



# **NHGRI Genomic Data Science Analysis, Visualization, and Informatics Lab-space Clinical Resource (ACR)**

**Ken Wiley, Jr. & Chris Wellington**  
**National Advisory Council for Human Genome Research**

# Analysis platform

**Terra:** 284 public workspaces

**Dockstore:** 1,051 analysis workflows

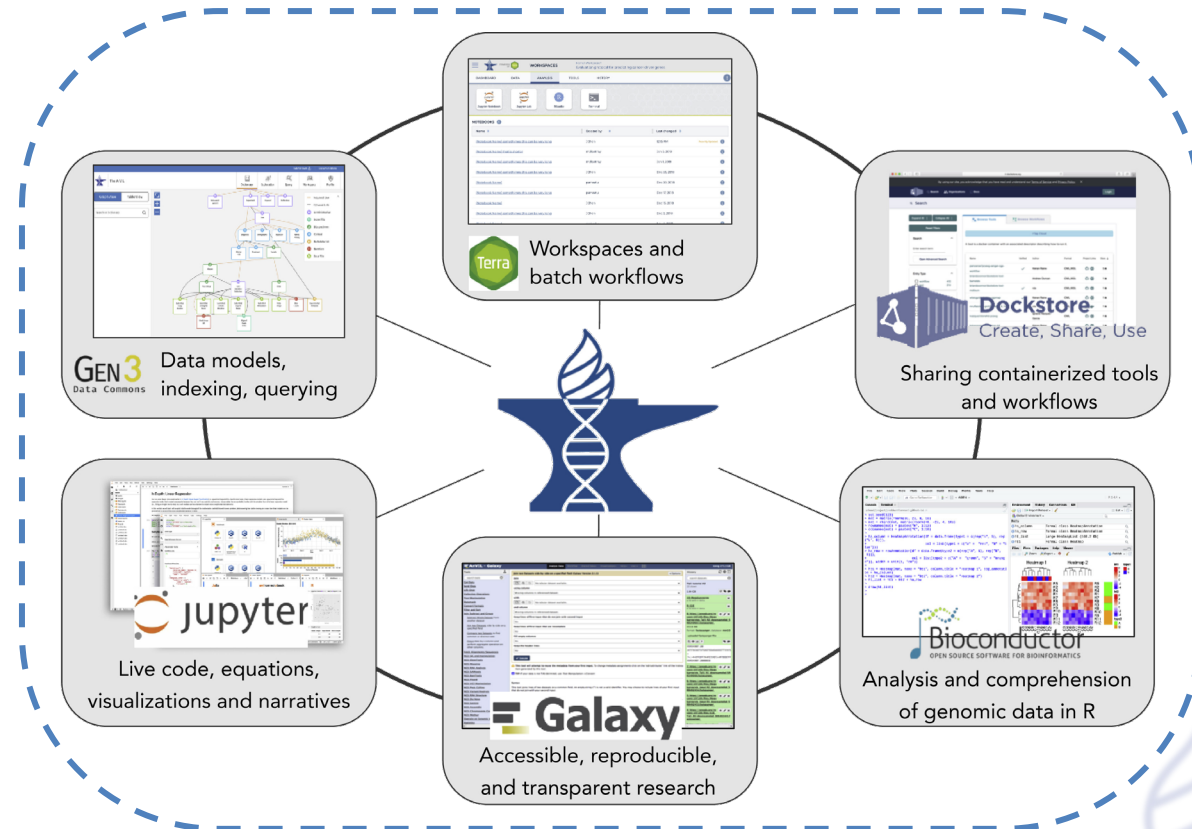
**Bioconductor:** 2,083 software packages

