Breakout Session 6:

Migration to Cloud of the Oncogenomics Next Generation Sequencing Pipelines & Databases for CCDI and Other Pediatric Cancers

Dr. Javed Khan
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Migration to Cloud of the Oncogenomics Next Generation Sequencing Pipelines & Databases for CCDI and Other Pediatric Cancers

PI: Dr. Javed Khan

Current Project Personnel: Hsien-Chao Chou, Vineela Gangalapudi, Vishal Koparde, Jun Wei and Patrick Zhao

AWS ProSupport: Kevin Sayers

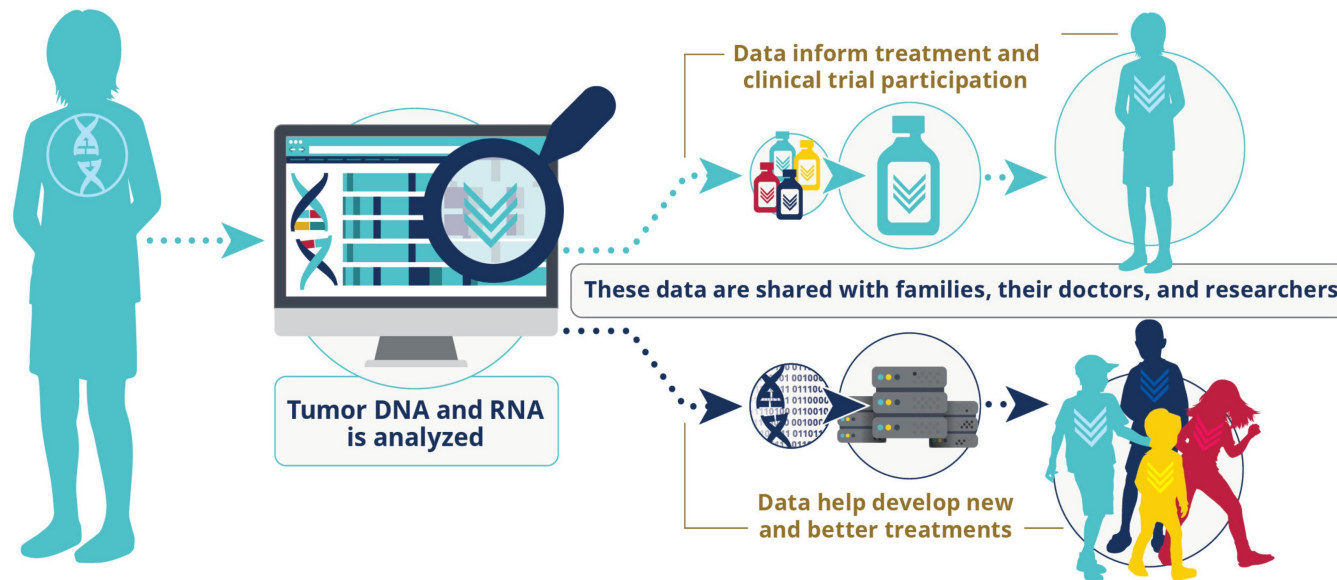2024 NIH/ODSS Cloud Supplement Program PI Meeting
January 17-18, 2024

Overarching Goals

- Develop cloud-based state-of-the art next generation sequencing analysis (NGS) pipeline based on best practice
- Develop a secure cloud-based comprehensive, genomic integrated browser for visualization and exploration of clinical (patient-centric) and research (cohort summary data) for pediatric cancers
- Support hypothesis generation, publications, and grant applications
- Complimentary to existing browsers (cBioPortal, Genomic Data Commons Data Portal, St. Jude Cloud, and UCSC Treehouse)
- Building on the existing Oncogenomics Clinical NGS pipeline and ClinOmics Portal

Background: Childhood Cancer Data Initiative (CCDI) Molecular Characterization Initiative (MCI)


NATIONAL CANCER INSTITUTE

WHAT IS THE

CCDI Molecular Characterization Initiative?

Data inform treatment and clinical trial participation

These data are shared with families, their doctors, and researchers

Tumor DNA and RNA is analyzed

Data help develop new and better treatments

Source: https://www.cancer.gov/research/areas/childhood/childhood-cancer-data-initiative

Generate clinical grade next generation sequencing (NGS) and methylation data from every child, adolescent, and young adult diagnosed with childhood cancer, enrolled in Children's Oncology Group (COG) trials nationwide

Childhood Cancer Data Initiative (CCDI) Oncogenomics Cloud Project
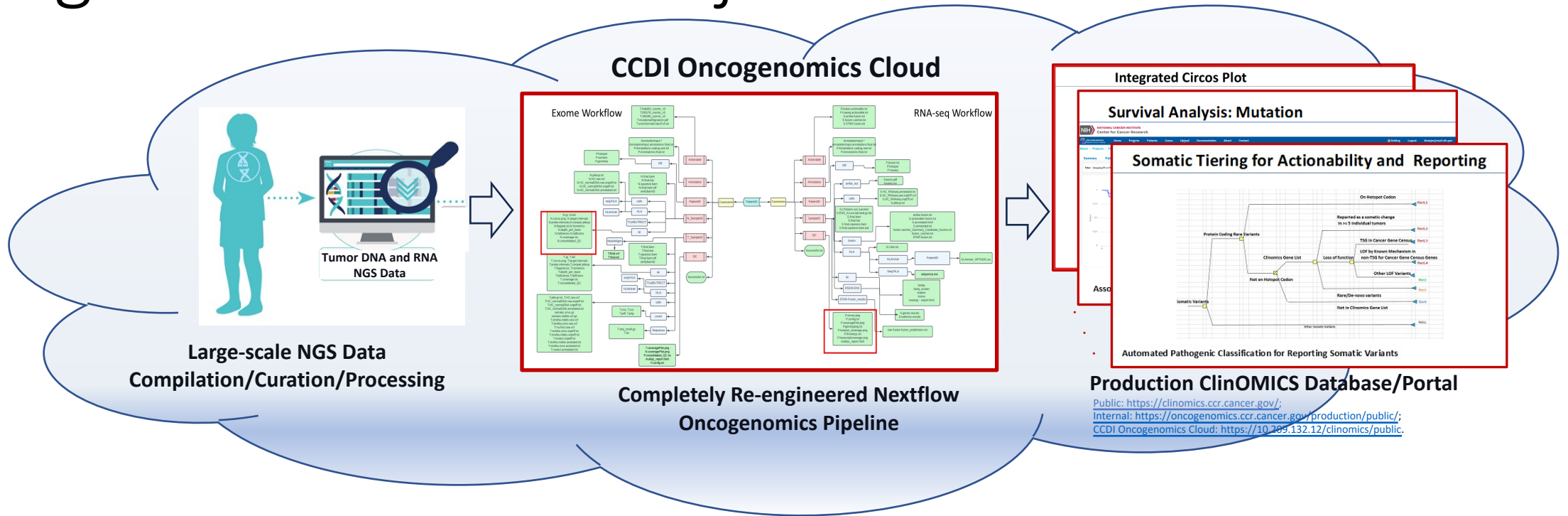
Data

