

Experiences Sharing Genomics Data

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PROBLEM: Genome data held in silos, unshared, not standardized

- No one institute has enough on its own to make progress
- Every clinician should be able to compare their genomes to others

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We need a network to share

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Global Alliance
for Genomics & Health

Collaborate. Innovate. Accelerate.

200+ Genomic Data Initiatives Globally

Clinical/Genomic Medicine

40

Initiatives

Research

70

Initiatives

National

21

From 15 Countries

Cohorts

64

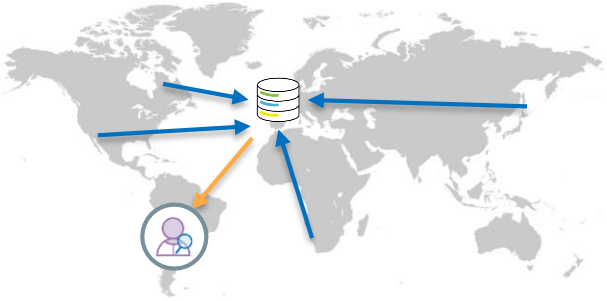
Globally

Data Federation Model for Global Genome Sharing

Global Alliance for Genomics & Health

Data Commons

Basic research consented for data sharing

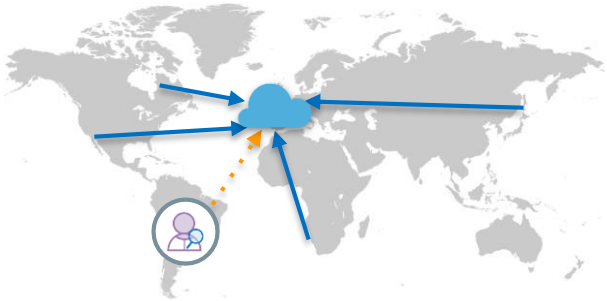


Aggregate data globally

Download, analyze locally

Cloud Commons

Large scale research datasets

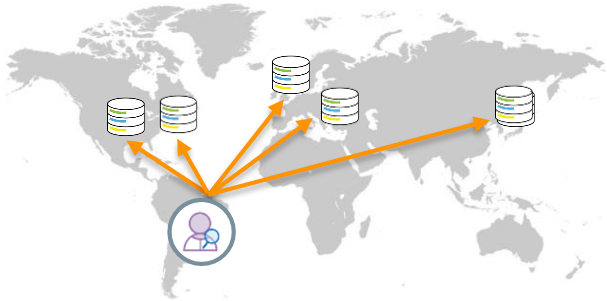


Aggregate data globally

Analyze centrally in secure cloud

Data Federation

New approach for genomics initiatives



Host data locally

Visit data remotely and collate results

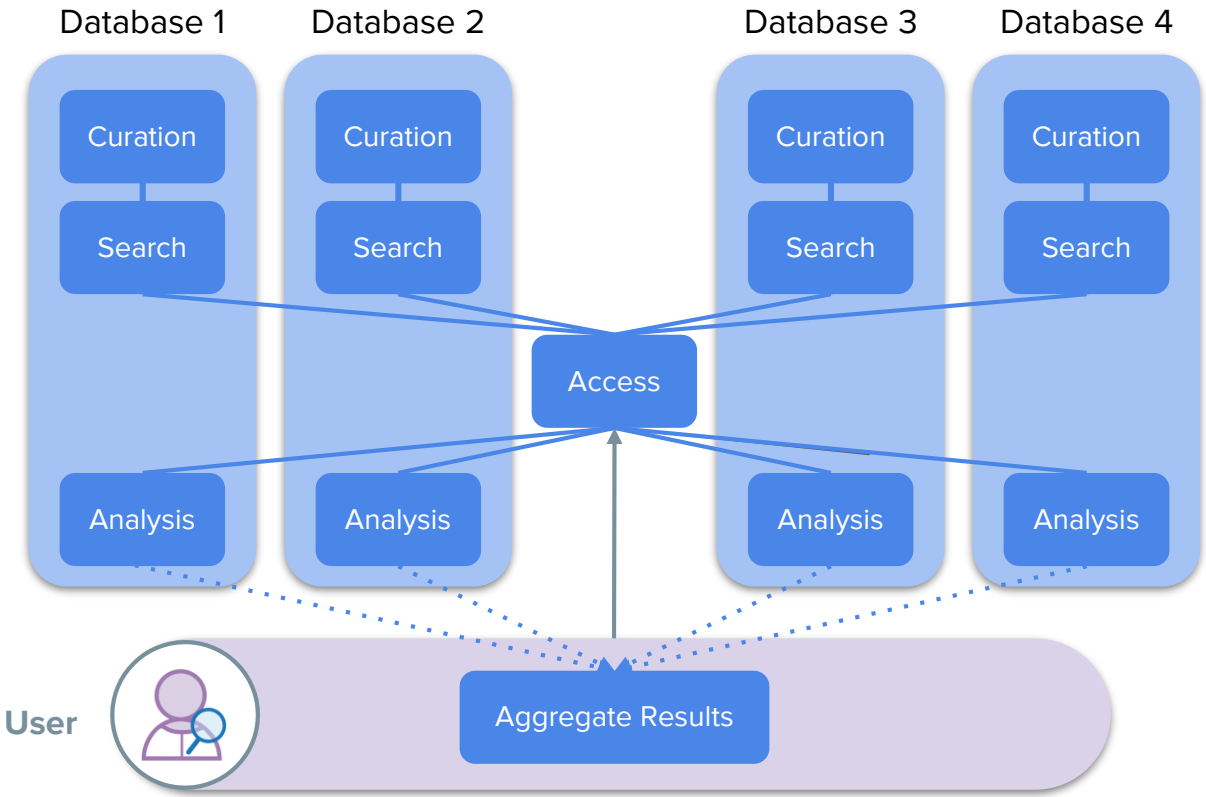
User

Data transmission

Analysis traveling to the data

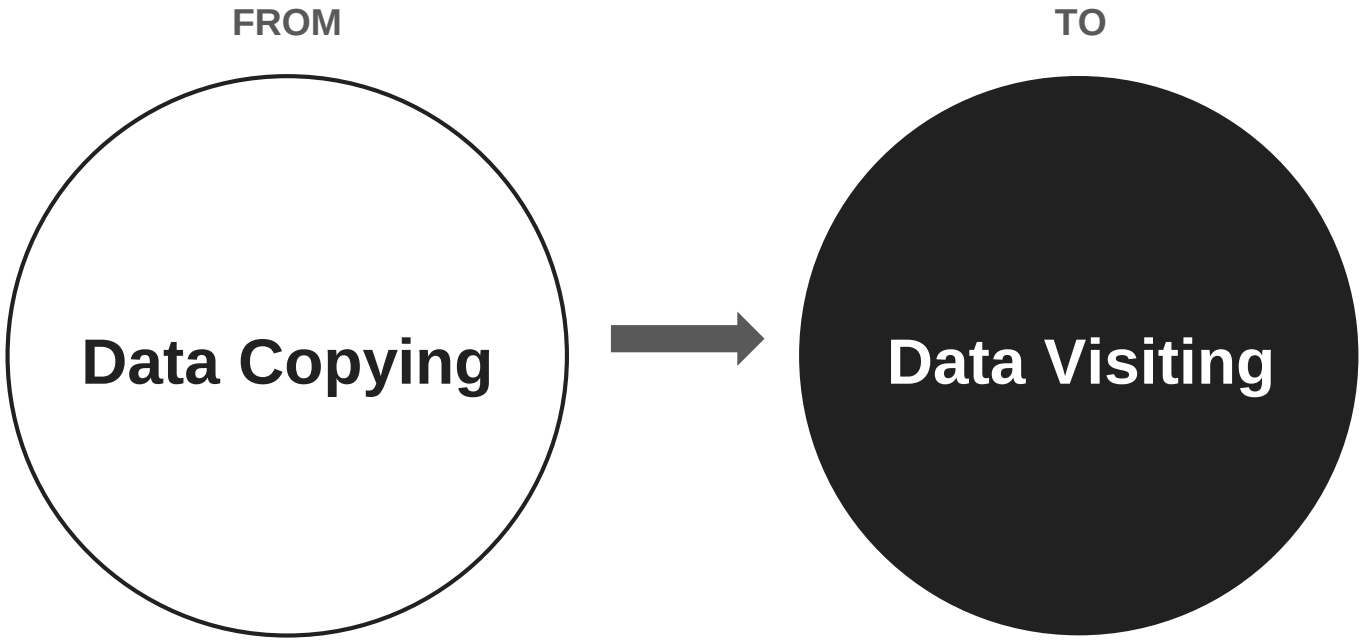
Federated analysis of cooperating genome databases

Global Alliance for Genomics & Health



A New Paradigm for Genome Sharing

Global Alliance for Genomics & Health

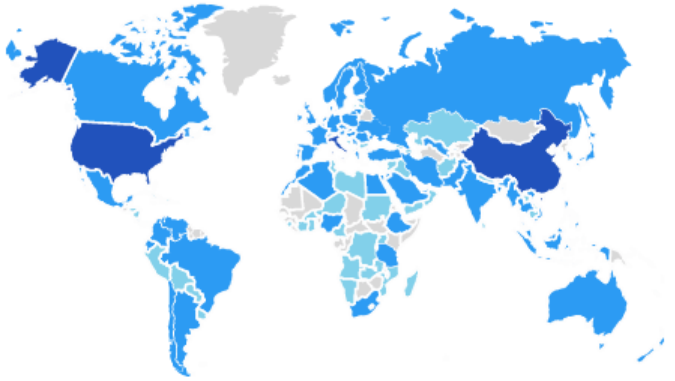


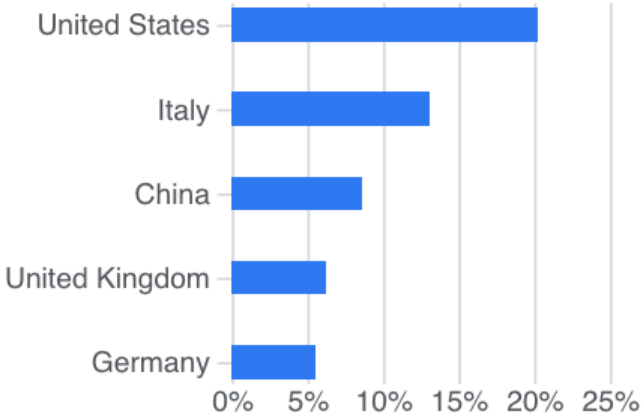
Case Study: BRCA Exchange validated more than 65,000 genetic variants of the BRCA1 and 2 genes

