Accessing Data from the Genomics of Drug Sensitiviy (GDSC) Website

Contents

Introduction

The Genomics of Drug Sensitivity in Cancer project provides carefully curated and multifaceted statistical data on how well different drugs target different cancers in different cell lines. These data allow researches to study higher-order connections computationally, and also inform future in-vitro experiments. They are becoming invaluable for understanding cancer and developing treatments.

I am exploring this data to help build a graph database that will define genes, cell lines, cancers, and drugs as entities with other variables as connections between them. Doing this requires data tables that are clean, properly formatted, and well-harmonized. Computation work relies on data being presented in a uniform way so that the programmer does not need to handle a host of formatting edge-cases either by hand or with large amounts of code that have nothing to do with the actual analysis. Then programmers have to do those things, it becomes nearly impossible to do reproducible analysis and guarantee their results to be free of human error.

In preparing the GDSC data to enter into a relational database and then a graph database, I discovered numerous issues. Some of these are convenience issues, such as similar data having different column names in different files and data in Excel files containing multiple, heterogeneous sheets. Some of the issues exposed missing but essential information about data tables, such as when they were last updated, and how they relate to other apparently similar data tables. Unfortunately, I also found some catastrophic problems such as tables with mislabeled columns and missing column names.

I collected my observations in this notebook for three reasons.

- As a guide for myself to know how to process the GDSC tables
- As a guide for someone who joins this project or picks it up down the road
- As information for the GDSC project to help them identify data issues and perhaps improve their data quality, uniformity, harmonization, and access.

Note on Reproducible Research

The world of computational science research has learned that a scientific study is incomplete if it includes the results of computational analysis but not the computer code that produced those results. Reproducible research means providing the computational tools to reproduce results as well as the results themselves.

The first step in any reproducible research project is cleaning and harmonizing data. This means cleaning data to make sure data are in exactly the same consistent format wherever they appear. For example, (Yes|No) should always be in that format, and not (y|n) or (1|0). Column names for matching variables should always be the same. Column names should be in a consistent format for importing into data analysis programs. This means no spaces or hyphens and periods should be avoided. Filenames should be as consistent as possible to facilitate automation and searching. Etc.

I'm hoping that in light of the information in this analysis the GDSC project will consider providing a way to access their data which tries to meet the needs of computational scientists as much as possible. Given the inconsistencies I found, it might be that the best solution would be to host the data in a relational database, and have back-end processes that provide the tables in Excel files such as are available now for those who prefer them in that format.

Accessing GDSC Data

There are three places on the website to access data files. However, documentation is scarce regarding how these files are related. We looked at the different ways of accessing data and tried to understand how they relate.

Metadata Pages and Table Exports

The website has three dedicated pages for downloading metadata that describes the entities (genes, drugs, cells, etc.) referred to in the data containing the results: Compounds (drugs), Features, Cell Lines

- *Compounds - Cancerrxgene - Genomics of Drug Sensitivity in Cancer*

- *Cancer Features - Cancerrxgene - Genomics of Drug Sensitivity in Cancer*

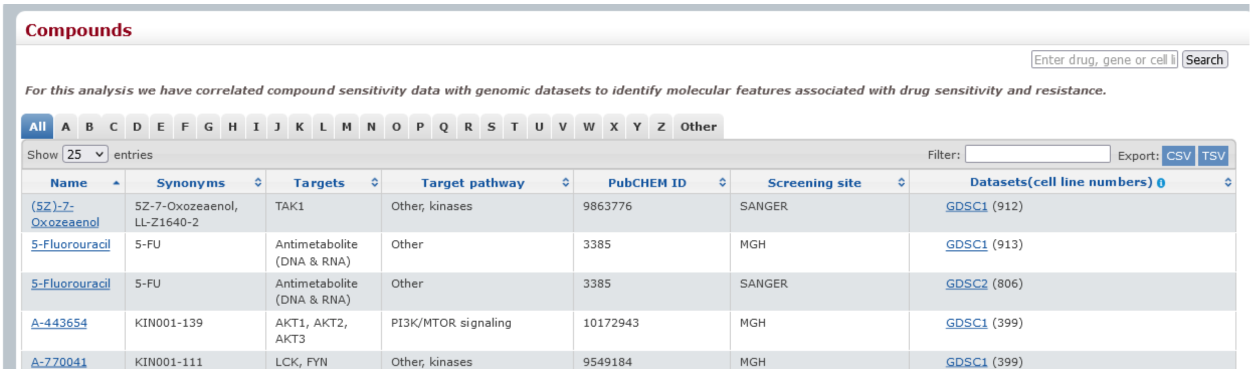
- *Cancer Cell Lines - Cancerrxgene - Genomics of Drug Sensitivity in Cancer*

Each has a table preview and also export buttons for CSV and TSV. However, the way the exported data is put into columns is different than in the preview table and include a column (the last) of unknown significance. More importantly, the the columns in the exported data are incomplete and sometimes incorrect.

