Transposable elements and Scientific cloud computing

Group Meeting - Jan 2018

Agenda

- Introduction: TEs in the human genome
- Transposable elements activity in healthy tissues
- Scientific computing on Seven Bridges
- Future steps
    - Transposable elements activity in human tumors

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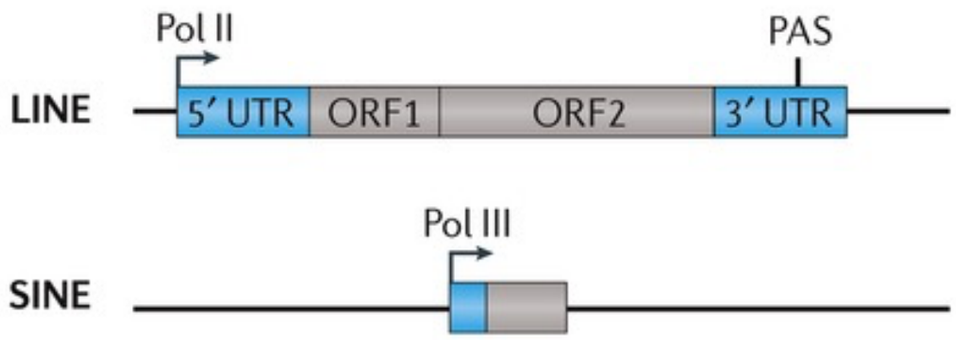
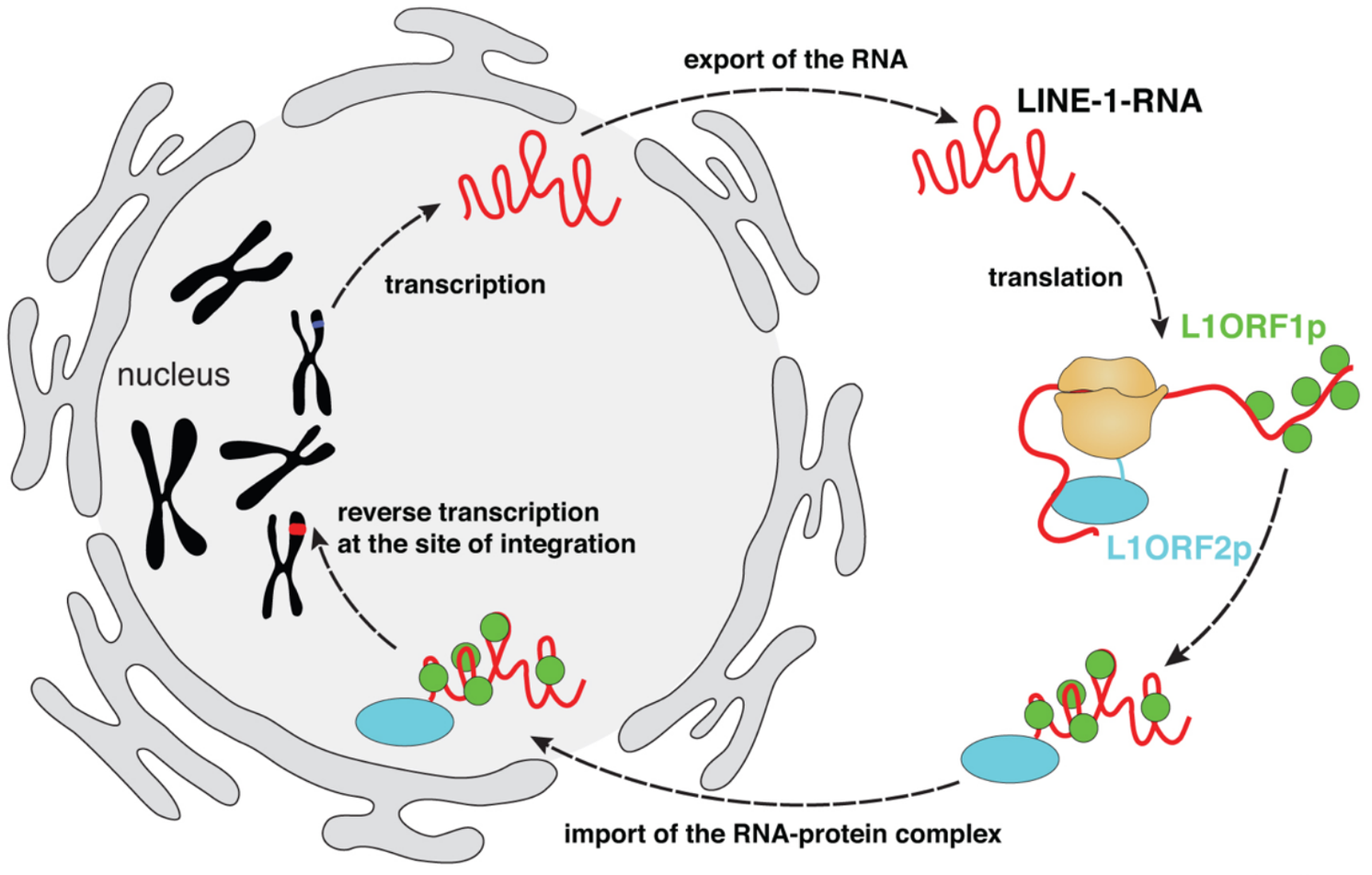
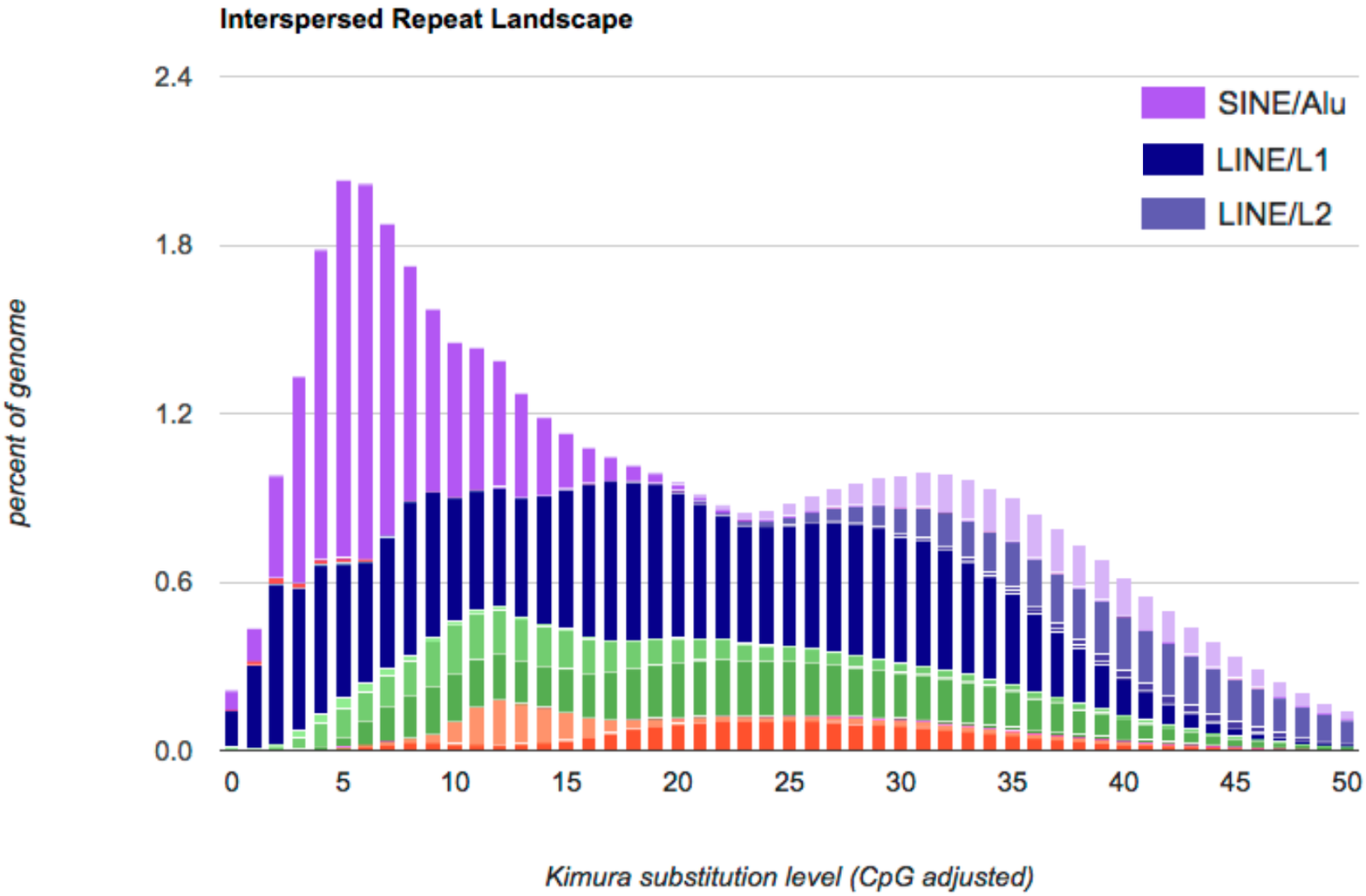
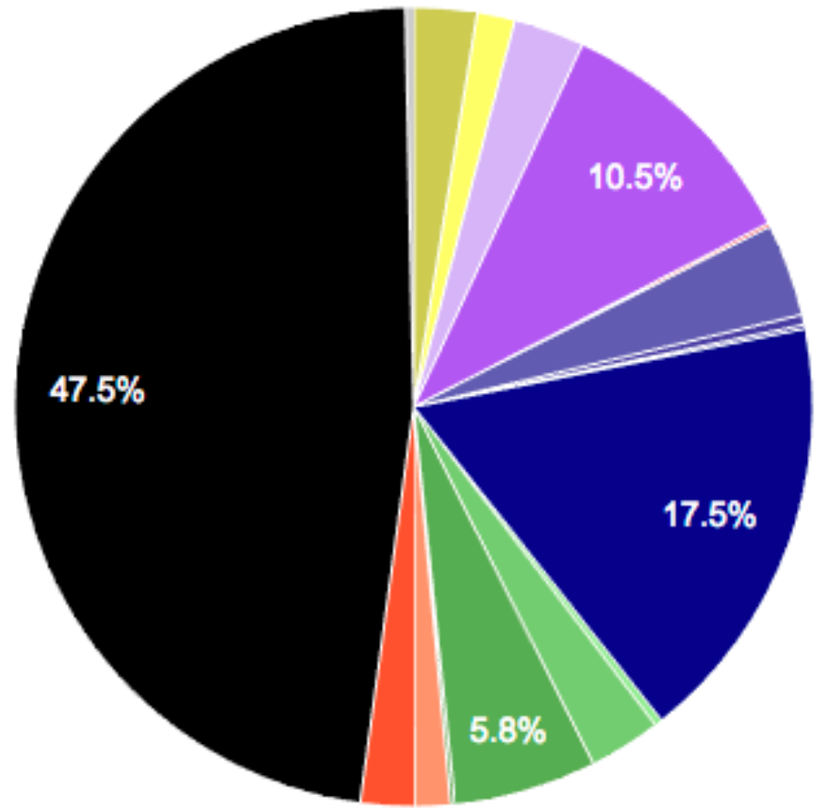
(retro)Transposable elements