**Galaxy:** 8,568 tools  
(incl. PharmCat)

**Jupyter, Gen3, seqr...**



**Global Alliance**  
for Genomics & Health  
Collaborate. Innovate. Accelerate.



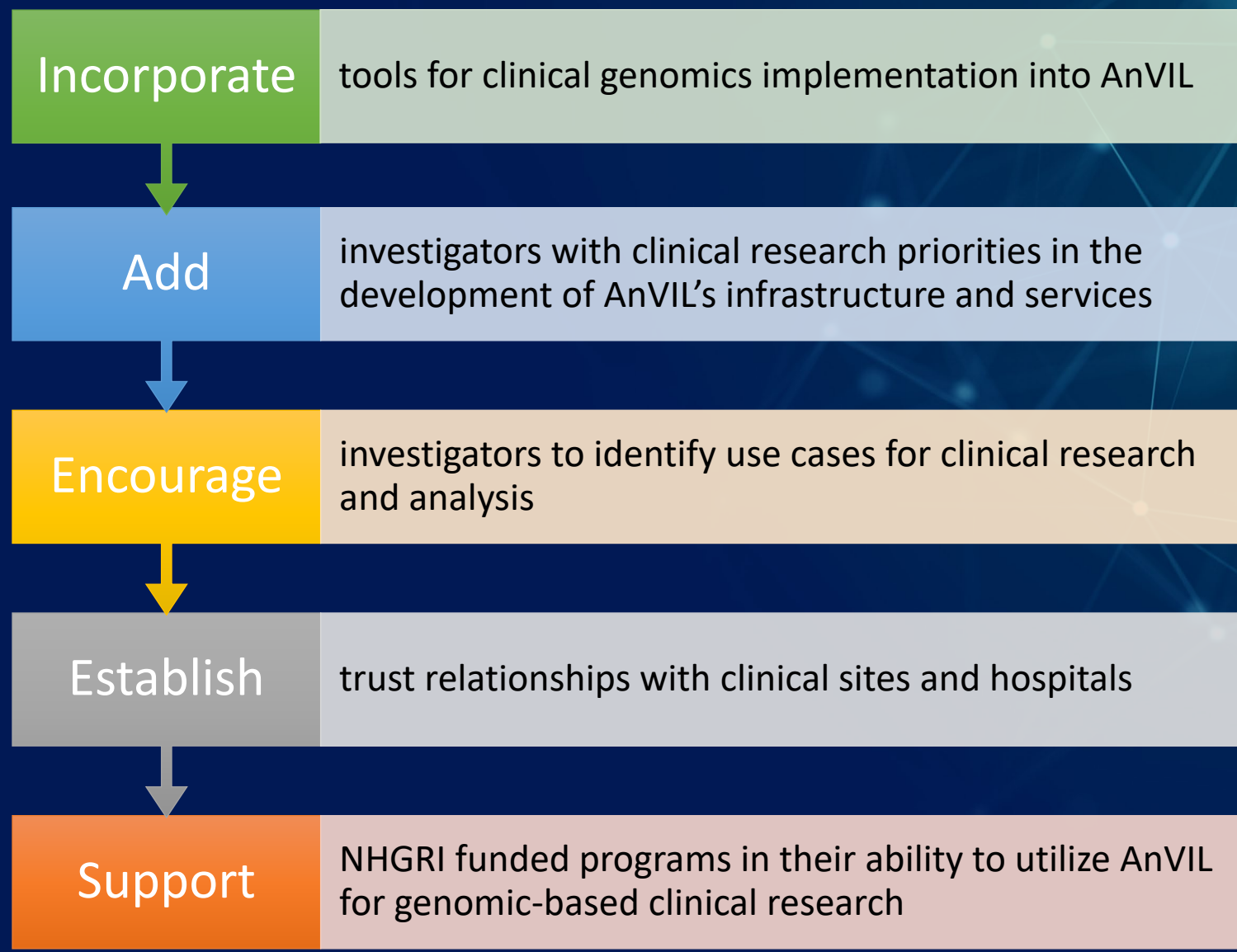
**FedRAMP**

FedRAMP certified



Implemented on  
**Google Cloud Platform**

# Support For The Clinical Research Community



# Approach, Requirement, & Process

A comprehensive approach is needed for AnVIL to serve the genomic based clinical research community

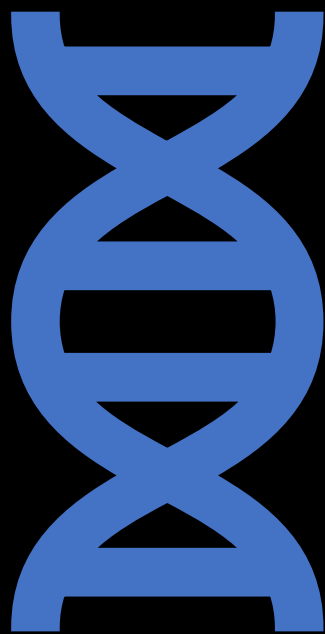
```
graph TD; A[A comprehensive approach is needed for AnVIL to serve the genomic based clinical research community] --> B[Requires clinical research expertise to add to the existing AnVIL team]; B --> C[Open competition to address both];
```

