

# Public Datasets of Pharmacogenomics Data

# Outline

1. In Vitro - In Vivo - Clinical Data
2. Publicly Available Large Datasets in Pharmacogenomics
  - a. In Vitro
  - b. In Vivo
  - c. Clinical
3. Web Applications and Portals
  - a. PharmacoDB
  - b. CellMinerCDB/COMPARE
  - c. clue.io
4. Bioinformatics Tools for Accessing Pharmacogenomics Data

# Model Systems for Pharmacogenomic Discovery

## Clinical Data is Gold Standard

Why care about pharmacogenomics data in model systems?

- Cannot answer all questions:
  - Patient: 1 treatment regime at a time
  - Treatment with drug alters patient tumours
  - Response data in patients is noisy
  - Ethics

# (Model) System Determines Dataset Size

Clinical:

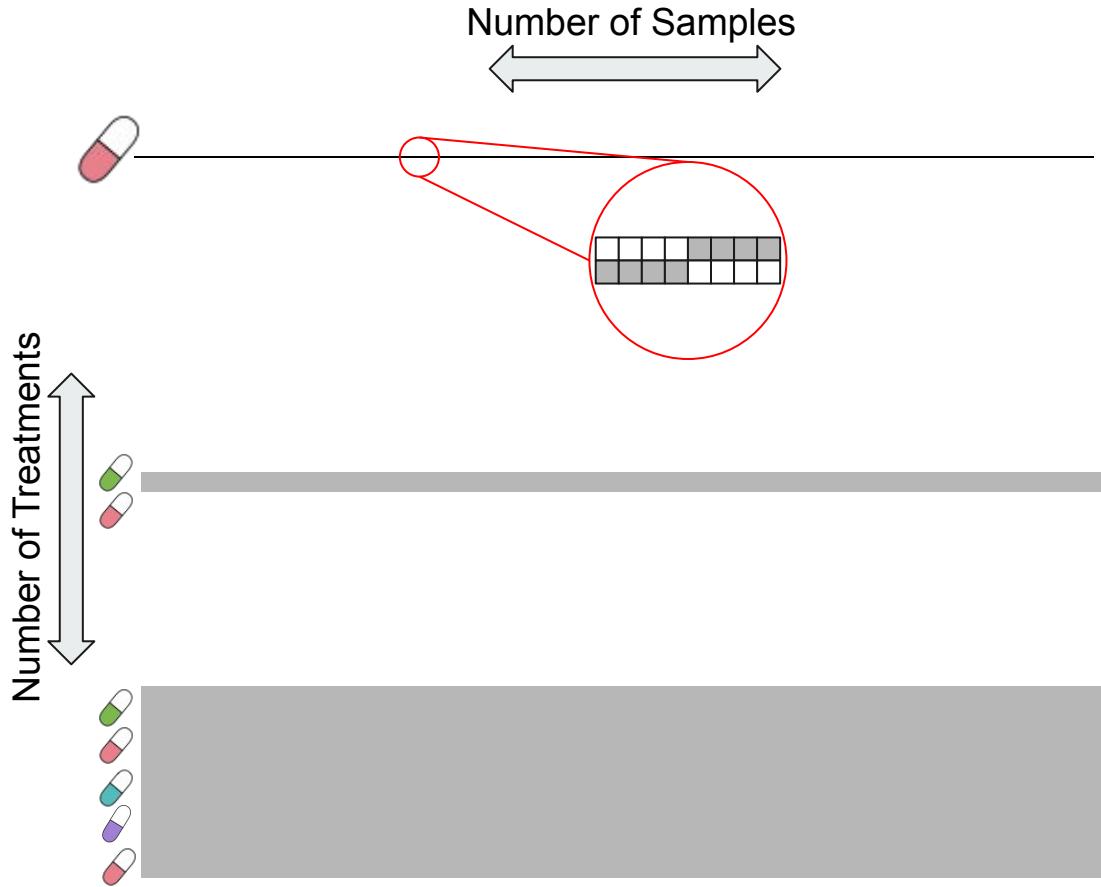
1000s patients achievable  
<10s treatments (1 per patient)

In Vivo:

1000 models (PDX)  
10s treatments

In Vitro:

1000 Cell Lines  
100s treatments



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# **Non-Exhaustive Survey of Public Pharmacogenomics Datasets**

# Data sharing for In Vitro Pharmacogenomics

**NCI60/DTP**  
Since 1997  
59 cell lines  
60,000+ drugs

**JCFR39**  
Since 1999  
39 cell lines  
557 drugs

**CMap**  
Sep 2006  
5 cell lines  
1,309 drugs

**GSK**  
Apr 2010  
311 cell lines  
19 drugs

**PGP**  
Jan 2012  
87 cell lines  
2 drugs

**GRAY**  
Feb 2012  
54 cell lines  
74 drugs

**L1000**  
Jan 2012  
77 cell lines  
20,431 drugs

**GNE**  
Dec 2014  
675 cell lines  
5 drugs

**GRAY'**  
Oct 2013  
70 cell lines  
90 drugs

**CTRP**  
Aug 2013  
242 cell lines  
354 drugs

**CCLE**  
Mar 2012  
1061 cell lines  
24 drugs

**GDSC**  
Mar 2012  
727 cell lines  
140 drugs

**CTRPv2**  
Sep 2015  
860 cell lines  
481 drugs

**gCSI**  
May 2016  
410 cell lines  
16 drugs

**GDSC1000**  
June 2016  
1124 cell lines  
256 drugs

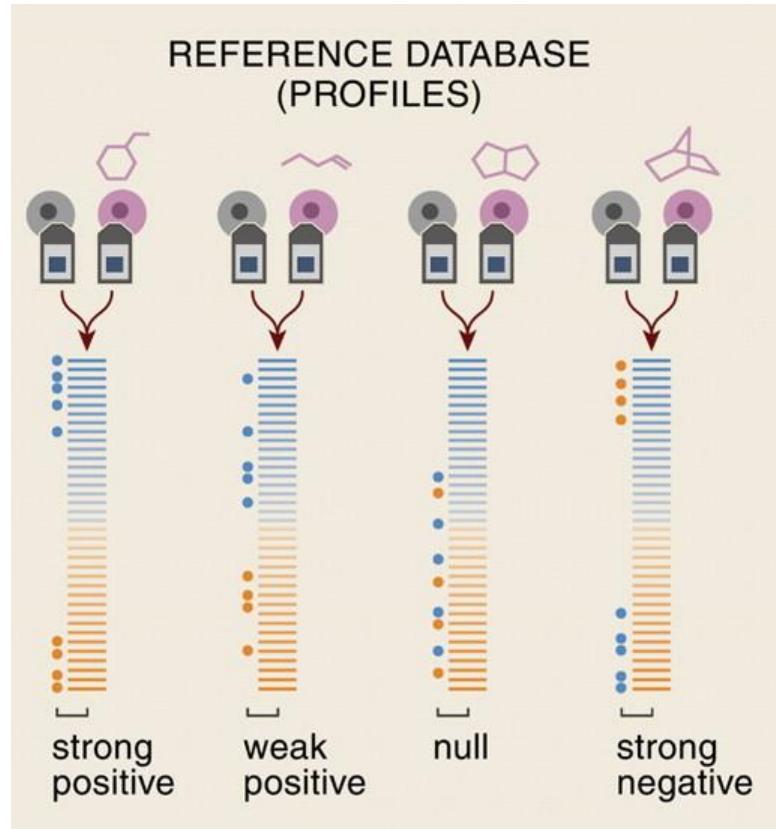
**FIMM**  
Dec 2016  
106 cell lines  
308 drugs

More to come... 6

# Perturbation Datasets

The Connectivity Map Team at the Broad

- 2006: CMAP
  - Affy Microarray Gene Expression (~20k)
  - 5 Cell lines
  - ~1200 Compounds
- Next Generation: L1000
  - Luminex Platform: 1k Landmark Genes
  - 3-77 Cell Lines
  - 27k+ Perturbagens (7.5k genetic)



# Sensitivity Datasets – Immortalized Cancer Cell Lines

NCI-60:

88,000+ Compounds

60 Cell Lines

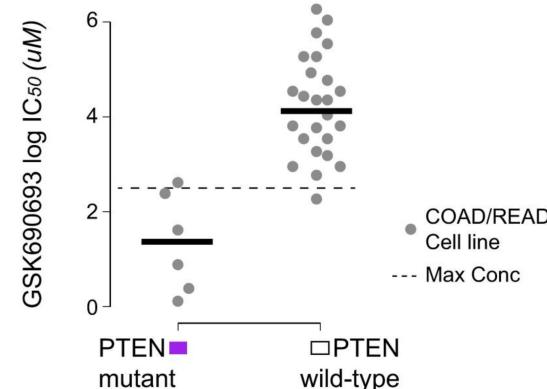
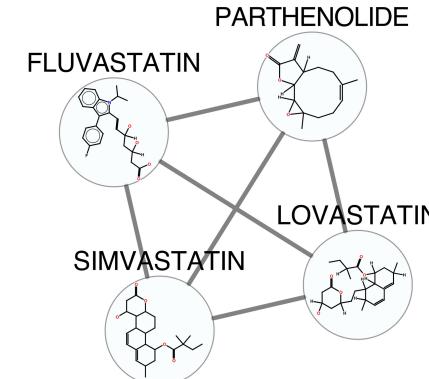
CCLE+CTRPV2

GDSC1000

100s Compounds

~1000 Cells

Many more datasets!



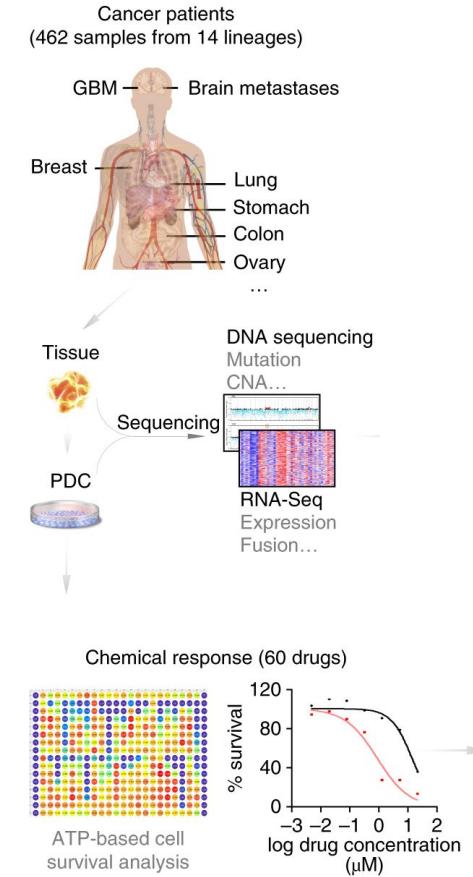
# Sensitivity Datasets – ex Vivo Screening

## BeatAML Initiative

562 Patient Derived Cells  
122 Compounds

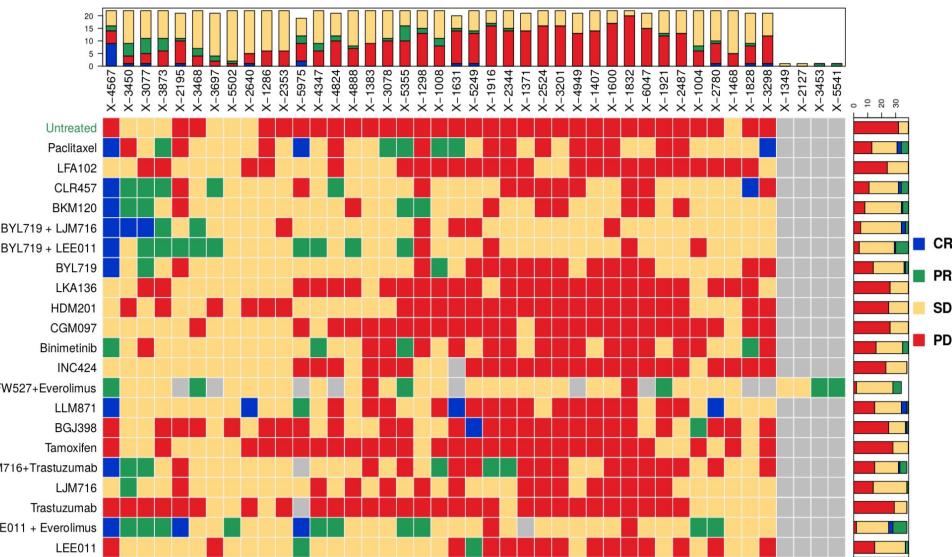
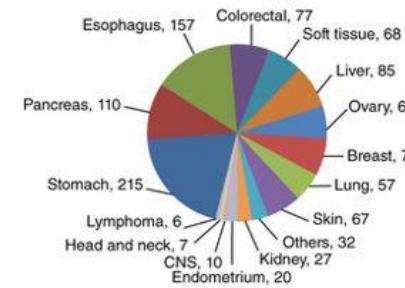
## Samsung Medical Centre PanCancer

462 Patient Derived Cells  
60 Compounds



# PDX are the Workhorse of in Vivo Pharmacogenomics

Novartis PDX Encyclopedia:  
1075 Models (~250 Patients)  
60 Drugs



Gao, H. et al. High-throughput screening using patient-derived tumor xenografts to predict clinical trial drug response. *Nature Medicine* 21, 1318–1325 (2015).  
Mer, A. S. et al. Integrative pharmacogenomics analysis of patient-derived xenografts. *Cancer Res* 0349.2019 (2019).

# Clinical Data, where to find it?

Not very many completely public datasets available!

Multiple Myeloma CoMMpass:  
1150 Patients  
Largely Standard of Care



<https://research.themmrf.org/>

ClinicalTrial.gov:  
Contact Study Investigators

AACR Genie:  
Could be the future?  
Clinical Annotation still very expensive!



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# **Web Tools to Interrogate Pharmacogenomics Data**

# Common Pharmacogenomics Questions

Has my drug of interest **X** been tested in public data?

Which model should I use for my experiments with drug  
**X**?

What gene knockdowns are most similar in effect to my  
drug **X**?

# Demos – Feel free to follow along!

## PharmacoDB:

7 large in Vitro Pharmacogenomics Studies

[www.pharmacodb.ca](http://www.pharmacodb.ca)

## CellMinerCDB:

Explore NCI-60+:

<https://discover.nci.nih.gov/cellminercdb/>

## clue.io:

Portal for the L1000 dataset:

[clue.io](http://clue.io)

# References

CMAP:

Lamb, J. et al. The Connectivity Map: Using Gene-Expression Signatures to Connect Small Molecules, Genes, and Disease. *Science* 313, 1929–1935 (2006).

L1000:

Subramanian, A. et al. A Next Generation Connectivity Map: L1000 Platform and the First 1,000,000 Profiles. *Cell* 171, 1437-1452.e17 (2017).

CCLE:

Barretina, J. et al. The Cancer Cell Line Encyclopedia enables predictive modelling of anticancer drug sensitivity. *Nature* 483, 603–607 (2012).

CTRPv2:

Seashore-Ludlow, B. et al. Harnessing Connectivity in a Large-Scale Small-Molecule Sensitivity Dataset. *Cancer Discovery* (2015). doi:10.1158/2159-8290.CD-15-0235

GDSC1000:

Iorio, F. et al. A Landscape of Pharmacogenomic Interactions in Cancer. *Cell* 166, 740–754 (2016).

# References

BeatAML:

Tyner, J. W. et al. Functional genomic landscape of acute myeloid leukaemia. *Nature* 562, 526 (2018).

Samsung Patient Derived Tumour Cells:

Lee, J.-K. et al. Pharmacogenomic landscape of patient-derived tumor cells informs precision oncology therapy. *Nature Genetics* 50, 1399 (2018).

Novartis PDXE:

Gao, H. et al. High-throughput screening using patient-derived tumor xenografts to predict clinical trial drug response. *Nature Medicine* 21, 1318–1325 (2015).

MMRF CoMMpass:

Craig, D. W. et al. Interim Analysis Of The Mmrf Commpass Trial, a Longitudinal Study In Multiple Myeloma Relating Clinical Outcomes To Genomic and Immunophenotypic Profiles. *Blood* 122, 532–532 (2013).

