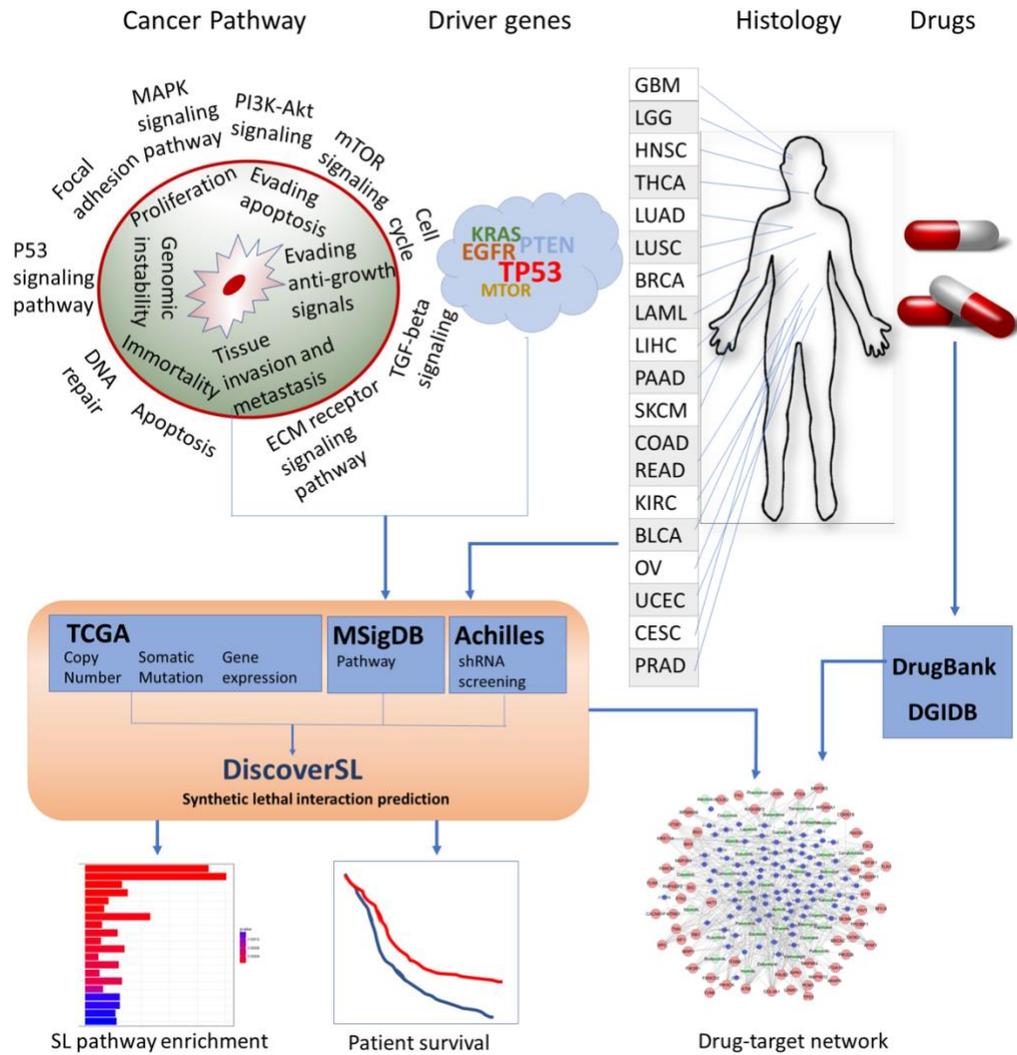


SL BioDiscovery Portal

The Synthetic Lethality BioDiscovery portal (SL-BioDP) is a comprehensive web tool for systematic exploration and functional analysis of cancer-specific synthetic lethal (SL) interactions of known [cancer susceptibility genes](#). It hosts SL interactions predicted using *DiscoverSL*: a machine-learning algorithm for multi-omic TCGA cancer data-driven synthetic lethal interactions. It provides extensive cross-references and user-friendly querying interfaces to support SL-related research. This web portal currently hosts SL interactions for 18 cancer types ([Portal Data Summary](#)).

Genes are included in the SL model if they are found to have protein-coding non-synonymous mutations in 5 or more unique TCGA samples.

Overview: Integration of data used in SL BioDiscovery Portal



A. Data Summary

B. Search Methods:

1. Search by Gene

2. Search by Cancer Type

3. Search by Drug

4. Investigate Inferred Drug Synergy

Data Summary

Differential gene expression was determined using TCGA RNAseqV2 Level 3 data. For each tumor type, tumor samples were compared to pooled normal samples.



Synthetic Lethality BioDiscovery Portal

The Synthetic Lethality BioDiscovery portal (SL-BioDP) is a comprehensive web tool for systematic exploration and functional analysis of cancer-specific synthetic lethal (SL) interactions of known cancer susceptibility genes. It hosts SL interactions predicted using **DiscoverSL**, a machine-learning algorithm for multi-omic TCGA cancer data-driven synthetic lethal interactions. It provides extensive cross-references and user friendly querying interfaces to support SL-related research. This web portal currently hosts SL interactions for 18 cancer types ([Portal Data Summary](#)).

*** We recommend using Chrome and Firefox. Some functionalities may not be well supported on Internet Explorer (IE).

GENE CANCER DRUG INFERRED DRUG SYNERGY DOCUMENTATION CONTACT US

Search by one or more HUGO gene symbols or Entrez ID

- For prediction of SL interactions, search is limited to the cancer survival **SL Primary Gene list**
- Results of SL predictions and drug interactions are presented by sequential selection of available options by the user
- Results are summarized into 3 main pages initiated by gene search:
 - Selection of Cancer types
 - Selection of SL pairs
 - Drug interaction

Gene Search:

Gene Symbol
 Entrez Gene ID

Enter gene list:
Type to start searching ...

OR Upload gene list from file:

Click [Portal Data Summary](#) for a summary of gene expression and mutation data.

Whole Genome dataset summary

Cancer code	Cancer name	Sample_Count	Total_Gene_Count	Gene_Count_U.P	Gene_Count_Down
BLCA	Blastic Unblastoid Carcinoma	408	21889	1676(9%)	491(4%)
BRCA	Breast invasive carcinoma	1100	21889	1666(7%)	774(4%)
CEC	Cervical squamous cell carcinoma and endocervical adenocarcinoma	306	21889	3519(16%)	1517(7%)
COADREAD	Colon and Rectum adenocarcinoma	382	21889	1434(7%)	1083(5%)
GBM	Glioblastoma multiforme	166	21889	2151(10%)	1446(9%)
HNSC	Head and Neck squamous cell carcinoma	522	21889	869(4%)	1202(5%)
KIRC	Kidney renal clear cell carcinoma	554	21889	1808(8%)	806(4%)
LAML	Acute Myeloid Leukemia	173	21889	2853(13%)	4882(22%)
LOG	Brain Lower Grade Glioma	530	21889	1903(9%)	3625(17%)
LIHC	Liver hepatocellular carcinoma	373	21889	1610(8%)	2261(10%)
LUAD	Lung adenocarcinoma	517	21889	2368(11%)	564(3%)
LUSC	Lung squamous cell carcinoma	501	21889	2448(11%)	1282(6%)
OV	Ovarian serous cystadenocarcinoma	307	21889	1737(8%)	3081(14%)
PAAD	Pancreatic adenocarcinoma	179	20423	1417(7%)	1338(7%)
PRAD	Prostate adenocarcinoma	498	21889	4022(18%)	418(2%)
SKCM	Skin Cutaneous Melanoma	472	21889	1019(5%)	3141(14%)
THCA	Thyroid carcinoma	509	21889	479(4%)	230(1%)
UCEC	Uterine Corpus Endometrial Carcinoma	177	21889	1851(9%)	1022(5%)

Cancer code	Cancer name	Total Number of All Mutations	Total Number of Non-synonymous Mutations	Average Non-synonymous Mutations per Sample	Number of Samples	Number of Genes	Top Mutated Genes (Ranked by Number of Samples affected)
BLCA	Blastic Unblastoid Carcinoma	39231	29469	236	1302	11362	TTN(9779)P53(84)MUC16(43)KMT2D(36)ARID1A(35)
BRCA	Breast invasive carcinoma	49158	35484	72	962	17281	PIK3CA(19)PTEN(16)TP53(15)SCN1B(13)GATA3(9)
CEC	Cervical squamous cell carcinoma and endocervical adenocarcinoma	45302	35883	185	194	15428	TTN(69)PIK3CA(5)MUC16(4)GATA3(3)MUC16(3)

For a table summarizing pathways, genes, and cancer types used in the model, select **SL Primary Gene List**.

