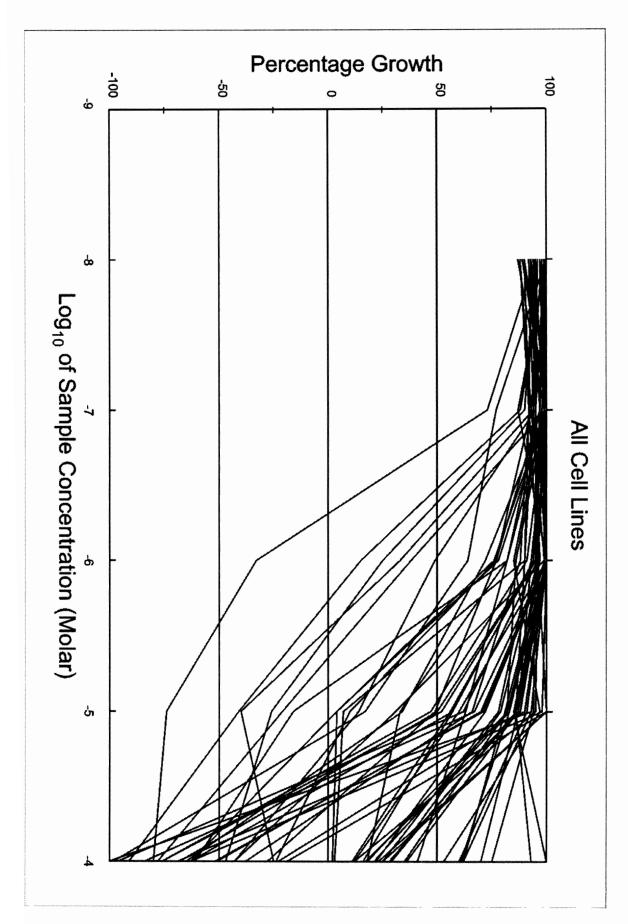


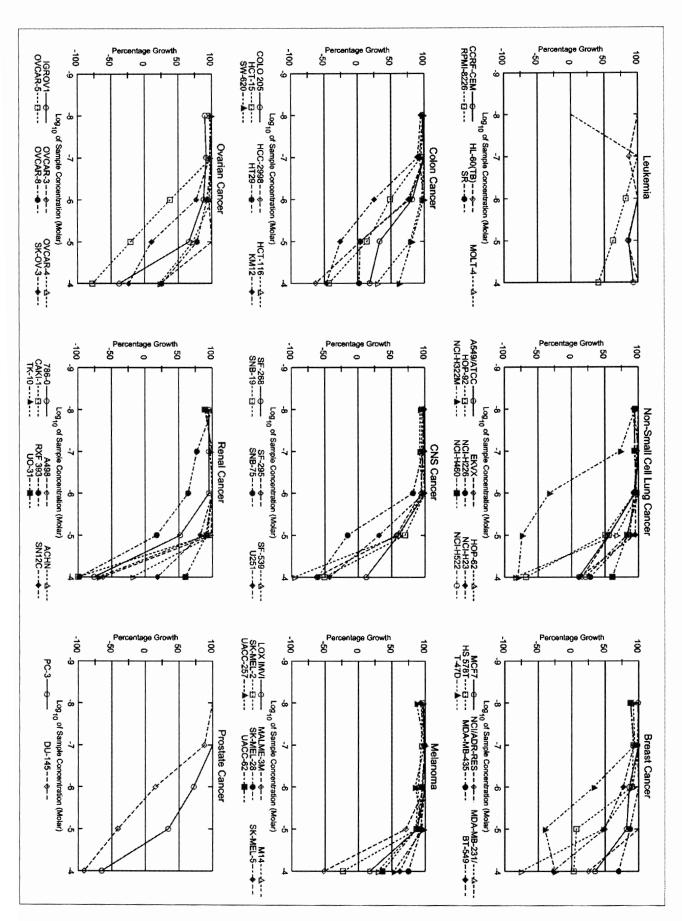




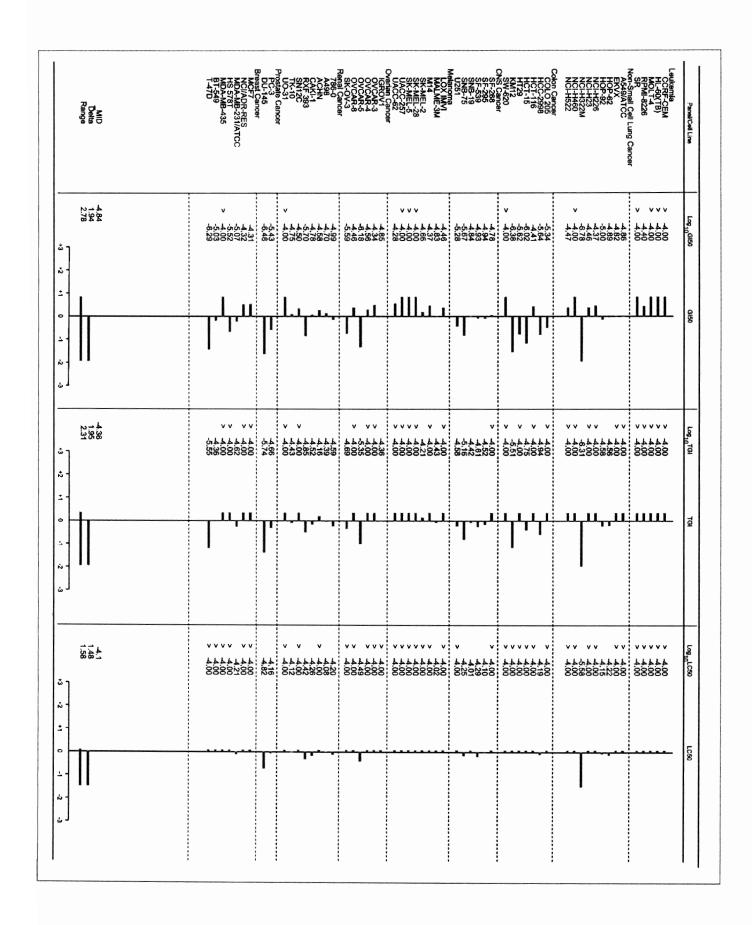
Breast Cancer MCF7 NCI/ADR-RES NCI/ADR-RES MIDA-MB-23/ATCC HS 578T HS 578T MDA-MB-435 BT-549 T-47D	Prostate Cancer PC-3 DU-145	Renal Cancer 786-0 A498 ACHN CAKI-1 RXF 393 SN12C TK-10 UC-31	Ovarian Canoor IGROV1 OVCAR-3 OVCAR-4 OVCAR-6 OVCAR-6 SK-OV-3	Melanoma LOX IMVI MALMESM M14 SK-MEL-2 SK-MEL-2 SK-MEL-2 UACC-257 UACC-62	CNS Cancer SF-288 SF-295 SF-539 SNB-19 SNB-75 U251	Colon Cancer COLO 205 HCC-2988 HCT-116 HCT-15 HTZ9 KM12 SW-620	Non-Small Cell Lung C A549/ATCC ENVX ENVX HOP-92 HOP-92 NCI-H228 NCI-H228 NCI-H322M NCI-H4450 NCI-H452	HL-80(TB) K-562 MOLT-4 RPMI-8226 SR	Panel/Cell Line
0.287 0.406 C 0.377 0.426 0.475 0.377 0.627	0.356 0.220	0.322 1.109 0.204 0.399 0.768 0.613 0.656	0.818 0.406 0.443 0.366 0.099 0.651	0.193 0.484 0.350 0.662 0.254 0.234 1.047	0.364 0.476 0.385 0.501 0.725 0.247	0.211 0.549 0.124 0.223 0.168 0.388 0.094	Cancer 0.311 0.469 0.185 0.918 0.473 0.491 0.554 0.236 0.854	0.495 0.612 0.355 0.889 0.315	Time Zero
37 1.702 37 1.702 96 1.399 97 1.096 26 0.884 75 1.553 77 0.810 27 1.303	56 1.055 20 0.909	22 1,332 1,751 1,751 1,4 0,852 1,9 0,495 1,388 1,388 1,388 1,388 1,388 1,388 1,388	18 1.969 0.761 1041 13 1.041 13 0.854 19 0.501	33 1.301 34 0.804 360 1.086 37 1.243 384 0.737 384 1.432 387 2.222 387 2.222	94 1.169 76 1.311 95 1.324 91 1.378 95 1.093 17 1.261	11 0.919 1.615 19 1.615 24 1.085 24 1.512 23 1.512 38 1.123 38 1.475 34 0.655	11 1.725 39 1.358 35 0.553 36 1.316 1.391 1.391 1.391 1.391 1.391 1.391 1.391 1.391 1.391 1.391 1.391 1.391 1.391 1.391 1.391 1.391 1.391	15 1.317 12 2.050 15 1.309 16 2.328 15 1.230	C B