AACR Genie:

The AACR Project GENIE Consortium. AACR Project GENIE: Powering Precision Medicine through an International Consortium. *Cancer Discovery* 7, 818–831 (2017).

# References

PharmacоДB:

Smirnov, P. et al. PharmacоДB: an integrative database for mining in vitro anticancer drug screening studies. Nucleic Acids Res 46, D994–D1002 (2018).

Cell Miner CDB:

Rajapakse, V. N. et al. Integrative analysis of pharmacogenomics in major cancer cell line databases using CellMinerCDB. bioRxiv 292904 (2018). doi:10.1101/292904

clue.io:

Not Yet Published in Peer Reviewed Article: clue.io



# Demo Appendix

# PHARMACODB

MINE MULTIPLE CANCER PHARMACOGENOMIC DATASETS

Tissue (



7  
DATASETS

41  
TISSUES

1,691  
CELL LINES

19,933  
GENES

759  
COMPOUNDS

650,894  
EXPERIMENTS

# PHARMACODB

MINE MULTIPLE CANCER PHARMACOGENOMIC DATASETS

MDA-MB-231



CELL LINE

MDA-MB-231

7

DATASETS

3

759  
COMPOUNDS

650,894  
EXPERIMENTS

# MDA-MB-231

## Synonyms

| Sources              | Names Used |
|----------------------|------------|
| CCLE, GDSC1000, gCSI | MDA-MB-231 |
| GRAY, FIMM, CTRPv2   | MDAMB231   |
| UHNBreast            | mdamb231   |
| PharmacoGx           | MDA-MB-231 |

## Tissue Type

breast

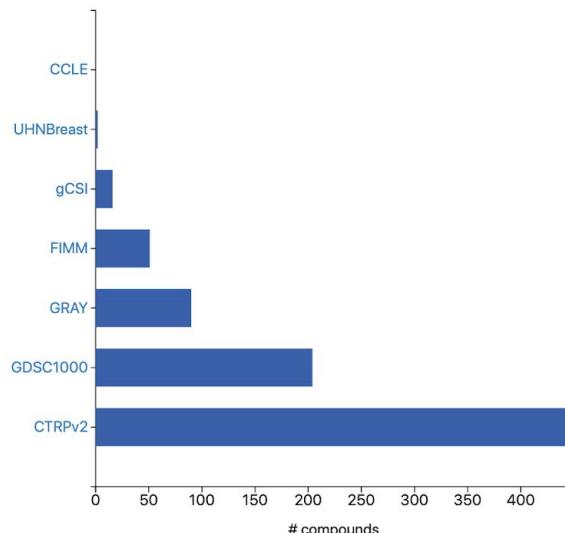
## Disease(s)

NCIt, C5214, Breast adenocarcinoma

## Link(s)

Cellosaurus

Number of compounds tested with MDA-MB-231 per dataset



Download SVG

## Compounds tested with MDA-MB-231

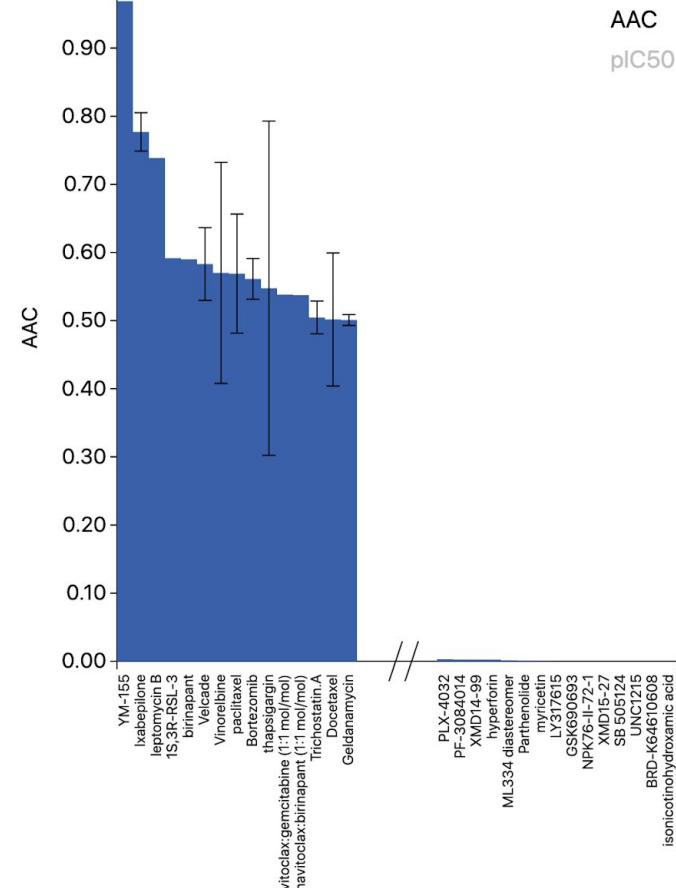
647 compounds have been tested with this cell line, using data from 6 dataset(s).

Search compound names ...



| Compounds ▲ | Datasets ▲                           | Experiments ▲ |
|-------------|--------------------------------------|---------------|
| GSK1838705  | GRAY                                 | 8             |
| paclitaxel  | gCSI, GRAY, FIMM, CT RPV2, UHNBreast | 8             |
| Bortezomib  | gCSI, GRAY, FIMM, CT RPV2            | 8             |
| Erlotinib   | gCSI, GRAY, FIMM, CT RPV2, UHNBreast | 7             |
| Vorinostat  | GDSC1000, gCSI, GRA Y, FIMM, CTRPv2  | 7             |
| Gefitinib   | GDSC1000, GRAY, FIMM, CTRPv2         | 7             |
| Doxorubicin | GDSC1000, gCSI, GRA Y, FIMM, CTRPv2  | 7             |

