# TP53 Mutations in Cell Lines compendium

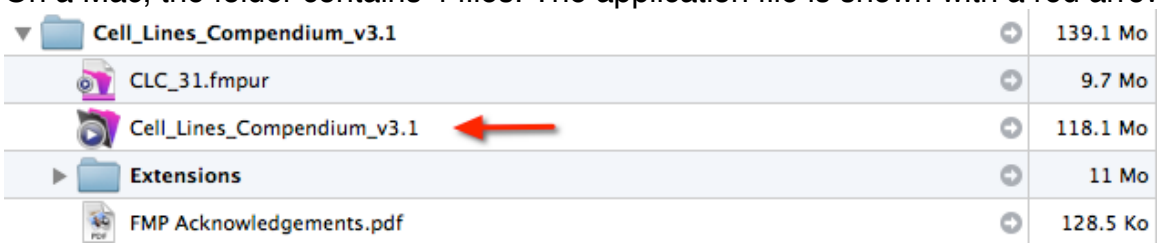
## Installation:

To install the compendium

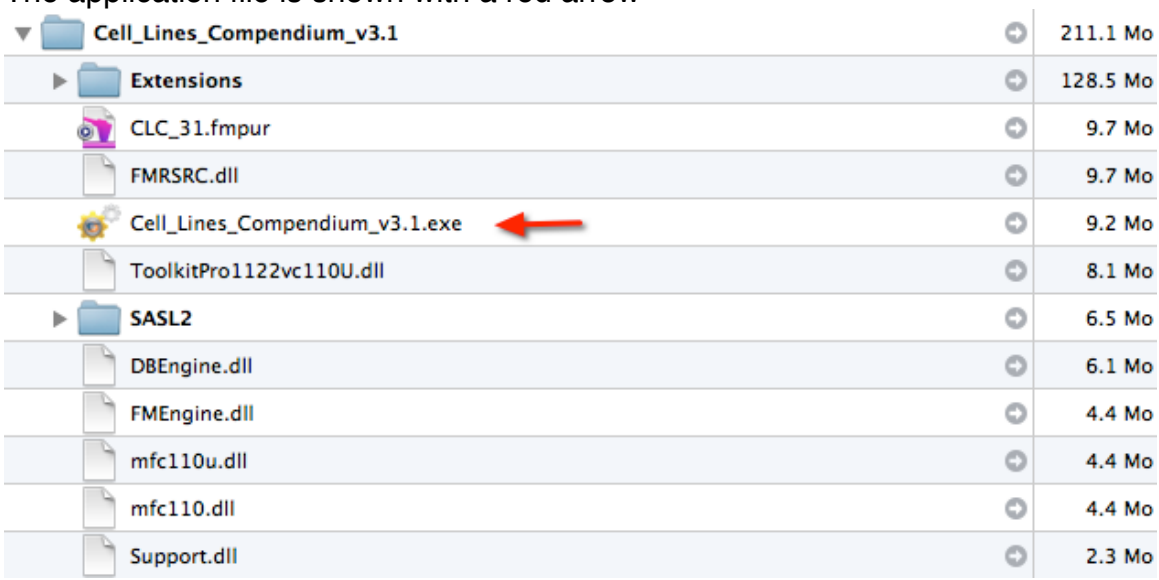
I) Decompress the file
You can unzip .zip  files in Windows XP, Vista, 7, and Mac OS X by using unzipping software that supports the file extension.

