How to retrieve the alterations_across_samples.tsv file for your analysis → go to https://www.cbioportal.org/

Quick Sear	rch Beta!	Download			Please cite: Cerami et al., 2012 & Gao et al., 201	3 What's New	@cbioporta
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t Studies for Visi	ualization & A	Analysis:	1 study selected (1739 samples) Deselect all		Search 👻	cBioPortal @cbioportal It's a small addition, but	
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	2	Cancer Cell Line Encyclopedia (Novartis/Broad, Nature 20 NCI-60 Cell Lines (NCI, Cancer Res 2012)	⁰¹²⁾ (Broad, 2019)		1020 samples 🔀 🖉 🗳 67 samples 🔀 🖉 🗳		
	10	Adrenal Gland				Cases by Top 2	
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	2	Adrenocortical Carcinoma (TCGA, PanCancer Atlas)			92 samples () 🖉 🕼	Lung	
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	3	Ampullary Carcinoma				Kidney Stomach	
nd Neck	13	Ampullary Carcinoma (Baylor College of Medicine, Cell R	lepons 2016)		160 samples 🔀 🎒 🗳	Myeloid	
	17	Biliary Tract				Bladder Skin	
	8	Cholangiocarcinoma Cholangiocarcinoma (MSK, Clin Cancer Res 2018)	2. Click "Query By	/ Gene"	195 samples 🚯 🛃 🚱	Uterus Head/Neck	
	21	 Cholangiocarcinoma (National Cancer Centre of Singapor Cholangiocarcinoma (National University of Singapore, National University) 			15 samples 🛛 🖉 😓 8 samples 🛈 🖉 🚱	Ovary Thyroid	
bid	20	Cholangiocarcinoma (TCGA, Firehose Legacy) Cholangiocarcinoma (TCGA, PanCancer Atlas)	★		51 samples 🔀 📾 📞 36 samples 🔂 🖉 🔩	Liver	
cBioP C	ortal GENOMICS	1 study selected (1739 samples) D Data Sets Web API R/MATLAB T	eselect all Query By Gene of Expl	ore Selected Studies		Pancreas	
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		MRNA Expression z-Scores (RNA Enter a z-score threshold ± 2.0	Seq RPKM) 🕑	should be included	in your analysis		
				×	4. Select Case Set		
ect Patient/Ca ild your own cas it our enhanced	se set,	All samples (1739)					
ld your own cas	se set,	All samples (1739)		X •			

Supplementary Figure 1. Step-by-spec guide how to retrieve the 'alterations_across_samples.tsv' file from https://www.cbioportal.org/ part 1. After selecting the Cancer Cell Line Encyclopedia (Broad, 2019), click 'Query by Gene'. On the following page genomic alteration types can be chosen and and genes of interest entered.

5. Enter your genes of interest

BRAF

MAP2

PTEN

✓ All gene symbols are valid.

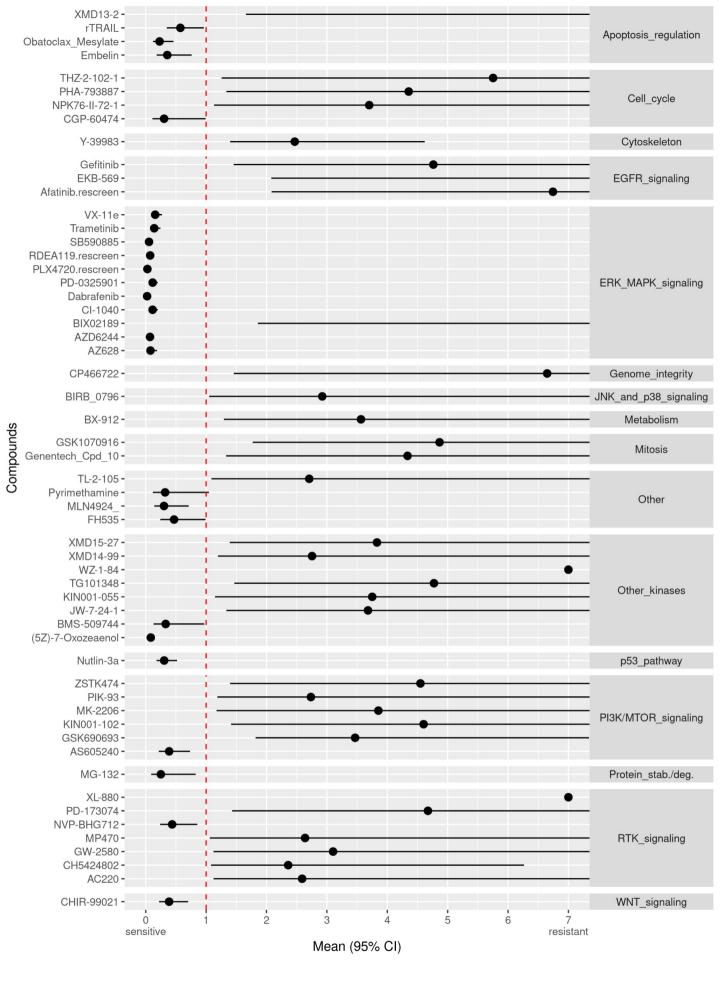
6. Click "Submit Query"

