



COSMIC - Catalogue of Somatic Mutations in Cancer

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

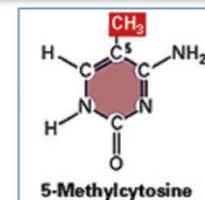
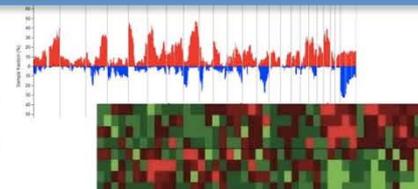
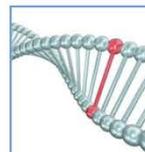
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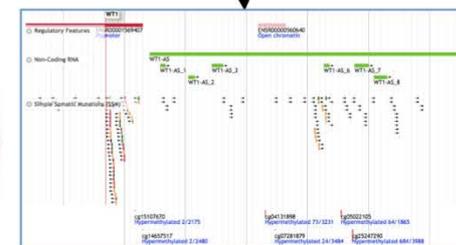
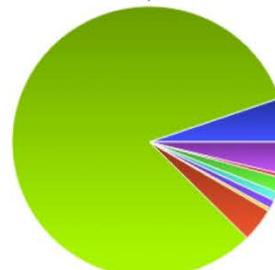
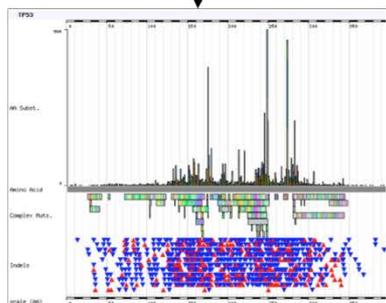
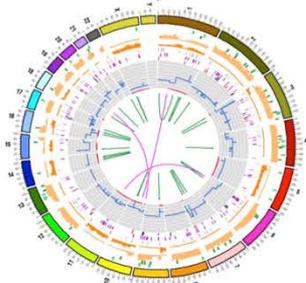
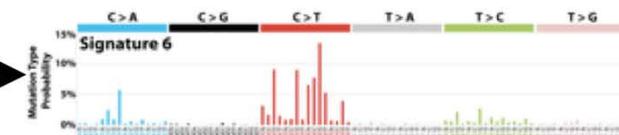
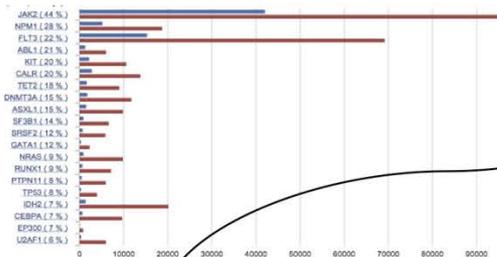
The COSMIC Project

Expert knowledge curation

Large-scale cancer genomics

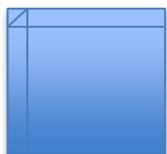


Curate, Integrate, Combine

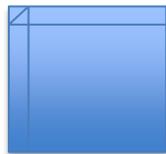


Data In

Large-scale systematic screens



ICGC/TCGA/CGP



Publication
datasheets

QC (data input
format, details
& noise)

Data Extraction

GRCh37 co-ords
& allele seqs

Sample Details

QC (standardise)

ATRAC

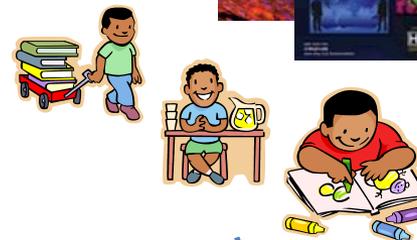


Genic annotation
(HGVS syntax)

QC (sequence and
annotation checks)

Broad
genomic
data

Detailed genic analyses



QC (reject ~30%)

Deep
genic
data

Standardisation

COSMIC

COSMIC v82, released 03-AUG-17

COSMIC, the Catalogue Of Somatic Mutations In Cancer, is the world's largest and most comprehensive resource for exploring the impact of somatic mutations in human cancer.

Start using COSMIC by searching for a gene, cancer type, mutation, etc. below.

 SEARCH

Projects

COSMIC is divided into several distinct projects, each presenting a separate dataset or view of our data:

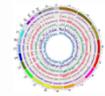
-  **COSMIC**
The core of COSMIC, an expert-curated database of somatic mutations
-  **Cell lines project**
Mutation profiles of over 1,000 cell lines used in cancer research
-  **COSMIC-3D**
An interactive view of cancer mutations in the context of 3D structures
-  **Cancer Gene Census**
A catalogue of genes with mutations that are causally implicated in cancer

Data curation

-  [Gene curation](#) — details of our manual curation process
-  [Gene fusion curation](#) — details of our curation process for gene fusions
-  [Genome Annotation](#) — information on the annotation of genomes
-  [Drug Resistance](#) — curation of mutations conferring drug resistance

COSMIC News

[Follow @cosmic_sanger](#)



COSMIC Release v82

What's new in v82? The August updates include the completion and launch of the restyled website. The full curation of four new genes: BTK, DROSHA, EPAS1 and KEAP1, a substantial update to SMAD4 and a new fusion pair NUP214-ABL1. [More...](#)



The new website has launched

The restyled website is complete and we have now switched it over as the main website with the old COSMIC site becoming legacy. [More...](#)



Cancer Gene Census, Hallmarks and the new tier system

The Cancer Gene Census has had a thorough re-evaluation as part of integrating the Hallmarks of Cancer feature. This feature, initially released in May, has now had a substantial update to include 226 genes. [More...](#)

Tools

-  [Cancer browser](#) — browse COSMIC data by tissue type and histology
-  [Genome browser](#) — browse the human genome with COSMIC annotations
-  [CONAN](#) — the COSMIC copy number analysis tool
-  [GA4GH Beacon](#) — access COSMIC data through the [GA4GH Beacon Project](#)
-  [COSMIC in BigQuery](#) — search COSMIC via the [ISB Cancer Genomics Cloud](#)

Help

-  [Downloads](#) — data that you can download from our SFTP site
-  [Documentation](#) — view our help documentation
-  [FAQ](#) — a compilation of our Frequently Asked Questions
-  [Release notes](#) — information about the latest COSMIC release
-  [Licensing FAQ](#) — information about our licensing policy

- Search for Disease, Gene, Variant, Sample, Study in either search bar
- Much information is open to public, but some features require a subscription/login.
- News window in upper right.
- Tools – Cancer Browser
- Data Curation information and details
- Release Notes – inform of new additions/advancements to COSMIC

Select Data Source - COSMIC vs. Cell Lines



The screenshot shows the COSMIC website header with a navigation menu. The 'Projects' dropdown is open, and 'Cell Lines Project' is highlighted with a yellow box. Below the menu, there is a search bar and a 'Projects' section with descriptions for COSMIC and the Cell Lines Project.

COSMIC
Catalogue Of Somatic Mutations In Cancer

Projects ▾ Data ▾ Tools ▾ News ▾ Help ▾ About ▾ Search COS

COSMIC

Cell Lines Project

COSMIC-3D

Cancer Gene Census

COSMIC legacy site

eg *Braf, COLO-829, Carcinoma, V600E, BRCA-UK, Campbell*

Projects

COSMIC is divided into several distinct projects, each presenting a separate dat

COSMIC
The core of COSMIC, an expert-curated database of somatic mutation:

Cell lines project
Mutation profiles of over 1,000 cell lines used in cancer research

- Cell Lines Project and COSMIC house different data.
- To select a cell line to look into, look at the Cell Line Browser, or NCI-60 Browser if applicable

Cell Lines Data

- Once you select a cell line to view, sample page opens.
- Menu on left – click on any item in menu to navigate to that item or scroll to desired information.

Sample
COSS905991

- Overview
- Circos
- Genome browser
- Variants
- Mutation spectrum
- Sequence context
- Heatmap
- Non-mutant genes
- References

[Reset page](#)

Overview

This tab shows an overview of the data that we have for this sample. You can read more about these

Sample information

Sample name [OVCAR-8](#)

COSMIC sample ID COSS905991

Tumour location Ovary (Carcinoma)
View this tissue/histology in the [Cancer Browser](#)

Screening method n/a

Source	Sample type Cultured Sample
	Cell line source primary
	Sample source cell-line

Microsatellite instability (MSI)

BAT25	stable
BAT26	stable
D5S346	stable
D2S123	stable
D17S250	stable

Curated features n/a

Tumour details n/a

Individual details

Age	Unknown
Family	Unknown

- Overview– cell line information: sample type, demographics, institute, microsatellite stability, STR Profile, Sequence stats, and Downloadable files
- Mutation Spectrum tab – information can be matched to mutation profiles through COSMIC Home Page
- Sequence Context tab – bases flanking mutations
- Heatmap tab – shows frequent mutations



COSMIC
Catalogue Of Somatic Mutations In Cancer



CANCER
GENOMICS
CONSORTIUM

Educating for best practices in clinical cancer genomics

Cell Lines Variants tab

- Can view by variant type – tabs in window
 - Breakpoints: search by hg38 coordinates
- Exportable in .TSV and .CSV
- Click on Gene name to go to gene page
- Click on mutation nomenclature to go to mutation page – can determine mutation recurrence in cell lines dataset and pathway involvement

Mutations Fusions Breakpoints Non-Coding mutation CNV & Expression

Show 10 entries

Export: **CSV** TSV Search:

