Cancer Data Analytics on the ISB-CGC platform

April 9, 2021 www.isb-cqc.org





Agenda for Today's Presentation

- An introduction to the ISB-CGC role in the CRDC
- The data analysis avenues accessible via the ISB-CGC
 - Web tools
 - Google VMs
 - Google BigQuery
- Examples of analyses run with our tools

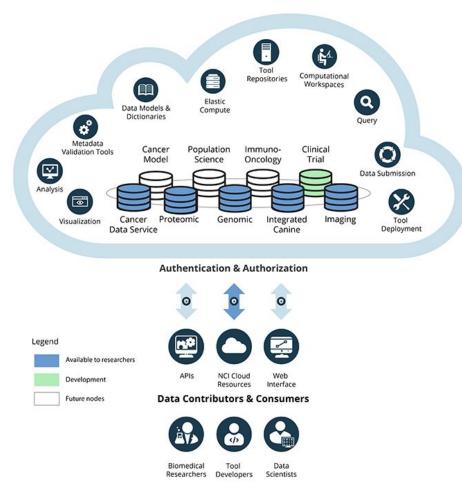


The CRDC Today

The CRDC is a cloud-based data science infrastructure that provides secure access to large, comprehensive, and expanding collections of cancer research data. Users can explore and use analytical and visualization tools for data analysis in the cloud.

The Cloud Resources have >3,000 on average active users per month from >500 institutions around the world

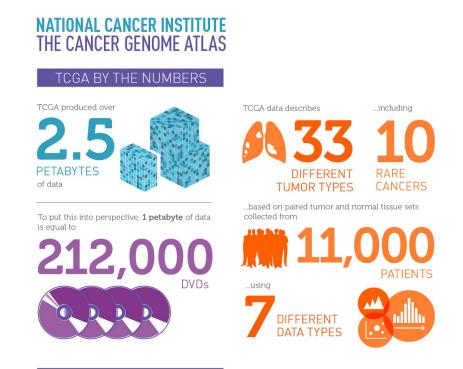
NCI Cancer Research Data Commons (CRDC)



ISB-CGC provides Data as a Service (DaaS) solutions to the rapid growth of cancer data

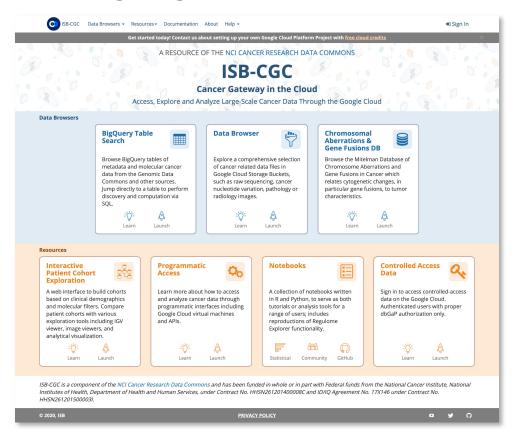
Common problems of big data:

- Data discovery is onerous
- Transfer speeds become bottlenecks with scaling data size
- Availability of data can be tenuous



TCGA RESULTS & FINDINGS

The ISB-CGC landing page provides access to our resources







Our mission at ISB-CGC

To make NCI multi-omics cancer data as well as high-performance compute resources available via the Google Cloud Platform through multiple modes:

- Interactive web tools for cohort building and data discovery
- Easily accessible and query-able tables for multivariate data analysis
- Advanced pipeline and workflow execution on Google Cloud virtual machines
- Intentionally a "thin" layer on top of Google Cloud
 - Easy access to Google Tools
 - Direct access to NCI datasets
 - Raw GC bucket files
 - structured "BigQuery" tables for interactive data mining)



The data analysis avenues accessible via the ISB-CGC



Three entry points for exploring cancer data on ISB-CGC

DASHBOARD

Your Dashboard > Cohorts >

Create Cohort - Filters

TCGA DATA

WORKBOOKS ▼

PROGRAMS -

Selected Filters

ANALYSES -

CCLE DATA

GENES & miRNAs ▼

VARIABLES ▼

TARGET DATA

COHORTS -

Save As New Cohort

Clear All

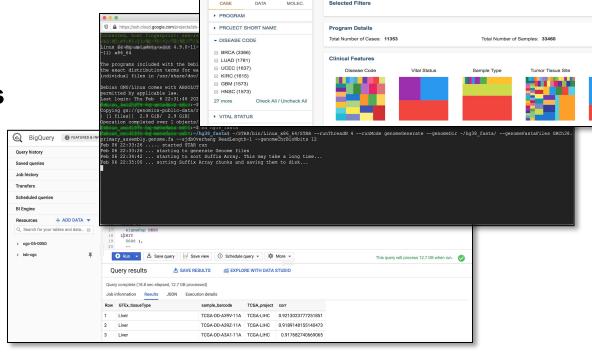
USER DATA

Gender



Google VMs

BigQuery



Some example use-cases of each major entry point

Interactive web-based exploration

- Select a subset of TCGA samples based on clinical or molecular characteristics
- Compare one cohort to another
- Upload a small private dataset to analyze in conjunction with TCGA data
- etc...

Interactive cancer data exploration and analysis

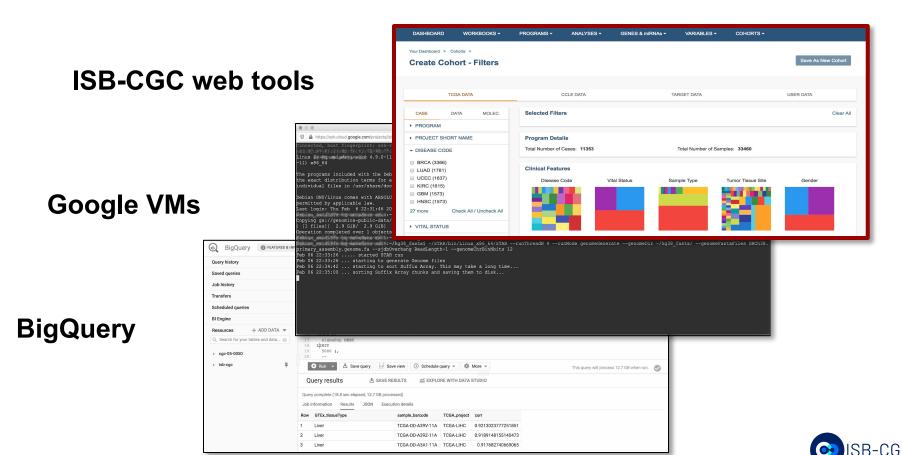
- Interactive data exploration in BigQuery
- Use R or Python to perform custom multivariate analyses
- Directly run statistical tests on data in BigQuery using custom functions
- etc...

