The *All of Us* Research Program Genome Centers

All of Us
RESEARCH PROGRAM

NIH
National Institutes of Health

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What is the NIH *All of Us* Research Program?

All of Us RESEARCH PROGRAM | The Future of Health Begins With You

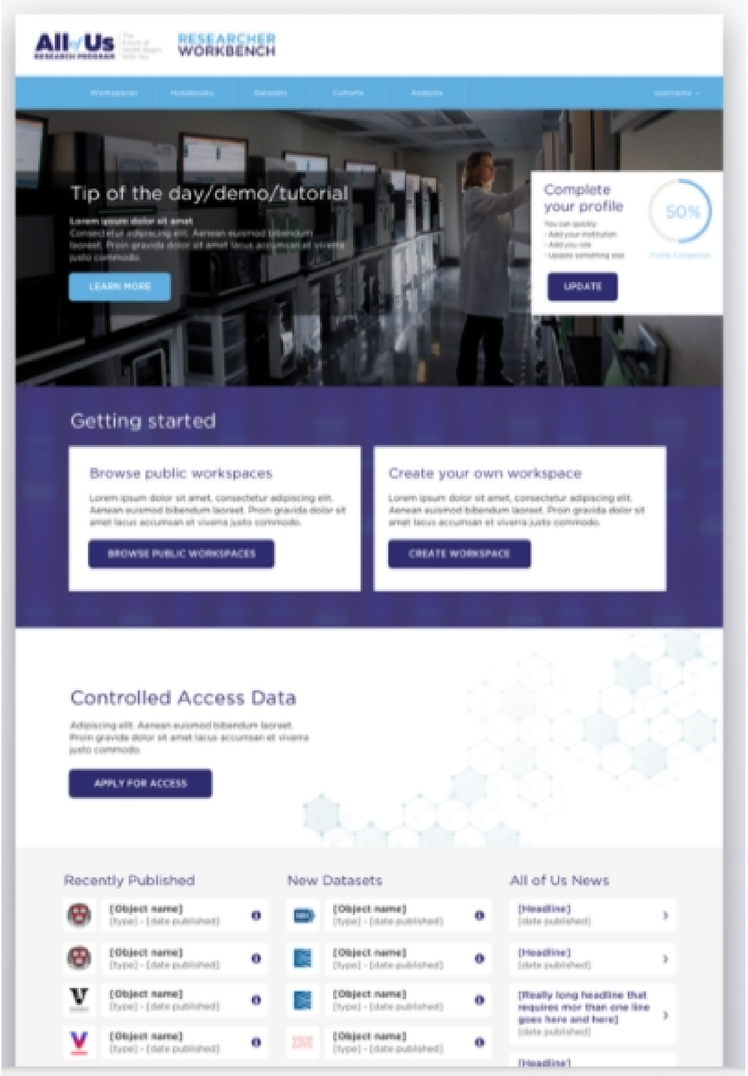
The *All of Us* Research Program is a historic, longitudinal effort to **gather data from one million or more people** living in the United States **to accelerate research and improve health**. By taking into account individual differences in **lifestyle, socioeconomics, environment, and biology**, researchers will uncover paths toward delivering **precision medicine – or individualized prevention, treatment, and care – for all of us**.

"*All of Us* is among the most ambitious research efforts that our nation has undertaken!"

NIH Director Francis Collins, M.D., Ph.D.

What is the promise for researchers?

- The opportunity to **save time and resources** and **accelerate your research breakthroughs** by leveraging:
  - A **rich resource of data**, including biospecimens and increasingly robust electronic health records.
  - A **longitudinal dataset** that will follow participants as they move, age, develop relationships, get sick, and try treatments.
  - A **diverse cohort of participants**, including people both healthy and sick, from all walks of life and all parts of the country.
  - Both raw data and data that is already **cleaned and curated**.
  - **Robust computing and analytic tools** to support complex data analyses in a **secure data environment**.
  - A group of **engaged participants** who may be eager to participate in ancillary studies.
- The ability to easily **share workspaces and analyses** with research partners and reviewers.
- The chance to learn from the program's pilots and experiments and **leverage innovations** for other studies and cohorts.



We are collecting, evaluating, and curating initial datasets*;* availability in 2019.

