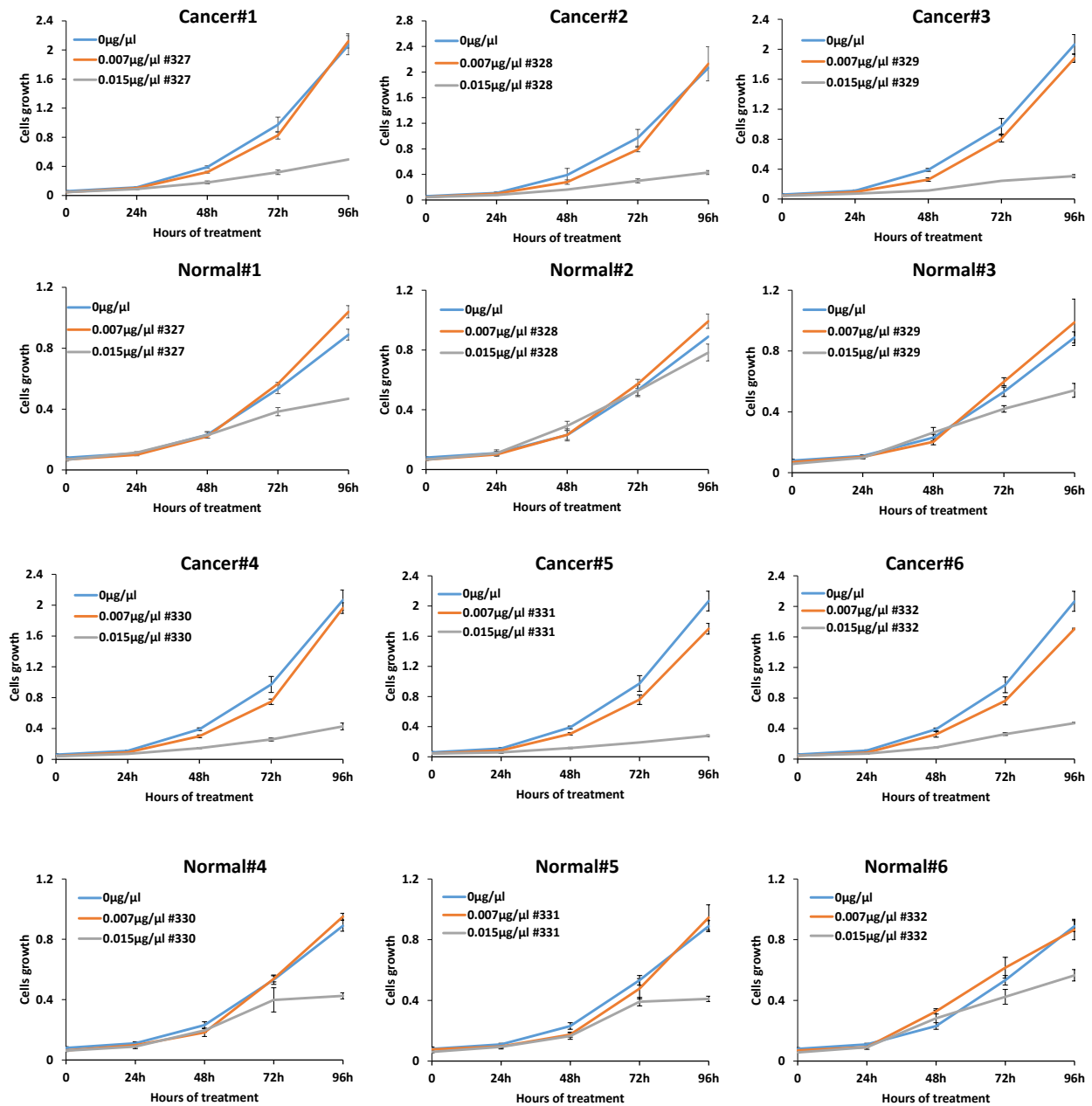
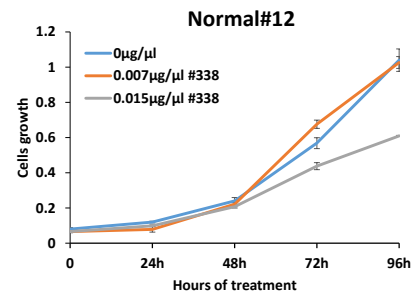
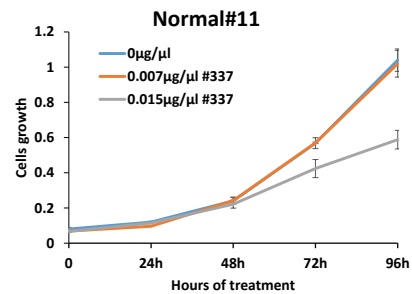
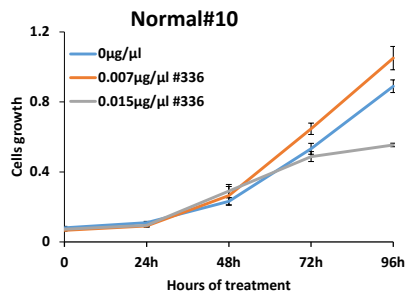
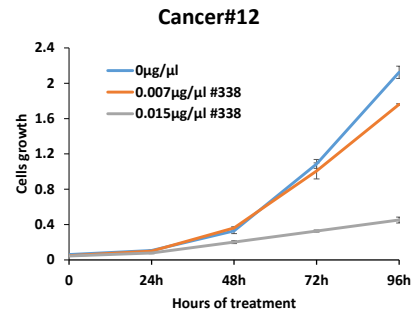
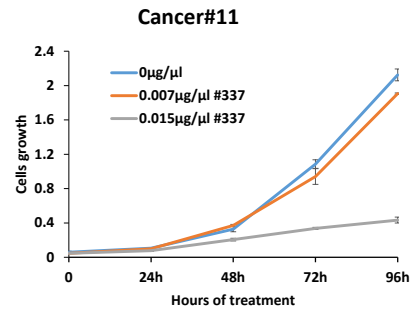
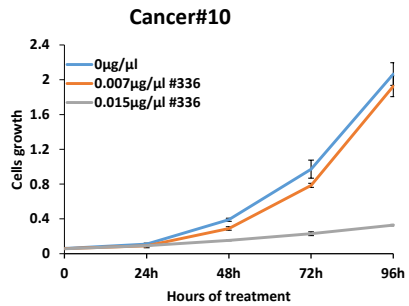
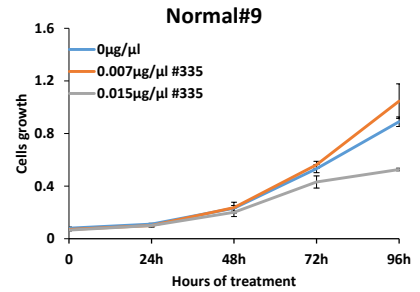
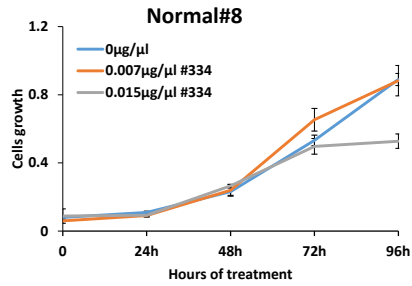
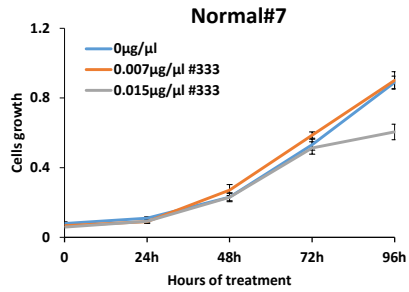
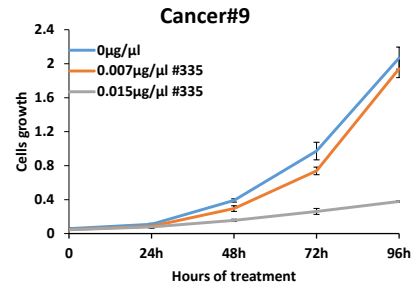
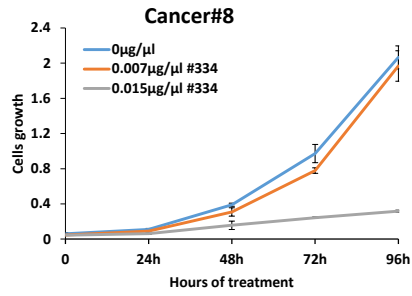