Solution:
BRCA Exchange

BRCA Exchange aggregates "big data" on *BRCA* variants from research and health care databases around the globe. The **Evidence-based Network for the Interpretation of Germline Mutant Alleles (ENIGMA)***

contributes expert classifications for each variant.
Patients, clinicians, and others can review these details to inform their decisions on cancer prevention, screening, and intervention.





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ENIGMA

How to share BRCA information from patients

- Variant interpretation relies on data from patients and their families. It requires **sharing treatments and outcomes**.
- Patient information is private and cannot be shared directly.
- But, the information needed for variant interpretation is not the individual private, patient-level information. It is variant-level summary data.
- We can share the variant-level summary data.

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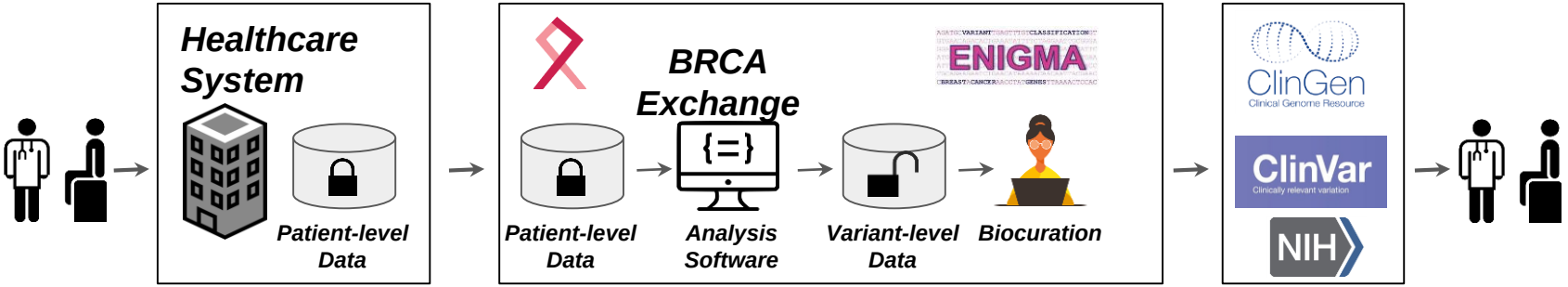
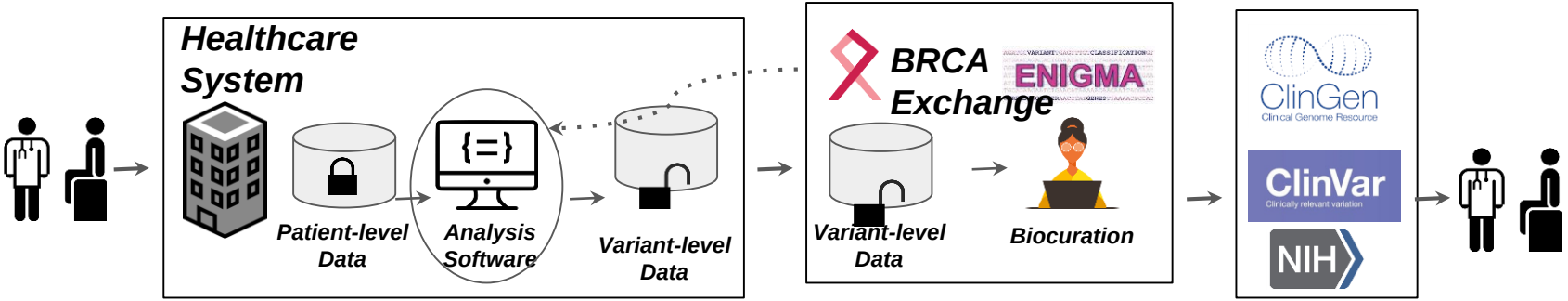
Privacy-preserving data sharing through federated analysis