Gene	Transcript	Census Gene	AA Mutation	CDS Mutation	Somatic status	Zygoty	Validated	Type	Position
ABCC8	ENST00000389817	No	p.V222M	c.664G>A	Previously Reported	Homozygous	Verified	Substitution - Missense	11:17461741..17461741 g e!
ABCG8	ENST00000272286	No	p.D369Y	c.1105G>T	Previously Reported	Heterozygous	Verified	Substitution - Missense	2:43872116..43872116 g e!
ABCG8	ENST00000272286	No	p.L269L	c.807C>G	Unknown	Heterozygous	Unverified	Substitution - coding silent	2:43852711..43852711 g e!
ABI3BP ENST00000383691	ENST00000383691	No	p.T175fs*31	c.523delA	Unknown	Heterozygous	Unverified	Deletion - Frameshift	3:100824933..100824933 g e!
ABI3BP ENST00000471714	ENST00000471714	No	p.T898fs*31	c.2692delA	Unknown	Heterozygous	Unverified	Deletion - Frameshift	3:100824933..100824933 g e!
ABLIM2	ENST00000447017	No	p.C177F	c.530G>T	Unknown	Homozygous	Unverified	Substitution - Missense	g 4:8080727..8080727 e!
ABLIM2 ENST00000296372	ENST00000296372	No	p.C177F	c.530G>T	Unknown	Homozygous	Unverified	Substitution - Missense	g 4:8080727..8080727 e!
ABLIM2 ENST00000361737	ENST00000361737	No	p.C177F	c.530G>T	Unknown	Homozygous	Unverified	Substitution - Missense	g 4:8080727..8080727 e!
AC008537_5-2	ENST00000359667	No	p.V32I	c.94G>A	Unknown	Homozygous	Unverified	Substitution - Missense	19:40910603..40910603 g e!
AC010872_2	ENST00000405799	No	p.S1547C	c.4640C>G	Unknown	Heterozygous	Unverified	Substitution - Missense	2:21142107..21142107 g e!

Showing 1 to 10 of 584 entries

First Previous **1** 2 3 4 5 ... 59 Next Last

Mutation Filter: Mutation In Genes Recurrence Mutation Ty **Apply**

Mutation Filters

- Scroll right to see expandable mutation filters.



Mutation Filters ?

- [-] Mutation Impact i**
 - Pathogenic
 - Neutral
- [-] Genes**
 - All
 - Cancer Gene Census
- [-] Recurrence i**
 - Recurrent Substitutions
 - Recurrent Inframe Indels
 - Recurrent Terminations
- [+] Mutation Type**

Apply **Reset**

CNV and Expression Data

- Under/over expression
 - Z-Score
- CN Type
 - Minor allele
 - Copy number observed
 - Hg38 coordinates
- Average Ploidy

Mutations Fusions Breakpoints Non-Coding mutation **CNV & Expression**

Table Information Hide

The average ploidy of the genome is **3.10**. The table currently shows only **high value (numeric)** copy number data. Copy number segments are excluded if the total copy number and minor allele values are unknown.

Click [here](#) to include all copy number data. For more detailed information about copy number data and gain/loss definitions click [here](#).

Show entries Export: Search:

Gene	Expression	Expr Level (Z-Score)	CN Type	Minor Allele	Copy Number	CN Segment Posn.	Average Ploidy	Study	CNV
ACER3	Over ▲	3.16	Gain ▲	1	9	11:76722647..78387682 / / 3 1	3.10	619	6414491
AKT2	Over ▲	4.59	Gain ▲	1	11	19:39279756..40449204 / / 3 1	3.10	619	6495293
ALG8	Over ▲	4.35	Gain ▲	1	9	11:76722647..78387682 / / 3 1	3.10	619	6414491
ALG8_ENST00000376156	-	-	Gain ▲	1	9	11:76722647..78387682 / / 3 1	3.10	619	6414491
AQP11	Normal	0.96	Gain ▲	1	9	11:76722647..78387682 / / 3 1	3.10	619	6414491
B3Gn-T6	-	-	Gain ▲	1	9	11:76722647..78387682 / / 3 1	3.10	619	6414491
BLVRB	Normal	-1.22	Gain ▲	1	11	19:39279756..40449204 / / 3 1	3.10	619	6495293

Searching in COSMIC

- Search by disease type – brings you to Cancer Browser – see slides 24-30
- Search by gene – brings you to search results page that can link to gene/mutation overview (same format as Cell Lines Project)
- Search by mutation – bring you to mutation overview page (same format as Cell Lines Project)
- All data are derived directly from a cited data source
 - Usually a PubMed ID

Gene Overview Page

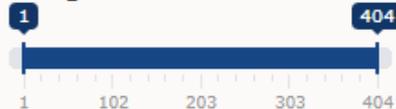
- Overview
- Gene view
- Genome browser
- Tissue distribution
- Mutation distribution
- Drug resistance
- Variants
- References

[Reset page](#)

Filters

[Show advanced filters](#)

Range



Coordinate system

- Amino-acid
- cDNA

- Several Items on Menu on left panel
 - Gene view – view domains within gene and where mutations reside
 - Genome browser - view genomic context
 - Overview – general information
 - Tissue – expression/mutations in each tissue type
 - Distribution – what kind of mutations observed?
 - Drug Resistance – do mutations confer drug resistance
 - Variants – table of observed variants in gene
 - References – curated references for gene

Gene Overview Page

Gene

PTEN

Overview

This section gives an overview of the selected gene, along with links to any related data and resources.

- Overview
- Gene view
- Genome browser
- Tissue distribution
- Mutation distribution
- Drug resistance
- Variants
- References

[Reset page](#)

Filters

[Show advanced filters](#)

Range



Coordinate system

- Amino-acid
- cDNA

Summary

Gene name PTEN
COSMIC gene ID COSG15
Genomic coordinates [10:87864470..87965472](#) (positive strand)
Synonyms BZS, MGC11227, MHAM, MMAC1, PTEN1, P60484, ENSG00000171862
COSMIC-3D There are **6** structures for **PTEN**. View them in [COSMIC-3D](#).



Number of samples 73549 unique samples
3765 unique samples with mutations

Alternative transcripts n/a

Sequences You can see various sequences for this gene:
[cDNA](#) (ENST00000371953)
[Protein](#) (PTEN)
[Transcript and protein aligned](#) (ENST00000371953+PTEN)

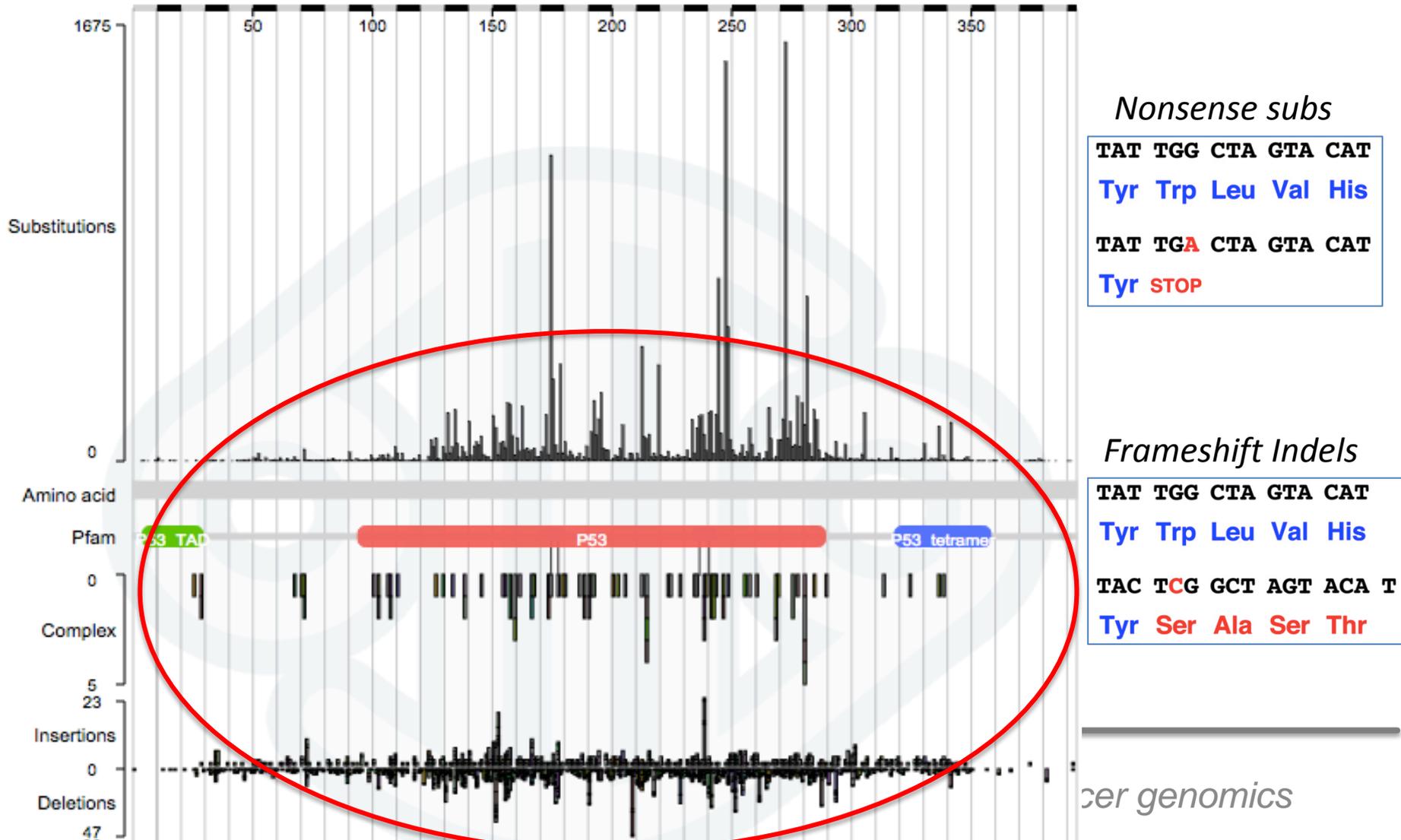
Attributes Census gene Curated gene Mouse gene Hallmark gene