2 1.841 2 1.527 9 1.527 6 1.067 4 0.862 3 1.623 0 0.765 3 1.334	5 1.061 9 0.894	1.368 1.750 1.750 2.0.845 5.0.505 8.1.353 8.1.353 8.2.567 1.258 1.258	9 2.099 11 0.784 11 1.066 14 0.897 11 0.531 1 1.479	11 1.329 4 0.863 6 1.113 3 1.287 7 0.771 2 1.321 2 2.204 7 2.300	9 1.238 1 1.277 4 1.366 8 1.408 13 1.153	9 0.981 5 1.666 5 1.171 2 1.510 3 1.186 5 1.584 5 0.674	5 1.721 5 1.369 8 1.369 3 0.554 6 1.324 6 1.324 1 1.468 1 1.332 3 1.332 6 1.968	7 1.459 0 2.217 9 1.464 8 2.841 0 1.335	<u>6</u>
7 1.430 7 1.051 7 1.051 7 1.051 7 1.083 2 0.883 3 1.638 5 0.763 4 1.400	1.068 0.886	8 1.406 0 1.741 5 0.894 5 0.554 5 1.337 7 2.486 8 1.413 1 1.559	9 2.082 4 0.809 6 1.117 7 0.966 11 0.482 9 1.565	9 1.364 3 0.861 3 1.238 7 1.300 7 0.764 11 1.293 4 2.240 0 2.214	8 1.265 7 1.271 6 1.301 8 1.475 3 1.142 4 1.298	91 0.930 6 1.565 71 1.157 0 1.528 6 1.181 4 1.679 4 0.649	1 1.615 9 1.338 9 1.567 4 1.276 7 1.037 8 1.520 2 1.464 8 2.072 8 2.279	9 1.491 7 2.341 4 1.533 4 2.798 5 1.513	-7.1
1.663 1.454 1.034 0.582 1.514 0.782 0.348	0.336 0.072	1.361 1.726 0.837 0.529 1.335 2.433 1.370	1.558 0.738 0.701 0.781 0.521 0.468	1.366 0.827 1.157 1.287 0.685 1.267 2.200 2.222	1.182 1.209 1.289 1.481 0.979 1.086	0.214 0.656 1.129 0.640 0.109 0.291 0.545	0.217 1.036 0.541 1.272 1.053 1.461 0.137 1.988 2.253	1.548 2.373 1.515 2.091 1.517	Aean Opti -6.1