Direct Command line Access to Google virtual machines

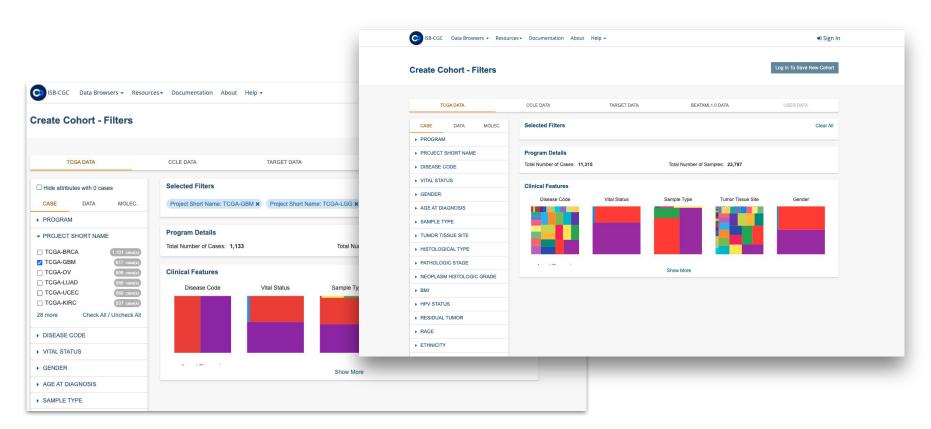
- Test new algorithm on hundreds or thousands of BAM or FASTQ files
- Run novel image segmentation method across whole-slide images
- etc...



Three entry points for exploring cancer data on ISB-CGC

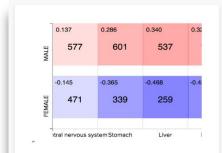


Interactive cohort-building using the ISB-CGC





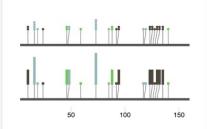
ISB-CGC has several interactive apps to generate quick plots



Cubby Hole Plot

Used to plot two categorical features. Boxes are colored by their related p-values.

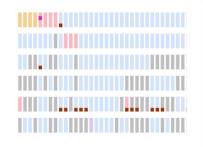
Start A New Workbook Cubby Hole Plot



SeqPeek

This visualization shows where somatic mutations have been observed on a linear representation of a specific protein. Each horizontal strip represents the protein, with data from different tumor types (aka cohorts or studies) shown stacked one on top of the other.

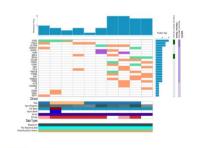
Start A New Workbook SegPeek



OncoPrint

Used to plot multiple genomic alteration (somatic mutation) events across a set of samples by heatmap. OncoPrint is developed and provided by cBioPortal.

Start A New Workbook OncoPrint



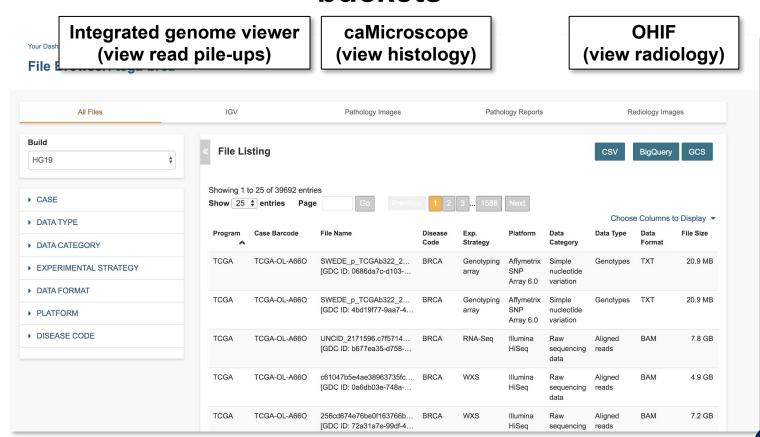
OncoGrid

Used to view multiple genomic alteration (somatic mutation) events, clinical data, available files across a set of cases by interactive heatmap. OncoGrid library is developed at Ontario Institute for Cancer Research (OICR).

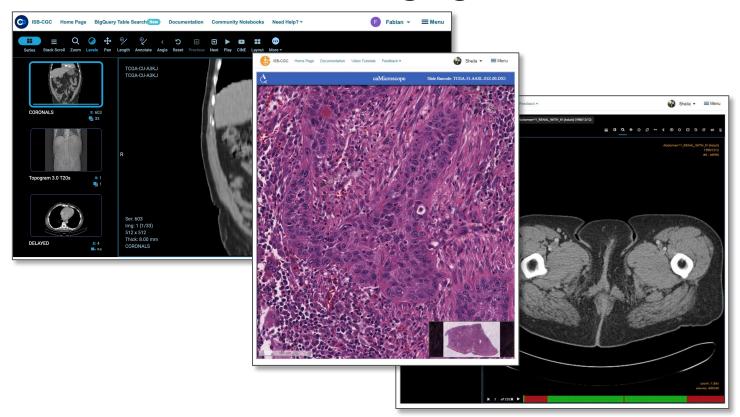
Start A New Workbook OncoGrid



File browser to browse the data hosted in cloud buckets



Interactive image viewers allows for browsing of cancer imaging data





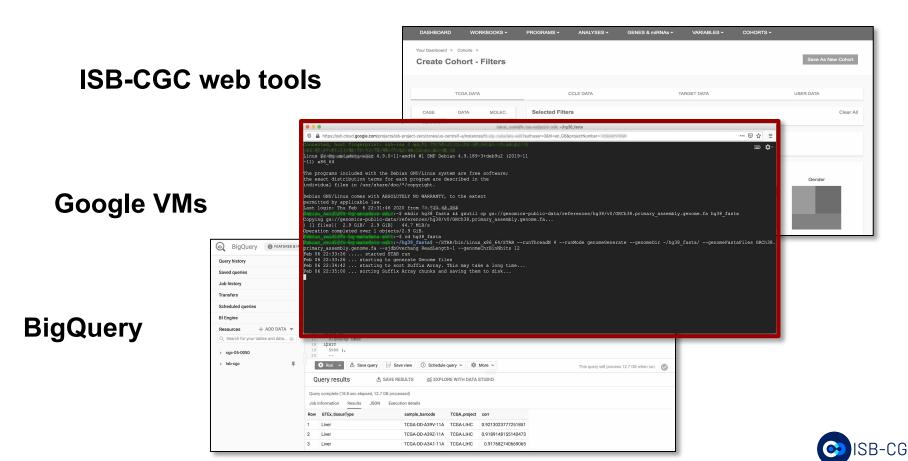
Mitelman database is also hosted by ISB-CGC