Requires clinical research expertise to add to the existing AnVIL team

Open competition to address both



## ACR Goal



ACR will leverage the existing AnVIL ecosystem to provide a suite of interoperable clinical components to assist users in the transition to a collaborative all-digital environment to foster genomic-based clinical research




# ACR Clinical Components

Implementing and deploying clinical software, tools, and workflows



Developing innovative methods for storing, generating, and returning clinical results



Outreach and education tailored for the clinical genomic research community



Data access and security

# Implementing and deploying clinical software, tools, and workflows

- Provide user-friendly open-source software, tools, and workflows to visualize and analyze relationships between and among heterogeneous datasets
- Provide a foundation for users to conduct research and development of digital health applications

Outreach and  
education  
tailored for the  
clinical  
genomic  
research  
community

Expand existing AnVIL outreach and educational resources to include:

- focus group sessions
- assisting investigators in developing use cases
- education sessions to serve specific groups
- soliciting and addressing ACR related users' feedback



# Developing innovative methods for storing, generating, and returning clinical results

Develop and implement pilots using FHIR and GA4GH standards and APIs

Assist investigators in understanding how AnVIL can facilitate genomic-based clinical research

# Data access and security



ACR is expected to adhere to the data access and security requirements of AnVIL



Address the security needs of clinical research sites in making AnVIL a HIPAA compliant resource.



# ACR Team Expertise

Clinical informatics

Cloud platform experience

Leverage and combine diverse datasets to conduct genomic-based clinical research analysis

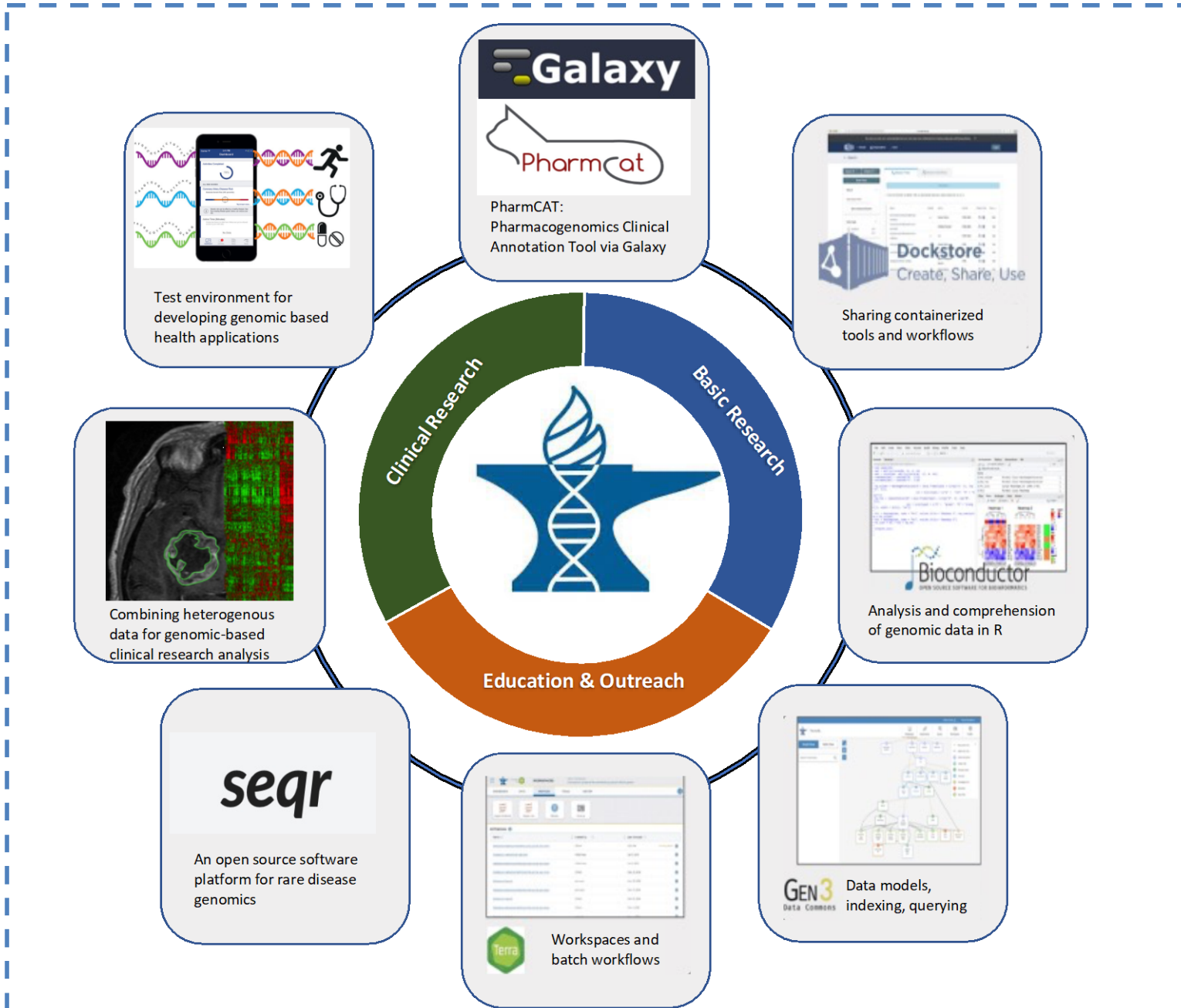
Building trust relationships with clinical research sites and hospitals

