

NCI Proteomic Data Commons Scientific Committee Meeting

09/28/2020, 5:00 – 6:00 PM ET

NATIONAL CANCER INSTITUTE CONTRACT: 20X042F01



The Team

- ESAC Inc., Rockville, MD
 Anand Basu, Program Manager
 Ratna (Rajesh) Thangudu, Project Lead
 Michael Holck, Technical Lead
- Leidos Biomedical., Fredrick, MD
 John Otridge, Program Manager
 Sudha Venkatachari, Project Manager

- University of Washington, Seattle, WA
 Michael J MacCoss (Chair, Scientific Committee)
- Georgetown University, Washington, DC
 Nathan Edwards (SME Data Analysis)
- Spectragen Informatics LLC, WA
 Paul Rudnick (SME Data Analysis)
- National Cancer Institute, Bethesda, MD
 Henry Rodriguez
 Erika Kim















Agenda

- PDC overview & goals Mike MacCoss (15 min)
 - SC goals and responsibilities
 - Expectations what specific feedback/inputs we seek from the SC
- CRDC Overview Allen Dearry/Erika Kim (10 min)
- Current data and where we are today, Interoperability, System Architecture Rajesh Thangudu (10 min)
- Data harmonization, APIs, CDAP and other pipelines Paul Rudnick (10 min)
- Open discussion (15min)



The PDC Scientific Committee

Member

Alexey Nesvizhskii, Ph.D.

University of Michigan

Amanda Paulovich, M.D., Ph.D.

Fred Hutchinson Cancer Research Institute

Bing Zhang, Ph.D.

Baylor College of Medicine

Eric Deutsch, Ph.D.

Institute for Systems Biology

Oliver Bogler, Ph.D.

CCT/NCI

Sam Payne, Ph.D.

Brigham Young University



PDC -- High Level Goals

- Unsilo mass spectrometry data. Bring data into a common location that satisfy Findability, Accessibility, and Reusability
- Move from a situation where people move data to local tools to where people move their tools to the data.
- Shift from a 'data graveyard model' to a 'data workspace model'
- Make it feasible for pipelines to be released with data during publication to improve reproducibility
- Improve meta-data annotations. Ensure data is annotated well using common vocabularies but that the process is non-onerous.



PDC Scientific Committee Responsibilities

- Provide constructive criticism on the work we have performed to date.
- Help us define the scope of the PDC.
- Help us prioritize our short-term and long-term to-do list.
- Provide comments about the UI/UX.
- Identify key collaborators to best demonstrate features and to contribute valuable cancer proteomics datasets
- Identify critical tools and workflows to integrate with the PDC to facilitate data reanalysis.
- Identify specific features that can make proteogenomic data accessible to cancer biologists and clinicians



PDC Scientific Committee Commitment

- A 1-hour scientific committee meeting per quarter
- Occasional individual calls/emails regarding a specific issue we need input up to 1-hour per week max.



Overview of CRDC

Dr Allen Dearry

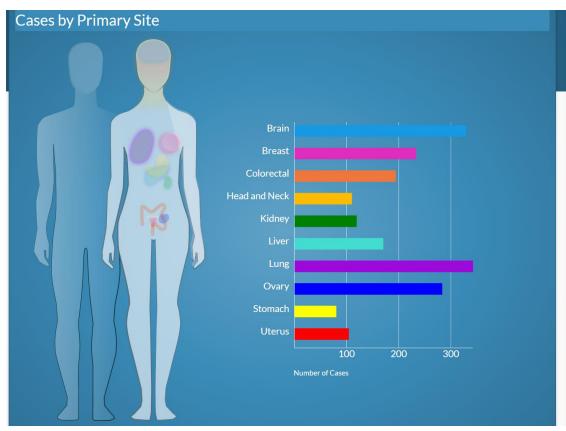


Current data and where we are today, Interoperability

R Rajesh Thangudu



PDC- Current status



Cases by Disease Type	
Breast Invasive Carcinoma	233
Chromophobe Renal Cell Carcinoma	1
Clear Cell Renal Cell Carcinoma	116
Colon Adenocarcinoma	164
Early Onset Gastric Cancer	80
Glioblastoma	100
Head and Neck Squamous Cell Carcinoma	110
Hepatocellular Carcinoma	170
Lung Adenocarcinoma	216
Lung Squamous Cell Carcinoma	118
Ovarian Serous Cystadenocarcinoma	283
Papillary Renal Cell Carcinoma	2
Pediatric/AYA Brain Tumors	219
Rectum Adenocarcinoma	30
Uterine Corpus Endometrial Carcinoma	104



PDC by the numbers



STUDIES

From large programs and also smaller labs.