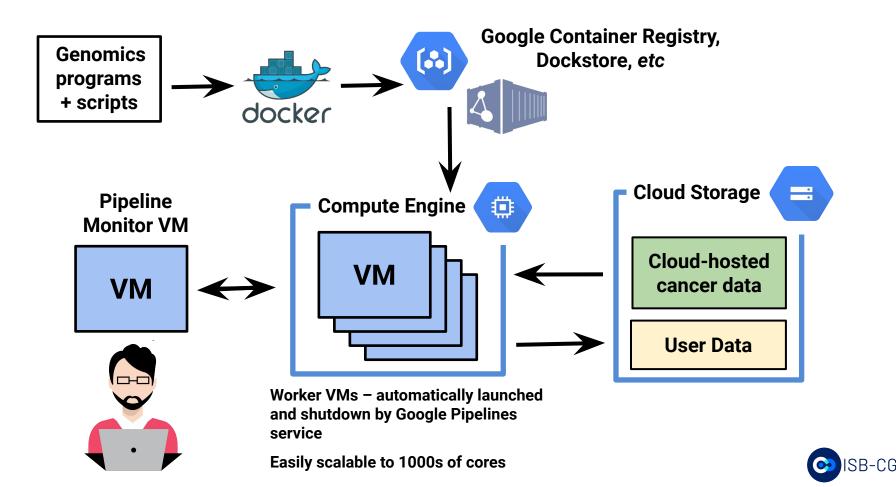
Also ongoing work towards hosting the TP53 database soon



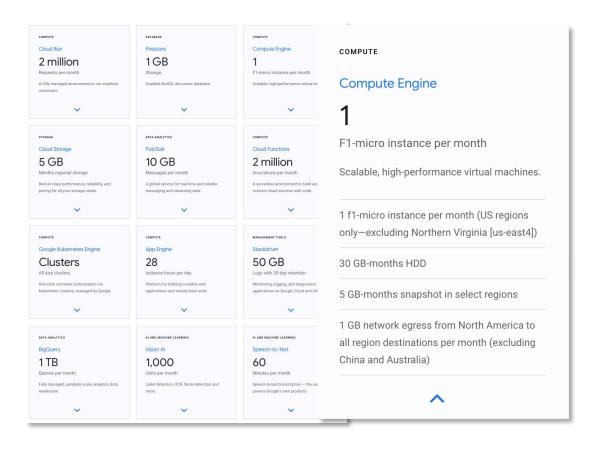
Three entry points for exploring cancer data on ISB-CGC



Advanced workflow execution on -omics data enabled by ISB-CGC



Google Cloud Platform Free Tier lets you perform small scale computes with no cost!

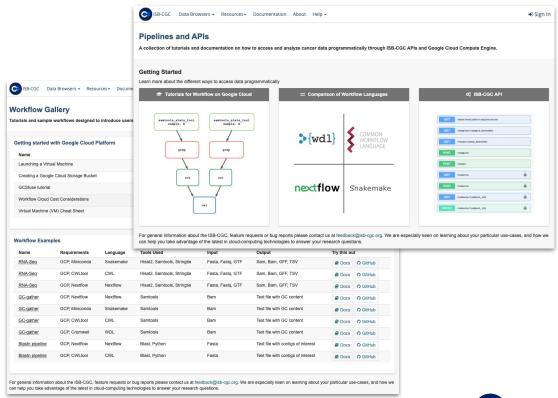




We have several workflow and pipeline tutorials at ISB-CGC

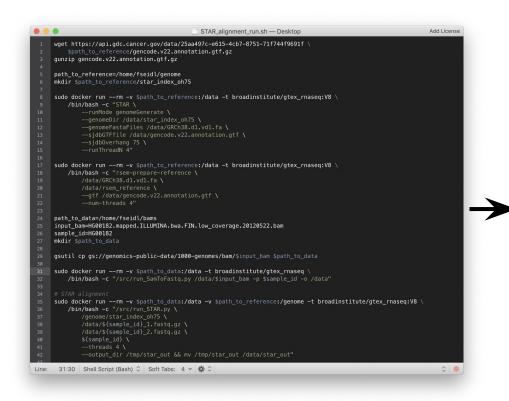
Tutorials and sample workflows designed to introduce and enable users on how to run workflows in CWL, Nextflow, Snakemake and WDL on GCP

https://isb-cgc.appspot.com/
programmatic access/





Example RNASeq quantification workflow using a Docker image



Row	HGNC_gene_symbol	gene_id	normalized_count
1	RELN	5649	5092.9882
2	DDX49	54555	1233.9143
3	OCSTAMP	128506	1.2346
4	RUFY4	285180	0.9481
5	SLC6A4	6532	1.0684
6	NOXA1	10811	14.8593
7	TAGLN2	8407	3785.6545
8	ZNF484	83744	40.8805
9	RNF217	154214	167.8584
10	RHOC	389	2670.3879
11	RNF219	79596	136.9329
12	MANEA	79694	797.0085
13	PALB2	79728	174.2287
14	MRPL35	51318	803.0303
15	IQSEC1	9922	2266.2474
16	FAM57B	83723	1.3774
17	CFLAR	8837	1108.9744
18	MAML2	84441	79.8898



Easily run batches of jobs in the cloud using dsub

Overview

dsub is a command-line tool that makes it easy to submit and run batch scripts in the cloud.

The dsub user experience is modeled after traditional high-performance computing job schedulers like Grid Engine and Slurm. You write a script and then submit it to a job scheduler from a shell prompt on your local machine.

Today dsub supports Google Cloud as the backend batch job runner, along with a local provider for development and testing. With help from the community, we'd like to add other backends, such as a Grid Engine, Slurm, Amazon Batch, and Azure Batch.

Getting started

You can install dsub from PyPI, or you can clone and install from github.

```
dsub \
    --name kallisto_quant \
    --project ${GS_PROJECT} \
    --zones 'us-*' \
    --image "nareshr/kallisto:v0.43" \
    --input "KALIDX=${GS_BUCKET}/Homo_sapiens.GRCh37.cdna.all.kal.idx" \
    --input "FASTQ=${GS_BUCKET}/All_CCLE_customDB.fastq" \
    --output-recursive "KALOUT=${GS_BUCKET}/output" \
    --logging ${GS_BUCKET}/log \
    --min-cores 8 \
    --command 'kallisto quant -i ${KALIDX} -o ${KALOUT} -b 100 --single -l 180 -s 20 -t 8 ${FASTQ}' \
    --wait
```

Google Cloud Life Sciences

Features

Cost-optimized compute

Google Cloud's Healthcare and Life Sciences team has optimized the most popular methods—like GATK, DeepVariant, and Sentieon—to run on GCP.

Flexible machine sizes

Take advantage of Compute Engine, our infrastructure as a service (laaS), to run large-scale workloads on virtual machines and pay only for what you use.

Built for batch processing

Preemptible VMs for affordable batch processing on fault-tolerant workloads to save you time and money.

