

Medical and genomic tools and databases

Precision Oncology Course





Gene & Protein DBs

Functional Enrichment

Cancer Collections & Browsers

Therapy response

Cancer dependencies

Survival, Clinical & other useful info

Gene & Protein DBs

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Genes

NCBI Gene

http://www.ncbi.nlm.nih.gov/gene/

Ensembl

http://www.ensembl.org/

GeneCards

http://www.genecards.org/

Expression Atlas

https://www.ebi.ac.uk/gxa/home

Network of Cancer Genes

http://ncg.kcl.ac.uk/index.php

GTEx

http://www.gtexportal.org/

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Protein

Tumor Protein Atlas https://www.proteinatlas.org/

The Human Protein Atlas https://www.proteinatlas.org/

Gene & Protein DBs

Exercise 1: Using NCBI gene.

- Go to NCBI's Gene database
- Do an Advanced search for
 - Organism: homo sapiens
 - Gene/Protein Name: EGFR



On which chromosome is the gene located?

http://www.ncbi.nlm.nih.gov/gene/

Gene & Protein DBs

Exercise 1: Using NCBI gene.

Look at the **GeneRIFs** of this gene. GeneRIFs are short sentences that describe the function of a gene product that are extracted from scientific publications. NCBI encourages scientists to submit these GeneRIFs together with the Pubmed ID of the publication to the Gene database and curates the submissions. In this way you don't have to go through the scientific literature yourself to get idea about the function of a gene product.

What is the function of the protein encoded by this gene?

Check out al other info that you find here for EGFR and try to do a search on your favourite gene to see if you can find any new info on it.

Gene & Protein DBs

Exercise 2: Using Ensembl

Search the human EGFR gene.

- Select the Human genome to search in
- Search for EGFR
- Click Go
- Click the EGFR (Human gene) link to go to the gene page of EGFR.



Ensembl

http://www.ensembl.org/

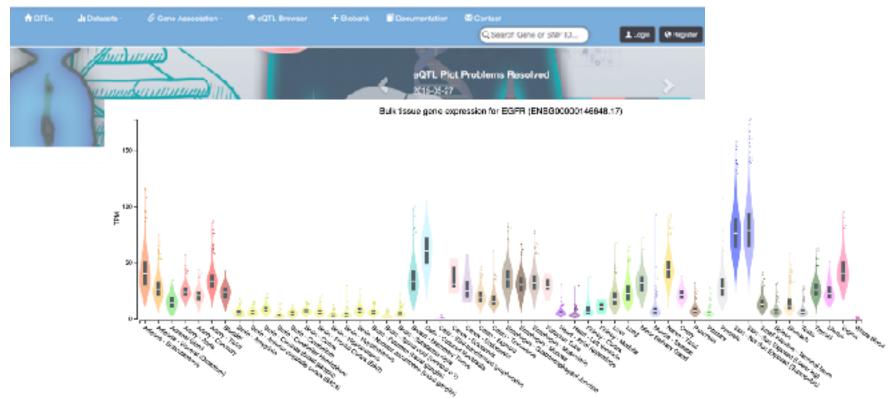
Gene & Protein DBs

Exercise 2: Using Ensembl

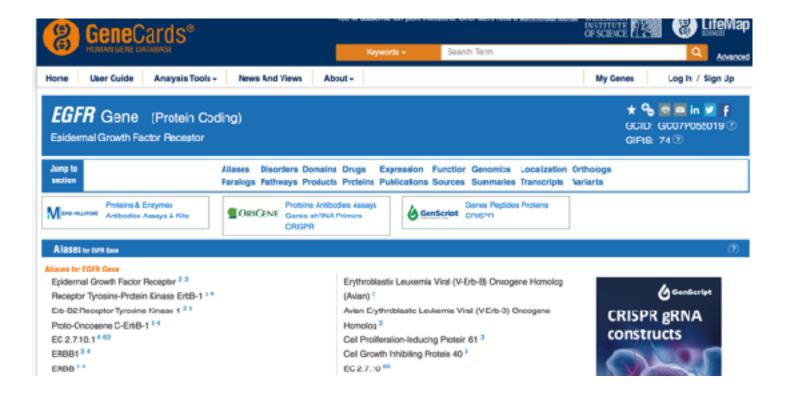
- On which chromosome and which strand of the genome is this gene located?
- How many transcripts (splice variants) does this gene have?
- How many CCDS are annotated for this gene?
- What's the name of the longest transcript?
- How long is the protein it encodes?
- Compare the sequence of the two longest protein-coding transcripts.