ACQUISITION TYPES

Data Dependent Acquisition
Data Independent Acquisition.



VOLUME

25 TB data including raw and processed data and supplementary information



EXPERIMENTAL TYPES

Lable Free iTRAQ TMT



ANALYTICAL FRACTIONS

Proteome, Phosphoproteome, Acetylome, Glycoproteome, Ubiquitylome



PRIMARY SITES

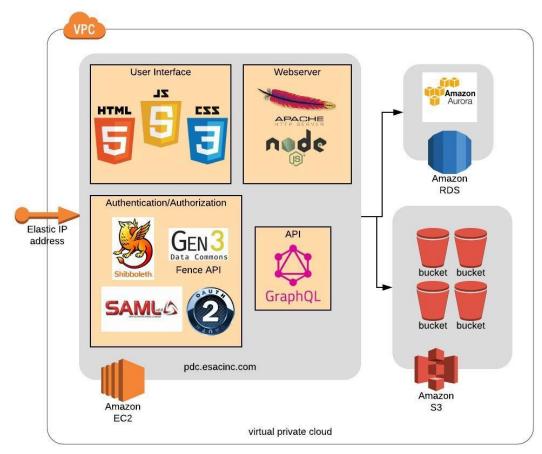
15 cancer types from 11 primary sites





PDC Technology Stack

- PDC Data Portal is a web-based application for querying and viewing Proteomic data
 - Also provides an API for programmatic access
- PDC Workspace is a web-based application for submitting raw data to the PDC for processing
 - Requires authentication (supports Google, NIH/eRA)
- Both work through any browser

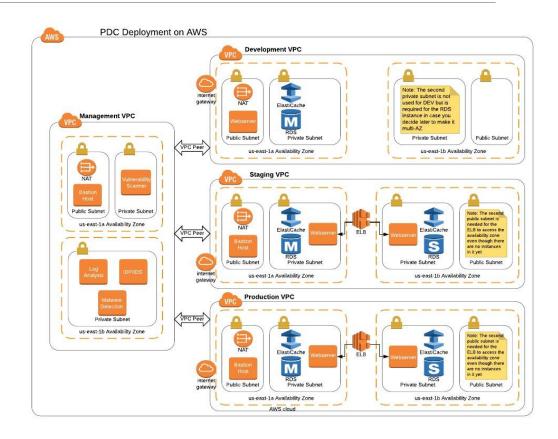




PDC Infrastructure

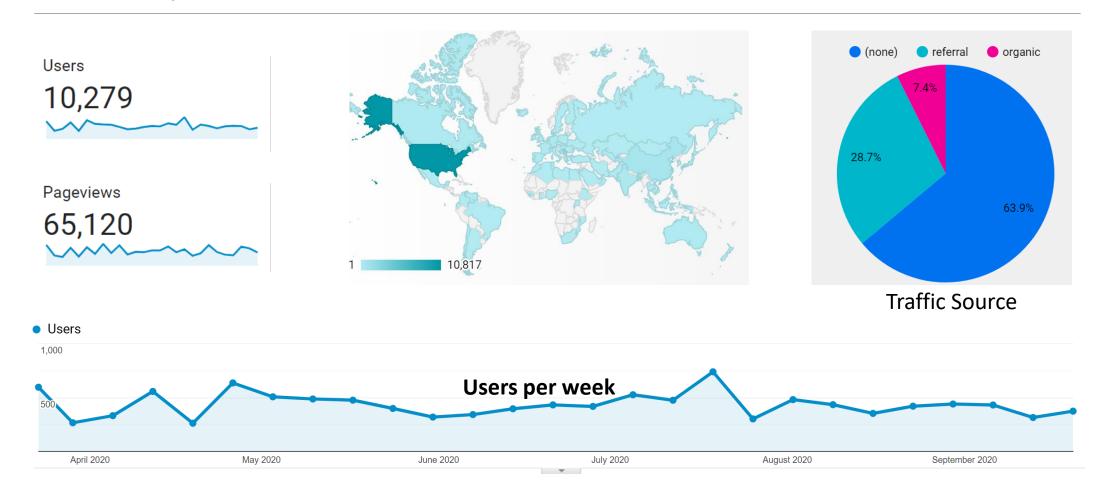
- PDC is FedRAMP and FISMA complaint system with Authority To Operate (ATO) under cancer.gov domain issued on January 15, 2020
 - 278 Security controls across 26 operational areas were planned and implemented
- PDC deployment is based on NIST architecture

