

## TP53 Mutations in Cell Lines compendium

### Installation:

To install the compendium

I) Decompress the file

You can unzip .zip files in Windows XP, Vista, 7, and Mac OS X by using unzipping software that supports the file extension.

II) Drag the folder to any folder on your hard drive. The “Applications” folder is recommended, but not required.

On a Mac, the folder contains 4 files. The application file is shown with a red arrow

▼ Cell_Lines_Compendium_v3.1	➡	139.1 Mo
CLC_31.fmpur	➡	9.7 Mo
Cell_Lines_Compendium_v3.1	➡	118.1 Mo
▶ Extensions	➡	11 Mo
FMP Acknowledgements.pdf	➡	128.5 Ko

On a PC with Windows, the folder contains 46 files (All files do not appear on the figure). The application file is shown with a red arrow

▼ Cell_Lines_Compendium_v3.1	➡	211.1 Mo
▶ Extensions	➡	128.5 Mo
CLC_31.fmpur	➡	9.7 Mo
FMRSRC.dll	➡	9.7 Mo
Cell_Lines_Compendium_v3.1.exe	➡	9.2 Mo
ToolkitPro1122vc110U.dll	➡	8.1 Mo
▶ SASL2	➡	6.5 Mo
DBEngine.dll	➡	6.1 Mo
FMEngine.dll	➡	4.4 Mo
mfc110u.dll	➡	4.4 Mo
mfc110.dll	➡	4.4 Mo
Support.dll	➡	2.3 Mo

## Detailed description of the "Search by Cancer" panel

Menu Cancers Mutations Names

### SEARCH BY CANCER

Cancer

1 All ☐

1 Tumor Type 1 Astrocytoma

1 Tumor Type 2

1 Tumor Type 3

Reset the search criteria

2 TP53 Status

3 Mutant Frequency

4 Complexity

5 Variant Classification

All ☐

Wild Type ☐

Mutant ☒

All ☐

Frequent (100+) ☒

Unfrequent (10-99) ☐

Rare (1-9) ☐

All ☐

One mutant per cell line ☒

Two mutants per cell line ☐

Multiples mutants per cell line ☐

All ☐

Missense mutation ☒

Silent mutation ☐

Nonsense mutation ☐

Frameshift mutation ☐

Tandem mutation ☐

GO

The user can perform the search for all cancer types or can choose up to three different types of cancer (green stamp 1).

Four filters are available to refine the search:

*TP53 status (green stamp 2):*

Cell line expressing wild-type or mutant TP53

After selecting cell lines that express wild-type TP53, the other three filters are dimmed, as they are related to mutant TP53.

*Mutant frequency (green stamp 3):*

Mutants have been classified into three categories according to their frequencies in the database; frequent (more than 100 occurrences); infrequent (between 10 and 100 occurrences in the database; rare (between 1 and 9 occurrences in the database).

*Complexity (green stamp 4):*

Complexity refers to the number of mutations in the cell line. Although the majority of cell lines have only one mutation, a few cell lines express two or more mutations.

*Variant classification (green stamp 5):*

The user can choose a specific type of mutation such as missense, nonsense, silent, tandem or frameshift.

## Detailed description of the "Search by mutant" panel

The screenshot shows the 'Search by mutant' panel with the following elements:

- Green Stamp 1:** Points to the 'Tumor Type 1' dropdown menu, which is currently set to 'Esophageal SCC'. Below it are 'Tumor Type 2' and 'Tumor Type 3' dropdowns.
- Green Stamp 2:** Points to the 'Codon Position' section, which includes an 'All' checkbox and three input fields labeled 'aa 1', 'aa 2', and 'aa 3'.
- Green Stamp 3:** Points to the 'Mutant Frequency' section, which includes an 'All' checkbox and three radio button options: 'Frequent (100+)', 'Unfrequent (10-99)', and 'Rare (1-9)'. The 'Frequent (100+)' option is selected.
- Green Stamp 4:** Points to the 'Variant Classification' section, which includes an 'All' checkbox and six radio button options: 'Missence mutation', 'Silent mutation', 'Nonsense mutation', 'Frameshift mutation', and 'Tandem mutation'. The 'Nonsense mutation' option is selected.

Other visible elements include a 'Cancer' label, a 'Reset the search criteria' button, and a 'GO' button at the bottom.

The user can perform the search for all cancer types or can choose up to three different types of cancer (green stamp 1).