0.127 0.217 0.217 0.422 0.251 0.087 0.151 0.238	0.043	0.017 0.186 0.005 0.126 0.540 0.203 0.166 0.144	0.230 0.120 0.186 0.062 0.120 0.050	0.099 0.166 0.004 0.268 0.046 0.015 0.286 0.296	0.125 0.144 0.037 0.248 0.151 0.004	0.062 0.112 0.014 0.015 0.051 0.144 0.021	0.148 0.181 0.059 0.864 0.165 0.250 0.115 0.105	0.656 0.995 1.255 0.320 0.388	Mean Optical Densities -6.1 -5.1
0.355 0.427 0.035 0.221 0.338 0.281 0.500	0.171	0.166 -0.052 0.011 0.288 0.369 0.199 0.393 0.393	0.493 0.327 0.447 0.102 0.366 0.386	0.024 0.432 0.075 0.538 0.310 0.076 0.827	0.354 0.324 0.264 0.479 0.575	0.247 0.252 -0.026 -0.019 0.255 0.376	0.382 0.295 0.084 0.478 0.274 0.098 0.334 0.304	0.261 0.454 0.255 0.639 0.213	
1 9 7 9 9 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	98 98	100 100 100 100 100 100 100 100 100 100	100 100 111 100 100 111	103 103 107 108 103 103	100 mm 10	103 103 103 103	105 105 105 105 105 105 105 105 105 105	117 112 116 136	Log10 Concentration
12 4 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	102 97	107 98 107 161 92 92 117	110 110 120 120 120	106 118 119 119 110 106 88 88 97	1 1 1 8 8 8 1 2 2 2 2 2 2 2 2 2 2 2 2 2	8 1 2 2 3 8 2	92 114 117 117 116	121 120 123 133 131	7.1
97 98 98 94 44	57 6	100 0 0 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	2 6 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8	98 88 88 88 88 88 88 88 88 88 88 88 88 8	8 6 7 8 8 R	888825	-36 97 98 98 98 108 1108	122 122 131 131	.6.1