PDC went live on March 23, 2020



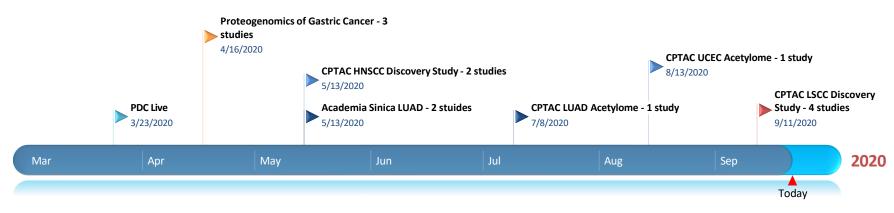


PDC Analytics – since March 23, 2020





PDC timeline since launch

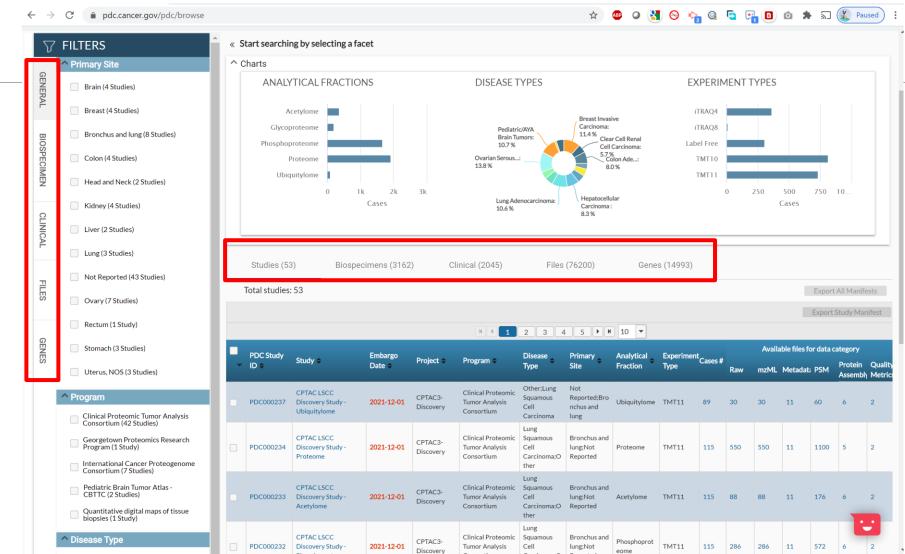


Release includes

- raw data
- clinical data, experimental design
- processed data open formats, PSM, Protein parsimony
- post processing for visualization
- API access



https://pdc.cancer.gov



STUDY SUMMARY: CPTAC UCEC Discovery Study - Proteome

123 Cases

154 Aliquots SUMMARY

PDC Study Identifier P
Study ID c
Study Name C

Experimental Strategy

PDC000125 c935c587-0cd1-11e9-a064-0a9c39d33490 CPTAC UCEC Discovery Study - Proteome Embargo Release Date June 1, 2019

Analytical Fraction Proteome

Disease Types Uterine Corpus Endometrial Carcinoma

Project ID CPTAC3-Discovery

Description ?

Protocol ?

Experimental Design ?

Clinical ?

Biospecimens ?

Workflow ?

DUA 🕜

Data Use Agreement

CPTAC requests that data users abide by the same principles that were previously established in the Fort Lauderdale and Amsterdam meetings. The recommendations from the Fort Lauderdale meeting (2003) on best practices and principles for sharing large-scale genomic data address the roles and responsibilities of data producers, data users and funders of community resource projects. The aim of the recommendations is to establish and maintain an appropriate balance between the interests that data users have in rapid access to data and the needs that data producers have to publish and receive recognition for their work. The conclusion of the attendees at the Fort Lauderdale meeting was that a "responsible use" approach for secondary data users would be sufficient to ensure that the efforts of data producers will be recognized. "Responsible use" was defined as allowing data producers to have the opportunity to publish the initial global analyses of the data within a reasonable period of time prior to secondary

In 2008, the NCI's OCCPR organized a workshop to discuss how and when proteomics data should be released. The result was the Amsterdam Principles that established guidelines for the timing of data release, comprehensiveness of a dataset, data format, deposition to repositories, quality metrics, and responsibility for proteomic data release. Participants agreed that mass spectrometry output data files should be available to support the claims of proteomics publications. In 2010, NCI's OCCPR convened a follow-on workshop to address quality metrics for proteomics with an emphasis on mass spectrometry. As a sign of solidarity for these principles, four peer-reviewed journals simultaneously published the corollary to Amsterdam Principles.