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

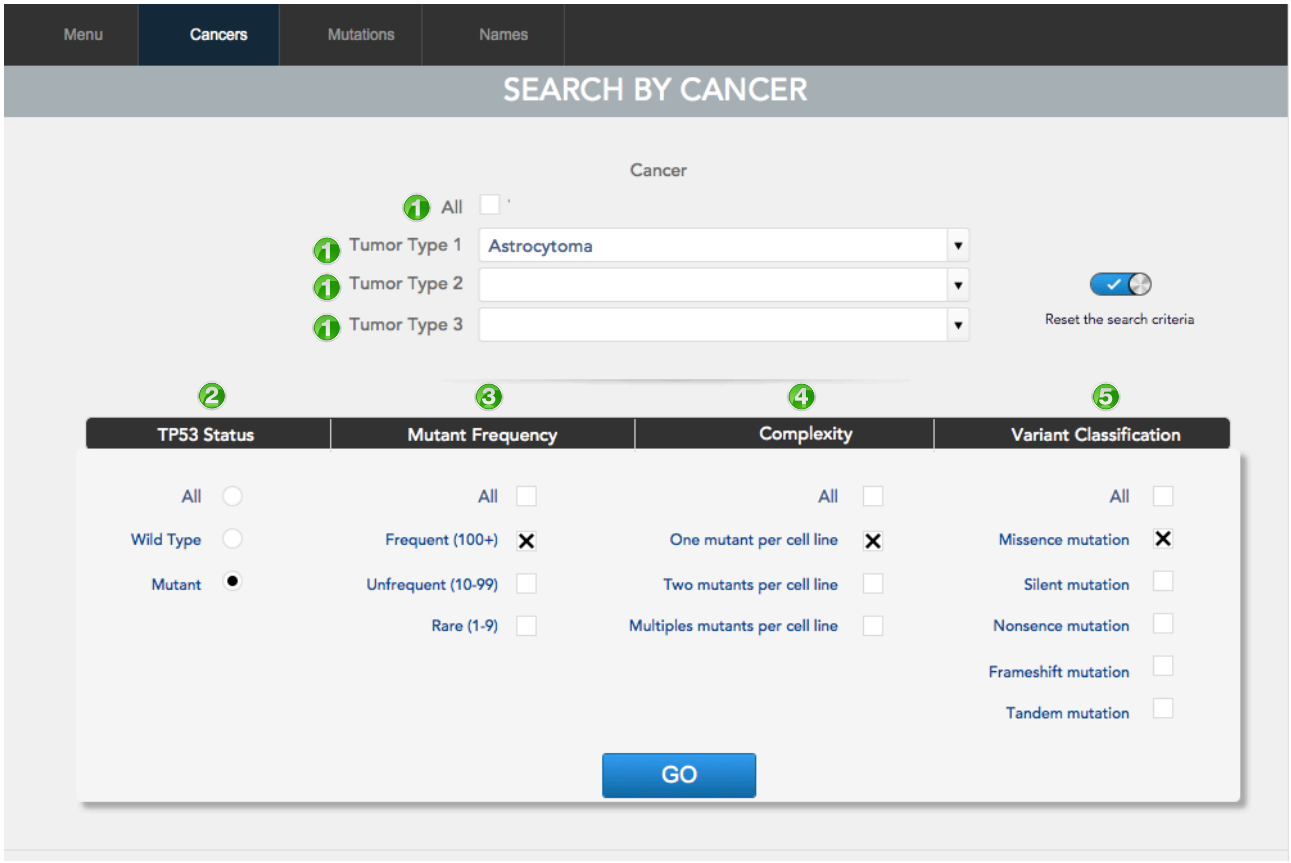
On a Mac, the folder contains 4 files. The application file is shown with a red arrow




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



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




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).