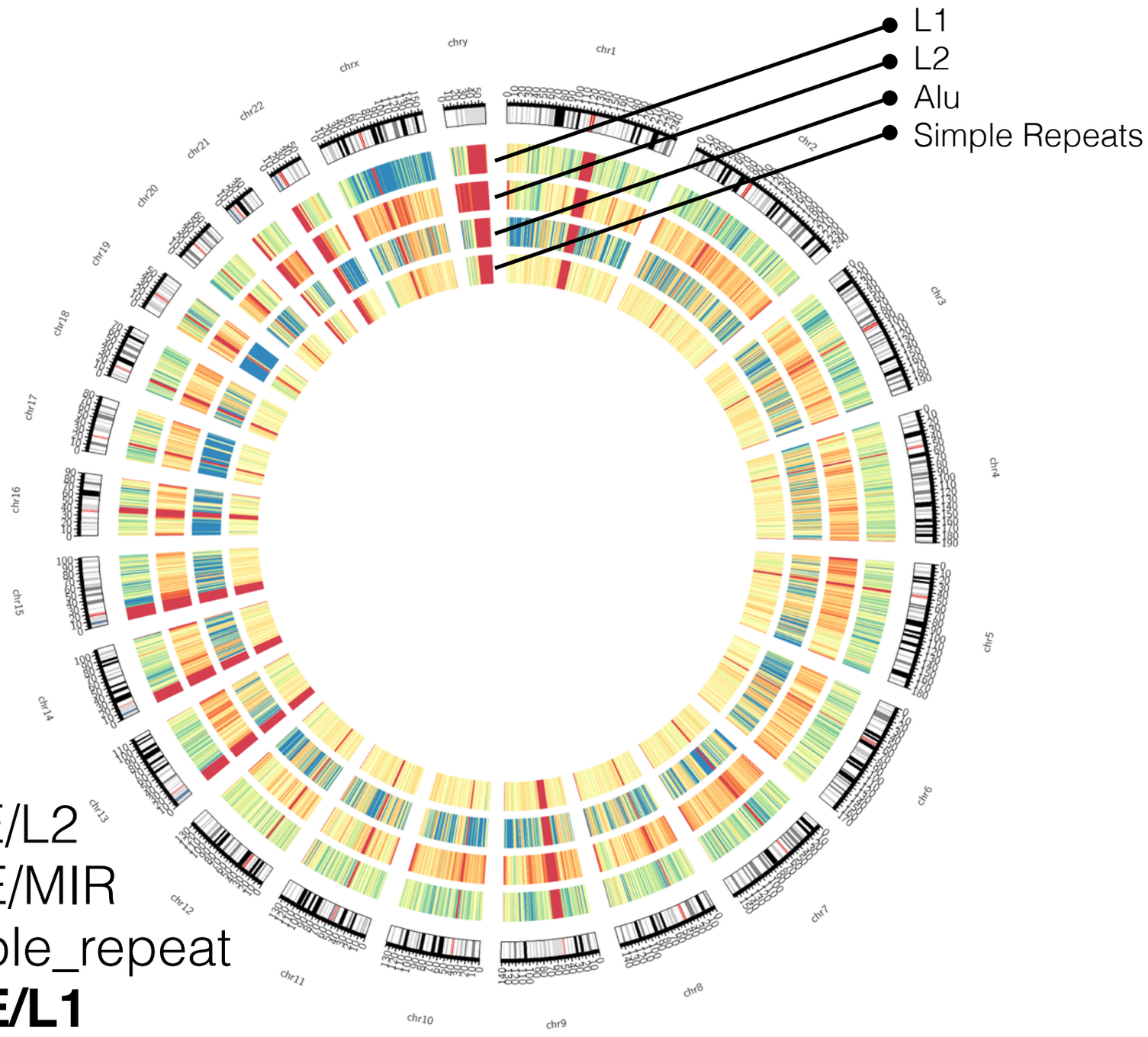
Repetitions in our genome





534,592	LINE/L2
611,412	SINE/MIR
700,455	Simple_repeat
978,523	**LINE/L1**
1,238,490	**SINE/Alu**

Transposable element density



534,592	LINE/L2
611,412	SINE/MIR
700,455	Simple_repeat
978,523	**LINE/L1**
1,238,490	**SINE/Alu**

Some open questions about LINE-1 biology:

- Are LINE-1 completely silenced in somatic tissue?
- There are papers describing the activity of LINE-1 in tumors, but surprisingly, none about ALUs
- LINE-1 causes huge disruptions in the genome, what is their impact in tumor evolution?

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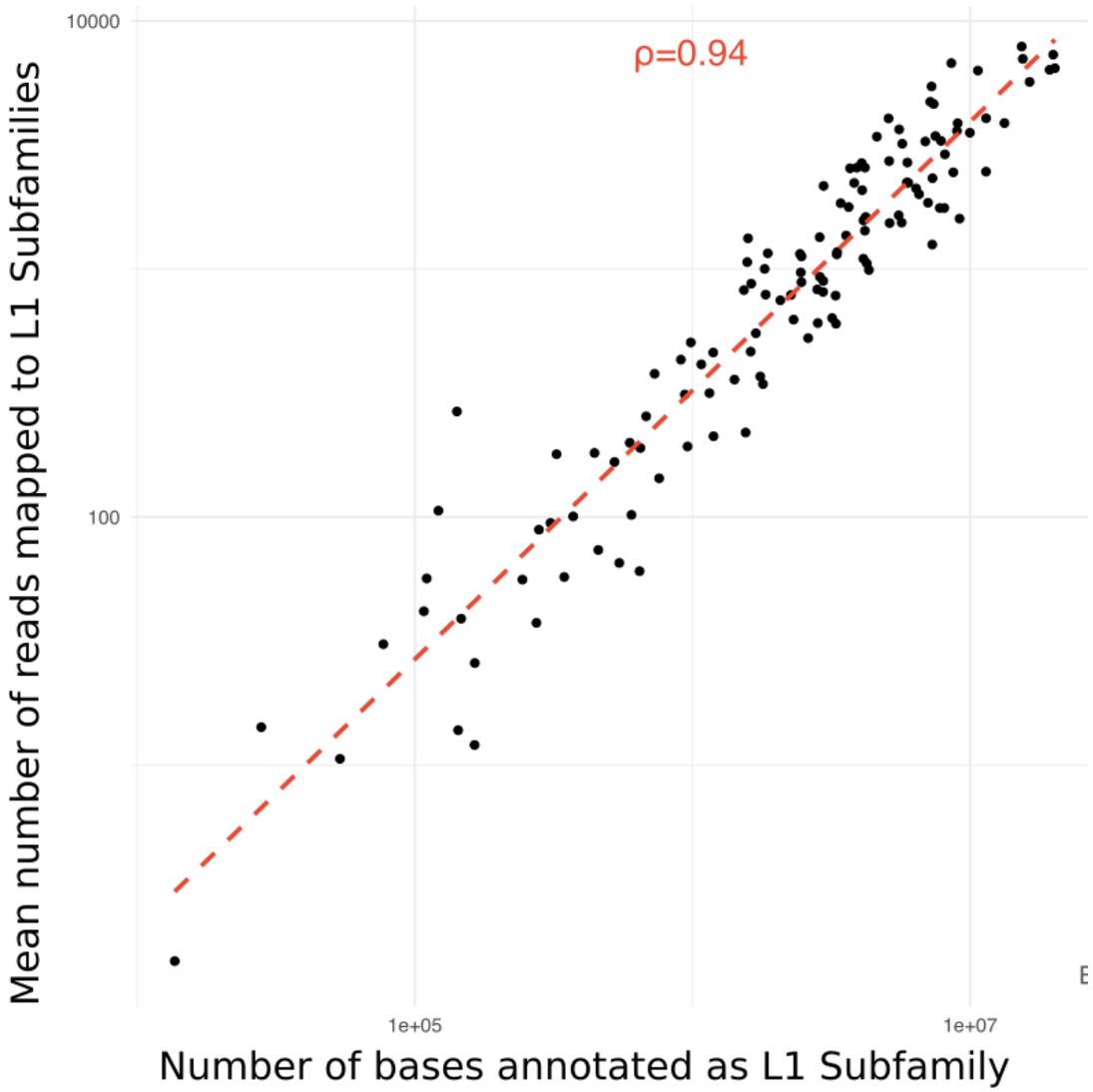
TeXP model

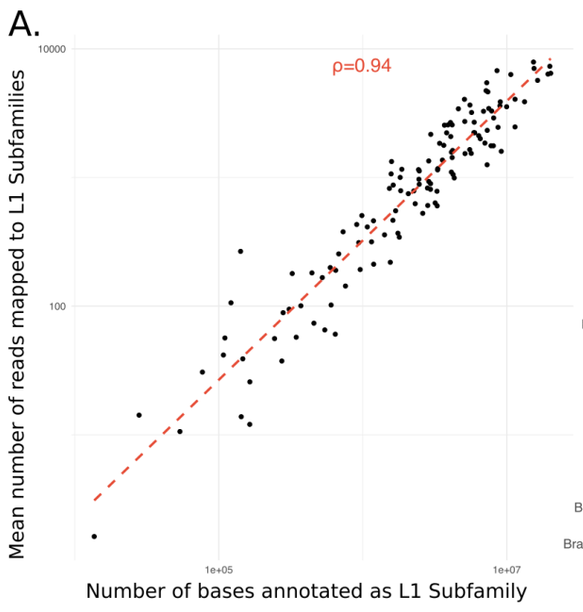
- Are LINE-1 completely silenced in somatic tissue?

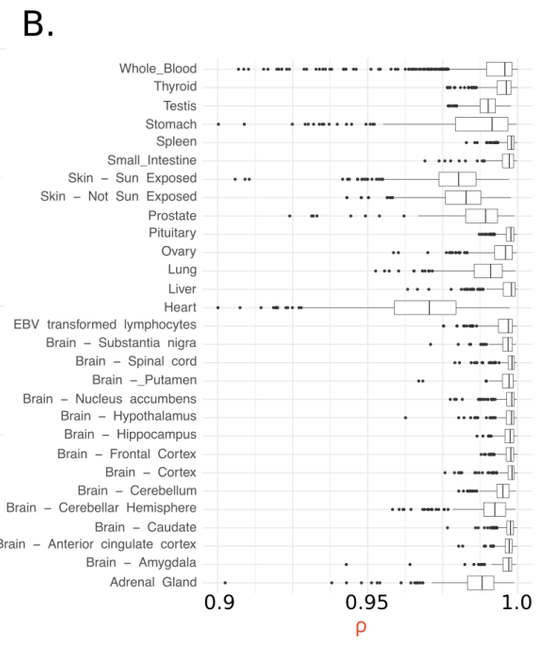


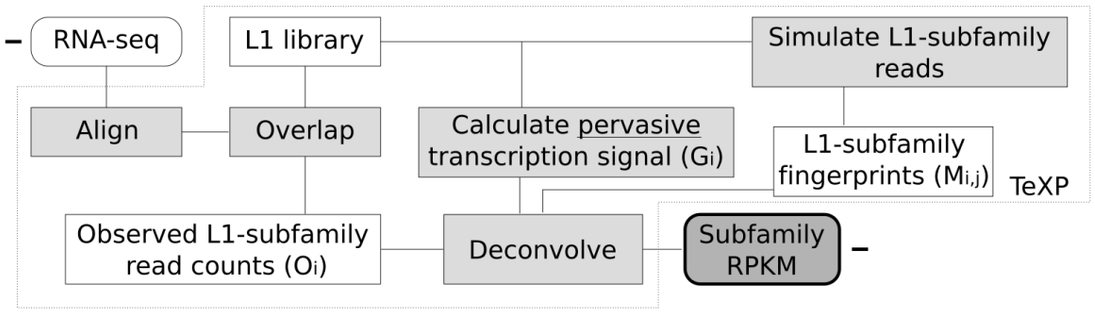
TeXP model

$$O_i = T(G_i \epsilon_{pervasive} + M_{i,j} \varepsilon_j)$$

Noise from pervasive transcription







Oi is the observed number of reads mapping to L1Hs;

T is the total number of reads mapped to L1 instances;

Gi defines the proportion of L1 bases in the genome annotated as subfamily i;

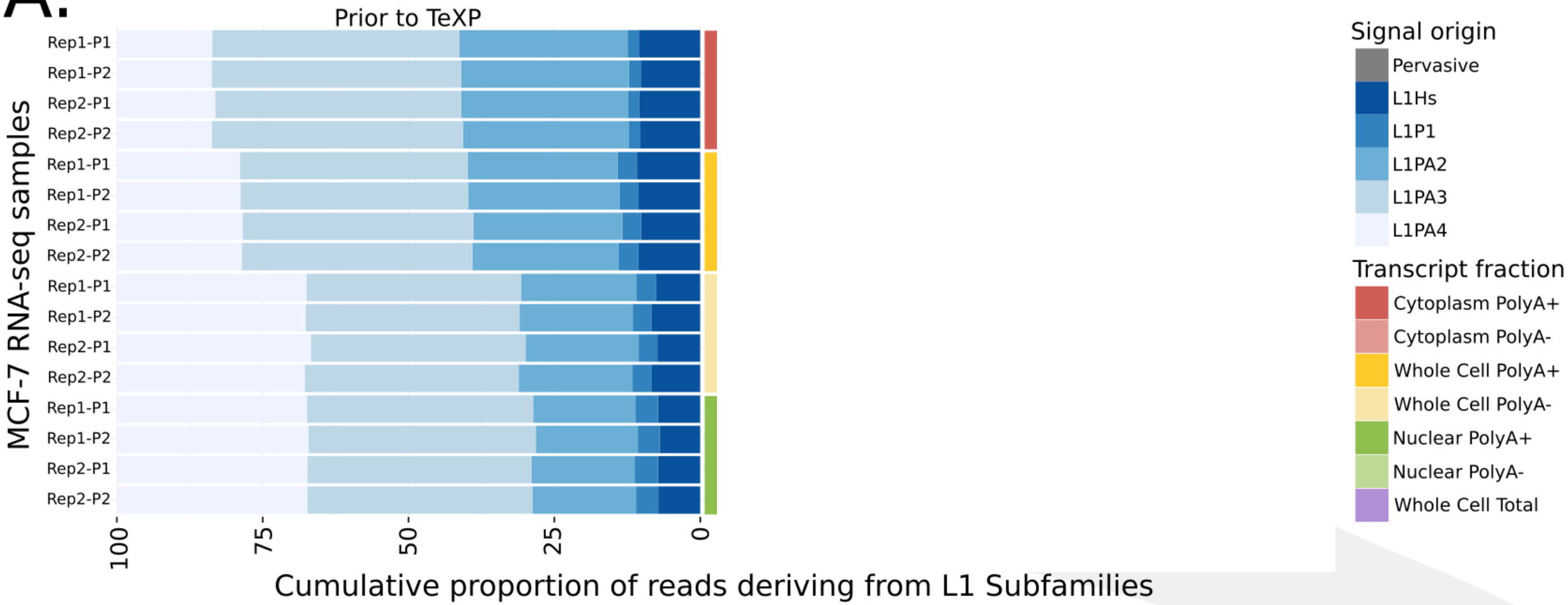
Epervasive is the percentage of reads emanating from pervasive transcription;