Three filters are available to refine the search:

*Codon position (green stamp 2):*

The user can choose up to three different codons (e.g. 175 and 213 and 248).

*Mutant frequency (green stamp 3):*

Mutants have been classified into three categories according to their frequencies in the database; frequent (more than 100 occurrences); infrequent (between 10 and 100 occurrences in the database; rare (between 1 and 9 occurrences in the database).

*Variant classification (green stamp 4):*

The user can choose a specific type of mutation such as missense, nonsense, silent, tandem or frameshift.

## Detailed description of the "Search by Names" panel

Menu Cancers Mutations **Names**

SEARCH BY NAMES

0 - 9 A - C D - F G - I J - L M - O P - R S - U V - Z NCI-60 cell lines

91 Items

Click on the name

010627NSGF	110	201T	526	8505C
1	111	20842P	58	866MT
107	1861	20M	59M	8823
121	19	2211M	6	8823
121LN	1LN	30966M	6	8842
122LN	2	32	607B	8902
123	2081	3522 S2	622	8988S
124	2098	380	624	9
136-2	2207	4	63	92VU040
1402P	2218	4197	639-V	92VU041
14362M	222	42-MG-BA	64	92VU059
1455	2224	42-MG-BA	647-V	
154	22Rv1	440	647-V	
16396M	23132-87	451Lu	697	
17697M	2319	4686M	769-P	
1833	2436	486P	786-0	
183A	253J	518A2	786-0	
185	2774	5637	8-MG-BA	
1890	293	584	8305C	
1994	2L1	59	8402	

The various cell lines can be browsed by using the various tabs (red stamp 1). A specific tab devoted to the NCI-60 panel is available (red stamp 2).

Clicking on the cell name opens the mutation description panel.

Mutant List

SEARCH BY MUTANTS

2 files

CRITERIA

1

Cancer

Esophageal SCC

2

Codon Position

3

Frequency

Frequent (100+)

4

Variant Classification

Nonsense Mutation

5

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Sample ID	ATCC	Cancer	cDNA variant	Protein variant	Complexity	Tand Class	Variant Classification	Rec. Numb.	WAF1 %	Reference
TE-14		Esophageal SCC	c.637C>T	p.R213*	SM		Nonsense_Mutation	619		2932
TE-15		Esophageal SCC	c.1024C>T	p.R342*	DMU		Nonsense_Mutation	175		2249

The mutant list is displayed after selecting the various criteria.  
The top row summarizes the various criteria selected for the search.  
The list includes 11 informative items.

<b>Sample ID</b>	Name of the cell line
<b>ATCC</b>	ATCC number if available
<b>Cancer</b>	Cancer type
<b>cDNA variant</b>	Position of the mutation using the full length cDNA as reference
<b>Protein variant</b>	Position of the mutation using the full length protein as reference
<b>Complexity</b>	<p>Number of mutations in the cell line.</p> <p><b>SM</b>: Single mutational event in the tumor;</p> <p><b>DMU</b> (Double Mutation Unknown): Two p53 mutations in the same tumor but their allelic distribution is unknown;</p> <p><b>DMD</b> (Double Mutation Different allele): Two p53 mutations in the same tumor on two different p53 alleles;</p> <p><b>DMD</b> (Double Mutation Same allele): Two p53 mutations in the same tumor on the same p53 allele;</p> <p><b>MM</b> (Multiple Mutations): More than two p53 mutations in the same tumor.</p>
<b>Tandem class</b>	<p>The majority of tandem mutations are found in skin tumors.</p> <p>Two types of tandem mutation can occur in the open reading frame of the TP53 gene (or any other gene).</p> <p><b>T1</b>: each substitution targets two different codons.  e.g.: codons 247 and 248 of the TP53 gene: AAC - CCG -&gt; AAT- TGG  Although two codons are targeted, the mutation is considered to be a single mutational event linked to UV exposure  c.[741C-&gt;T;742C-&gt;T]  In the majority of T1 tandem mutations, the first substitution does not change the amino acid residue and leads to a synonymous change.</p> <p><b>T2</b>: each substitution targets the same nucleotide.  e.g.: codon 151, TCC -&gt;TTT  This mutation is considered to be a single mutational event linked to UV exposure  c.[530C-&gt;T;531C-&gt;T]</p>
<b>Variant classification</b>	Translational effect of the mutation. (missense, nonsense, silent, or frameshift)
<b>Rec Numb.</b>	Number of occurrences of the mutant in the database
<b>Waf1 %</b>	Residual transcriptional activity of the mutant on the WAF1 promoter (% compared to wild-type p53).
<b>Reference</b>	Reference identification number

Clicking on the cell name opens the mutation description panel.