Fully integrated with GCP

Experience the power of Google Cloud's infrastructure with fast virtual machines, scalable storage, serverless data warehouses, and fully managed databases with GCP integration to tools like Cloud Spanner and BigQuery.

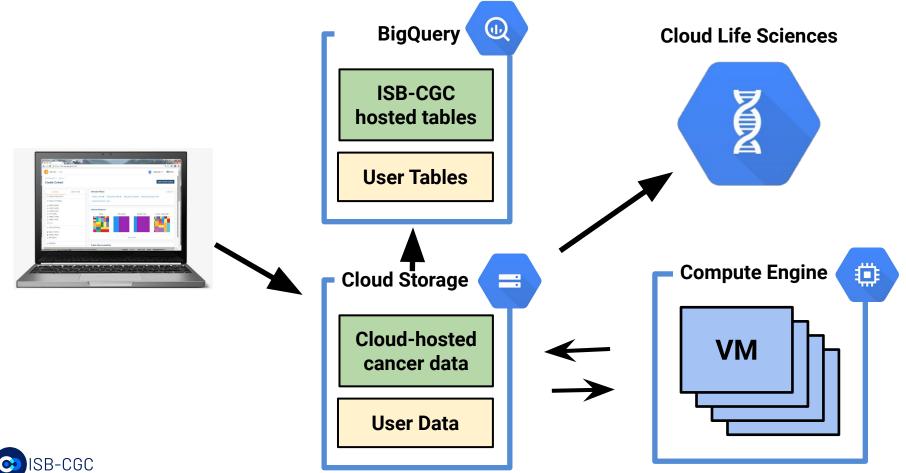
Open and interoperable

Use the tools and workflows you already know and enjoy support for open industry standards like Global Alliance for Genomics and Health.

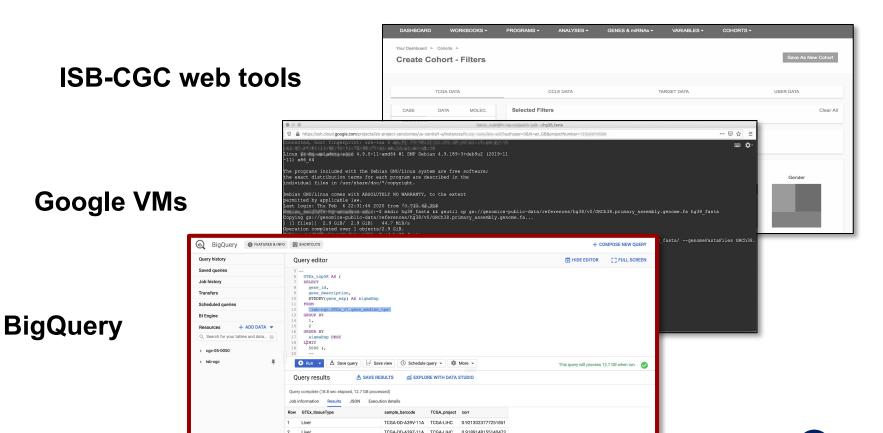
Ready for AI / ML

Bring your data closer to public datasets and advanced analytics that come along with GCP.

Example end-to-end workflow analysis on ISB-CGC

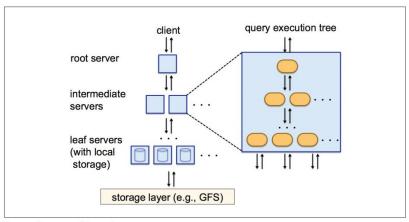


Three entry points for exploring cancer data on ISB-CGC



Attributes of Google BigQuery that make it ideal for cancer data analytics

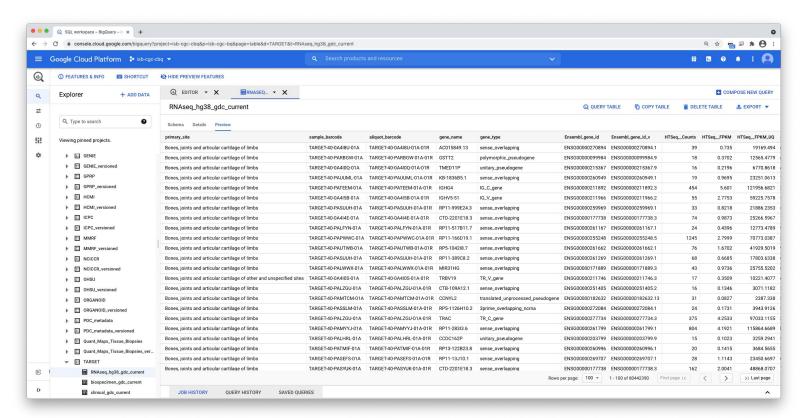
- Columnar database ideal for storing tabular data (RNA sequencing etc.)
- Query speed is automatically scaled by multiprocessing
- Powerful SQL language interface, including user defined functions
- Can join tables based on shared variables
- ISB-CGC combines data of a similar type into single BigQuery tables
 - For example: ~150 individual MAF files were combined to generate a single table