Compounds (i.e. Drugs)

Table Preview

Records: 518
Columns: `Name`, `Synonyms`, `Targets`, `Target pathway`, `PubCHEM ID`, `Screening site`, `Datasets (cell line numbers)`



Compounds

For this analysis we have correlated compound sensitivity data with genomic datasets to identify molecular features associated with drug sensitivity and resistance.

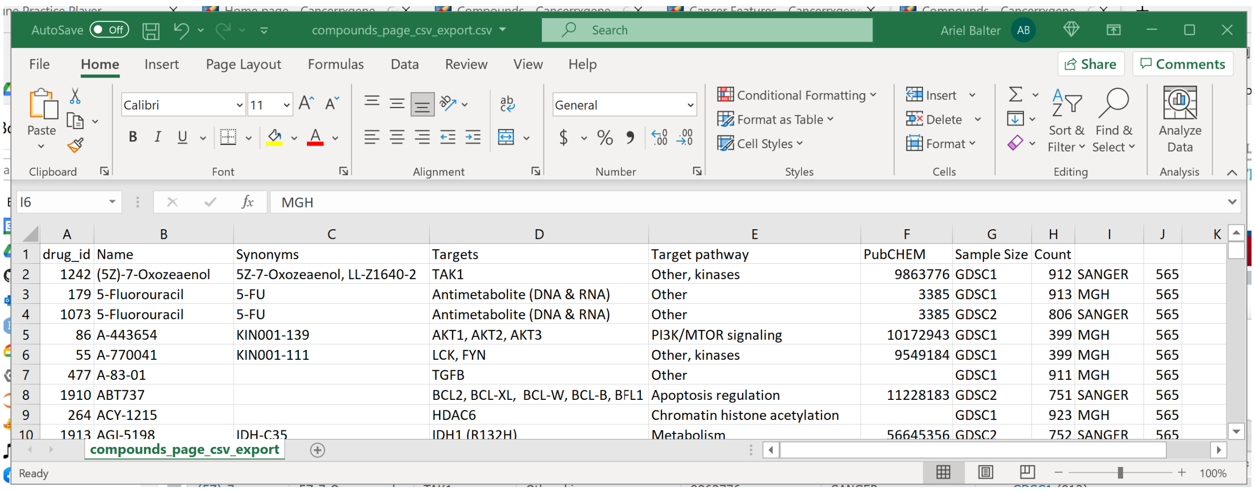
Enter drug, gene or cell li
Search
All A B C D E F G H I J K L M N O P Q R S T U V W X Y Z Other
Show 25 entries
Filter:
Export: CSV TSV

Name	Synonyms	Targets	Target pathway	PubCHEM ID	Screening site	Datasets(cell line numbers)
(5Z)-7-Oxozeaenol	5Z-7-Oxozeaenol, LL-Z1640-2	TAK1	Other, kinases	9863776	SANGER	GDSC1 (912)
5-Fluorouracil	5-FU	Antimetabolite (DNA & RNA)	Other	3385	MGH	GDSC1 (913)
5-Fluorouracil	5-FU	Antimetabolite (DNA & RNA)	Other	3385	SANGER	GDSC2 (806)
A-443654	KIN001-139	AKT1, AKT2, AKT3	PI3K/MTOR signaling	10172943	MGH	GDSC1 (399)
A-770041	KIN001-111	LCK, FYN	Other, kinases	9549184	MGH	GDSC1 (399)

CSV export

Records: 565
Columns: `drug_id`, `Name`, `Synonyms`, `Targets`, `Target pathway`, `PubCHEM`, `Sample Size`, `Count`

The exported CSV is called `Drug_list<timetamp>.csv`.