to write more powerful queries 🗹

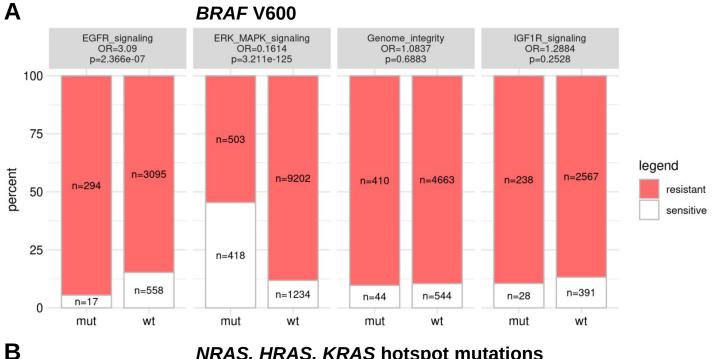
Submit Query

		torials FAQ News Visualize Your Data About	7. Click "Downloa	ad"		Login
Modify Query 🗦	Cancer Cell Line Encyclopedia (Broad, 2019 All samples (1739 patients/samples) - BRAF, MAP2 &			Queried genes are altered in 65	56 (38%) of queried patients/sam	nples 💊
OncoPrint Cance	er Types Summary Mutual Exclusivity Plots	Mutations Co-expression Comparison CN Segments Path	ways Download			
Add Clinical Tracks (41	I ▼ Add Heatmap Tracks 4 ▼ Sort ▼ Mut	tations • View • Download • Q 26 % Q H				
Profiled in Cop						
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BRAF	18%*					
MAP2	11%*					
PTEN	20%* • • • •					
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Copy-number Alteration	s (OOL is not in effect)	Tab Delimited Format Transposed Matrix				
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Unaltered samples: List	of samples without any alteration	🚯 Copy 🛆 Download 🛛 Query 🕏 Virtual Study				
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mRNA expression (RNA	A-Seq RPKM) 0	Tab Delimited Format A Transposed Matrix				
Treatment response: IC		Tab Delimited Format Transposed Matrix				
Treatment response: Z-s		Tab Delimited Format A Transposed Matrix				
Treatment response: AU	JC 🖸	Tab Delimited Format A Transposed Matrix				
Gene Alteration Fre	quency				olumns 🗸	Q
Gene Symbol	Num Samples Alte	ered Percent Samp	les Altered 🔻			
PTEN	335		20.1%			
BRAF	308		18.5%	7. Dowi	nload .tsv file	
MAP2	188		11.3%			
		Showing 1-3 of 3				
Type of Genetic Alte	erations Across All Samples				olumns 🕶	Q
Study ID	Sample ID	Patient ID	Altered v E	BRAF MAP2	PTEN	
ccle_broad_2019	NCIH1694_LUNG	NCIH1694_LUNG	1 H	HIGH AMP, HIGH	no alteration	
ccle_broad_2019	P3HR1_HAEMATOPOIETIC_AND_LYMPHOID_T	ISSUE P3HR1_HAEMATOPOIETIC_AND_LYMPHOID_TISS	UE 1 r	no alteration no alteration	HIGH, Q17*	
ccle_broad_2019	HUT78_HAEMATOPOIETIC_AND_LYMPHOID_T	ISSUE HUT78_HAEMATOPOIETIC_AND_LYMPHOID_TISS	JE 1 r	no alteration no alteration	HOMDEL	
ccle_broad_2019	UMUC3_URINARY_TRACT	UMUC3_URINARY_TRACT		no alteration no alteration	HOMDEL	
ccle_broad_2019	HOS_BONE	HOS_BONE		IOMDEL no alteration	no alteration	
colo broad 2010	ULINET UXEMATODOLETIC AND LVMDUOID T		1 1	IONDEI no alteration	no alteration	

