The ISB Cancer Genomics Cloud

Workshop at NCI

May 24th 2016

Institute for Systems Biology
Revolutionizing Science. Enhancing Life.

Google Cloud Platform

CSRA

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Our Goals for this Workshop

for YOU

- to understand what the ISB-CGC platform provides
- to know how to find and use the data and tools that suit your needs
- to know your way around the Google Cloud Platform

for US

- to better understand your use-cases, research goals, and needs
- to get feedback & suggestions
    - new data or metadata, sources, and/or formats?
    - new features?
    - new tools?
    - other ideas?

What the ISB-CGC is…

Open platform integrated with the Google Cloud, providing Data, Tools, and Code Samples for a broad range of users

- Data as a Service (DaaS)
  - TCGA clinical and molecular data (multiple formats and technologies)
  - Genome- and Platform-Reference data (*eg* GENCODE, miRTarBase, Kaviar, *etc*)
  - Additional open-access data sets (*eg* CCLE)
- Tools & Applications (SaaS)
  - web app allows interactive and custom visualizations of the TCGA data
  - R and Python examples to get you started implementing your own custom analyses
  - programmatic API endpoints to supplement Google APIs
  - framework to help you use the new Google Pipelines API to run and manage tens of thousands of compute tasks

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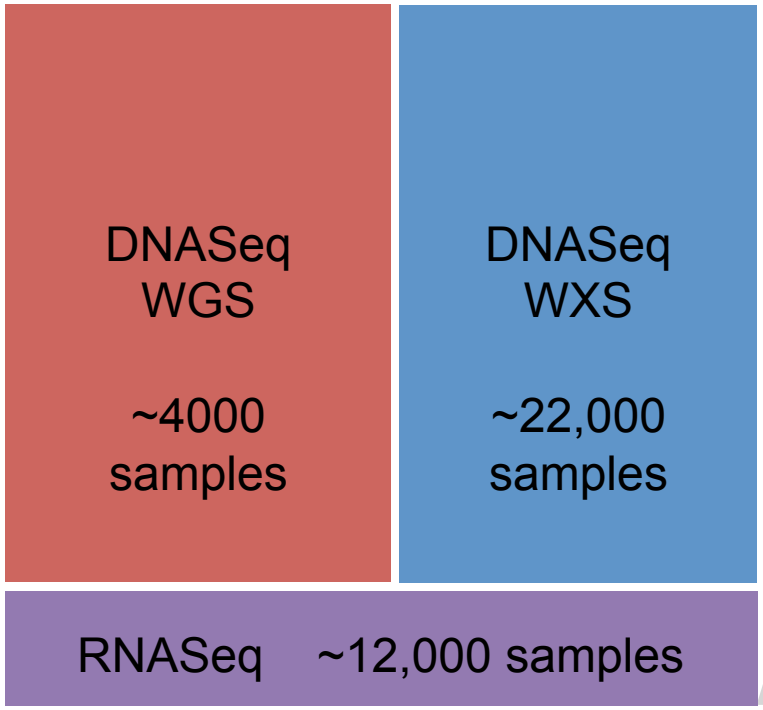
You are the builder

What the ISB-CGC is *not* …

- a repository from which to *download* large data sets
  - bring *your* tools and data to the cloud, to work with *our* tools and data!
- a "walled garden" with a *single* entrance
  - only "fence" is around the controlled-access data, but once you have a key, you can choose the path you prefer (GUI, CLI, API)
- a repository of "approved" or "recommended" pipelines for performing standard tasks
  - best left to the research community (*eg* DREAM challenges, GA4GH, PCAWG, tools developers, and you!)

TCGA Size & Complexity

>1 PB of sequence data
(controlled access)



~400,000 files of
heterogeneous data
(mostly open-access)