GTEx http://www.gtexportal.org/





GeneCards http://www.genecards.org/



Tumor protein atlas http://www.proteinatlas.org/

EGFR







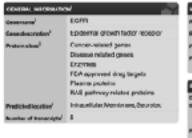










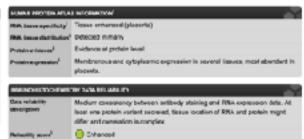


TRADES ATLAS.

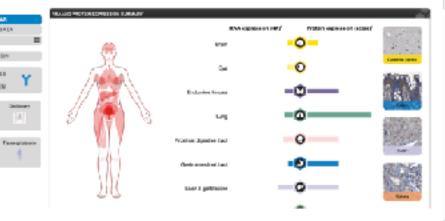
TIGELES

ANTIBODIES AND VALIDATION

PRIMARY DATA



BRADITZOC _HMAD19530 . GABODDOSS _CASREE185 _CABDITISS4



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Gene Expression Signatures

MSigDB

http://software.broadinstitute.org/gsea/msigdb/annotate.jsp

Enrichr

http://amp.pharm.mssm.edu/Enrichr/

Harmonizome

http://amp.pharm.mssm.edu/Harmonizome//

GeneMania

http://genemania.org/

Functional Enrichment

Exercise: Using EnrichR

- Go to https://maayanlab.cloud/Enrichr/
- Expand into a gene set the term:
 triple negative breast cancer
- Submit the query
- Go to the Diseases/Drugs section
- Check the COVID-19 related gene sets 2021 collection

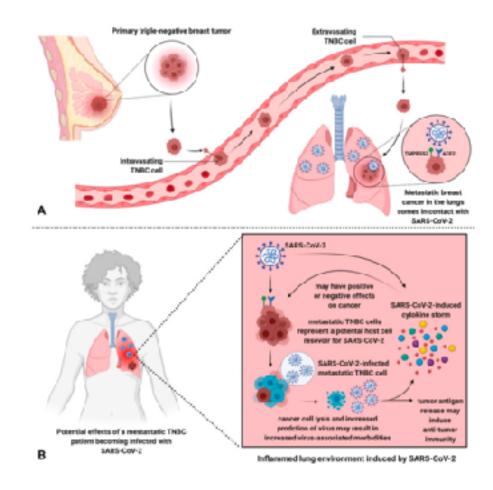


Functional Enrichment

Metastatic breast cancer cells may represent an additional host cell SARS-CoV-2 reservoir, leading to increased viral load and virusassociated morbidities, and unknown consequences on the progression of the cancer.

Source:

Brown JM, Wasson MD, Marcato P. Triple-Negative Breast Cancer and the COVID-19 Pandemic: Clinical Management Perspectives and Potential Consequences of Infection. Cancers. 2021 Jan;13(2). DOI: 10.3390/cancers13020296. PMID: 33467411; PMCID: PMC7830590.



MSigDB http://www.software.broadinstitute.org/gsea/msigdb



MSigDB Home

- About Collections
- Browse Gene Sets.
- Search Gene Sets
- Investigate Gene Sets
- View Gene Families
- Help.



Molecular Signatures Database v6.2

Overview

The Molecular Signatures Database (MSigDB) is a collection of annotated gene sets for use with GSEA software. From this web site, you can

- Search for gene sets by keyword.
- Browse gene sets by name or collection.

Collections

The MSigDB gene sets are divided into 8 major collections:



hallmark gene sets are coherently expressed signatures derived by aggregating many MSigDB gene sets to represent well-defined biological states or processes.

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Pathways and Networks

Networks: STRING http://string-db.org

PATHIVAR

http://pathivar.babelomics.org

WikiPathways

https://www.wikipathways.org/index.php/WikiPathways

KEGG

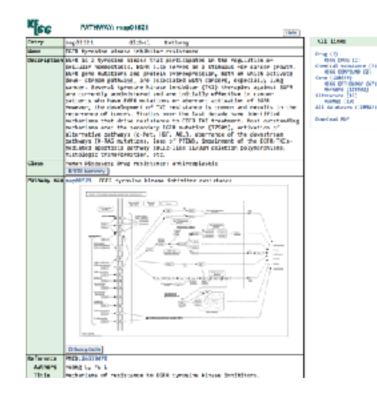
https://www.genome.jp/kegg/

Functional Enrichment

Exercise: Using KEGG

- Go to https://www.genome.jp/kegg/
- Load a map of the EGFR tyrosine kinase inhibitor resistance pathwaypathway

What are the names of the chemical compounds that are related to the EGFR pathway according to KEGG?