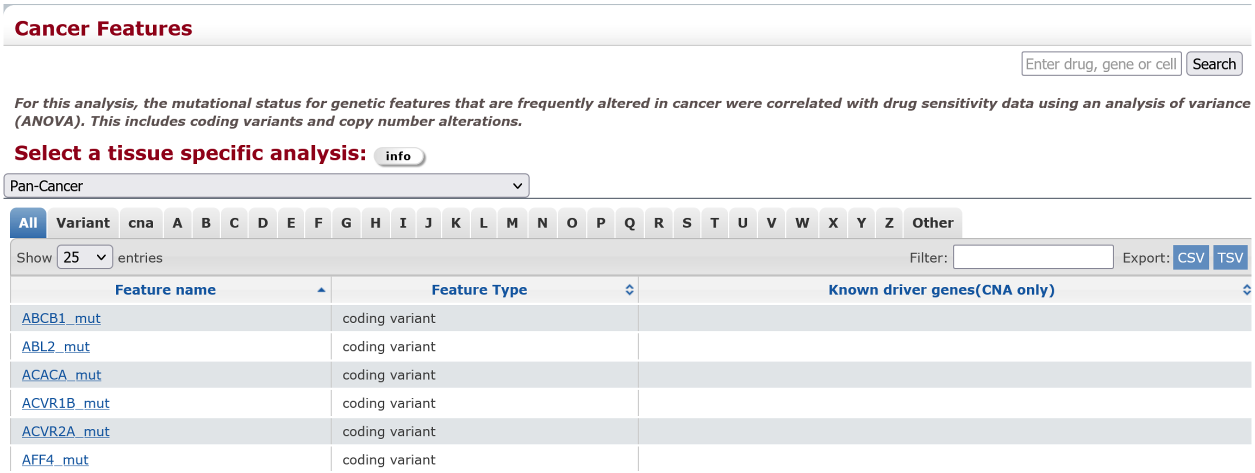
	A	B	C	D	E	F	G	H	I	J
1	drug_id	Name	Synonyms	Targets	Target pathway	PubCHEM	Sample Size	Count		
2	1242	(5Z)-7-Oxozeaenol	5Z-7-Oxozeaenol, LL-Z1640-2	TAK1	Other, kinases	9863776	GDSC1	912	SANGER	565
3	179	5-Fluorouracil	5-FU	Antimetabolite (DNA & RNA)	Other	3385	GDSC1	913	MGH	565
4	1073	5-Fluorouracil	5-FU	Antimetabolite (DNA & RNA)	Other	3385	GDSC2	806	SANGER	565
5	86	A-443654	KIN001-139	AKT1, AKT2, AKT3	PI3K/MTOR signaling	10172943	GDSC1	399	MGH	565
6	55	A-770041	KIN001-111	LCK, FYN	Other, kinases	9549184	GDSC1	399	MGH	565
7	477	A-83-01		TGFB	Other		GDSC1	911	MGH	565
8	1910	ABT737		BCL2, BCL-XL, BCL-W, BCL-B, BFL1	Apoptosis regulation	11228183	GDSC2	751	SANGER	565
9	264	ACY-1215		HDAC6	Chromatin histone acetylation		GDSC1	923	MGH	565
10	1913	AGI-5198	IDH-C35	IDH1 (R132H)	Metabolism	56645356	GDSC2	752	SANGER	565

The CSV export is missing the `Screening site` column, which should be after `PubCHEM` (`PubCHEM ID` in the table preview) and before `Sample Size`. The sample size is include in parenthesis in the table preview and called the confusing term "cell line numbers." The `Count` column in the export appears to be the number of records in the export, so is the same in all records.

Cancer Features

Preview

Records: 693
Columns: `Feature name`, `Feature type`, `Known driver genes(CNA only)`



Cancer Features

Enter drug, gene or cell | Search

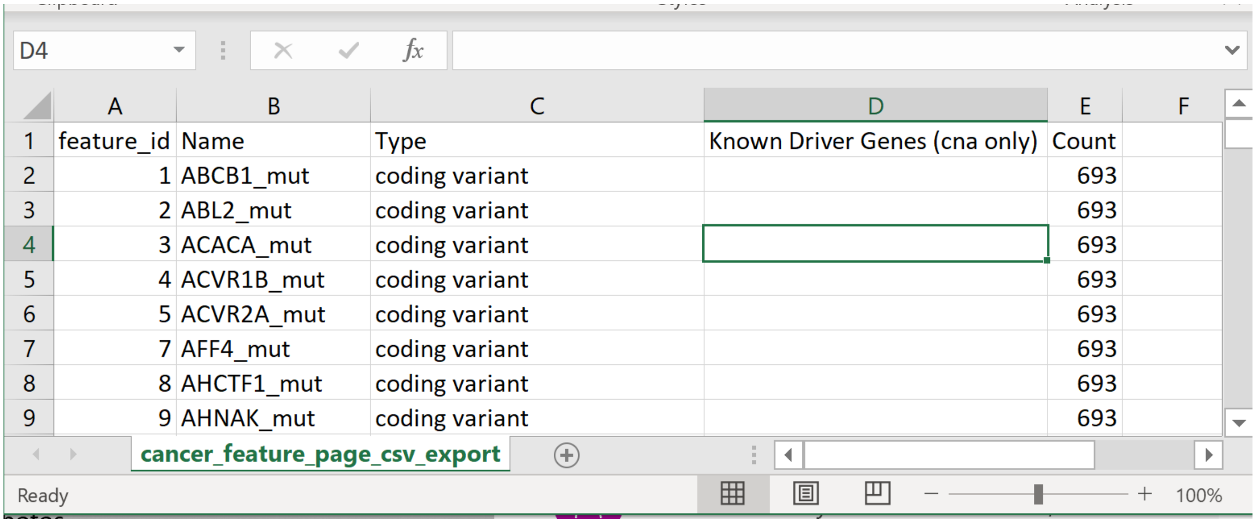
For this analysis, the mutational status for genetic features that are frequently altered in cancer were correlated with drug sensitivity data using an analysis of variance (ANOVA). This includes coding variants and copy number alterations.