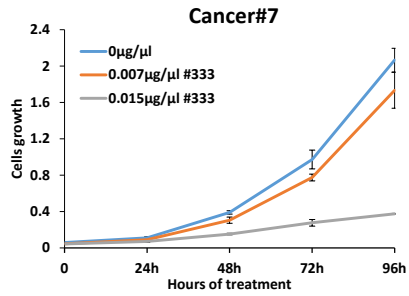
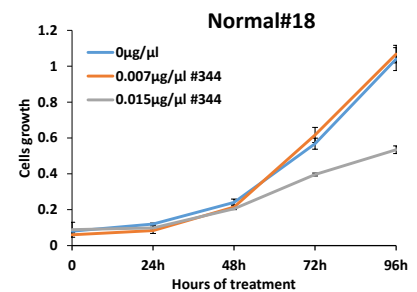
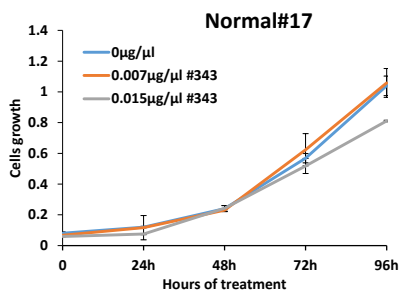
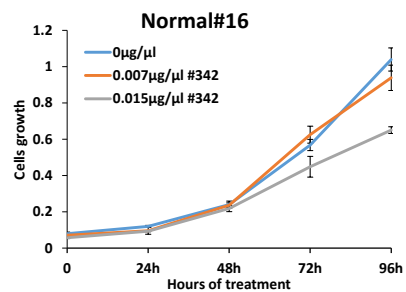
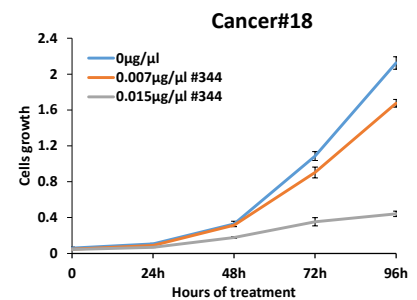
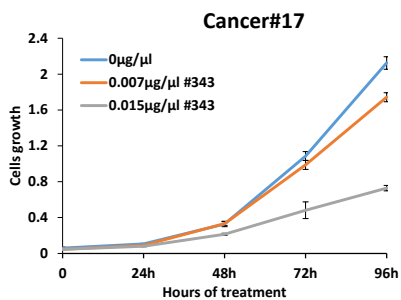
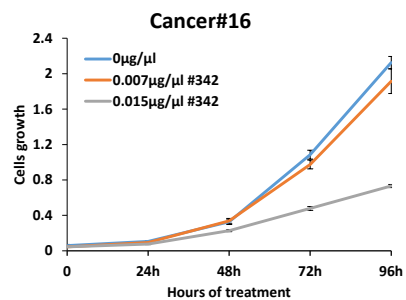
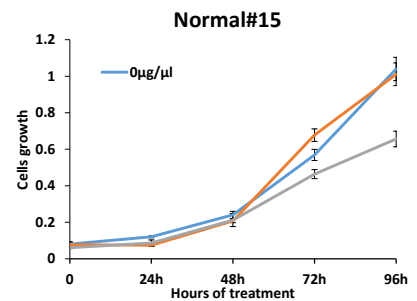
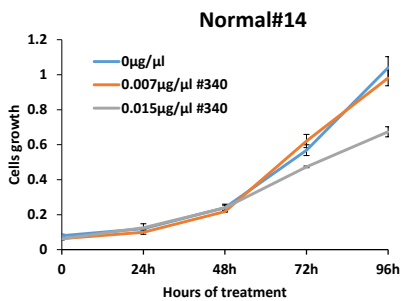
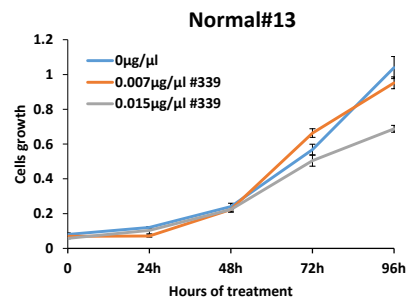
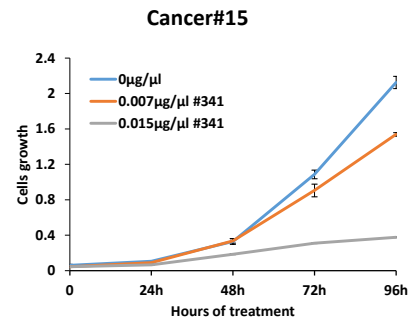
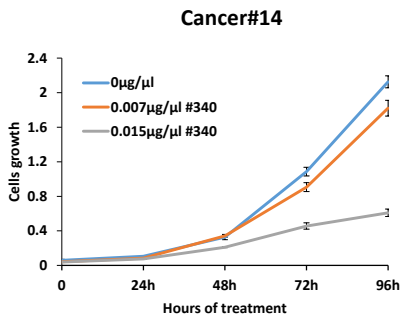
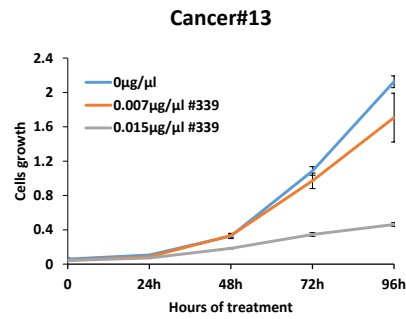