Functional Enrichment

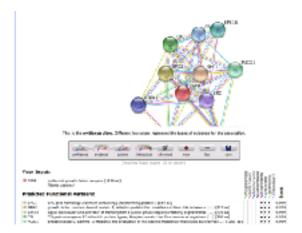
Exercise: Using STRING

Go to the STRING <u>website</u> http://string-db.org

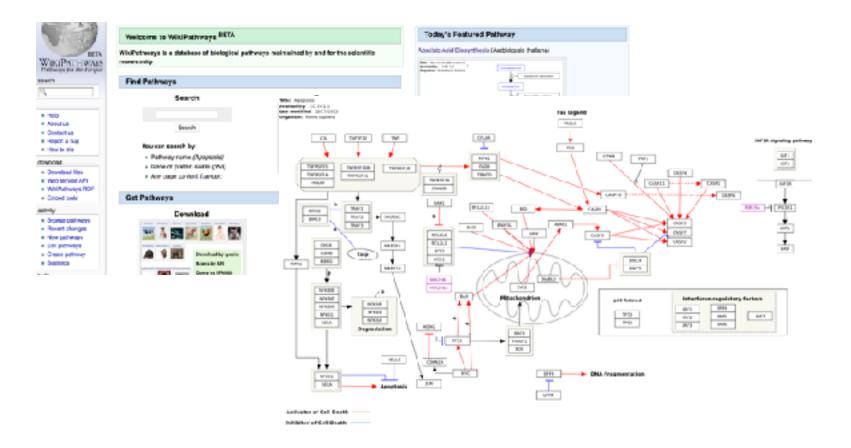
How to find the interaction network of a protein?

On the top of the results page, the interaction network is visualized.

- The network nodes are proteins.
- The edges represent the predicted functional associations.
- The color of the edges reflects the evidence:
 - Red line indicates the presence of fusion evidence
 - Green line neighborhood evidence
 - Blue line cooccurrence evidence
 - Purple line experimental evidence
 - Yellow line textmining evidence
 - Light blue line database evidence
 - Black line coexpression evidence.



Wikipathways https://www.wikipathways.org/index.php/WikiPathways



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Collections

NCI60

https://discover.nci.nih.gov/cellminer/

Cancer Cell Line Encyclopedia https://portals.broadinstitute.org/ccle

International Cancer Genome Consortium http://dcc.icgc.org/

The Cancer Genome Atlas https://cancergenome.nih.gov/

COSMIC

http://cancer.sanger.ac.uk/cosmic/

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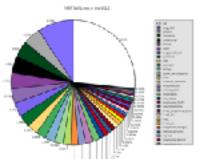
Cell lines

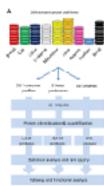
NCI60

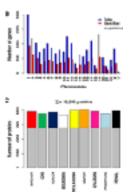
https://discover.nci.nih.gov/cellminer/

Cancer Cell Line Encyclopedia https://portals.broadinstitute.org/ccle









Amin Moghaddas Gholami, Hannes Hahne, Zhixiang Wu, Florian Johann Auer, Chen Meng, Mathias Wilhelm, Bernhard Kuster, Global Proteome Analysis of the NCI-60 Cell Line Panel, Cell Reports, Volume 4, Issue 3, 2013, Pages 609-620, ISSN 2211-1247 https://doi.org/10.1016/i.celrep.2013.07.018.

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https://discover.nci.nih.gov/cellminer/

Cancer Cell Line Encyclopedia https://portals.broadinstitute.org/ccle

samples

Tumor

The Cancer Genome Atlas https://cancergenome.nih.gov/

International Cancer Genome Consortium http://dcc.icgc.org/

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Collections

NCI60

samples

Tumor

https://discover.nci.nih.gov/celli

Cancer Cell Line Encycloped https://portals.broadinstitute.org

The Cancer Genome Atlas https://cancergenome.nih.gov/





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https://discover.nci.nih.gov/cellminer/

Cancer Cell Line Encyclopedia
https://portals.broadinstitute.org/ccle



@ ICGC Data Portal

International Cancer Genome Consortium http://dcc.icgc.org/



Cancerprojects	55
Cancer primary sites	21
Donors	12,979
Simple comade mutations	16,159,160
Mutated genes	57,523

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https://discover.nci.nih.gov/cellminer/