Select a tissue specific analysis: info

Pan-Cancer

Feature name	Feature Type	Known driver genes(CNA only)
ABCB1_mut	coding variant	
ABL2_mut	coding variant	
ACACA_mut	coding variant	
ACVR1B_mut	coding variant	
ACVR2A_mut	coding variant	
AFF4_mut	coding variant	

CSV Export



	A	B	C	D	E	F
1	feature_id	Name	Type	Known Driver Genes (cna only)	Count	
2	1	ABCB1_mut	coding variant		693	
3	2	ABL2_mut	coding variant		693	
4	3	ACACA_mut	coding variant		693	
5	4	ACVR1B_mut	coding variant		693	
6	5	ACVR2A_mut	coding variant		693	
7	7	AFF4_mut	coding variant		693	
8	8	AHCTF1_mut	coding variant		693	
9	9	AHNAK_mut	coding variant		693	

The exported file is called `Feature_list<timestamp>.csv`

Records: 693
Columns: `feature_id`, `Name`, `Type`, `Known Driver Genes(cna only)`, `Count`

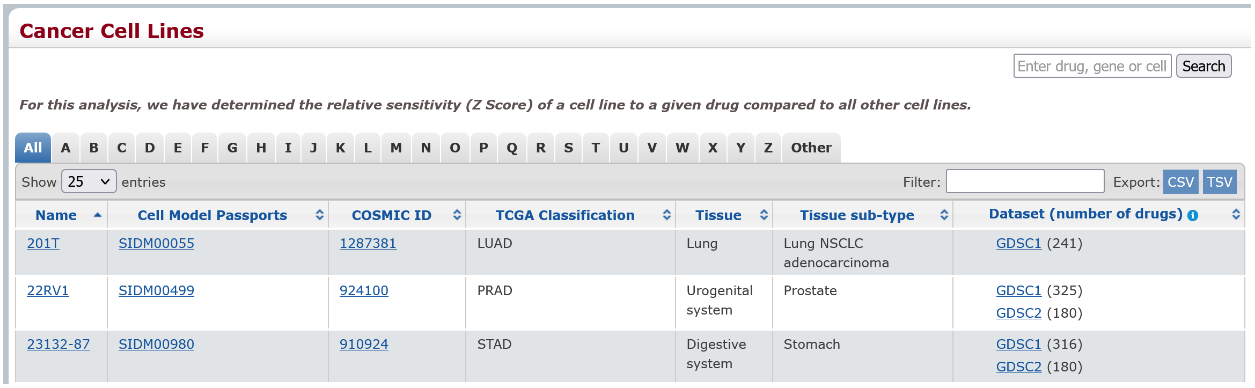
The `Feature name` in the table preview is called `Name` in the export. `Feature Type` in the table preview is called `Feature Name` in the export. Note the inconsistent use of capitals.

Cell Lines

This appears to be a condensed version of the table described here.

Table Preview

Records: 988
Columns: `Name`, `Cell Model Passports`, `COSMIC ID`, `TCGA Classification`, `Tissue`, `Tissue sub-type`, `Dataset (number of drugs)`



Cancer Cell Lines

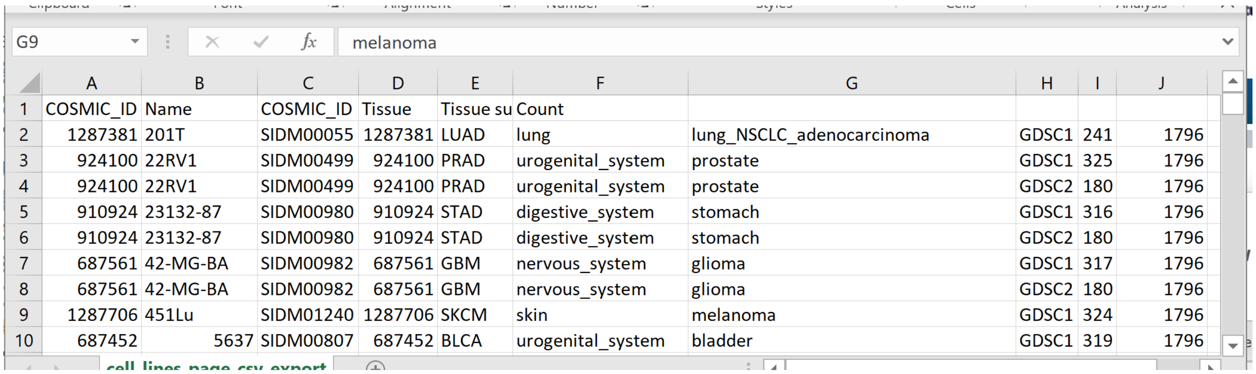
For this analysis, we have determined the relative sensitivity (Z Score) of a cell line to a given drug compared to all other cell lines.