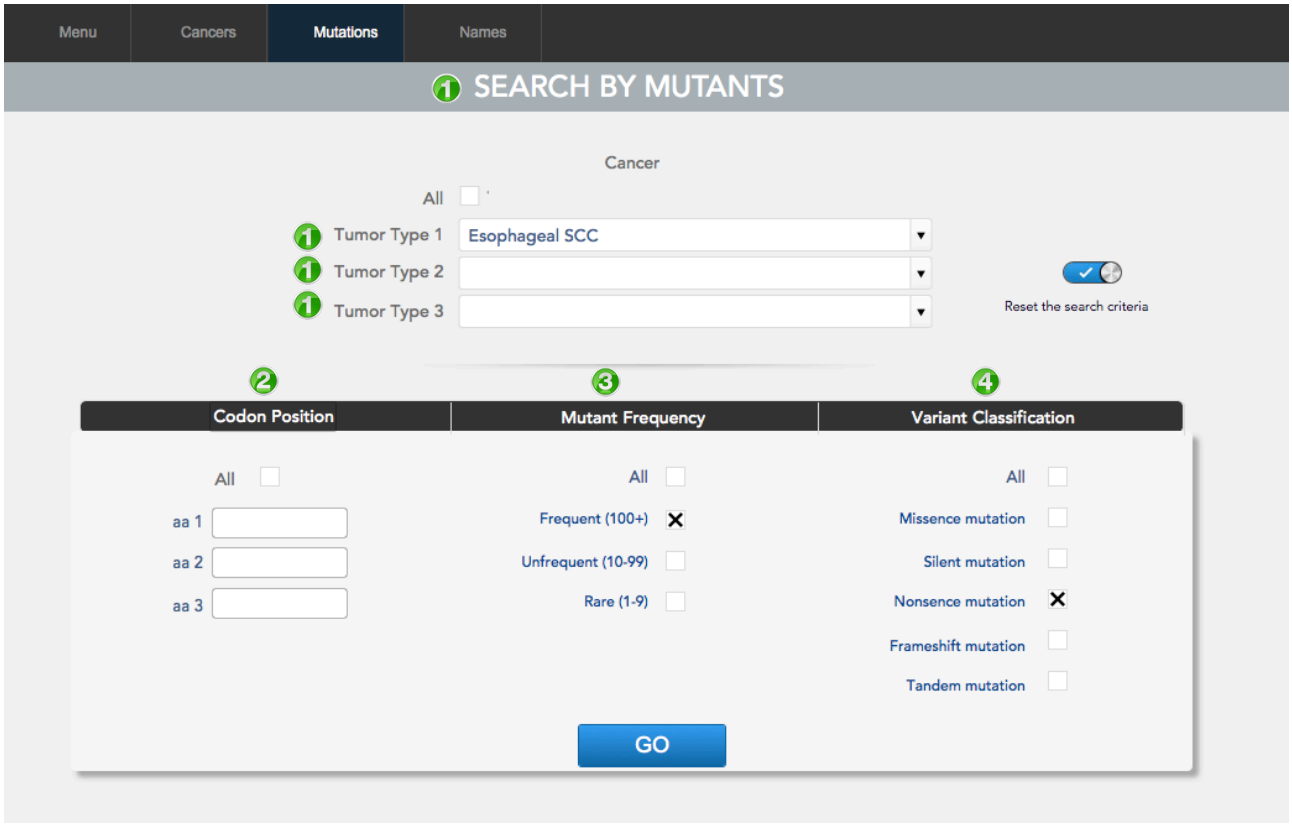
*Complexity (green stamp 4):*

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 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).