Cancer Cell Line Encyclopedia https://portals.broadinstitute.org/ccle





International Cancer Genome Consortium

http://dcc.icgc.org/



Service or

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NCI60

https://discover.nci.nih.gov/cellminer/

Cancer Cell Line Encyclopedia https://portals.broadinstitute.org/ccle

International Cancer Genome Consortium http://dcc.icgc.org/

The Cancer Genome Atlas https://cancergenome.nih.gov/

Both

COSMIC

http://cancer.sanger.ac.uk/cosmic/

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Browsers

cBio Portal for Cancer genomics

http://www.cbioportal.org/

Integrative Onco Genomics

https://www.intogen.org/

Oncomine

https://www.oncomine.org/resource/login.html

TumorPortal

http://www.tumorportal.org/

XenaBrowser

https://xena.ucsc.edu/

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GDSC

http://www.cancerrxgene.org

Cancer Cell Line Encyclopedia http://www.broadinstitute.org/ccle/

Cancer Therapeutics Response Portal http://www.broadinstitute.org/ctrp/

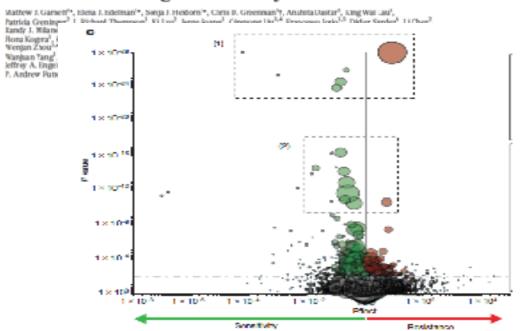
Open Targets
https://www.opentargets.org/

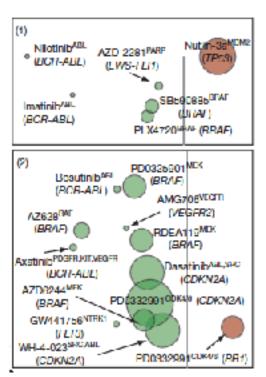
Connectivity Map https://clue.io/

PanDrugs
http://pandrugs.bioinfo.cnio.es/

Genomics of drug sensitivity in cancer https://www.cancerrxgene.org/

Systematic identification of genomic markers of drug sensitivity in cancer cells





Garnett et al. Nature 2012

Therapy response

Exercise: Using GDSC

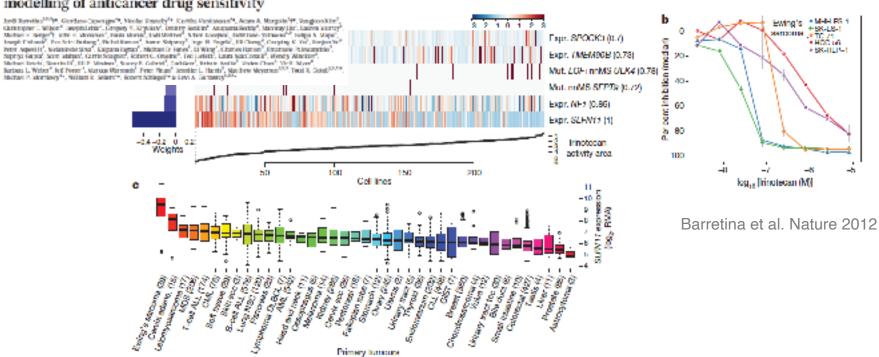
- Go to the GDSC website
- Look for the EGFR gene

To which drugs are sensitive the EGFR mutated cell lines?

- Choose a compound of interest
- Look for other sensitivity/resistance associations related to that same compound

Cancer cell line encyclopedia https://www.broadinstitute.org/ccle

The Cancer Cell Line Encyclopedia enables predictive modelling of anticancer drug sensitivity



PanDrugs https://pandrugs.bioinfo.cnio.es

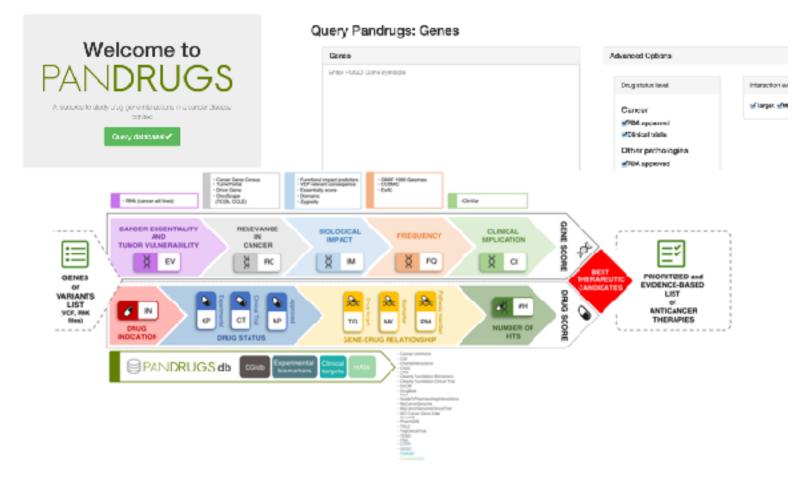
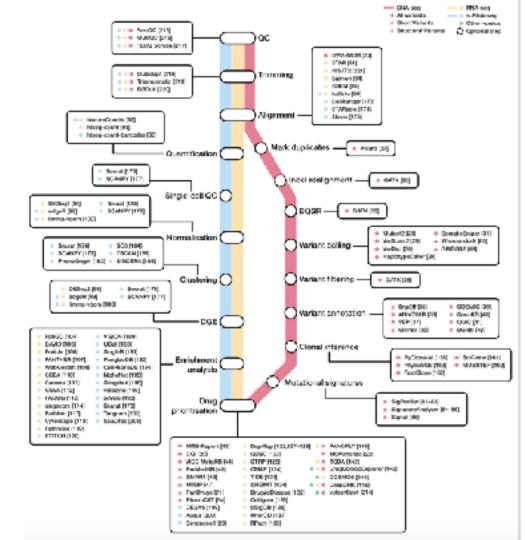