What is the promise for participants?

- An opportunity to help **fight disease** and improve the health of future generations.
- A chance to **learn about your own health**, including personalized risk factors or exposures.
- The ability and choice to **access your own data**, including genomic information.
- An opportunity to **ensure that your community is included** in the studies that lead to new understanding and new treatments.
- A chance to **learn about additional research opportunities** that may interest you.
- The choice to **meet others like you**, perhaps even joining some of them to propose & do research.

This is a long-term relationship and the value to participants (and researchers) will grow over time.

All of Us Genome Centers – timeline

- May 23: Publish Funding Opportunity for *All of Us* Genome Centers (OT-PM-18-002 https://allofus.nih.gov/sites/default/files/fa_genome_centers_OT_18.pdf)
- July 12 - Application receipt date
- August – Review of applications
- September – Negotiation of awards

- Late 2018: Begin data generation
- 2019: Genomic data become available on AoU Research Portal; initiate responsible return of results pilot phase

AoU Genomics Platform

Workflows for the AoU Genomics Platform.

The Research Workflow is shown in the box.

The Biobank ships DNA samples to the Genome Centers (GC1 and GC2) for genotyping and whole genome sequencing. All data generation in the GCs is conducted in a CLIA-certified environment.

Products of analysis pipelines are uploaded to the Data & Research Center (DRC), including variant calls and interpretation (in program-defined regions) and metadata.

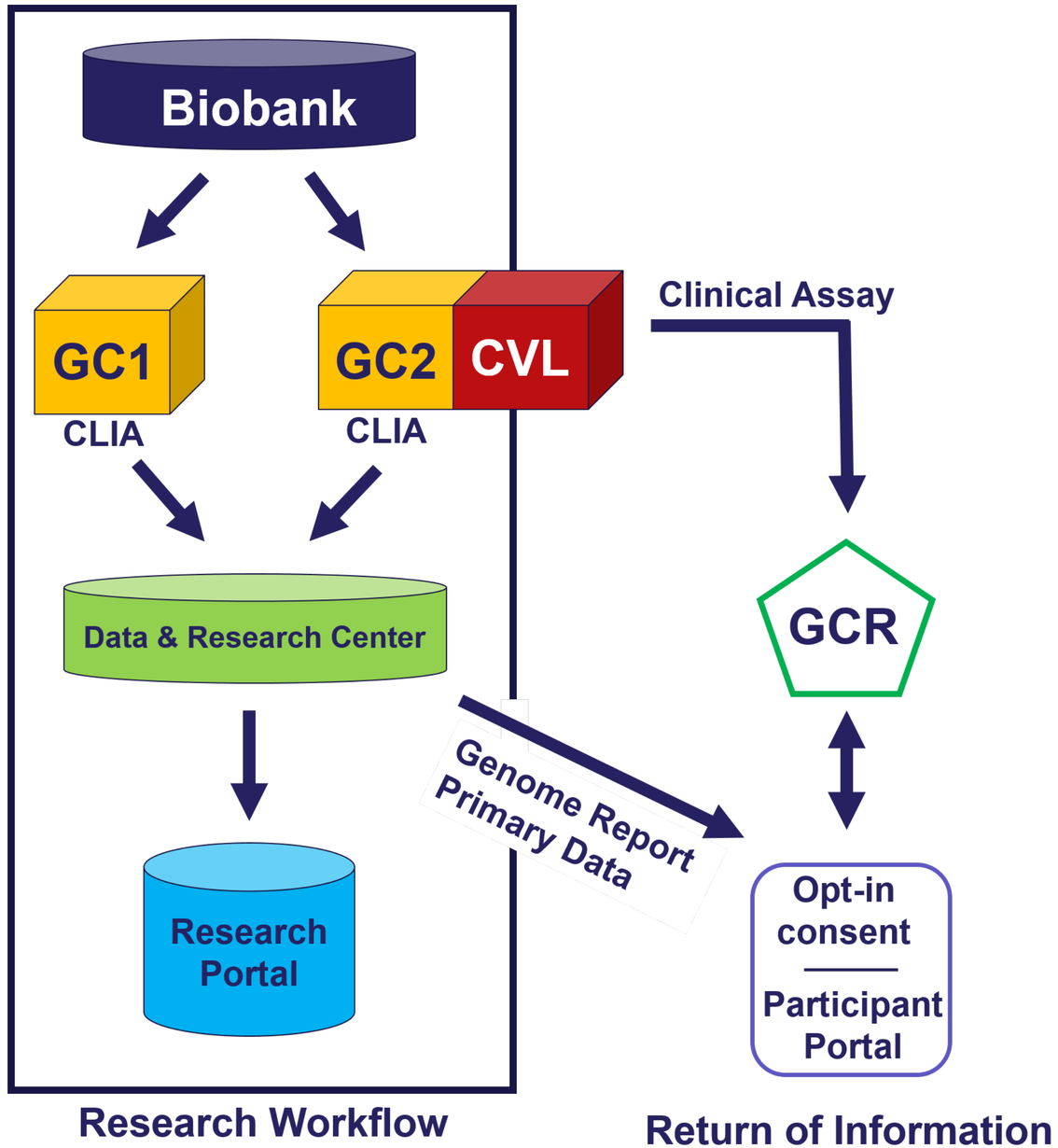
The DRC curates these data and makes available in the Research Portal.