## MDA-MB-231: AAC



← Previous

1 2 3 ... 64 65 Next →

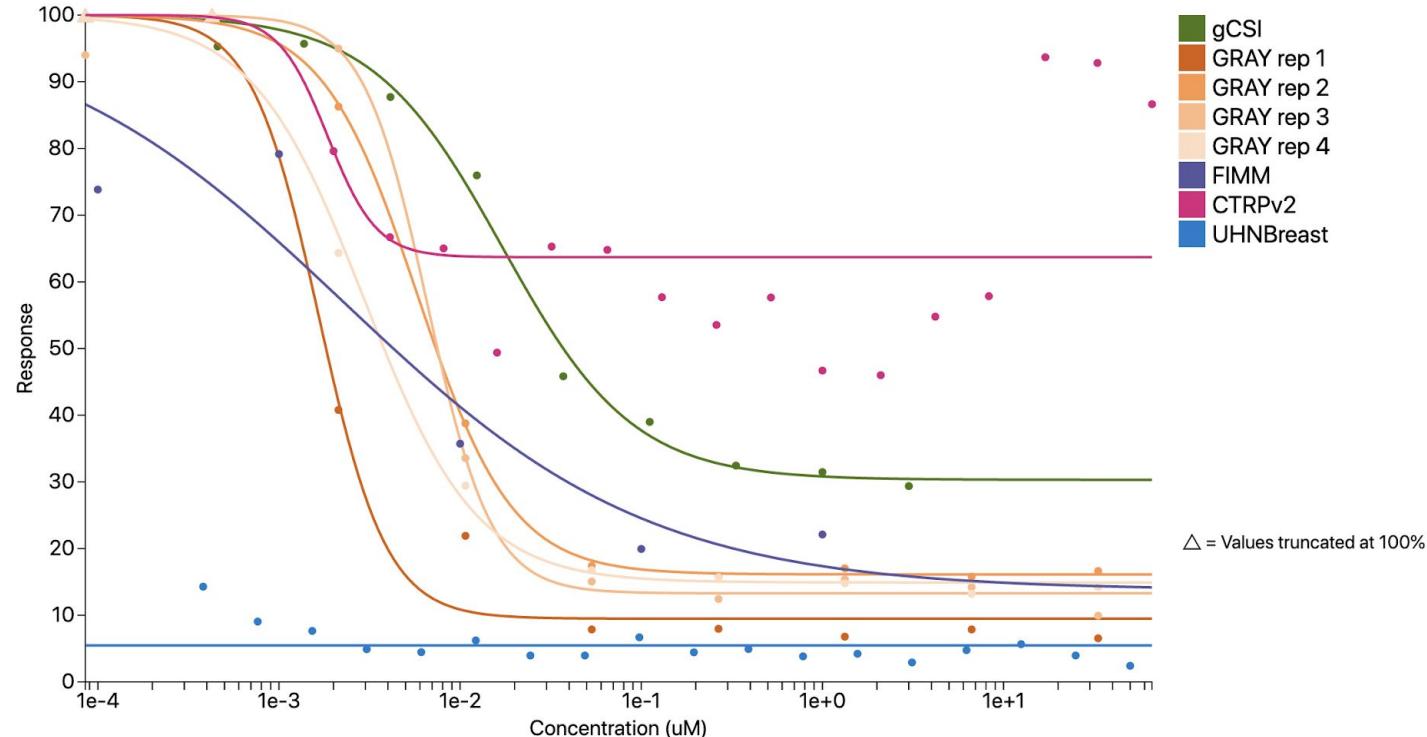
Download CSV

## Available Molecular Profiling in PharmacoGx

# of profiles of each type per dataset

| Datasets  | rna | rnaseq | mutation | cnv |
|-----------|-----|--------|----------|-----|
| CCLE      | 1   | 1      | 1        | 1   |
| GDSC1000  | 1   | -      | -        | -   |
| gCSI      | -   | 1      | -        | 1   |
| GRAY      | -   | 1      | -        | -   |
| FIMM      | -   | -      | -        | -   |
| CTRPv2    | -   | -      | -        | -   |
| UHNBreast | -   | 1      | -        | -   |

# MDA-MB-231 treated with paclitaxel



# Summary Statistics

| Dataset    | AAC (%) | IC50 ( $\mu$ M) | EC50 ( $\mu$ M) | Einf (%) | DSS <sub>1</sub> (arb.) |
|------------|---------|-----------------|-----------------|----------|-------------------------|
| gCSI       | 40.893  | 0.0371          | 0.0171          | 30.302   | 0.36                    |
| GRAY rep 1 | 69.628  | 0.00182         | 0.00166         | 9.494    | 0.677                   |
| GRAY rep 2 | 56.366  | 0.00735         | 0.00581         | 16.133   | 0.536                   |
| GRAY rep 3 | 57.425  | 0.00749         | 0.0066          | 13.291   | 0.554                   |
| GRAY rep 4 | 61.643  | 0.0038          | 0.00295         | 14.906   | 0.586                   |
| FIMM       | 54.393  | 0.00428         | 0.00229         | 13.748   | 0.493                   |
| CTRPv2     | 35.675  | N/A             | 0.00186         | 63.694   | 0.285                   |
| UHNBreast  | 94.532  | 1.03e-06        | 1e-06           | 5.469    | 0.939                   |

[Download CSV](#)

SITE

HOME

ABOUT

DOCUMENTATION

TOOLS

EXPLORE

BATCH QUERY

SEARCH

DATATYPES

DATASETS

CELL LINES

TISSUES

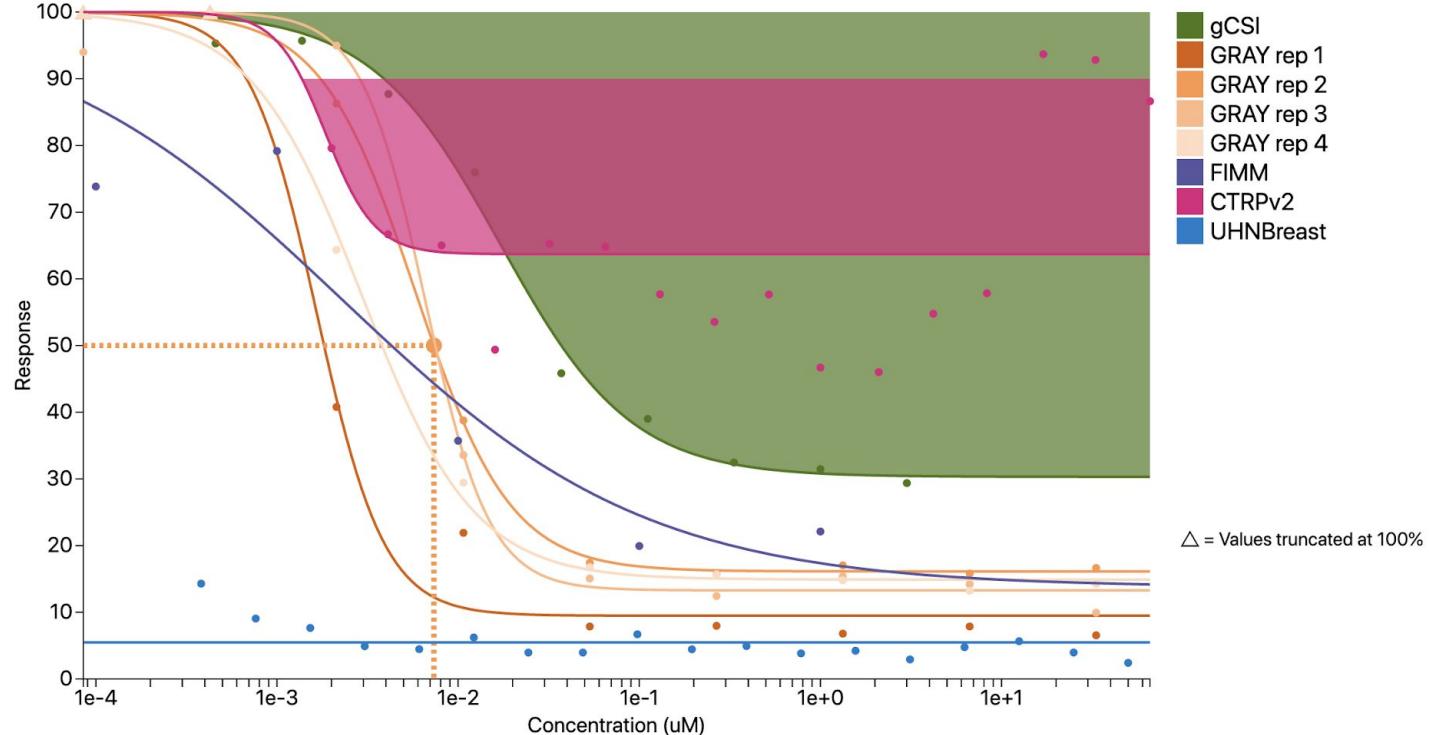
**BHKLAB**

The MaRS Center

TMDT room 11-310

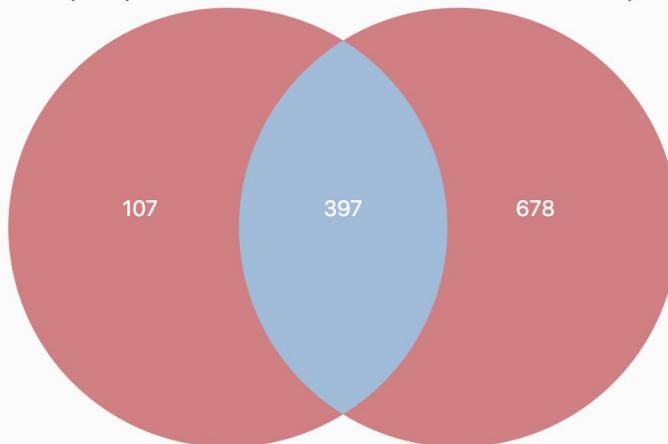
9101 College Street, Toronto, ON

## MDA-MB-231 treated with paclitaxel



## Cell Lines: CCLE + GDSC1000

CCLE (504)      GDSC1000 (1075)



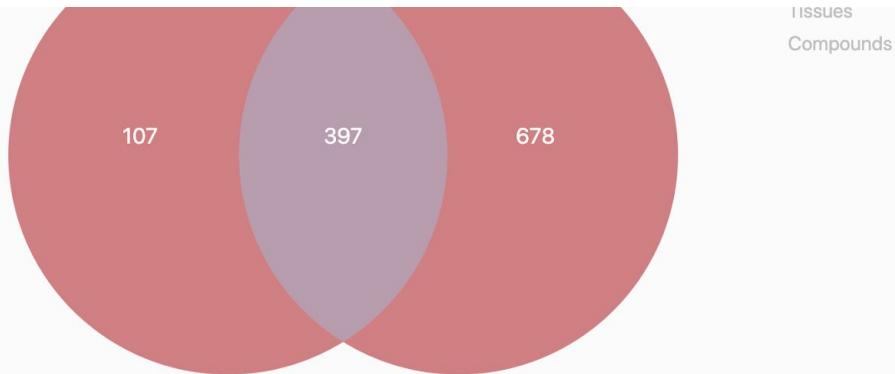
Show:

Cell Lines

Tissues

Compounds

Download SVG



[Download SVG](#)

|         |           |           |
|---------|-----------|-----------|
| HDQ-P1  | JHH-2     | BT-474    |
| A375    | OC-314    | KMS-12-BM |
| TOV-21G | SK-N-FI   | SK-N-AS   |
| HCT-15  | HSC-2     | OV-90     |
| SCC-25  | SNU-398   | NCI-H2452 |
| P3HR-1  | KELLY     | SNU-182   |
| SW48    | RPMI-8402 | SK-ES-1   |
| KG-1    | MC116     | HT-1080   |
| LN-229  | KYSE-450  | MEC-1     |
| SW780   | TYK-nu    | KYSE-410  |



# lapatinib

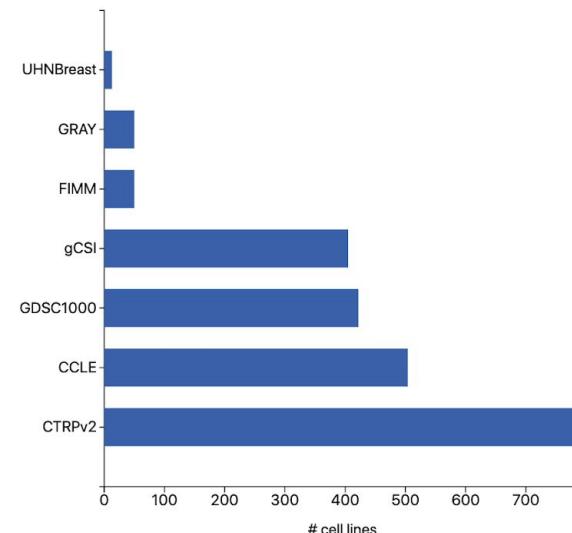
## Synonyms

| Sources                                | Names Used |
|--|------------|
| CCLE, GDSC1000, GRAY, FIMM, UH NBreast | Lapatinib  |
| gCSI, CTRPv2                           | lapatinib  |
| PharmacoGx                             | lapatinib  |

## External IDs

| Database  | Identifier   |
|-----------|--|
| Smiles:   | CS(=O)(=O)CCNCC1=CC=C(O1)C2=C C3=C(C=C2)N=CN=C3NC4=CC(=C(C =C4)OCC5=CC(=CC=C5)F)Cl |
| Inchikey: | BCFGMOOMADDAQU-UHFFFAOYS A-N   |

Number of cell lines tested with lapatinib (per dataset)



Download SVG

## Top molecular features associated with response to lapatinib

Search gene names ...



| Feature Type | Gene ▲  | Dataset ▲ | Stat ▲ | Standardized Coefficient ▲ | Nominal ANOVA p-value ▲ |
|--------------|---------|-----------|--------|----------------------------|-------------------------|
| mRNA         | ERBB2   | CCLE      | AAC    | 0.57                       | 3e-33                   |
| mRNA         | PGAP3   | CCLE      | AAC    | 0.45                       | 7e-26                   |
| mRNA         | GRB7    | CCLE      | AAC    | 0.49                       | 5e-24                   |
| mRNA         | ERBB2   | gCSI      | AAC    | 0.51                       | 1e-17                   |
| mRNA         | ERBB2   | CTRPv2    | AAC    | 0.31                       | 1e-17                   |
| mRNA         | STARD3  | CCLE      | AAC    | 0.36                       | 3e-17                   |
| mRNA         | S100A14 | CCLE      | AAC    | 0.43                       | 4e-17                   |
| mRNA         | EPN3    | CCLE      | AAC    | 0.43                       | 8e-17                   |
| mRNA         | MAL2    | CCLE      | AAC    | 0.47                       | 4e-16                   |
| mRNA         | JUP     | CCLE      | AAC    | 0.41                       | 2e-15                   |

← Previous

1

2

3

...

10269

10270

Next →

# ERBB2

## Synonyms

|                  |                 |
|------------------|-----------------|
| Ensembl Gene ID: | ENSG00000141736 |
|------------------|-----------------|

## Links

|           |       |
|-----------|-------|
| Genecard: | ERBB2 |
|-----------|-------|

## Compounds tested targeting ERBB2

9 compounds have been tested on ERBB2, using data from 7 dataset(s).

Search compound names ...



| Compounds ▲ | Datasets ▲  | Experiments ▲ |
|-------------|---|---------------|
| Erlotinib   | CCLE, GDSC1000, gCSI, GRAY, FIMM, CTRPv2, UHNBreast | 2345          |
| Iapatinib   | CCLE, GDSC1000, gCSI, GRAY, FIMM, CTRPv2, UHNBreast | 2302          |
| BMS-536924  | GDSC1000, CTRPv2                                    | 2234          |
| Vandetanib  | CCLE, FIMM, CTRPv2                                  | 1381          |

## Top compounds associated with response to ERBB2

Search compound names ...



| Feature Type | Compound ▲ | Dataset ▲ | Stat ▲ | Standardized Coefficient ▲ | Nominal ANOVA p-value ▲ |
|--------------|------------|-----------|--------|----------------------------|-------------------------|
| mRNA         | CP724714   | GDSC1000  | AAC    | 0.47                       | 4e-39                   |
| mRNA         | lapatinib  | CCLE      | AAC    | 0.57                       | 3e-33                   |
| mRNA         | neratinib  | CTRPv2    | AAC    | 0.38                       | 2e-26                   |
| mRNA         | lapatinib  | gCSI      | AAC    | 0.51                       | 1e-17                   |
| mRNA         | lapatinib  | CTRPv2    | AAC    | 0.31                       | 1e-17                   |
| mRNA         | BIBW2992   | CTRPv2    | AAC    | 0.29                       | 5e-15                   |
| mRNA         | canertinib | CTRPv2    | AAC    | 0.26                       | 8e-12                   |
| mRNA         | ibrutinib  | CTRPv2    | AAC    | 0.29                       | 7e-11                   |
| mRNA         | lapatinib  | GDSC1000  | AAC    | 0.35                       | 8e-10                   |
| mRNA         | EKB-569    | GDSC1000  | AAC    | 0.19                       | 1e-07                   |

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1

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...

85

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Next →



Univariate Analyses

Regression Models

Metadata

Search IDs

Help

CellMinerCDB enables exploration and analysis of cancer cell line pharmacogenomic data across different sources. If publishing results based on this site, please cite: Rajapakse.VN, Luna.A, Yamade.M et al. iScience, Cell Press. 2018 Dec 12.

Plot Data

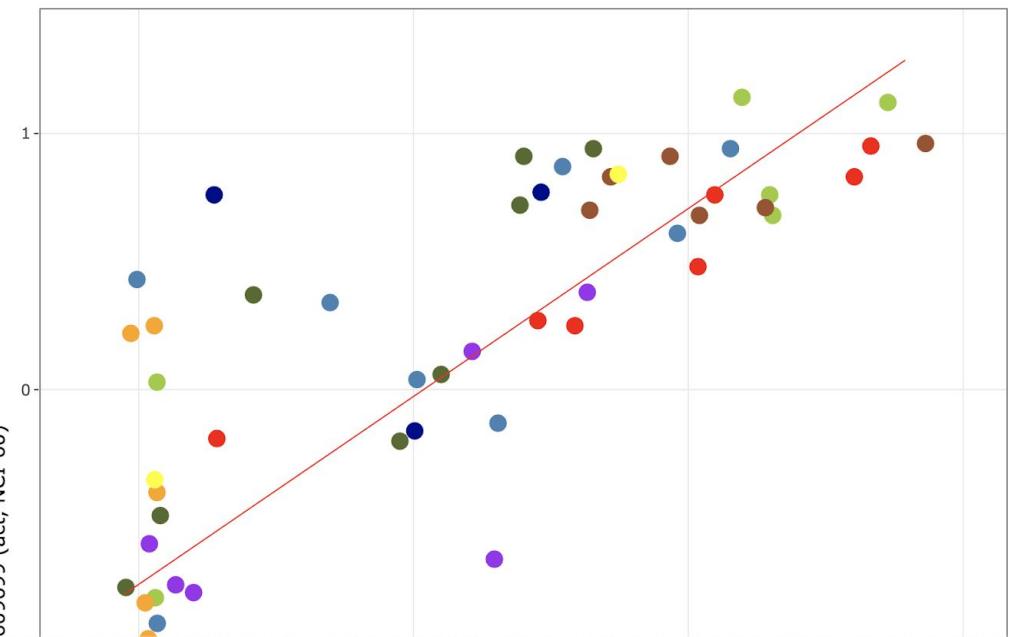
View Data

Compare Patterns

Tissue Correlation



609699 (act, NCI-60) vs. SLFN11 (exp, NCI-60)  
Pearson correlation ( $r$ )=0.78, p-value=3.3e-13



