Continuation of the Gabriella Miller Kids First Pediatric Research Program

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https://www.youtube.com/watch?v=U6Tq85GSg3g

Concept Clearance: Kids First Phase 3

TITLE: The Gabriella Miller Kids First Pediatric Research Program

Objective: Accelerate collaborative research leading to better prevention, diagnoses, and treatments for patients and families with pediatric cancer and structural birth defects.

- ❑ Enable Data Generation including Clinic-based Sequencing and New –Omics Data
- ❑ Enhance Development of Data Resources
- ❑ Support Expert-Driven Activities to Increase the Value of Kids First Data

Funds Available: $12.6-25 million per year (pending legislative action)

Program Duration: 5 or 10 years (pending legislative action)

Council Action: Vote for approval of the continuation for the Gabriella Miller Kids First Pediatric Research Program.

Kids First Program Origin

Gabriella Miller's Pediatric Cancer Advocacy Continues to Empower Research Across Pediatric Conditions

Oct 2013 - Gabriella Miller, childhood cancer advocate, died at age 10 from an aggressive brain cancer.

April 2014 - Gabriella Miller Kids First Research Act authorizes $12.6 million/year for 10 years to NIH for pediatric research.

Vision:

"Alleviate suffering from childhood cancer and structural birth defects by **fostering collaborative research** to uncover the etiology of these diseases and **supporting data sharing** within the pediatric research community"

The Kids First Working Group

Collaborating to Accelerate Discoveries in Pediatric Research

KIDS FIRST WORKING GROUP

National Institutes of Health
Office of Strategic Coordination - The Common Fund

Eunice Kennedy Shriver National Institute of Child Health and Human Development

National Heart, Lung and Blood Institute

NATIONAL CANCER INSTITUTE

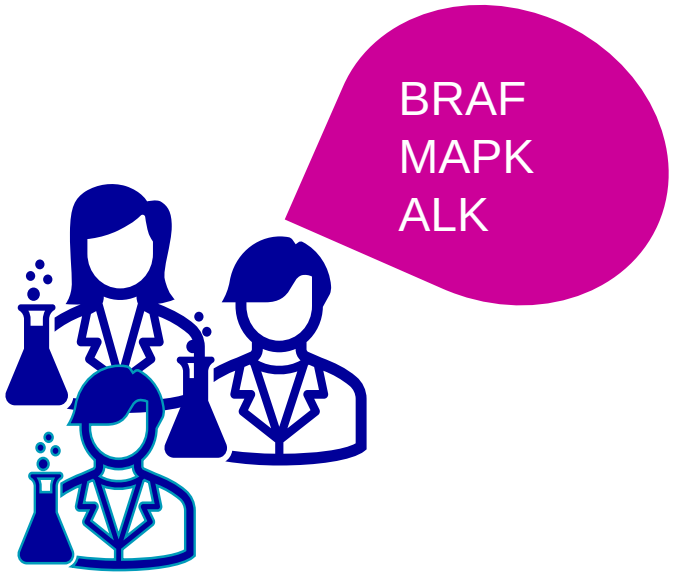
National Human Genome Research Institute

The Kids First Working Group is charged with building a cloud-based genomic data resource to share data and **accelerate collaborative research** leading to **better prevention, diagnosis, and treatments for patients and families** with pediatric cancer and structural birth defects.

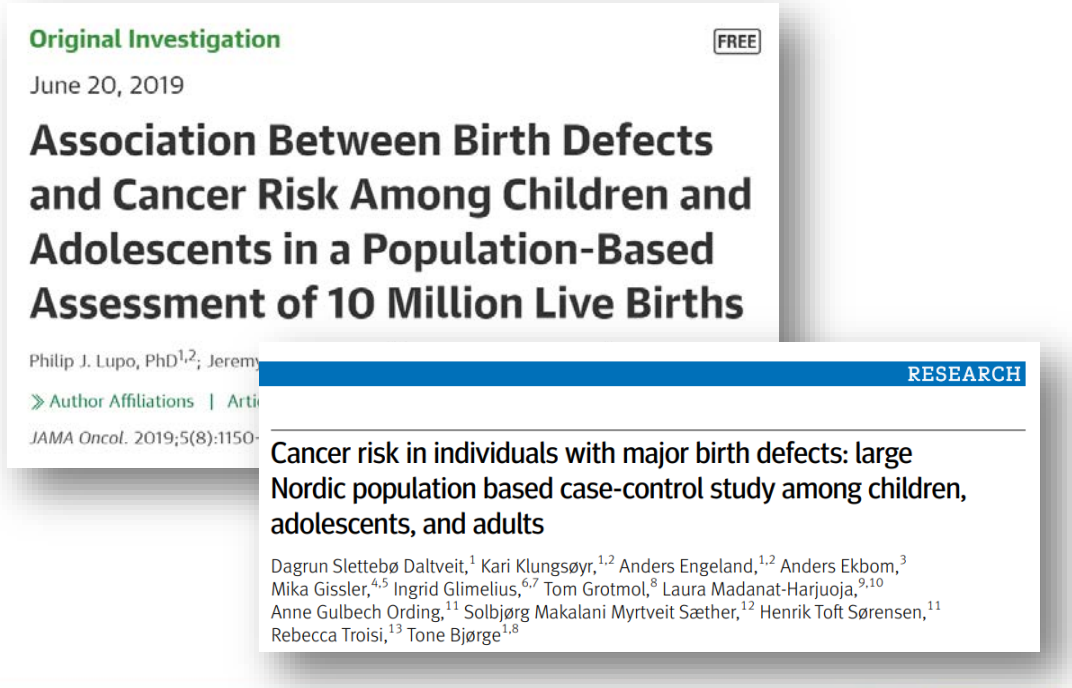
NIDCR	**NIAAA**	**NIDDK**	**NEI**	**NIAID**	**ORIP**
NIDA	**NINDS**	**NIEHS**	**NIAMS**	**NCATS**	**CDC**