Navigate the gene page by selecting an item from the left menu or scrolling through page.

p53 – an inactivating mutation profile

p53 is oncogenic when its activity is destroyed by inactivating mutations: **Loss - of - function.**

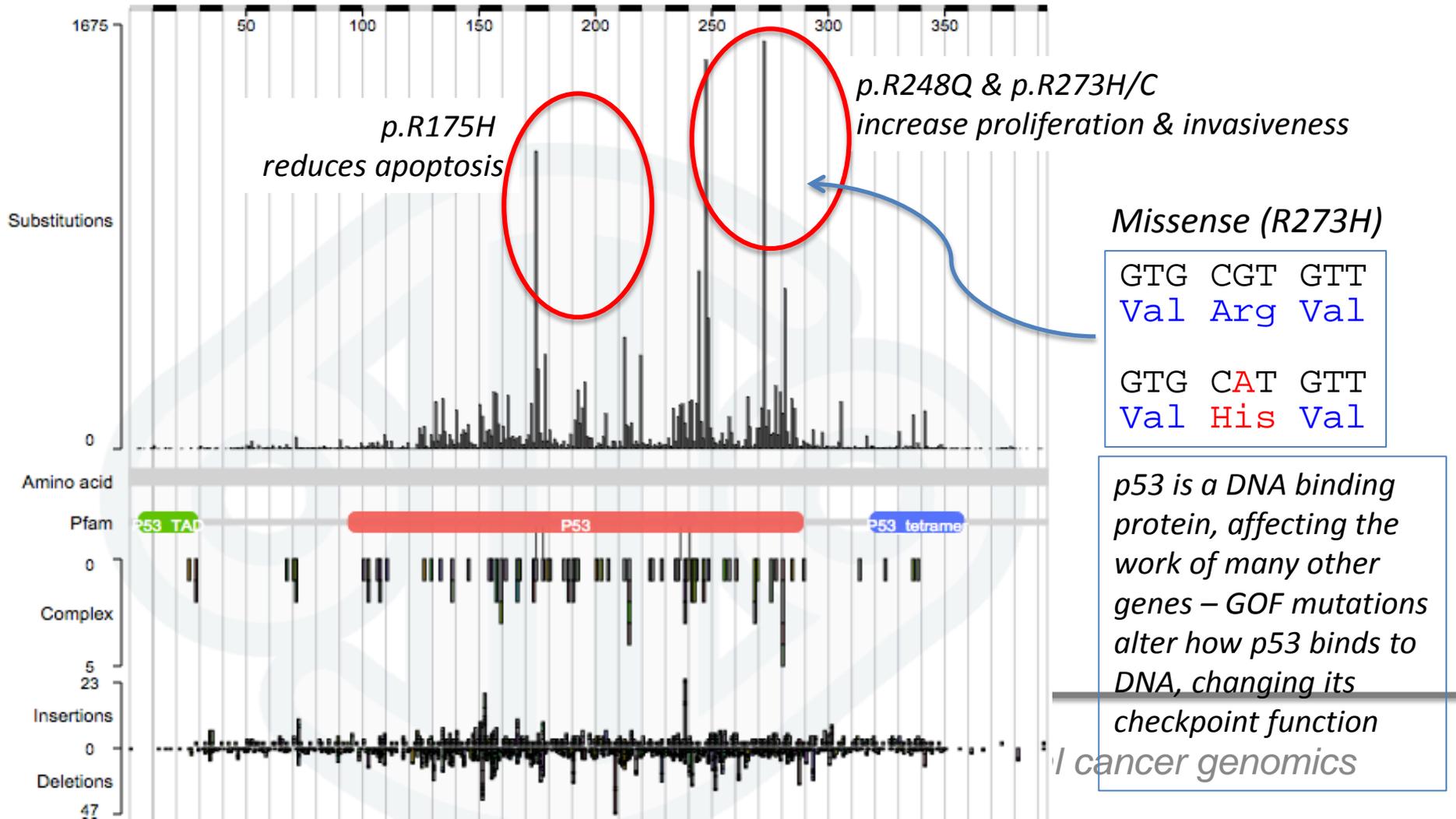
including substitutions, insertions and deletions which cause an early STOP codon



p53 – dominant missense mutations

However, specific p53 mutations also show **Gain – of – function**

- key missense substitutions cause an increase in malignancy
- and cause resistance to chemotherapies (eg cisplatin)



Mutation Overview

- Overview – general mutation information
- Tissue distribution – mutation frequency in tissue types
- Samples – table of affected samples
- Pathways Affected – table of affected pathways
 - Click link to go to WikiPathways
- References – links to relevant publications

Mutation Overview Page

COSMIC BETA
Catalogue Of Somatic Mutations In Cancer

Projects ▾ Data ▾ Tools ▾ News ▾ Help ▾ About ▾ Search COSMIC... SEARCH

Mutation Overview

COSM474

- Overview
- Tissue distribution
- Samples
- Pathways affected
- References

[Reset page](#)

This section shows a general overview of the selected mutation. It describes the source of the mutation i.e gene name and sequence level. You can see more information on our [help pages](#).

Mutation ID COSM474

Gene name [BRAF](#)

AA mutation p.V600R (Substitution - Missense, position 600, V→R)

CDS mutation c.1798_1799GT>AG (Complex)

Nucleotides inserted ag

Genomic coordinates GRCh38, [7:140753336..140753337](#), view [Ensembl contig](#)

CDD [NP_004324.2](#)

HomoloGene [3197](#), view the [multiple sequence alignment](#)

Ever confirmed somatic? Yes

FATHMM prediction n/a (score 0.00)

Remark n/a

Recurrent n/a

Drug resistance n/a

Cancer Gene Census

Projects

COSMIC is divided into several distinct projects, each presenting a separate dataset or view of our data:



COSMIC

The core of COSMIC, an expert-curated database of somatic mutations



Cell lines project

Mutation profiles of over 1,000 cell lines used in cancer research



COSMIC-3D

An interactive view of cancer mutations in the context of 3D structures



Cancer Gene Census

A catalogue of genes with mutations that are causally implicated in cancer

- Main Links under “Projects” Section on COSMIC home page.
- List is in table format and (with license) is exportable in .CSV or .TSV format.
- Genes marked as Hallmarks of Cancer have more functional descriptions available

– Click on



Cancer Gene Census

The Cancer Gene Census (CGC) is an ongoing effort to catalogue those genes for which mutations have been causally implicated in cancer. The original census and analysis was published in [Nature Reviews Cancer](#).

The census is not static but rather is updated regularly/as needed. In particular we are grateful to Felix Mitelman and his colleagues in providing information on more genes involved in uncommon translocations in leukaemias and lymphomas. Currently, more than 1% of all human genes are implicated via mutation in cancer. Of these, approximately 90% have somatic mutations in cancer, 20% bear germline mutations that predispose to cancer and 10% show both somatic and germline mutations.

Show 10 entries

Export: [CSV](#) [TSV](#) Search:

Gene Symbol	Name	Entrez GeneID	Genome Location	Hallmark	Chr Band	Somatic	Germline	Tumour Types(Somatic)	Tumour Types(Germline)	Cancer Syndrome	Tissue Type	Molecular Genetics	Role in Cancer	Muta Typ
ABL1	abl-interactor 1	10006	10:26748570-26860863		10p11.2	yes		AML			L	Dom	TSG; fusion	T
ABL1	v-abl Abelson murine leukemia viral oncogene homolog 1	25	9:130835447-130885683		9q34.1	yes		CML; ALL; T-ALL			L	Dom	oncogene; fusion	T; Mis
ABL2	c-abl oncogene 2; non-receptor tyrosine kinase	27	1:179107718-179143044		1q24-q25	yes		AML			L	Dom	oncogene; fusion	T
ACKR3	atypical chemokine receptor 3	57007	2:222908773-222941654		2q37.3	yes		lipoma			M	Dom	oncogene; fusion	T
ACSL3	acyl-CoA synthetase long-chain family	2181	2:222908773-222941654		2q36	yes		prostate			E	Dom	fusion	T

Cancer Gene Census

Census

- Cancer Gene Census
- Breakdown
- Abbreviations

[Reset page](#)

Cancer Gene Census

The Cancer Gene Census (CGC) is an ongoing effort to catalogue those genes...
The census is not static but rather is updated regularly/as needed. In particular...
lymphomas. Currently, more than 1% of all human genes are implicated via...
show both somatic and germline mutations.

Show entries

Gene Symbol ▲	Name ◆	Entrez GeneId ◆	Genome Location ◆	Hallmark ◆
ABI1	abl-interactor 1	10006	10:26748570-26860863	

- Click on buttons near the top of the browser or scroll down to see the “Breakdown” of the types of gene abnormalities in the Census or abbreviations used in the table.

Hallmarks of Cancer

COSMIC
Catalogue Of Somatic Mutations In Cancer

Projects ▾ Data ▾ Tools ▾ News ▾ Help ▾ About ▾ Search COSMIC... **SEARCH** Login ▾

ACKR3

atypical chemokine receptor 3

Function summary
scavenger receptor for chemokine CXCL12 in vascular endothelium [\[PubMed\]](#)

Role in cancer [oncogene](#)

Types of alteration in cancer overexpressed in breast cancer [\[PubMed\]](#)

Hallmarks of Cancer

Promotes

- proliferative signalling
promotes tumour growth in breast cancer [\[PubMed\]](#)
- invasion and metastasis
limits metastasis in breast cancer [\[PubMed\]](#)

Suppresses



Drug Resistance

- Main Link under “Data Curation” section on COSMIC home page.
- Resistance Data are available for 12 genes:
 - ABL1, ALK, BRAF, EGFR, ESR1, FLT3, KIT, MAP2K1, MAP2K2, PDGFRA, SMO, MET
- Table to view drug and resistance mutation frequency

Drug Resistance

- Manually curated list of genes that can carry resistance mutations to particular drugs.
- Click on gene name in table to see Gene Page. Scroll down to to the drug resistance section

Gene
EGFR

Drug resistance

This section shows the drugs that have been used to treat **EGFR** mutant tumours. In the tabs below genes.