- Blood
- Bowel
- Brain\_CNS
- Breast
- Kidney
- Lung
- Ovary
- Prostate
- Skin

## x-Axis Cell Line Set

NCI-60

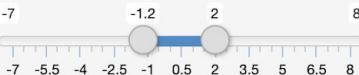
## x-Axis Data Type

exp: mRNA Expression (Z-Score)

Identifier: (e.g. topotecan or  
SLFN11)

SLFN11

## x-Axis Range



## y-Axis Cell Line Set

NCI-60

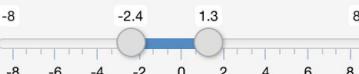
## y-Axis Data Type

act: Drug Activity

Identifier: (e.g. topotecan or  
SLFN11)

topotecan

## y-Axis Range



### x-Axis Cell Line Set

GDSC-MGH-Sanger

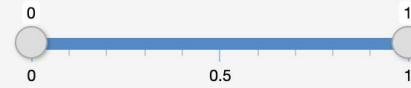
### x-Axis Data Type

met: DNA Methylation

Identifier: (e.g. topotecan or  
SLFN11)

MGMT

### x-Axis Range



### y-Axis Cell Line Set

GDSC-MGH-Sanger

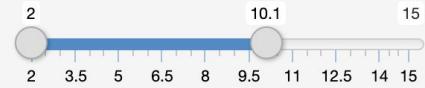
### y-Axis Data Type

exp: mRNA Expression (log2)

Identifier: (e.g. topotecan or  
SLFN11)

MGMT

### y-Axis Range



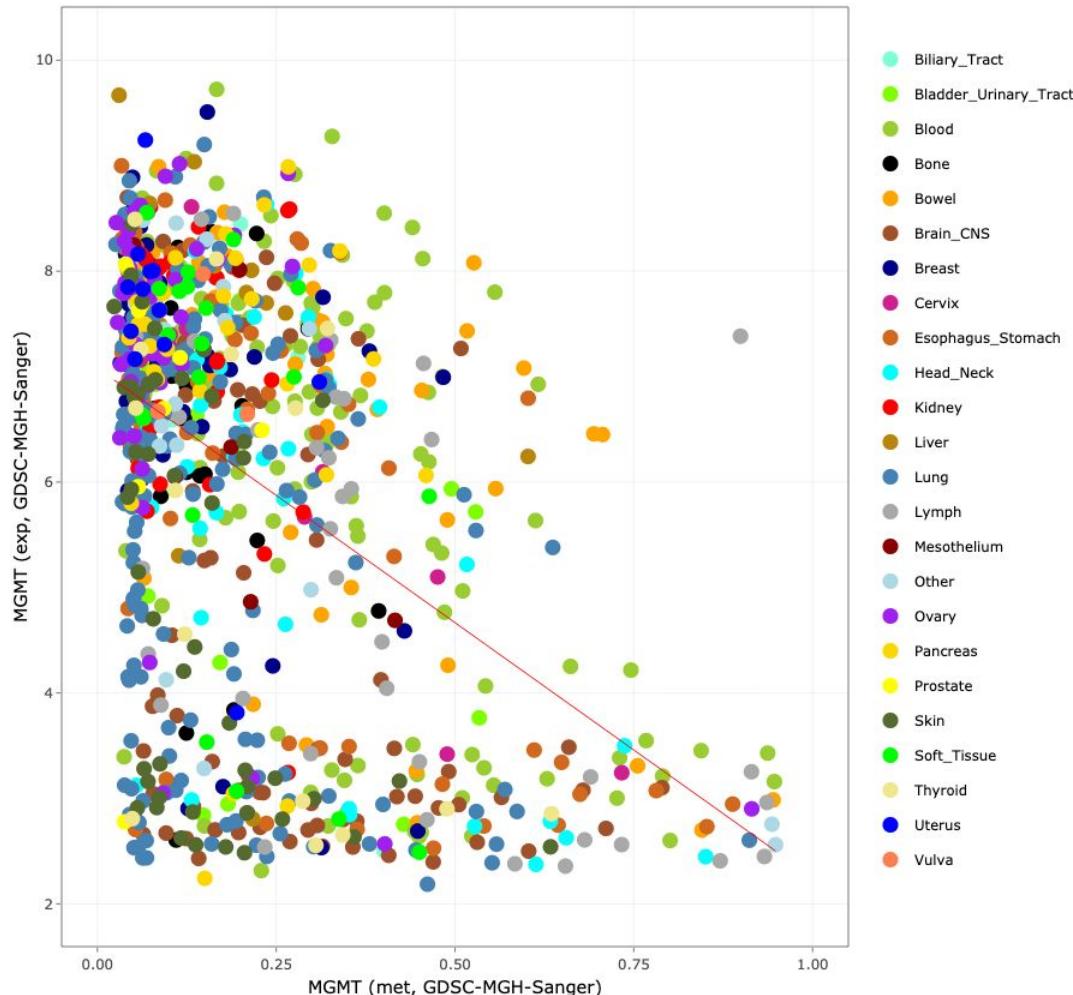
### Select Tissues

To include

To exclude

MGMT (exp, GDSC-MGH-Sanger) vs. MGMT (met, GDSC-MGH-Sanger)

Pearson correlation ( $r$ )=-0.46, p-value=2e-52



**Cell Line Set**

GDSC-MGH-Sanger ▾

**Response Data Type**

act: Drug Activity (-log10[IC50M]) ▾

**Response Identifier:**

plx4720

**Predictor Data Type/s**

exp: mRNA Expression (log2)  
 met: DNA Methylation  
 mut: DNA Mutation  
 mda: Miscellaneous phenotypic data

**Minimum Predictor Range (for first listed data type):**

0 5

**Predictor Identifiers: (Case-Sensitive, e.g. SLFN11 BPTF)**

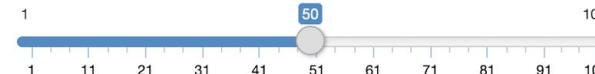
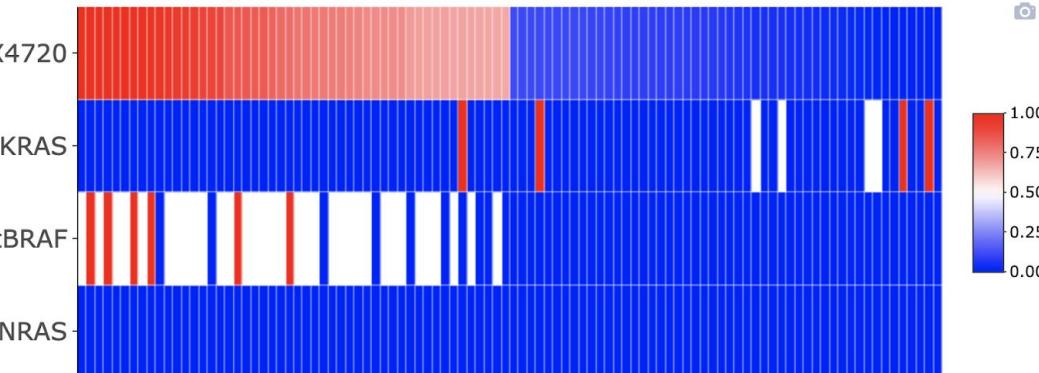
KRAS BRAF NRAS

**Select Tissues**

- To include  
 To exclude

**Select Tissue/s of Origin**

Heatmap Data Plot Cross-Validation Technical Details Partial Correlation

**Number of High/Low Response Lines to Display:** Use Row Color Scale

Select cell line or feature name to highlight heatmap columns or rows, respectively.

