

# How to retrieve the alterations\_across\_samples.tsv file for your analysis

→ go to <https://www.cbioportal.org/>

**1. Select data set: Cancer Cell Line Encyclopedia (Broad, 2019)**

**2. Click "Query By Gene"**

**3. Select alteration types which should be included in your analysis**

**4. Select Case Set**

**5. Enter your genes of interest**

**6. Click "Submit Query"**

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**6. Click "Submit Query"**

**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 genes of interest entered.

7. Click "Download"

Modify Query Cancer Cell Line Encyclopedia (Broad, 2019) Queried genes are altered in 656 (38%) of queried patients/samples  
 All samples (1739 patients/samples) - BRAF, MAP2 & PTEN

OncoPrint Cancer Types Summary Mutual Exclusivity Plots Mutations Co-expression Comparison CN Segments Pathways Download



Download

Downloadable Data Files

Copy-number Alterations (OQL is not in effect)	Tab Delimited Format   Transposed Matrix
Mutations (OQL is not in effect)	Tab Delimited Format   Transposed Matrix
mRNA Expression z-Scores (RNA Seq RPKM)	Tab Delimited Format   Transposed Matrix
Altered samples: List of samples with alterations	Copy   Download   Query   Virtual Study
Unaltered samples: List of samples without any alteration	Copy   Download   Query   Virtual Study
Sample matrix: List of all samples where 1=altered and 0=unaltered	Copy   Download
mRNA expression (RNA-Seq RPKM)	Tab Delimited Format   Transposed Matrix
Treatment response: IC50	Tab Delimited Format   Transposed Matrix
Treatment response: Z-score of IC50	Tab Delimited Format   Transposed Matrix
Treatment response: AUC	Tab Delimited Format   Transposed Matrix

Gene Alteration Frequency

Gene Symbol	Num Samples Altered	Percent Samples Altered
PTEN	335	20.1%
BRAF	308	18.5%
MAP2	188	11.3%