Mi,j is the mappability fingerprint (defined bellow) that describes what is the proportion of reads emanating from the signal i that maps to L1 subfamily j;

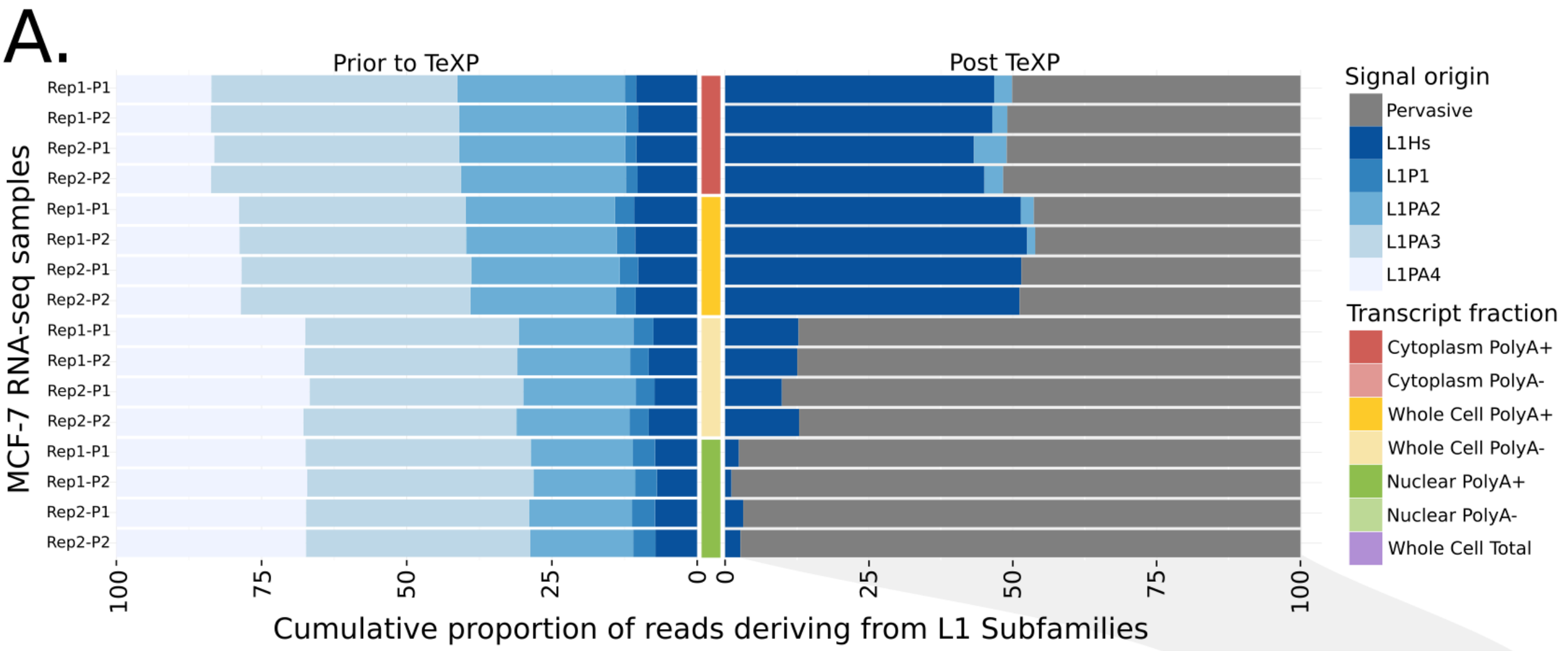
Ej is the percentage of reads emanating from the L1 Subfamily .

TeXP Validation

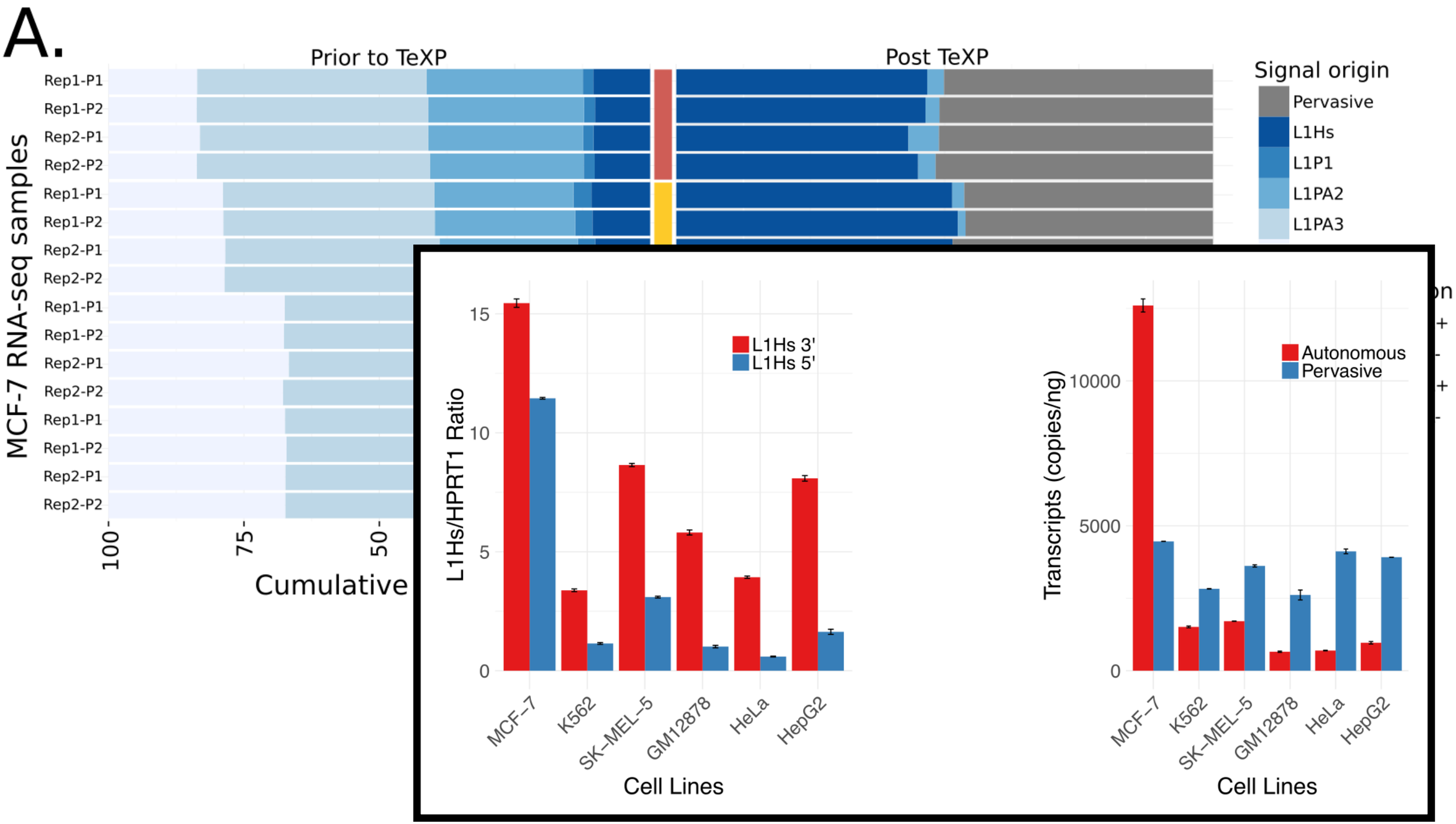
A.