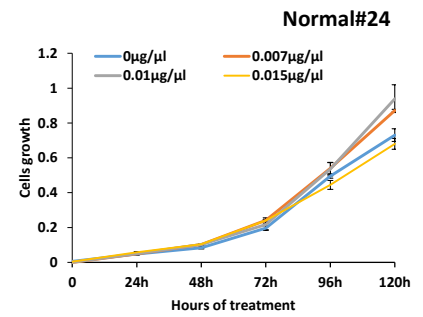
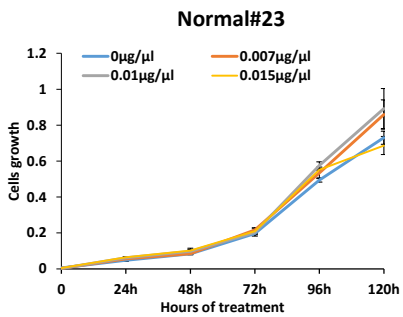
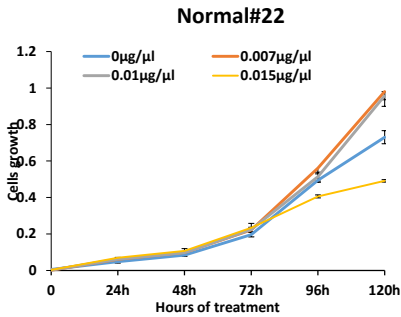
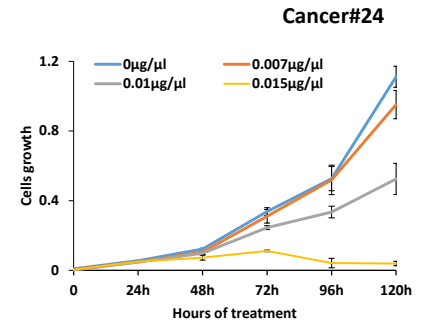
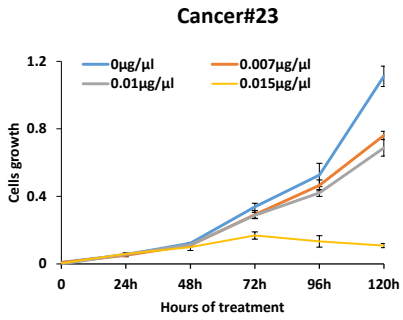
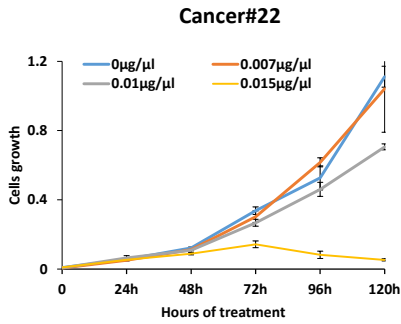
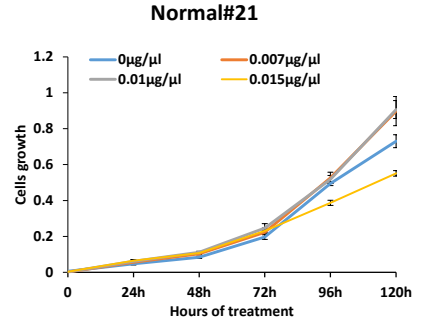
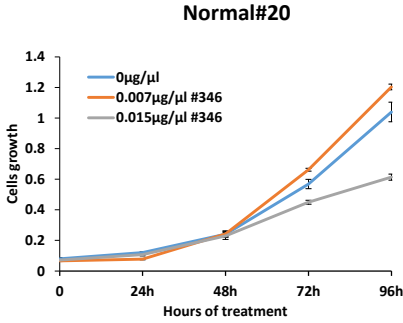
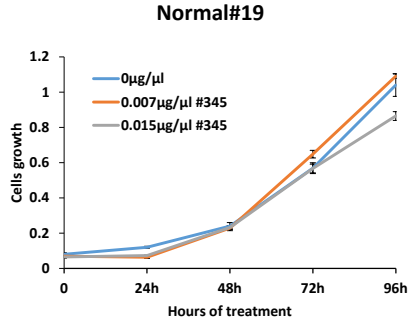
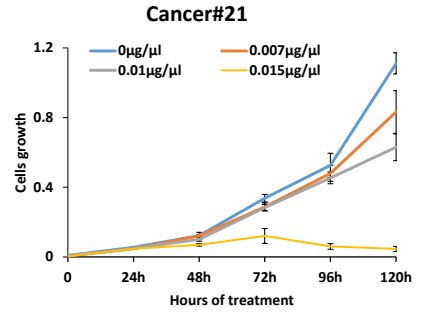
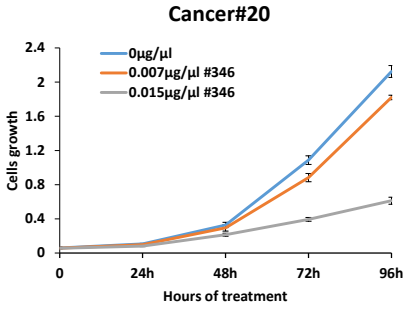
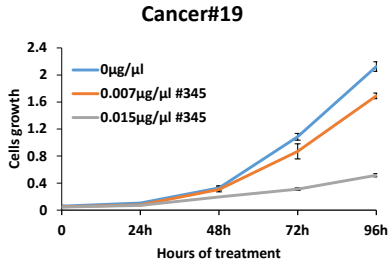