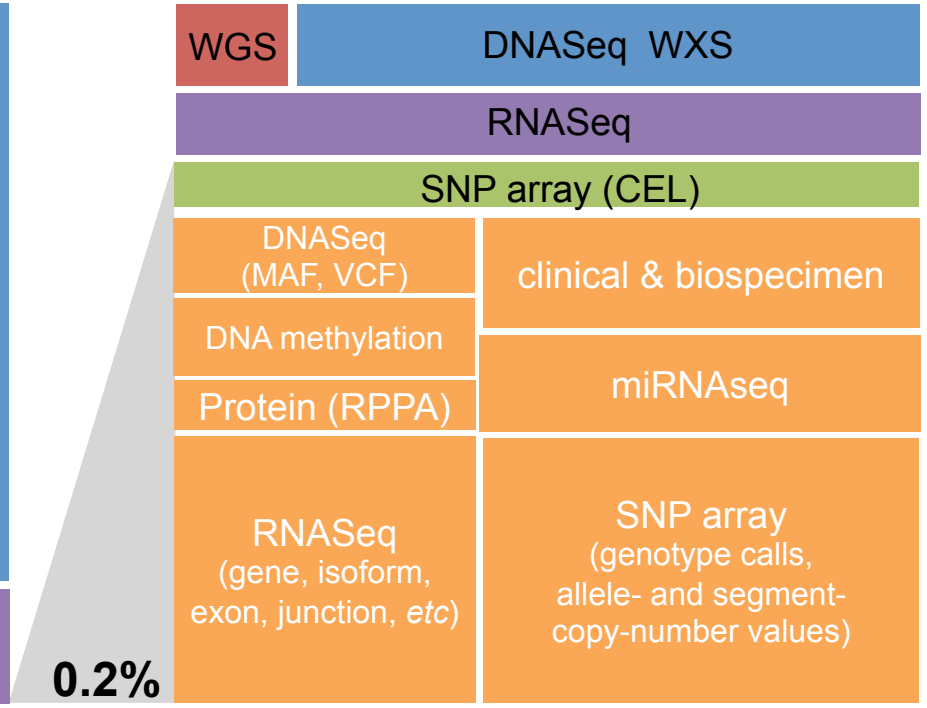


Table Details: Clinical_data

Schema

ParticipantBarcode	STRING	NULLABLE	Describe this field...
Study	STRING	NULLABLE	Describe this field...
Project	STRING	NULLABLE	Describe this field...
ParticipantUUID	STRING	NULLABLE	Describe this field...
TSSCode	STRING	NULLABLE	Describe this field...
age_at_initial_pathologic_diagnosis	INTEGER	NULLABLE	Describe this field...
anatomic_neoplasm_subdivision	STRING	NULLABLE	Describe this field...
batch_number	INTEGER	NULLABLE	Describe this field...
bcr	STRING	NULLABLE	Describe this field...
clinical_M	STRING	NULLABLE	Describe this field...
clinical_N	STRING	NULLABLE	Describe this field...
clinical_T			
clinical_stage			
colorectal_cancer			
country			
vital_status			
days_to_birth			
days_to_death			
days_to_last_known_alive			
days_to_last_followup			
days_to_initial_pathologic_diagnosis			
days_to_submitted_specimen_dx			
ethnicity			
frozen_specimen_anatomic_site			
gender			
gleason_score_combined			
histological_type			
history_of_colon_polyps			

Table Details: Somatic_Mutation_calls

Schema

ParticipantBarcode	STRING	NULLABLE	Describe this field...
Tumor_SampleBarcode	STRING	NULLABLE	Describe this field...
Tumor_AliquotBarcode	STRING	NULLABLE	Describe this field...
Tumor_SampleTypeLetterCode	STRING	NULLABLE	Describe this field...
Normal_SampleBarcode	STRING	NULLABLE	Describe this field...
Normal_AliquotBarcode	STRING	NULLABLE	Describe this field...
Normal_SampleTypeLetterCode	STRING	NULLABLE	Describe this field...
Study	STRING	NULLABLE	Describe this field...
Annotation_Transcript	STRING	NULLABLE	Describe this field...
CCLE_ONCOMAP_Total_Mutations_In_Gene	INTEGER	NULLABLE	Describe this field...
COSMIC_Total_Alterations_In_Gene	INTEGER	NULLABLE	Describe this field...
Center	STRING	NULLABLE	Describe this field...
Chromosome	STRING	NULLABLE	Describe this field...
DNARepairGenes_Role	STRING	NULLABLE	Describe this field...
DbSNP_RS	STRING	NULLABLE	Describe this field...
DbSNP_Val_Status	STRING	NULLABLE	Describe this field...
DrugBank	STRING	NULLABLE	Describe this field...
End_Position	INTEGER	NULLABLE	Describe this field...
Entrez_Gene_Id	INTEGER	NULLABLE	Describe this field...
GC_Content			
GENCODE_Transcript_Name	S		
GENCODE_Transcript_Status	S		
GENCODE_Transcript_Type	S		
GO_Biological_Process	S		
GO_Cellular_Component	S		
GO_Molecular_Function	S		
Gene_Type	S		
Genome_Change	S		

Table Details: Biospecimen_data

Schema

ParticipantBarcode	STRING	NULLABLE	Describe this field...
SampleBarcode	STRING	NULLABLE	Describe this field...
SampleTypeLetterCode	STRING	NULLABLE	Describe this field...
SampleType	STRING	NULLABLE	Describe this field...
Study	STRING	NULLABLE	Describe this field...
Project	STRING	NULLABLE	Describe this field...
SampleTypeCode	STRING	NULLABLE	Describe this field...
avg_percent_lymphocyte_infiltration	FLOAT	NULLABLE	Describe this field...
avg_percent_monocyte_infiltration	FLOAT	NULLABLE	Describe this field...
avg_percent_necrosis	FLOAT	NULLABLE	Describe this field...
avg_percent_neutrophil_infiltration	FLOAT	NULLABLE	Describe this field...
avg_percent_normal_cells	FLOAT	NULLABLE	Describe this field...
avg_percent_stromal_cells	FLOAT	NULLABLE	Describe this field...
avg_percent_tumor_cells	FLOAT	NULLABLE	Describe this field...
avg_percent_tumor_nuclei	FLOAT	NULLABLE	Describe this field...
batch_number	INTEGER	NULLABLE	Describe this field...
bcr	STRING	NULLABLE	Describe this field...
days_to_collection	FLOAT	NULLABLE	Describe this field...
days_to_sample_procurement	FLOAT	NULLABLE	Describe this field...
is_ffpe			
max_percent_lymphocyte_infiltrat			
max_percent_monocyte_infiltratic			
max_percent_necrosis			
max_percent_neutrophil_infiltrati			
max_percent_normal_cells			
max_percent_stromal_cells			
max_percent_tumor_cells			
max_percent_tumor_nuclei			

Table Details: Copy_Number_segments

Schema

ParticipantBarcode	STRING	NULLABLE	Describe this field...
SampleBarcode	STRING	NULLABLE	Describe this field...
SampleTypeLetterCode	STRING	NULLABLE	Describe this field...
AliquotBarcode	STRING	NULLABLE	Describe this field...
Study	STRING	NULLABLE	Describe this field...
Platform	STRING	NULLABLE	Describe this field...
Chromosome	STRING	NULLABLE	Describe this field...
Start	INTEGER	NULLABLE	Describe this field...
End	INTEGER	NULLABLE	Describe this field...
Num_Probes	INTEGER	NULLABLE	Describe this field...