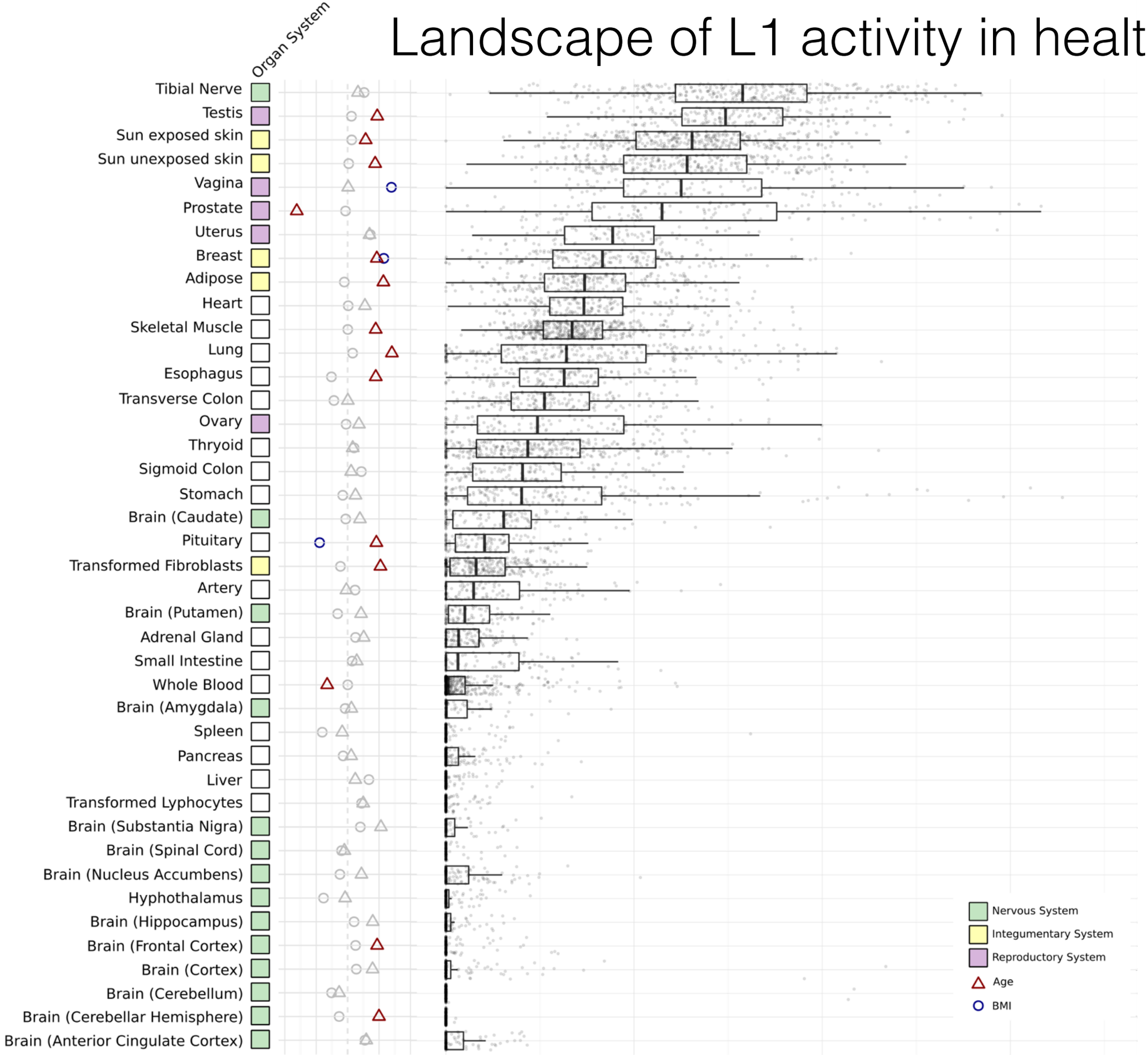
TeXP Validation



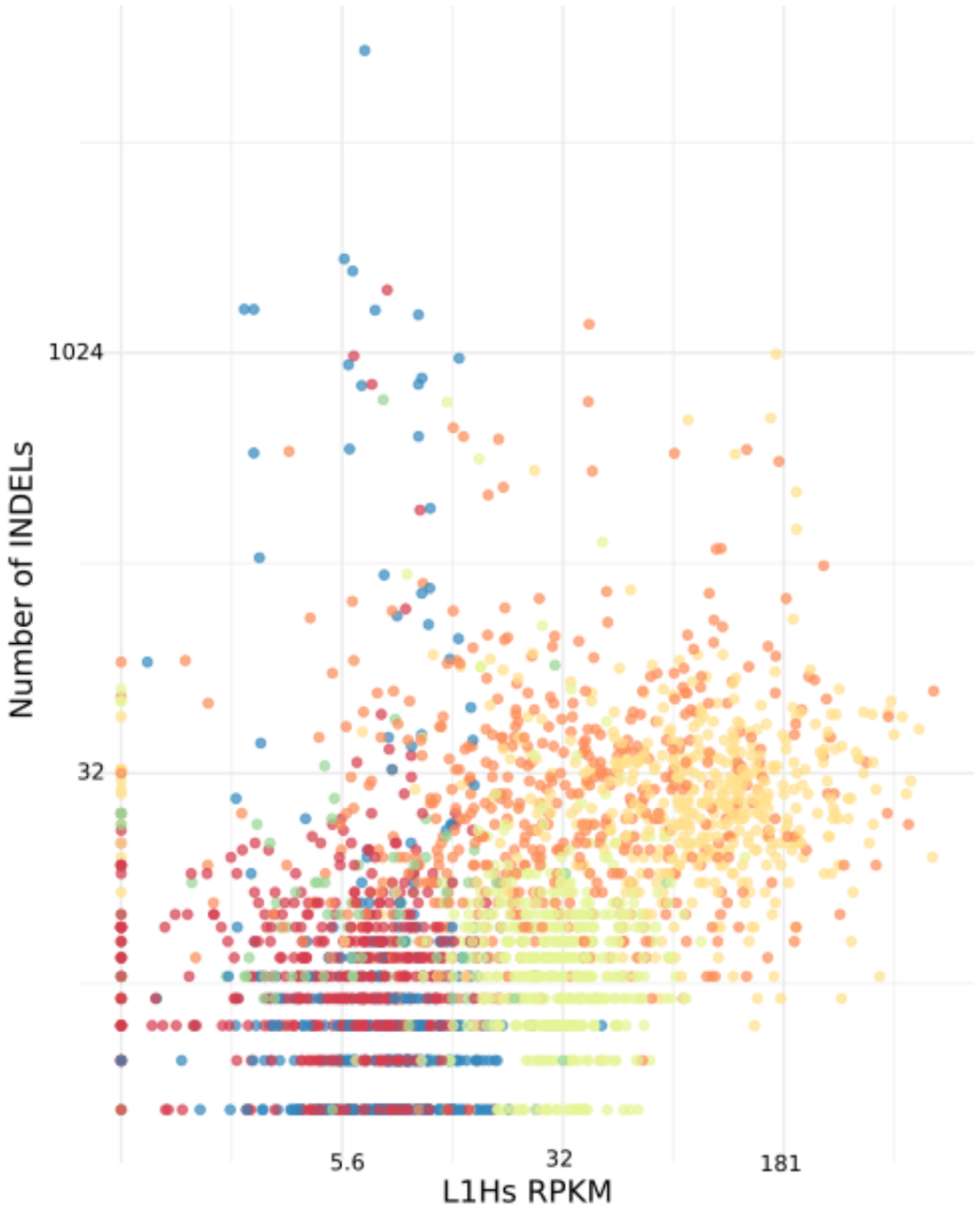
TeXP Validation

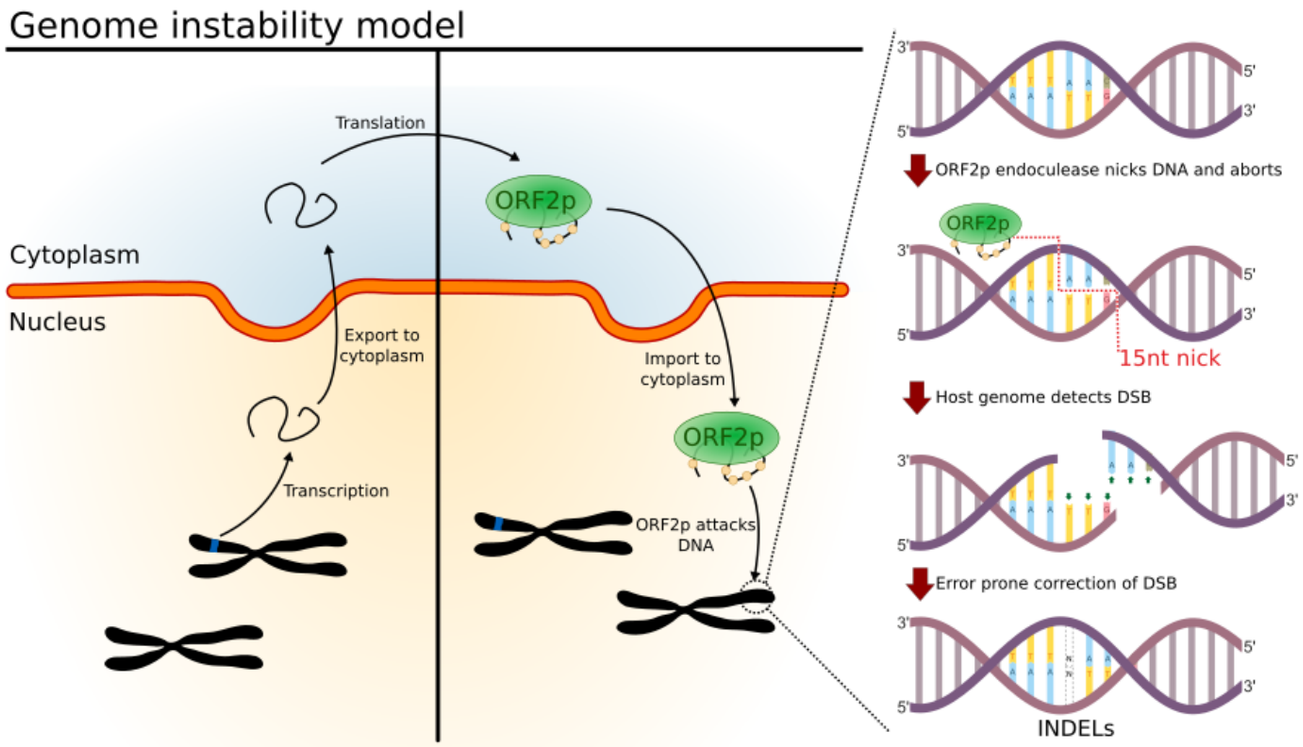


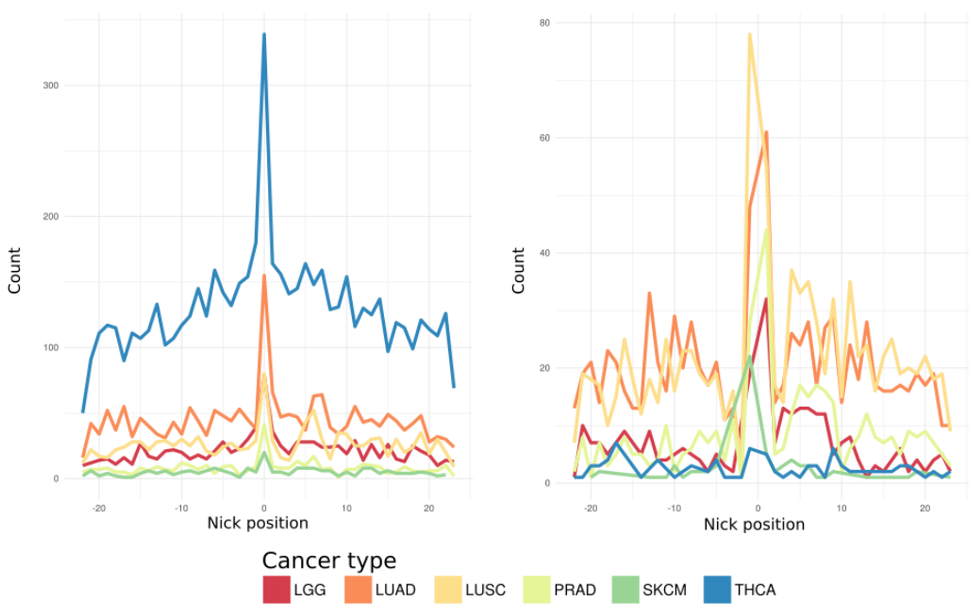
Landscape of L1 activity in healthy tissues



Correlation between L1 expression and Number of INDELs in tumors







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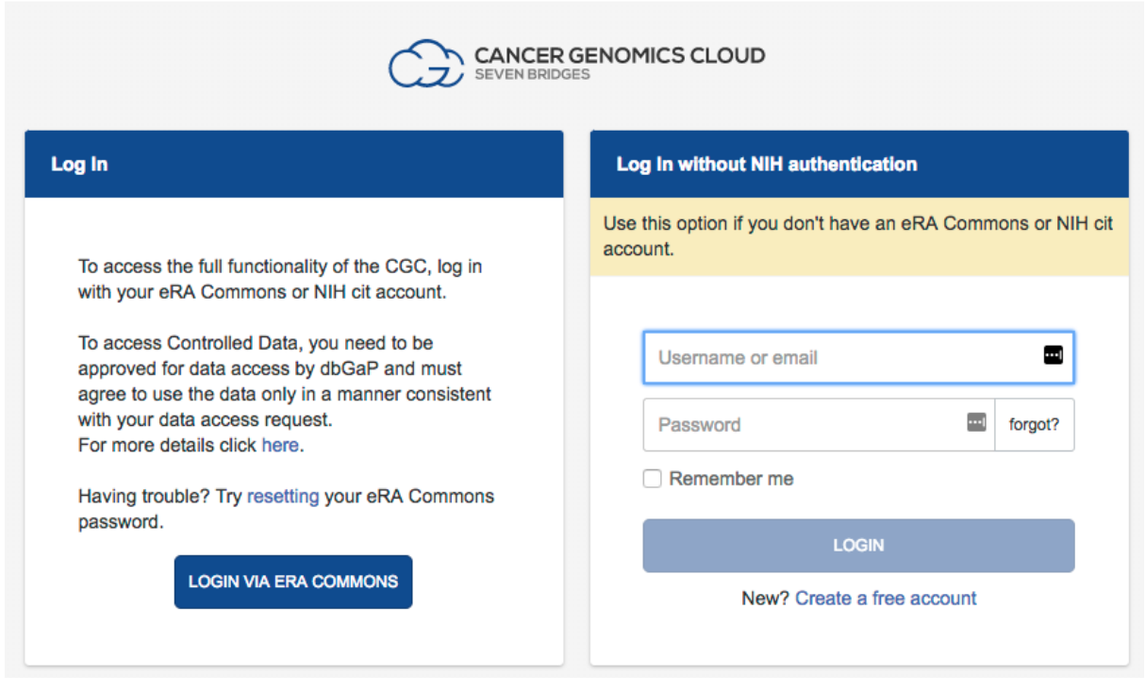
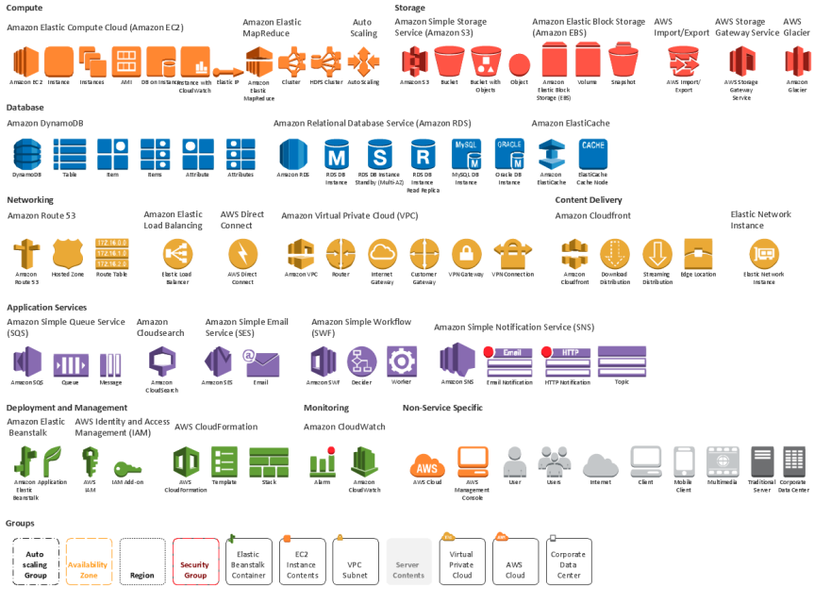
Seven Bridges CGC