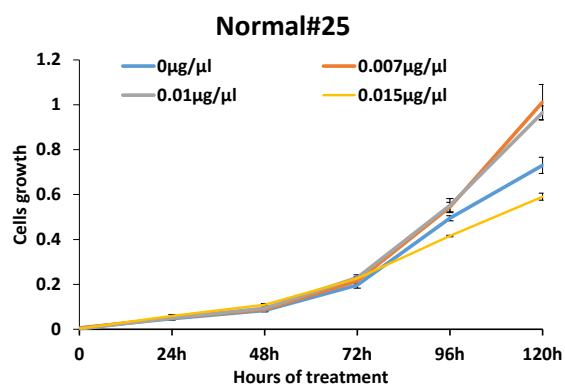
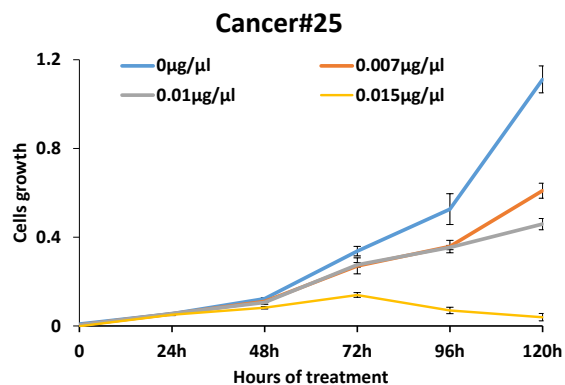
Supplementary Figures