You can change the list of drugs that are used to filter data in the panels below; click the name of a

Afatinib Erlotinib Gefitinib Osimertinib Tyrosine Kinase Inhibitor - NS

Update drugs

Genes Mutations

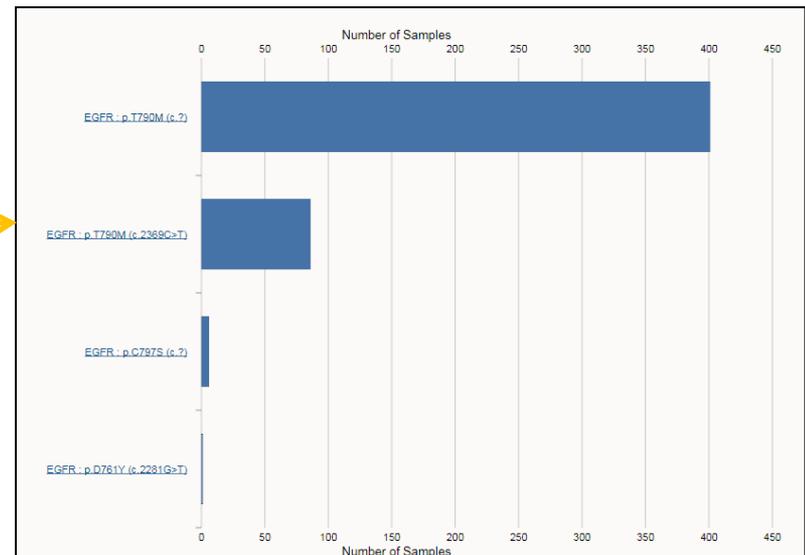
Mutations in the following genes confer resistance to one or more of the selected drugs.



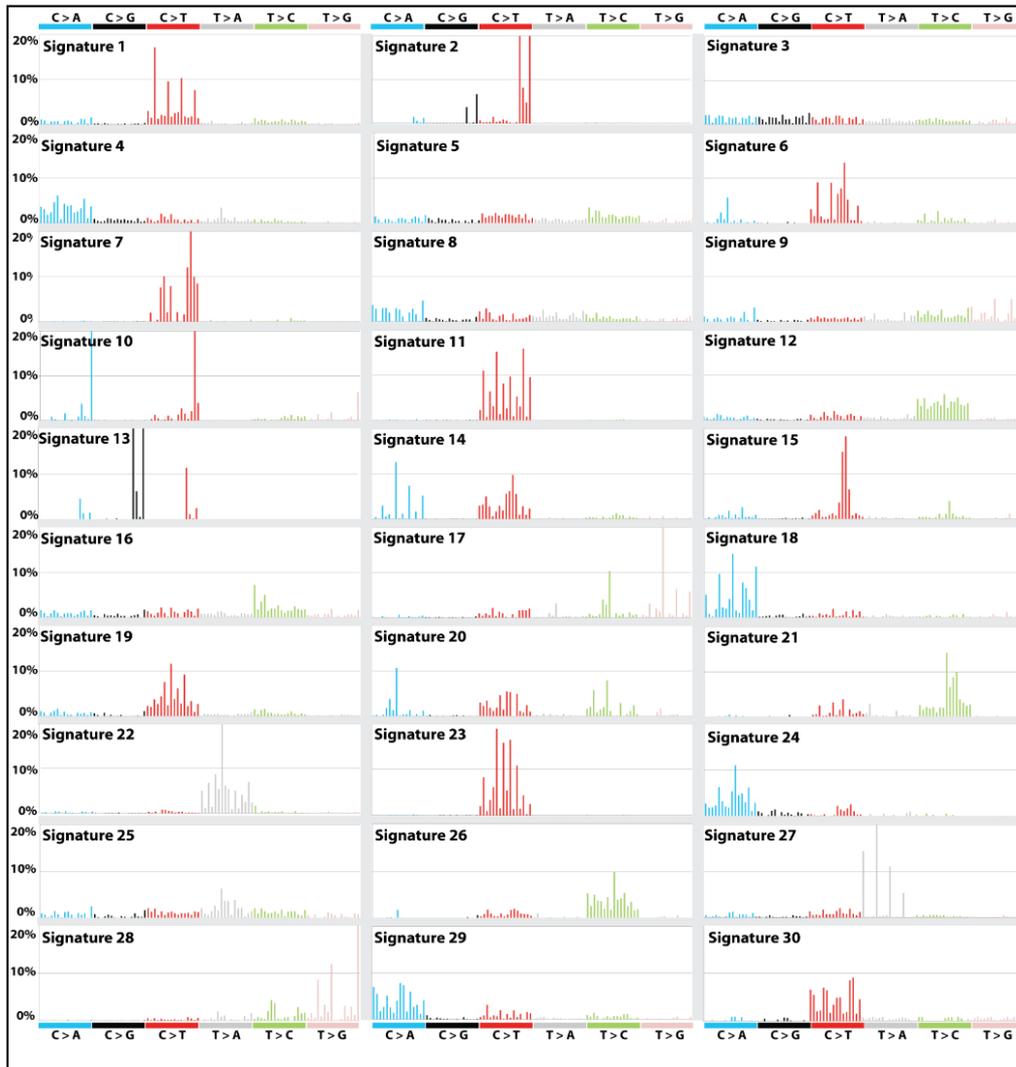
Colour	Gene	Unique resistant samples	Unique resistant mutations	Frequency (%)
Blue	EGFR	494	4	73.29
Green	ABL1	177	57	26.26
Red	MET	2	1	0.30
Orange	NF2	1	2	0.15
	Total	674	64	

Reset page

Filters
Show advanced filters



Mutational Signatures



- Selection under “Data” in top banner.
- Describes mutational signatures in detail and specifies diseases that carry each mutational signature.

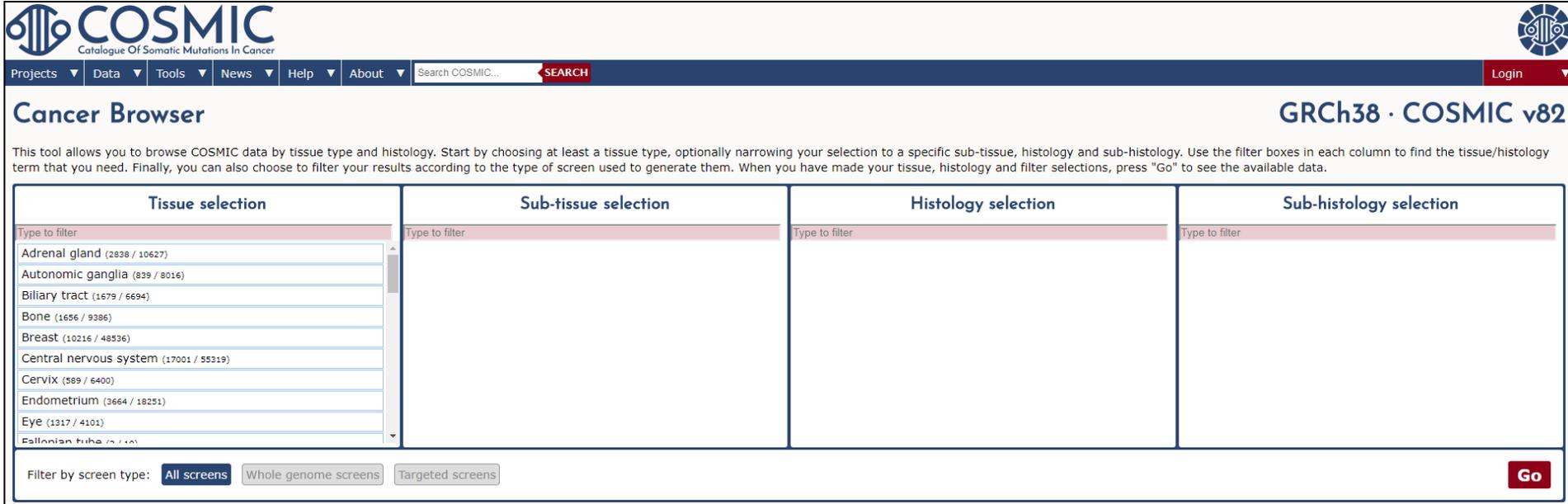
GRCh37 Cancer Archive

- If your lab has not converted to hg38, there is an option to view GRCh37/hg19 information on COSMIC.
- Under “Projects” in top banner, select GRCh37 archive to see legacy site.

Data Curation

- Other links under Expert Curation section on home page
 - **Gene Curation:** list of all genes with deep curation completed. Curation details included on Curated Genes page. Click on gene to go to gene page.
 - **Gene Fusion Curation:** list of all gene fusions with deep curation completed for solid tumors. Click on pair of gene to go to fusion overview page.
 - Fusion Overview page – information about in what kind of tissue fusion was observed and PMID.
 - **Genome Annotation:** Information and parameters used to analyze data.
 - **Drug Resistance:** See slides 19-20.