Large-scale tumor Whole Transcriptome and tumor/normal Whole Exome <u>from every child and adolescent young adult</u>
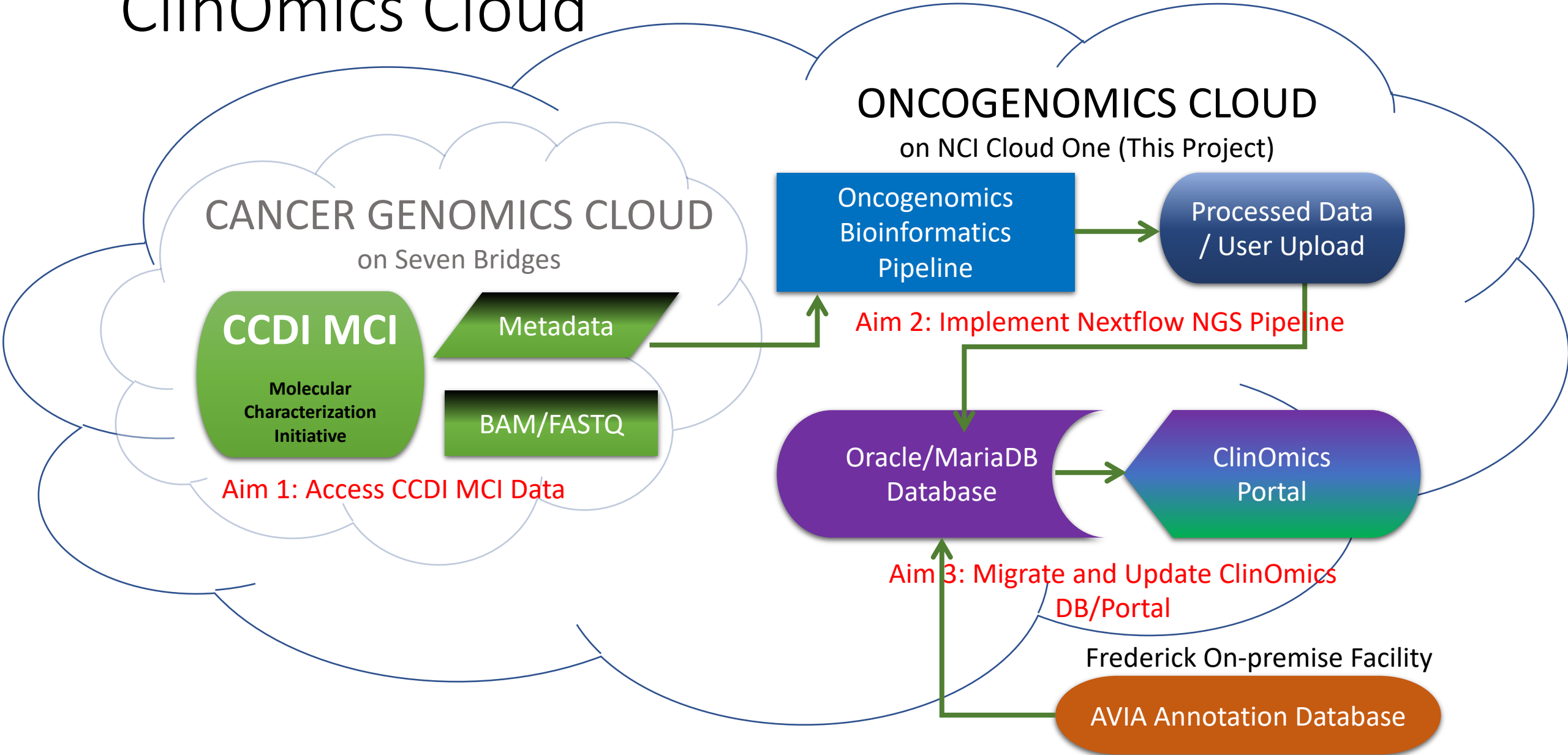
Oncogenomics NGS Pipeline

Processing and analyzing large-scale Transcriptomic and WES datasets

ClinOmics DB/Portal

Bring the CCDI MCI and other pediatric cancer genomics data to the fingertips of researchers and clinicians.

ODSS support of NCI data science project for exploratory use of the cloud via the STRIDES Initiative in FY2023, 2024

ClinOmics Cloud

CANCER GENOMICS CLOUD
on Seven Bridges

ONCOGENOMICS CLOUD
on NCI Cloud One (This Project)