Traditional Data Sharing



Federated Analysis

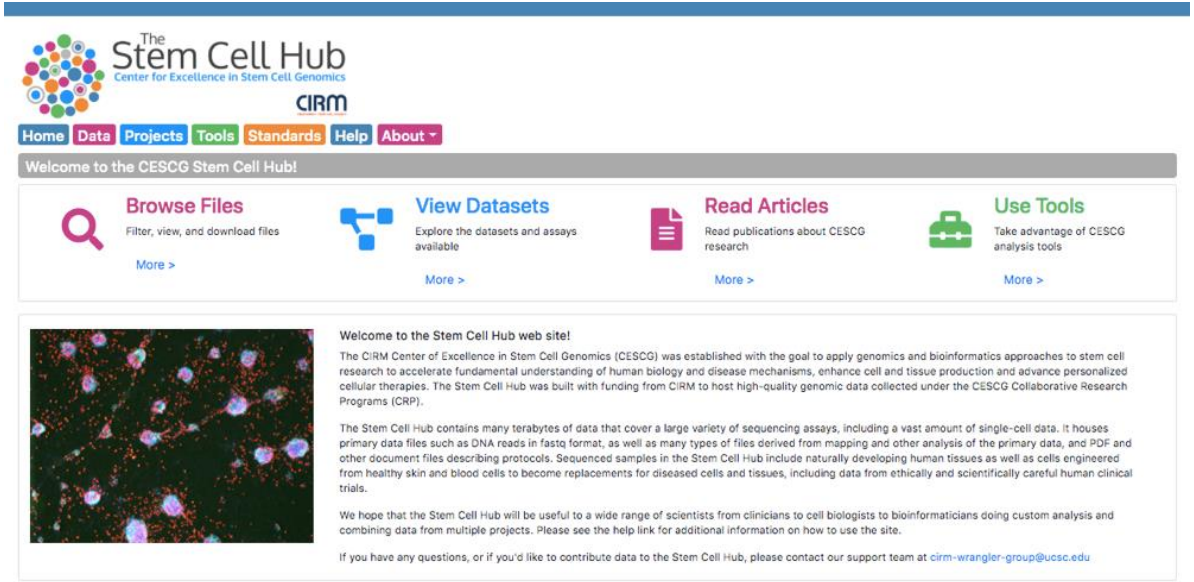


Example: Federated analysis collaboration with BioBank Japan

- BioBank Japan has a large cohort of cancer patients and controls, which they cannot share directly.
- We shared a Docker container with them to analyze their patient cohort
- The container generated variant-level data, which we are now using together with the ENIGMA Consortium to interpret BRCA variants!

BIOBANK JAPAN

2nd Case Study: California Institute for Regenerative Medicine Stem Cell Genomics Hub



https://cirm.ucsc.edu

84 TB of data in 180,170 files from 18 CIRM research labs

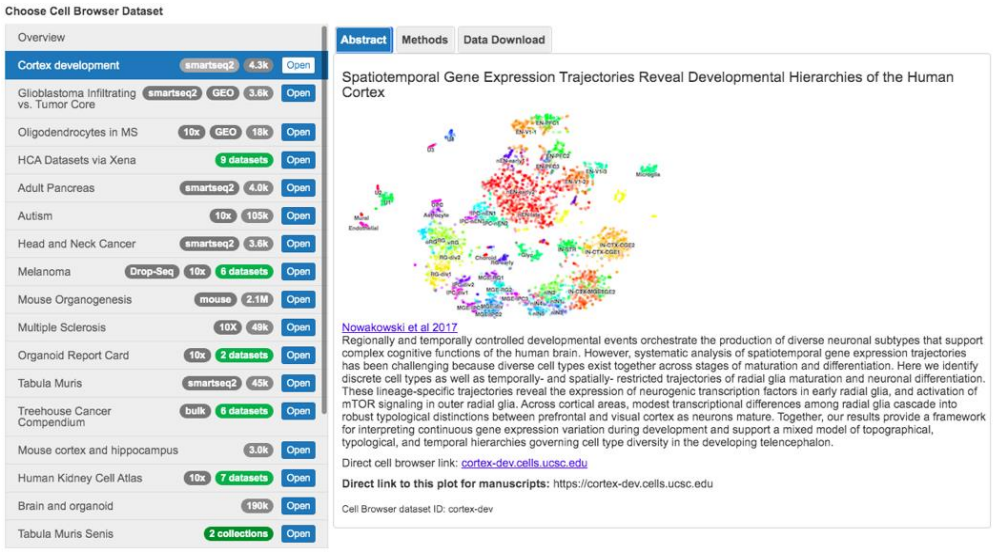
6.7 TB of that data is **currently publicly available;** the rest is pre-publication

The data are **Machine-Learning Ready***

*https://www.acd.od.nih.gov/documents/presentations/12132019AI_FinalReport.pdf

Cell Browser

The Cell Browser is a software **tool using a 2D viewer** to represent single-cell RNA expression



https://cells.ucsc.edu/

Integrates CIRM data with global single-cell data, including HCA

Shows **expression data for individual cells**

Allows for a **visual comparison** of large datasets consisting of many cells

Includes overlays of **metadata, marker gene levels, cell clustering and more**

Useful for comparing single-cell layout/batch correction methods

Coordinated with Human Cell Atlas (HCA)