All A B C D E F G H I J K L M N O P Q R S T U V W X Y Z Other
Show 25 entries
Filter:
Export: CSV TSV

Name	Cell Model Passports	COSMIC ID	TCGA Classification	Tissue	Tissue sub-type	Dataset (number of drugs)
201T	SIDM00055	1287381	LUAD	Lung	Lung NSCLC adenocarcinoma	GDSC1 (241)
22RV1	SIDM00499	924100	PRAD	Urogenital system	Prostate	GDSC1 (325) GDSC2 (180)
23132-87	SIDM00980	910924	STAD	Digestive system	Stomach	GDSC1 (316) GDSC2 (180)

Exported CSV

Records: 1798
Columns: `COSMIC_ID`, `Name`, `COSMIC_ID`, `Tissue`, `Tissue sub-type`, `Count`



	A	B	C	D	E	F	G	H	I	J
1	COSMIC_ID	Name	COSMIC_ID	Tissue	Tissue su	Count				
2	1287381	201T	SIDM00055	1287381	LUAD	lung	lung_NSCLC_adenocarcinoma	GDSC1	241	1796
3	924100	22RV1	SIDM00499	924100	PRAD	urogenital_system	prostate	GDSC1	325	1796
4	924100	22RV1	SIDM00499	924100	PRAD	urogenital_system	prostate	GDSC2	180	1796
5	910924	23132-87	SIDM00980	910924	STAD	digestive_system	stomach	GDSC1	316	1796
6	910924	23132-87	SIDM00980	910924	STAD	digestive_system	stomach	GDSC2	180	1796
7	687561	42-MG-BA	SIDM00982	687561	GBM	nervous_system	glioma	GDSC1	317	1796
8	687561	42-MG-BA	SIDM00982	687561	GBM	nervous_system	glioma	GDSC2	180	1796
9	1287706	451Lu	SIDM01240	1287706	SKCM	skin	melanoma	GDSC1	324	1796
10	687452	5637	SIDM00807	687452	BLCA	urogenital_system	bladder	GDSC1	319	1796

The COSMIC_ID *data* values are repeated in two columns: `COSMIC_ID` and `Tissue`. The `Cell Model Passports` data values in the preview are under a 2nd column called `COSMIC_ID` in the CSV Export. The columns in the CSV export, in order, should be:

`COSMIC_ID`, `Name`, `Cell_Model_Passports`, `COSMIC_ID` (which should not be there at all), `Tissue`, `Tissue_Subtype`, `Dataset`, `number_of_drugs`

The large difference in size between the export and preview needs investigation. Has the amount of data doubled between the preview and export?

Final Comments

There are some serious issues here with exported files formatted incorrectly. The number of records shown in the Cell Lines preview is roughly 50% of the number in the export. Do these two represent the same data?

- Correct the export process.
- Offer more description on the relationship between the previews and the export data.

Column names should be harmonized and consistent.

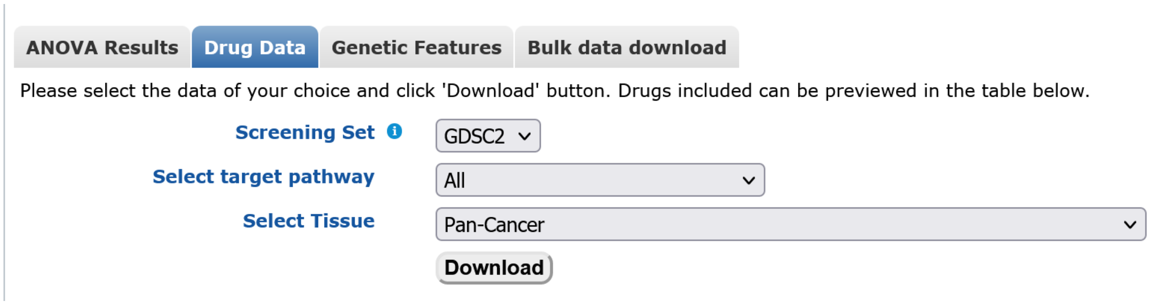
- Some columns have a space before words in parenthesis, some don't.
- Similar columns are named the same in different tables. If it is called "Feature_name" in one table, it should not be called "Name" in another.
- The best format for column headings is title-case with underscores instead of spaces. All lower with underscores is also good. This greatly facilitates use in other applications such as databases, dataframes,

etc.