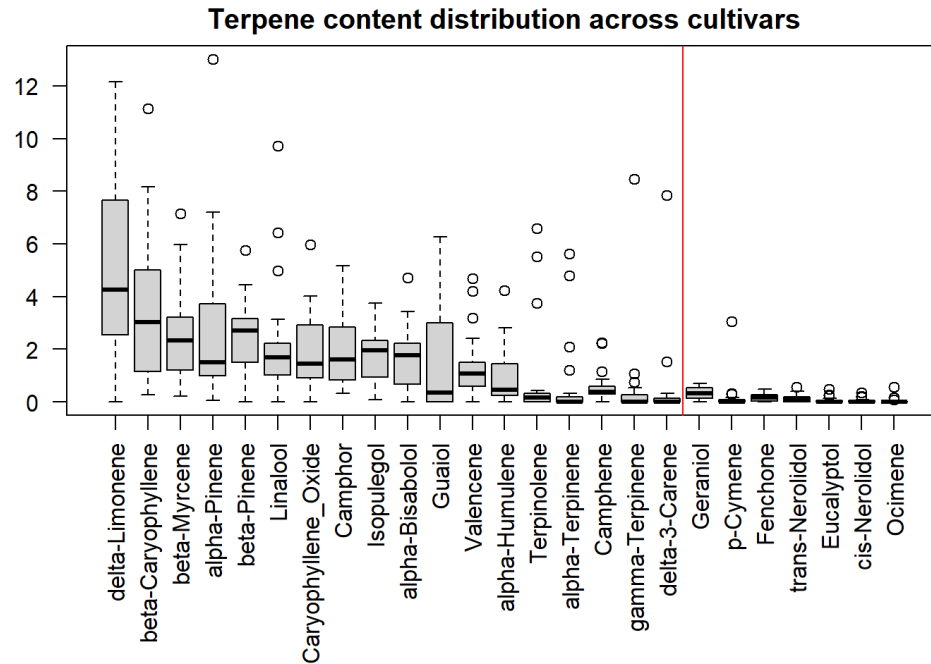








Supplementary Figure S1. Inhibition of growth of breast cancer cell line HCC1806 and normal cell line BJ-5ta. Y axis indicates arbitrary units of cell growth as measured by MTT assay. X axis indicates time of the cell growth/extraction application. Data (average of three replicates with SD) are shown as a cell growth curve measured for 96-120 h after application of three different concentrations of extracts #1-#25.



Supplementary Figure S2. Terpene content distribution across cultivars. Y axis shows the concentrations of terpenes in ug/ul. Data are shown as an average from 25 lines, with SD. Data outliers are shown as open circles. Terpenes to the right of the red line were removed from further analysis that included clustering and PCA.