Genes from 10 Pathways and Significant Driver Genes included in SL prediction model*

GENE_SET	HALLMARK	BLCA	BRCA	CEC	COADREAD	GBM	HNSC	KIRC	LAML	LOG	LIHC	LUAD	LUSC	OV	PAAD	PRAD	SKCM	THCA	UCEC	UNIQUE_TOTAL
DRIVER_GENE		17	18	13	10	11	21	6	7	14	16	14	7	4	8	6	14	3	24	87
KI67_APOPTOSIS	RESISTING CELL DEATH	6	14	6	2	4	14	5	1	3	8	6	4	1	2	5	13	0	26	53
KI67_ECM_RECEPTOR_INTERACTION	ACTIVATING INVASION & METASTASIS	14	22	9	0	5	20	20	0	0	29	40	32	6	3	6	0	0	0	64
KI67_FOCAL_ADHESION	SUSTAINING PROLIFERATIVE SIGNALING	23	28	21	1	11	24	29	0	4	30	30	20	8	6	13	11	2	0	158
KI67_MAPK_SIGNALING_PATHWAY	SUSTAINING PROLIFERATIVE SIGNALING	10	18	19	2	7	20	20	2	3	31	30	27	3	9	5	10	4	0	166
KI67_MTOR_SIGNALING_PATHWAY	SUSTAINING PROLIFERATIVE SIGNALING	2	10	6	1	3	16	4	0	2	10	11	4	0	1	2	22	1	20	34
KI67_P53_SIGNALING_PATHWAY	GENOME INSTABILITY & MUTATION	7	12	5	1	3	16	8	1	2	9	6	6	1	2	4	26	1	19	37
KI67_TGF_BETA_SIGNALING_PATHWAY	EVADING GROWTH SUPPRESSORS	2	2	2	0	0	10	1	0	0	4	4	2	0	2	1	9	0	12	18
REACTOME_CELL_CYCLE	SUSTAINING PROLIFERATIVE SIGNALING	25	28	21	2	6	27	24	5	1	30	28	20	3	10	0	0	0	0	196
REACTOME_DNA_REPAIR	GENOME INSTABILITY & MUTATION	9	20	6	0	1	22	10	0	0	13	10	6	2	0	3	6	0	0	44
REACTOME_PI3K_AKT_ACTIVATION	DEREGULATING CELLULAR ENERGETICS	3	11	6	1	3	7	6	0	3	9	5	3	0	1	4	13	0	13	22
UNIQUE_TOTAL		75	130	68	11	24	236	81	12	13	134	135	108	16	19	31	361	5	382	623

References:

1. Douglas Hanahan, Robert A. Weinberg. (2011) Hallmarks of Cancer: The Next Generation. Cell, 144(5), 646-674.
2. Subramanian, A., Tamayo, P. et al. (2005) Gene set enrichment analysis: a knowledge-based approach for interpreting gene-wide expression profiles. Proc Natl Acad Sci U S A. 102:15545-15550.
3. Bailey ME, Tokheim C et al. (2018) Comprehensive Characterization of Cancer Driver Genes and Mutations. Cell
4. Hallmarks of Cancer Panel Collection

1. Search by Gene

To investigate specific genes, first make sure you are on the GENE tab

GENE CANCER DRUG INFERRED DRUG SYNERGY DOCUMENTATION CONTACT US

Search by one or more HUGO gene symbols or Entrez ID

- For prediction of SL interactions, search is limited to the cancer survival SL Primary Gene list
- Results of SL predictions and drug interactions are presented by sequential selection of
- Results are summarized into 3 main pages initiated by gene search:
 1. Selection of Cancer types
 2. Selection of SL pairs
 3. Drug interaction

Toggle radio buttons to search by different criteria

Gene Search

Gene Symbol
 Entrez Gene ID

Enter gene list:
TP53, BRCA1

OR Upload gene list from file:
Browse... No file selected.

Search

Enter new-line, comma, or space-delimited list, or upload gene list from file

HINT ONLY: Please type in the entire name/id in the input area above

Input	Gene_Symbol	Gene_Entrez_ID
BRCA1	BRCA1	672
BRCA1	BRCA1P1	394269

Helpful hints are offered as you type. When you are done, click Search.

Click for mutation details

Gene: TP53; Histology: BRCA; Number of unique samples with mutation: 30; Total number of mutations: 320

cancer	gene	Variant_Classification	Variant_Type	Chromosome	Start_Position	End_Position	Strand	Mutation_Status	HGVSc	HGVSp_Short	Tumor_Sample_Barcode	Matched_Norm_Sample_Barcode	dbSNP_RS	
1	BRCA	TP53	Missense_Mutation	SNP	17	7578406	7578406	-1	Somatic	c.524G>A	p.R175H	TCGA-A1-A0SI-01	TCGA-A1-A0SI-10	
2	BRCA	TP53	Missense_Mutation	SNP	17	7578532	7578532	-1	Somatic	c.398T>A	p.M133K	TCGA-A1-A0SK-01	TCGA-A1-A0SK-10	
3	BRCA	TP53	Nonsense_Mutation	SNP	17	7578382	7578382	-1	Somatic	c.548C>G	p.S183*	TCGA-A1-A0SP-01	TCGA-A1-A0SP-10	

Gene Mutation status from available cancer types

Select Cancer types and filter parameters to search for SL prediction results (note: if the SL Model column is crossed out, it means the gene is not in SLDB as SL primary gene.)

Please select categories

Select All	Cancer Type	In SL Model as SL Primary Gene		# of Samples with Mutation vs All Samples	
		BRCA1	TP53	BRCA1	TP53
<input type="checkbox"/>	BC (breast) BRCA (Breast invasive carcinoma)	✓	✓	13/1100(1.18%)	301/1100(27.36%)
<input type="checkbox"/>	Bladder (bladder) BLCA (Bladder Urothelial Carcinoma)	✗	✓	4/408(0.98%)	64/408(15.69%)
<input type="checkbox"/>	Blood (Blood) LAML (Acute Myeloid Leukemia)	✗	✓	0/173(0.00%)	16/173(9.25%)
<input type="checkbox"/>	CNS (central_nervous_system) GBM (Glioblastoma multiforme)	✗	✓	4/166(2.41%)	84/166(50.60%)
<input type="checkbox"/>	CNS (central_nervous_system) LGG (Brain Lower Grade Glioma)	✗	✓	0/530(0.00%)	146/530(27.55%)
<input type="checkbox"/>	CX (cervix) CESC (Cervical squamous cell carcinoma and endocervical adenocarcinoma)	✗	✓	5/306(1.63%)	9/306(2.94%)
<input type="checkbox"/>	Liver (liver) LIHC (Liver hepatocellular carcinoma)	✓	✓	9/373(2.41%)	116/373(31.10%)
<input type="checkbox"/>	LI (large_intestine) COADREAD (Colon and Rectum adenocarcinoma)	✗	✓	6/382(1.57%)	120/382(31.41%)
<input type="checkbox"/>	Lung (lung) LUAD (Lung adenocarcinoma)	✗	✓	7/517(1.35%)	106/517(20.50%)
<input type="checkbox"/>	Lung (lung) LUSC (Lung squamous cell carcinoma)	✗	✓	10/501(2.00%)	145/501(28.94%)
<input type="checkbox"/>	OV (ovary) OV (Ovarian serous cystadenocarcinoma)	✗	✓	11/307(3.58%)	276/307(89.90%)
<input type="checkbox"/>	PANC (pancreas) PAAD (Pancreatic adenocarcinoma)	✗	✓	1/307(0.32%)	11/307(3.58%)
<input type="checkbox"/>	PC (prostate) PRAD (Prostate adenocarcinoma)	✗	✓	1/307(0.32%)	11/307(3.58%)
<input type="checkbox"/>	RC (kidney) KIRC (Kidney renal clear cell carcinoma)	✓	✓	5/534(0.94%)	15/534(2.81%)
<input type="checkbox"/>	SKIN (skin) SKCM (Skin Cutaneous Melanoma)	✓	✓	18/472(3.81%)	56/472(11.86%)
<input type="checkbox"/>	THYROID (thyroid) THCA (Thyroid carcinoma)	✗	✗	1/509(0.20%)	3/509(0.59%)
<input type="checkbox"/>	UADT (upper_aerodigestive_tract) HNSC (Head and Neck squamous cell carcinoma)	✓	✓	11/522(2.11%)	366/522(70.11%)
<input type="checkbox"/>	Uterine (uterine) UCEC (Uterine Corpus Endometrial Carcinoma)	✓	✓	12/177(6.78%)	69/177(38.98%)

A green check mark indicates that the gene is included in the SL model as the SL primary gene

Search SL Interaction

Change number of hits to display [Enter]:

Change Pvalue of Survival cutoff (0~1) [Enter]:

Limit to Reported SL only: Yes No

Search for synthetic lethal partners:

- Choose type(s) of cancer
- Select number of hits to display per gene, per cancer type
- Choose Pvalue of Survival cutoff, from 0 (most significant) to 1 (least significant)
- Toggle Yes to limit pairs to reported SL only
- Click Search

The resulting page displays primary genes searched and interactor genes predicted by the SL model, as restricted by previous search parameters. Column descriptions are below. Click to view graphs, plots, and to download data.