CCDI MCI
Molecular Characterization Initiative

Metadata

BAM/FASTQ

Aim 1: Access CCDI MCI Data

Oncogenomics Bioinformatics Pipeline

Processed Data / User Upload

Aim 2: Implement Nextflow NGS Pipeline

Oracle/MariaDB Database

ClinOmics Portal

Aim 3: Migrate and Update ClinOmics DB/Portal

Frederick On-premise Facility
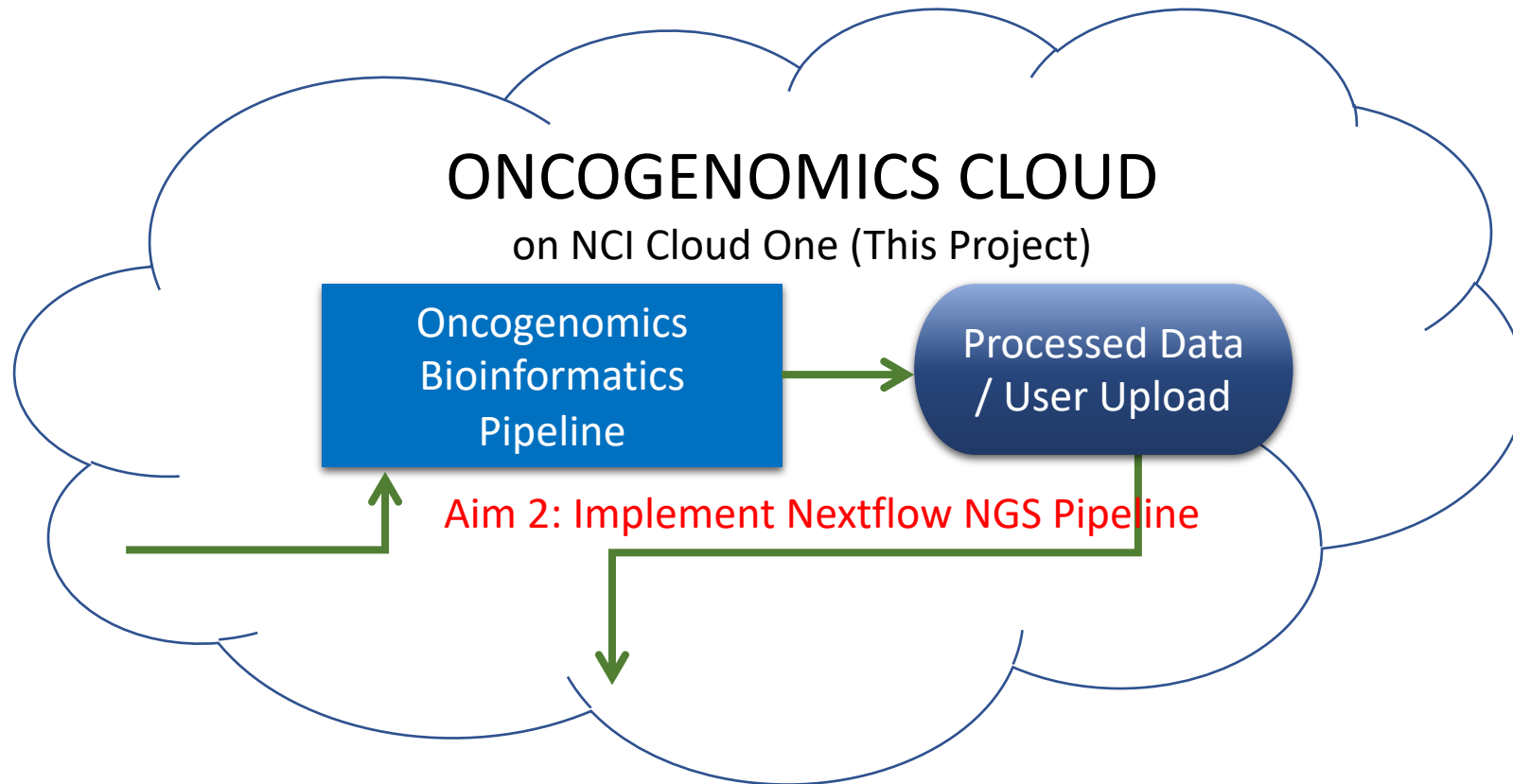
AVIA Annotation Database

Aim #1: Directly accessing the CCDI Molecular Characterization Initiative (MCI) data in Cancer Genomics Cloud (CGC)

- Explore security and data sharing policies and technological means to directly access the CCDI MCI data in CGC hosted in Seven Bridges.

- Direct access to MCI data in CGC would avoid or reduce data download/egress costs of data analysis via S3 bucket sharing in the AWS cloud.

- The cross-cloud architecture would improve the data transfer, computational, and cost efficiencies of research.