Agreeing to abide by these principles and the CPTAC Publication Guidelines is required to gain access to CPTAC data.

Common Data Analysis Pipeline (PDC Harmonization) data 🕐		
Data Category	Files (n=1639)	
Peptide Spectral Matches (Open Standard)	408	
Peptide Spectral Matches (Text)	408	
Processed Mass Spectra (Open Standard)	408	
Protein Assembly (Text)	5	
Quality Metrics (Text)	1	
Quality Metrics (Web)	1	
Raw Mass Spectra (Proprietary)	408	

External References	
Clinical Proteomic Tumor Analysis Consortium	S043
Database of Genotypes and Phenotypes	phs001287
Related PDC studies	

Supplementary data 🔮			
Data Category		Files (n=16)	
Alternate Processing Pipeline (Archive)		3	
Other Metadata (Document)		13	
	Explore protein quantitation from PDC Common Data Analysis pipeline (CDAP) through heatmaps		
PUBLICATIONS			



Yongchao Dou, Emily A. Kawaler, Daniel Cui Zhou, Tao Liu, David Fenyo, et al., Cell (2020). Vol. 180, Issue 4, p729–748 https://doi.org/10.1016/j.cell.2020.01.026 ×



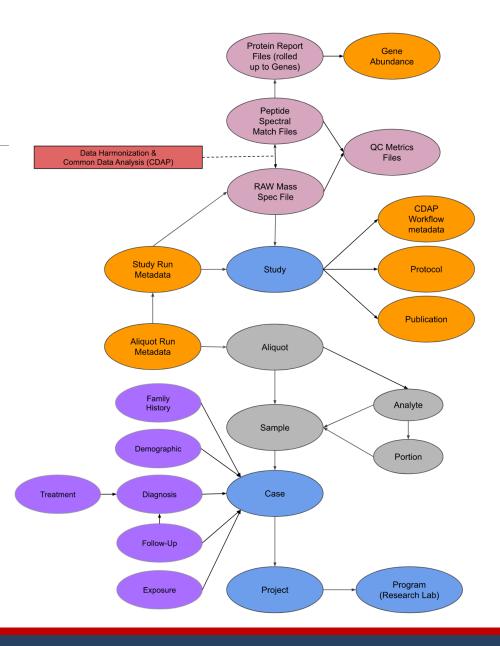
Data Model, Standards, Semantics

Robust Data Model

 Representing the data in a structured manner that allows to collect and distribute data and metadata effectively and efficiently

Consistency of Metadata

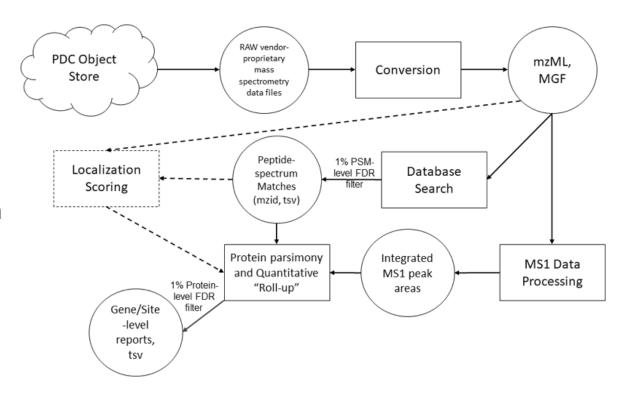
- Reuse clinical metadata and standards from caDSR, NCIt, ICD
- Use HUPO PSI Controlled Vocabulary of proteomics





Data harmonization

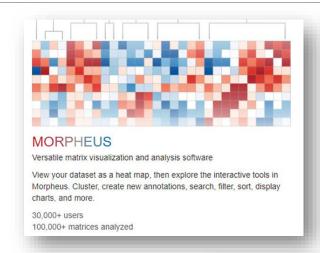
- Harmonization starts with assigning standard identifiers, data integrity checks, adherence to standards and PDC data model.
- All of the data is processed through a common data analysis pipeline (CDAP) for removing data analysis variables, enabling comparisons across datasets.