Table Details: DNA_Methylation_betas

Schema

ParticipantBarcode	STRING	NULLABLE	Describe this field...
SampleBarcode	STRING	NULLABLE	Describe this field...
SampleTypeLetterCode	STRING	NULLABLE	Refer: https://tcga-data.nci.nih.gov/datareports/codeTablesReport.htm
AliquotBarcode	STRING	NULLABLE	The Aliquot ID is an identifier/barcode of TCGA data. Refer: https://wiki.nci.nih.gov/display/TCGA/TCGA+barcode
Platform	STRING	NULLABLE	Refer: https://tcga-data.nci.nih.gov/datareports/codeTablesReport.htm
Study	STRING	NULLABLE	TCGA disease type
Probe_Id	STRING	NULLABLE	Illumina's CpG loci IDs. Refer: http://www.illumina.com/content/dam/illumina-marketing/documents/products/technotes/technote_cpg_loci_identification.pdf
Beta_Value	FLOAT	NULLABLE	The beta value (β) is used to estimate the methylation level of the CpG locus using the ratio of intensities between methylat

Table Details: Annotations

Schema

annotationId	INTEGER	NULLABLE	Describe this field...
annotationCategoryId	INTEGER	NULLABLE	Describe this field...
annotationCategoryName	STRING	NULLABLE	Describe this field...
annotationClassification	STRING	NULLABLE	Describe this field...
annotationNoteText	STRING	NULLABLE	Describe this field...
Study	STRING	NULLABLE	Describe this field...
itemTypeName	STRING	NULLABLE	Describe this field...
itemBarcode	STRING	NULLABLE	Describe this field...
AliquotBarcode	STRING	NULLABLE	Describe this field...
ParticipantBarcode	STRING	NULLABLE	Describe this field...
SampleBarcode	STRING	NULLABLE	Describe this field...
dateAdded	STRING	NULLABLE	Describe this field...
dateCreated	STRING	NULLABLE	Describe this field...
dateEdited	STRING	NULLABLE	Describe this field...

Table Details: mRNA_UNC_HiSeq_RSEM

Schema

ParticipantBarcode	STRING	NULLABLE	Describe this field...
SampleBarcode	STRING	NULLABLE	Describe this field...
AliquotBarcode	STRING	NULLABLE	Describe this field...
Study	STRING	NULLABLE	Describe this field...
SampleTypeLetterCode	STRING	NULLABLE	Describe this field...
Platform	STRING	NULLABLE	Describe this field...
original_gene_symbol	STRING	NULLABLE	Describe this field...
HGNC_gene_symbol	STRING	NULLABLE	Describe this field...
gene_id	INTEGER	NULLABLE	Describe this field...
normalized_count	FLOAT	NULLABLE	Describe this field...

Table Details: Protein_RPPA_data

Schema

ParticipantBarcode	STRING	NULLABLE	Describe this field...
SampleBarcode	STRING	NULLABLE	Describe this field...
SampleTypeLetterCode	STRING	NULLABLE	Describe this field...
AliquotBarcode	STRING	NULLABLE	Describe this field...
Study	STRING	NULLABLE	Describe this field...
Gene_Name	STRING	NULLABLE	Describe this field...
Protein_Expression	FLOAT	NULLABLE	Describe this field...
Protein_Name	STRING	NULLABLE	Describe this field...
Protein_Basename	STRING	NULLABLE	Describe this field...
Phospho	STRING	NULLABLE	Describe this field...
antibodySource	STRING	NULLABLE	Describe this field...
validationStatus	STRING	NULLABLE	Describe this field...

Table Details: mRNA_BCGSC_HiSeq_RPKM

Schema

ParticipantBarcode	STRING	NULLABLE	Describe this field...
SampleBarcode	STRING	NULLABLE	Describe this field...
SampleTypeLetterCode	STRING	NULLABLE	Describe this field...
AliquotBarcode	STRING	NULLABLE	Describe this field...
Study	STRING	NULLABLE	Describe this field...
Platform	STRING	NULLABLE	Describe this field...
	NTEGER	NULLABLE	Describe this field...
	TRING	NULLABLE	Describe this field...
	TRING	NULLABLE	Describe this field...
	LOAT	NULLABLE	Describe this field...
	TRING	NULLABLE	Describe this field...