- Pathway to access other childhood cancer genomics data hosted in AWS cloud
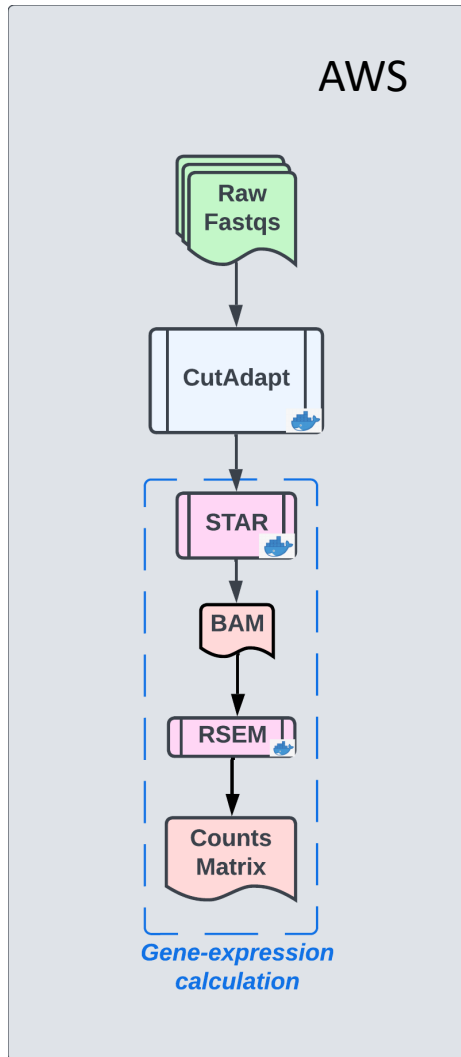
Aim #1 Ongoing: Accessing MCI Data in CGC
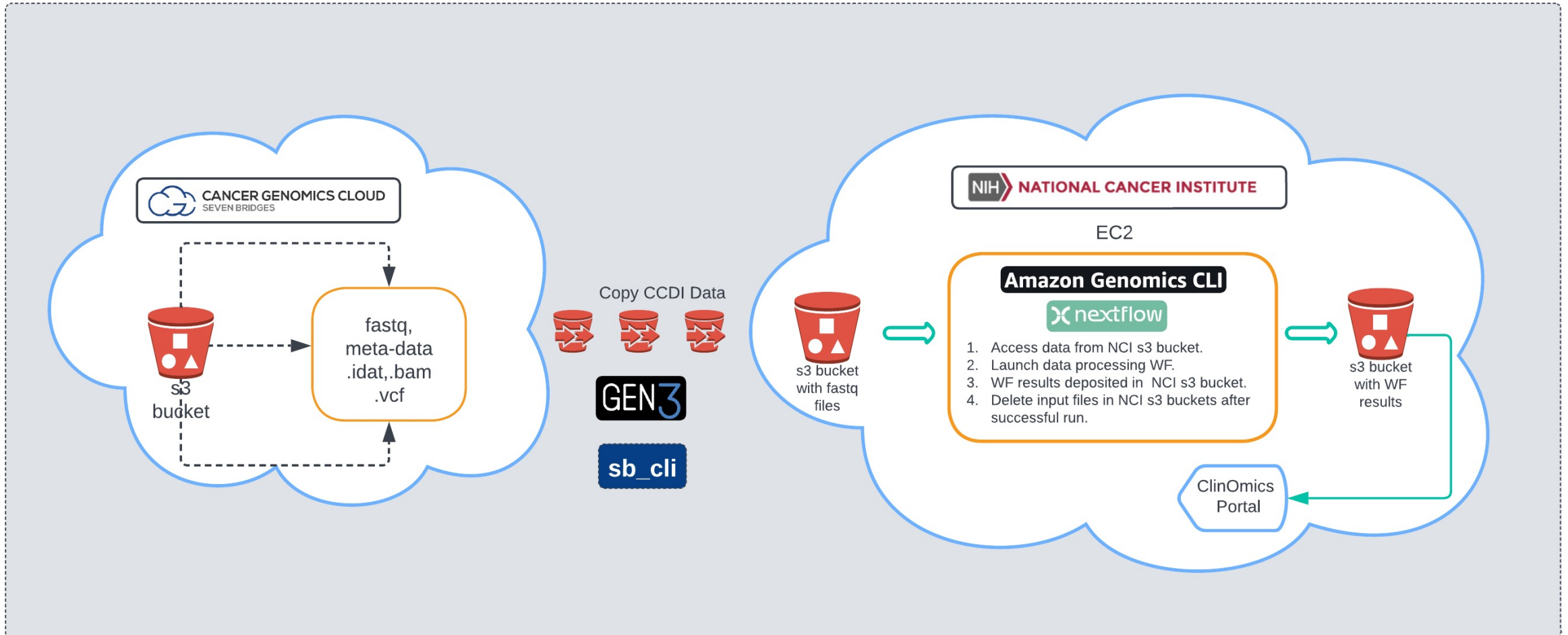
Aim #2: Develop and Deploy Oncogenomics NGS Pipeline in the AWS Cloud

Oncogenomics Pipeline – Conversion to Nextflow

AWS

Raw Fastqs → CutAdapt → STAR → BAM → RSEM → Counts Matrix

Gene-expression calculation

| Technical Feature/Metric	Snakemake	nextflow
dryrun	✓	✗
"bin" folder	✗	✓
"variable" input	✗	✓
HPC<->Cloud interoperability	✗	✓
s3 fs support	✗	✓
direct GitHub support	✗	✓
inbuilt SLURM support	✗	✓
better regex support	✗	✓
code simplicity	✓	✗

Achieved: Minimal Viable Product (MVP) in Year 1

Re-engineered Oncogenomics RNA-seq Pipeline, deployable on Biowulf, AWS Cloud Computing Platform, and other High-performance environments.

RNASeq

- Gene Expression
- QC
- Fusion Detection
- HLA Calling
- Variant Calling
- HLA

Easy to append new features or switch between genome versions (hg19<->hg38)
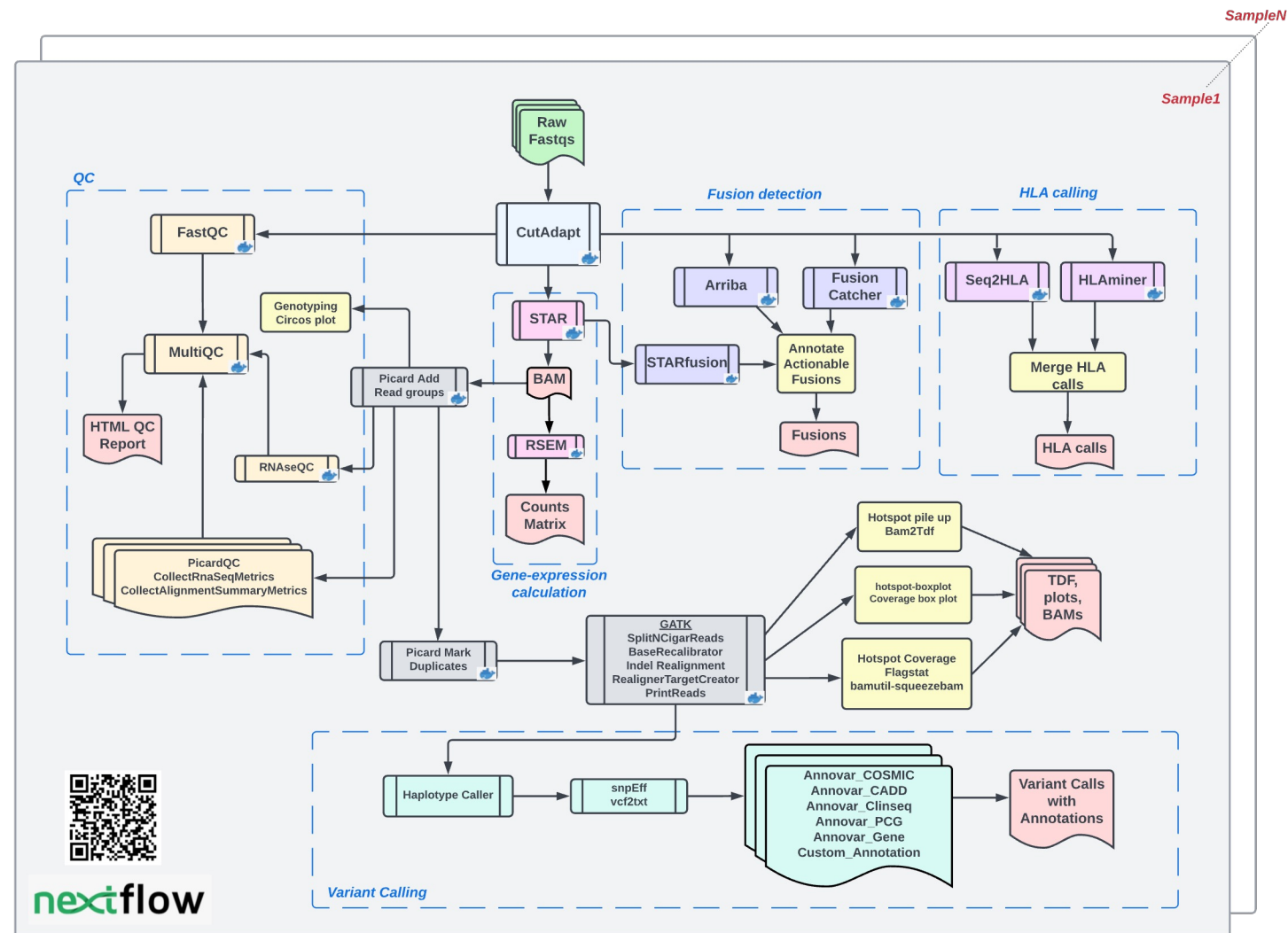
Ongoing: Exome Workflow – Year 1, 2