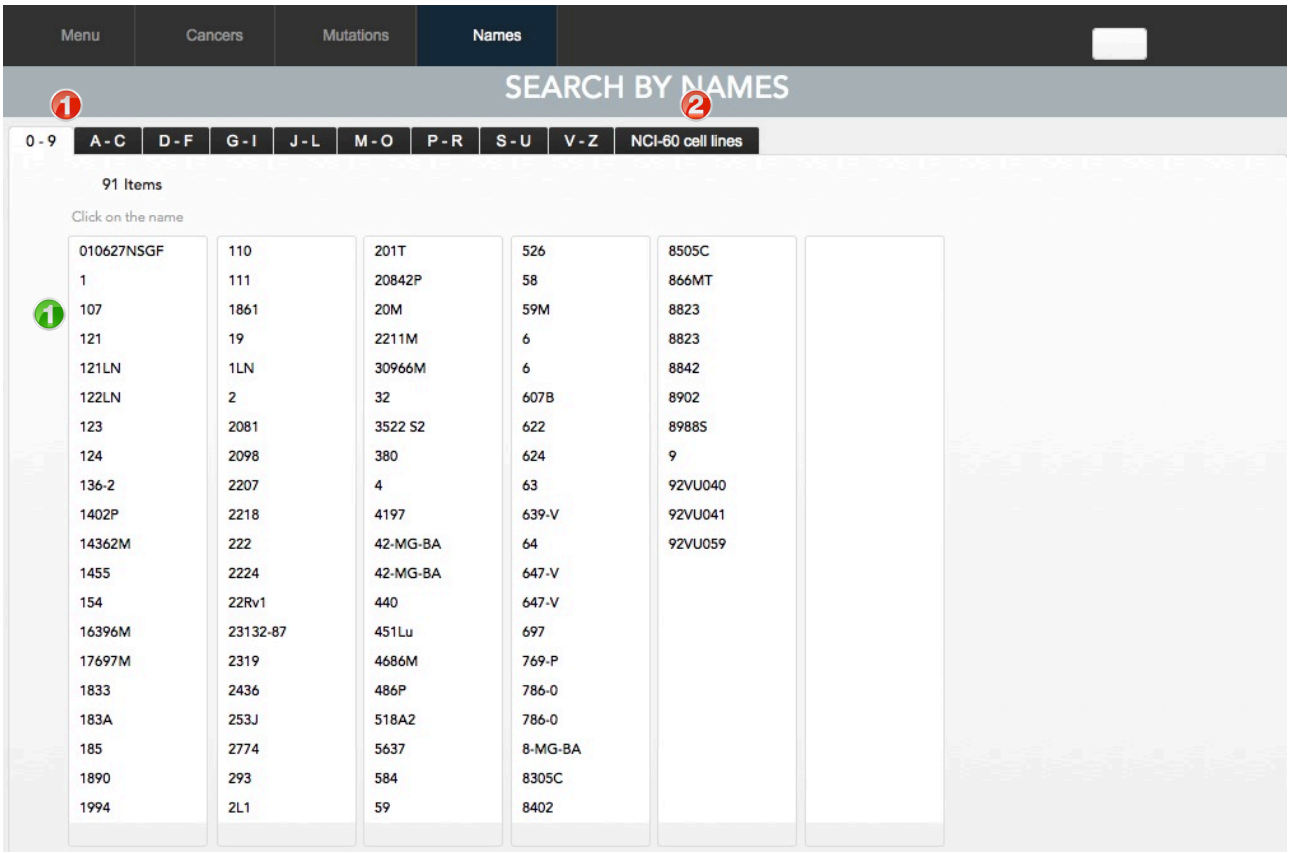
*Mutant frequency (green stamp 3):*

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.

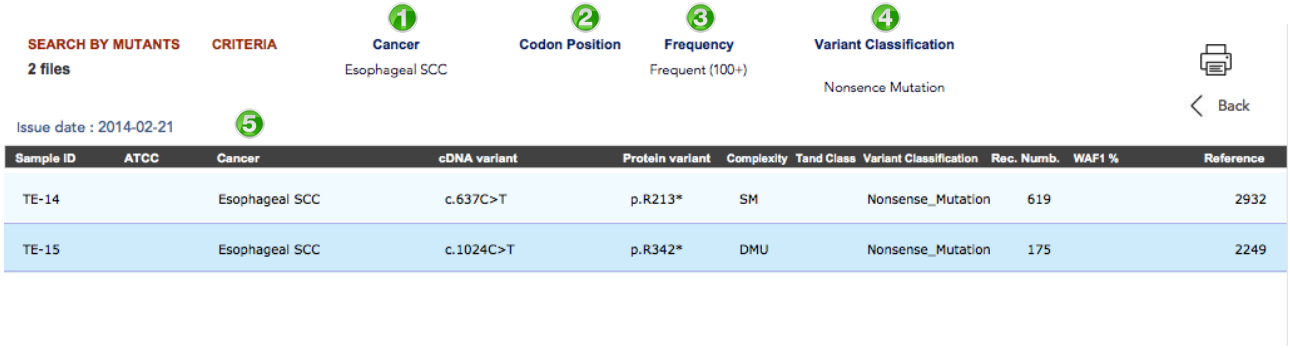
**Detailed description of the "Search by Names" panel**