Schema

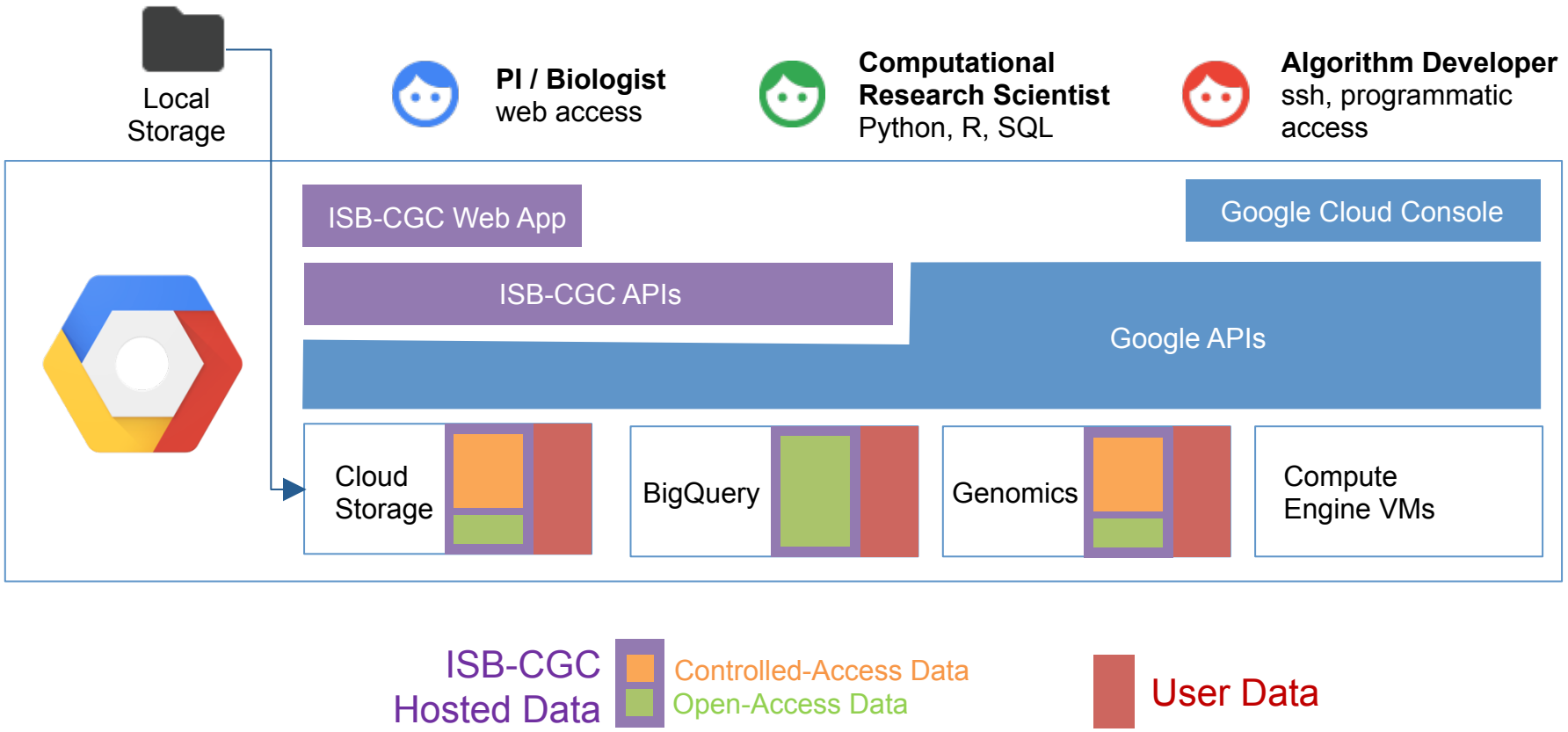
Table Details: miRNA_expression

Schema

ParticipantBarcode	STRING	NULLABLE	Describe this field...
SampleBarcode	STRING	NULLABLE	Describe this field...
AliquotBarcode	STRING	NULLABLE	Describe this field...
SampleTypeLetterCode	STRING	NULLABLE	Describe this field...
Study	STRING	NULLABLE	Describe this field...
Platform	STRING	NULLABLE	Describe this field...
mirna_id	STRING	NULLABLE	Describe this field...
mirna_accession	STRING	NULLABLE	Describe this field...
normalized_count	FLOAT	NULLABLE	Describe this field...

ISB-CGC Approach

- build an open platform that can grow and evolve to satisfy a broad range of users and use-cases
- leverage the best existing tools and technologies, as they are released
- collaborate with the research community in areas of data standards, containers and workflows, *etc*
- provide a range of examples and tutorials to get newcomers up and running quickly!