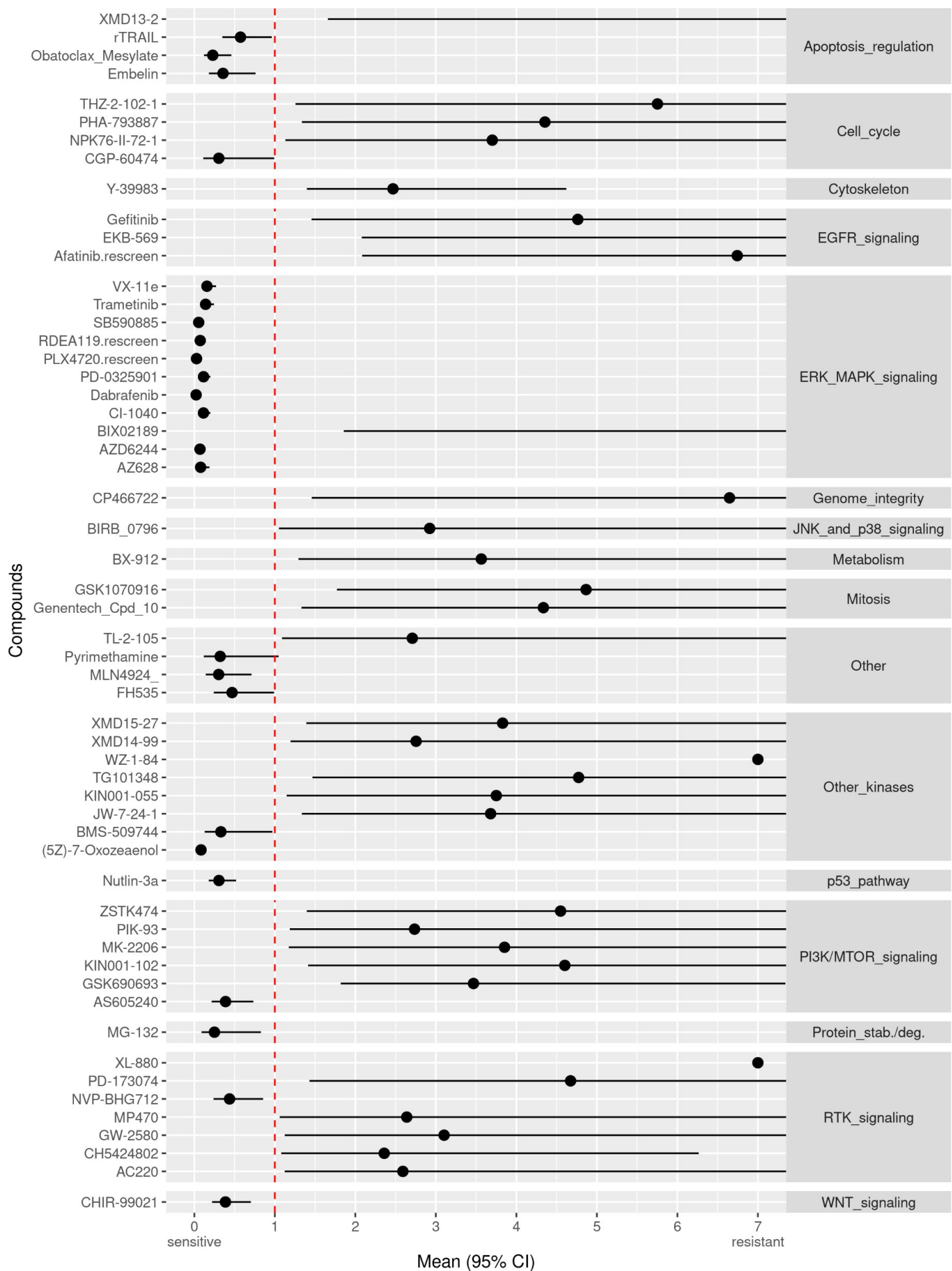
Showing 1-3 of 3

7. Download .tsv file

Type of Genetic Alterations Across All Samples

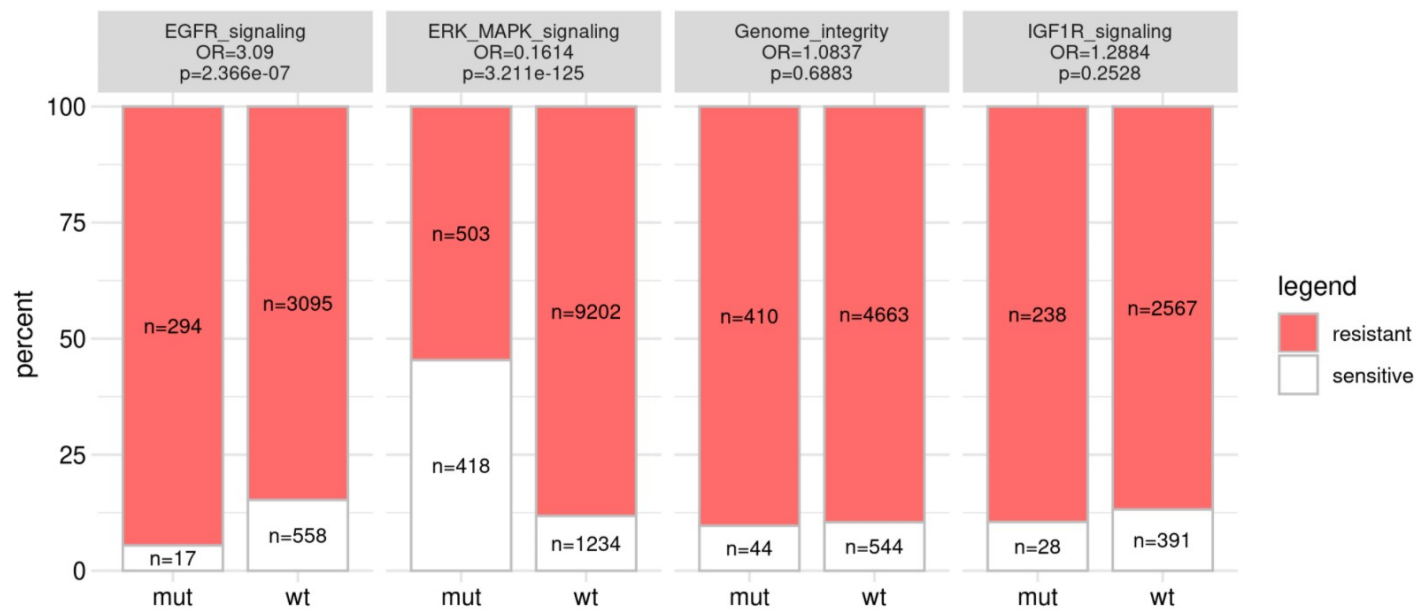
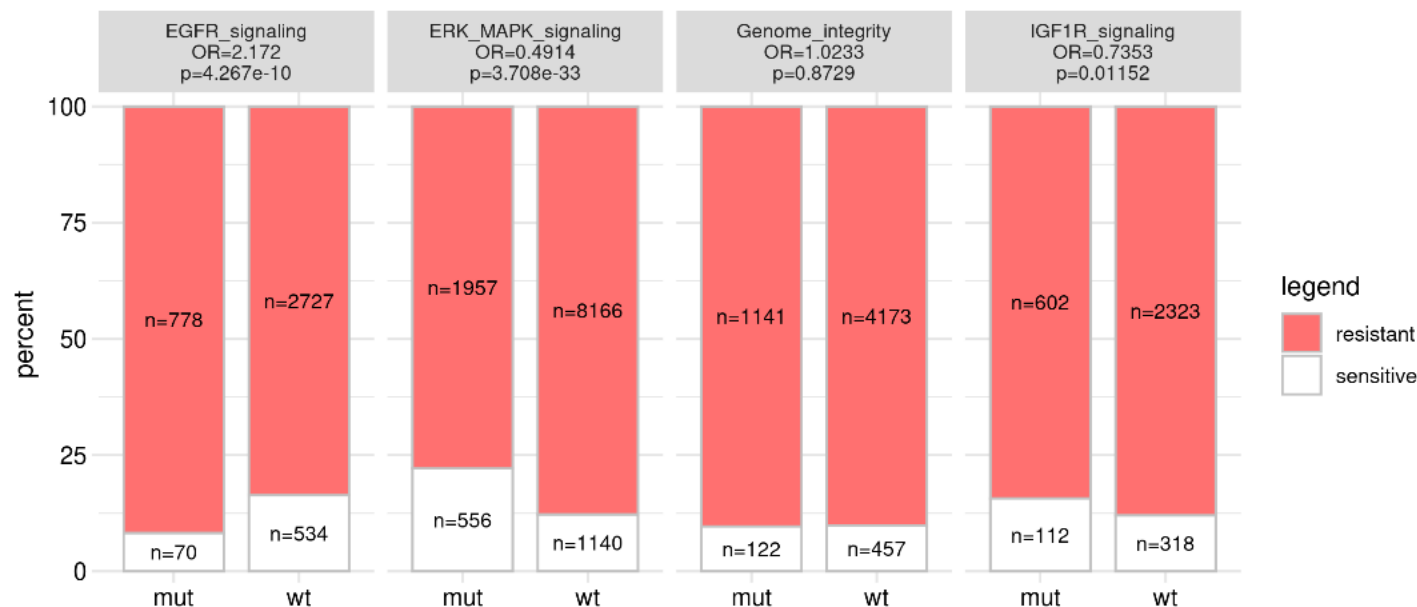
Study ID	Sample ID	Patient ID	Altered	BRAF	MAP2	PTEN
ccl_broad_2019	NCIH1694_LUNG	NCIH1694_LUNG	1	HIGH	AMP, HIGH	no alteration
ccl_broad_2019	P3HR1_HAEMATPOIETIC_AND_LYMPHOID_TISSUE	P3HR1_HAEMATPOIETIC_AND_LYMPHOID_TISSUE	1	no alteration	no alteration	HIGH, Q17*
ccl_broad_2019	HUT78_HAEMATPOIETIC_AND_LYMPHOID_TISSUE	HUT78_HAEMATPOIETIC_AND_LYMPHOID_TISSUE	1	no alteration	no alteration	HOMDEL
ccl_broad_2019	UMUC3_URINARY_TRACT	UMUC3_URINARY_TRACT	1	no alteration	no alteration	HOMDEL
ccl_broad_2019	HOS_BONE	HOS_BONE	1	HOMDEL	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.