Supplementary Tables

Supplementary Table S1. Enrichment of cannabinoids upon

extraction	THC	CBD	CBGA	TOTAL
#1	3.19	9.38	5.16	3.40
#2	4.13	10.33	5.86	4.29
#3	3.30	4.20	3.64	3.37
#4	3.17	3.84	3.45	3.23
#5	3.01	4.62	3.19	3.09
#6	2.89	2.83	2.35	2.86
#7	2.85	6.92	3.27	2.94
#8	3.12	3.44	2.73	3.14
#9	2.33	1.77	1.36	2.25
#10	2.33	5.09	2.31	2.40
#11	4.39	3.57	4.06	4.32
#12	3.04	3.55	3.09	3.05
#13	3.33	4.75	2.40	3.31
#14	2.76	7.55	2.77	2.84
#15	2.45	3.39	1.94	2.46
#16	2.76	4.24	4.96	2.87
#17	1.95	3.18	1.62	1.98
#18	2.85	4.31	3.03	2.91
#19	3.31	1.14	1.91	3.14
#20	2.91	8.98	4.19	3.06
#21	2.54	2.17	1.59	2.45
#22	2.83	3.22	2.10	2.80
#23	3.52	8.14	3.14	3.58
#24	2.31	1.57	1.41	2.20
#25	2.21	8.12	2.79	2.28
Average	2.94	4.81	2.97	2.97

Numbers show the enrichment of each tested cannabinoid, calculated by dividing the concentration in the extracts by the concentration in the flowers.

Supplementary Table S2. Concentration of terpenes in the flower extracts, ug/ul

	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13
δ -Limonene	8.06	3.76	4.12	6.36	9.68	4.25	4.33	0	12.15	7.65	0.88	5.45	8.36
β -Myrcene	5.98	0.82	0.79	0.52	2.79	2.65	0.85	3.78	1.21	7.16	5.67	2.1	2.07
α -Pinene	3.11	0.69	7.2	13.01	2.31	0.55	0.86	6.86	4.75	1.61	3.85	1.01	1.52
β -Caryophyllene	2.1	11.1	0.74	0.93	2.52	8.15	0.85	2.87	5.05	3.73	5.08	8.18	1.63
β -Pinene	1.87	0.92	3.44	5.75	2.7	0.92	4.33	0	3.15	1.84	3.99	2.99	1.5
Camphor	1.62	2.52	1.55	2.95	0.82	2.3	0.31	0.4	2.13	0.76	2.97	1.54	1.11
Isopulegol	0.81	3.43	1.45	1.75	2.13	3.46	0.45	2.54	3.75	2.24	1.96	2.54	1.26
Valencene	0.79	4.68	0.2	0.45	0.5	3.19	0	1.07	1.5	0.83	1.38	2.04	0.68
Geraniol	0.59	0.61	0	0.55	0	0.31	0	0.47	0.31	0	0.1	0.13	0.21
Camphene	0.52	0.32	0.33	0.31	0.86	0.25	0.34	2.26	1.16	0.62	0.07	0.37	0.59
Caryophyllene Oxide	0.49	5.98	1.24	0.97	1.45	2.91	0.7	0	2.47	3	2.59	3.22	0.24
Terpinolene	0.42	0	0.28	0	0.36	0.22	0	0	0.32	0.19	0.07	0.17	0.38
Eucalyptol	0.27	0	0.23	0	0	0	0	0	0.12	0	0	0	0
trans-Nerolidol	0.09	0	0.09	0	0	0.18	0	0	0.23	0	0.56	0.04	0.1
α -Bisabolol	0	4.71	1.38	1.18	0.68	2.73	0.31	1.78	2.63	2.22	1.44	1.1	0.68
α -Humulene	0	4.24	0.36	0	0	1.72	0	0.23	0.47	0.35	1.44	2.8	0.31
α -Terpinene	0	0.2	0	0.32	0	0	0	0	0	0	0	0.11	0
cis-Nerolidol	0	0	0	0	0	0	0	0	0	0	0.04	0.08	0
δ -3-Carene	0	0	0	0	0.3	0	0	7.84	0	0	0	0	0
Fenchone	0	0.41	0.48	0.41	0.34	0.13	0.18	0	0.21	0.36	0.08	0.06	0.26
γ -Terpinene	0	0	0.53	0	0	0	0	0	1.08	0	0	0	0
Guaiol	0	0.27	0.67	0	0	3.74	0	3.53	6.28	0	0.06	0.07	0.65
Linalool	0	2.22	1.09	0	3.14	1.53	1.26	4.98	6.43	1.8	1.2	1.7	2
Ocimene	0	0	0	0.56	0	0	0	0	0	0	0	0	0
p-Cymene	0	0	0	0.3	0	0	0	0	0	0	0.08	0.09	0
Total	26.72	46.92	25.77	38.23	30.58	39.19	12.15	38.61	55.4	34.36	33.51	35.79	23.55
	#14	#15	#16	#17	#18	#19	#20	#21	#22	#23	#24	#25	
δ -Limonene	3.6	8.68		8.44	4.97	4.27	4.99	1.01	0.58	2.55	2.78	0	
β -Myrcene	0.99	3.01	2.32	3.19	2.12	1.27	2.93	0.21	5.92	3.22	4.08	2.04	
α -Pinene	3.72	4.79	0.63	1.3	1.3	0.05	0.82	1.37	1.69	0.99	1.5	1.23	
β -Caryophyllene	0.83	3.87	4.55	7.62	3.53	3.02	4.08	0.28	1.14	1.01	1.25	5	
β -Pinene	0.92	1.81	2.25	4.36	2.58	3.03	1.19	0.15	3.14	2.93	2.8	4.44	
Camphor	1.24	3.07	0.75	1.66	3.88	5.16	1.93	2.85	0.6	3.25	0.78	1.25	
Isopulegol	0.8	2.52	1.95	0.99	1.15	1.99	2.34	2.32	0.08	0.33	0.54	0.93	
Valencene	0	4.21	2.41	1.21	1.34	0.72	1.99	0.68	0	1.13	0.59	1.36	
Geraniol	0	0.46	0.14	0.46	0.57	0.67	0.19	0.63	0.14	0.7	0.13	0.35	
Camphene	0.24	0.45	0.37	0.61	0.09	0.6	0.3	2.22	0.05	0	0.46	0.56	