Gene Synthetic Lethality Interaction Search Result Summary

Gene Name: TP53, BRCA1

Select SL pair(s) and filters to search for drug interactions. This page also provides option for users to check SL-pair of interest and visualize associated significant pathways

SL Data Download

Default sort is by Pvalue of Survival. Click column headers to sort by different parameters.

Select All	SL Primary Gene	SL Interactor Gene	cBioportal Search	Cancer	SL Score	Correlation Coefficient	Pvalue of Mutual Exclusivity	Pvalue of RNAi	Pvalue of Amplification	Pvalue of Survival	Reported In
<input type="checkbox"/>	TP53	KANK2	gsk3l1.combustion	BRCA	0.92	-0.0584	0.3761	0.0000	0.0000	0.104	
<input type="checkbox"/>	TP53	ENTHD1	gsk3l1.combustion	BRCA	0.88	0.0148	0.7223	0.0000	0.0000	0.816	
<input type="checkbox"/>	BRCA1	ZBTB46	gsk3l1.combustion	BRCA	0.87	-0.0368	0.0000	0.0000	0.0000	0.968	N
<input type="checkbox"/>	BRCA1	SLFN12L	gsk3l1.combustion	BRCA	0.81	0.0000	0.0000	0.0000	0.0000	NA	N

View and download all data

Search for Interactions of Chemicals/Drugs

Select Drug Database: **DrugBank** and **DCIdb**

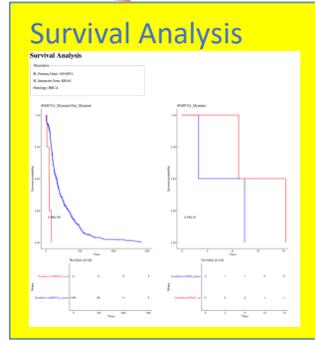
Select Parameters:

Change number of hits to display [Enter]: 10

Limit to ATC drug only: Yes No

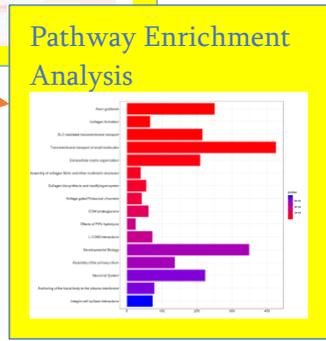
NCBI

cBioPortal search



Gene Expression Heatmap by Cancer Type

Cancer	SL Primary Gene	Pathway Enrichment of SL partners
BRCA	TP53	
BRCA	BRCA1	



Column Descriptions

SL Primary Gene: When gene is mutated, drugs are known to target the SL partner, or 'SL Interactor Gene'.

SL Interactor Gene: Gene targeted by drugs when the 'SL Primary Gene' is mutated.

cBioPortal Search: Information such as mutation, copy number, and expression data from the TCGA PanCancer Atlas Studies for both 'SL Primary Gene' and 'SL Interactor Gene'.

Cancer: Cancer type.

SL Score: Unified score calculated by a random forest regression model which combines four features for the SL pair: differential expression, expression correlation, mutual exclusivity and shared pathways.

Correlation Coefficient: Pearson's correlation coefficient of expression (RNA-Seq V2) of the SL gene pair.

P-value of Mutual Exclusivity: P-value for mutual exclusivity of mutation event for the SL gene pair.

P-value of RNAi: P-value for conditional essentiality of the interactor gene in presence of mutation in the input gene; calculated from Achilles shRNA screening data.

P-value of Amplification: P-value for relative targetability of the interactor

gene in presence of mutation in the input gene; calculated from relative change in the copy number alteration (TCGA) of the interactor gene in samples +/- input gene mutation.

P-value of Survival: P-value for difference in TCGA patient disease-free survival in cases in under-expression vs over-expression of the interactor gene, in presence of mutation in the input gene.

Reported SL: SL interactions reported in literature.

Reference: Literature reference for the reported SL interaction.

On the same page, choose synthetic lethal pairs to investigate their interactions with drugs/chemicals. If a drug/chemical interaction is known, a genetic interaction search result summary will be shown on the next page after clicking submit.

Gene Synthetic Lethality Interaction Search Result Summary

Gene Name: TP53, BRCA1

Select SL pair(s) and filters to search for drug interactions. This page also provides option for users to check SL-pair of interest and visualize associated significant pathways

[SL Data Download](#)

Select All	SL Primary Gene	SL Interactor Gene	cBioportal Search	Cancer	SL Score	Correlation Coefficient	Pvalue of Mutual Exclusivity	Pvalue of RNAi	Pvalue of Amplification	Pvalue of Survival	Reported SL	Reference
<input checked="" type="checkbox"/>	TP53	MTBP	cBioportal Search	BRCA	0.96	0.0535	0.0000	0.0000	0.0000	0.0132	Y	22585861
<input type="checkbox"/>	TP53	DCAF13	cBioportal Search	BRCA	0.96	0.0477	0.0000	0.0000	0.0000	0.0555	Y	22585861
<input checked="" type="checkbox"/>	BRCA1	ZNF625	cBioportal Search	BRCA	0.95	0.2277	0.0000	0.4821	0.0000	0.79	Y	22585861
<input type="checkbox"/>	BRCA1	SLX4	cBioportal Search	BRCA	0.95	0.3572	0.0000	0.0000	0.0000	0.98	Y	17094803

Search for Interactions of Chemicals/Drugs

Select Drug Database (DrugBank and DGI(d)b):

DGI(d)b

Select Parameters:

Change number of hits to display [Enter]:

Limit to ATC drug only: Yes No

Limit to drug for cancer used by NCI: Yes No

If you have pair of genes of your interest from cancer types in SLDB, you can search

Pair of genes search

Gene Symbol 1 [Enter]:

Gene Symbol 2 [Enter]:

Gene Expression Heatmap by Cancer Type

Pathway Enrichment Analysis

Cancer	SL Primary Gene	Pathway Enrichment of SL partners
BRCA	TP53	
BRCA	BRCA1	

Gene Synthetic Lethality Interaction Search Result Summary

Gene Name: EGFR and ERBB2

Select All	SL Primary Gene	SL Interactor Gene	cBioportal Search	Cancer	SL Score	Correlation Coefficient	Mutual Exclusivity	Pvalue of RNAi	Pvalue of Amplification	Pvalue of Survival	Reported SL
<input type="checkbox"/>	EGFR	ERBB2	cBioportal Search	LUAD	0.37	0.34	0.00	0.00	0.00	0.20	Y
<input type="checkbox"/>	EGFR	ERBB2	cBioportal Search	LIHC	0.60	0.23	0.00	0.00	0.00	0.00	Y
<input type="checkbox"/>	EGFR	ERBB2	cBioportal Search	HNSC	0.38	0.21	0.00	0.00	0.00	0.00	Y
<input type="checkbox"/>	ERBB2	EGFR	cBioportal Search	BRCA	0.44	0.02	0.00	0.00	0.00	0.00	N
<input type="checkbox"/>	ERBB2	EGFR	cBioportal Search	LIHC	0.38	0.03	0.00	0.00	0.00	0.00	N
<input type="checkbox"/>	ERBB2	EGFR	cBioportal Search	LUAD	0.37	0.03	0.00	0.00	0.00	0.00	N
<input type="checkbox"/>	ERBB2	EGFR	cBioportal Search	HNSC	0.41	0.21	0.00	0.00	0.00	0.00	N
<input type="checkbox"/>	EGFR	ERBB2	cBioportal Search	HNSC	0.39	0.03	0.00	0.00	0.00	0.00	N
<input type="checkbox"/>	ERBB2	EGFR	cBioportal Search	HNSC	0.42	0.03	0.00	0.00	0.00	0.00	N
<input type="checkbox"/>	ERBB2	EGFR	cBioportal Search	UCEC	0.37	0.02	0.00	0.00	0.00	0.00	N

Search for Interactions of Chemicals/Drugs

Select Drug Database (DrugBank and DGI(d)b):

DGI(d)b

Select Parameters:

Change number of hits to display [Enter]:

Limit to ATC drug only: Yes No

Limit to NCI Approved drug only: Yes No

Choose database and filter by drugs by:
Anatomical Therapeutic Chemical Classification System (ATC)
and/or
Drugs for Cancer used by NCI
then click Submit

Or, enter additional gene pairs not listed above, then click Submit. This will display a search results page similar to above. Choose pairs of interest and again click Submit.