Cancer Browser



The screenshot shows the COSMIC Cancer Browser interface. At the top, there is a navigation bar with links for Projects, Data, Tools, News, Help, and About, along with a search bar and a Login button. The main heading is "Cancer Browser" and the version is "GRCh38 · COSMIC v82". Below the heading, a descriptive paragraph explains the tool's purpose. The main content area is divided into four columns: "Tissue selection", "Sub-tissue selection", "Histology selection", and "Sub-histology selection". Each column has a "Type to filter" input field. The "Tissue selection" column is currently populated with a list of tissues and their corresponding mutation counts. At the bottom, there is a "Filter by screen type" section with buttons for "All screens", "Whole genome screens", and "Targeted screens", and a "Go" button.

COSMIC
Catalogue Of Somatic Mutations In Cancer

Projects ▾ Data ▾ Tools ▾ News ▾ Help ▾ About ▾ Search COSMIC... **SEARCH** Login ▾

Cancer Browser

GRCh38 · COSMIC v82

This tool allows you to browse COSMIC data by tissue type and histology. Start by choosing at least a tissue type, optionally narrowing your selection to a specific sub-tissue, histology and sub-histology. Use the filter boxes in each column to find the tissue/histology term that you need. Finally, you can also choose to filter your results according to the type of screen used to generate them. When you have made your tissue, histology and filter selections, press "Go" to see the available data.

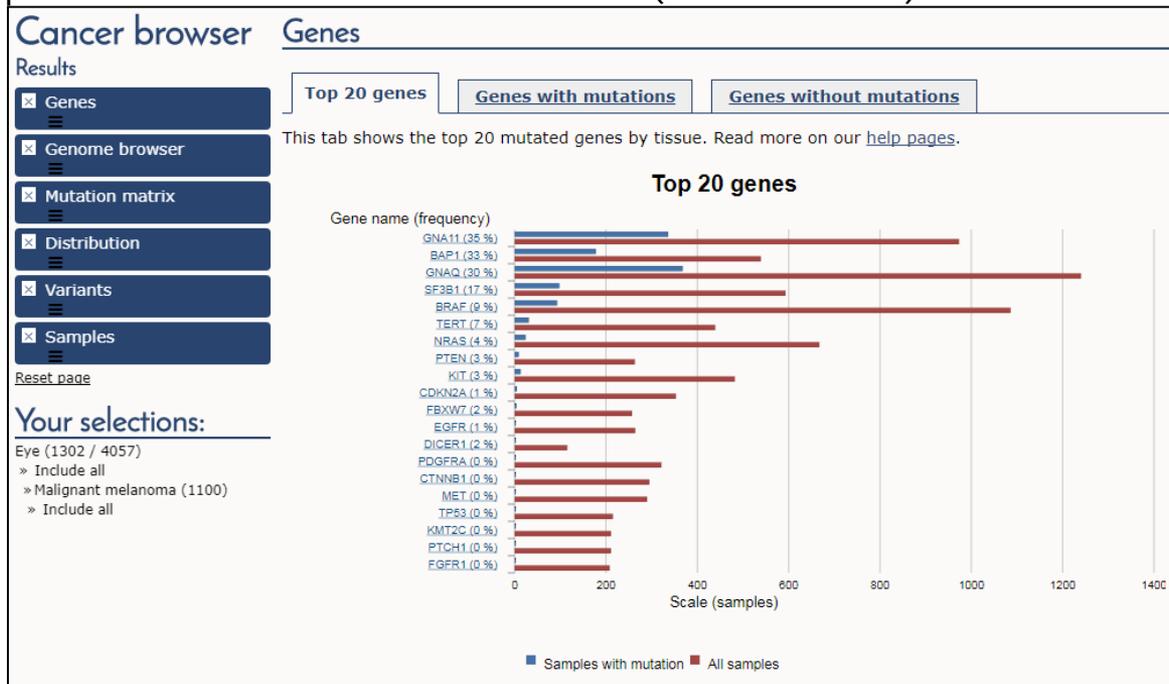
Tissue selection	Sub-tissue selection	Histology selection	Sub-histology selection
Type to filter Adrenal gland (2838 / 10627) Autonomic ganglia (839 / 8016) Biliary tract (1679 / 6694) Bone (1656 / 9386) Breast (10216 / 48536) Central nervous system (17001 / 55319) Cervix (589 / 6400) Endometrium (3664 / 18251) Eye (1317 / 4101) Fallopian tube (1 / 1)	Type to filter	Type to filter	Type to filter

Filter by screen type:

- Main link under "Tools" on home page
- Select tumor of interest by tissue and histology
- Press 'Go' in lower right corner of window

Cancer Browser

- Opens to bar graph of top 20 mutated genes in your selected type of cancer.
- In table format you can view and filter genes with and without mutations by mutation frequency or number of samples tested.
 - Exportable in .CSV or .TSV format (with license)

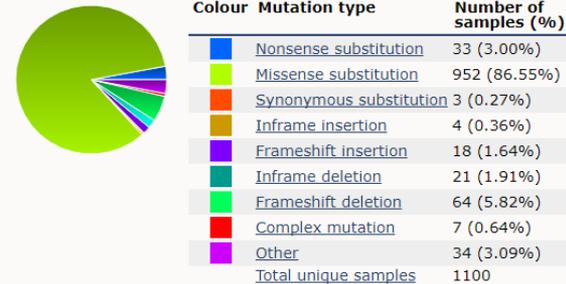


Cancer Browser: Distribution

- Distribution of mutations within your selected cancer type.
- Substitutions are described similarly base>base (not shown)
- Indels described by size in bps (Insertions displayed similar to deletions)

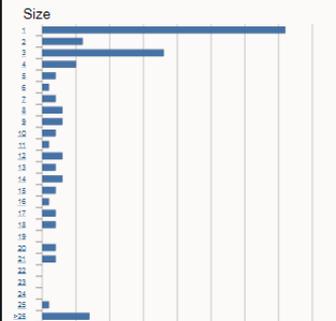
Summary

An overview of the types of mutation observed.



Deletions

This histogram shows the distribution of deletion size across samples. You can see [all samples with deletions](#).



Cancer Browser: Variants

- Observed Fusions, Mutations, Methylation status, and CNV/Expression data given in table format.
 - Exportable in .CSV and .TSV format (with license)
 - Click on mutations for mutation overview
 - Click on fusion pairing for Fusion overview
 - Click on gene for gene overview.

Variants

[Fusions](#) |
 [Mutations](#) |
 [Methylation](#) |
 [CNV & Expression](#)

This tab shows genes with mutations in the selected tissue/histology. Read more on our [help pages](#).

Show entries

Export: [CSV](#) [TSV](#) Search:

Genes	Samples	CDS Mutation	AA Mutation
AACS	E22	c.1122-9G>A	p.?
ABCA13	E11	c.14779-8delG	p.?
ABCA13	E19	c.14513G>A	p.R4838Q
ABCA13	E1	c.6308T>C	p.I2103T
ABCA13 FNST00000435803	E11	c.14944-8delG	p.?
ABCA13 FNST00000435803	E19	c.14678G>A	p.R4893Q
ABCA13 FNST00000435803	E1	c.6473T>C	p.I2158T
ABCA3	E12	c.2215G>A	p.G739R
ABCA5	E14	c.3430-6C>T	p.?
ABCA6	E20	c.792-5_792-2delTTTA	p.?

Cancer Browser: Samples

- Table of mutated and non-mutated samples
 - Exportable in .TSV or .CSV (with license)
 - Click on sample ID for sample overview page

Sample Overview Page

Sample

COSS1898448

- Overview
- Circos
- Genome browser
- Variants
- Mutation spectrum
- Sequence context
- Heatmap
- Non-mutant genes
- References

Reset page

Overview

This tab shows an overview of the data that we have for this sample. You can read more about these data on our [help pages](#).

Sample information

Sample name	NB-1110
COSMIC sample ID	COSS1898448
Tumour location	Autonomic ganglia (Neuroblastoma) View this tissue/histology in the Cancer Browser
Screening method	Whole exome screening
Source	
Sample type	NS
Origin of sample	NS
Sample source	NS

Microsatellite instability (MSI)

Curated features	n/a
Tumour details	n/a

Individual details

Age	Unknown
Normal tissue tested	Unknown
Gender	Unknown

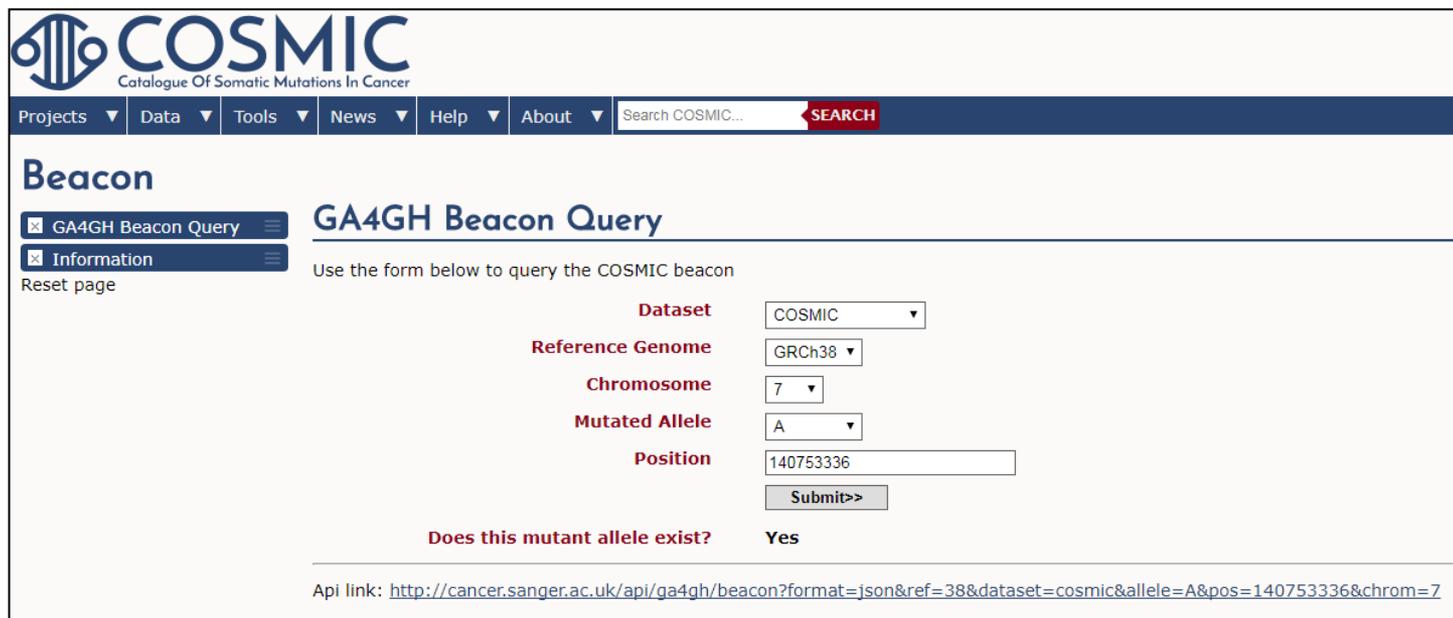
Other samples linked to the same individual