Re-engineered Oncogenomics Exome Pipeline, deployable on Biowulf, AWS Cloud Computing Platform, and other High-performance environments.

Data generated

- Actionable Germline
- Actionable Somatic
- HLA
- Copy number variant
- Mutation signature
- Mutational burden
- MSI
- Neoantigen
- Immune infiltrate

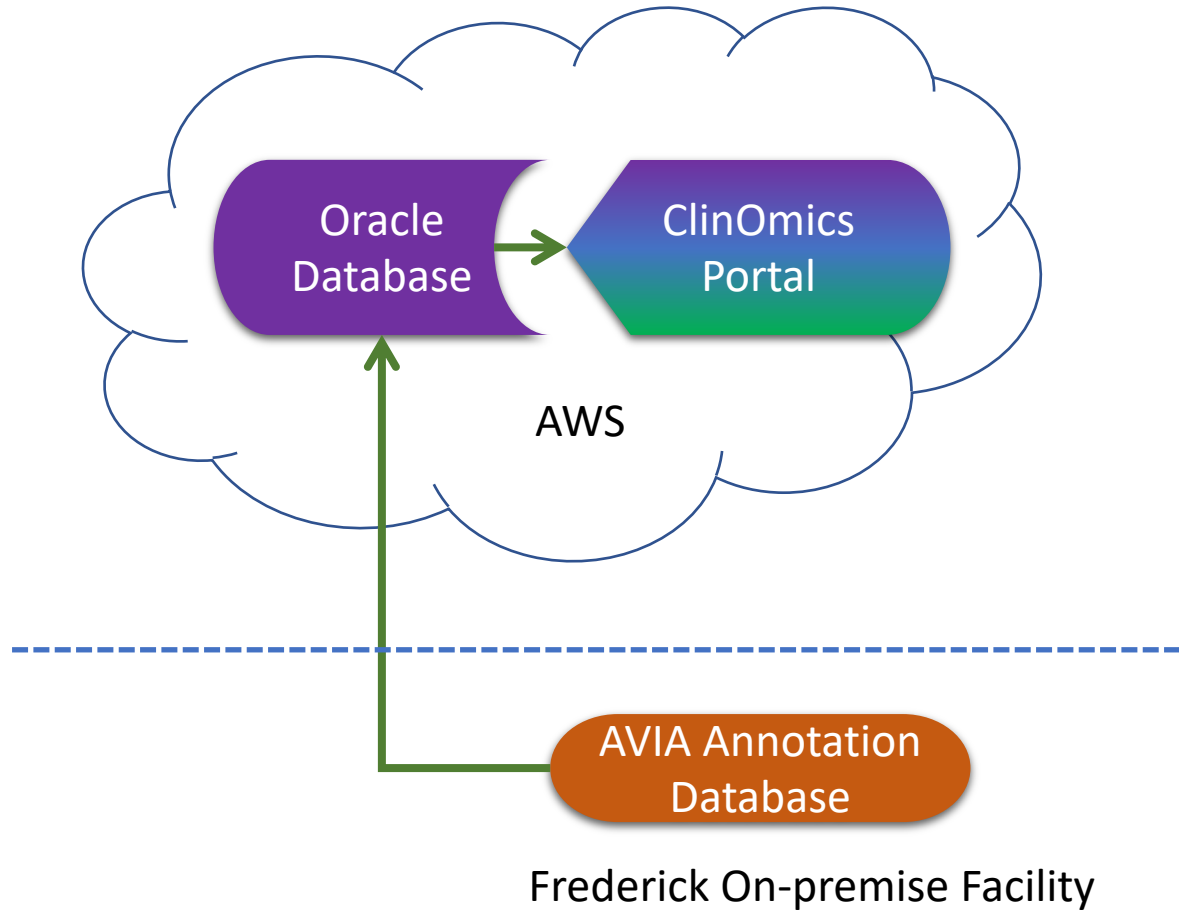Easy to append new features or switch between genome versions (hg19<->hg38)
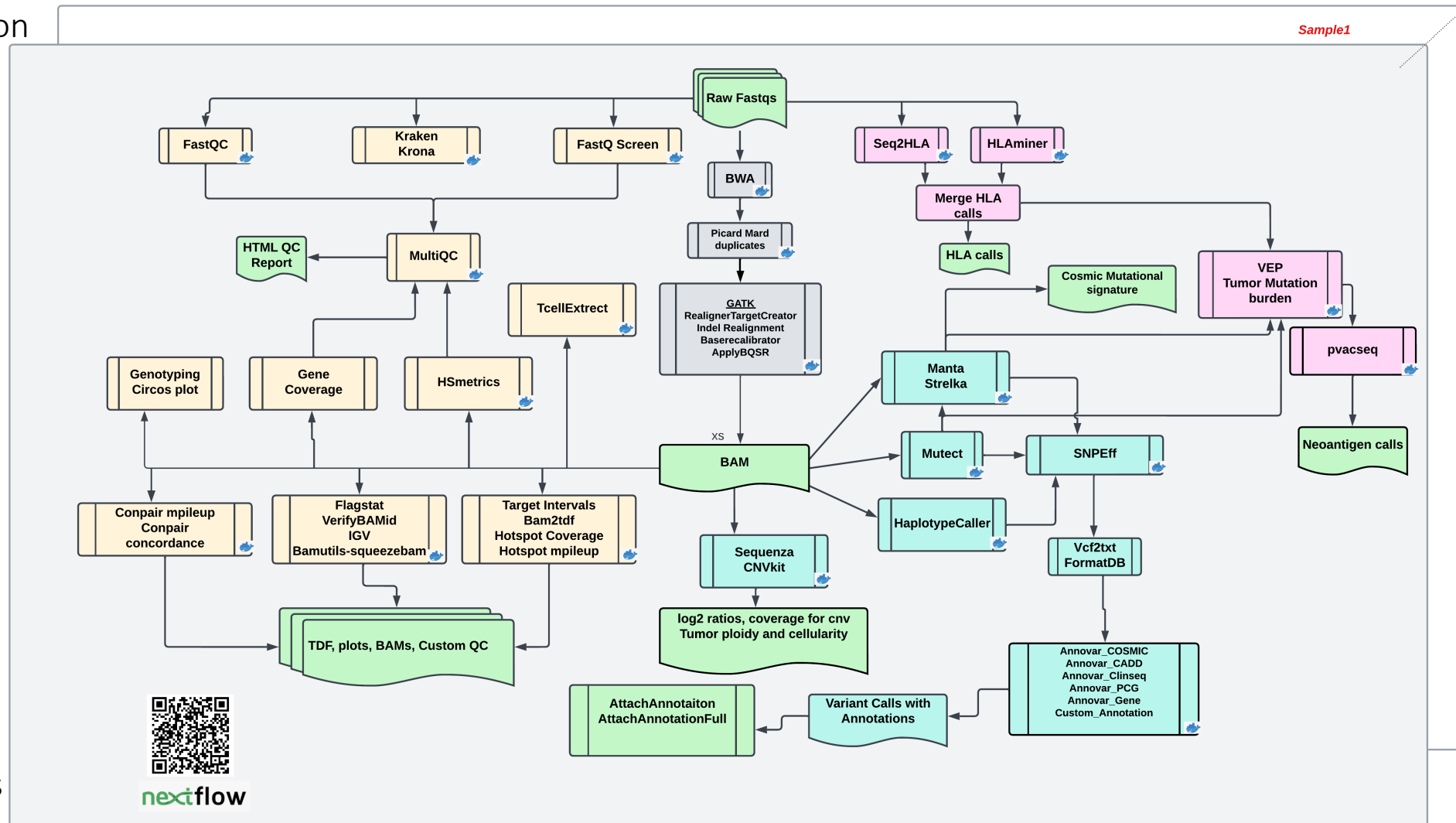
Aim #3: Migrating DB/Web Portal to AWS