Panel view

CLOSE

1

Cell line 8-MG-BA

< Panel >

Click to toggle the panels

P1

ATCC

Cancer

Protein variant

cDNA variant

Complexity

Mutation\_Type

Exon / Intron

Domain

Structure

Post\_Translation

Variant\_Classification

Variant\_Comment

Astrocytoma

p.R273C

c.817C>T

SM

B

8

HCD V - DNA binding

Beta Strand S1

Missense\_Mutation

Exonic\_Mutation

UMD Comment Frequency

UMD Comment Outliers

UMD Comment Activity

UMD Comment Splicing

This is a hot spot mutant

This mutant is inactive

No potential effect on splicing

Frcy in the UMD database

Activity

SIFT

Polyphen

Mut Assessor

Provean

CONDel

Comments

1177

.91

Damaging

probably damaging

medium

Deleterious

deleterious

Mutation in COSMIC database

P2

UMD ID

COSMIC ID

Gene reference

HG19

HG18

cDNA reference

t1

t2

t3

t4

t5

t6

t7

t8

Protein reference

P1 (TP53\_alpha)

P3 (TP53\_beta)

P4 (TP53\_gamma)

P8 (Delta40\_TP53\_alpha)

P9 (Delta 40\_TP53\_beta)

P10 (Delta 40\_TP53\_gamma)

P5 (Delta 133\_TP53\_alpha)

P6 (Delta 133\_TP53\_beta)

P7 (Delta 133\_TP53\_gamma)

P11 (Delta160\_TP53\_alpha)

P12 (Delta160\_TP53\_beta)

P13 (Delta160\_TP53\_gamma)

25522

10659

chr17:g.7577121C>T

chr17:g.7517846C>T

LRG\_321t1:c.817C>T

LRG\_321t2:c.814C>T

LRG\_321t3:c.817C>T

LRG\_321t4:c.817C>T

LRG\_321t5:c.421C>T

LRG\_321t6:c.421C>T

LRG\_321t7:c.421C>T

LRG\_321t8:c.934C>T

LRG\_321p1:p.R273C

LRG\_321p3:p.R273C

LRG\_321p4:p.R273C

LRG\_321p8:p.Y234C

LRG\_321p9:p.Y234C

LRG\_321p10:p.Y234C

LRG\_321p5:p.C141C

LRG\_321p6:p.C141C

LRG\_321p7:p.C141C

LRG\_321p11:p.L114C

LRG\_321p12:p.L114C

LRG\_321p13:p.L114C

Clicking on the name of the cell line opens panel 1 (red stamp 1).  
 Panel two (red stamp 2) can be toggled by using the arrows at the top or in the middle of the panel.

Panel 1

ATCC	An official reference is available for several cell lines distributed by repository centers
Cancer	Cancer name
Protein variant	Mutation nomenclature according to <a href="#">HGVS</a> standards using the protein sequence as reference. Full length TP53 protein isoform is used (393 aa)
cDNA variant	Mutation nomenclature according to <a href="#">HGVS</a> standards using the coding sequence as reference. (1 is the A of the start ATG): reference sequence <a href="#">NM_000546.5</a>
Complexity	<b>SM:</b> Single mutational event in the tumor; <b>DMU</b> (Double Mutation Unknown): Two p53 mutations in the same tumor but their allelic distribution is unknown; <b>DMD</b> (Double Mutation Different allele): Two p53 mutations in the same tumor on two different p53 alleles; <b>DMD</b> (Double Mutation Same allele): Two p53 mutations in the same tumor on the same p53 allele; <b>MM</b> (Multiple Mutation): More than two p53 mutations in the same tumor.  Tandem mutations are considered to be a single event in the tumor, as they originate from a single alteration to two adjacent nucleotides.
Mutation type	<b>B:</b> single missense mutation <b>D:</b> deletion <b>I:</b> insertion <b>T:</b> tandem mutation <b>ID:</b> indel mutation
Exon / Intron	Localization of the mutation