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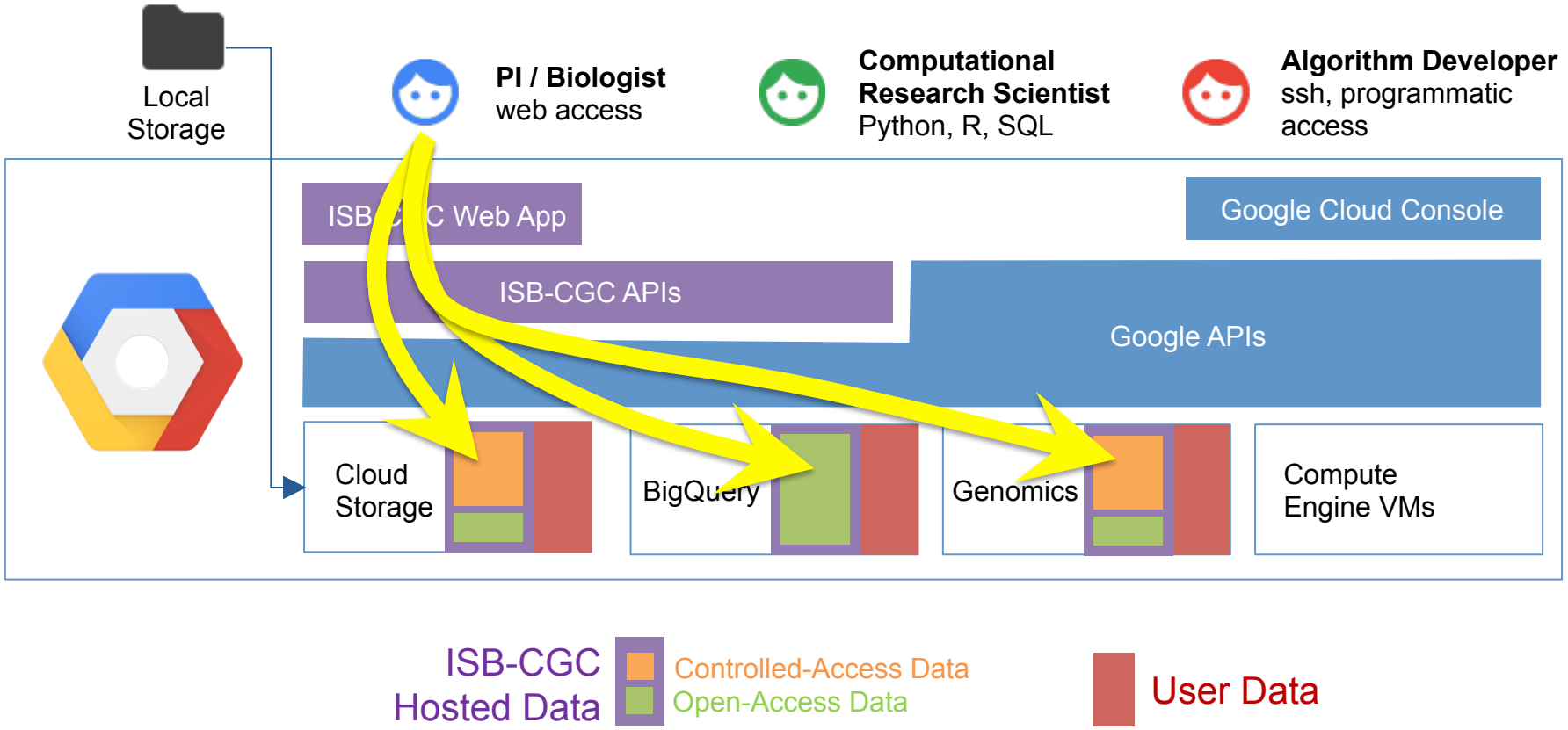
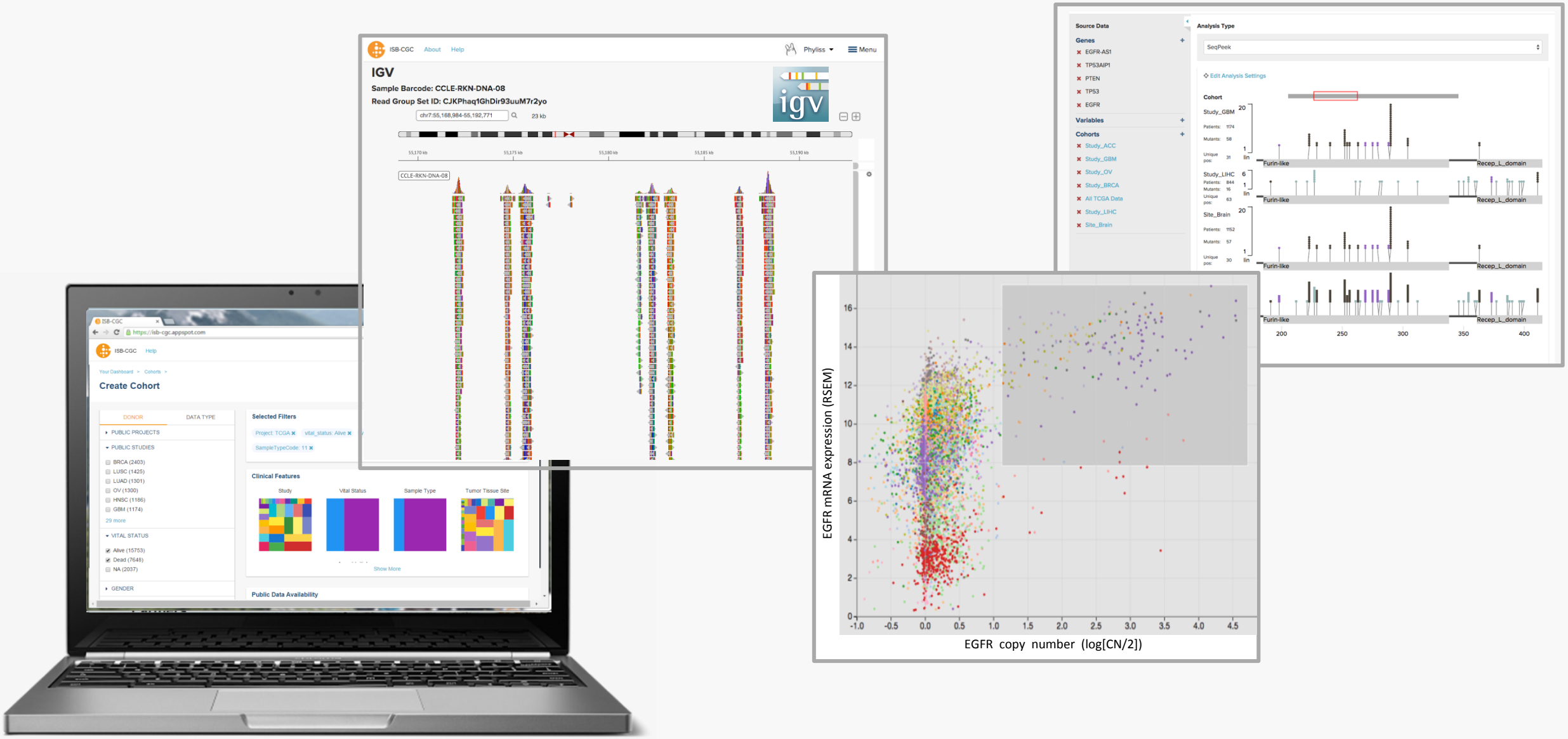