Supplier	n/a
External links	n/a
STR profile data	n/a
Sequence statistics	n/a

- Click on menu on left side of page or scroll to desired information
- Primary reference(s) and/or large study name are available in the reference section

GA4GH Beacon

- Main link under “Tools” on COSMIC home page
- GA4GH = Global Alliance for Genomics and Health – see Information section
- Shared URL format for query
 - <http://cancer.sanger.ac.uk/api/ga4gh/beacon/query?chrom=?;pos=?;allele=?>
- Can query if COSMIC or Cell Lines Project has observed a specific mutation at a designated genomic locus.



The screenshot shows the COSMIC website's GA4GH Beacon Query interface. At the top is the COSMIC logo and navigation menu. The main heading is "Beacon" with a sub-heading "GA4GH Beacon Query". There are two tabs: "GA4GH Beacon Query" (selected) and "Information". Below the tabs is a "Reset page" link. The form contains several fields: "Dataset" (COSMIC), "Reference Genome" (GRCh38), "Chromosome" (7), "Mutated Allele" (A), and "Position" (140753336). A "Submit>>" button is located below the position field. Below the form, there is a question "Does this mutant allele exist?" with the answer "Yes". At the bottom, an "Api link" is provided: <http://cancer.sanger.ac.uk/api/ga4gh/beacon?format=json&ref=38&dataset=cosmic&allele=A&pos=140753336&chrom=7>

COSMIC-3D

COSMIC-3D

A platform for understanding cancer mutations in the context of 3D protein structure.

[Learn more](#)

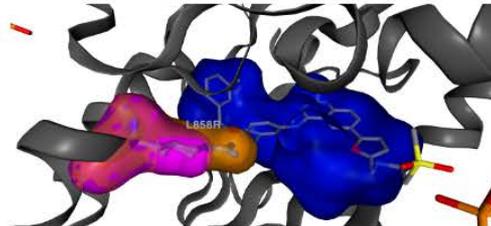
Visualise mutations



Overlay three types of cancer mutation, or a heatmap of missense recurrence, onto protein structure to add an extra dimension to COSMIC cancer genomic data.

[Explore »](#)

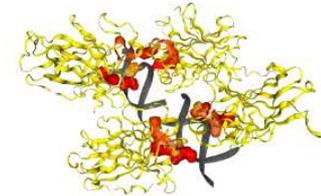
Generate hypotheses



See indicative models of missense mutants and generate hypotheses as to the effects of the mutation on protein structure and drug binding.

[Explore »](#)

Understand impact



Infer functional consequences from a different perspective on cancer mutation data.

[Explore »](#)

Getting Started

Search for a gene or protein, e.g. BRAF, EGFR, or BRCA2...

or

[Show me a demo!](#)

COSMIC – 3D

EGFR P00533 In Census 150 structures

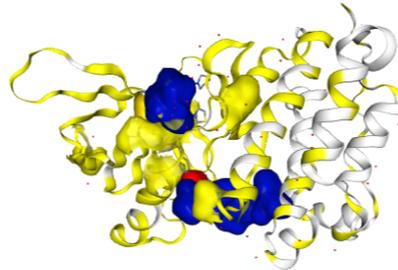
Single Structure Mode 

Receptor tyrosine kinase binding ligands of the EGF family and activating several signaling cascades to convert extracellular cues into appropriate cellular responses.

 External Links  Toggle Usage Hints  Share

3LZB/A/LEU834



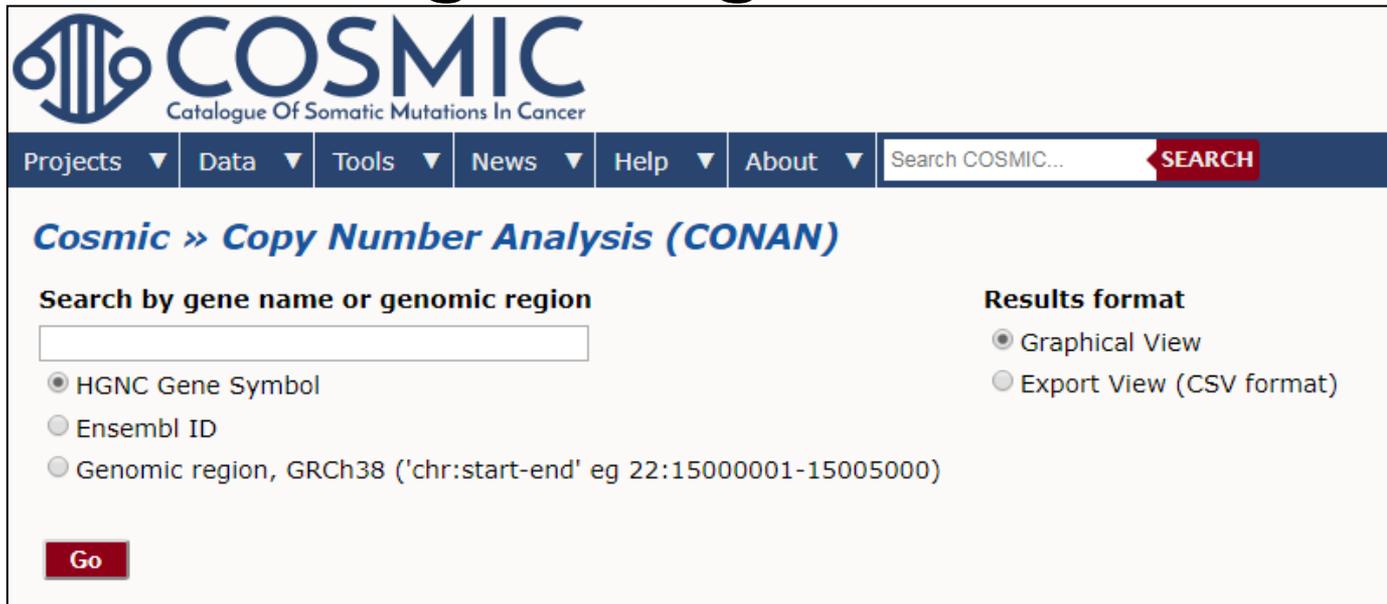
- SNV frequency depicted by yellow/orange segments
- Predicted small molecule binding sites in blue.
- Can take screenshot, pop screen out, drag mouse or click button to rotate protein structure for better view. 
- Several viewing and toggle options
- Protein property information
- UniProt sequence information and mutation information integrated.
- There are so many features within this application. Check them out!

COSMIC BigQuery

- If you have a COSMIC account, register at no charge for access to BigQuery.
- Research based queries of large datasets at minimal cost per query.
- Supports Standard SQL programming language and can be accessed by R
- <http://isb-cancer-genomics-cloud.readthedocs.io/en/latest/sections/COSMIC.html>

CONAN

- CONAN = COpy Number ANalysis – under “Tools” on Home page.
- Search by gene (HGNC or Ensembl) or genomic region (hg38)



The screenshot shows the COSMIC website interface for the CONAN tool. At the top, the COSMIC logo and name are displayed. Below the logo is a navigation bar with dropdown menus for Projects, Data, Tools, News, Help, and About. A search bar is located to the right of the navigation bar, with the text "Search COSMIC..." and a red "SEARCH" button. The main content area is titled "Cosmic » Copy Number Analysis (CONAN)". Below the title, there is a section for "Search by gene name or genomic region" with a text input field. Underneath the input field are three radio button options: "HGNC Gene Symbol" (selected), "Ensembl ID", and "Genomic region, GRCh38 ('chr:start-end' eg 22:15000001-15005000)". To the right of the search options is a "Results format" section with two radio button options: "Graphical View" (selected) and "Export View (CSV format)". At the bottom left of the search section is a red "Go" button.

CONAN

Cosmic » Copy Number Analysis (CONAN) » BAP1 ?