Gene Synthetic Lethality Interaction Search Result Summary

Gene Name: EGFR and ERBB2

Select All	SL Primary Gene	SL Interactor Gene	cBioportal Search	Cancer	SL Score	Correlation Coefficient	Mutual Exclusivity	Pvalue of RNAi	Pvalue of Amplification	Pvalue of Survival	Reported SL
<input type="checkbox"/>	EGFR	ERBB2	cBioportal Search	LUAD	0.37	0.34	0.00	0.00	0.00	0.20	Y
<input type="checkbox"/>	EGFR	ERBB2	cBioportal Search	LIHC	0.60	0.23	0.00	0.00	0.00	0.00	Y
<input type="checkbox"/>	EGFR	ERBB2	cBioportal Search	HNSC	0.38	0.21	0.00	0.00	0.00	0.00	Y
<input type="checkbox"/>	ERBB2	EGFR	cBioportal Search	BRCA	0.44	0.02	0.00	0.00	0.00	0.00	N
<input type="checkbox"/>	ERBB2	EGFR	cBioportal Search	LIHC	0.38	0.03	0.00	0.00	0.00	0.00	N
<input type="checkbox"/>	ERBB2	EGFR	cBioportal Search	LUAD	0.37	0.03	0.00	0.00	0.00	0.00	N
<input type="checkbox"/>	ERBB2	EGFR	cBioportal Search	HNSC	0.41	0.21	0.00	0.00	0.00	0.00	N
<input type="checkbox"/>	EGFR	ERBB2	cBioportal Search	HNSC	0.39	0.03	0.00	0.00	0.00	0.00	N
<input type="checkbox"/>	ERBB2	EGFR	cBioportal Search	HNSC	0.42	0.03	0.00	0.00	0.00	0.00	N
<input type="checkbox"/>	ERBB2	EGFR	cBioportal Search	UCEC	0.37	0.02	0.00	0.00	0.00	0.00	N

Search for Interactions of Chemicals/Drugs

Select Drug Database (DrugBank and DGI(d)b):

DGI(d)b

Select Parameters:

Change number of hits to display [Enter]:

Limit to ATC drug only: Yes No

Limit to NCI Approved drug only: Yes No

The resulting page displays a comprehensive list of drugs and target genes from your search. Gene/drug interactions are pulled from the chosen database, either DGIdb or Drugbank.

Chemical/Drug Interaction Search Result Summary

Parameters

Genes: TP53, BRCA1

From [DGIdb](#)

[Download Full Drug-target Interaction Data from DGIdb](#)

Click column headers to sort

Targeted_Gene	Drug Name	CID	Function	Chemical_Sources	NCI_Approval_Status	Reference
TP53	epirubicin	41867	ATC	Y	22903472	
TP53	decitabine	451668	ATC	Y	2596101	
TP53	etoposide	36462	ATC	Y	27659046	
TP53	mitomycin C	52146	ATC	Y	26855148	
TP53	bortezomib	19815	ATC	Y		
TP53	dabrafenib	19815	ATC	Y		
TP53	dasatinib	19815	ATC	Y		
TP53	cyclophosphamide	19815	ATC	Y		
TP53	trametinib	19815	ATC	Y		

Targeted Gene Symbol	Drug Name	CID	Function	Chemical Sources	Drug used by NCI	References
TP53	epirubicin	41867	ATC	Y	22903472	
TP53	decitabine	451668	ATC	Y	2596101	
TP53	etoposide	36462	ATC	Y	27659046	
TP53	mitomycin C	52146	ATC	Y	26855148	
TP53	bortezomib	19815	ATC	Y		
TP53	dabrafenib	19815	ATC	Y		
TP53	dasatinib	19815	ATC	Y		
TP53	cyclophosphamide	19815	ATC	Y		
TP53	trametinib	19815	ATC	Y		

CID: PubChem Compound Identification, a non-zero integer [PubChem](#) accession identifier for a unique chemical structure.

Chemical Sources: Anatomical Therapeutic Chemical ([ATC](#)) Classification

Drugs used by NCI: Drugs for cancer, or conditions related to cancer, used by [NCI](#)

2. Search by Cancer Type



Click on CANCER tab to explore differential gene expression in each cancer type

Synthetic Lethality BioDiscovery Portal

The Synthetic Lethality BioDiscovery portal (SL-BioDP) is a comprehensive web tool for systematic exploration and functional analysis of cancer-specific synthetic lethal (SL) interactions of known cancer susceptibility genes. It hosts SL interactions predicted using *DiscoverSL*: a machine-learning algorithm for multi-omic TCGA cancer data-driven synthetic lethal interactions. It provides extensive cross-references and user friendly querying interfaces to support SL-related research. This web portal currently hosts SL interactions for 18 cancer types ([Portal Data Summary](#)).

*** We recommend using Chrome and Firefox. Some functionalities may not be well supported On Internet Explorer (IE).

The screenshot shows the 'CANCER' tab selected in the navigation menu. Below the menu, there is a search instruction: 'Search by cancer type to view the mutation status in the cancers for the selected genes'. A list of bullet points describes the results and search process. A search form is visible with a 'Cancer Type Menu' dropdown, input fields for 'Change p-value [Enter]: 0.05' and 'Change number of hits to display [Enter]: 10', and a radio button for 'Limit to genes in SL model only: Yes No'. A 'Search' button is located at the bottom of the form.

Select parameters to search by a specific tissue type, including a p-value filter for tumor to normal differential gene expression.
Set 'Limit to genes in SL model only' filter to yes and

Gene expression and Mutation status in the selected cancer type

Select gene(s) and filter parameters to search

Download data
Gene Expression Full Data Export
Histology: BRCA

Click for mutation details

| pos | chr | hg19 | refseq | hg38 | transcript |
|-----|-----|--------|--------|--------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 1 | 10 | 108034 | BRCA | 108034 | BRCA |

Please select gene(s)

Full Gene Expression Data Access

Select All	Gene Symbol	In SL Model as SL Pri	Pvalue	logFC	Gene Expression logCPM	# of Unique Samples with Mutation vs. Total Samples
<input type="checkbox"/>	TNXB	✔	5.66e-306	-3.99e+0	5.84e+0	9/1100(0.82%)
<input type="checkbox"/>	CACNA1S	✔	2.61e-242	-6.59e+0	1.01e+0	8/1100(0.73%)
<input type="checkbox"/>	ACTN2	✔	1.86e-222	-5.91e+0	4.29e+0	10/1100(0.91%)
<input type="checkbox"/>	TLN2	✔	1.87e-182	-1.86e+0		
<input type="checkbox"/>	FLNC	✔	1.07e-180	-3.02e+0		
<input type="checkbox"/>	VWF	✔	5.76e-158	-2.04e+0	7.99e+0	11/1100(1.00%)
<input type="checkbox"/>	COL6A6	✔	1.45e-144	-3.16e+0	2.40e+0	15/1100(1.36%)
<input type="checkbox"/>	MYLK	✔	1.69e-129	-2.16e+0	7.49e+0	10/1100(0.91%)
<input type="checkbox"/>	HJURP	✔	2.02e-120	3.58e+0	4.05e+0	7/1100(0.64%)
<input type="checkbox"/>	COL11A1	✔	1.09e-107	6.23e+0	7.85e+0	8/1100(0.73%)

A green check mark indicates that the gene is in the SL model.

Search SL Interaction

Change number of hits to display [Enter]:

Change Pvalue of Survival cutoff (0~1) [Enter]:

Limit to Reported SL only: Yes No

- Search for synthetic lethal partners:
- Choose primary genes of interest
 - Select number of hits to display per gene, per cancer type
 - Choose Pvalue of Survival cutoff, from 0 (most significant) to 1 (least significant)
 - Toggle Yes to limit pairs to reported SL only
 - Click Search

The resulting page displays selected primary genes and interactor genes predicted by the SL model, as restricted by previous search parameters. Column descriptions are below. Click to view graphs, plots, and to download data.

Gene Synthetic Lethality Interaction Search Result Summary

Gene Name: **TNXB,CACNA1S**

Select SL pair(s) and filters to search for drug interactions. This page also provides option for users to check SL-pair of interest and visualize associated significant pathways

[SL Data Download](#)

Default sort is by Pvalue of Survival. Click column headers to sort by different parameters.