688 ± 6 ± 68	88	-98 -98 -75 -75	-92 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	\$ 7 \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	-98 -70 -98	26. 26. 26. 27. 28. 27. 28. 27. 28. 27. 28. 28. 29. 29. 29. 29. 29. 29. 29. 29. 29. 29	5.55 5.79 5.79 5.79 5.79 5.79 5.79 5.79	8 × × 27 28	Percent Growth
98845V2	ģ 52	4888864	682584	-122 -136 -100	សង់ 2 4 ½ k	ස්ද්රීම් ස	244844	±8888	7
1.53E-6 1.74E-6 2.30E-6 4.27E-7 1.37E-6 1.44E-6 1.91E-7	2.28E-7 1.44E-7	1.39E-6 1.36E-6 1.32E-6 1.97E-6 1.65E-6 1.29E-6 1.59E-6 1.46E-6	9.55E-7 1.38E-6 5.98E-7 1.21E-6 2.23E-7	1.72E-6 1.61E-6 1.43E-6 1.58E-6 1.27E-6 1.44E-6 1.31E-6	1.52E-6 1.30E-6 1.33E-6 1.80E-6 1.01E-6 1.14E-6	2.43E-7 2.55E-7 1.42E-6 4.16E-7 1.87E-7 2.26E-7 1.17E-6	1.66E-7 9.67E-7 1.44E-6 1.93E-6 1.73E-6 1.67E-7 1.67E-7 1.67E-5	3.92E-6 4.28E-6 1.73E-5 1.27E-6 3.42E-6	GI50
8.70E-6 2.13E-6 2.61E-6 3.05E-6 3.94E-7	6.65E-7 2.92E-7	2.48E-6 2.57E-6 2.37E-6 3.46E-6 4.28E-6 2.74E-6 2.96E-6 2.84E-6	2.22E-6 2.79E-6 2.40E-6 > 7.50E-5 4.85E-7	3.63E-6 3.13E-6 2.49E-6 3.33E-6 2.26E-6 2.62E-6 2.36E-6	3.04E-6 2.70E-6 2.46E-6 3.66E-6 2.19E-6 2.15E-6	9.71E-7 2.59E-6 1.36E-6 5.03E-7 2.42E-6	2.42E-6 2.89E-6 6.49E-6 2.94E-6 3.64E-7 3.68E-5	1,47E-5 2,41E-5 4,42E-5 2,76E-6 1,18E-5	TGI
> 7.50E-5 2.85E-5 > 7.50E-5	2.59E-6 5.88E-7	4.89E-6 4.27E-6 5.42E-5 5.82E-6	4.77E-6 > 7.50E-5	8.10E-6 4.35E-6 4.25E-6	4.05E-6	3.51E-6 4.70E-6 3.39E-6	5.82E-6 > 7.50E-5 7.97E-6 > 7.50E-5	> 7.50E-5 > 7.50E-5 > 7.50E-5 > 7.50E-5	LC50