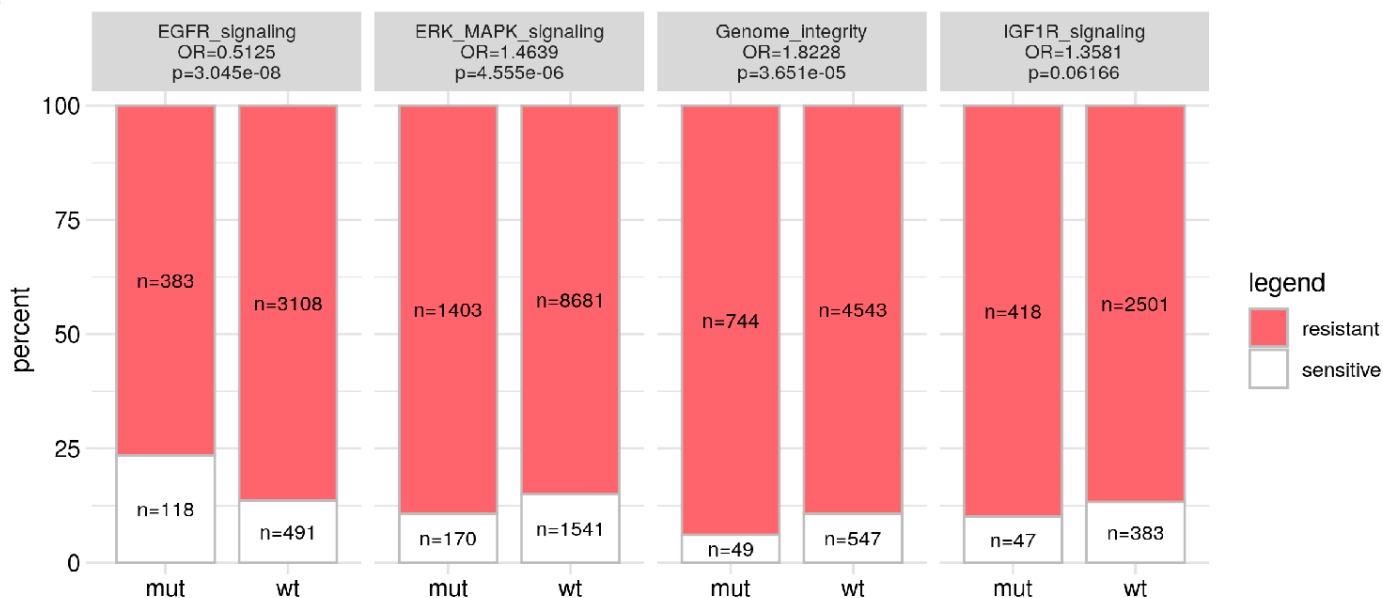
**A*****BRAF* V600****B*****NRAS, HRAS, KRAS* hotspot mutations**