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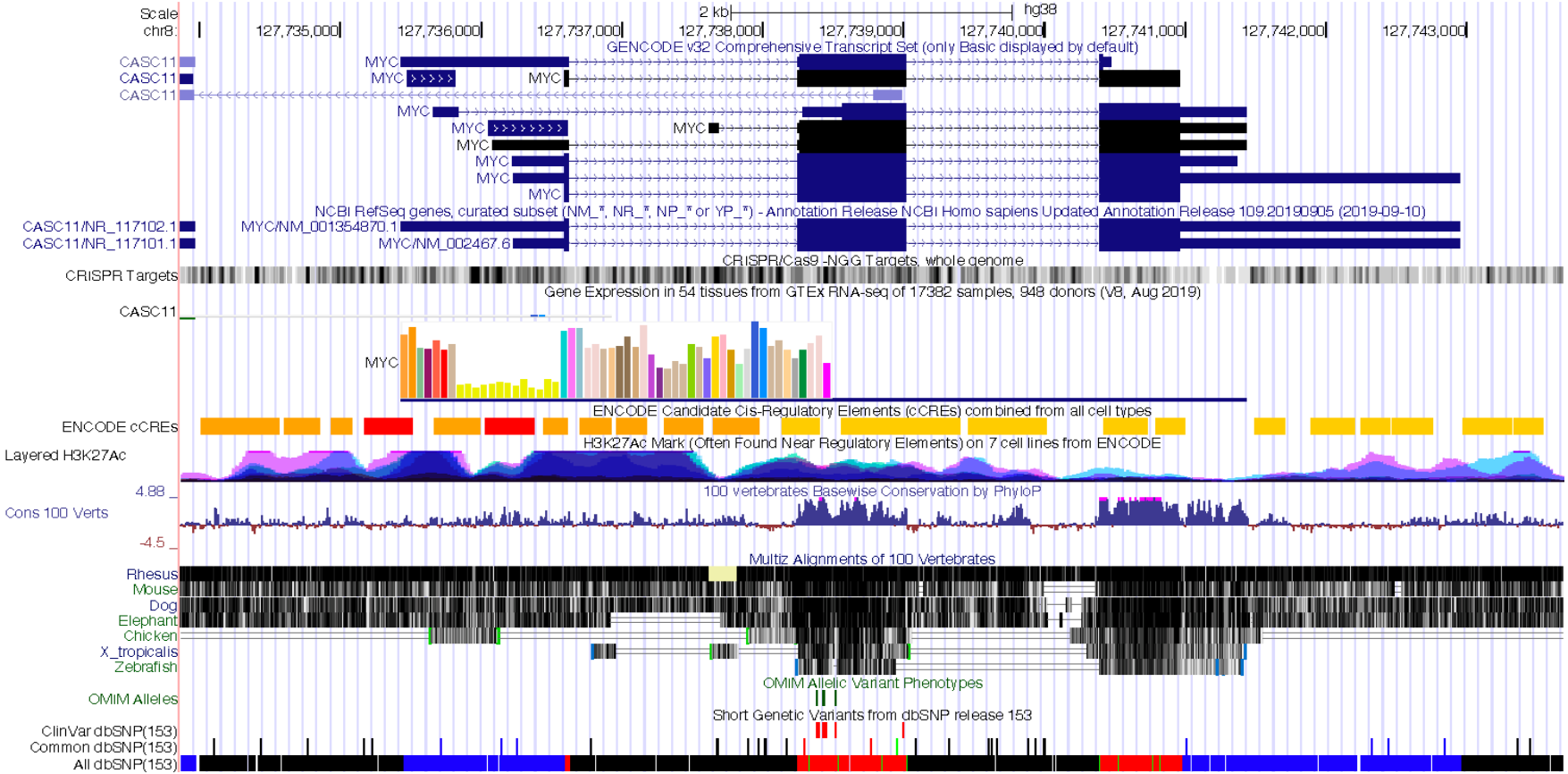
Genome Browser



https://genome.ucsc.edu/

Gen-2 CIRM Data will be in the Data Biosphere

Scalable and interoperable computing resource for the genomics scientific community

Cloud-based infrastructure

- Highly elastic; shared analysis and computing environment

Data access and security

- Genomic and single cell datasets, phenotypes and metadata
- Securely housed, large datasets generated by NHGRI, NHLBI, NCI, CZI funded programs and HCA community, as well as other initiatives / agencies

Collaborative computing environment for datasets and analysis workflows

- Storage, scalable analytics, data visualization
- Security, training & outreach, with new models of data access
    - ...for both users with limited computational expertise and sophisticated data scientist users