PDC Analysis tools

- Morpheus viewer a heatmaps visualization tool from Broad Institute for view expression data
- PepQuery a peptide-centric search engine for novel peptide identification and validation from Bing Zhang's lab
- Jbrowse a genome browser for viewing peptides on the genomic coordinates







PDC Data Submission

- A data submission template with examples is available
- A video tutorial and step by step guide
- UI menu driven and tsv files in predefined format
- Can request to set up a program or lab and have full control of the metadata
- Data remains private and modifiable until release

Join NCI Proteomic Data Portal







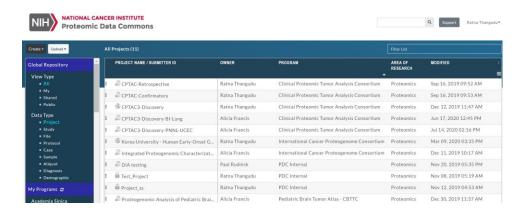


Upload Files

Create Studies

Share Data

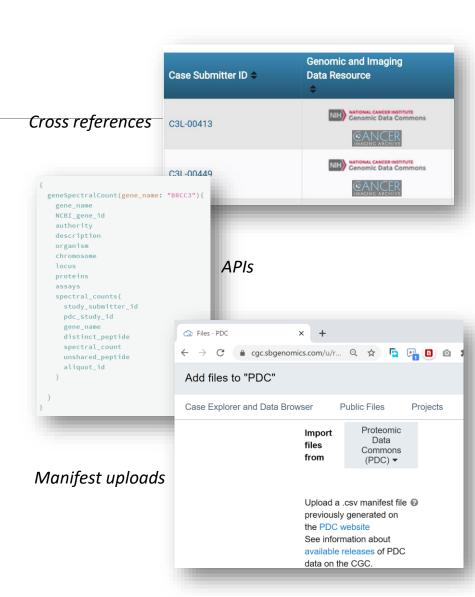
Analyze Data





Interoperability

- Data standards and harmonization will help both general users and also the CCDH and CDA
- Large suite of graphQL based APIs to provide flexibility for programmatic access
- Cross-referencing other multiomic resources
- Data files indexed by CRDC DCF service for easy access from analytical platforms such as SBG
- Authorization and authentication through DCF Fence API which allows users to register using their existing credentials such as Google, NHI, eRA, etc





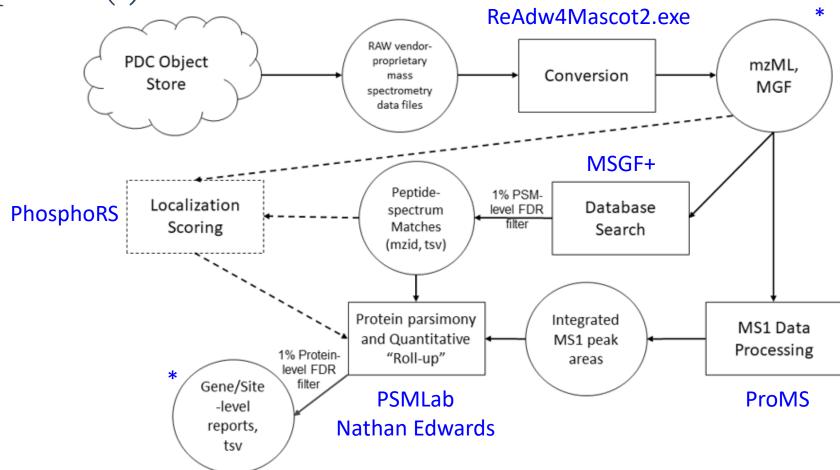
Data harmonization, APIs, CDAP and other pipelines