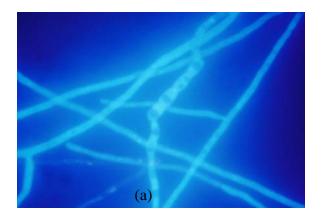


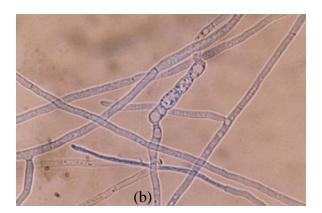




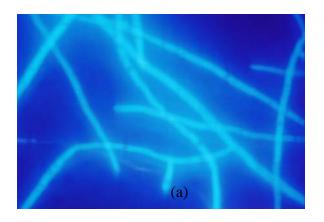
MDA-MB-231/ATCC OHS 578T CMDA-MB-435 CBT-549 CT-47D	Breast Cancer MCF7 NCIADR-RES	Prostate Cancer PC-3 DU-145	Renal Cancer 786-0 A498 ACHN CAK:1 CAK:1 SN12C TK:10 UO-31	Ovarian Cancer IGROV1 OVCAR-3 OVCAR-4 OVCAR-8 OVCAR-8 SK-OV-3	Melanoma LOX IMVI MALME-3M M14 SK-MEL-2 SK-MEL-28 SK-MEL-28 SK-MEL-5 UACC-257 UACC-62	CNS Cancer SF-268 SF-295 SF-399 SNB-19 SNB-75 U251	Colon Cancer COLO 205 HCC-2988 HCT-116 HCT-15 HT29 KM12 SW-520	Non-Small Cell Lung A549/ATCC EKVX HOP-82 HOP-92 NCI-H226 NCI-H233 NCI-H328 NCI-H328 NCI-H328 NCI-H328	Leukemia CCRF-CEM HL-60(TB) MOLT-4 RPMI-8226 SR	Panel/Cell Line
0.452 0.482 0.683	0.353	0.197 0.270	0.577 1.303 0.391 0.470 0.747 0.417 0.595 0.584	0.525 0.398 0.364 0.641 0.426 0.440	0.270 0.514 0.512 0.352 0.890 0.278 0.329 0.748 0.470	0.231 0.678 0.671 0.691 0.573 0.275	0.340 0.634 0.123 0.304 0.132 0.290 0.186	Cancer 0.308 0.549 0.406 0.512 0.512 0.581 0.612 0.557 0.215	0.581 0.274 0.251 0.695 0.222	Time Zero
1.258 0.987 1.663 1.544	1.817	0.825 1.197	2.270 1.859 1.223 1.115 1.394 1.713 1.271 2.027	1.791 1.346 1.305 2.105 2.015 1.094	1.595 0.959 1.229 1.909 1.246 1.710 1.857 2.271	1.098 2.223 2.103 1.625 1.155 1.286	1.410 1.855 1.131 1.557 1.228 1.284	1.475 1.732 1.312 1.312 0.871 1.850 1.735 1.532 2.184 0.686	2.129 0.777 1.003 2.041 0.400	뎦
1.307 1.701 1.443	1.801	0.882 1.236	2.190 1.801 1.288 1.156 1.450 1.732 1.224 1.869	1.661 1.404 1.291 2.059 2.093	1.550 0.979 1.191 1.953 1.270 1.619 1.713 2.307	1.081 2.301 2.304 1.590 1.141 1.279	1.376 1.836 1.102 1.612 1.241 1.232 1.380	1.539 1.736 1.262 0.869 1.873 1.861 1.481 1.481 2.094	2.227 0.867 1.001 2.071 0.534	-8.0