Association Between Structural Birth Defects and Childhood Cancer

Shared mutations and drug targets across pediatric conditions



Cancer risk increased among children with birth defects


Original Investigation FREE

June 20, 2019

Association Between Birth Defects and Cancer Risk Among Children and Adolescents in a Population-Based Assessment of 10 Million Live Births

Philip J. Lupo, PhD[1,2]; Jeremy

Author Affiliations | Arti

JAMA Oncol. 2019;5(8):1150-

RESEARCH

Cancer risk in individuals with major birth defects: large Nordic population based case-control study among children, adolescents, and adults

Dagrun Slettebø Daltveit,[1] Kari Klungsøyr,[1,2] Anders Engeland,[1,2] Anders Ekbom,[3] Mika Gissler,[4,5] Ingrid Glimelius,[6,7] Tom Grotmol,[8] Laura Madanat-Harjuoja,[9,10] Anne Gulbech Ording,[11] Solbjørg Makalani Myrtveit Sæther,[12] Henrik Toft Sørensen,[11] Rebecca Troisi,[13] Tone Bjørge[1,8]

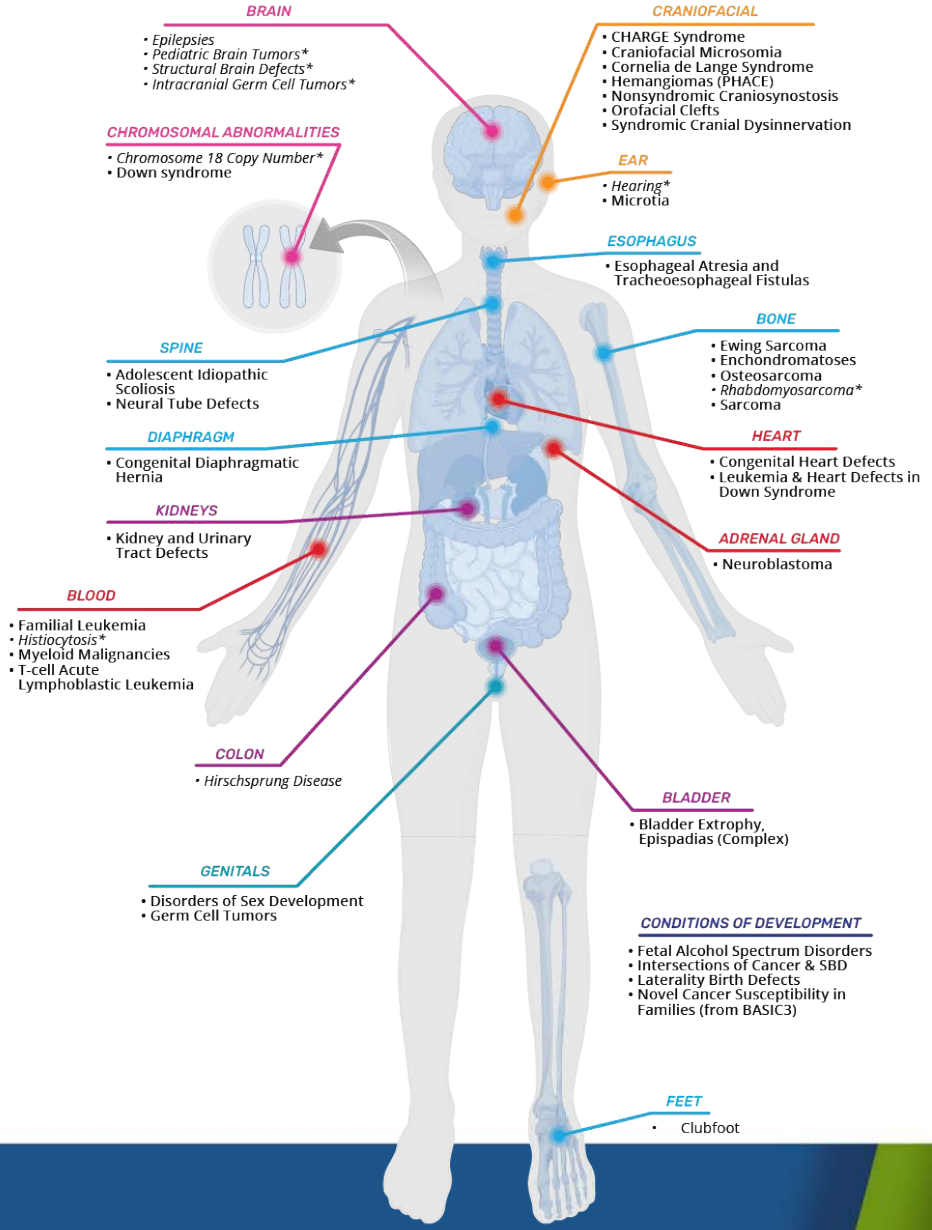
Kids First Current Priorities

Funds Available: $12.6-25 million per year

- Add more –omics data types for childhood cancer and structural birth defects
- Development of the Data Resources
- Support expert-driven research activities to increase the value of Kids First data

Kids First Data Resource Addresses Unmet Need

- **33** cohorts released at dbGaP
- **27,000+** genomes available from affected children and families
- **620+** approved data access requests for secondary use by NIH Kids First Data Access Committee



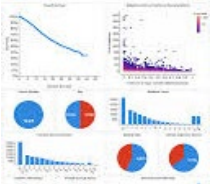
Kids First Cloud-Based Resources

Data Resource Portal

Entry point. Query, search, discover, build & visualize synthetic cohorts

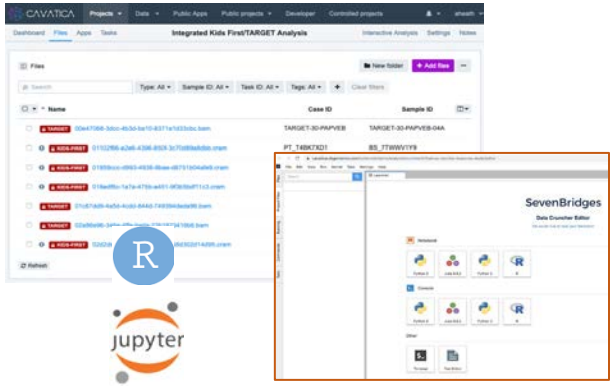
Knowledge Base Integrations (PedcBioPortal)

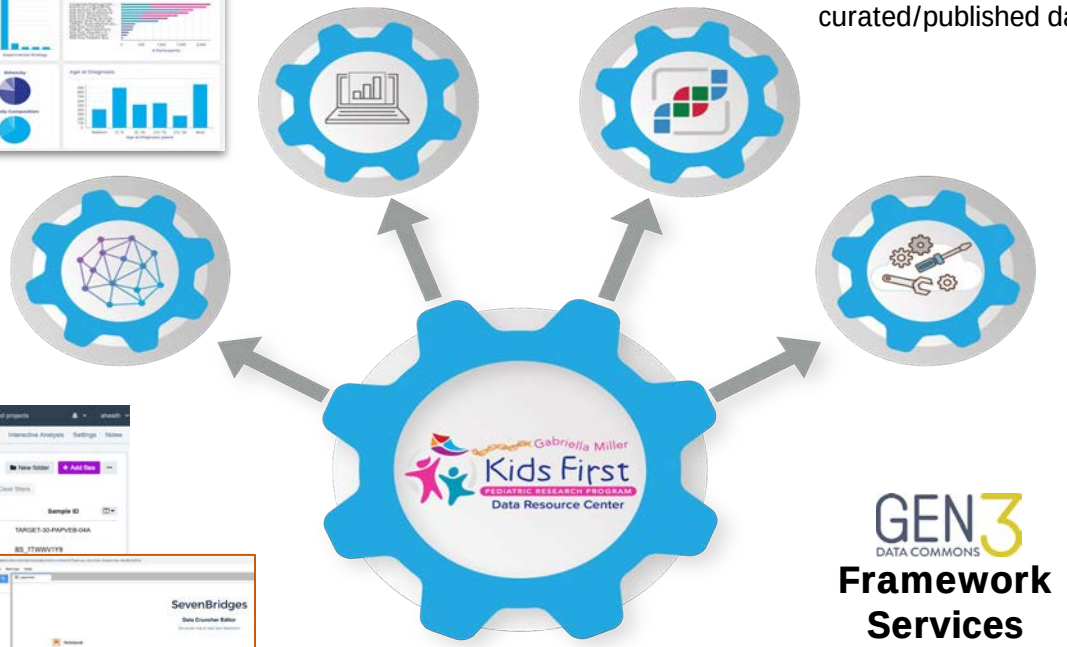
Integrations with existing curated/published data visualizations