Front-End

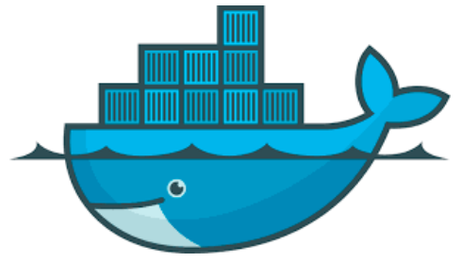


Amazon AWS



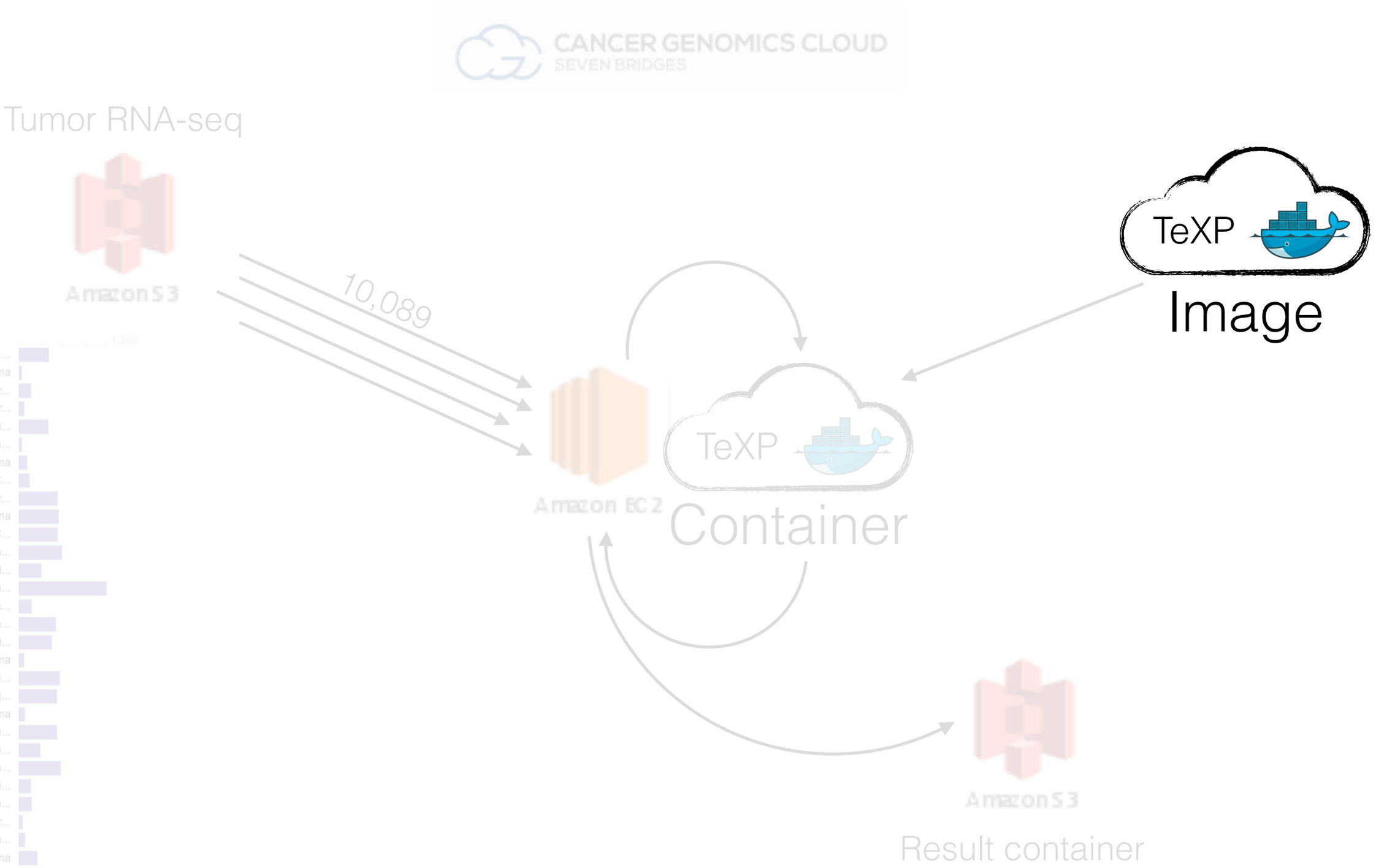
Rabix CWL

[Reproducible Analysis for Bioinformatics]

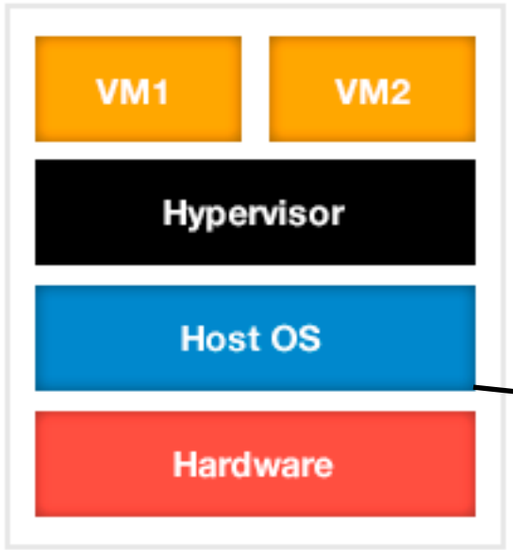


Docker

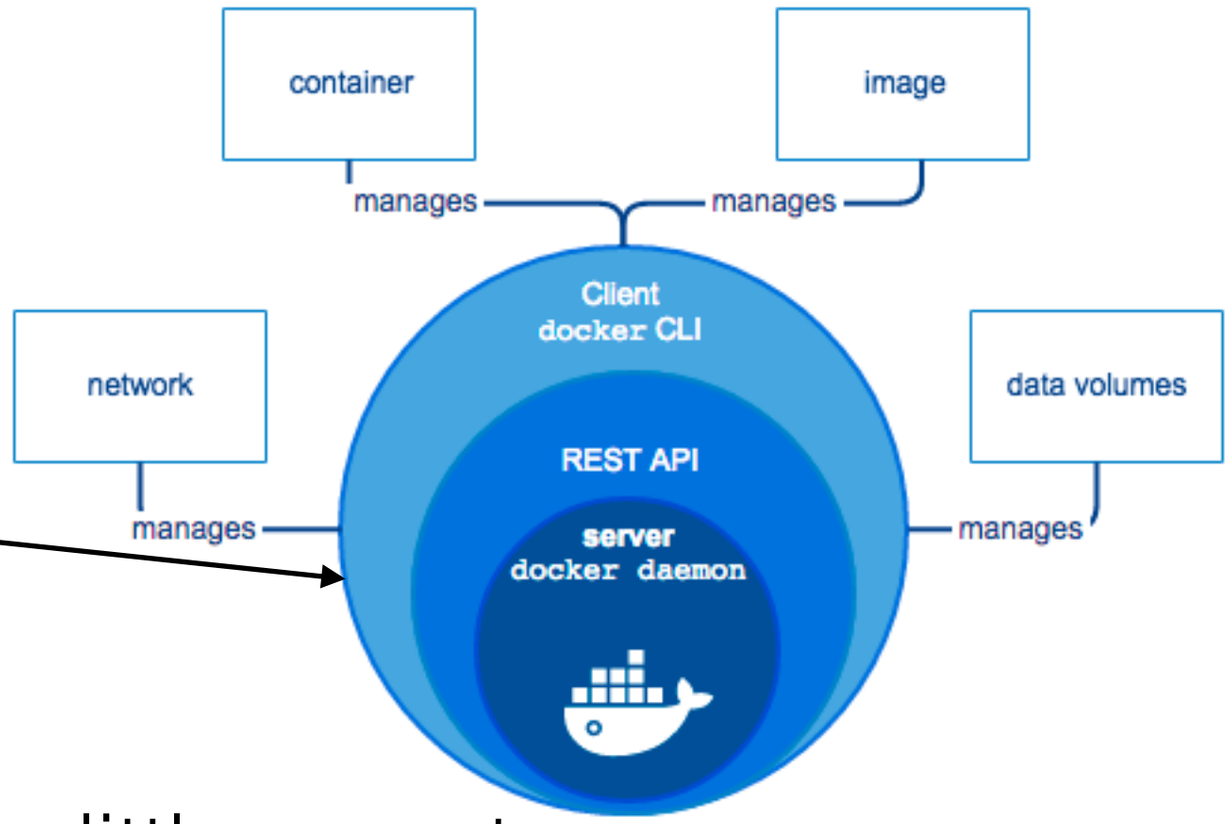
CGC Life cycle



Docker?



Hosted Hypervisor



except for a dirty little secret:
MacOS and Windows don’t have this especial container implementation. So Both run over VMs!

Defining your docker "VM"

Dockerfile

```
FROM debian:stretch
RUN apt-get update

##################
#Install binaries dependencies
##################

RUN apt-get install -y \
    bedtools=2.26.0+dfsg-3 \
```

$ docker build -t fnavarro/temp:latest ./Dockerfile

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```
Building in Docker Cloud's infrastructure...
Cloning into '.'...
.
Reset branch 'master'
Your branch is up-to-date with 'origin/master'.
Pulling cache layers for fnavarro/texp:latest...
Done!
KernelVersion: 4.4.0-93-generic
Arch: amd64
BuildTime: 2017-08-17T22:50:04.828747906+00:00
ApiVersion: 1.30
Version: 17.06.1-ce
MinAPIVersion: 1.12
GitCommit: 874a737
Os: linux
GoVersion: go1.8.3
Starting build of index.docker.io/fnavarro/texp...
Step 1/12 : FROM debian:stretch
---> da653cee0545
Step 2/12 : RUN apt-get update
---> Using cache
---> 17904f776045
Step 3/12 : RUN apt-get install -y bedtools
---> Using cache
---> eea5e6affff4
```

```
FROM debian:stretch
RUN apt-get update

#################
#Install binaries dependencies

RUN apt-get install -y \
        samtools=1.3.1-3 \
             […]
        wget

#################
#Install Wgsim

#################
#Download Libraries

RUN wget rep_annotation.hg38.tar.bz2
RUN wget bowtie2.hg38.tar.bz2

#################
#Install R packages dependencies

#################
#Install TeXP

ADD https://api.github.com/repos/gersteinlab/texp/git/refs/heads/master version.json
RUN mkdir -p /src; \
        cd /src ; \
        git clone https://github.com/gersteinlab/texp.git