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



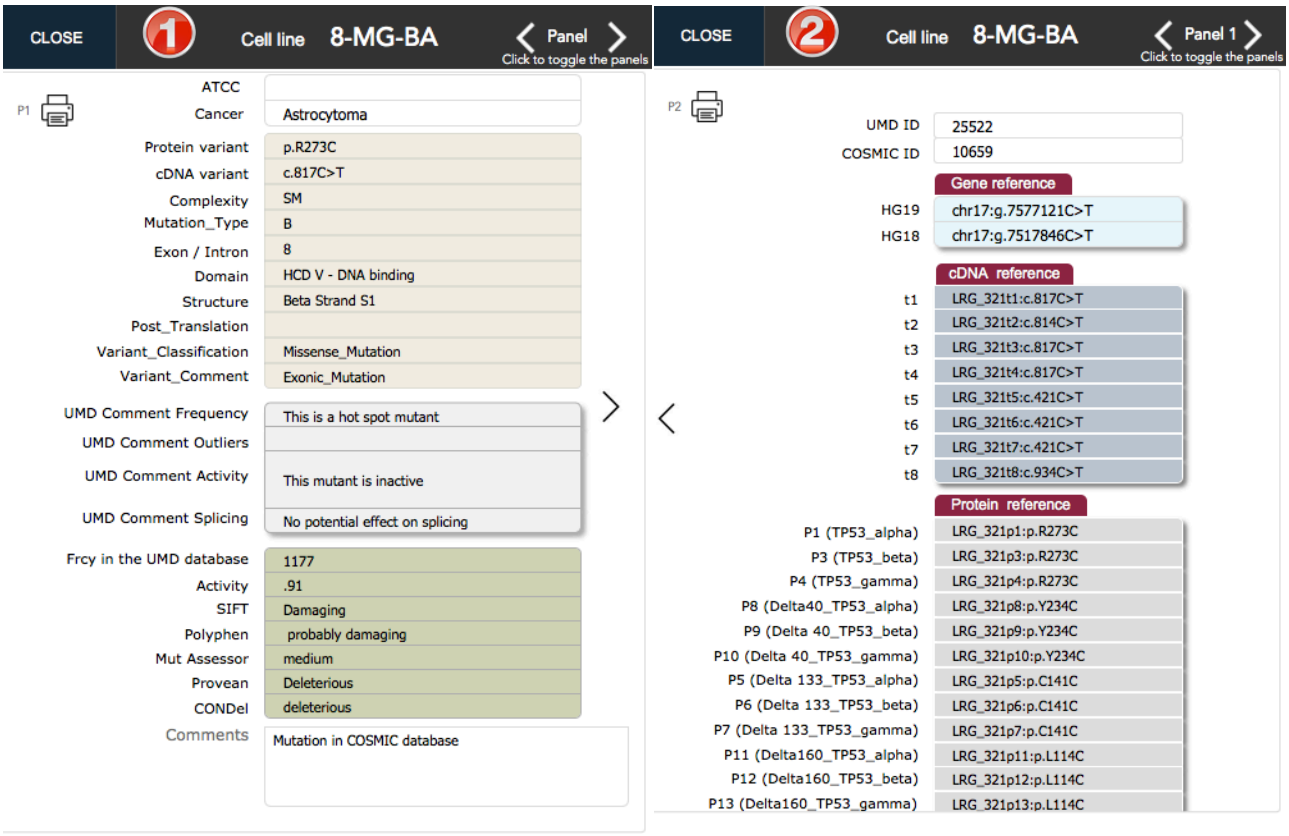

| Sample ID | ATCC | Cancer | cDNA variant | Protein variant | Complexity | Tand Class | Variant Classification | Rec. Numb. | WAF1 % | Reference |
|---|---|---|---|---|---|---|---|---|---|---|
| TE-14 | | Esophageal SCC | c.637C>T | p.R213* | SM | | Nonsense_Mutation | 619 | | 2932 |
| TE-15 | | Esophageal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

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

Clicking on the cell name opens the mutation description panel.

**Panel view**




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 HGVS standards using the protein sequence as reference. Full length TP53 protein isoform is used (393 aa) |
| cDNA variant | Mutation nomenclature according to HGVS standards using the coding sequence as reference. (1 is the A of the start ATG): reference sequence NM_000546.5 |
| Complexity | **SM:** Single mutational event in the tumor;<br>**DMU** (Double Mutation Unknown): Two p53 mutations in the same tumor but their allelic distribution is unknown;<br>**DMD** (Double Mutation Different allele): Two p53 mutations in the same tumor on two different p53 alleles;<br>**DMD** (Double Mutation Same allele): Two p53 mutations in the same tumor on the same p53 allele:<br>**MM** (Multiple Mutation): More than two p53 mutations in the same tumor.<br><br>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:** single missense mutation<br>**D**: deletion<br>**I**: insertion<br>**T**: tandem mutation<br>**ID:** indel mutation |
| Exon / Intron | Localization of the mutation |