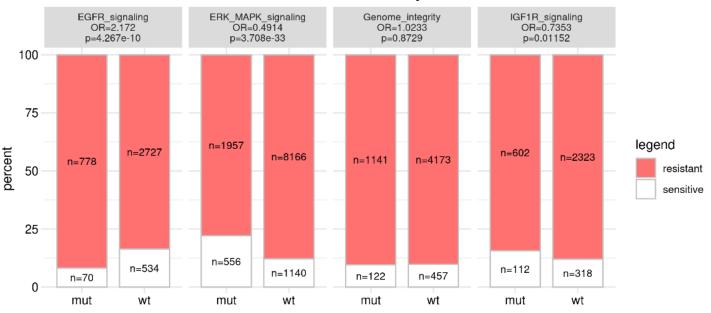
Supplementary Figure 2. Step-by-spec guide how to retrieve the 'alterations_across_samples.tsv' file from cBioPortal part 2. Under the last tab 'Download', the section 'Type of Genomic Alterations Across All Samples' can be found and the 'alterations_across_samples.tsv' file can be downloaded with the cloud symbol on the right site.



Supplementary Figure 3. Associations of drug response to single compounds and BRAFV600 mutations. Forest plot with OR and confidence intervals given for compounds with p<0.05 (fisher's exact tests). Comparisons with groups of the size zero with infinite confidence intervals are depicted as single points at OR=0 (sensitive) or OR=7 (resistant). Analysis performed across entities.

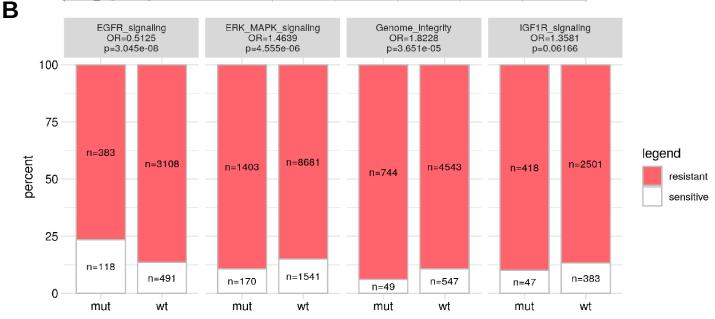


NRAS, HRAS, KRAS hotspot mutations



Supplementary Figure 4. Cell lines with activating changes in BRAF V600 (A) and in RAS genes (B) show sensitivity to ERK/MAPK inhibition. For each pathway (grey boxes) two barplots show numbers of cell lines pooled in the changed/mutated group (mut) and in the wild type (wt). Percent of resistant (red) and sensitive (white) cell lines indicated on the y-scale. Odds ratios (OR) for resistance in the altered cell lines above each bar plot: OR >1: resistance of altered cell lines to drugs in this pathway, OR<1: sensitivity.