Download Heatmap Data

**Cell Line Set**

GDSC-MGH-Sanger ▾

**Response Data Type**

act: Drug Activity (-log10[IC50M]) ▾

**Response Identifier:**

plx4720

**Predictor Data Type/s**

exp: mRNA Expression (log2)  
 met: DNA Methylation  
 mut: DNA Mutation  
 mda: Miscellaneous phenotypic data

**Minimum Predictor Range (for first listed data type):**

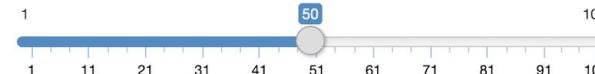
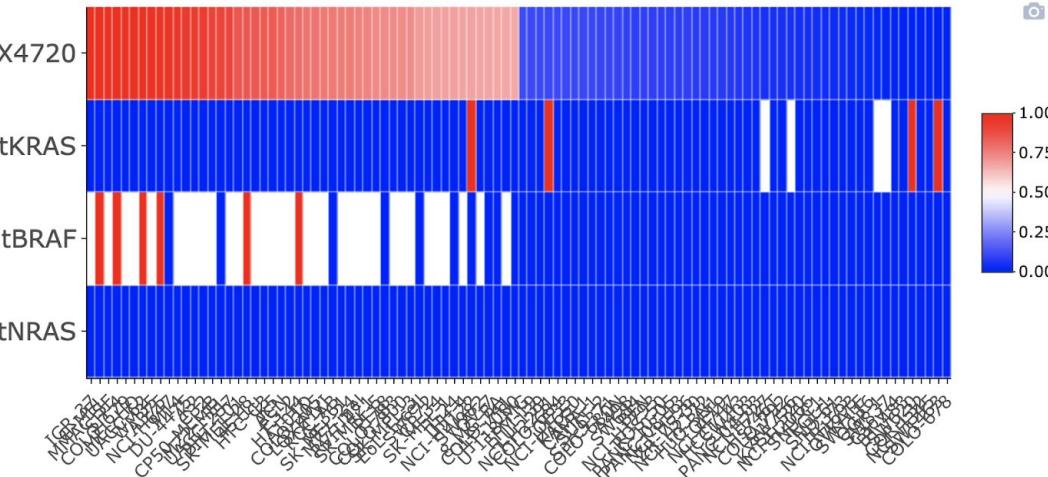
0 5  
 0.5 1 1.5 2 2.5 3 3.5 4 4.5 5

**Predictor Identifiers: (Case-Sensitive, e.g. SLFN11 BPTF)**

KRAS BRAF NRAS

**Select Tissues**

- To include
- To exclude

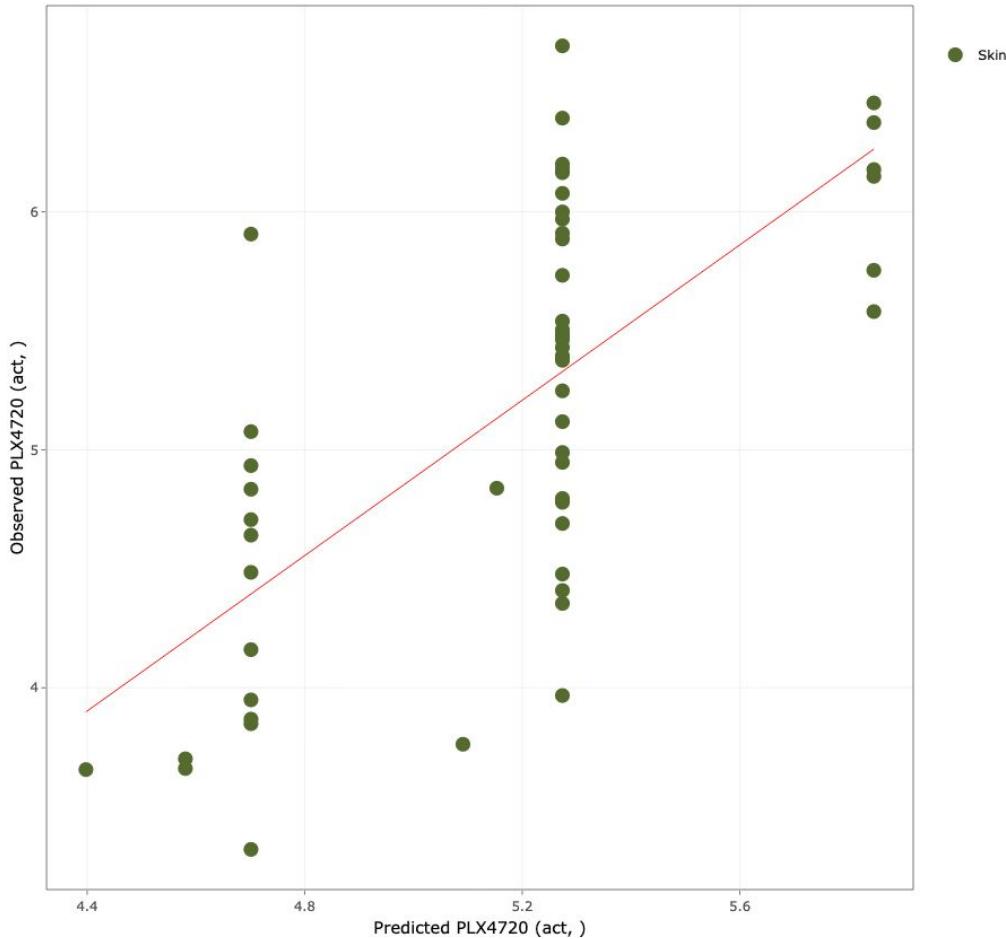
**Select Tissue/s of Origin**
[Heatmap](#)   [Data](#)   [Plot](#)   [Cross-Validation](#)   [Technical Details](#)   [Partial Correlation](#)
**Number of High/Low Response Lines to Display:** Use Row Color Scale

Select cell line or feature name to highlight heatmap columns or rows, respectively.

Download Heatmap Data



Observed PLX4720 (act, ) vs. Predicted PLX4720 (act, )  
Pearson correlation ( $r$ )=0.68, p-value=1.1e-08





# ConnectivityMap

Unravel biology with the world's largest perturbation-driven gene expression dataset.



> TYPE COMPOUND, GENE, MoA, OR PERTURBAGEN CLASS TO SEE OVERVIEW  
> TYPE A SLASH CHARACTER "/" TO SEE LIST OF COMMANDS

DATA VERSION: 1.1.1.2 / SOFTWARE VERSION: 1.1.1.42

## USING CONNECTIVITY MAP TO IDENTIFY ENVIRONMENTAL CARCINOGENS

Most chemicals in commerce have not been evaluated for their carcinogenic potential. The de facto gold-standard approach to carcinogen testing adopts the 2-y rodent bioassay, a time-consuming and costly procedure. High-throughput *in vitro* assays are a promising alternative for addressing the limitations in carcinogen screening.

Amy Li et al. developed a screening process for predicting chemical carcinogenicity and genotoxicity, as well as characterizing modes of actions, using *in vitro* gene expression profiles from the L1000 platform. Computational classifiers achieved 72.2% Area Under the ROC Curve (AUC) for predicting carcinogenicity and 82.3% AUC for predicting genotoxicity, suggesting that such methods could provide a scalable approach to characterizing potential hazards of commonly used chemicals.

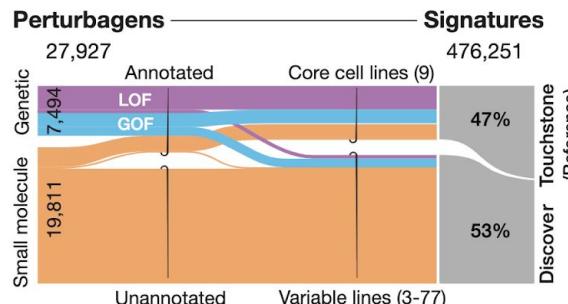
This publication is available via open access:

A. Li et al. (2019). The Carcinogenome Project: *In Vitro* Gene Expression Profiling of Chemical Perturbations to Predict Long-Term Carcinogenicity. *Environmental Health Perspectives*, 127(4).