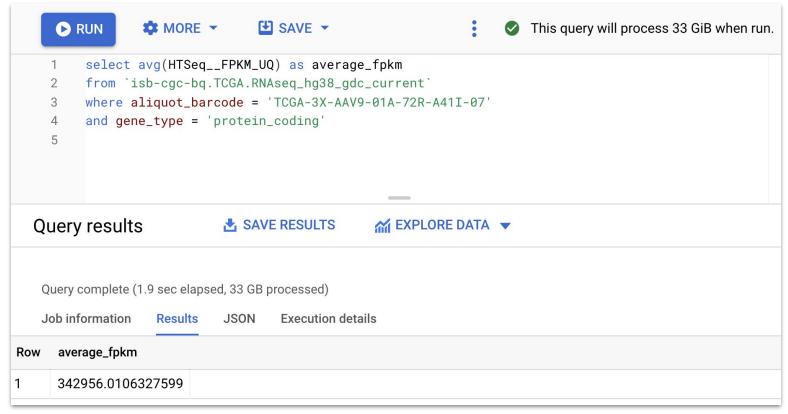
Tree architecture of Dremel

You can think of individual BigQuery tables very simply as a tabular database

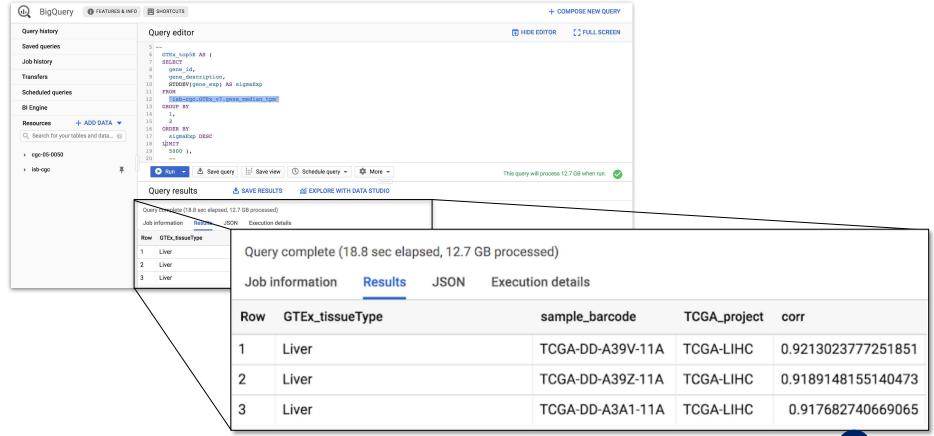




The unique benefit is that you can mine these data quickly and cheaply



Analyze correlation between TCGA samples & GTEx tissue types quickly and cheaply



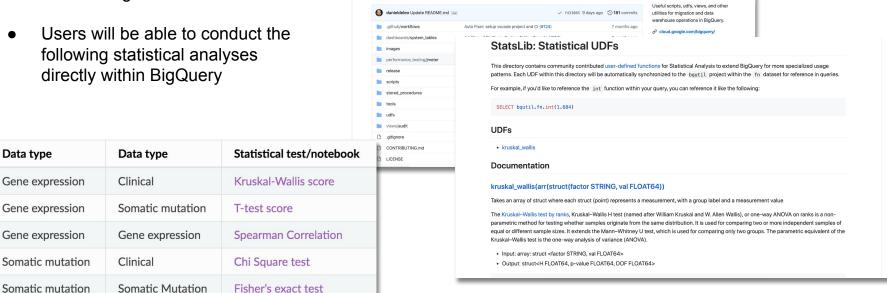


Custom User Defined Functions allow users to expand beyond the default functionality

☐ GoogleCloudPlatform / bigguery-utils

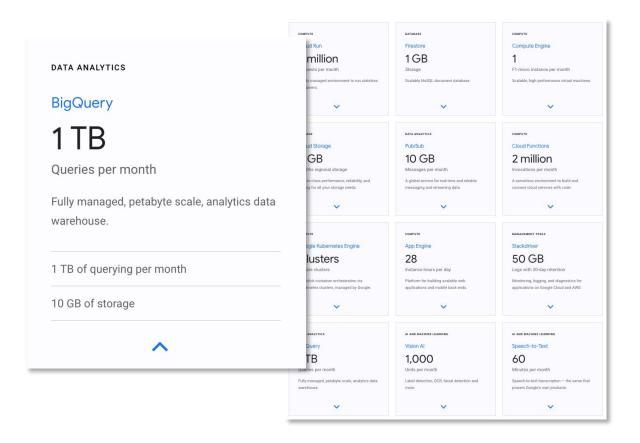
P master ▼ P 13 branches O tags

 We are contributing commonly used statistical methods as UDFs to the Google BQ StatsLib



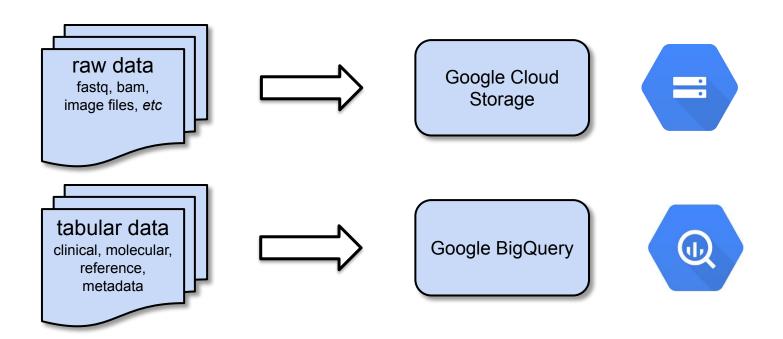


Google Cloud Platform Free Tier lets you perform introductory queries at no cost





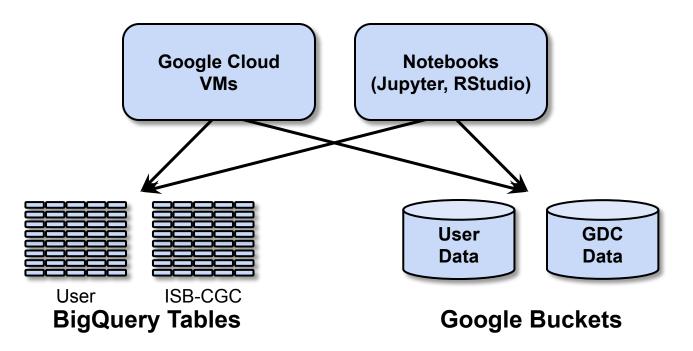
How do users access data on ISB-CGC?





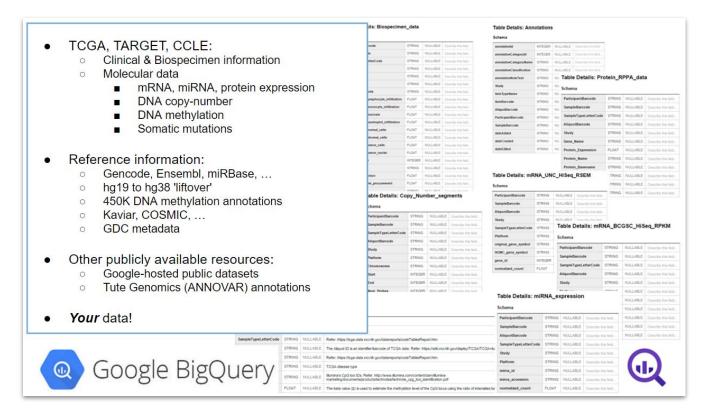
Multiple easy avenues for computing on data on ISB-CGC

ISB-CGC enables full command line access to analyze cloud hosted data via a collection of powerful tools and technologies along with the ability to install your own tools





In total, ISB-CGC hosts multiple TBs of cancer research data across 440 open-access BigQuery tables





This is potentially overwhelming for data discovery, we have a table search UI to help