Table 1: Bioinformatics tools for genomics-based drug prioritisation.

	-			
Name	Description	Input	Output	URL
MTB-Report [43]	R script that filters and classifies cancer variants into levels of evidence using gene-drug databases.	Tables with SNVs, CNVs and gene fusions (somatic).	Molecular Tumour Board (MTB) report with actionable variants in PDF.	https://github.com/jperera- bel/MTB-Report
Cancer Genome Interpreter (CGI) [20]	Web tool that annotates cancer variants and identifies potential oncogenic alterations and genomic biomarkers of drug response.	List of SNVs, indels, CNVs and/or gene fusions (somatic).	Downloadable tables of a) Annotated variants, including information about the oncogenicity and biological consequence, and b) drug- variant associations with evidence level and response prediction.	https:// www.cancergenomeinterpret er.org/home
VICC MetaKB [44]	Web tool for cancer variant interpretation that harmonises 6 different variant annotation knowledgebases with information about variant, gene, disease and drug associations and their corresponding evidence levels.	List of variants (somatic), including gene fusions, genes, diseases and/or drugs.	Interactive report with variant- gene-disease-drug associations, each one with its evidence label and supporting links.	https:// search.cancervariants.org/#*
PreMedKB [45]	Web tool for integrating information on diseases, genes, variants, drugs, and the relationships between any two or more of these four components.	List of short variants (somatic), genes, drugs and/or diseases.	Interactive semantic network displaying components as nodes and their relationships as edges. Results can be downloaded in either JSON or PNG format.	http://www.fudan-pgx.org/ premedkb/index.html#/home
SMART Cancer Navigator [46]	Web application for variant interpretation that associates the corresponding genes to diseases, known drugs and relevant clinical trials.	List of short variants (somatic and germline).	Interactive report with variant, gene, disease and drug information.	https://smart-cancer- navigator.github.io/home
PanDrugs [21]	Web tool to prioritise anticancer drug treatments according to individual genomics data. PanDrugs computes two scores, the Gene Score (GScore) and the Drug Score (OScore). The Score ranges from 0 to 1 and is estimated according to gene essentiality and tumoral vulnerability, gene relevance in cancer, the biological impact of mutations, the frequency of gene alterations and their clinical implications. The DScore ranges from -1 to 1, considers drug indication and status, gene-drug associations and number of hits and estimates resistance (negative values) or sensitivity (positive values).	VCF, a list or a ranking of genes or a drug query (somatic).	Report with a prioritised list of anticancer therapies. PanDrugs resolves the Best Therapeutic Candidates based on the accumulated and weighted scoring of the GScore and the DScore.	https://www.pandrugs.org/#9/
MTBP [47]	Web tool that annotates somatic and germline short variants (SNVs and indels) functionally and clinically, categorising the cancer biomarkers (diagnosis, prognosis and drug response) found in the tumour.	VCF or a list of short variants (somatic and germline).	HTML report with annotated variants, the evidence supporting the variants' functional classification and their associated actionability.	https://mtbp.org/
PharmCAT [54]	A tool for identifying germinal variants, inferring patient's haplotypes and diplotypes and suggesting treatments following the Clinical Pharmacogenetics Implementation Consortium (CPIC)	VCF (germline).	HTML/JSON report with drug suggestions based on germinal variants.	https://pharmcat.org/

The bioinformatics roadmap for therapy selection in cancer genomics

Jiménez-Santos et al. 2022 coming soon



Connectivity Map https://clue.io





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: 1.1.1.36

CONNECTIVITY MAP LAUNCHES THIRD CROWDSOURCED CONTEST

The Connectivity Map team at the Broad Institute is happy to announce its latest crowdsourced contest, launched in collaboration with the Laboratory for Innovation

challenge is focused on enhancing the CMap

1,000 in total prizes available. Register today

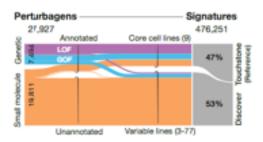
The aim is to generate perturbational profiles across multiple cell and perturbation types