# Budget Summary

- Three Cooperative Agreement (U24) awards
- Five years, FY 2023 - FY 2027
- AnVIL renewal: Limited to AnVIL Primary awardees
- ACR: Excludes AnVIL Primary Awardees

	<b>FY23</b>	<b>FY24</b>	<b>FY25</b>	<b>FY26</b>	<b>FY27</b>
<b>ACR</b>	<b>\$1.5M</b>	<b>\$1.5M</b>	<b>\$1.5M</b>	<b>\$1.5M</b>	<b>\$1.5M</b>
<b>AnVIL Renewal</b>	<b>\$6.5M</b>	<b>\$6.5M</b>	<b>\$6.5M</b>	<b>\$6.5M</b>	<b>\$6.5M</b>

# A Secure, Federated Data Analysis Ecosystem



**NAME:** Lyle, Jonathan      **DOB:** 12/26/1979      **ADMISSION ID:** PMAA-1245  
**DOB:** 12/26/1979      **MRN:** 12345678      **ADMISSION ID:** PMAA-1245  
**Sex:** Male      **Specimen:** Blood, Peripheral      **Referring Physician:** MedDoc  
**Ref:** Education      **Referral:** 12345678      **Referring Facility:** MedSys  
**Indication for testing:** Clinical diagnosis of hypertrophic cardiomyopathy, MedSys  
**Test:** WGS-pak, InvScribe, WGS-GS

**GENOME REPORT**

**RESULT SUMMARY**  
Sequencing of the individual genome was performed and covered 99.7% of all positions of 64 coverage or higher, resulting in over 2.2 billion variants compared to a reference genome. These data were analyzed to identify previously reported variants of potential clinical relevance as well as novel variants that could potentially be relevant to disease based on existing knowledge. All results are summarized on page 1 with further details on subsequent pages.

**1. RESULTS RELEVANT TO INDICATION FOR TESTING**  
For the patient with a diagnosis of cardiomyopathy, we received an variants found in 62 genes with known association with hereditary cardiomyopathy disease and identified the pathogenic variant below. The result is consistent with the molecular clinical diagnosis.

Disease	Phenotype	Gene	Variant	Classification
Cardiomyopathy	Left ventricular hypertrophy	MYH7	c.1085C>T (p.S361Y)	Pathogenic
Additional disease		MYH7	c.1085C>T (p.S361Y)	Pathogenic

**2. OTHER VARIANTS OF MEDICAL SIGNIFICANCE (INCIDENTAL FINDINGS)**

**A. MONOGENIC DISEASE RISK: 0 VARIANTS IDENTIFIED**  
This test did not identify any genetic variants that may be responsible for existing disease or the development of disease in this individual's lifetime.

**B. CANCER RISK: 2 VARIANTS IDENTIFIED**  
This test identified carrier status for 2 additional recessive disorders.

Disease	Phenotype	Gene	Variant	Classification
Autosomal recessive	Autosomal recessive	ANKRD18	c.1085C>T (p.S361Y)	Pathogenic
Autosomal recessive	Autosomal recessive	ANKRD18	c.1085C>T (p.S361Y)	Pathogenic

**C. PHARMACOGENOMIC ASSOCIATIONS**  
This test identified the following pharmacogenomic associations. Additional pharmacogenomic results may be requested, but will require additional molecular confirmation prior to disclosure.

Variant	Relevant drug treatment	Risk and Dosing Information
CYP2D6	Typical response to codeine	
MTHFR	Intermediate response to oral contraceptives and other folic acid supplements	
UGT1A1	Typical response to irinotecan	



The **Forefront**  
of **Genomics**<sup>®</sup>