Domain	<p>Domains of the TP53 protein</p> <p><b>HCD I to V:</b> Highly Conserved Domains I to V;  <b>DNA Binding:</b> DNA binding domain;  <b>Negative regulation:</b> carboxy-terminus of the p53 protein associated with negative regulation of p53 DNA binding activity;  <b>Transactivation:</b> transactivation domain of the p53 protein  <b>TAD1:</b> transactivation domain 1  <b>TAD2:</b> transactivation domain 2  <b>Proline Rich:</b> Proline-rich domain of the p53 protein;  <b>NES:</b> Nuclear export signal of p53;  <b>NLS:</b> Nuclear localization signal of p53;  <b>Oligomerization:</b> Tetramerization domain of the p53 protein.  <b>NA:</b> No specific domain available</p>
Structure	Structural motif of the TP53 protein according to the analysis described by <a href="#">Cho et al. (1994)</a>
Post Translation	Displays potential posttranslational modifications at the position of the mutant
Variant classification	Translational effect of the mutation. (missense, nonsense, silent, or frameshift)
Variant comment	Specific comment concerning the consequences of the mutation
UMD comment frequency	Specific information related to the frequency of the mutation
UMD comment outliers	Indicates whether or not the mutation is associated with outlier publications
UMD comment activity	Specific information related to the frequency of the mutation in the database
UMD comment splicing	Indicates whether the mutation can alter splicing
Frequency	Occurrence of this mutant in the database
Activity	Residual transcriptional activity of mutant p53 on the WAF1 promoter (% compared to wild-type p53)
SIFT	Predicted pathogenicity using SIFT algorithm
Polyphen	Predicted pathogenicity using Polyphen algorithm
Mutassessor	Predicted pathogenicity using Mutassessor algorithm
Provean	Predicted pathogenicity using Provean algorithm
Condel	Predicted pathogenicity using Condel algorithm
Comment	Final comment

## Panel 2

UMD_ID	Unique file identifier
COSMIC_ID	Mutation identifier used in COSMIC
HG19	Localization of the mutation in the TP53 gene using HG19 as reference
HG18	Localization of the mutation in the TP53 gene using HG18 as reference
<i>Mutation nomenclature and coordinates used below are expressed according to HGVS and the LRG</i>	
Transcript t1	Localization of the mutation in transcript 1
Transcript t2	Localization of the mutation in transcript 3
Transcript t3	Localization of the mutation in transcript 3
Transcript t4	Localization of the mutation in transcript 4
Transcript t5	Localization of the mutation in transcript 5
Transcript t6	Localization of the mutation in transcript 6
Transcript t7	Localization of the mutation in transcript 7
Transcript t8	Localization of the mutation in transcript 8
Protein p1 (TP53)	Localization of the mutation in protein p1
Protein p3 (TP53_beta)	Localization of the mutation in protein p3
Protein p4 (TP53_gamma)	Localization of the mutation in protein p4
Protein p8 (Delta_40_TP53)	Localization of the mutation in protein p8
Protein p9 (Delta_40_TP53_beta)	Localization of the mutation in protein p9
Protein p10 (Delta_40_TP53_gamma)	Localization of the mutation in protein p10
Protein p5 (Delta_133_TP53_alpha)	Localization of the mutation in protein p5

Protein p6 (Delta_133_TP53_beta)	Localization of the mutation in protein p6
Protein p7 (Delta_133_TP53_gamma)	Localization of the mutation in protein p7
Protein p11 (Delta_160_TP53_alpha)	Localization of the mutation in protein p11
Protein p12 (Delta_160_TP53_beta)	Localization of the mutation in protein p12
Protein p13 (Delta_160_TP53_gamma)	Localization of the mutation in protein p13



## TP53 mutant display

Example: Cell line 42-MG-BA from the NCI-60 panel that expressed two TP53 mutants

CLOSE
1
Cell line 42-MG-BA
Panel 2 >
Click to toggle the panels

P1

ATCC	
Cancer	glioma
Protein variant	p.T211I
cDNA variant	c.632C>T
Complexity	DMU
Mutation_Type	B
Exon / Intron	6
Domain	DNA binding
Structure	
Post_Translation	Thr Phosphorylation
Variant_Classification	Missense_Mutation
Variant_Comment	Exonic_Mutation