The far side of the diagram shows the return of information workflow.

ACMG59 pathogenic and likely pathogenic variants will be validated by clinical assay in the Clinical Validation Laboratory (CVL) within a GC.

The clinical report will be sent to the Genetic Counseling Resource (GCR) for communication with the participant. This requires a consent encounter with the participant.

The participant also may consent to receive a Genome Report with additional information assembled by the DRC as well as provided the opportunity to download a primary data file.



All of Us Genome Centers – Objectives

OTA, 1 to 2 awards, 5 yr award period, yr1 budget = $15M direct costs, yr2-5 multiple cost proposals

1. **Large-scale data generation and analysis**
   - **Rapid deployment and scale-up of genotyping array, 100k yr1 then 200k per year**
     - Platform to be determined
   - **Ramp up for whole genome sequencing, >10k yr1 then scale *to be determined***
     - Require proposal for up to 200k WGS per year
   - **Data analysis includes methods for variant interpretation for clinical utility**
   - **Innovation for population-scale genomics including cost efficiencies**
2. **Clinical Validation Laboratory**
   - **CLIA/CAP validation of ACMG gene variants including clinical report**
3. **Other review criteria**
   - **Investigator and Organization experience with large-scale genomics**
   - **QA/QC plan**
   - **Cost proposal**

Budget Year	# Genotype Assays	# WGS Assays
Yr1	100,000	>10,000
Yr2	200,000	A. 25,000 B. 50,000 C. 100,000
Yr3	200,000	A. 50,000 B. 100,000 C. 200,000
Yr4	200,000	A. 50,000 B. 100,000 C. 200,000
Yr5	200,000	A. 50,000 B. 100,000 C. 200,000

Other Transactions Authority

- The Other Transactions (OT) award mechanism is not a grant, cooperative agreement or contract.
- Only a few NIH Institutes/Centers have this authority.
- For the *All of Us* Research Program, the National Center for Advancing Translational Sciences (NCATS) manages the OT awards.
- All applicants (PI, AOR, Project Team) should read and be familiar with the Other Transaction Award Policy Guide for NIH Precision Medicine Initiative Research Programs. (The NIH Grants Policy Statement does not apply to OT awards.)
- OT allows NIH the flexibility to alter the course of projects in real-time to meet the overarching programmatic goal. This means awarded activity can be expanded, modified, partnered, not supported, or later discontinued based on program needs.
- If selected for award, applicants should expect significant ongoing involvement from NIH.

Two Step Submission Process

- All applicants must complete the two-step submission process.
  - Step One – email submission
  - Step Two – application submission via the NIH eRA ASSIST System
- Step One is required and MUST be completed by the deadline.
- Step Two is also required however applicants will not be penalized for late submissions due to technical difficulties.
- To complete Step Two, you must complete the NIH Commons Registration first. If you already have a Commons Registration, you do not need to re-register.
- The pdf documents submitted for both Step One and Step Two should be identical.

This presentation and Questions & Answers will be posted at https://allofus.nih.gov/funding/current-funding-opportunities

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