1.282 1.634 1.486	1.868	0.864 1.087	2.190 1.890 1.324 1.187 1.246 1.759 1.248 2.028	1.695 1.361 1.276 2.198 2.117 1.073	1.577 0.948 1.174 1.906 1.280 1.740 1.846 2.313	1.173 2.178 1.995 1.574 1.136 1.277	1.498 2.222 1.171 1.497 1.251 1.184 1.313	1.563 1.706 1.326 0.884 1.876 1.679 1.268 2.075	2.148 0.712 1.080 2.091 0.830	Mean -7.0
1.183 0.934 1.681 1.347	1.619	0.647 0.406	2.192 1.888 1.319 1.148 1.161 1.715 1.287 2.051	1.641 1.313 1.325 1.192 1.907 0.944	1.690 1.006 1.141 1.984 1.203 1.744 1.694 2.191	1.112 2.127 2.050 1.648 1.049 1.278	1.213 1.559 1.093 0.921 0.985 0.540 1.396	1.418 1.660 1.369 0.852 1.763 1.685 0.375 2.122 0.724	2.226 0.781 1.129 1.797 0.928	Optical
0.832 0.520 1.489 1.107	1.560	0.408 0.160	1.452 1.847 1.224 1.073 0.856 1.474 1.205 1.903	1.355 1.375 1.044 0.509 1.672 0.508	1.442 0.828 1.104 1.783 1.190 1.610 1.826 2.039	0.755 1.564 1.555 1.343 0.482 0.592	0.697 0.679 0.922 0.485 0.178 0.214 1.174	0.963 1.227 1.014 0.692 1.681 1.678 0.146 1.852	1.918 0.701 1.062 1.543 0.776	-5.0
0.109 0.495 1.275 0.495	0.871	0.068 0.024	0.140 0.486 0.319 -0.001 0.017 0.017 0.650 0.183 1.452	0.328 0.612 0.571 0.140 0.830 0.336	0,498 0,245 0,606 0,684 1,007 1,188 1,339 1,116	0.334 0.254 0.030 0.339 0.222 0.156	0.528 0.238 0.238 0.419 0.172 0.158 0.154 0.938	0.433 0.743 0.066 0.163 0.943 0.747 0.747 0.114 1.416	2.025 0.784 1.343 1.253 0.690	4.0 -8.0
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នៃនងន	និនិ	æ 🕏	106 112 108 112 108 108	១៩៩១៩ ១	D 9 D D D 9 9 9 9	89889 5	890 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	5 2 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	101 87 110 104 341	-7.0 P