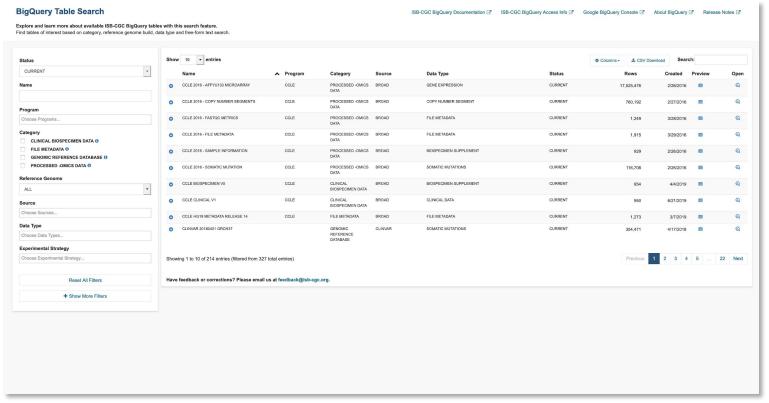
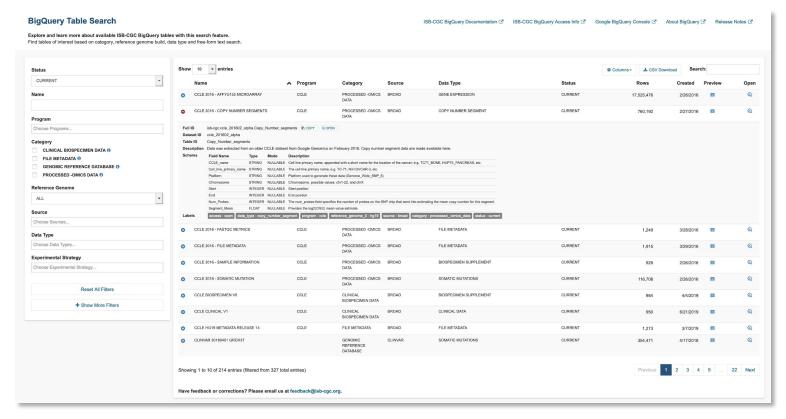




Table schemas are easily accessible through this UI





Benefits of the ISB-CGC BigQuery Table Search

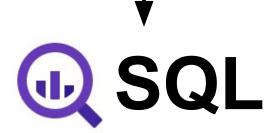
- Allows users to browse and learn more about available ISB-CGC BigQuery tables
- Each table has been curated to include detailed table and field descriptions as well as table labels
- Identify table(s) of interest by filtering (e.g. by reference genome build, data type, category) or via free-form text search
- Get a snapshot of table contents by previewing the first few (~10) lines
- Found a table of interested? An "open" button takes users directly to the GCP BigQuery Console.





Use Google BigQuery to easily connect your research to public datasets

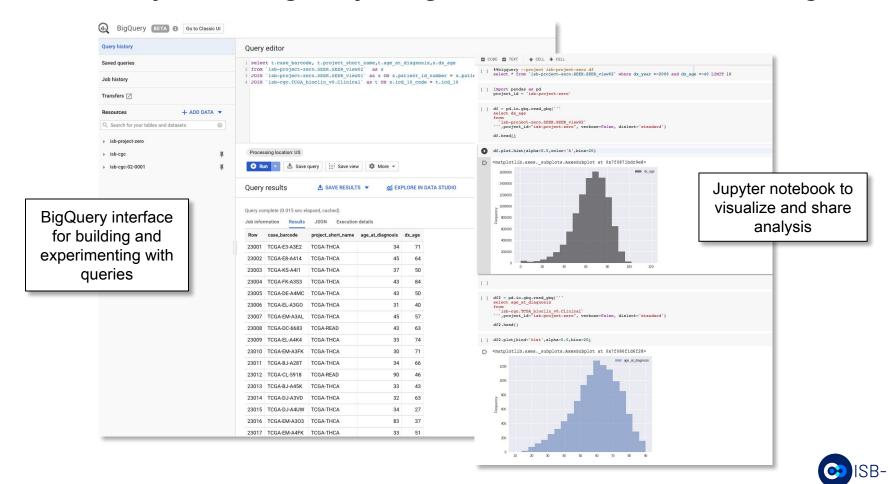
ISB-CGC and Other Public Datasets



Private User Data and Derived Results

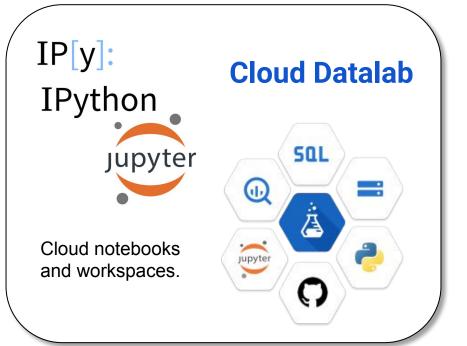


Tables can be joined in BigQuery using SQL to draw connections amongst data



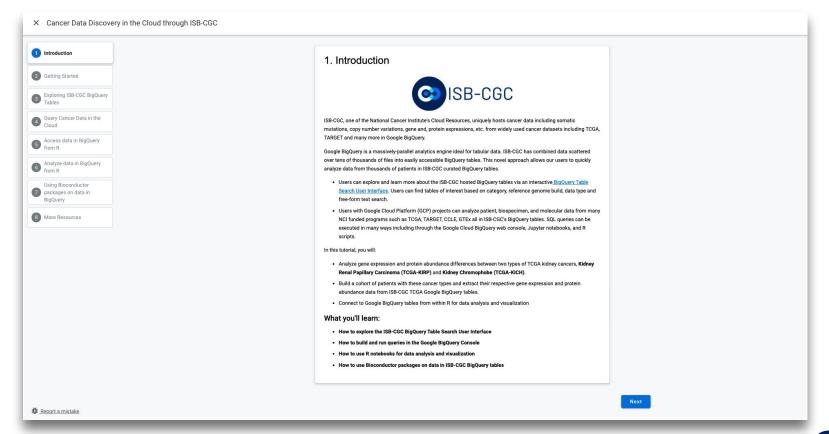
BigQuery integrates with a variety of commonly used analysis tools







Interactive step-by-step guide on BigQuery data analysis



Some examples of analyses run with our tools



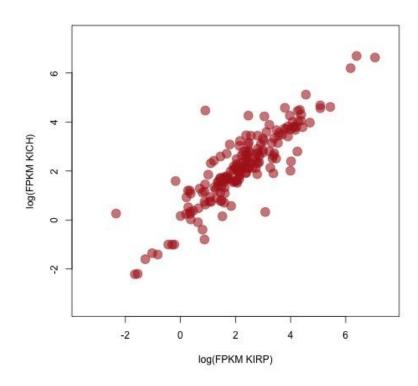
BigQuery can be used to join tables of different data types

```
1 with gexp as
          (SELECT
              project_short_name,
              case_barcode,
             gene name.
              avg(HTSeq__FPKM) as mean_gexp
          FROM 'isb-cgc.TCGA_hg38_data_v0.RNAseq_Gene_Expression'
 8 ~
          WHERE
 9
              project_short_name in ('TCGA-KIRP', 'TCGA-KICH')
10
              AND gene_type = 'protein_coding'
11 ~
          GROUP BY
12
              project_short_name, case_barcode, gene_name
13
14 v pexp as
          (SELECT
16
              project_short_name,
17
              case_barcode, gene_name,
18
              avg(protein_expression) as mean_pexp
19
          FROM 'isb-cgc.TCGA_hg38_data_v0.Protein_Expression'
20 ~
          WHERE
21
              project_short_name in ('TCGA-KIRP', 'TCGA-KICH')
22 V
          GROUP BY
23
              project short name, case barcode, gene name
24
25 V SELECT
26
          gexp.project_short_name.
27
          gexp.case_barcode,
28
          gexp.gene_name,
29
          gexp.mean_gexp,
30
          pexp.mean_pexp
31 V FROM gexp
32
          inner join pexp
33
34
          gexp.project_short_name = pexp.project_short_name
35
          AND gexp.case_barcode = pexp.case_barcode
36
          AND gexp.gene_name = pexp.gene_name
```