Paul Rudnick



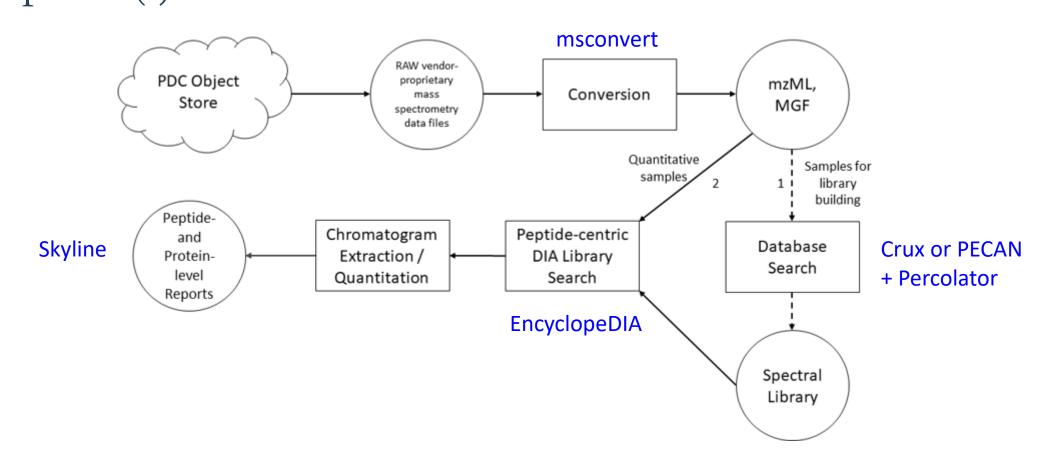
Harmonization (DDA): Common Data Analysis

Pipeline(s): 2013-current





Harmonization (DIA): Common Data Analysis Pipeline(s): 2018-current





How to aliquots map to TMT channels for a given study?

Gets experimental design for a PDC Study ID

?query={ studyExperimentalDesign (pdc_study_id: "{pdc_study_id}") { pdc_study_id, study_run_metadata_id,

Show samples </>

{ pdc_study_id, study_run_metadata_id, study_run_metadata_submitter_id, study_id, study_submitter_id, analyte, acquisition_type, experiment_type, plex_dataset_name, experiment_number, number_of_fractions, label_free, itraq_113, itraq_114, itraq_115, itraq_116, itraq_117, itraq_118, itraq_119, itraq_121, tmt_126, tmt_127n, tmt_127c, tmt_128n, tmt_128c, tmt_129n, tmt_129c, tmt_130n, tmt_130c, tmt_131, tmt_131c } }

Example from Swagger page.

https://pdc.cancer.gov/graphql studyExperimentalDesign PRETTIFY HISTORY https://proteomic.datacommons.cancer.gov/graphql studyExperimentalDesign(pdc_study_id: "PDC000120") pdc_study_id study run metadata id study_run_metadata_submitter_id study_id study_submitter_id analyte acquisition_type experiment_type plex_dataset_name experiment_number number_of_fractions label_free itraq_113 itrag_114 itraq_115 18 itraq_116 19 itrag 117 itrag 118 itraq_119 itraq_121 tmt_126 tmt_127n tmt_127c tmt 128n tmt 128c tmt_129n tmt 129c tmt_130n tmt_130c tmt_131 tmt 131c

COPY CURL "studyExperimentalDesign": ["pdc_study_id": "PDC000120", "study_run_metadata_id": "92c14909-56cc-11e8-b664-00a098d917f8". "study_run_metadata_submitter_id": "S039-1-1", "study_id": "bdcd3802-57b8-11e8-b07a-00a098d917f8", "study_submitter_id": "S039-1", "analyte": "Proteome", "acquisition_type": "DDA", "experiment_type": "TMT10", "plex_dataset_name": "01CPTAC_BCprospective_Proteome_BC_20160911", "experiment_number": 80, "number_of_fractions": "25", "label_free": "", "itrag 113": null, "itraq_114": "", "itraq_115": "", "itraq_116": "", "itraq_117": "", "itrag_118": null, "itraq_119": null, "itraq_121": null, "tmt_126": "ef52c640-13a9-4855-9ce2-0be77a_D2", "tmt_127n": "6d34d499-167e-42aa-9790-316fca_D2", "tmt_127c": "2e700669-85b0-43fa-a9c7-3eaf5a_D2", "tmt_128n": "079b5600-6afc-4785-bb22-48cfab_D2", "tmt_128c": "0bb9d596-774e-452b-9c89-a6643c_D2", "tmt_129n": "31b13596-554e-452f-91a4-7e67a8_D2", "tmt_129c": "12ce8313-6c54-4bee-a996-1aa7f8_D2", "tmt_130n": "392b8aa4-9f99-4250-b693-326260_D2", "tmt_130c": "09659708-7747-4d59-a3b9-e221e0_D2", "tmt_131": "Internal Reference - Pooled Sample", "tmt 131c": null



Jupyter Notebook Example

Proteomic Data

This notebook attempts to demonstrate the following:

- Using the Proteome Data Commons (PDC) API to retreive relative protein express Common Data Analysis Pipeline (<u>CDAP</u>). More information on the PDC implmenta
- 2. Using the PDC API to retrieve the associated clinical metadata.
- 3. Formatting the data for analysis.
- 4. Clustering the data using the Seaborn clustermap package.
- 5. Visualizing the clustermap / heatmap.