https://clinomics.ccr.cancer.gov/

Cloud/On-premise Databases Sync for Up-to-date AVIA Annotations

Oncogenomics DB for Clinical and Research Applications

Project Level Summary Data

Home / Projects / RNAseq_Landscape_Manuscript

🔍 Gene: _____

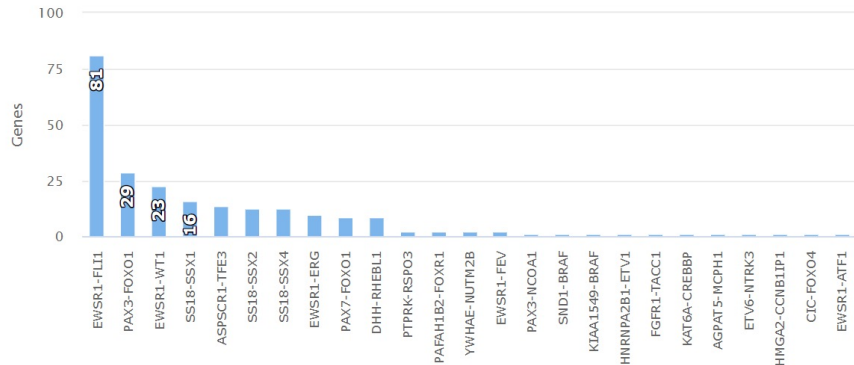| Summary | Patients | Samples | Cases | Mutations | TIL | Fusions | Expression | CNV | Survival | QC | Users |

Project ID: 25861   **Version:** hg19   **Project Group:** 1   **Project Name:** RNAseq_Landscape_Manuscript

Patients: 786   **Cases:** 294   **Samples:** 1696   **Processed Patients:** 785   **Processed Cases:** 259
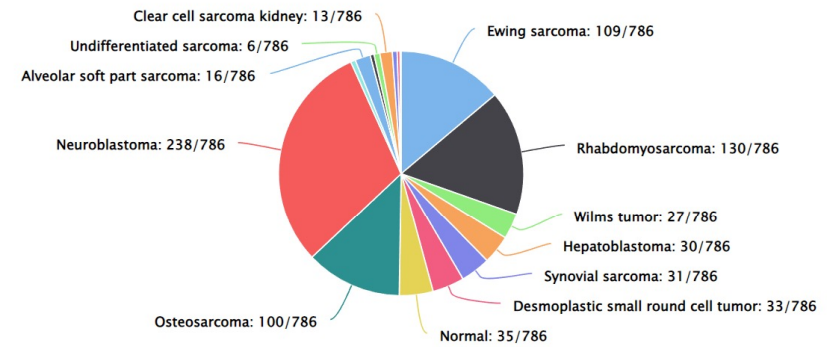
Survival: 240   **Exomes:** 569   **Panels:** 0   **RNAseq:** 935   **Whole Genome:** 192