Ensembl:[3:52402288-52409878](#) | Cosmic:[BAP1](#)

Results for BAP1

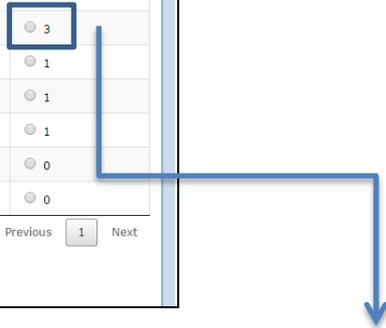
[Go](#)

Show All entries Search:

Tissues	Amplification	Homozygous Deletion	LOH
Breast (1749)	<input type="radio"/> 0	<input type="radio"/> 1	<input type="radio"/> 2
Central nervous system (1093)	<input type="radio"/> 0	<input type="radio"/> 0	<input type="radio"/> 2
Cervix (313)	<input type="radio"/> 0	<input type="radio"/> 3	<input type="radio"/> 0
Eye (80)	<input type="radio"/> 0	<input type="radio"/> 2	<input type="radio"/> 0
Kidney (1027)	<input type="radio"/> 0	<input type="radio"/> 2	<input type="radio"/> 5
Large intestine (771)	<input type="radio"/> 0	<input type="radio"/> 0	<input type="radio"/> 2
Lung (1185)	<input type="radio"/> 0	<input type="radio"/> 1	<input type="radio"/> 3
Oesophagus (220)	<input type="radio"/> 0	<input type="radio"/> 0	<input type="radio"/> 1
Pleura (108)	<input type="radio"/> 0	<input type="radio"/> 3	<input type="radio"/> 1
Skin (630)	<input type="radio"/> 0	<input type="radio"/> 0	<input type="radio"/> 1
Stomach (501)	<input type="radio"/> 0	<input type="radio"/> 1	<input type="radio"/> 0
Urinary tract (419)	<input type="radio"/> 1	<input type="radio"/> 1	<input type="radio"/> 0

Showing 1 to 12 of 12 entries Previous 1 Next

[Go](#)



Cosmic » Copy Number Analysis (CONAN) » BAP1 ?

Ensembl:[3:52402288-52409878](#) | Cosmic:[BAP1](#)

Results for BAP1

Show All entries Search:

Sample Name	Sample ID	CNV
TCGA-35-5375-01	1780088	LOH
TCGA-95-7043-01	1914101	LOH
TCGA-MP-A4TF-01	2194749	LOH

Showing 1 to 3 of 3 entries

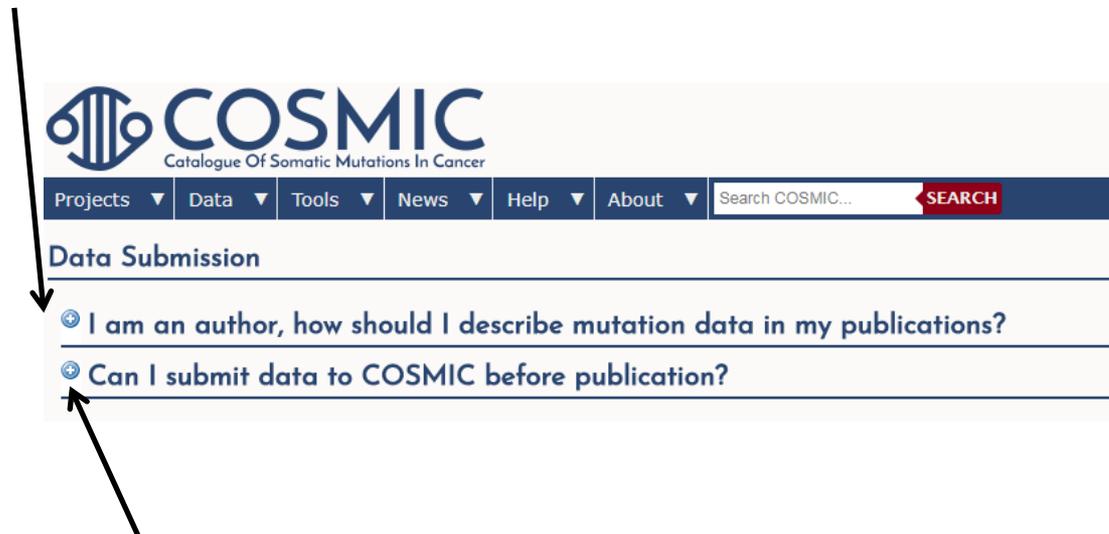
Previous 1 Next

Data Downloads

- Main Link under “Data” on Home Page
- Need license to download data
- Depending on the data you would like to download, you may need to download off of a SFTP site using a FTP tool like WinSCP or Filezilla

Data Submission

- Under Help → Data Submission
- Using COSMIC data or describing mutation data in results



- Submitting Data to COSMIC

Other Links Under Data

- Genome Annotation
- Datasheets – details about COSMIC versions
- Help – links to helpful overview resources
- FAQ – Frequently Asked Questions

Scenario #1

- You are a laboratory professional trying to identify genes to put on your lab's new breast carcinoma NGS panel.
 - Cancer Browser
 - Search Cancer Gene Census

Cancer Browser Query

Cancer Browser

GRCh38 · COSMIC v82

This tool allows you to browse COSMIC data by tissue type and histology. Start by choosing at least a tissue type, optionally narrowing your selection to a specific sub-tissue, histology and sub-histology. Use the filter boxes in each column to find the tissue/histology term that you need. Finally, you can also choose to filter your results according to the type of screen used to generate them. When you have made your tissue, histology and filter selections, press "Go" to see the available data.

Tissue selection	Sub-tissue selection	Histology selection	Sub-histology selection
Type to filter Adrenal gland (2838 / 10627) Autonomic ganglia (839 / 8016) Biliary tract (1679 / 6694) Bone (1656 / 9386) Breast (10216 / 48536) Central nervous system (17001 / 55219) CERVIX (589 / 6400) Endometrium (3664 / 18251) Eye (1317 / 4101) Fallopian tube (73 / 201)	Type to filter Include all Extramammary (70) Nipple (14) NS (10132)	Type to filter Include all Carcinoma (9018) Carcinoma in situ (266) Hyperplasia (66) NS (2) Other (864)	Type to filter Include all Acinic cell carcinoma (8) Adenoid cystic carcinoma (6) Basal (triple-negative) carcinoma (259) Ductal carcinoma (1514) Ductolobular carcinoma (22) ER-HER-positive carcinoma (15) ER-positive carcinoma (252) ER-PR-HER-positive carcinoma (28) ER-PR-negative carcinoma (130)
Filter by screen type: <input checked="" type="checkbox"/> All screens <input type="checkbox"/> Whole genome screens <input type="checkbox"/> Targeted screens			Go

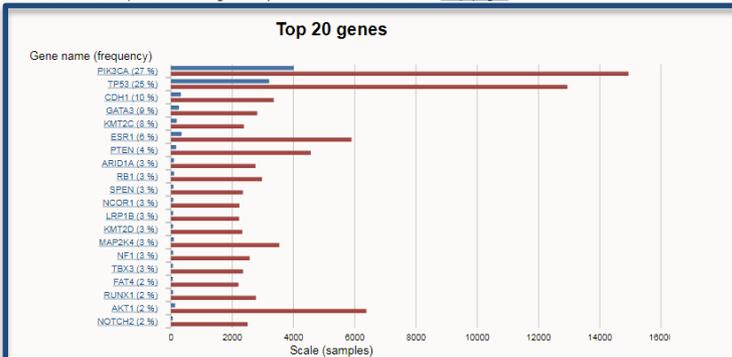
Cancer brow... Genes

Results

- Genes
- Genome browser
- Mutation matrix
- Distribution
- Variants
- Samples

Top 20 genes Genes with mutations Genes without mutations

This tab shows the top 20 mutated genes by tissue. Read more on our [help pages](#).



Search Cancer Gene Census

GRCh38 · COSMIC v85

Cancer Gene Census

The Cancer Gene Census (CGC) is an ongoing effort to catalogue those genes for which mutations have been causally implicated in cancer. The original census and analysis was published in [Nature Reviews Cancer](#).

The census is not static but rather is updated regularly/as needed. In particular we are grateful to Felix Mitelman and his colleagues in providing information on more genes involved in uncommon translocations in leukaemias and lymphomas. Currently, more than 1% of all human genes are implicated via mutation in cancer. Of these, approximately 90% have somatic mutations in cancer, 20% bear germline mutations that predispose to cancer and 10% show both somatic and germline mutations.

 Show entries

 Export: [CSV](#) [TSV](#) Search:

Gene Symbol	Name	Entrez GeneId	Genome Location	Hallmark	Chr Band	Somatic	Germline	Tumour Types(Somatic)	Tumour Types(Germline)	Cancer Syndrome	Tissue Type	Molecular Genetics	Role in Cancer
AKT1	v-akt murine thymoma viral oncogene homolog 1	207	14:104770341-104792643		14q32.32	yes		breast; colorectal; ovarian; NSCLC			E	Dom	oncogene
APOBEC3B	apolipoprotein B mRNA editing enzyme catalytic subunit 3B	9582	22:38982454-38992445		22q13.1		yes		breast cancer		E	Rec	oncogene; TSG
ARID1A	AT rich interactive domain 1A (SWI-like)	8289	1:26696404-26780756		1p35.3	yes		clear cell ovarian carcinoma; RCC; breast			E	Rec	TSG; fusion
ARID1B	AT rich interactive domain 1B	57492	6:156778104-157207891		6q25.1	yes		breast; hepatocellular carcinoma			E	Rec	TSG
BAP1	BRCA1 associated protein-1 (ubiquitin carboxy-terminal hydrolase)	8314	3:52402288-52409878		3p21.31-p21.2	yes	yes	uveal melanoma; breast; NSCLC; RCC	mesothelioma; uveal melanoma		E	Rec	TSG
BRCA1	familial breast/ovarian cancer gene 1	672	17:43045678-43124096		17q21	yes	yes	ovarian	breast; ovarian	hereditary breast/ovarian cancer	E	Rec	TSG