WORKDIR /src/texp/
CMD ["/src/texp/TeXP.sh"]
```

TeXP Dockerfile

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RUN mkdir -p /src; \
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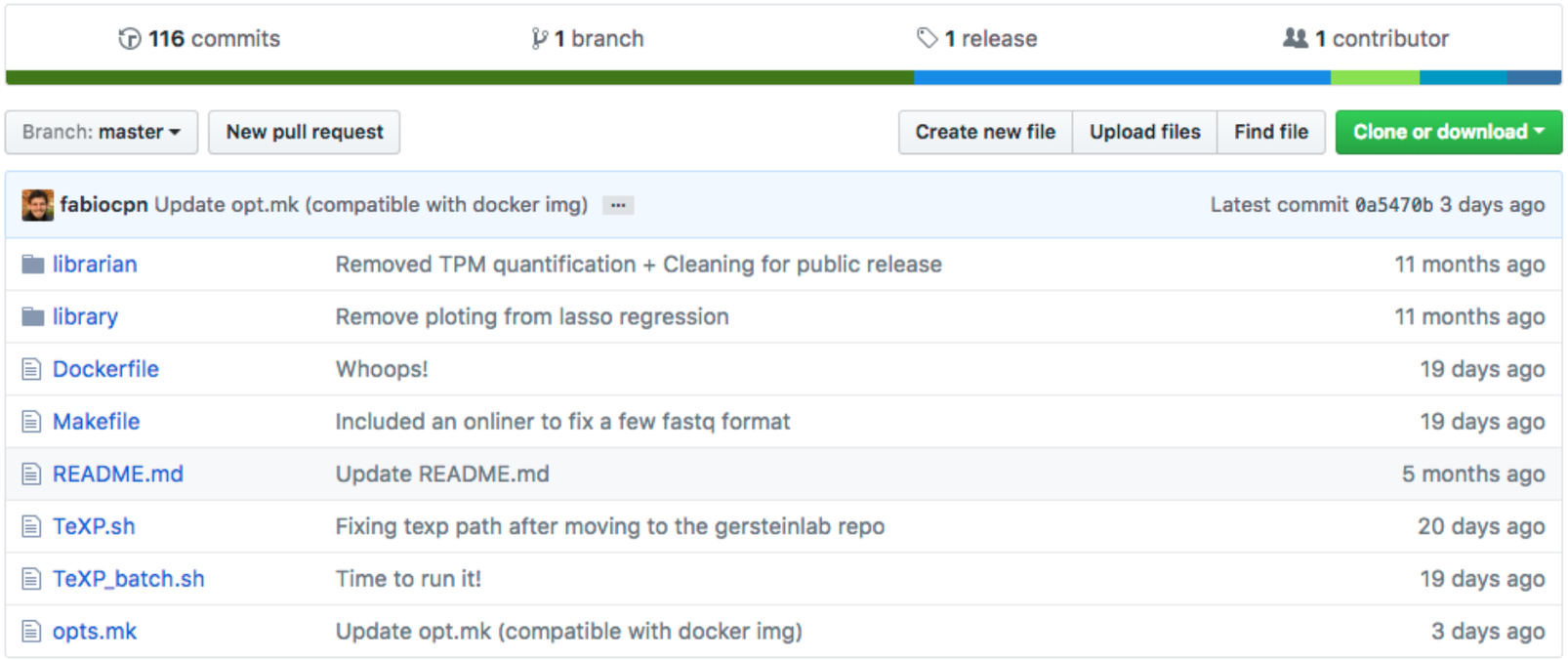
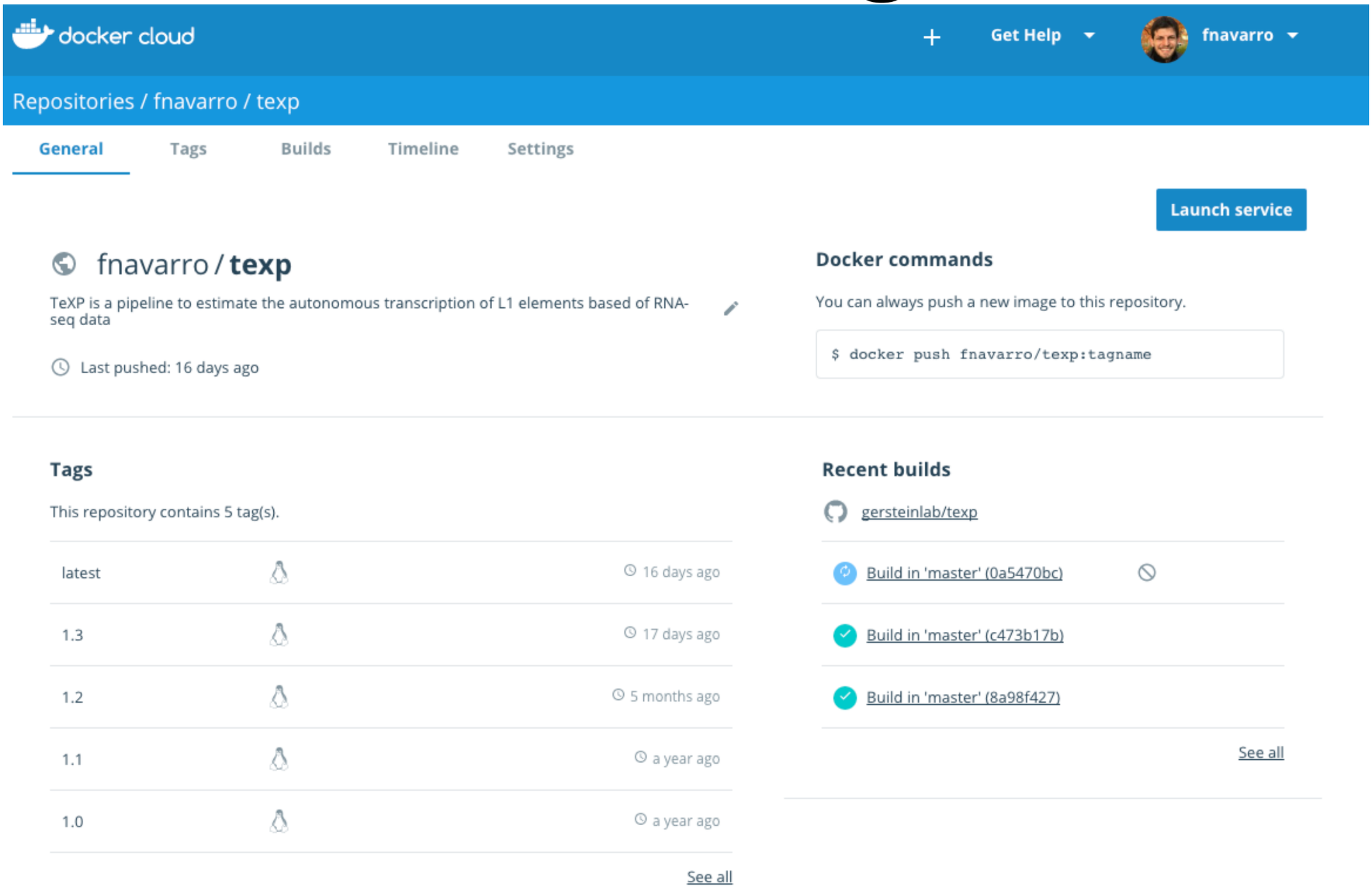
        git clone https://github.com/gersteinlab/texp.git

WORKDIR /src/texp/
CMD ["/src/texp/TeXP.sh"]
```



https://github.com/gersteinlab/texp.git

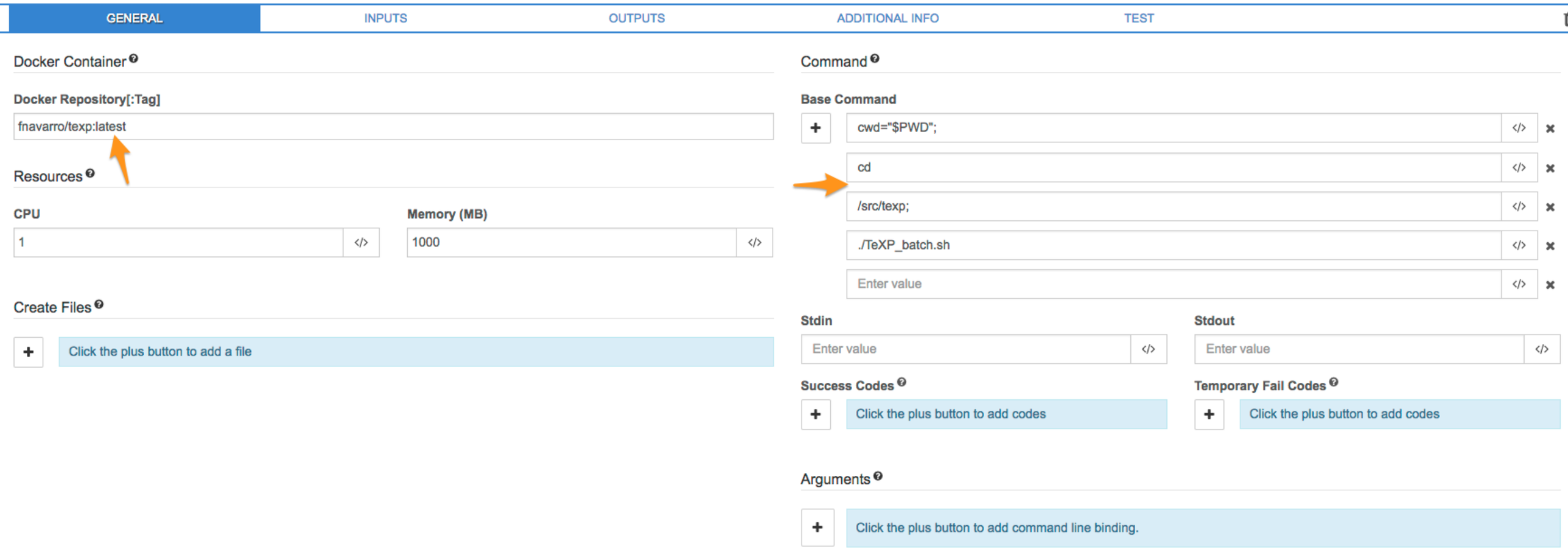
docker.io + github



docker run -it fnavarro/texp:latest /bin/bash

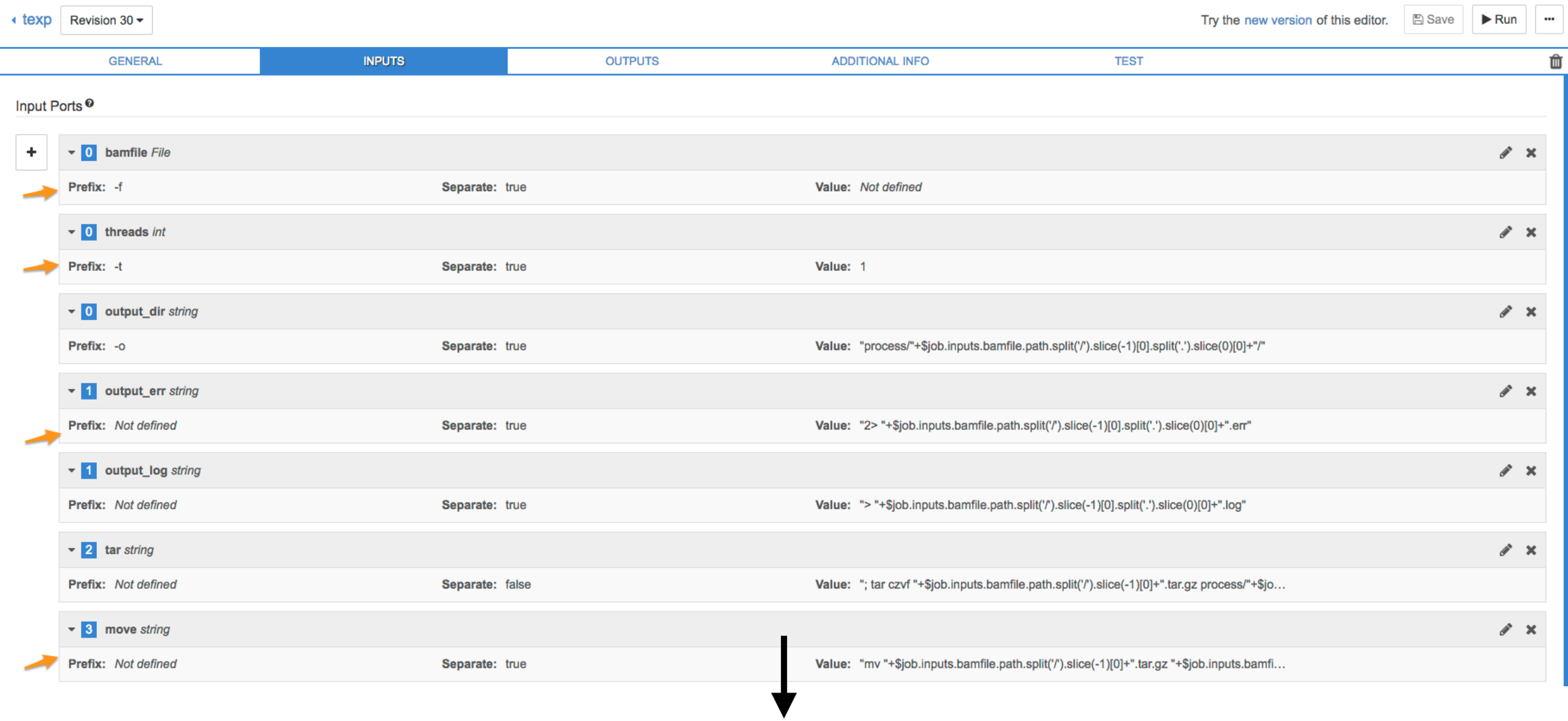
Setting up TeXP on CGC

Setting up TeXP on CGC (1)



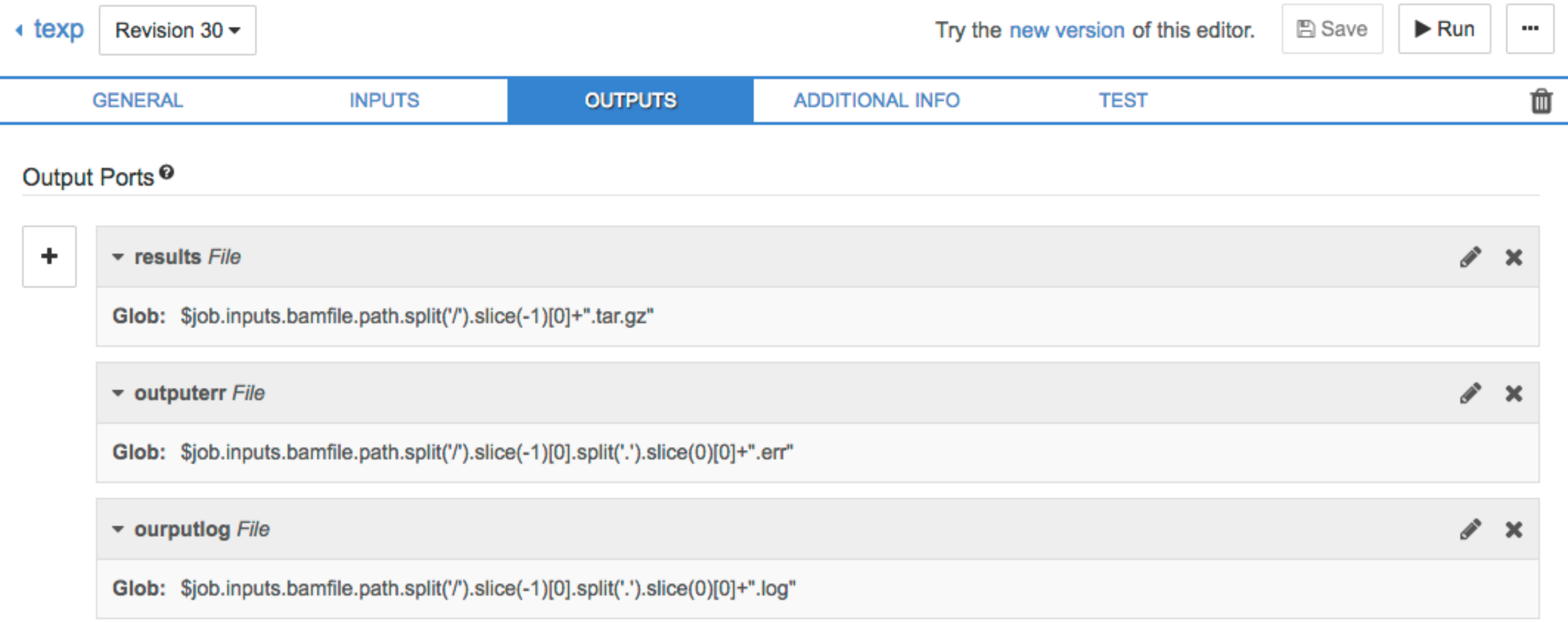
docker pull fnavarro/texp:latest; cwd="$PWD"; cd /src/texp; ./TeXP_batch.sh