- Column names should be as descriptive as possible. It's obvious that `Number of drugs` and `cell line numbers` are both terms for sample size.

Downloads Page

The Downloads page has a UI where you can select three table preview/download options (ANOVE Results, Drug Data, Genetic Features), and an option for "Bulk Data Downloads."



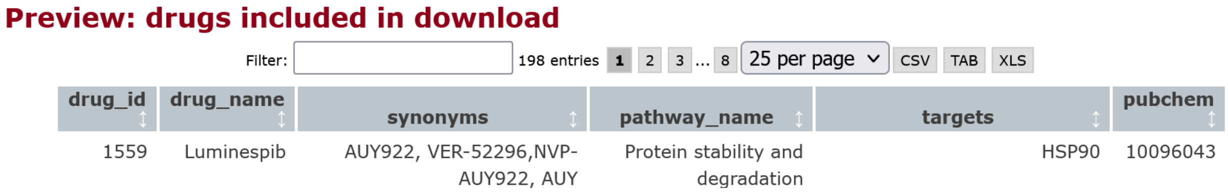
Please select the data of your choice and click 'Download' button. Drugs included can be previewed in the table below.

Screening Set: GDSC2

Select target pathway: All

Select Tissue: Pan-Cancer

The ANOVA Results and Drug data show a table preview of what appears to be a list of drugs and targets used in the study. However, the table has 198 button, which seems like it must be truly a "preview." There is a "Download" button as well as buttons on the table preview to export Tab, CSV, or XLS. I will compare them to the metadata to see if the table is comprehensive or



Preview: drugs included in download

Filter:

198 entries

drug_id	drug_name	synonyms	pathway_name	targets	pubchem
1559	Luminespib	AUY922, VER-52296,NVP-AUY922, AUY	Protein stability and degradation	HSP90	10096043

The "Bulk Data Download" option leads to a page with FTP links for individual files, as well as a link to an FTP directory with both current and archival data.

ANOVA Results

The ANOVA data file is called `PANCANCER_ANOVA_<timestamp>.csv`.

Records: 124483
Columns: `drug_name`, `drug_id`, `drug_target`, `target_pathway`, `feature_name`, `n_feature_pos`, `n_feature_neg`, `ic50_effect_size`, `log_ic50_mean_pos`, `log_ic50_mean_neg`, `log_max_conc_tested`, `log_max_conc_tested_2`, `feature_ic50_t_pval`, `feature_delta_mean_ic50`, `feature_pos_ic50_var`, `feature_neg_ic50_var`, `feature_pval`, `tissue_pval`, `msi_pval`, `fdr`, `tissue_type`, `screening set`

This is likely the same data as in the FTP download file `ANOVA_results_GDSC2_20Feb20.xlsx` described here, but perhaps more up-to-date given the slightly larger number of records.

Drug Data

The data file is called `PANCANCER_IC_<timestamp>.csv`. "IC" refers to the IC50 results which are a key data element.

Records: 135242
Columns: `Drug name`, `Drug Id`, `Cell line name`, `Cosmic sample Id`, `TCGA classification`, `Tissue`, `Tissue sub-type`, `IC50`, `AUC`, `Max conc`, `RMSE`, `Z score`, `Dataset version`

This is likely the same data as in the FTP download file `GDSC2_fitted_dose_response_25Feb20.csv` described here.

Genetic Features

The data file is called `PANCANCER_Genetic_feature__<timestamp>.csv`.

Records: 583305
Columns: `cell_line_name`, `cosmic_sample_id`, `gdsc_desc1`, `gdsc_desc2`, `tcga_desc`, `genetic_feature`, `is_mutated`, `recurrent_gain_loss`, `genes_in_segment`

Notice the full lower-case “feature,” apparent lack of the plural “s,” and the double underscore “__” preceding the timestamp.

There is no comparable file in the FTP download.

This file has a very serious problem. It uses raagged rows without any warning. The last column `genes_in_segment` is meant to contain an array of genes. However, the genes are simply separated by commas *which is the field delimiter used in the file*! When you view the file in Excel, the program simply adds columns for these genes. When you try to import the file into a data analysis environment such as R or Python, you get an error because the file has more record fields than columns. If you work around the error, you simply get unnamed columns that contain the genes as in Excel.

In short, this file is unusable in its current form. I wrote the following code that converts the file into a tab-delimited format with the list of `genes_in_segment` comma delimited. In this format the file is ready for reading into R or Python or inserting into a database.