377589	110 86	57	222223233 2223233	77 33 36 28	107 111 90 107 95 102 85	988 55 98 4 55 98 55 98 4 55	96 96 97 98	79 88 88 88 88 88 88 88	106 101 117 82 396	Percent G -5.0
498747	1 8	¥ <u>¥</u>	93 93 93 94 95 95 95 95 95	103 de 10	88 94 88 87	-16 31 31	33 14 14 18	56 57 57 50 57 50 83 83	86 108 53	Growth -5.0
	3 K	94 65	-76 -63 -63 -98 -98 -69	223 223 23 24 24 25 25 25 25 25 25 25 25 25 25 25 25 25	7 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	ភនិនិញ្ចុំជំង	842555	2288822	93 145 145 263	4.0
× 3.03m-6 9.38m-6	4.89E-5	3.70E-6 3.30E-7	1.03E-5 2.64E-5 1.66E-5 1.96E-6 1.96E-6 3.13E-5 1.79E-5	1.41E-5 4.56E-5 2.77E-5 6.60E-7 3.44E-5 2.55E-6	3.46E-5 1.47E-5 4.26E-5 2.18E-5 > 1.00E-4 > 1.00E-4 5.30E-5	1.64E-5 1.15E-5 1.19E-5 1.46E-5 2.11E-6 5.31E-6	4.52E-6 2.27E-6 3.85E-5 9.64E-7 2.39E-6 4.13E-7 7 1.00E-4	1.37E-5 1.51E-5 1.30E-5 1.00E-5 4.27E-5 3.42E-5 1.65E-7 1.00E-4 3.40E-5	v 1.00mA v 1.00mA v 1.00mA v 1.00mA	GI50
× 1.00m-4 4.38m-5	> 1.00E-4	2.18E-5 1.83E-6	2.54m-5 5.98m-5 3.04m-5 1.40m-5 > 1.00m-4 > 1.00m-4	4.32m.5 > 1.00m.4 > 1.00m.4 4.43m.6 > 1.00m.4 2.02m.5	> 1,00m-4 3,75m-5 > 1,00m-4 6,17m-5 > 1,00m-4 > 1,00m-4 > 1,00m-4	> 1.00E-4 3.01E-5 2.47E-5 3.78E-5 6.87E-6 2.62E-5	1.14m-5 1.14m-5 1.00m-4 1.77m-5 1.00m-4 3.07m-6	> 1.00E4 > 1.00E4 2.79E5 2.65E5 > 1.00E4 > 1.00E4 > 1.00E4 - 1.00E4	v 1.00m4 v 1.00m4 v 1.00m4 v 1.00m4	TGI
0.15E-5 0.15E-5 0.100E-4 0.100E-4	> 1.00E.4	6,98E-5 1.51E-5	6.27E-5 8.33E-5 > 1.00E-4 5.51E-5 3.83E-5 > 1.00E-4 > 1.00E-4	v 1.00m v 1.00m v 1.00m v 1.00m v 1.00m	> 1.00E4 9.56E-5 > 1.00E4 > 1.00E4 > 1.00E4 > 1.00E4 > 1.00E4	v 1.00m.4 7.86m.5 5.13m.5 9.81m.5 5.62m.5 v 1.00m.4	> 1.00E4 6.46E5 7 1.00E4 > 1.00E4 > 1.00E4 > 1.00E4	> 1,00E4 > 1,00E4 > 9,9E-5 7,01E-5 > 1,00E4 > 1,00E4 > 1,00E4 > 1,00E4 > 1,00E4	v 1.00m4 v 1.00m4 v 1.00m4 v 1.00m4	LC50