Description: RNAseq_Landscape_Manuscript
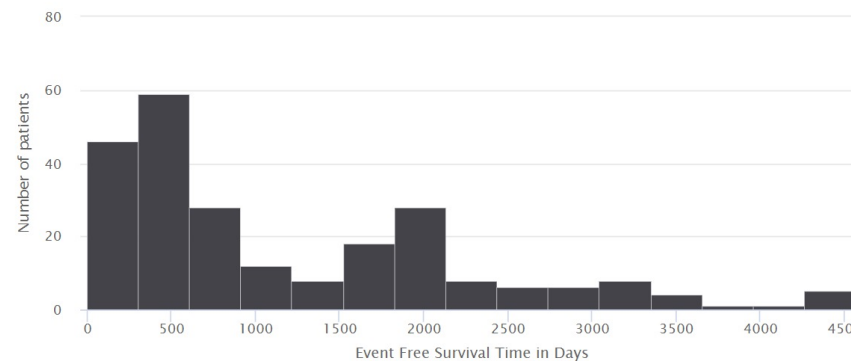
Fusion – Tier 1.1

Diagnosis

Clear cell sarcoma kidney: 13/786
Undifferentiated sarcoma: 6/786
Alveolar soft part sarcoma: 16/786
Neuroblastoma: 238/786
Osteosarcoma: 100/786
Ewing sarcoma: 109/786
Rhabdomyosarcoma: 130/786
Wilms tumor: 27/786
Hepatoblastoma: 30/786
Synovial sarcoma: 31/786
Desmoplastic small round cell tumor: 33/786
Normal: 35/786

Diagnosis	Number
Alveolar soft part sarcoma	16
Clear cell sarcoma	3
Clear cell sarcoma kidney	13
Desmoplastic small round cell tumor	33
Ewing like sarcoma	1
Ewing sarcoma	109
Hepatoblastoma	30

Showing 1 to 17 of 17 entries

Event Free Survival Time in Days

Vital Status

NoValue: 1/786
: 1/786
Alive: 131/786
Dead
Number of patients: 107/786 (13.6%)
Dead: 107/786
NA: 546/786
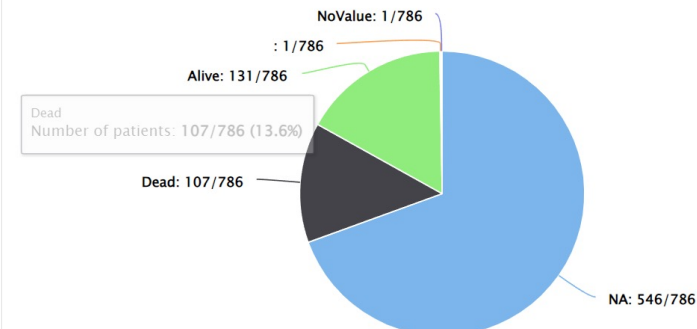
Visual Validation of Variant, Germline vs. Somatic, Tumor evolution   Association of MYOD1 Mutation with Outcome in Rhabdomyosarcoma   Automated Pathogenic Classification for Reporting Somatic Variants

Variant annotation – AVIA (Annotation, Visualization and Impact Analysis)

- Seamless integration with AVIA (https://avia-abcc.ncifcrf.gov/)
- AVIA provides up-to-date customized OpenCRAVAT based annotation
  - Reported database (CBioPortal, ICGC, Genie and PCG)
  - Population frequency
  - Protein annotation
  - Functional prediction
  - Epigenetics information
  - Clinical information
  - Basic gene information

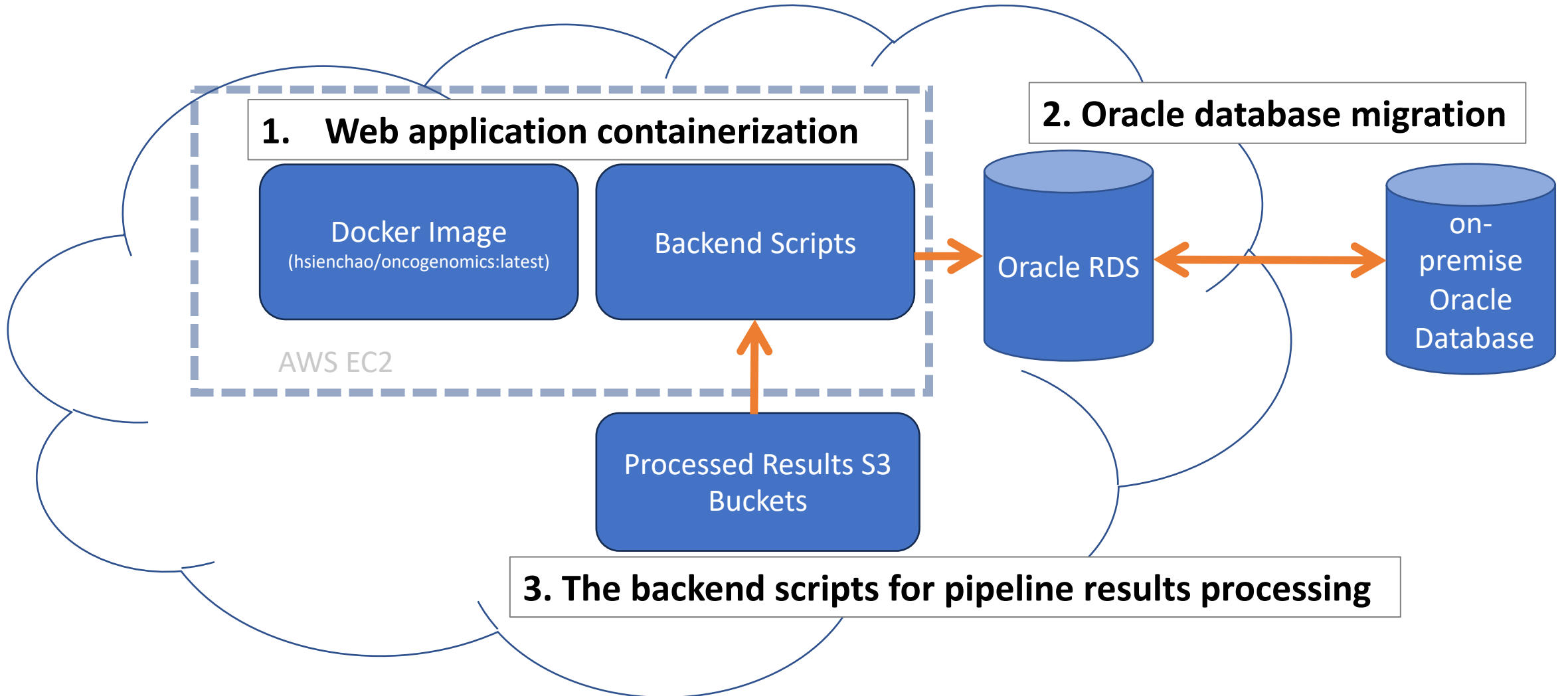| Gene: **PTH2** | Chr: **chr19** | Start: **49926533** | End: **49926533** | Ref: **G** | Alt: **C** |