Bash code for reformatting the file

```
### Convert button-downloaded genetic features to
### tab-delimited with the last column, `genes_in_segment` as a comma-delimited array
curl -o genetic_features.csv https://www.cancerrxgene.org/downloads/download/genetic_feature

paste \
  <(cut -d"," -f1-8 genetic_features.csv | tr "," "\t") \
  <(cut -d"," -f9- genetic_features.csv) \
  > genetic_features.tsv
```

Example of reading into R

```
### load the file
gdsc_genetic_features_raw =
  read.csv(
    "genetic_features.tsv",
    sep="\t",
    stringsAsFactors = F
  )

gdsc_genetic_features =
  gdsc_genetic_features_raw %>%

  ### Turn the comma-delimited genes into arrays
  rowwise() %>%
  mutate(genes_in_segment =  str_split(genes_in_segment, ",")) %>%

  ### Add column for number of genes (just because)
```

cell_line_name	genetic_feature	genes_in_segment	number_of_genes
697	cnaPANCAN13	CARD8 , ZNF114	2
697	cnaPANCAN14	GRIN2D, GRWD1	2
697	cnaPANCAN23	ELAC1 , RP11-729L2.2, SMAD4	3
697	cnaPANCAN25	HMSD , SERPINB8	2
697	cnaPANCAN38	ERCC6 , ERCC6-PGBD3, PGBD3	3
697	cnaPANCAN46	ARHGAP19-SLIT1, SLIT1	2
697	cnaPANCAN53	DPYSL4, STK32C	2
697	cnaPANCAN54	ADAM8, KNDC1, UTF1 , VENTX	4
697	cnaPANCAN56	IGF2 , INS , INS-IGF2, TH	4
697	cnaPANCAN64	HBE1, HBG2	2

```
  mutate(number_of_genes = length(genes_in_segment))

gdsc_genetic_features %>%
  select(cell_line_name, genetic_feature, genes_in_segment, number_of_genes) %>%
  filter(number_of_genes > 1 & number_of_genes < 5) %>%
  head(10) %>%
  kable() %>%
  kable_styling(
    bootstrap_options = c(
      "condensed",
      full_width = F,
      font_size = 8
      )
    )
```

Final Comments

The column names are nicely harmonized and in a consistent format. The files appear to be properly formatted as well.

If the ANOVA data is, indeed, more up-to-date, the website should say so, and give the date of the last dataset change. Perhaps even a changelog.

The name “Drug Data” is extremely non-descriptive. Without studying the tables, one would have no idea that these same data are called “Fitted Dose Response” elsewhere.

The filename for Genetic Features should consistent: `PANCANCER_Genetic_Features_<timestamp>.csv`

Bulk (FTP) Downloads

The Bulk data download page Bulk data download page provides FTP links to both archival and current data.

The current links (10/1/2021) are for the files:

- `FTP_ANOVA_results_GDSC2_20Feb20.xlsx`
- `FTP_GDSC2_fitted_dose_response_25Feb20.csv`
- `FTP_QC.xlsx`
- `FTP_Cell_Lines_Details.xlsx`
- `FTP_GDSC2_fitted_dose_response_25Feb20.xlsx`
- `FTP_screened_compunds_rel_8.2.csv`

ANOVA

Records: 121580
Columns: drug_name, drug_id, target, target_pathway, feature_name, n_feature_pos, n_feature_neg, ic50_effect_size, log_ic50_mean_pos, log_ic50_mean_neg, log_max_conc_tested, feature_ic50_t_pval, feature_delta_mean_ic50, feature_pos_ic50_var, feature_neg_ic50_var, feature_pval, tissue_pval, msi_pval, fdr, tissue_type, dataset_version

This appears to be a less up-to-date version of the data described here

Screened Compounds

Records: 518
Columns: DRUG_ID, SCREENING_SITE, DRUG_NAME, SYNONYMS, TARGET, TARGET_PATHWAY

This is the same data table described here.

Fitted Dose Response

CSV

Records: 135242
Columns: DATASET, NLME_RESULT_ID, NLME_CURVE_ID, COSMIC_ID, CELL_LINE_NAME, SANGER_MODEL_ID, TCGA_DESC, DRUG_ID, DRUG_NAME, PUTATIVE_TARGET, PATHWAY_NAME, COMPANY_ID, WEBRELEASE, MIN_CONC, MAX_CONC, LN_IC50, AUC, RMSE, Z_SCORE

This is the same data table described here.

XLSX

Records: 125242
Columns: DATASET, NLME_RESULT_ID, NLME_CURVE_ID, COSMIC_ID, CELL_LINE_NAME, SANGER_MODEL_ID, TCGA_DESC, DRUG_ID, DRUG_NAME, PUTATIVE_TARGET, PATHWAY_NAME, COMPANY_ID, WEBRELEASE, MIN_CONC, MAX_CONC, LN_IC50, AUC, RMSE, Z_SCORE

This is the same data table described here.