**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.

**A**

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

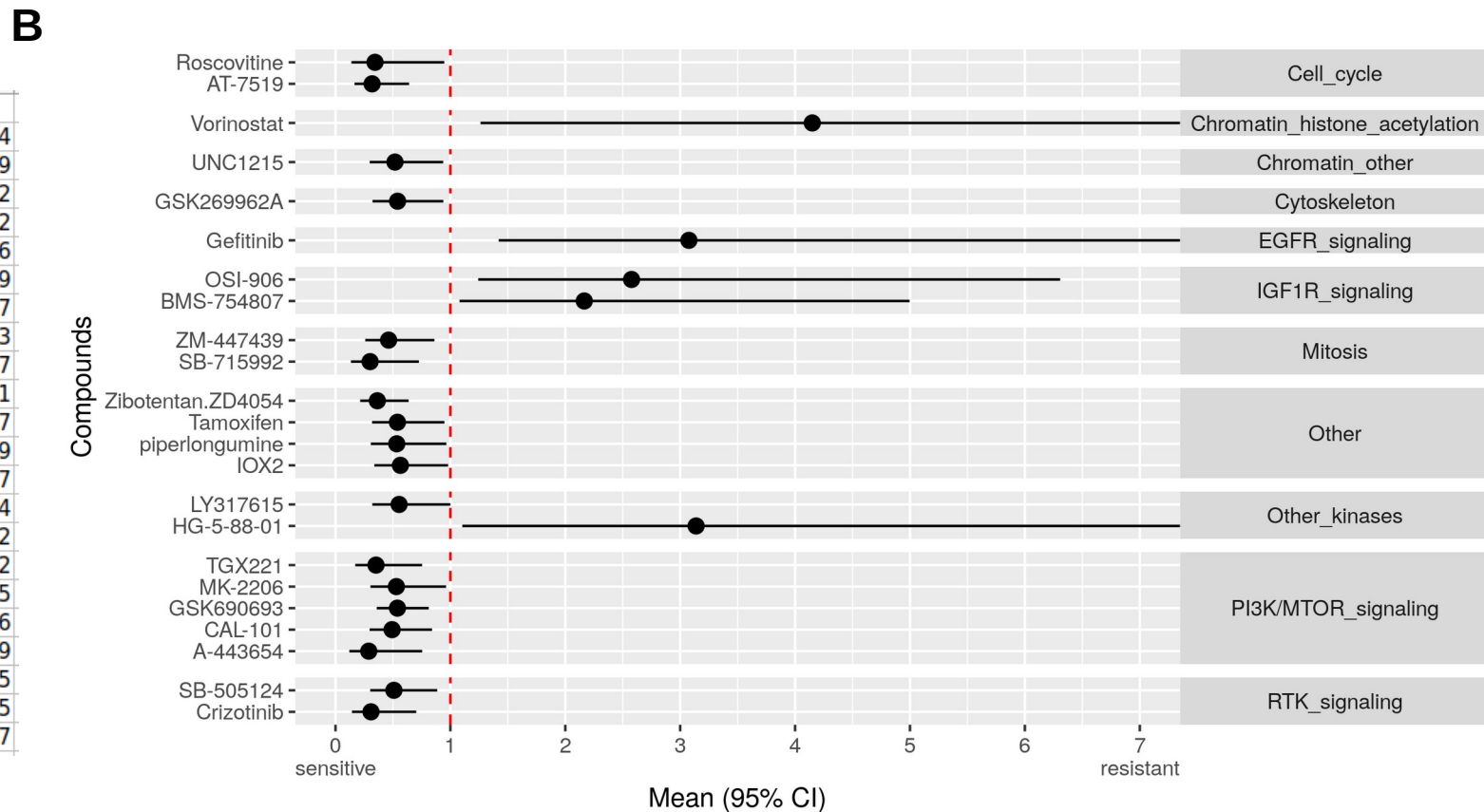
**B**



**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  $\pm 2$ ) 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).

**A**

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



**C**

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%
CDH1	114	112	11.4%
GATA3	101	97	9.9%
MAP3K1	98	71	7.2%
KMT2C	83	70	7.1%
NCOR1	42	40	4.1%
PTEN	37	35	3.6%
SPEN	44	33	3.4%
MAP2K4	32	32	3.3%

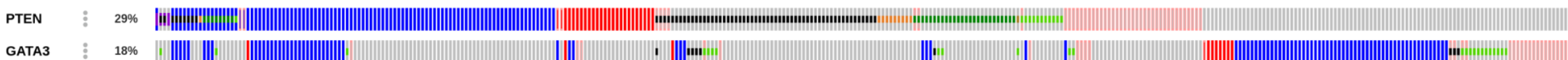
**D** Breast Invasive Carcinoma (TCGA Firehose legacy)

A	B	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)

A	B	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

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



Cancer Cell Line Encyclopedia (Broad, 2019), n=921, point mutations, co-occurrence p<0.001, q<0.001



**Supplementary Figure 6. PTEN and GATA3. (A)** Drug sensitivity of the CCLC 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.