NHLBI TOPMed

HUMAN CELL ATLAS

NIH National Heart, Lung, and Blood Institute

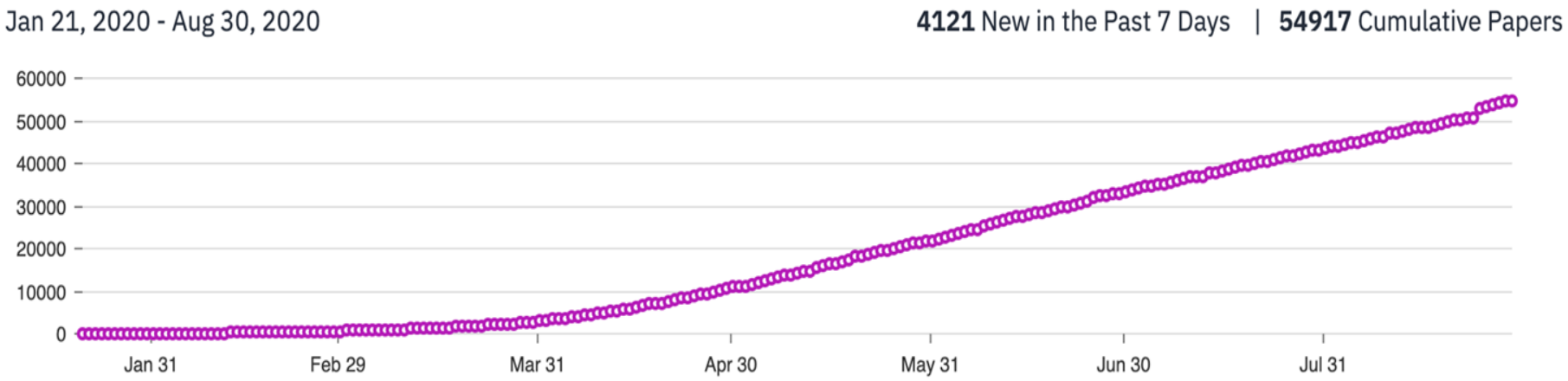
BioData CATALYST

AnVIL

LungMAP

DATA BIOSPHERE

Case Study: SARS-CoV-2 Research is generating data at an astonishing pace



In April 2020, SARS CoV-2 papers had a doubling time of ~14.5 days.

(The virus doubling time then was ~7 days)