Cell Lines Details

Sheet: "Cell line details"

Records: 1002
Columns: Sample Name, COSMIC identifier, Whole Exome Sequencing (WES), Copy Number Alterations (CNA), Gene Expression, Methylation, Drug Response, GDSC Tissue descriptor 1, GDSC Tissue descriptor 2, Cancer Type (matching TCGA label), Microsatellite instability Status (MSI), Screen Medium, Growth Properties

This appears to be an expanded version of the data table described here. However this table has slightly more records. Does this mean it is more complete or up-to-date?

Sheet: "COSMIC tissue classification"

Records: 1029
Columns: Line, COSMIC_ID, Site, Histology

Sheet: "Decode"

Misc. small lookup tables - TCGA Tissue Classification - Microsatillite instability data - Growth media

Comments:

The column “Line”, in “Cell_Line_Details”.”COSMIC tissue classification” should be “Cell_Line.”

The column “Sample Name” in “Cell_Line_Details”.”Cell line details” has cell line names (similar to the “Line” column in the “Cosmic Tissue Classification”) table. But they refer to unique cell lines in the COSMIC database.

The QC table has a sheet “Lines” (should be “Cell Lines”) that maps COSMIC names to “GDSC Name”s. I’m guessing this is what is in the “Sample Name” column. As described below, it would be advisable to simply use the COSMIC name.

In that case, the “Sample Name” column could simply be called Cell_Lines” because it is clear in the context of this set of data that different cell lines were used as samples. The term “sample name” is best used when the investigator has assigned their own unique identifier to each sample that does not have a direct reference outside of the study.

QC

Sheet: “Readme”

“We have compared the STR profiles (where available) to those profiles published by the repositories to confirm that the cell line name and its STR profile is consistent with its name sake in at least one repository. Three columns are given for each STR, allele A, allele B and allele X, the data has been adjusted to give the best fit for alleles A and B and identity was determined using these calls. Any additional alleles are listed as allele X (multiple additional alleles are comma separated).”

Sheet: “Lines”

Records: 1025
Columns: `GDSC Name`, `COSMIC Name`, `COSMIC ID`

This is a lookup table that maps “GDSC Name,” which is apparently the internal name used for the cell line samples, to the corresponding “COSMIC Name”. Comparing the two columns, I found only 5 out of 1025 names that were different, and that was because the GDSC Name allowed spaces where the COSMIC name used underscores. It’s hard to see the reason for introducing a new variable for this purpose.

Sheet: “STR Data”

Two tables in the same sheet!!!

Table 1 Records: 1013
Rows: [Cell] `Line`
Columns: `Summary Score`, `CGP STR Profile` with subcolumns for some designation number
Values: I think Chromosomes.

Table 2 Records: 886
Rows: `Sample used for scoring STR profile (repository and catalogue number)`
Columns: `Published STR Profile` with subcolumns
Values: I think chromosomes.

Sheet: “SNP Data”

Records: 1025
Rows: [Cell] `Line`
Columns: Accesion numbers (rs)
Values: Variants? Each is a single nucleotide, two nucleotides, or N. Variant on one allele or both?

Sheet: "MSI"

Records: 1025
Rows: [Cell] `Line`
Columns: `BAT25`, `BAT26`, `D17S250`, `D2S123`, `D5S346`, `Summary`
Values: `[stable | unstable | failed]`, `MSI-[L | S | H]`

Sheet: "SNP Details"

Records: 97
Columns: `SNP`, `Chr`, `Position`, `Chr`, `Position`, `Sense_Primer`, `Antisense_Primer`
Note: Some SNPs have a GS number not an rs number. They have two columns for `Chr` and `Position`. The rest have rs numbers and only use one `Chr`/`Position` pair.

Comments

This Excel file has multiple sheets with lookup tables and metadata. Given that they are lookup tables, it is not clear why the file is called "QC" which implies "quality control" in the sense of analyzing data consistency or quality (think `fastqc`).

While for a given investigator in their personal use it would be ok to have Excel files with multiple sheets, and even heterogeneous data in some of those sheets, for data analysis this poses huge problems. It hinders the data being processed programmatically, which impedes reproducibility and risks introducing errors.

Including data in this format is not wrong. But for data analysis, these data should also be provided in individual CSV files with appropriate documentation.

Data Dictionaries

The FTP download has two sparse data dictionary files:

- "GDSC_Fitted_Data_Description.pdf"
- "GDSC_Raw_Data_Description.pdf"

They contain a small amount if information describing some of the data columns