The results are intended to help idenify clusters of samples (tumors) displaying similar

These are the required imports. Install them using pip if needed.

```
In [1]: import requests
  import pandas as pd
  import seaborn as sns
  import matplotlib.pyplot as plt
```

Next, set up the query parameters.

The first one is study_submitter_id. These can be retrieved using an API like this one

```
In [2]: study_submitter_id = 'S015-1' # S015-1 is TCGA-Breast(iTRAQ4)
```

Next, select the data type to retrieve for the given study. A table of data_types is availal here. In brief, these values are log2 transformed ratio of the sample to the control chan normalization.

```
In [3]: data_type = 'log2_ratio' # Retrieves CDAP iTRAQ or TMT data
```

Next, set the number of samples to retrieve. Samples are identified by their aliquot_sut currently recommended during the initial PDC development period. Higher values may

```
In [4]: max_aliquots = 25
```

Next, the expression data GraphQL query is set up. Adding the study_submitter_id a

```
Let's do the same thing for the clinical data.
```

Now we can define a function to make the <u>GraphQL</u> Post query. This will get called one new to GraphQL, you can also try your queries <u>here</u>.

```
In [7]: def query_pdc(query):
    URL = 'https://pdc-dev.esacinc.com/graphql'
    # Send the POST graphql query
    print('Sending query.')
    pdc_response = requests.post(URL, json={'query': query})

# Set up a data structure for the query result
    decoded = dict()

# Check the results
    if pdc_response.ok:
    # Decode the response
        decoded = pdc_response.json()
    else:
    # Response not OK, see error
    pdc_response.raise_for_status()
    return decoded
```

```
In [11]: decoded = query_pdc(metadata_query)
matrix = decoded['data']['clinicalMetadata']
metadata = pd.DataFrame(matrix, columns=matrix[0]).set_index
print('Created a dataframe of these dimensions: {}'.format(m
```

Sending query.
Created a dataframe of these dimensions: (111, 4)

We can then set up a color mapping function for the clinical annotations

```
In [12]: def get_colors(df, name, color) -> pd.Series:
    s = df[name]
    su = s.unique()
    colors = sns.light_palette(color, len(su))
    lut = dict(zip(su, colors))
    return s.map(lut)
```

Next, call get_colors() to map the tumor_stage and primary_diagnosis attrit

```
In [13]: stage_col_colors = get_colors(metadata, 'tumor_stage', 'red'
diagnosis_col_colors = get_colors(metadata, 'primary_diagnos
```

And, finally, generate the large clustermap.

Retrieve the expression data and convert it into a pandas dataframe.

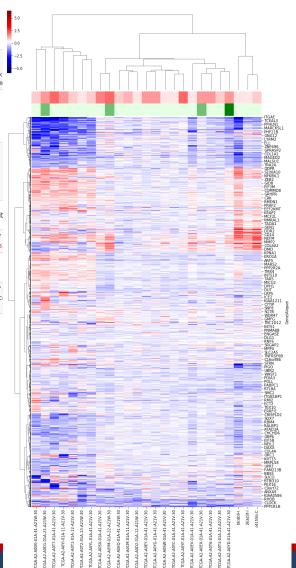
```
In [8]: decoded = query_pdc(exp_data_query)
matrix = decoded['data']['paginatedDataMatrix']['dataMatrix']

# Aliquots are first row, gene names are first column
ga = pd.DataFrame(matrix[1:], columns=matrix[0]).set_index('Gene/Aliquot')
print('Created a dataFrame of these dimensions: {}'.format(ga.shape))
Sending query.
```

Created a dataframe of these dimensions: (10625, 25)

Since the expression values are returned as strings, we need to convert those to floats and deal with missing data.