Results from Queries

Cancer Genome Browser
Query (Criteria \geq 3% mutated)
= 16 genes

- PIK3CA
- TP53
- CDH1
- GATA3
- KMT2C
- ESR1
- PTEN
- RB1
- SPEN
- ARID1A
- NCOR1
- KMT2D
- MAP2K4
- NF1
- TBX3
- LRP1B

Cancer Gene Census Query
= 32 genes

- CCND1
- KEAP1
- NOTCH1
- GATA3
- SMARCD1
- ESR1
- MAP3K13
- NCOR1
- TP53
- AKT1
- ARID1B
- TBX3
- ERBB2
- BRCA1
- BRCA2
- FOXA1
- CDKN1B
- ARID1A
- PBRM1
- SALL4
- EP300
- PIK3CA
- ETV6
- NTRK3
- CTCF
- PPM1D
- CASP8
- CDH1
- MAP3K1
- MAP3K4
- RB1
- BAP1

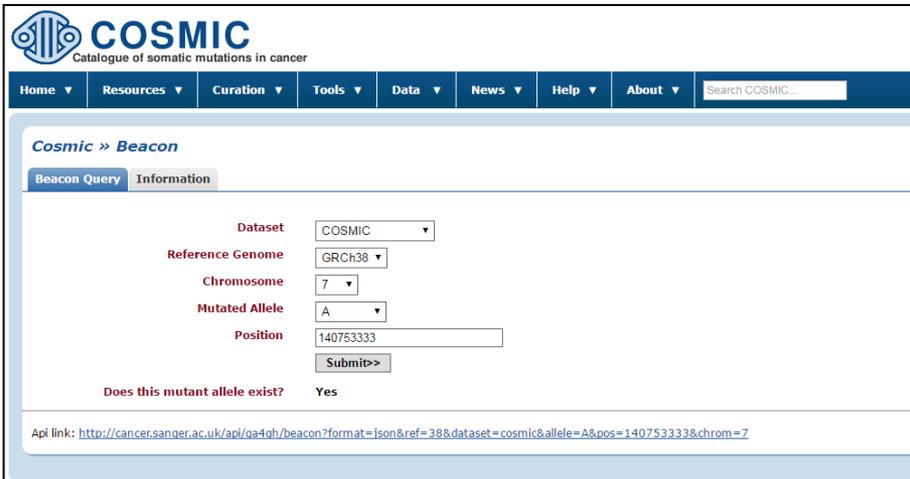
9 genes overlap between two lists = 39 total genes

Scenario #2

- A whole genome sequencing (WGS) case in your lab has a mutation that you haven't observed before. Does this mutant allele exist in COSMIC?
 - GA4GH Beacon
 - Chr7:140753333 (BRAF)
 - Mutated Allele = A

Yes – this is in COSMIC

- Mutation can be found in Genome browser on BRAF gene page or by entering the AA mutation or CDS Mutation Nomenclature



COSMIC
Catalogue of somatic mutations in cancer

Home ▾ Resources ▾ Curation ▾ Tools ▾ Data ▾ News ▾ Help ▾ About ▾

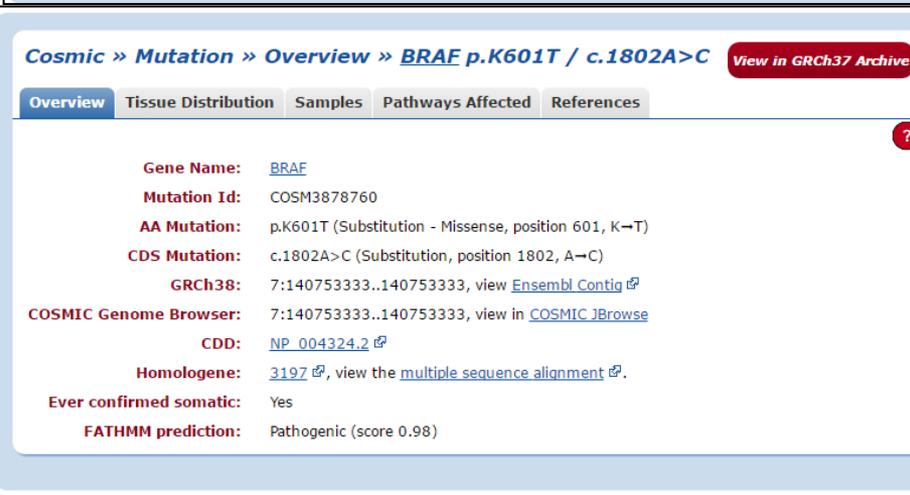
Cosmic » Beacon

Beacon Query Information

Dataset: COSMIC ▾
 Reference Genome: GRCh38 ▾
 Chromosome: 7 ▾
 Mutated Allele: A ▾
 Position: 140753333

Does this mutant allele exist? Yes

Api link: <http://cancer.sanger.ac.uk/api/qa4qh/beacon?format=json&ref=38&dataset=cosmic&allele=A&pos=140753333&chrom=7>



Cosmic » Mutation » Overview » BRAF p.K601T / c.1802A>C

Overview Tissue Distribution Samples Pathways Affected References

Gene Name: [BRAF](#)

Mutation Id: COSM3878760

AA Mutation: p.K601T (Substitution - Missense, position 601, K→T)

CDS Mutation: c.1802A>C (Substitution, position 1802, A→C)

GRCh38: 7:140753333..140753333, view [Ensembl Contig](#)

COSMIC Genome Browser: 7:140753333..140753333, view in [COSMIC JBrowse](#)

CDD: [NP_004324.2](#)

Homologene: [3197](#), view the [multiple sequence alignment](#).

Ever confirmed somatic: Yes

FATHMM prediction: Pathogenic (score 0.98)

Scenario #3

- Your lab is building a Pan Cancer List based on multiple resources.
 - Cancer Gene Census

Using Data from Cancer Gene Census

- If you have a license, download as .CSV or .TSV
 - This is useful as Excel if you'd like to sort data in different ways to stratify genes based on other criteria in COSMIC's table.
- Cancer Gene Census is updated with most version releases of COSMIC.

Scenario #4

- Mate Pair sequencing has picked up a translocation your lab has not yet reported.
 - NUP98/KDM5A
 - Search in “Gene fusion curation” under Data Curation

Curated Fusions

Fusions

Gene fusions, or translocations, resulting from chromosomal rearrangements are the most common mutation class. They lead to chimeric transcripts or to deregulation of genes through juxtapositioning of novel promoter or enhancer regions.

Gene fusions are manually curated from peer reviewed publications by expert COSMIC curators. A comprehensive literature curation is completed for each fusion pair when it is released in the database. Currently COSMIC includes information on fusions involved in solid tumours. Annotation of fusions associated with leukaemias and lymphomas will be added.

Select a gene pair from the list to go to the Overview page for that fusion and see all curated fusions for that pair, as well as the tissue types in which they were found and the associated publications. Many additional data points are curated for individuals (e.g. age, gender), tumour (e.g. stage, drug response) and samples (e.g. histology, sample source). This information can be found on the Sample Overview page.

Show entries

Search:

Genes	Samples	Mutations	Papers
NUP98/KDM5A_ENST00000399788	77	4	1

Showing 1 to 1 of 1 entries (filtered from 290 total entries)

Previous Next

- Click on fusion gene pairing to open fusion overview.
- Link to PMID and/or large scale studies on Reference tab.

Cosmic » Fusion » Overview » [NUP98:KDM5A_ENST00000399788](#)

[View in GRCh37 Archive](#)

[Fusions](#) [Tissues](#) [References](#)

Genes [NUP98 ->KDM5A_ENST00000399788](#)

Mutation ID	5' Partner Gene				3' Partner Gene				No. of Mutations	Mutation Frequency
	Gene Name	Last Observed Exon	Inferred Breakpoint	Inserted Sequence	Gene Name	First Observed Exon	Inferred Breakpoint	Inserted Sequence		
COSF2292	NUP98	13	1963	-	KDM5A_ENST00000399788	27	4819	-	1	25%
COSF2294	NUP98	?	?	-	KDM5A_ENST00000399788	?	?	-	3	75%
Total Mutations									4	100%

Scenario #5

- Your lab has a significant pool of data that you would like to contribute to COSMIC to enhance the knowledgebase.
 - COSMIC is exploring collaborative relationships with institutions aiming to release anonymized somatic mutation calls in COSMIC
 - COSMIC will highlight these laboratories in their webpages and strongly cite them as sources.
 - Contact COSMIC directly
 - Simon Forbes (Head of COSMIC): saf@sanger.ac.uk
 - COSMIC Helpdesk: cosmic@sanger.ac.uk

Future Features: Coming Soon

- Guide to Actionability
- Organoids
 - Data release for the [Human Cancer Model Initiative](#)
 - Better laboratory models – in preparation
- Cancer Mutation Census
 - identify driver mutations across all diseases

Online Tutorials

- COSMIC Site Overview:
<https://www.youtube.com/watch?v=whxIL86gnKA>
- Sample Data Tutorial:
https://www.youtube.com/watch?v=5dqInH8_LAo
- Cancer Browser Tutorial:
<https://www.youtube.com/watch?v=k477uAiKx74>
- Gene Pages Tutorial:
<https://www.youtube.com/watch?v=2FD5RabgK6o>
- Fusions Tutorial:
<https://www.youtube.com/watch?v=M9ILszjsuAw>
- COSMIC Search Tutorial:
<https://www.youtube.com/watch?v=SVfloi4hfNM>
- **DISCLAIMER:** These tutorials all provide instruction on how to use older versions of COSMIC. The latest version of COSMIC looks different and has different features.

Citation

- Forbes et al. COSMIC: somatic cancer genetics at high-resolution. *Nucleic Acids Research* (2017)45(D1):D777-D783. Available online: <https://doi.org/10.1093/nar/gkw1121>

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