Web access for the PI / Biologist:



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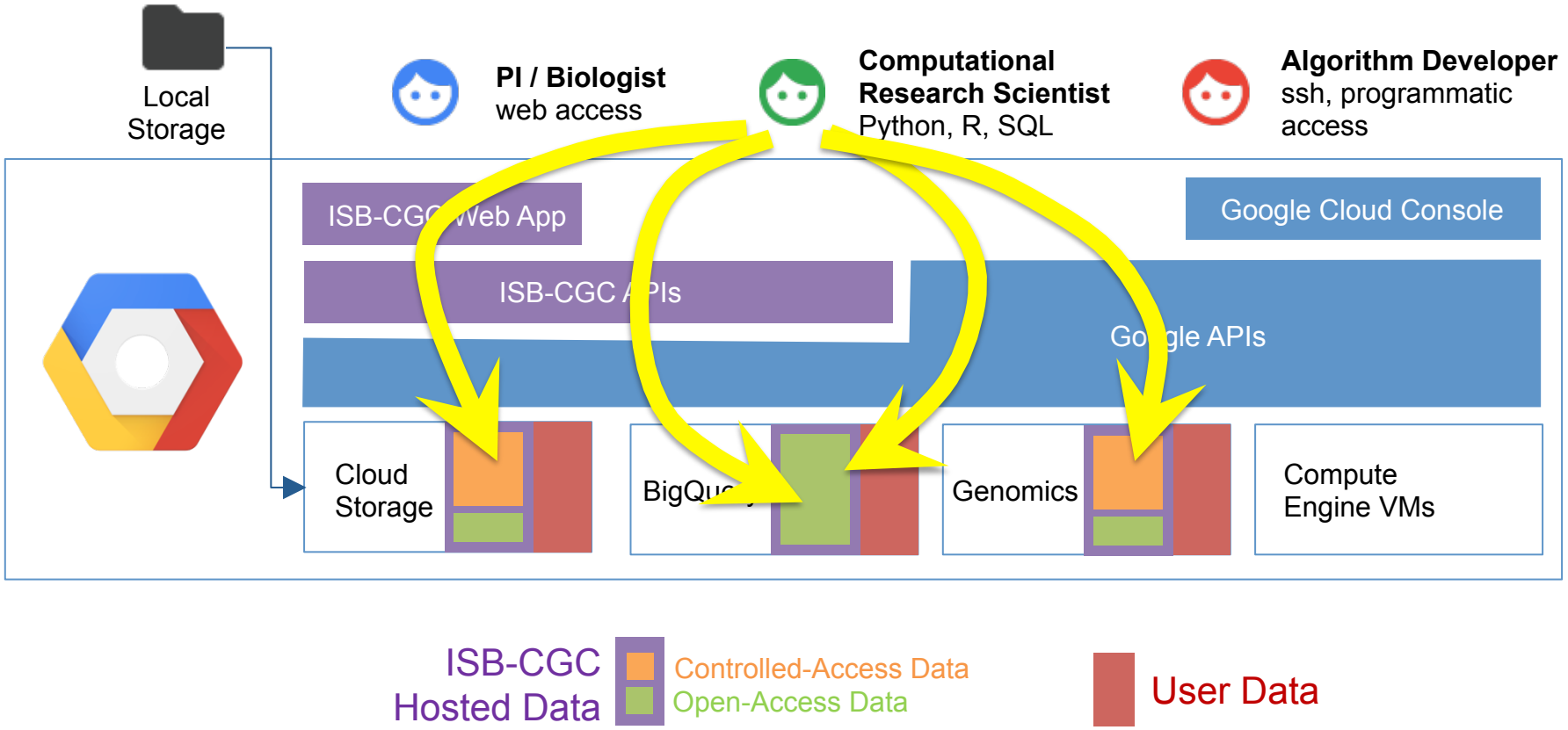


Python, R, and SQL for the Computational Scientist:

IPython Interactive Computing

SQL

RStudio

Google Cloud Datalab — Copy Number segments (autosaved)

Notebook · Add Code · Add Markdown · Delete · Move Up · Move Down · Run · Clear · Reset Session

Copy Number segments (Broad)

The goal of this notebook is to introduce you to the Copy Number (CN) segments B

This table contains all available TCGA Level-3 copy number data produced by the B Genome Wide SNP6 array, as of October 2015. (Actual archive dates range from A recent archives (e.g. broad.mit.edu_UCEC.Genome_Wide_SNP_6.Level_3.143.) types was downloaded from the DCC, and data extracted from all files matching th Each of these segmentation files has six columns: Sample, Chromosome, Start, End During ETL the sample identifer contained in the segmentation files was mapped to the SDRF file in the associated mage-tab archive.