Query complete (3.6 sec elapsed, 36.5 GB processed) Job information Results JSON Execution details					
1	TCGA-KIRP	TCGA-BQ-5882	CASP9	4.36721774268	-0.77899630325
2	TCGA-KIRP	TCGA-BQ-5893	CASP9	3.51383227626	-0.00487536525000024
3	TCGA-KIRP	TCGA-UZ-A9PV	CASP9	5.18471681617	0.608095901
4	TCGA-KIRP	TCGA-HE-7130	CASP9	9.66588010427	1.26419392825
5	TCGA-KIRP	TCGA-BQ-7051	CASP9	4.960828359680001	0.16363261725
6	TCGA-KIRP	TCGA-B9-A5W7	CASP9	3.48913273215	0.4692597255
7	TCGA-KIRP	TCGA-B9-A69E	CASP9	2.31606330472	-0.79851830675
8	TCGA-KIRP	TCGA-IA-A83W	CASP9	7.0151441055	0.0390634209999998
9	TCGA-KIRP	TCGA-KV-A74V	CASP9	3.6511469304	0.58510363975
10	TCGA-KIRP	TCGA-DW-7963	CASP9	2.72821430732	-0.0676392402500001
11	TCGA-KIRP	TCGA-B1-A470	CASP9	4.38451034062	-0.30207994575
12	TCGA-KIRP	TCGA-SX-A7SM	CASP9	5.19366866041	-0.12840562825
13	TCGA-KIRP	TCGA-BQ-7061	CASP9	5.52320872773	-0.4549548795
14	TCGA-KIRP	TCGA-AL-A5DJ	CASP9	3.94040060142	-0.22713179975
15	TCGA-KIRP	TCGA-B9-A8YH	CASP9	4.40211877405	0.307956009
16	TCGA-KIRP	TCGA-J7-A8I2	CASP9	5.40615807819	0.9955787775
17	TCGA-KIRP	TCGA-IZ-8196	CASP9	4.76919558442	0.0767987447499998
18	TCGA-KIRP	TCGA-UZ-A9PR	CASP9	5.16376898893	0.41371152025
19	TCGA-KIRP	TCGA-BQ-5875	CASP9	3.445547761625	-0.35423371525
20	TCGA-KIRP	TCGA-SX-A7SS	CASP9	3.32930470316	-0.12148286825
21	TCGA-KIRP	TCGA-DW-7840	CASP9	4.47098482015	-0.1197760605



This query can be executed and the results downloaded and plotted from R

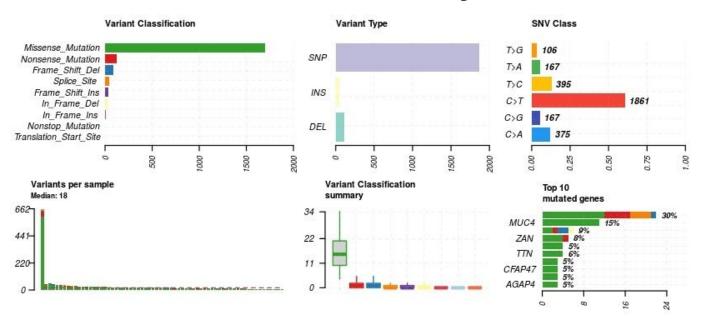


Lots of data types can directly be plugged into Bioconductor pipelines

```
SELECT
    Hugo_Symbol,
    Start_Position,
    End Position,
    Reference_Allele,
    Tumor_Seq_Allele2,
    Variant Classification,
    Variant_Type,
    sample_barcode_tumor
FROM
     `isb-cgc.TCGA_hg38_data_v0.Somatic_Mutation`
WHERE
    project short name = 'TCGA-KICH'"
maf kich <- bg table download(bg project query (project, query = sgl kich))
colnames(maf kich)[9] <- "Tumor Sample Barcode"</pre>
kich <- read.maf(maf_kich)</pre>
plotmafSummary(maf = kich, rmOutlier = TRUE,
                addStat = 'median', dashboard = TRUE,
                titvRaw = FALSE
```

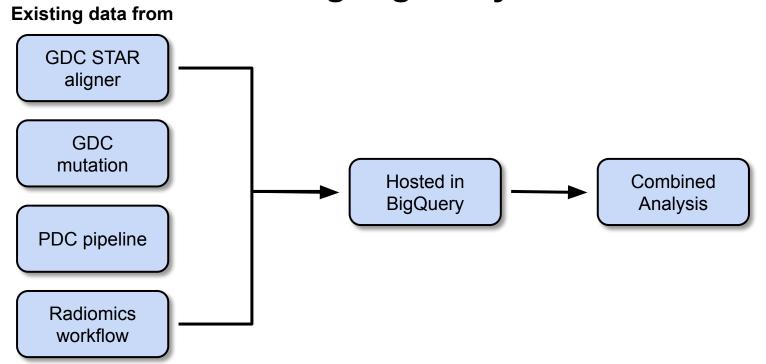


A plot of MAF characteristics using the Bioconductor maftools library





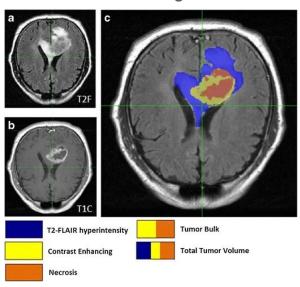
Connecting existing genomics, proteomics, and radiomics data from the respective data commons using BigQuery

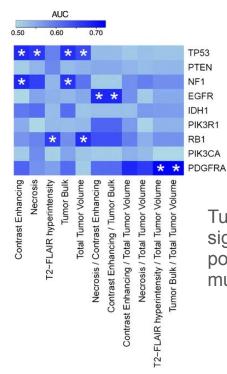




Collaboration between ISB-CGC Cloud Resource and IDC

Tumor identification and characterization by machine learning





Tumor features have significant predictive power about the mutations present

Gutman, et al. Diagnostic Neuroradiology 2015



We have created workflows to join data and run statistical tests

Generated significance values from the correlation between gene expression and tumor features