| | |
|---|---|
| Domain | Domains of the TP53 protein<br><br>**HCD I to V**: Highly Conserved Domains I to V;<br>**DNA Binding**: DNA binding domain:<br>**Negative regulation:** carboxy-terminus of the p53 protein associated with negative regulation of p53 DNA binding activity;<br>**Transactivation:** transactivation domain of the p53 protein<br>**TAD1:** transactivation domain 1<br>**TAD2:** transactivation domain 2<br>**Proline Rich**: Proline-rich domain of the p53 protein;<br>**NES:** Nuclear export signal of p53;<br>**NLS:** Nuclear localization signal of p53;<br>**Oligomerization:** Tetramerization domain of the p53 protein.<br>**NA**: No specific domain available |
| Structure | Structural motif of the TP53 protein according to the analysis described by Cho et al. (1994) |
| Post Translation | Displays potential posttranslational modifications at the position of the mutant |
| Variant classification | Translational effect of the mutation.<br>(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 |

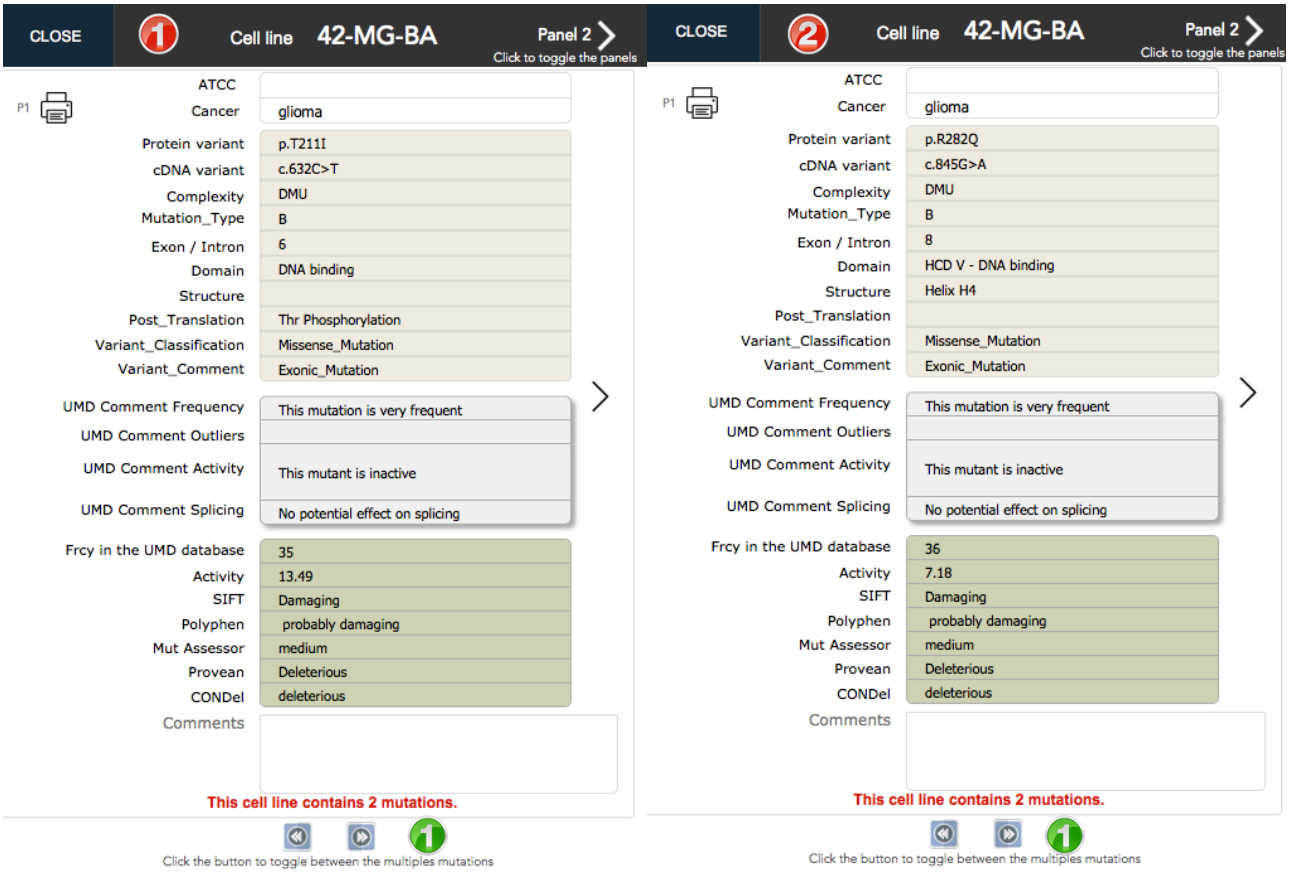
***Panel 2***

| | |
|---|---|
| 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 |
| *Mutation nomenclature and coordinates used below are expressed according to HGVS and the LRG* | |
| 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