Select All	SL Primary Gene	SL Interactor Gene	cBioportal Search	Cancer	SL Score	Correlation Coefficient	Pvalue of Mutual Exclusivity	Pvalue of RNAi	Pvalue of Amplification	Pvalue of Survival	Reported SL	Reference
<input type="checkbox"/>	TNXB	TRAF1	cBioPortal Search	BRCA	0.88	0.1203	0.0000	0.0000	0.0000	0.0837	N	
<input type="checkbox"/>	TNXB	LRRC40	cBioPortal Search	BRCA	0.89	-0.0971	0.0000	0.0000	0.0000	0.262	N	
<input type="checkbox"/>	CACNA1S	HMCN1	cBioPortal Search	BRCA	0.86	-0.0191	0.0000	0.0000	0.0000	0.437	N	
<input type="checkbox"/>	CACNA1S	ITPR1D1	cBioPortal Search	BRCA	0.89	-0.0048	0.0000	0.0000	0.0000	NA	N	

Search for Interactions of Chemicals/Drugs
Select Drug Database ([DrugBank](#) and [DGIdb](#)):

NCBI

cBioPortal search

If you have pair of genes of your interest from cancer types in SLDB, you can search here directly. ([SL Primary Gene list](#))

Pair of genes search
Gene Symbol 1 [Enter]:
Gene Symbol 2 [Enter]:

Gene Expression Heatmap by Cancer Type

Pathway Enrichment Analysis

Cancer	SL Primary Gene	Pathway Enrichment of SL partners
BRCA	TNXB	View Pathway
BRCA	CACNA1S	View Pathway

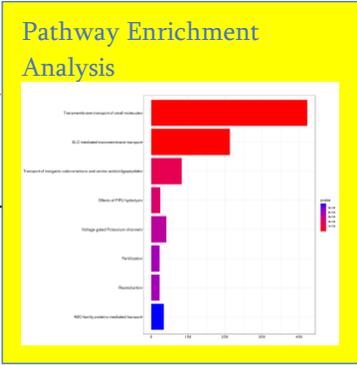
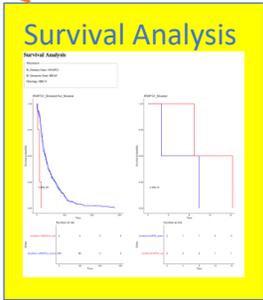
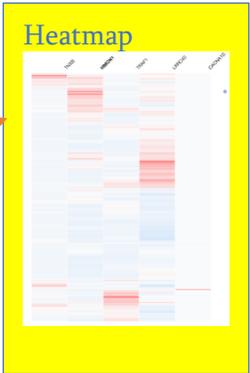
Pathway Enrichment Analysis

View and download all data

SL Full Data Export

NCBI

cBioPortal search



Column Descriptions

SL Primary Gene: When gene is mutated, drugs are known to target the SL partner, or 'SL Interactor Gene'.

SL Interactor Gene: Gene targeted by drugs when the 'SL Primary Gene' is mutated.

cBioPortal Search: Information such as mutation, copy number, and expression data from the TCGA PanCancer Atlas Studies for both 'SL Primary Gene' and 'SL Interactor Gene'.

Cancer: Cancer type.

SL Score: Unified score calculated by a random forest regression model which combines four features for the SL pair: differential expression, expression correlation, mutual exclusivity and shared pathways.

Correlation Coefficient: Pearson's correlation coefficient of expression (RNA-Seq V2) of the SL gene pair.

P-value of Mutual Exclusivity: P-value for mutual exclusivity of mutation event for the SL gene pair.

P-value of RNAi: P-value for conditional essentiality of the interactor gene in presence of mutation in the input gene; calculated from Achilles shRNA screening data.

P-value of Amplification: P-value for relative targetability of the interactor

gene in presence of mutation in the input gene; calculated from relative change in the copy number alteration (TCGA) of the interactor gene in samples +/- input gene mutation.

P-value of Survival: P-value for difference in TCGA patient disease-free survival in cases in under-expression vs over-expression of the interactor gene, in presence of mutation in the input gene.

Reported SL: SL interactions reported in literature.

Reference: Literature reference for the reported SL interaction.

On the same page, choose synthetic lethal pairs to investigate their interactions with drugs/chemicals. If a drug/chemical interaction is known, a genetic interaction search result summary will be shown on the next page after clicking submit.

Gene Synthetic Lethality Interaction Search Result Summary

Gene Name: TNXB,CACNA1S

Select SL pair(s) and filters to search for drug interactions. This page also provides option for users to check SL-pair of interest and visualize associated significant pathways

[SL Data Download](#)

Select All	SL Primary Gene	SL Interactor Gene	cBioportal Search	Cancer	SL Score	Correlation Coefficient	Pvalue of Mutual Exclusivity	Pvalue of RNAi	Pvalue of Amplification	Pvalue of Survival	Reported SL	Reference
<input type="checkbox"/>	TNXB	NEU4	cBioportal Search	BRCA	0.96	0.0644	0.0000	0.0000	0.0000	0.642	N	
<input type="checkbox"/>	TNXB	TNIP3	cBioportal Search	BRCA	0.96	-0.0454	0.9836	0.0000	0.0000	0.924	N	
<input type="checkbox"/>	CACNA1S	PDZK1P1	cBioportal Search	BRCA	0.94	0.0000	0.0000	0.0000	0.0000	NA	N	
<input type="checkbox"/>	CACNA1S	TEDC2	cBioportal Search	BRCA	0.94	0.0000	0.0000	0.0000	0.0000	NA	N	

Search for Interactions of Chemicals/Drugs

Select Drug Database (DrugBank and DGIdb):

Select Parameters:

Change number of hits to display [Enter]:

Limit to ATC drug only: Yes No

Limit to drug for cancer used by NCI: Yes No

Choose database and filter by drugs by:
Anatomical Therapeutic Chemical Classification System (ATC)
and/or
Drugs for Cancer used by NCI
then click Submit

If you have pair of genes of your interest from cancer types in SLDB, you can search

Pair of genes search

Gene Symbol 1 [Enter]:

Gene Symbol 2 [Enter]:

Or, enter additional gene pairs not listed above, then click Submit. This will display a search results page similar to above. Choose pairs of interest and again click Submit.

[Gene Expression Heatmap by Cancer Type](#)

Pathway Enrichment Analysis

Cancer	SL Primary Gene	Pathway Enrichment of SL partners
BRCA	TNXB	
BRCA	CACNA1S	

Genetic Interaction Search Result Summary

Gene Name:

Select All	Input Gene	Interactor Gene Symbol	cBioportal Search	Cancer	Predicted P	Correlation Coefficient	Mutual Exclusivity	Pval(RNAi)	TTestMutAmpl	Survival	Reported SL
<input type="checkbox"/>	ERBB2	EGFR	cBioportal Search	BRCA	0.46	-0.02	0.00	0.00	0.00	0.215	N

Search for Interactions of Chemicals/Drugs

Select Drug Database (DrugBank and DGIdb):

Select Parameters:

Change number of hits to display [Enter]:

Limit to ATC drug only: Yes No

Limit to NCI Approved drug only: Yes No

The resulting page displays a comprehensive list of drugs and target genes from your search. Gene/drug interactions are pulled from the chosen database, either DGIdb or Drugbank.

Chemical/Drug Interaction Search Result Summary

Parameters

Genes:
MYLK,TLN2,COL11A1,FLNC,VWF,TNXB,HJURP,COL6A6,ACTN2,CACNA1

Targeted Gene	Drug Name	CID	Drug used by NCI	References
VWF	thalidomide	5426	Y	12871448
VWF	mitomycin C	5746	Y	2104558
VWF	indole alkaloid	5978	Y	3875694
VWF	prednisone	5865	Y	3146197
IDH1	lomustine	3950	Y	26762204
IDH1	decitabine	451668	Y	24077826
IDH1	temozolomide	5394	Y	25210856
IDH1	vandetanib	3081361	Y	25210856

From [DGIdb](#)

[Download Full Drug-target Interaction Data from DGIdb](#)

Targeted Gene Symbol	Drug Name	CID	Drug used by NCI	References
VWF	thalidomide	5426	Y	12871448
VWF	mitomycin C	5746	Y	2104558
VWF	indole alkaloid	5978	Y	3875694
VWF	prednisone	5865	Y	3146197
IDH1	lomustine	3950	Y	26762204
IDH1	decitabine	451668	Y	24077826
IDH1	temozolomide	5394	Y	25210856
IDH1	vandetanib	3081361	Y	25210856

Click column headers to sort

CID: PubChem Compound Identification, a non-zero integer [PubChem](#) accession identifier for a unique chemical structure.

Chemical Sources: Anatomical Therapeutic Chemical ([ATC](#)) Classification

Drugs used by NCI: Drugs for cancer, or conditions related to cancer, used by [NCI](#)

3. Search by Drug

Click on the DRUG tab
Toggle radio buttons to search by different criteria

GENE **DRUG** INFERRED DRUG SYNERGY DOCUMENTATION CONTACT US

Search by drug name or Pubchem chemical index (CID) number to show genes reported to interact with the selected drug

- Results of SL predictions and drug interactions are presented by sequential selection of provided options by the user
- Results are summarized into 4 main pages initiated by drug search:
 1. Gene drug interactions (sourced from DGldb or Drug bank); The presented drug target(s) will query against the SL interaction database as SL interactor gene;
 2. Selection of Cancer types
 3. Selection of SL pairs
 4. Drug interaction

Drug Search

Drug Name
 CID

Enter drug list:
tamoxifen, erlotinib

OR Upload drug list from file:
 No file selected.

Select Drug Target Database (DrugBank and DGldb) :
DGldb

Select Parameters:
Change number of hits to display [Enter]: 10
Limit to genes in SL model only: Yes No

HINT ONLY: Please type in the entire name/id in the input area above

Input	Drug_Name	Drug_CID
erlotinib	Erlotinib	176870

Enter new-line, comma, or space-delimited list, or upload gene list from file

Select database
Toggle button to limit genes to SL model only

Helpful predictions are offered as you type. When you are done, click Search.