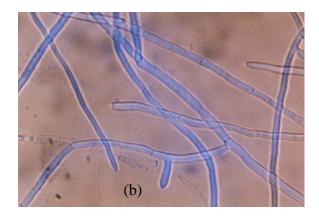






Mycelia of F. solani after exposure with coumarine (a) under fluorescence microscope (b) under light microscope





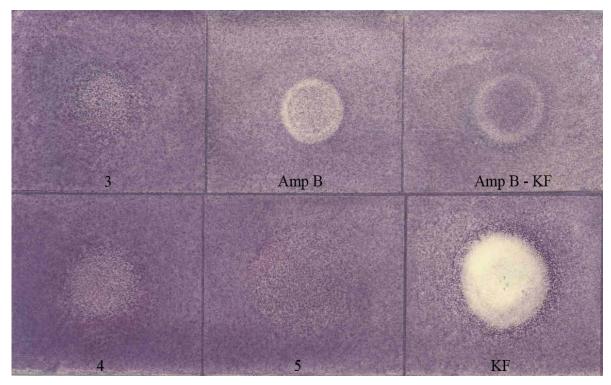
Mycelia of *F. oxysporium* after exposure with coumarine (a). under fluorescence microscope (b) under light microscope

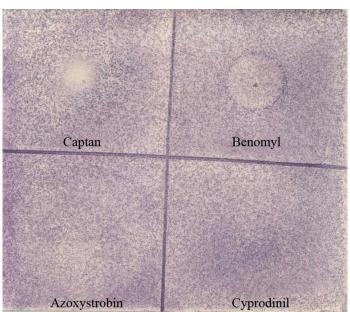


Mycelia untreated with fluorescence compound under fluoresence microscope: no autofluoresence has been observed



KF-coumarine under fluorescence microscope

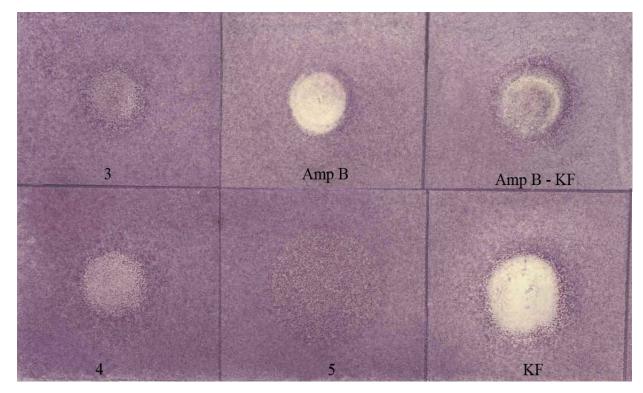




Bioautography plate of 3, 4 and 5 against Fusarium solani after spraying with MTT.

Standards: Amp B: amphotericin B, AmpB-KF: Amphotericin B plus KF (1:1), Captan, Benomyl, Azoxystrobin and Cyprodinil.

Control: KF: kahalalide F.



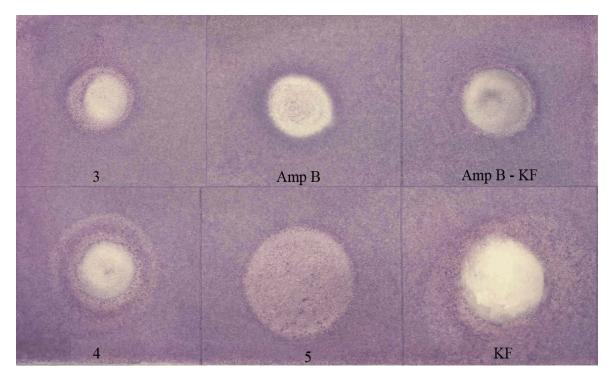


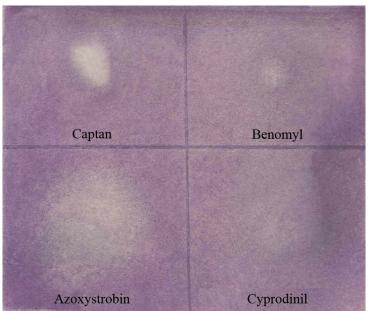
Bioautography plate of 3, 4 and 5 against Fusarium oxysporium after spraying with MTT.

Standards: Amp B: amphotericin B, AmpB-KF: Amphotericin B plus KF (1:1), Captan, Benomyl,

Azoxystrobin and Cyprodinil.

Control: KF: kahalalide F.





Bioautography plate of 3, 4 and 5 against Fusarium proliferatum after spraying with MTT.

Standards: Amp B: amphotericin B, AmpB-KF: Amphotericin B plus KF (1:1), Captan, Benomyl, Azoxystrobin and Cyprodinil.

Control: KF: kahalalide F.