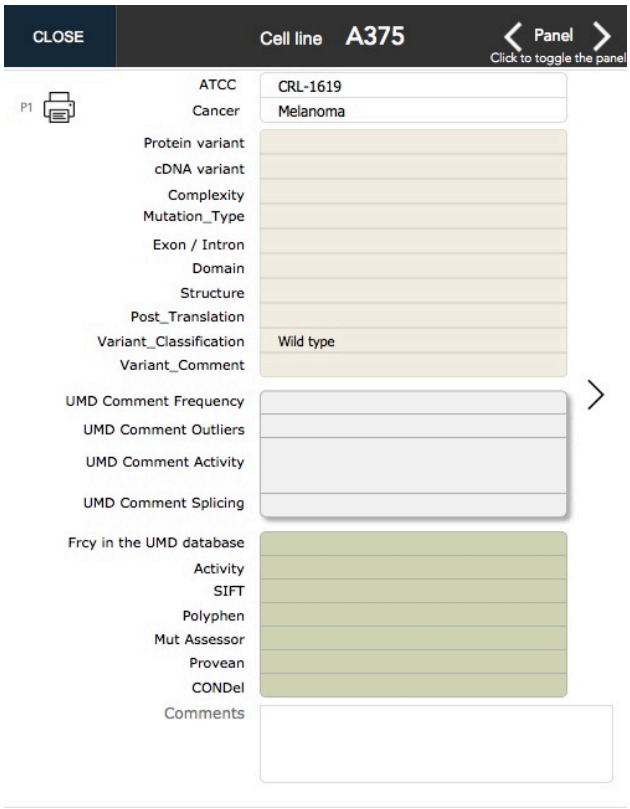
Example: Cell line 42-MG-BA from the NCI-60 panel that expressed two TP53 mutants



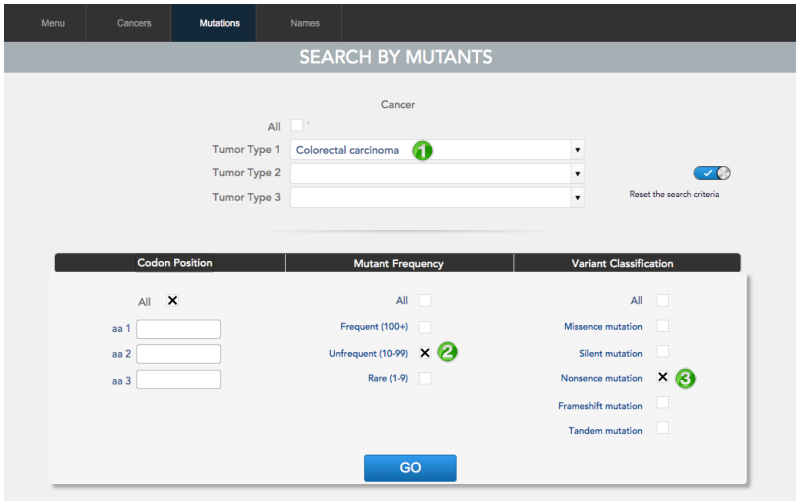

Cell lines with more than one mutation are included in the database. A specific message informs the user that more than one mutation is available. A specific button can be used (green stamp 1) to toggle between the two panels describing the two mutations (red stamps 1 and 2).
Cell lines with more than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

**TP53 mutant display**

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



## Searching for a specific set of TP53 mutants




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

**SEARCH BY MUTANTS** **CRITERIA** **Cancer** **Codon Position** **Frequency** **Variant Classification**

**8 files** Colorectal carcinoma All Unfrequent(10-99) Nonsence Mutation

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Issue date : 2014-02-21

| Sample ID | ATCC | Cancer | cDNA variant | Protein variant | Complexity | Tand Class | Variant Classification | Rec. Numb. | WAF1 % | Reference |
|---|---|---|---|---|---|---|---|---|---|---|
| C2BBe1 | | 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.