Each link gives information about the contents. Click to select genes of interest, then click Submit.

Gene drug interactions summary

Interactions shown were from curated data from DGIdb and Drug bank. Select gene(s) to search for SL prediction results

Search Target Gene for Drug

From DGIdb Dataset ([doc](#))

[Full Drug Targets Access](#)

Select All	Gene Symbol	CID	Drug Name	Function
<input type="checkbox"/>	EGFR	176870	erlotinib	inhibitor
<input type="checkbox"/>	KRAS	176870	erlotinib	
<input type="checkbox"/>	DDR2	176870	erlotinib	
<input type="checkbox"/>	PTEN	176870	erlotinib	
<input type="checkbox"/>	CDH1	176870	erlotinib	
<input type="checkbox"/>	FZR1	176870	erlotinib	
<input type="checkbox"/>	TP53	176870	erlotinib	
<input type="checkbox"/>	MET	176870	erlotinib	
<input type="checkbox"/>	RNMT	176870	erlotinib	
<input type="checkbox"/>	SLTM	176870	erlotinib	

Submit

Gene Search By Drug Full Data Export
Drug(s): tamoxifen ,erlotinib

Gene Symbol	CID	Drug Name	Function
1	176870	erlotinib	
2	176870	erlotinib	
3	176870	erlotinib	
4	176870	erlotinib	
5	176870	erlotinib	
6	176870	erlotinib	
7	176870	erlotinib	
8	176870	erlotinib	
9	176870	erlotinib	
10	176870	erlotinib	inhibitor
11	176870	erlotinib	
12	176870	erlotinib	
13	273324	tamoxifen	medication
14	176870	erlotinib	
15	176870	erlotinib	
16	176870	erlotinib	
17	176870	erlotinib	
18	176870	erlotinib	
19	176870	erlotinib	
20	176870	erlotinib	
21	176870	erlotinib	
22	176870	erlotinib	
23	176870	erlotinib	
24	176870	erlotinib	
25	176870	erlotinib	
26	176870	erlotinib	

NCBI - Gene

Gene: KRAS

Search results

Accession ID	Description	Location	Aliases	ORF
KRAS	KRAS proto-oncogene, GTPase	Chromosome 12	K-RAS, CFC2	198979
KRAS2	KRAS2 proto-oncogene, GTPase	Chromosome 12	K-RAS2	
KRAS3	KRAS3 proto-oncogene, GTPase	Chromosome 12	K-RAS3	
KRAS4	KRAS4 proto-oncogene, GTPase	Chromosome 12	K-RAS4	
KRAS5	KRAS5 proto-oncogene, GTPase	Chromosome 12	K-RAS5	
KRAS6	KRAS6 proto-oncogene, GTPase	Chromosome 12	K-RAS6	
KRAS7	KRAS7 proto-oncogene, GTPase	Chromosome 12	K-RAS7	
KRAS8	KRAS8 proto-oncogene, GTPase	Chromosome 12	K-RAS8	
KRAS9	KRAS9 proto-oncogene, GTPase	Chromosome 12	K-RAS9	
KRAS10	KRAS10 proto-oncogene, GTPase	Chromosome 12	K-RAS10	
KRAS11	KRAS11 proto-oncogene, GTPase	Chromosome 12	K-RAS11	
KRAS12	KRAS12 proto-oncogene, GTPase	Chromosome 12	K-RAS12	
KRAS13	KRAS13 proto-oncogene, GTPase	Chromosome 12	K-RAS13	
KRAS14	KRAS14 proto-oncogene, GTPase	Chromosome 12	K-RAS14	
KRAS15	KRAS15 proto-oncogene, GTPase	Chromosome 12	K-RAS15	
KRAS16	KRAS16 proto-oncogene, GTPase	Chromosome 12	K-RAS16	
KRAS17	KRAS17 proto-oncogene, GTPase	Chromosome 12	K-RAS17	
KRAS18	KRAS18 proto-oncogene, GTPase	Chromosome 12	K-RAS18	
KRAS19	KRAS19 proto-oncogene, GTPase	Chromosome 12	K-RAS19	
KRAS20	KRAS20 proto-oncogene, GTPase	Chromosome 12	K-RAS20	
KRAS21	KRAS21 proto-oncogene, GTPase	Chromosome 12	K-RAS21	
KRAS22	KRAS22 proto-oncogene, GTPase	Chromosome 12	K-RAS22	
KRAS23	KRAS23 proto-oncogene, GTPase	Chromosome 12	K-RAS23	
KRAS24	KRAS24 proto-oncogene, GTPase	Chromosome 12	K-RAS24	
KRAS25	KRAS25 proto-oncogene, GTPase	Chromosome 12	K-RAS25	
KRAS26	KRAS26 proto-oncogene, GTPase	Chromosome 12	K-RAS26	
KRAS27	KRAS27 proto-oncogene, GTPase	Chromosome 12	K-RAS27	
KRAS28	KRAS28 proto-oncogene, GTPase	Chromosome 12	K-RAS28	
KRAS29	KRAS29 proto-oncogene, GTPase	Chromosome 12	K-RAS29	
KRAS30	KRAS30 proto-oncogene, GTPase	Chromosome 12	K-RAS30	

PubChem

COMPOUND SUMMARY

erlotinib

PubChem CID: 176870

Structure: 

Chemical Safety: 

NCBI Key: [A04L3053\(D03603\)G1FFH9A256-0](#)

Molecular Formula: C17H19N5O4

UNII: J4T82NDC

Contents:

- 1 Structure
- 2 Names and Identifiers
- 3 Chemical and Physical Properties
- 4 Safety Information
- 5 Related Records
- 6 Chemical Vendors
- 7 Drug and Medication Information
- 8 Pharmacology and Biochemistry
- 9 Synonyms and Manufacturing
- 10 Identification
- 11 Safety and Hazards
- 12 Toxicity

Gene Mutation status from available cancer types

Click for mutation details

Gene	EGFR	History	BRCA	Number of unique samples with mutation	5	Total number of mutations	3						
1	BRCA	EGFR	Misense_Mutation	SNP	NA	5523574	5523574	NA	Somatic	c.815A>G	p.D114E	TCGA-A2-A43Z-01	TCGA-A2-A43Z-10
2	BRCA	EGFR	Misense_Mutation	SNP	NA	5524944	5524944	NA	Somatic	c.1315G>A	p.D115N	TCGA-AC-A23H-01	TCGA-AC-A23H-11
3	BRCA	EGFR	Misense_Mutation	SNP	NA	5521773	5521773	NA	Somatic	c.817A>G	p.T273A	TCGA-AO-A12G-01	TCGA-AO-A12G-10
4	BRCA	EGFR	Misense_Mutation	SNP	NA	5521107	5521107	NA	Somatic	c.300G>A	p.E114K	TCGA-AR-A23R-01	TCGA-AR-A23R-10
5	BRCA	EGFR	Misense_Mutation	SNP	NA	5521107	5521107	NA	Somatic	c.300G>A	p.E114K	TCGA-DB-A11F-01	TCGA-DB-A11F-10

Back to summary

Select Cancer types and filter parameters to search for SL prediction results (note: if the SL Model column is crossed out, it means the gene is not in SLDB as SL interactor gene.)