In order to work with BigQuery, you need to import the python bigquery module (g the name(s) of the table(s) you are going to be working with:

```
import gcp.bigquery as bq
cn_BQtable = bq.Table('isb-cgc:tcga_201510_alpha.Copy_Number_
```

From now on, we will refer to this table using this variable ($cn_BQtable), but we co table name each time.

Let's start by taking a look at the table schema:

```
%%bigquery schema --table $cn_BQtable
```

name	type	mode	description
ParticipantBarcode	STRING		
SampleBarcode	STRING		
SampleTypeLetterCode	STRING		
AliquotBarcode	STRING		
Study	STRING		
Platform	STRING		
Chromosome	STRING		
Start	INTEGER		
End	INTEGER		
Num_Probes	INTEGER		
Segment_Mean	FLOAT		

Unlike most other molecular data types in which measurements are available for a microRNAs, this data is produced using a data-driven approach for each aliquot ind sizes and positions of these segments can vary widely from one sample to another.

Now we'll use matplotlib to create some simple visualizations.

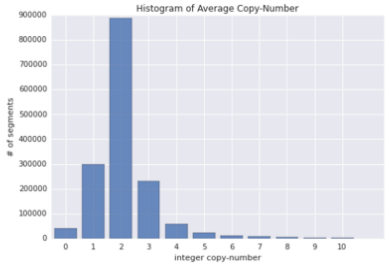
```
import numpy as np
import matplotlib.pyplot as plt
```

For the segment means, let's invert the log-transform and then bin the values to see what the distribu

```
%%sql --module getCNhist

SELECT
  lin_bin,
  COUNT(*) AS n
FROM (
  SELECT
    Segment_Mean,
    (2.*POW(2,Segment_Mean)) AS lin_CN,
    INTEGER(((2.*POW(2,Segment_Mean))+0.50)/1.0) AS lin_bin
  FROM
    $t
  WHERE
    ( (End-Start+1)>1000 AND SampleTypeLetterCode="TP" ) )
GROUP BY
  lin_bin
HAVING
  ( n > 2000 )
ORDER BY
  lin_bin ASC
```

```
CNhist = bq.Query(getCNhist,t=cn_BQtable).results().to_dataframe()
bar_width=0.80
plt.bar(CNhist['lin_bin']+0.1,CNhist['n'],bar_width,alpha=0.8);
plt.xticks(CNhist['lin_bin']+0.5,CNhist['lin_bin']);
plt.title('Histogram of Average Copy-Number');
plt.ylabel('# of segments');
plt.xlabel('integer copy-number');
```



The histogram illustrates that the vast majority of the CN segments have a copy-number value near 2 either side representing deletions (left) and amplifications (right).

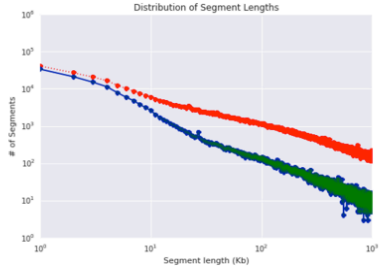
```
  bin
ORDER BY
  bin ASC
```

```
%%sql --module getSLhist_1k_amp

SELECT
  bin,
  COUNT(*) AS n
FROM (
  SELECT
    (END-Start+1) AS segLength,
    INTEGER((END-Start+1)/1000) AS bin
  FROM
    $t
  WHERE
    (END-Start+1)<1000000 AND SampleTypeLetterCode="TP" AND Segment_Mea
GROUP BY
  bin
ORDER BY
  bin ASC
```

```
SLhistDel = bq.Query(getSLhist_1k_del,t=cn_BQtable).results().to_datafr
SLhistAmp = bq.Query(getSLhist_1k_amp,t=cn_BQtable).results().to_datafr
```

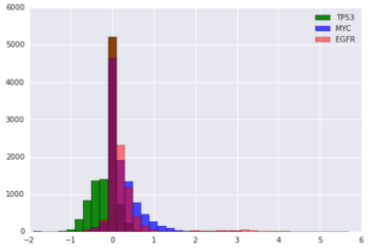
```
plt.plot(SLhist_1k['bin'],SLhist_1k['n'],'ro:');
plt.plot(SLhistDel['bin'],SLhistDel['n'],'bo-')
plt.plot(SLhistAmp['bin'],SLhistDel['n'],'go-',alpha=0.3)
plt.xscale('log');
plt.yscale('log');
plt.xlabel('Segment length (Kb)');
plt.ylabel('# of Segments');
plt.title('Distribution of Segment Lengths');
```



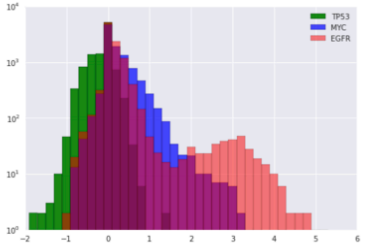
The amplification and deletion distributions are nearly identical and still seem to roughly follow a pov from this graph that a majority of the segments less than 10Kb in length are either amplifications or d lengths >100Kb are copy-number neutral.