Caryophyllene Oxide	0.81	2.78	1.31	3.53	0.39	1.74	4.01	1.28	1.16	0.92	1.67	3.37	
Terpinolene	0	0.09	0.07	0.2	0.01	0	0	3.76	6.59	5.53	0.28	0.12	
Eucalyptol	0	0		0.13	0	0	0	0	0.06	0.06	0.48	0.05	
trans-Nerolidol	0	0.05	0.41	0.01	0.36	0.18	0.35	0.56	0.07	0.14	0.02	0.12	
α -Bisabolol	0.42	2.15	2.25	1.01	3.44	2.2	1.96	2.11	0.56	0.36	2.28	1.89	
α -Humulene	0.24	1.1	1.93	0.51	1.41	1.5	2.42	1.12	0	0.51	0.06	0.27	
α -Terpinene	0	0	4.79	0	0	0.2	0.11	2.1	1.2	0	0	5.63	
cis-Nerolidol	0	0	0.06	0.08	0.06	0.18	0.22	0.34	0.02	0.02	0.03	0.02	
δ -3-Carene	0	0	0.03	0	0.24	0	0	1.54	0.32	0.13	0.2	0	
Fenchone	0	0.16		0.12	0.07	0.23	0	0.23	0.02	0.16	0.29	0.03	
γ -Terpinene	0	0.12		0	0.42	0.28	0	0.22	0.26	0.76	8.47	0	
Guaiol	0.39	0	2.72	0.03	4.04	5.07	0	3.07	1.17	0.09	2.99	0.35	
Linalool	1.01	9.73	2.48	2.78	0.65	1.73	0.51	2.12	0	0.84	1.31	2.17	
Ocimene	0	0		0	0	0	0	0	0	0.09	0.16	0	
p-Cymene	0.29	0	0.02	0.06	0	0	0	0.32	3.06	0	0	0.15	
Total	15.5	49.0	31.4	38.3	32.6	34.0	30.3	30.4	28.1	25.7	33.1	31.3	
		5	4		2	9	4	9	7	2	5	3	

Supplementary Table S3. CCE for various clustering methods

Clustering Method	Raw data	Scaled	Scaled and filtered
Ward.D2	0.46	0.65	0.66
Complete	0.74	0.71	0.72
McQuitty	0.77	0.85	0.86

Supplementary Table S4. Dunn index for various clustering methods

Clustering Method	Raw data	Scaled	Scaled and filtered
Ward.D2	0.33	0.37	0.36
Complete	0.29	0.45	0.44
McQuitty	0.38	0.60	0.64

Supplementary Table S5. Association between terpene content and anti-cancer activity

Terpene	Estimate	Std. Error	t value	Pr(> t)	Pval_BH
---------	----------	------------	---------	----------	---------

γ-terpinene	0.872	0.180	4.835	0.000*	0.002*
eucalyptol	9.558	3.176	3.010	0.006	0.094
β-caryophyllene	-0.240	0.145	-1.653	0.112	0.696
camphene	1.298	0.712	1.823	0.081	0.696
α-humulene	-0.627	0.384	-1.634	0.116	0.696
CBGA	1.512	1.171	1.291	0.210	0.699
d-limonene	-0.172	0.128	-1.345	0.192	0.699
camphor	-0.456	0.346	-1.318	0.201	0.699
fenchone	4.168	2.822	1.477	0.154	0.699
valencene	-0.413	0.344	-1.199	0.243	0.728

Asterisks show significant associations between the presence of terpenes and anti-cancer activity. The analysis was done using generalized linear models (GLM) with family “gaussian” specified. Resulting p-values were adjusted using Benjamini-Hochberg method.