Please select categories

Select All	Cancer Type	Genes --->	In SL Model as SL Interactor Gene			# of Samples with Mutation vs All Samples		
			EGFR	KRAS	DDR2	EGFR	KRAS	DDR2
<input type="checkbox"/>	BC (breast) BRCA (Breast invasive carcinoma)		✓	✓	✓	5/1100(0.45%)	6/1100(0.55%)	10/1100(0.91%)
<input type="checkbox"/>	Bladder (bladder) BLCA (Bladder Urothelial Carcinoma)		✓	✗	✓	3/408(0.74%)	0/408(0.00%)	2/408(0.49%)
<input type="checkbox"/>	Blood (Blood) LAML (Acute Myeloid Leukemia)		✓	✓	✗	2/173(1.16%)	8/173(4.62%)	2/173(1.16%)
<input type="checkbox"/>	CNS (central_nervous_system) GBM (Glioblastoma multiforme)		✓	✓	✓	77/166(46.39%)	2/166(1.20%)	2/166(1.20%)
<input type="checkbox"/>	CNS (central_nervous_system) LGG (Brain Lower Grade Glioma)		✓	✓	✓	15/530(2.83%)	1/530(0.19%)	1/530(0.19%)
<input type="checkbox"/>	COADREAD (Colon and Rectum adenocarcinoma)		✓	✓	✓	10/382(2.62%)	97/382(25.39%)	6/382(1.57%)
<input type="checkbox"/>	Lung (lung) LUAD (Lung adenocarcinoma)		✓	✓	✓	33/517(6.38%)	75/517(14.51%)	7/517(1.35%)
<input type="checkbox"/>	Lung (lung) LUSC (Lung squamous cell carcinoma)		✓	✓	✓	6/501(1.20%)	2/501(0.40%)	3/501(0.60%)
<input type="checkbox"/>	OV (ovary) OV (Ovarian serous cystadenocarcinoma)		✓	✗	✗	7/307(2.28%)	2/307(0.65%)	0/307(0.00%)
<input type="checkbox"/>	PANC (pancreas) PAAD (Pancreatic adenocarcinoma)		✓	✓	✓	1/179(0.56%)	136/179(75.98%)	3/179(1.68%)
<input type="checkbox"/>	PC (prostate) PRAD (Prostate adenocarcinoma)		✓	✓	✓	3/498(0.60%)	2/498(0.40%)	2/498(0.40%)
<input type="checkbox"/>	RC (kidney) KIRC (Kidney renal clear cell carcinoma)		✓	✗	✓	9/534(1.69%)	1/534(0.19%)	3/534(0.56%)
<input type="checkbox"/>	SKIN (skin) SKCM (Skin Cutaneous Melanoma)		✓	✓	✓	25/472(5.30%)	7/472(1.48%)	6/472(1.27%)
<input type="checkbox"/>	THYROID (thyroid) THCA (Thyroid carcinoma)		✓	✗	✓	0/509(0.00%)	4/509(0.79%)	0/509(0.00%)
<input type="checkbox"/>	UADT (upper_aerodigestive_tract) HNSC (Head and Neck squamous cell carcinoma)		✓	✗	✓	20/522(3.83%)	1/522(0.19%)	10/522(1.92%)
<input type="checkbox"/>	Uterine (uterine) UCEC (Uterine Corpus Endometrial Carcinoma)		✓	✓	✓	8/177(4.52%)	53/177(29.94%)	13/177(7.34%)

A green check mark indicates that the gene is included in the SL model as the [SL interactor gene](#)

Search SL Interaction

Change number of hits to display [Enter]:

Change Pvalue of Survival cutoff (0~1) [Enter]:

Limit to Reported SL only: Yes No

Search for synthetic lethal partners:

- Choose type(s) of cancer
- Select number of hits to display per gene, per cancer type
- Choose Pvalue of Survival cutoff, from 0 (most significant) to 1 (least significant)
- Toggle Yes to limit pairs to reported SL only
- Click Search

The resulting page displays selected primary genes and interactor genes predicted by the SL model, as restricted by previous search parameters. Column descriptions are below. Click to view graphs and plots, and to download data.

Gene Synthetic Lethality Interaction Search Result Summary

Gene Name: **DDR2,KRAS,EGFR**

Select SL pair(s) and filters to search for drug interactions. This page also provides option for users to check SL pair of interest and visualize associated significant pathways

SL Data Download Default sort is by Pvalue of Survival. Click column headers to sort by different parameters.

Select All	SL Primary Gene	SL Interactor Gene	cBioportal Search	Cancer	SL Score	Correlation Coefficient	Pvalue of Mutual Exclusivity	Pvalue of RNAi	Pvalue of Amplification	Pvalue of Survival	Reported SL	Reference
<input type="checkbox"/>	ANAPC4	KRAS		BRCA	0.84	0.0301	0.0000	0.0000	0.0000	0.433	Y	19490893
<input type="checkbox"/>	BRCA1	EGFR		BRCA	0.84	0.0352	0.0000	0.4713	0.0000	0.483	Y	3965078 23071597 23564760
<input type="checkbox"/>	CKAP5	KRAS		BRCA	0.84	0.2629	0.0000	0.0000	0.0000	0.758	Y	19490893
<input type="checkbox"/>	ATM	EGFR		BRCA	0.80	0.0011	0.0000	0.7093	0.0000	0.937	Y	3965078

Search for Interactions of Chemicals/Drugs

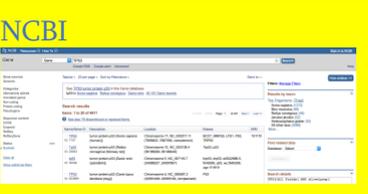
Select Drug Database (DrugBank and DGIdb) :

DGIdb

Select Parameters:

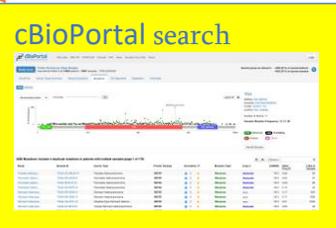
Change number of hits to display [Enter]: 10

NCBI



For cancer types in SLDB, you can search here directly. (SL Primary Gene list)

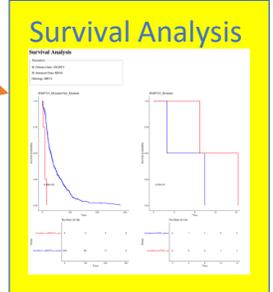
cBioPortal search



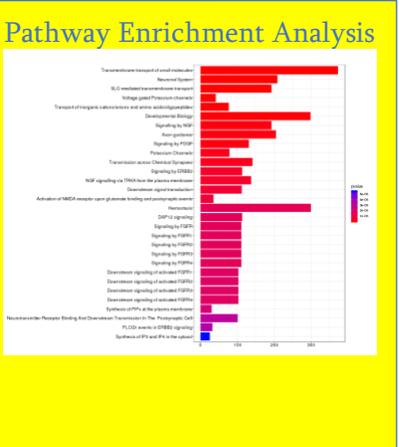
Heatmap



Survival Analysis



Pathway Enrichment Analysis



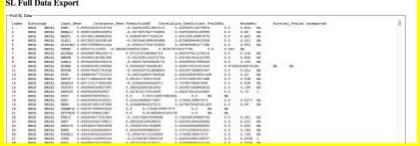
Gene Expression Heatmap by Cancer Type

Pathway Enrichment Analysis

Cancer	SL Primary Gene	Pathway Enrichment of SL partners
BRCA	ANAPC4	
BRCA	CKAP5	
BRCA	BRCA1	
BRCA	ATM	

View and download all data

SL Full Data Export



Column Descriptions

SL Primary Gene: When gene is mutated, drugs are known to target the SL partner, or 'SL Interactor Gene'.

SL Interactor Gene: Gene targeted by drugs when the 'SL Primary Gene' is mutated.

cBioPortal Search: Information such as mutation, copy number, and expression data from the TCGA PanCancer Atlas Studies for both 'SL Primary Gene' and 'SL Interactor Gene'.

Cancer: Cancer type.

SL Score: Unified score calculated by a random forest regression model which combines four features for the SL pair: differential expression, expression correlation, mutual exclusivity and shared pathways.

Correlation Coefficient: Pearson's correlation coefficient of expression (RNA-Seq V2) of the SL gene pair.

P-value of Mutual Exclusivity: P-value for mutual exclusivity of mutation event for the SL gene pair.

P-value of RNAi: P-value for conditional essentiality of the interactor gene in presence of mutation in the input gene; calculated from Achilles shRNA screening data.

P-value of Amplification: P-value for relative targetability of the interactor

gene in presence of mutation in the input gene; calculated from relative change in the copy number alteration (TCGA) of the interactor gene in samples +/- input gene mutation.

P-value of Survival: P-value for difference in TCGA patient disease-free survival in cases in under-expression vs over-expression of the interactor gene, in presence of mutation in the input gene.

Reported SL: SL interactions reported in literature.

Reference: Literature reference for the reported SL interaction.

On the same page, choose synthetic lethal pairs to investigate their interactions with other drugs/chemicals that target your gene of interest. If a drug/chemical interaction is known, a genetic interaction search result summary will be shown on the next page after clicking submit:

Gene Synthetic Lethality Interaction Search Result Summary

Gene Name: **DDR2, KRAS, EGFR**

Select SL pair(s) and filters to search for drug interactions. This page also provides option for users to check SL-pair of interest and visualize associated significant pathways

[SL Data Download](#)

Select All	SL Primary Gene	SL Interactor Gene	cBioportal Search	Cancer	SL Score	Correlation Coefficient	Pvalue of Mutual Exclusivity	Pvalue of RNAi	Pvalue of Amplification	Pvalue of Survival	Reported SL	Reference
<input type="checkbox"/>	ACTR1A	KRAS	cBioPortal Search	BRCA	0.91	-0.1656	0.0000	0.0000	0.0000	0.0389	Y	19490893
<input type="checkbox"/>	BRCA1	KRAS	cBioPortal Search	BRCA	0.91	0.2072	0.0000	0.2505	0.0000	0.438	Y	22585861
<input type="checkbox"/>	BRCA1	EGFR	cBioPortal Search	BRCA	0.84	0.0352	0.0000	0.4713	0.0000	0.483	Y	3965078 23071597 23564760
<input type="checkbox"/>	ATM	EGFR	cBioPortal Search	BRCA	0.80	0.0011	0.0000	0.7093	0.0000	0.937	Y	3965078

Choose database and filter by drugs by:
 Anatomical Therapeutic Chemical Classification System (ATC)
 and/or
 Drugs for Cancer used by NCI
 then click Submit

Search for Interactions of Chemicals/Drugs

Select Drug Database (DrugBank and DGIdb):

Select Parameters:
 Change number of hits to display [Enter]:
 Limit to ATC drug only: Yes No
 Limit to drug for cancer used by NCI: Yes No

If you have pair of genes of your interest from cancer types in SLDB, you can search here directly

Or, enter additional gene pairs not listed above, then click Submit. This will display a search results page similar to above. Choose pairs of interest and again click Submit.