- Small Molecules
 - 1300 FDA approved drugs
 - 5500 bioactive compounds
- Gene Knock-Outs and Over Expression

Data and Tools

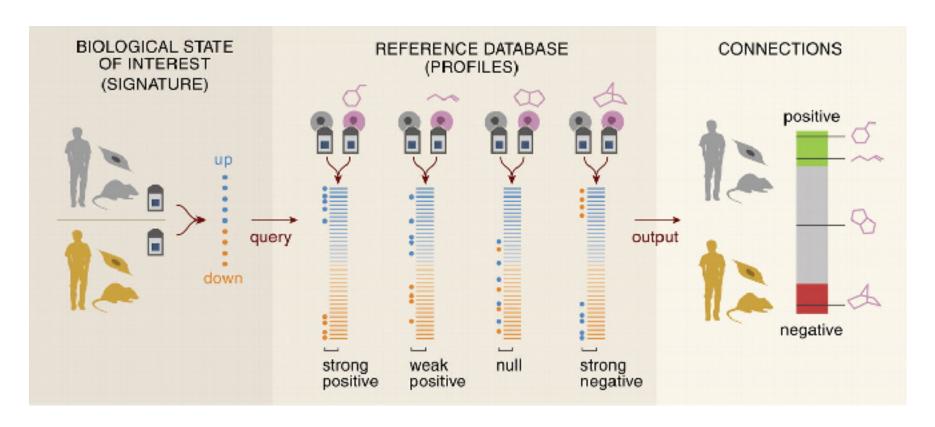
The CMap dataset of cellular signatures catalogs transcriptional responses of human cells to chemical and genetic perturbation. Here you can find the 1.3M L100) profiles and the tools for their analysis.

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.