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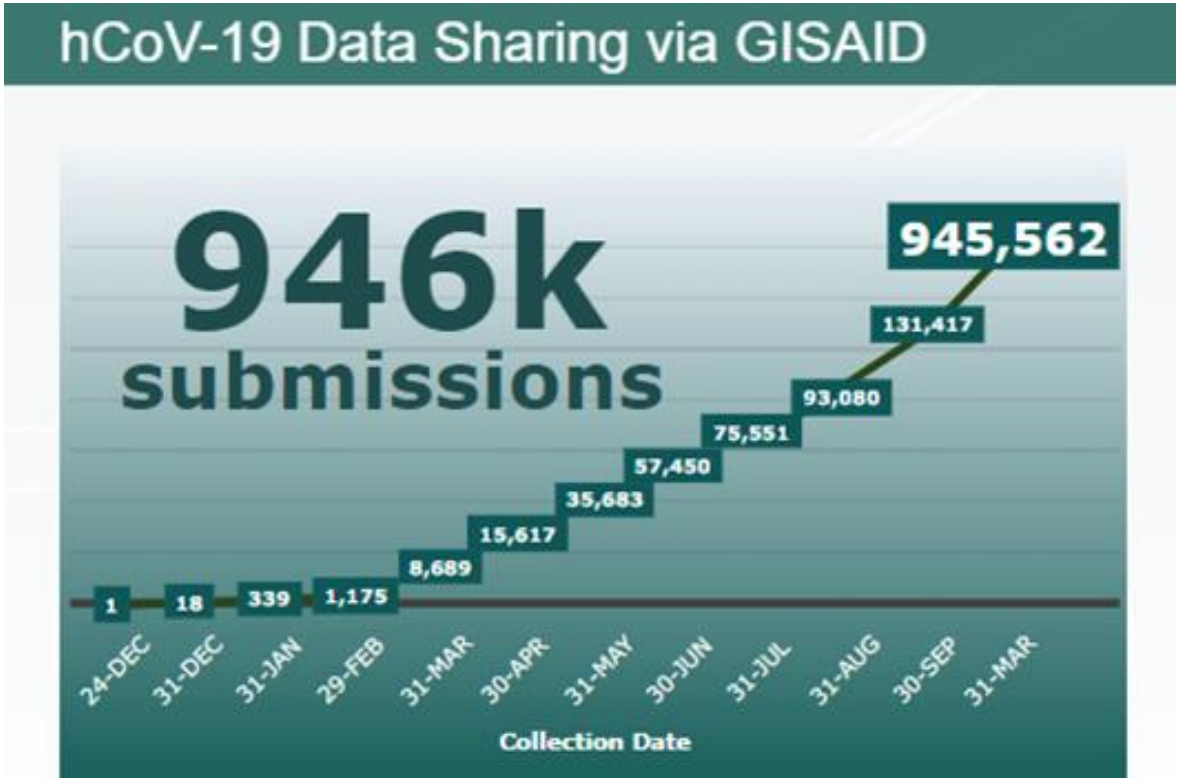
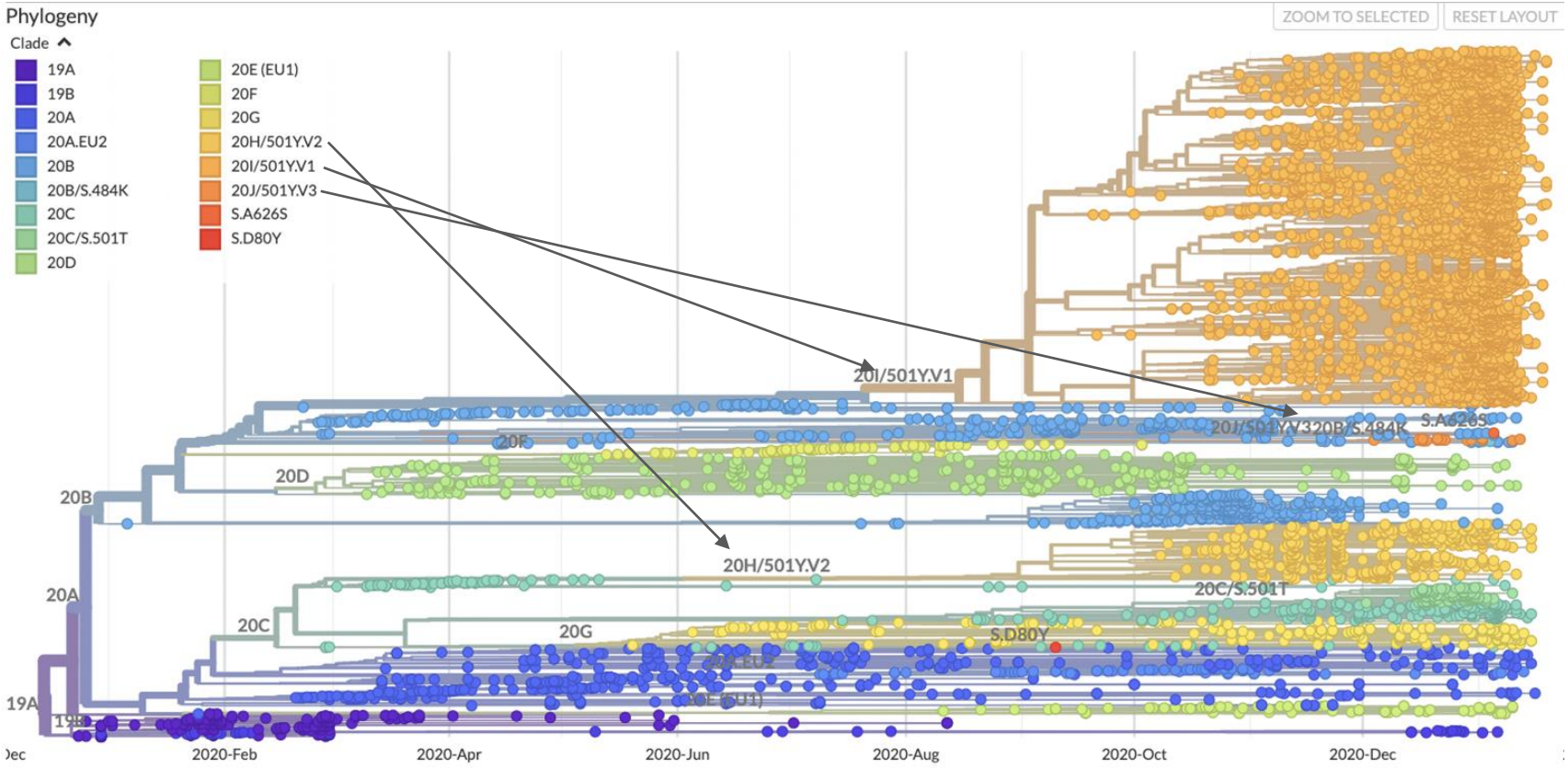
Genomic Data has also grown at an exponential rate