Pair of genes search

Gene Symbol 1 [Enter]:
 Gene Symbol 2 [Enter]:

Gene Expression Heatmap by Cancer Type

Pathway Enrichment Analysis

Cancer	SL Primary Gene	Pathway Enrichment of SL partners
BRCA	ACTR1A	
BRCA	BRCA1	
BRCA	ATM	

Genetic Interaction Search Result Summary

Gene Name:

Select All	Input Gene	Interactor Gene Symbol	cBioportal Search	Cancer	PdictionRF	Correlation Coefficient	Mutual Exclusivity	Pval(RNAi)	TTestMutAmp	Survival	Reported SL
<input checked="" type="checkbox"/>	ERBB2	EGFR	cBioPortal Search	BRCA	0.46	-0.02	0.00	0.00	0.00	0.215	N

Search for Interactions of Chemicals/Drugs

Select Drug Database (DrugBank and DGIdb):

Select Parameters:
 Change number of hits to display [Enter]:
 Limit to ATC drug only: Yes No
 Limit to NCI Approved drug only: Yes No

The resulting page displays a comprehensive list of drugs and target genes from your search. Gene/drug interactions are pulled from the chosen database, either DGIdb or Drugbank.

Chemical/Drug Interaction Search Result Summary

Parameters

Genes: SMC3,FANCM,TUBGCP2,DKC1,AKT3

From DGIdb

Download Full Drug-target Interaction Data from DGIdb

Click column headers to sort

Target Gene Symbol	Drug Name	CID	Function	Chemical Sources	Drug used by NCI	References
KRAS	lenalidomide	216326		ATC	Y	27458141
KRAS	taxol	34314		ATC	Y	22139013
KRAS	gefitinib	13631		ATC	Y	15696205 27338794 25870145
KRAS	dabrafenib	44462760		ATC	Y	27312529
KRAS	crizotinib	1626560		ATC	Y	27338794 25232318 26432108
KRAS	FOLFIRI	56842117		ATC	Y	28404754 25877855 2605843
KRAS	doxorubicin	31703		ATC	Y	21216929
KRAS	5-FU	3385		ATC	Y	26341920
KRAS	vandetanib	3081361		ATC	Y	
KRAS	dasatinib	3062316		ATC	Y	20956938
KRAS	nilotinib	644241		ATC	Y	26725216
KRAS	decitabine	451668		ATC	Y	25968887
KRAS	everolimus	6442177		ATC	Y	
KRAS	LBH589	6918837		ATC	Y	22693356 19490892 26725216
KRAS	ixabepilone	6445540		ATC	Y	26864210
KRAS	nonamib	24826799		ATC	Y	27338794

PubChem U.S. National Library of Medicine
 Lenalidomide
 PubChem CID: 216326
 Chemical Safety:
 ICD10: G80.0
 Molecular Formula: C₁₇H₁₅N₂O₂

PubMed NCBI
 A Phase I Trial to Evaluate Antibody-Dependent Cellular Cytotoxicity of Cetuximab and Lenalidomide in Advanced Colorectal and Head and Neck Cancer.
 Bettelei M, Mubareka S, Wang M, Dick M, Paul M, Ghossein M, Scapecchi S, Grossi D.
 ABSTRACT
 OBJECTIVE: To evaluate antibody-dependent cellular cytotoxicity (ADCC) via the innate immune system's ability to recognize MAb-coated cancer cells and activate immune effector cells. Lenalidomide is an immunomodulatory agent with the capacity to stimulate immune cell cytotoxic production and ADCC activity. This phase I trial evaluated the combination of cetuximab with lenalidomide in the treatment of advanced colorectal and head and neck squamous cell cancers (HNSCC). This trial included patients with advanced colorectal cancer or HNSCC. Treatment consisted of subcutaneous 500 mg cetuximab on every 14 days for 12 weeks with lenalidomide given orally days 1-21 on a 28-day cycle. Three dose levels of lenalidomide were evaluated (0.5, 2.0, 21 mg). Correlative studies included measurement of ADCC, FcγRIIIa polymorphism genotyping, measurement of serum cytokine levels, and flow cytometric analysis of immune cell subsets. Twenty-two patients were enrolled (19 colorectal cancer, 3 HNSCC). Fatigue was the only dose-limiting toxicity. One partial response was observed and 8 patients had stable disease at least 12 weeks. The recommended phase II dose is cetuximab 500 mg (mg) with lenalidomide 20 mg daily days 1-21. Correlative studies demonstrated a dose-dependent increase in natural killer cytotoxic activity with increasing doses of lenalidomide. Cetuximab and lenalidomide were well tolerated. There was a lenalidomide dose-dependent increase in ADCC with higher activity in patients enrolled in cohort 3 than those enrolled in cohorts 1/2. Although response was not a primary endpoint, there was evidence of antitumor activity for the combination therapy. Further investigation of lenalidomide as an immunomodulator in solid tumors is warranted. Mol Cancer Ther. 15(9):2244-50.

CID: PubChem Compound Identification, a non-zero integer [PubChem](#) accession identifier for a unique chemical structure.

Chemical Sources: Anatomical Therapeutic Chemical ([ATC](#)) Classification

Drugs used by NCI: Drugs for cancer, or conditions related to cancer, used by [NCI](#)

4. Investigate Inferred Drug Synergy

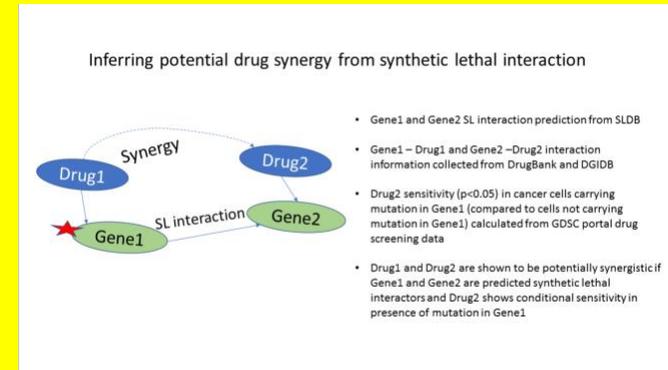
Inferring Potential Drug Synergy from Synthetic Lethal Interaction

• Please read [here](#) for more information

Potential Drug Synergy from SL Interaction by Cancer Types

Cancer Type	Cancer full name	Total number of Synergy
BRCA	BC (breast) BRCA (Breast invasive carcinoma)	73
BLCA	Bladder (bladder) BLCA (Bladder Urothelial Carcinoma)	40
LAML	Blood (Blood) LAML (Acute Myeloid Leukemia)	11
GBM	CNS (central_nervous_system) GBM (Glioblastoma multiforme)	20
LGG	CNS (central_nervous_system) LGG (Brain Lower Grade Glioma)	3
CESC	CX (cervix) CESC (Cervical squamous cell carcinoma and endocervical adenocarcinoma)	19
LIHC	Liver (liver) LIHC (Liver hepatocellular carcinoma)	33
COADREAD	LI (large_intestine) COADREAD (Colon and Rectum adenocarcinoma)	10
LUAD	Lung (lung) LUAD (Lung adenocarcinoma)	133
LUSC	Lung (lung) LUSC (Lung squamous cell carcinoma)	50
OV	OV (ovary) OV (Ovarian serous cystadenocarcinoma)	1
PAAD	PANC (pancreas) PAAD (Pancreatic adenocarcinoma)	3
PRAD	PC (prostate) PRAD (Prostate adenocarcinoma)	1

Click for information regarding drug synergy. Red star denotes mutation in Gene1



(Gene1-Drug1 interactions are considered regardless of mutation in Gene1.)

Click for a list of drug synergy pairs for each cancer type.

Histology: THCA; Total number of records: 6

index	drug_name1	gene_symbol1	drug_name2	PValue	hist_code	reference
1	Vemurafenib	BRAF	Temozolomide	4.24e-4	THCA	
2	Regorafenib	BRAF	Temozolomide	4.24e-4	THCA	
3	Dabrafenib	BRAF	Temozolomide	4.24e-4	THCA	
4	Dasatinib	BRAF	Temozolomide	4.24e-4	THCA	19190119
5	Temsirolimus	BRAF	Temozolomide	4.24e-4	THCA	
6	Encorafenib	BRAF	Temozolomide	4.24e-4	THCA	

[Back to summary](#)