Setting up TeXP on CGC (2)



-f /path/to/bamfile.ext -t 1 -o process/bamfile/ 2> bamfile.err > bamfile.log ; tar czvf bamfile.ext.tar.gz process/bamfile/; mv bamfile.ext.tar.gz bamfile.log bamfile.err $cwd

Setting up TeXP on CGC (3)

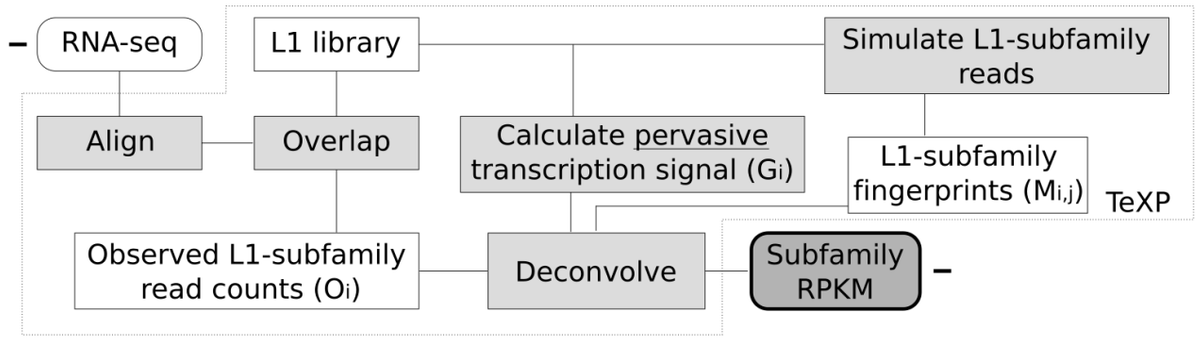


Setting up TeXP on CGC (4)

Create App workflow

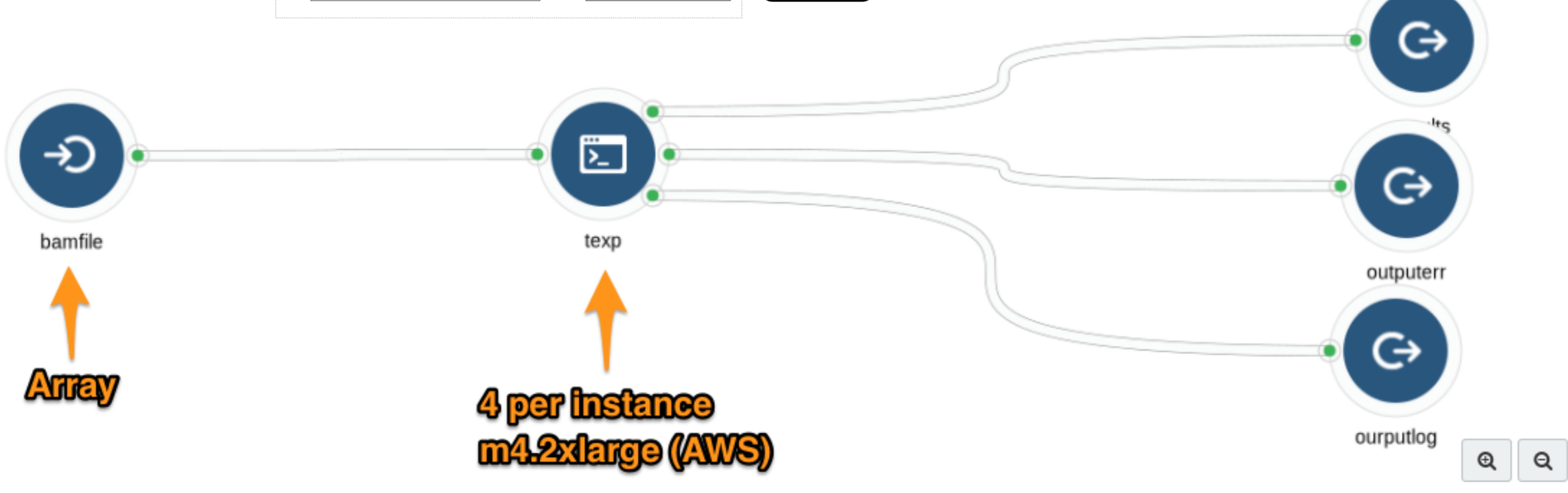
Description

No description.



process/UNCID_2332590/130718_UNC12-SN629_0321_AC2E6WACXX_ATGTCA_L007_1.fastq.err
process/UNCID_2332590/130718_UNC12-SN629_0321_AC2E6WACXX_ATGTCA_L007_1.fastq.log
process/UNCID_2332590/130718_UNC12-SN629_0321_AC2E6WACXX_ATGTCA_L007_1.fastq.stats

process/UNCID_2332590/130718_UNC12-SN629_0321_AC2E6WACXX_ATGTCA_L007_1.fastq:
L1HS_hg38.count
L1HS_hg38.count.corrected
L1HS_hg38.count.rpkm
L1HS_hg38.count.rpkm.corrected
L1HS_hg38.count.signal_proportions
qualityEncoding
read_length
re.bam
re.filtered.bam
re.filtered.bed
sorted.bam.bai
sorted.bam.tot
L1HS_hg38.signatures.txt



CGC Demo (3min)

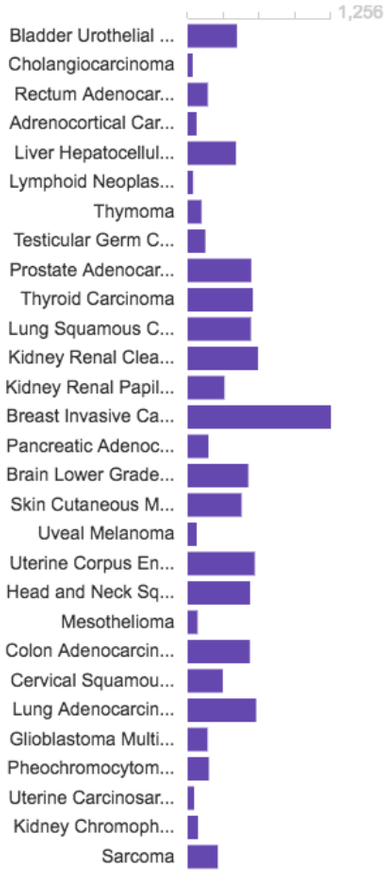
http://cgc.sbgenomics.com

CGC Life cycle

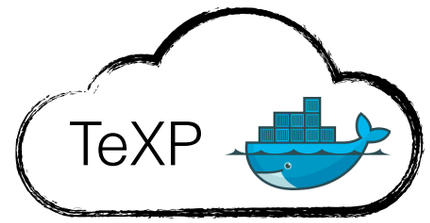
CANCER GENOMICS CLOUD
SEVEN BRIDGES

Tumor RNA-seq

Amazon S3



10,089



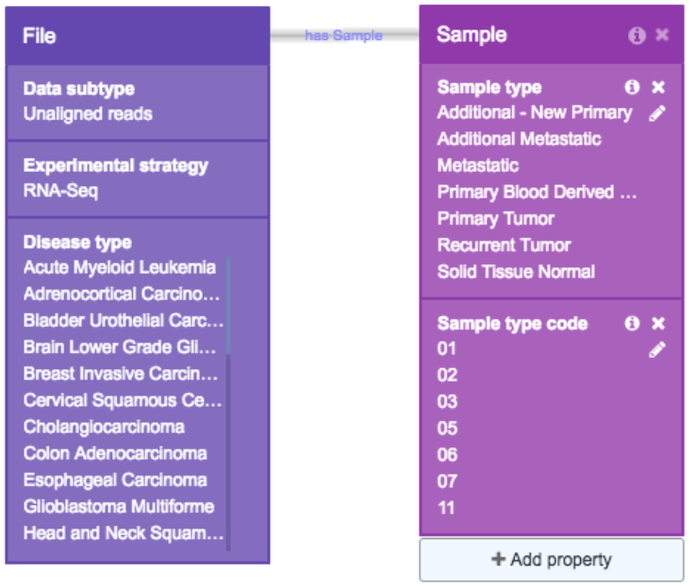
Image

Amazon EC2

Container

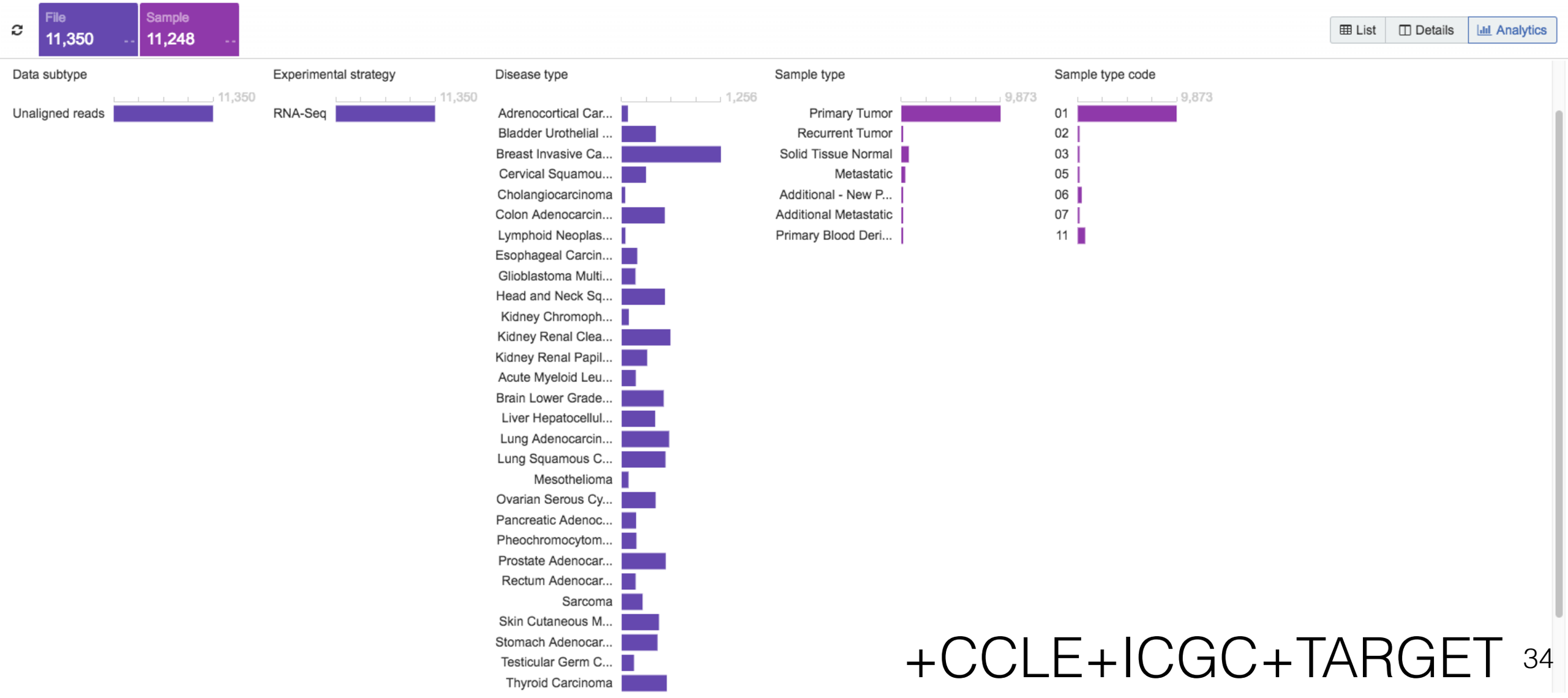
Amazon S3

Result container



TCGA data on CGC

(if you have authorized access)