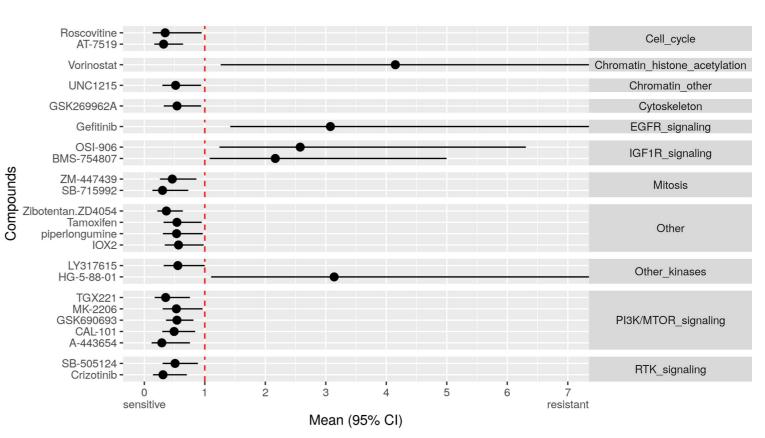
drug_group	OR	fisher p	chi p	lower	upper
Other_kinases	1.7062	6.284E-18	1.637E-16	1.5033	1.944
Other	1.4415	4.928E-10	1.518E-09	1.2813	1.6268
PI3K/MTOR_signaling	1.547	2.377E-08	6.958E-08	1.3219	1.8208
EGFR_signaling	0.5125	3.045E-08	5.1E-09	0.4093	0.6453
Chromatin_other	2.4925	7.835E-08	4.298E-07	1.753	3.6651
Cell_cycle	1.8093	3.169E-07	1.087E-06	1.4297	2.3241
DNA_replication	1.8182	1.372E-06	3.926E-06	1.415	2.3747
ERK_MAPK_signaling	1.4639	4.555E-06	7.653E-06	1.2407	1.7372
Cytoskeleton	1.6085	9.924E-06	1.556E-05	1.2993	2.0104
Chromatin_histone_acetylation	1.5991	1.753E-05	3.044E-05	1.286	2.011
p53_pathway	2.3501	2.495E-05	5.751E-05	1.5588	3.7104
Metabolism	2.0327	2.846E-05	7.154E-05	1.4407	2.9643
Genome_integrity	1.8228	3.651E-05	7.339E-05	1.361	2.4962
RTK_signaling	1.3427	5.285E-05	7.49E-05	1.1621	1.5585
Apoptosis_regulation	1.4639	0.001347	0.00156	1.16	1.8705
Mitosis	1.4984	0.001367	0.00174	1.1684	1.9519
JNK_and_p38_signaling	1.5021	0.006234	0.006583	1.1263	2.0447
IGF1R_signaling	1.3581	0.06166	0.05772	0.9956	1.8926
Protein_stab./deg.	1.2857	0.1425	0.1287	0.9358	1.8121
Chromatin_histone_methylation	1.4579	0.2131	0.1678	0.8656	2.6399
ABL_signaling	1.2925	0.4237	0.3568	0.7552	2.3686
WNT_signaling	1.0888	0.6632	0.6223	0.7747	1.566



Supplementary Figure 5. Cell lines with activating changes in *EGFR* or *ERBB2* show enhanced sensitivity to compounds targeting EGFR signaling. Analysis of activating changes (amplifications, mRNA high z-scores relative to diploid samples with z-score ± 2) across entities. **(A)** Sensitivity to a single pathway is observed with significance (highlighted in yellow) while altered cell lines appear resistant to most drugs from other pathways. **(B)** Odds ratios (OR) for resistance in the altered cell lines shown above each barplot (OR>1 indicates resistance, OR<1 sensitivity.

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drug_group	OR	fisher_p	chi_p	lower	upper
PI3K/MTOR_signaling	0.7473	3.26E-05	1.87E-05	0.6547	0.8554
IGF1R_signaling	1.8572	0.00048	0.00074	1.3048	2.7279
EGFR_signaling	1.569	0.00197	0.00225	1.1805	2.1232
Other	0.8624	0.00727	0.00646	0.7761	0.9602
RTK_signaling	0.8696	0.04557	0.04246	0.7611	0.9966
DNA_replication	1.2712	0.04825	0.04635	1.0075	1.6239
Cell_cycle	0.8388	0.08006	0.07331	0.6946	1.0197
Chromatin_histone_methylation	0.6564	0.09115	0.06961	0.4229	1.0533
Cytoskeleton	0.8482	0.102	0.0955	0.701	1.0317
Other_kinases	1.0789	0.1992	0.1906	0.9636	1.211
ERK_MAPK_signaling	1.1074	0.2082	0.2044	0.9471	1.3007
Apoptosis_regulation	0.896	0.331	0.3273	0.7236	1.1189
ABL_signaling	1.3101	0.4219	0.3347	0.7634	2.4057
Chromatin_histone_acetylation	1.0859	0.4422	0.4264	0.8873	1.34
Protein_stab./deg.	0.9001	0.481	0.4976	0.6736	1.2242
Chromatin_other	0.9378	0.6606	0.6645	0.7113	1.2532
p53_pathway	1.0698	0.7331	0.6865	0.7677	1.5225
JNK_and_p38_signaling	1.0241	0.891	0.8524	0.7862	1.3536
WNT_signaling	1.0386	0.9282	0.8226	0.7341	1.5039
Metabolism	1.0171	0.9395	0.8995	0.7599	1.3865
Genome_integrity	1.019	0.9481	0.8754	0.793	1.3265
Mitosis	0.9901	0.9538	0.9402	0.7931	1.2487