Supplementary Table S6. Association between terpene or cannabinoids content and IL-6 expression

Terpene	Estimate	Std. Error	t value	Pr(> t)	Pval_BH
p-cymene	0.663	0.191	3.463	0.002*	0.063*
camphor	-0.297	0.102	-2.907	0.008*	0.119
β-myrcene	0.177	0.067	2.627	0.015*	0.151
cis_nerolidol	-3.143	1.594	-1.971	0.061	0.456
CBD	-0.817	0.566	-1.443	0.162	0.542
geraniol	-0.817	0.566	-1.443	0.162	0.542
terpinolene	0.119	0.078	1.530	0.140	0.542
eucalyptol	1.763	1.193	1.478	0.153	0.542
trans-nerolidol	-1.296	0.781	-1.659	0.111	0.542
CBGA	0.401	0.395	1.015	0.321	0.812

Asterisks show significant associations between the presence of terpenes or cannabinoids and the change in expression of IL-6. The analysis was done using generalized linear models (GLM) with family “gaussian” specified. Resulting p-values were adjusted using Benjamini-Hochberg method.

Supplementary Table S7. Association between cannabinoids content and COX2 expression

Terpene	Estimate	Std. Error	t value	Pr(> t)	Pval_BH
trans-nerolidol	-0.789	0.431	-1.830	0.080	0.948
caryophyllene oxide	0.084	0.054	1.560	0.132	0.948
β -pinene	0.061	0.055	1.118	0.275	0.948
eucalyptol	0.735	0.681	1.080	0.291	0.948
fenchone	0.575	0.545	1.056	0.303	0.948
β -myrcene	-0.044	0.042	-1.047	0.306	0.948
α -bisabolol	0.067	0.072	0.932	0.361	0.948
cis_nerolidol	-0.802	0.949	-0.845	0.407	0.948
β -caryophyllene	0.023	0.028	0.825	0.418	0.948
geraniol	0.257	0.326	0.788	0.439	0.948

Associations were done between the presence of terpenes or cannabinoids and the change in expression of COX2. The analysis was done using generalized linear models (GLM) with family “gaussian” specified. Resulting p-values were adjusted using Benjamini-Hochberg method.

Supplementary Table S8. Association between terpene and cannabinoids content

Terpene	Estimate	Std. Error	t value	Pr(> t)	Pval_BH
α -pinene vs CBD	0.158	0.04	4.005	0.001	0.014
γ -terpinene vs CBGA	0.133	0.032	4.216	0.000	0.008
linalool vs CBGA	0.358	0.096	3.723	0.001	0.014

Associations was done between the presence of terpenes and cannabinoids content and the change in expression of IL-6. The analysis was done using generalized linear models (GLM) with family “gaussian” specified. Resulting p-values were adjusted using Benjamini-Hochberg method.

Supplementary Table S9. List of cultivars used for this study

	Cultivar	Location	Source
1	CB14 (no commercial name)	Squamish	Cloudburst Cannabis

2	CB2 (no commercial name)	Squamish	Cloudburst Cannabis
3	CB24 (no commercial name)	Squamish	Cloudburst Cannabis
4	CB10 (no commercial name)	Squamish	Cloudburst Cannabis
5	CB19 (no commercial name)	Squamish	Cloudburst Cannabis
6	Emperior	Nelson	Cannabis West Development
7	Artic Kush	Nelson	Cannabis West Development
8	Elevator Kush	Nelson	Cannabis West Development
9	Sunshine Pie	Nelson	Cannabis West Development
10	Diamond Haze	Nelson	Cannabis West Development
11	Spaceman Plus	Nelson	Cannabis West Development
12	Florida Gold	Nelson	Cannabis West Development
13	Citrus Splash	Nelson	Cannabis West Development
14	Glacier Goo	Nelson	Cannabis West Development
15	Zombie	Nelson	Cannabis West Development
16	Berry Delight	Nelson	Cannabis West Development
17	Aviator	Nelson	Cannabis West Development
18	CB17 (Mom) (no commercial name)	Squamish	Cloudburst Cannabis
19	CB17 (regular)(no commercial name)	Squamish	Cloudburst Cannabis
20	CB3 (no commercial name)	Squamish	Cloudburst Cannabis
21	CB11 (no commercial name)	Squamish	Cloudburst Cannabis
22	CB13 (no commercial name)	Squamish	Cloudburst Cannabis
23	CB5 (no commercial name)	Squamish	Cloudburst Cannabis
24	CB9 (no commercial name)	Squamish	Cloudburst Cannabis
25	CB22 (no commercial name)	Squamish	Cloudburst Cannabis