## Data and Tools

The CMap dataset of cellular signatures catalogs transcriptional responses of human cells to chemical and genetic perturbation. Here you can find the 1.3M L1000 profiles and the tools for their analysis.

A total of 27,927 perturbagens have been profiled to produce 476,251 expression signatures. About half of those signatures make up the Touchstone (reference) dataset generated from testing well-annotated genetic and small-molecular perturbagens in a core panel of cell lines. The remainder make up the Discover dataset, generated from profiling uncharacterized small molecules in a variable number of cell lines.



Start exploring the data by using the text-box on this page to look up perturbagens of interest in Touchstone. To see the suite of tools, including apps to query your gene expression signatures and analyze resulting connections, click on Tools in the menu bar.



PLX-4720

/home

PLX-4720

x

v

## PLX-4720

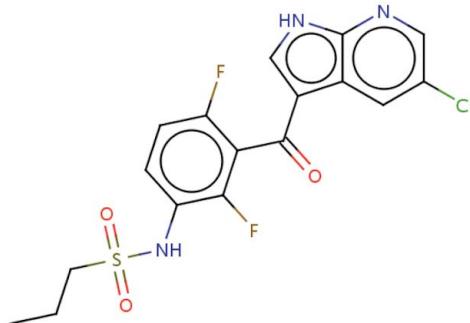
## CP PLX-4720

Synonym: S1152

RAF inhibitor, BRAF|KDR

ID: Broad | PubChem | ChEMBL | InChIKey | SMILES

BRD-K16478699



## Biological function

MOA: RAF inhibitor

CMap class: RAF inhibitor

Protein target: BRAF, KDR

## Profile status

View top  
connections/internal  
connectivities

/CONN

COMMAND [clue.io]

View/download signatures

/SIG

```
/conn "PLX-4720"
```

[/home](#) / PLX-4720 [/conn "PLX-4720"...](#)

## /conn "PLX-4720"

Top Connections (L1000)

Cell lines [Summary](#)

See all connections:



Export as...

The "score" column is the median connectivity score across the **selected perturbagens and cell lines**.

The top and bottom scores are shown separately for perturbagen classes, compounds, genetic perturbations (overexpressions and knockdowns).



cell\_id  
name  
type

### Perturbagen class

| score ▾ | type | name                                       | description |
|---------|------|--|-------------|
| 99.56   |      | Glycogen synthase kinase inhibitor         |             |
| 98.82   |      | VEGFR inhibitor                            |             |
| 98.11   |      | EGFR inhibitor                             |             |
| 97.54   |      | PKC inhibitor                              |             |
| 97.54   |      | Aminoacyl tRNA synthetases class II LOF    |             |
| 5.06    |      | BMP Signaling LOF                          |             |
| 4.69    |      | Nucleoside reverse transcriptase inhibitor |             |
| -1.29   |      | MDM inhibitor                              |             |
| -2.71   |      | Rho GTPase activating proteins LOF         |             |
| -5.23   |      | Integrin subunits beta LOF                 |             |

### Compound

| score ▾ | type   | name              | description  |
|---------|--------|-------------------|--|
| 99.97   | orange | PLX-4720          | RAF inhibitor  |
| 99.89   |        | sorafenib         | RAF inhibitor, FLT3 inhibitor, KIT inhibitor, PDGFR tyrosine kinase receptor |
| 99.86   |        | oligomycin-a      | ATP synthase inhibitor, ATPase inhibitor                                     |
| 99.82   |        | vermurafenib      | RAF inhibitor, protein kinase inhibitor                                      |
| 99.82   |        | tumatinib AG-1470 | EGFR inhibitor   |



## Compound

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|--------|------|--------------------|--|
| 99.97  |      | PLX-4720           | RAF inhibitor  |
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| 99.86  |      | oligomycin-a       | ATP synthase inhibitor, ATPase inhibitor   |
| 99.82  |      | vemurafenib        | RAF inhibitor, protein kinase inhibitor  |
| 99.82  |      | tyrphostin-AG-1478 | EGFR inhibitor   |
| 99.75  |      | CP466722           | ATM kinase inhibitor   |
| 99.75  |      | CGP-57380          | MAP kinase inhibitor, MAPK-interacting kinase inhibitor  |
| 99.75  |      | dasatinib          | KIT inhibitor, src inhibitor, Bcr-Abl kinase inhibitor, ephrin receptor inhibitor, PKC inhibitor   |
| 99.75  |      | SA-792987          | EGFR inhibitor, epidermal growth factor receptor (EGFR) inhibitor, tyrosine angiogenesis inhibitor, cereblon inhibitor, tumor apoptosis inducer, tumor n |
| 99.72  |      | erlotinib          | monoamine oxidase inhibitor  |
| -39.47 |      | lenalidomide       | tubulin inhibitor, dihydropteroate synthase inhibitor, microtubule inhibitor, P  |
| -44.64 |      | tetrindole         | opioid receptor agonist  |
| -45.73 |      | ABT-751            | acetylcholine release enhancer, dopamine release enhancer, GABA recept   |
| -52.36 |      | leu-enkephalin     | tubulin inhibitor, acetylcholinesterase inhibitor, microtubule inhibitor   |
| -59.16 |      | pregnenolone       | Phosphatidylinositol 3-kinase (PI3K) inhibitor, PI3K inhibitor   |
| -67.06 |      | albendazole        | GABA aminotransferase activator  |
| -72.82 |      | AS-605240          | MEK inhibitor, MAP kinase inhibitor, protein kinase inhibitor  |
| -90.67 |      | 3-methyl-GABA      | src inhibitor, Abl kinase inhibitor, Bcr-Abl kinase inhibitor, apoptosis stimula   |
| -96.31 |      | PD-0325901         |  |
| -98.80 |      | bosutinib          |  |

## Genetic

| score▼ | type | name     | description  |
|--------|------|----------|--|
| 99.75  |      | RAF1     | RAF family, v-raf-1 murine leukemia viral oncogene homolog 1                   |
| 99.72  |      | GNB1L    | WD repeat domain containing, guanine nucleotide binding protein (G prote       |
| 99.61  |      | CDC123   | cell division cycle 123 homolog (S. cerevisiae)                                |
| 99.47  |      | PHB2     | prohibitin 2   |
| 99.41  |      | KARS     | Aminoacyl tRNA synthetases / Class II, lysyl-tRNA synthetase                   |
| 99.37  |      | SERPINA6 | Serine (or cysteine) peptidase inhibitors, serpin peptidase inhibitor, clade A |
| 99.37  |      | FTSJ1    | FtsJ homolog 1 (E. coli)   |
| 99.33  |      | TMEM11   | transmembrane protein 11   |
| 99.30  |      | SGK3     | SGK family, serum/glucocorticoid regulated kinase family, member 3             |
| 99.30  |      | GLI1     | Zinc fingers, C2H2-type, GLI family zinc finger 1                              |
| -64.99 |      | MIF      | macrophage migration inhibitory factor (glycosylation-inhibiting factor)       |
| -67.77 |      | MMP1     | Matrix metallopeptidase, matrix metallopeptidase 1 (interstitial collagenase   |
| -68.44 |      | SHC4     | SH2 domain containing, SHC (Src homology 2 domain containing) family, r        |
| -73.30 |      | SC5D     | sterol-C5-desaturase (ERG3 delta-5-desaturase homolog, S. cerevisiae)-lik      |
| -74.81 |      | KLF5     | Kruppel-like transcription factors, Kruppel-like factor 5 (intestinal)         |
| -77.15 |      | CCND2    | cyclin D2  |
| -77.85 |      | MEST     | mesoderm specific transcript homolog (mouse)                                   |
| -79.10 |      | PSMD8    | Proteasome (prosome, macropain) subunits, proteasome (prosome, macro           |
| -79.42 |      | EIF1B    | eukaryotic translation initiation factor 1B                                    |
| -90.70 |      | CD14     | CD molecules, CD14 molecule  |