Connectivity Map https://clue.io



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Cancer Dependencies

DepMap

https://depmap.org/portal/

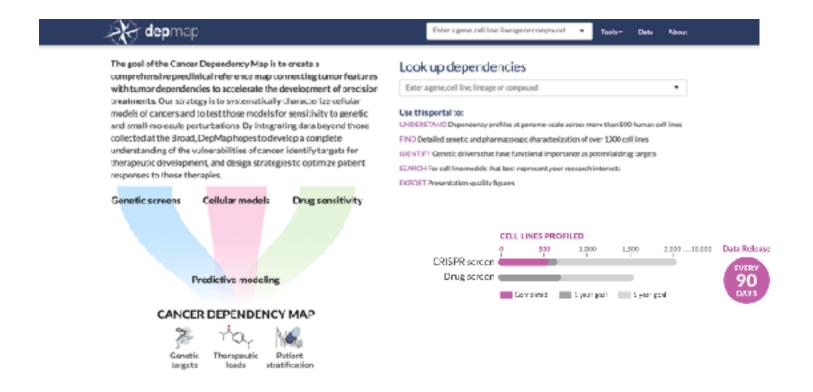
CancerGD

http://www.cancergd.org/

vulcanSpot

http://www.vulcanspot.org/

Cancer dependency map https://www.depmap.org/portal/



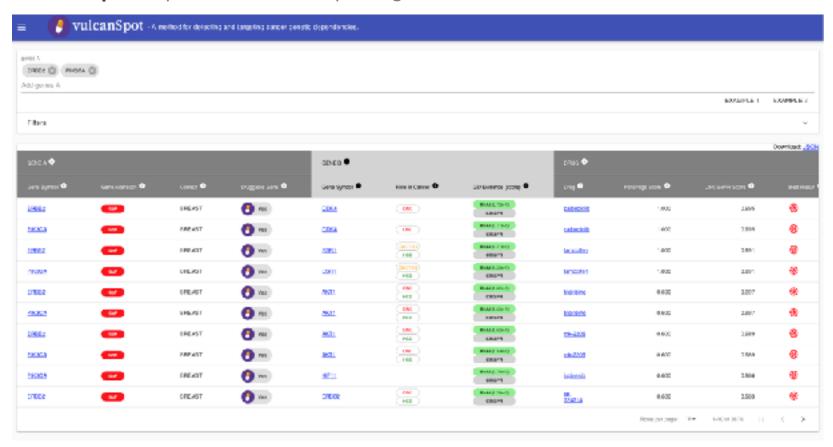
CancerGD https://www.cancergd.org

Search filter: Driver gener copes

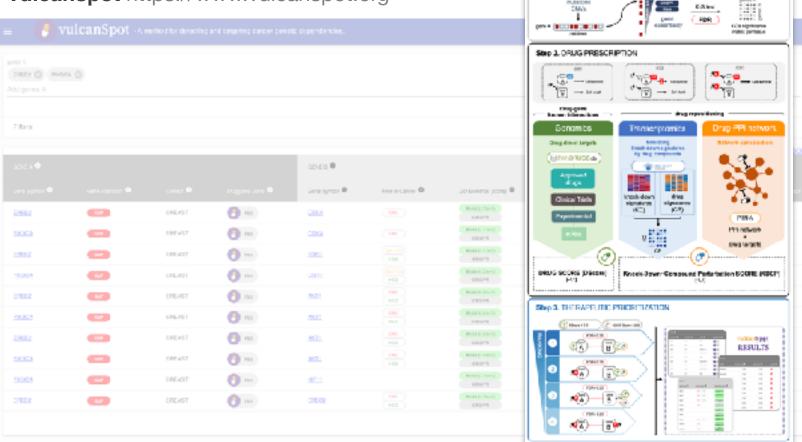
CancerGD: analysis of genetic dependencies in cancer

	General	Tillyan		9-				110000				oludy.			2031611		
Driver gene: ERBB2				Synonyms: HER-2 HER2 NEU CD340 NGL													
Gene	alteratio	n oo	nsidered	: An	nplification	s											
Gene Descripion: erb-b2 receptor tyrosine kinase 2																	
Extern	nal linka:	Gen	eCards I E	ntre	z i Ensembl	омито	ancerR	xGene I dBlot	Portal I	COSMICTO	anS/	R I UniProtKB I	GenomeRNA	l Ope	n Targets		
For dr	iver gen	e EF	BB2, a	otal	of 1990 d	ependen	icies v	ere found i	n tiss	ue type Pan	car	ncer in All stu	idies				
(Use so	rollbar at rig	ht of t	is table to s	orall c	lown, Click colu	ann header t	a sort by	that column. Clin	ok on the	e gene name in ti	he de	penancy column to	view the box-plot.	Entert	ext into the search box	at	
lop of oa	numn to ops	areary	THE THOSE I	s s ur s	i. In the Enect					5 ^r to liter results							
						Download	das CSV	file Down	leed as	Excellie	Strin	gdo Image St	ringdb interactiv	e fo	r 1990 rows (no	c 300)	
Depend	dency		P-value	٠	Effect ¢ size (%)	ΔScore	¢	Study	٠	Experiment	+	Multiple Hit ¢	String Interaction	•	Inhibitors		
Search	71									Type						¢	
			<0.05	•	>= 68.0	< 0.0			•	Туре	·			·		•	
MTOR		7	40.05 1 x 10 ⁻⁶	_	>= 68.0 92.5	< 0.0 -1.80		Cowley(2014	_	shfitNA	·	Yes	High	·	GDC-098/new)	_	
MTOR PSMC	ı							Cowley(2014 Marcotte(2012)		·				GDC-098)new] BORTEZO;new;		
	2		1 x 10 ⁻⁴		92.5	-1.80			2)	shfitNA	·			•			

vulcanspot https://www.vulcanspot.org



vulcanspot https://www.vulcanspot.org



Step 1. IDENTIFICATION OF GRNE DEPENDENCIES (GDv)

volenci@get

SUBSTITUTE OF

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VCF annotators

Variant Effect Predictor

http://www.ensembl.org/info/docs/tools/vep/index.html/

SnpEff

http://snpeff.sourceforge.net/

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Clinical Variants Annotators