And now we'll take a look at histograms of the average copy-number for these three genes. TP53 (in green) shows a significant number of partial deletions (CN<0), while MYC (in blue) shows some partial amplifications -- more frequently than EGFR, while EGFR (pale red) shows a few extreme amplifications (log2(CN/2) > 2). The final figure shows the same histograms on a semi-log plot to bring up the rarer events.

```
binWidth = 0.2
binVals = np.arange(-2+(binWidth/2.), 6-(binWidth/2.), binWidth)
plt.hist(tp53CN['avgCN'],bins=binVals,normed=False,color='green',alpha=0.9,label='TP53');
plt.hist(mycCN ['avgCN'],bins=binVals,normed=False,color='blue',alpha=0.7,label='MYC');
plt.hist(egfrCN['avgCN'],bins=binVals,normed=False,color='red',alpha=0.5,label='EGFR');
plt.legend(loc='upper right');
```




```
plt.hist(tp53CN['avgCN'],bins=binVals,normed=False,color='green',alpha=0.9,label='TP53');
plt.hist(mycCN ['avgCN'],bins=binVals,normed=False,color='blue',alpha=0.7,label='MYC');
plt.hist(egfrCN['avgCN'],bins=binVals,normed=False,color='red',alpha=0.5,label='EGFR');
plt.yscale('log');
plt.legend(loc='upper right');
```



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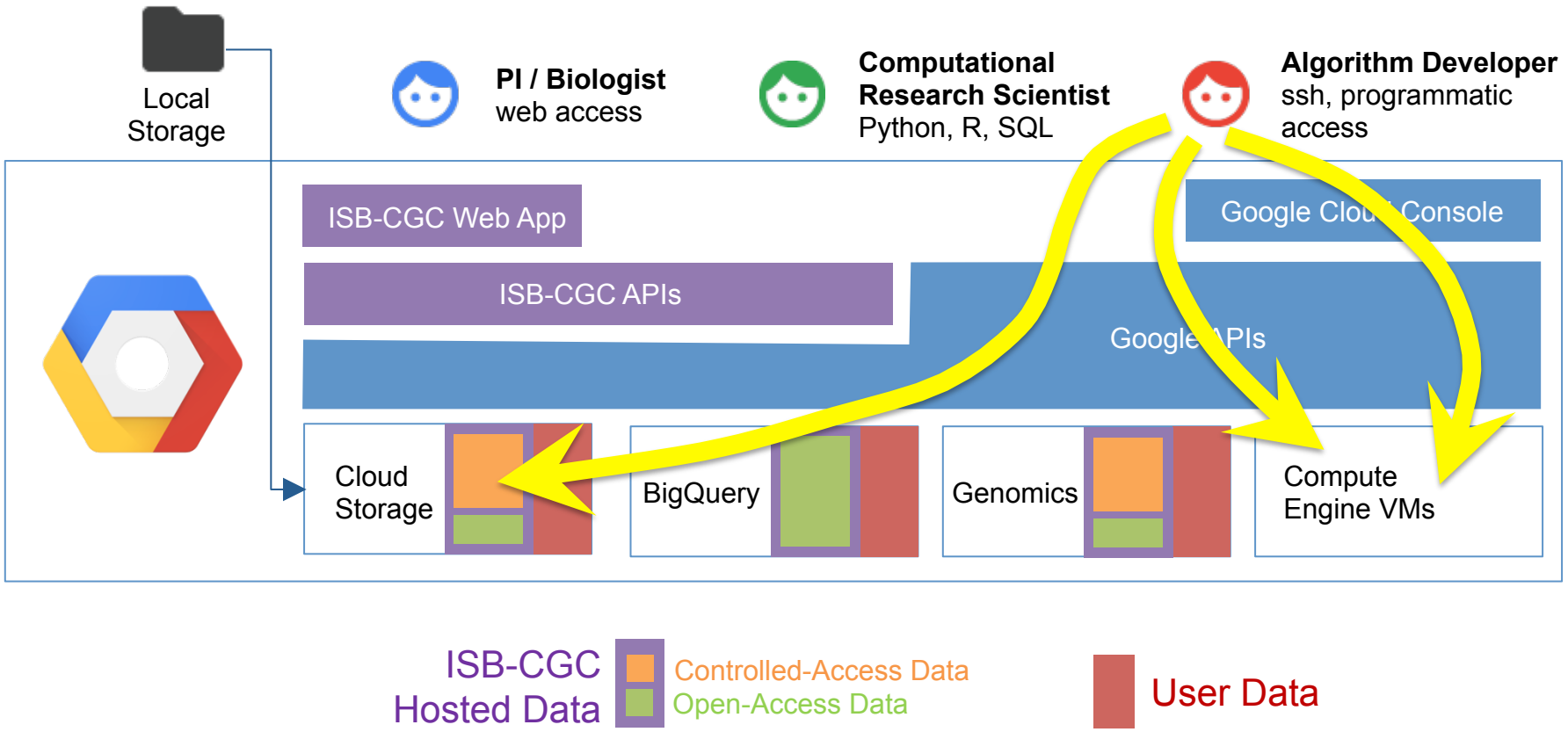

A generalizable workflow using Docker