The clustermap module within the Seaborn package does not allow for NaN values. So we must create a mask value that does not interfere much with the clustering and is likely to be unique. Not imputation is used. Missing data is a particularly tough challenge for proteomics data, particularly for phosphorylation studies. By using a value close to 0, we are saying that these are unchanged between samples. Better solutions may be used.





Seven Bridges Integration

ID

raw files

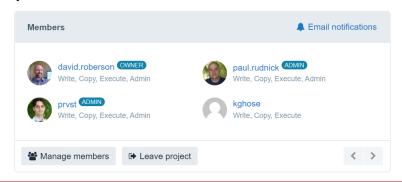
0 database name

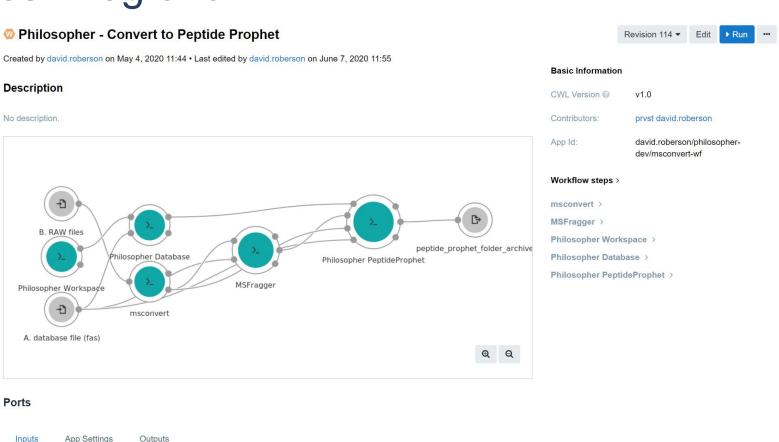
Label

A. database file (fas)

B. RAW files

- Direct loading of files by manifest generated on the PDC (i.e., no upload/download of data files)
- Applications added as Docker containers
- Pipelines designed using Rabbix (GUI for generating CWL)
- MSFragger + Prophets + TMT analysis of ccRCC dataset 23 plexes -> \$13.31





Required

Yes

Prefix

Format

FAS

RAW

Type

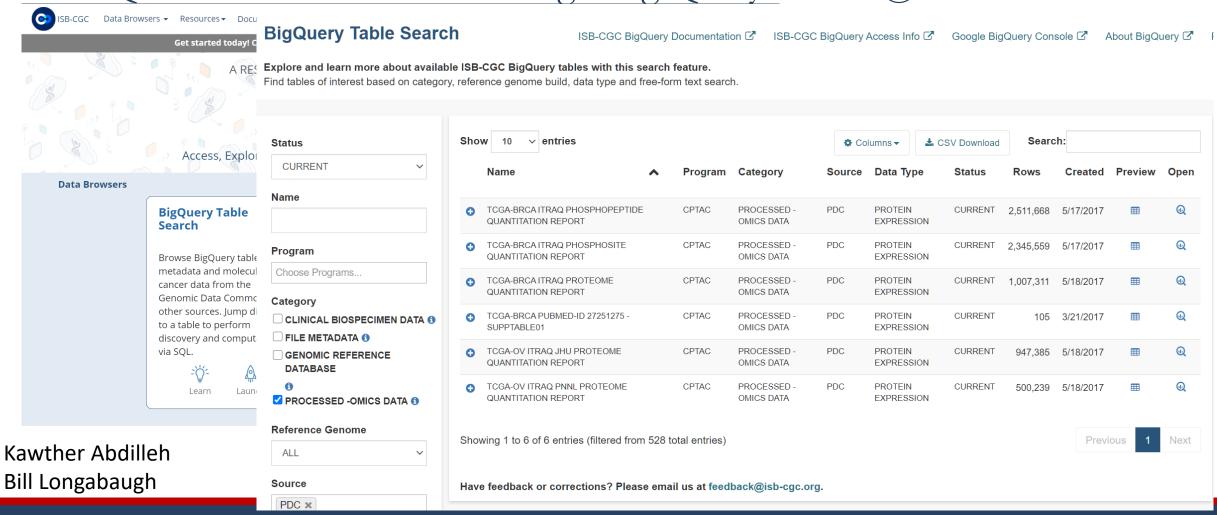
File

File array

Dave Roberson Manisha Ray Felipe Leprevost



PDC Quant Data Loaded into Google Big Query Tables @ ISB-CGC





Our Contact Information:

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