Population | Protein | Prediction | Epigenetics | **Reported** | Clinical | Gene

ICGC

Cbioportal

Pediatric

Annotator: **ICGC**

Description: **ICGC**

Column	Description	Value
ICGC	ICGC	Total count: 16 ID: MU46003

Project	Donors	Total Donors	Frequency
ESCA-CN	2	332	0.00602
LICA-CN	9	402	0.02239
LINC-JP	1	394	0.00254
LICA-FR	1	252	0.00397
GACA-JP	3	585	0.00513

Achieved: Migrating DB/Web Portal to AWS

https://clinomics.ccr.cancer.gov/

Ongoing: Migrating DB/Web Portal to AWS

https://clinomics.ccr.cancer.gov/

3. iTrust Authentication

iTrust Authentication

1. MariaDB migration

Docker Image

(hsienchao/oncogenomics:latest)

Backend Scripts

MariaDB RDS*

AVIA Annotation

2. DB independent AVIA integration

4. New Oncogenomics features:

- ssGSEA
- Hg38 support
- Methylation data
- ChIPseq/ATACseq/HiC

Processed Results S3 Buckets
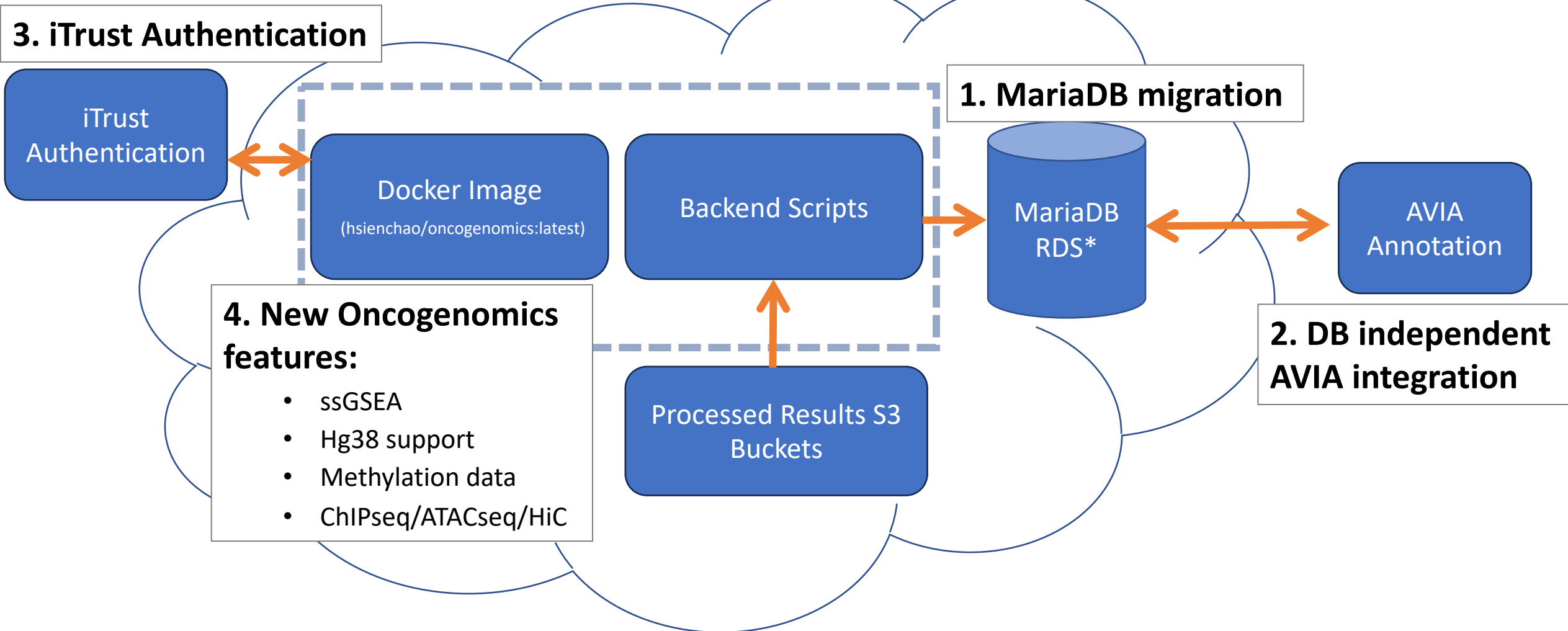
Achievements and future work

	Achievements/Products	Planned Future Work
Pipeline	Nextflow RNA- and DNA-seq Pipeline: https://github.com/CCRGeneticsBranch/AWS_POC_MVP_NF Pipeline Module Docker Containers: https://github.com/CCRGeneticsBranch/Dockers	• Add Whole Genome and Methylation workflow modules
Database and Web Portal	The Oncogenomics Database and Web Portal: https://10.209.132.12/clinomics/public The Oncogenomics Portal Source Code: https://github.com/CCRGeneticsBranch/Oncogenomics_v2 The Oncogenomics Portal Docker: https://github.com/CCRGeneticsBranch/Oncogenomics_docker	• Incorporate methylation data and tools, including diagnostic classification/ TSNE plots/ deconvolution

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- **Anney Che**
- **Parthav Jailwala**
- **Uma Mudunuri**
- **… …**

CCDI, CBIIT and AWS

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- **Sue Pan**
- **Kevin Sayers**
- **… …**

THANK YOU!