Using an initial feature set from Bakas, et al. Nature Scientific Data, 2017 to pilot analyses

tcga_gbm_radiomicFeatures

TCGA-02-0006 1996.08.23

TCGA-02-0009 1997.06.14

TCGA-02-0047 1998.12.15

TCGA-02-0068 2000.05.16

TCGA-02-0070 2000 07 10

TCGA-02-0075 1999.09.24

TCGA-02-0085 1999 01 30

10 TCGA-02-0087 1999 12 13

11 TCGA-02-0102 1997.12.15

12 TCGA-02-0106 1998.10.30

TCGA-02-0116 1997.03.22

TCGA-06-0119 2003.12.26

TCGA-06-0122 2004.09.14

TCGA-06-0130 2001.09.11

TCGA-06-0137 2001.12.24

TCGA-06-0138 2002.11.25

VOLUME ET VOLUME NET

50410

13224

8994

13892

25236

3852

1037

46904

35019

64595

17941

9138

49748

VOLUME ED

15723

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74657

25665

94553

66878

59124

11711

33130

30118

83133

48147

30952

129318

4349

11908

9905

11978

3169

26109

3277

42877

204

12627

1665

15826

736

2149

7195

⊞TCGA_G... ▼ X

Details Preview

+ ADD DATA

Explorer

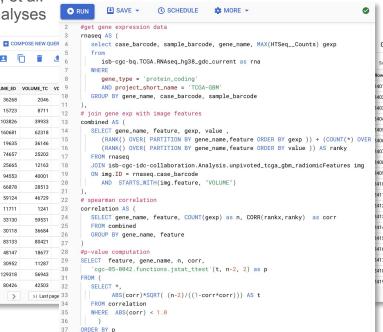
Q Type to search

Viewing pinned projects

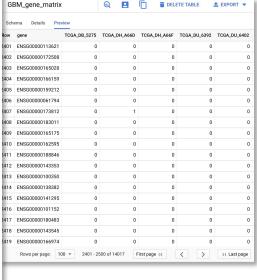
nih-sra-datastore

tcga gbm radiomicFeatures

tcga_lgg_radiomicFeatures



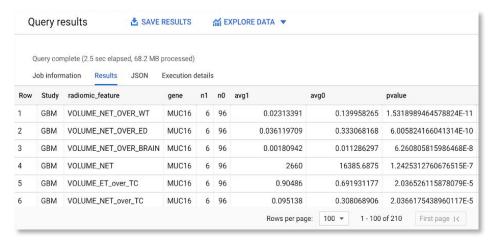
Subset of somatic mutations for each case id to be used for association analyses

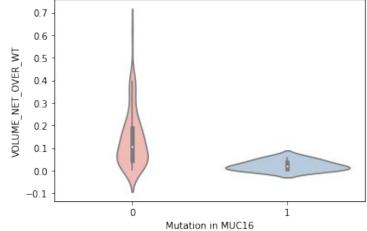




With more effort these cross-omics analyses could lead to novel insights

Using a simple t-test run via SQL in BigQuery we were able to replicate a significant association between a mutated MUC16 gene and an increased tumor volume as measured by radiology.

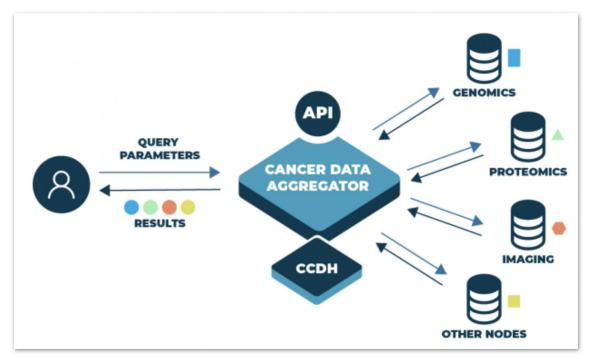






The Cancer Data Aggregator (CDA) is aimed to bridge data discovery between the Data Commons

Federated realtime search across nodes





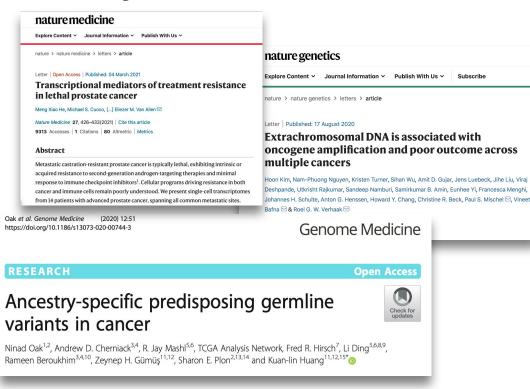
Some more workflows done by ISB-CGC end-users

Multiple PanCancer Atlas projects, including:

- Germline-variant calling
- Fusion gene analysis
- T-cell and B-cell receptor analysis
- viral DNA screening
- MYC pathway analysis (BQ)
- 8-oxoG filtering (MC3 project)

Other end-user projects include:

- SMC-RNA Dream challenge (supporting both the organizers and many participants)
- o tumor-specific alternative polyadenylation
- ML algorithm evaluation & benchmarking
- RNA seq alignment to novel transcriptome(s)
- mRNA expression quantitation
- targeted de-novo assembly
- structural variations (WGS + SNP6 data)
- metagenomics / cancer analysis
- statistical meta-analysis of miRNAs in cancer
- code/tutorial development
- o GDC hg38 TCGA miRNA QC (w/ BCGSC)



with many other manuscripts and grants currently in progress or submitted



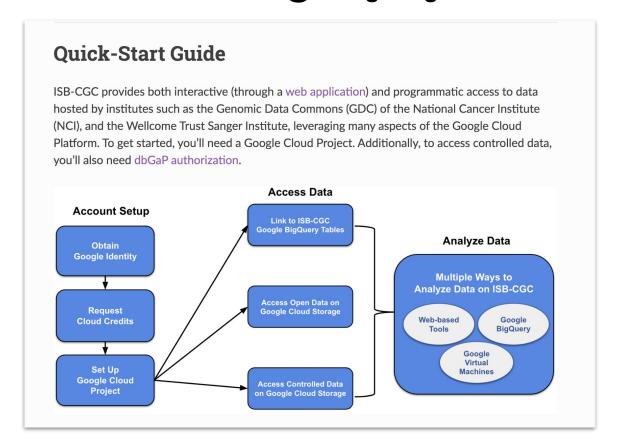
Resources to help you get started on ISB-CGC

- Our documentation can be found at: https://isb-cancer-genomics-cloud.readthedocs.io/
- Our workflow tutorials can be found at: https://isb-cgc.appspot.com/programmatic_access/
- Finally, a quick guide to BigQuery analysis is at: https://isb-cqc.appspot.com/how-to-discover/#0

For feedback/suggestions or need help getting starting, contact us at feedback@isb-cgc.org



Contact us about setting up your own Google Cloud Platform Project! feedback@isb-cgc.org



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Questions?