С

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Top 10 most frequently mutated genes in Breast Invasive Carcinoma (TCGA, Firehose Legacy)

Mutated Genes (982 profiled samples)								
▼ Gene	# Mut	#	Freq 👻					
PIK3CA ())	355	319	32.5%	^				
TP53 🔘	304	301	30.7%	1				
CDH1	114	112	11.4%					
GATA3 🛞	101	97	9.9%					
MAP3K1 🛞	98	71	7.2%					
KMT2C	83	70	7.1%					
NCOR1 (9)	42	40	4.1%					
PTEN 🔘	37	35	3.6%					
SPEN	44	33	3.4%					
MAP2K4	32	32	3.3%					

Breast Invasive Carcinoma (TCGA Firehose legacy)

Α	в	Log2 Odds Ratio	p-Value	q-Value ▲	Tendency
TP53	GATA3	1.604	<0.001	<0.001	Co-occurrence
NCOR1	MAP2K4	1.790	<0.001	<0.001	Co-occurrence
PIK3CA	GATA3	-1.416	<0.001	<0.001	Mutual exclusivity
TP53	PTEN	1.556	<0.001	<0.001	Co-occurrence
PIK3CA	PTEN	-1.516	<0.001	0.001	Mutual exclusivity
TP53	CDH1	-1.505	<0.001	0.002	Mutual exclusivity
GATA3	PTEN	1.331	<0.001	0.002	Co-occurrence
GATA3	KMT2C	0.926	0.006	0.029	Co-occurrence
KMT2C	NCOR1	1.020	0.006	0.029	Co-occurrence

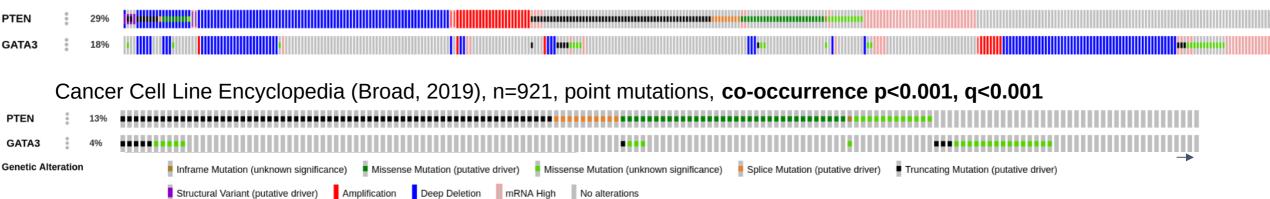
Cancer Cell Line Encyclopedia (Broad, 2019)

			•	•	
Α	в	Log2 Odds Ratio	p-Value	q-Value -	Tendency
NCOR1	MAP2K4	>3	<0.001	<0.001	Co-occurrence
TP53	MAP2K4	2.882	<0.001	<0.001	Co-occurrence
TP53	NCOR1	1.641	< 0.001	<0.001	Co-occurrence
GATA3	PTEN	1.213	<0.001	<0.001	Co-occurrence
GATA3	NCOR1	1.230	<0.001	<0.001	Co-occurrence
MAP3K1	NCOR1	1.260	< 0.001	<0.001	Co-occurrence

CCLE (Broad, 2019), n=921, point mutations, CNV, structural, mRNA, co-occurrence p<0.001, q<0.001

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Supplementary Figure 6. PTEN and GATA3. (A) Drug sensitivity of the CCLE cell lines associated with deactivating changes (homozygous deletions, splice variants, frameshift and nonsense mutations) in PTEN. (B) Odds ratios (Fisher's test p<0.05) of significant single compounds. (C) Co-mutation of PTEN and GATA3 in breast tumors and cancer cell lines. 10 most frequently mutated genes within Breast Invasive Carcinoma (TCGA, Firehose legacy; point mutations, www.cbioportal.org) and thereof (D) significant co-occurrence and mutual exclusivity (point mutations, structural and mRNA alterations) in breast cancer and the CCLE. (E) Co-occurrence of PTEN and GATA3 genetic changes in CCLE significant also for point mutations only (excluding structural and mRNA changes to rule out that co-occurrence is based solely on the localization on the same chromosome arm). Arrow indicates the presence of more wild type samples not depicted.