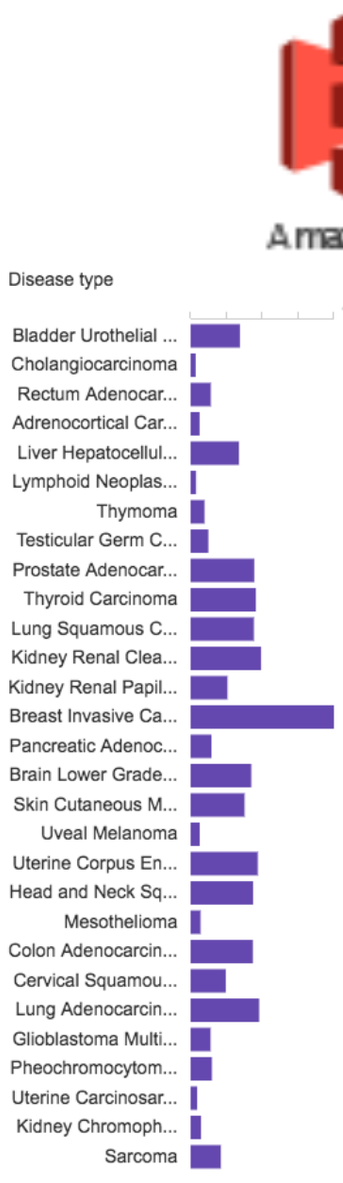


+CCLE+ICGC+TARGET

CGC Life cycle

CANCER GENOMICS CLOUD
SEVEN BRIDGES

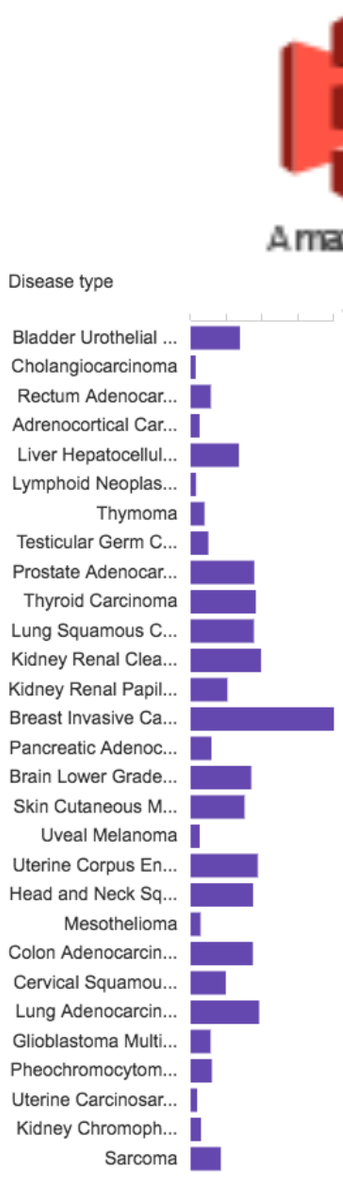
Tumor RNA-seq

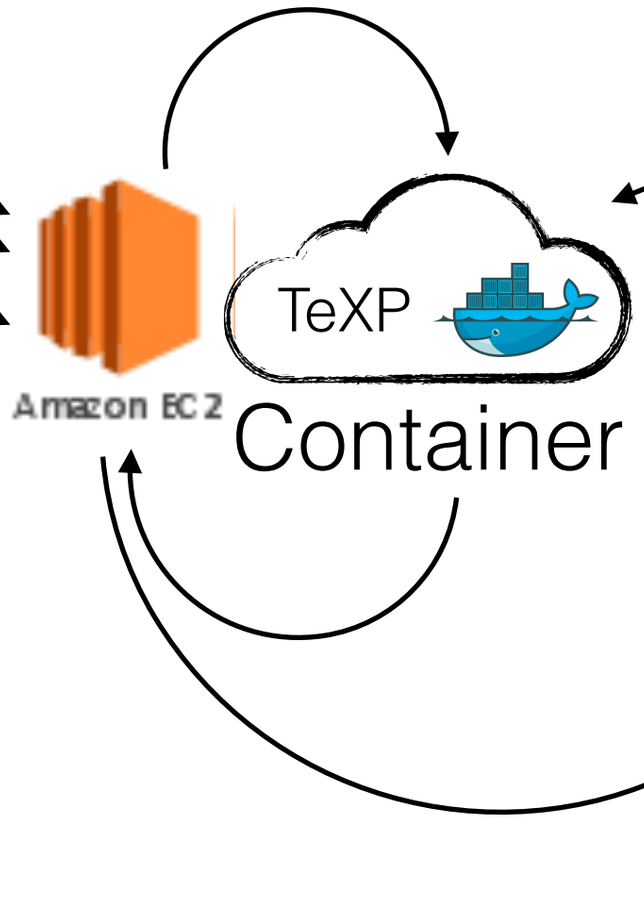


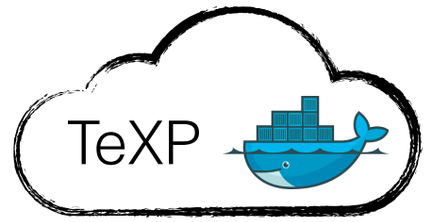
CGC Life cycle

CANCER GENOMICS CLOUD
SEVEN BRIDGES

Tumor RNA-seq







80 instances
= 640 proc

Result container

Doings things programmatically

- Python API to manage launching;

```
my_app = find_app(api, my_project, app_name)
tar_files = find_files(api, my_project, “tar")
my_project = find_project(api, project_name)

my_task = api.tasks.create(name="texp run"+str(task_id),
                           project=my_project, app=my_app,
                           inputs=inputs, run=True)
```

- Python API to manage files (download/rm);

```
output_files = find_files(api, my_project, “breaks")
for i, curr_file in enumerate(output_files):
     curr_file.download(path=‘auto_'+curr_file.name)
     curr_file.delete()
```

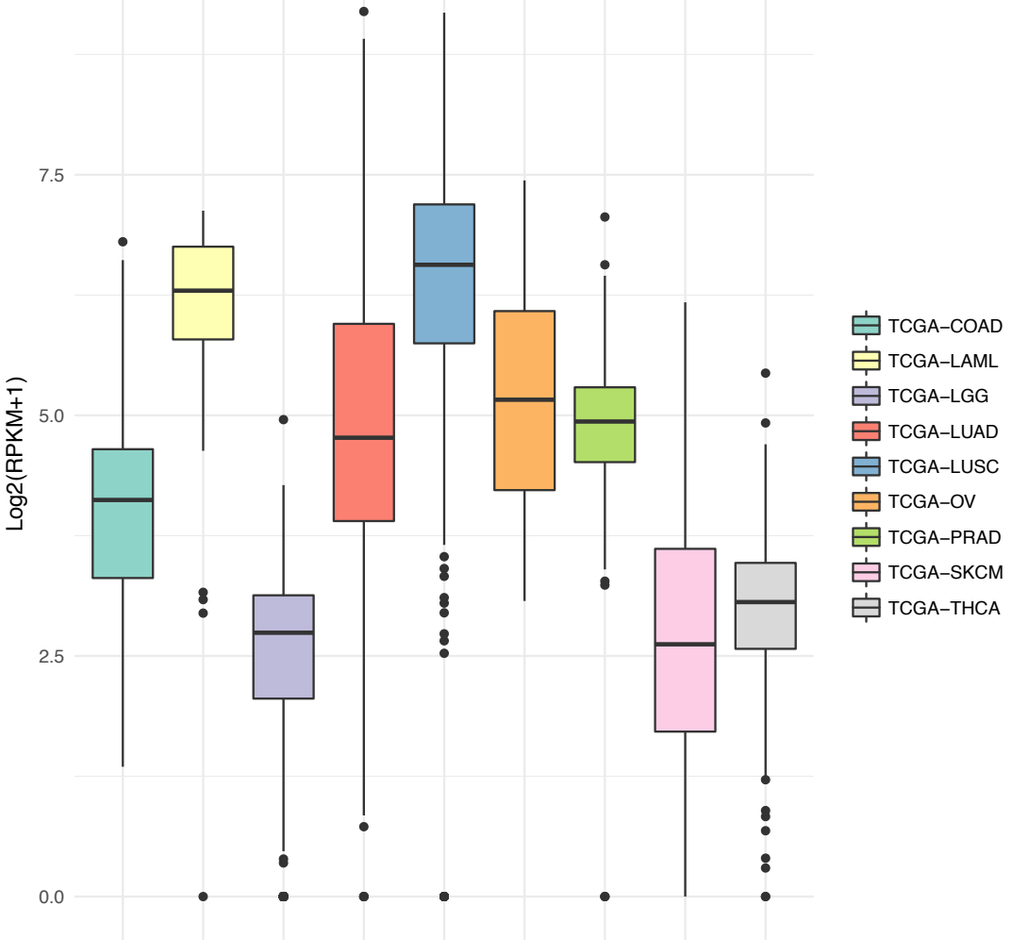
demo texp_6?

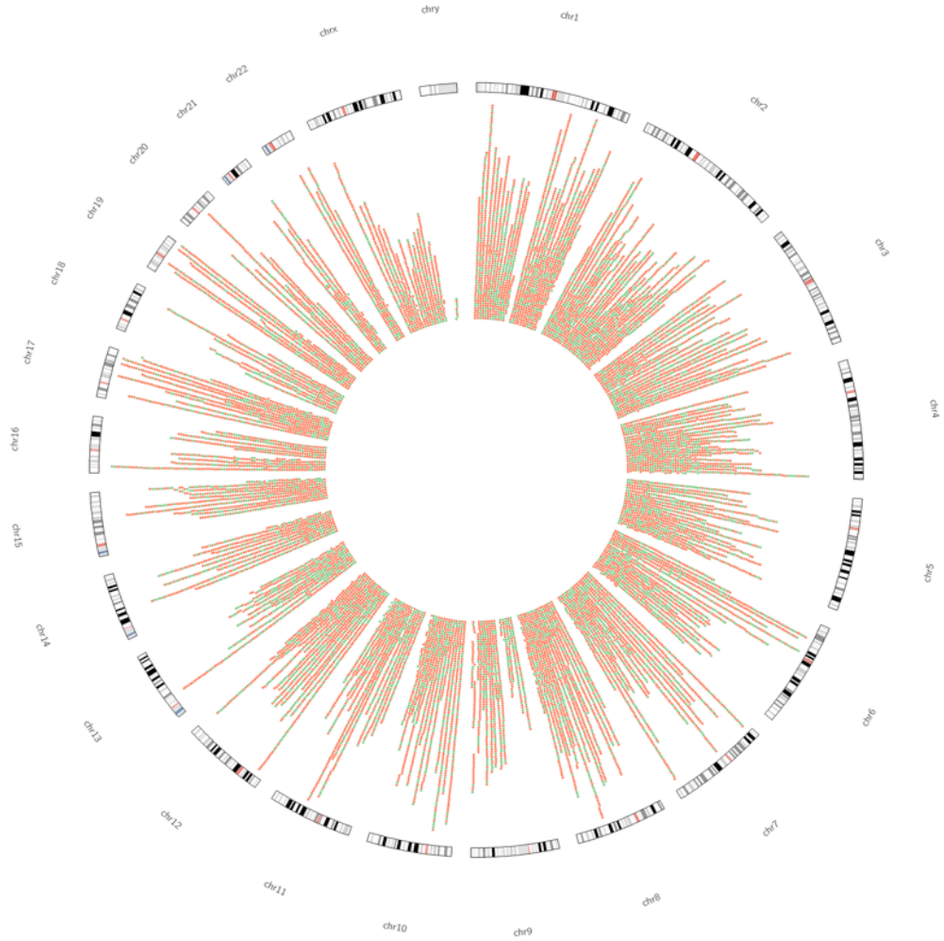
What have we learned so far?

- It’s fast-ish
- Mind the overhead of learning how to use all these tools
- It is kind of cheap
  - Break point analysis for all 4,880 TCGA WGS
    $1,800 - $0.36 p/ sample
  - TeXP for 3,900 RNA-seq samples
    $1200 - $0.30 p/ sample

Future steps

- Further explore the relationship between L1 transcription and genome instability





- Quantify the retrotransposition of ALUs in tumors

  75 samples -> 10,646 putative insertions

Acknowledgments

Mark Gerstein

Joel Rozowsky
Sushant Kumar
Prashant Emani
Timur Galeev
Gamze Gursoy
Jinrui Xu
Arif Harmanci
Eric Yu
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