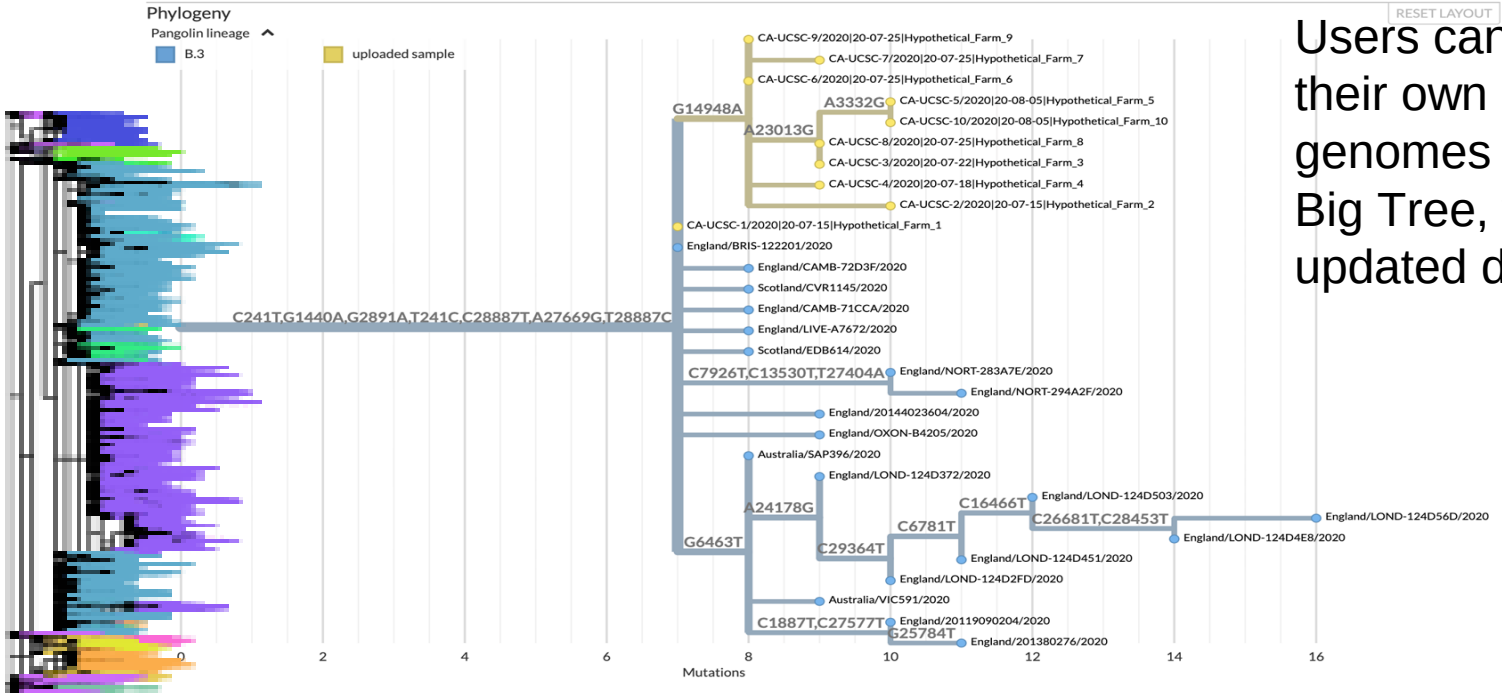


Now more than 1.2M genomes sequenced

New variants spread faster
Many show independent mutations to same alleles



We are the only lab that was able to maintain an accurate phylogenetic tree of >1M genomes



Users can add their own virus genomes to the Big Tree, which updated daily

>1M GISAID+public SARS-CoV-2 genome sequences, >1000 users/week

https://genome.ucsc.edu/cgi-bin/hgPhyloPlace

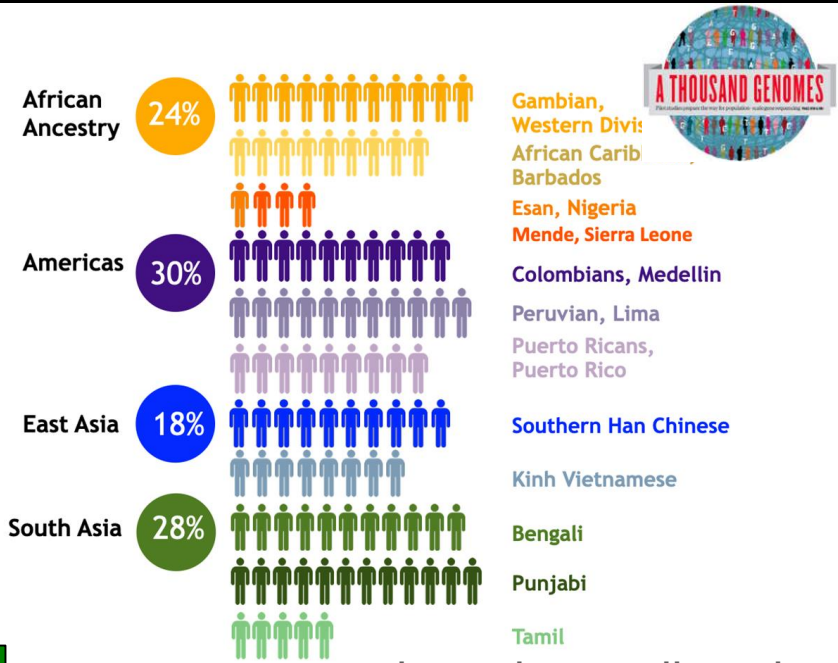
Data Sharing Issues for Pandemic Genome Tracking

- We were asked to “cease and desist” based on decade-old data sharing agreements (we refused)

- But the root issue is real: hardworking, underfunded scientists around the world contributing data deserve better recognition and reward

Latest Challenge: we must expand the one reference human genome to a Human Pangenome Reference

Global Genomic Partnerships



New international partnerships are needed to reach a more complete ”human pangenome reference”

- ✓ Represents genetic and geo. diversity
- ✓ Availability of low passage cell lines
- ✗ Strong Regional Scientific Partnerships

Take Home

The most important issue in data sharing is respect.

Respect for those who make the science possible by contributing data.

But that respect has to be earned with an equal amount of generosity.