UMD Comment Frequency

This mutation is very frequent

UMD Comment Outliers

UMD Comment Activity

This mutant is inactive

UMD Comment Splicing

No potential effect on splicing

Frcy in the UMD database

35

Activity

13.49

SIFT

Damaging

Polyphen

probably damaging

Mut Assessor

medium

Provean

Deleterious

CONDel

deleterious

Comments

This cell line contains 2 mutations.
Click the button to toggle between the multiples mutations

CLOSE
2
Cell line 42-MG-BA
Panel 2 >
Click to toggle the panels

P1

ATCC	
Cancer	glioma
Protein variant	p.R282Q
cDNA variant	c.845G>A
Complexity	DMU
Mutation_Type	B
Exon / Intron	8
Domain	HCD V - DNA binding
Structure	Helix H4
Post_Translation	
Variant_Classification	Missense_Mutation
Variant_Comment	Exonic_Mutation

UMD Comment Frequency

This mutation is very frequent

UMD Comment Outliers

UMD Comment Activity

This mutant is inactive

UMD Comment Splicing

No potential effect on splicing

Frcy in the UMD database

36

Activity

7.18

SIFT

Damaging

Polyphen

probably damaging

Mut Assessor

medium

Provean

Deleterious

CONDel

deleterious

Comments

This cell line contains 2 mutations.
Click the button to toggle between the multiples mutations

Cell lines with more than one mutation are included in the database. A specific message informs the user that more than one mutation is available. A specific button can be used (green stamp 1) to toggle between the two panels describing the two mutations (red stamps 1 and 2). Cell lines with more than 2 mutations are presented in a similar way.


## TP53 mutant display

Example: Cell line A375 that expressed wild-type TP53.

CLOSE

Cell line **A375**

< Panel >  
Click to toggle the panel

P1 

ATCC

CRL-1619

Cancer

Melanoma

Protein variant

cDNA variant

Complexity

Mutation\_Type

Exon / Intron

Domain

Structure

Post\_Translation

Variant\_Classification

Wild type

Variant\_Comment

UMD Comment Frequency

UMD Comment Outliers

UMD Comment Activity

UMD Comment Splicing

Frcy in the UMD database

Activity

SIFT

Polyphen

Mut Assessor

Provean

CONDel

Comments

## Searching for a specific set of TP53 mutants

Menu
Cancers
Mutations
Names

SEARCH BY MUTANTS

Cancer
All
Tumor Type 1
Colorectal carcinoma 1
Tumor Type 2
Tumor Type 3
Reset the search criteria

Codon Position
Mutant Frequency
Variant Classification

All X
aa 1
aa 2
aa 3

All
Frequent (100+)
Unfrequent (10-99) X 2
Rare (1-9)

All
Missense mutation
Silent mutation
Nonsense mutation X 3
Frameshift mutation
Tandem mutation

GO

The user can search for infrequent (green stamp 2) nonsense TP53 mutations (green stamp 3) in colorectal carcinoma (green stamp 1)

SEARCH BY MUTANTS

8 files

CRITERIA

Cancer

Colorectal carcinoma

Codon Position

All

Frequency

Unfrequent(10-99)

Variant Classification

Nonsense Mutation

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Sample ID	ATCC	Cancer	cDNA variant	Protein variant	Complexity	Tand Class	Variant Classification	Rec. Numb.	WAF1 %	Reference
C28Be1		Colorectal carcinoma	c.610G>T	p.E204*	SM		Nonsense_Mutation	75		2249
C80		Colorectal carcinoma	c.154C>T	p.Q52*	SM		Nonsense_Mutation	17		2051
CACO2	HTB-37	Colorectal carcinoma	c.610G>T	p.E204*	SM		Nonsense_Mutation	75		2051
CC20		Colorectal carcinoma	c.378C>G	p.Y126*	SM		Nonsense_Mutation	24		2051
Co84		Colorectal carcinoma	c.430C>T	p.Q144*	SM		Nonsense_Mutation	84		2258
LS-411N	CRL-2159	Colorectal carcinoma	c.378C>A	p.Y126*	SM		Nonsense_Mutation	15		2051
SNU-C1	CRL-5972	Colorectal carcinoma	c.497C>G	p.S166*	SM		Nonsense_Mutation	27		2249
SW403	CCL-230	Colorectal carcinoma	c.151G>T	p.E51*	SM		Nonsense_Mutation	11		2051

Only 8 cell lines meet the various criteria of this search request. They are listed in alphabetical order. The TP53 mutant display can be opened for each cell line after clicking the name of the cell line in column sample\_ID.