ClinVAR

http://www.ncbi.nlm.nih.gov/clinvar/

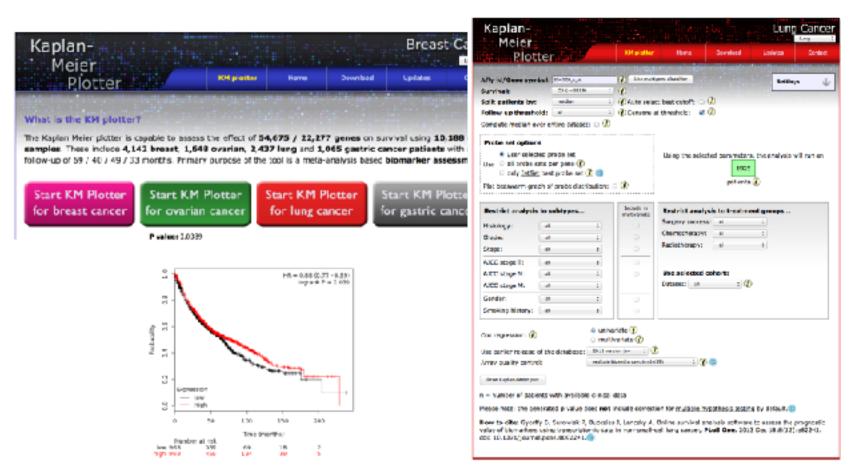
ExAC

http://exac.broadinstitute.org

gnomAD

http://gnomAD.broadinstitute.org

Survival Kaplan meier plotter http://kmplot.com/analysis/index.php



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Survival Analysis

https://www.tcga-survival.com/ Cell Reports 2022

https://bbisr.shinyapps.winship.emory.edu/ SurvivalGenie/

Survival: Kaplan Meier Plotter http://kmplot.com/analysis/index.php

Survival: Prognoscan

http://www.abren.net/PrognoScan

Other



April 2022 Update — Signal presents newly published single and double base substitution signature data derived from more than.

12,000 cancer samples recruited via the UK National Health Service. Click here to view all of the cancer signature data on Signal.

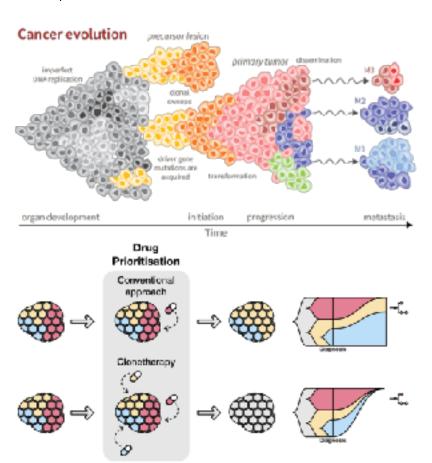
Discover Mutational Signatures Somatic mutations arise in the DNA of all the cells of the are the consequence of mutational processes that may b cellular activities, and are a key component in understant Different mutational processes generate observable path patterns are called mutational signatures.

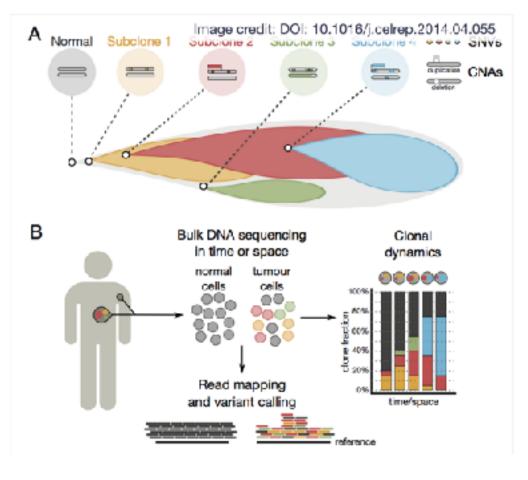




Tumour clonality

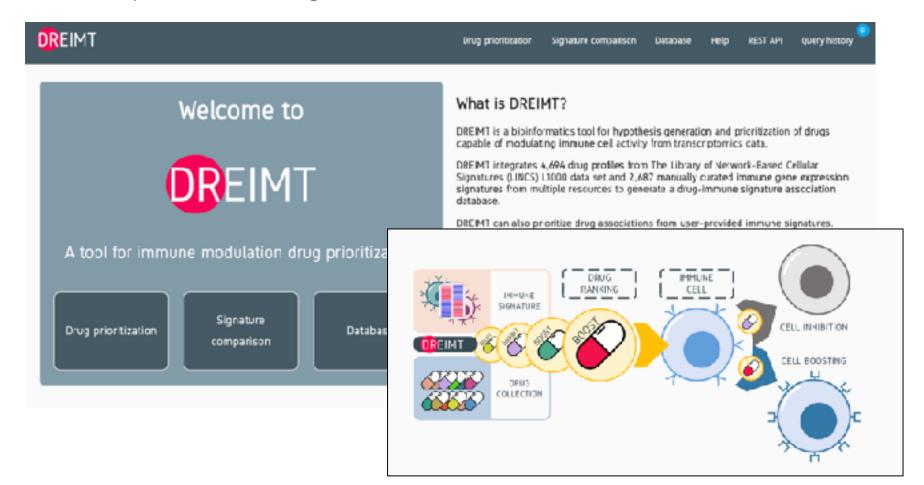
http://tracerx.co.uk/





PyClone2, FastClone, Subclone, etc

Dreimt https://www.dreimt.org/



Extra

Downloading the reference genome

- Gencode: https://www.gencodegenes.org/
- UCSC: https://hgdownload.soe.ucsc.edu/downloads.html

Downloading published experiments

- GEO: https://www.ncbi.nlm.nih.gov/geo/
- SRA: https://www.ncbi.nlm.nih.gov/sra
- Single Cell Portal: https://portals.broadinstitute.org/single_cell