Cavatica

Pull data from multiple sources into one workspace.
Use notebooks, bring-your-own or use available workflows.





Data Services

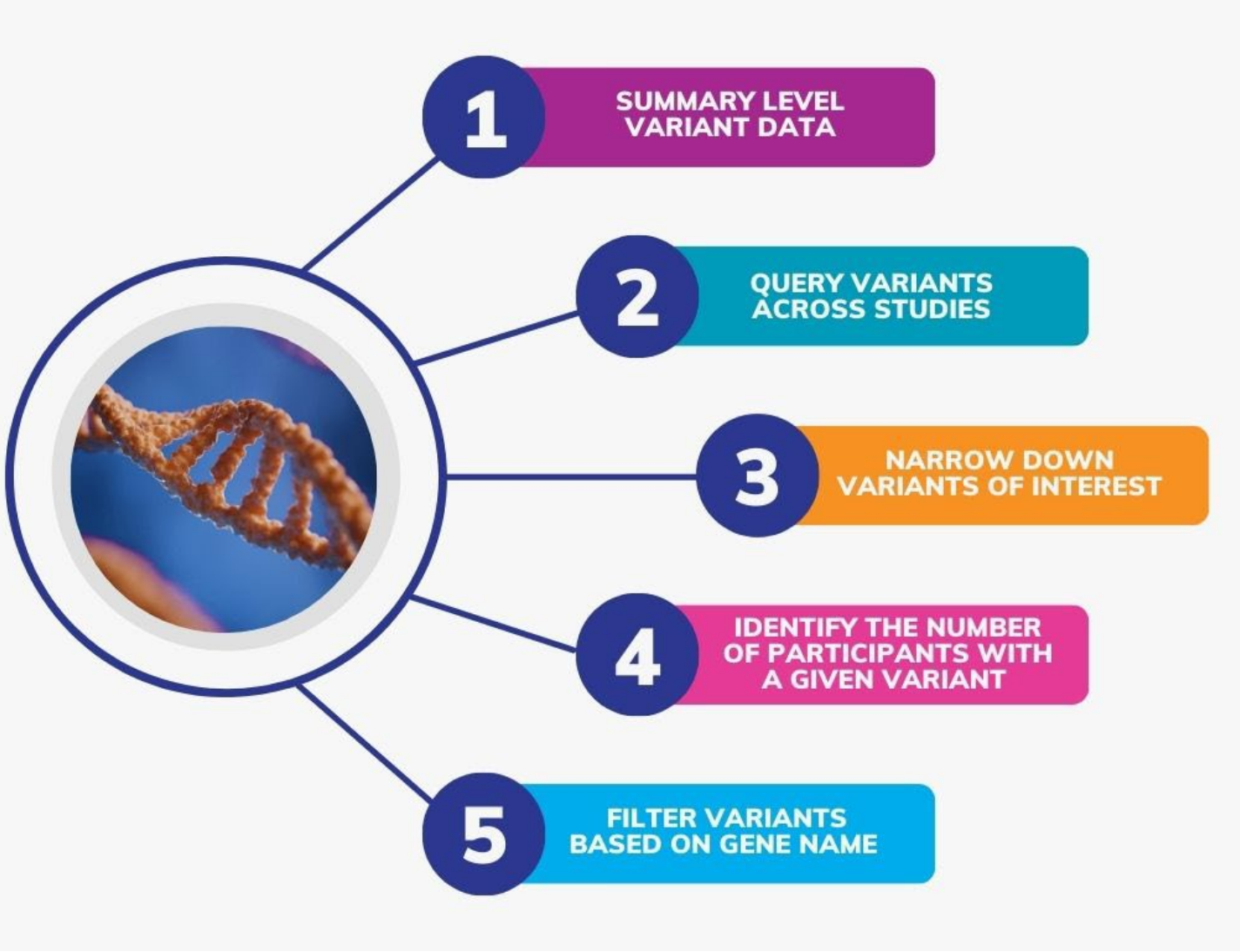
Exchange clinical data in FHIR-based data services for semantic interoperability and coordination

Framework Services

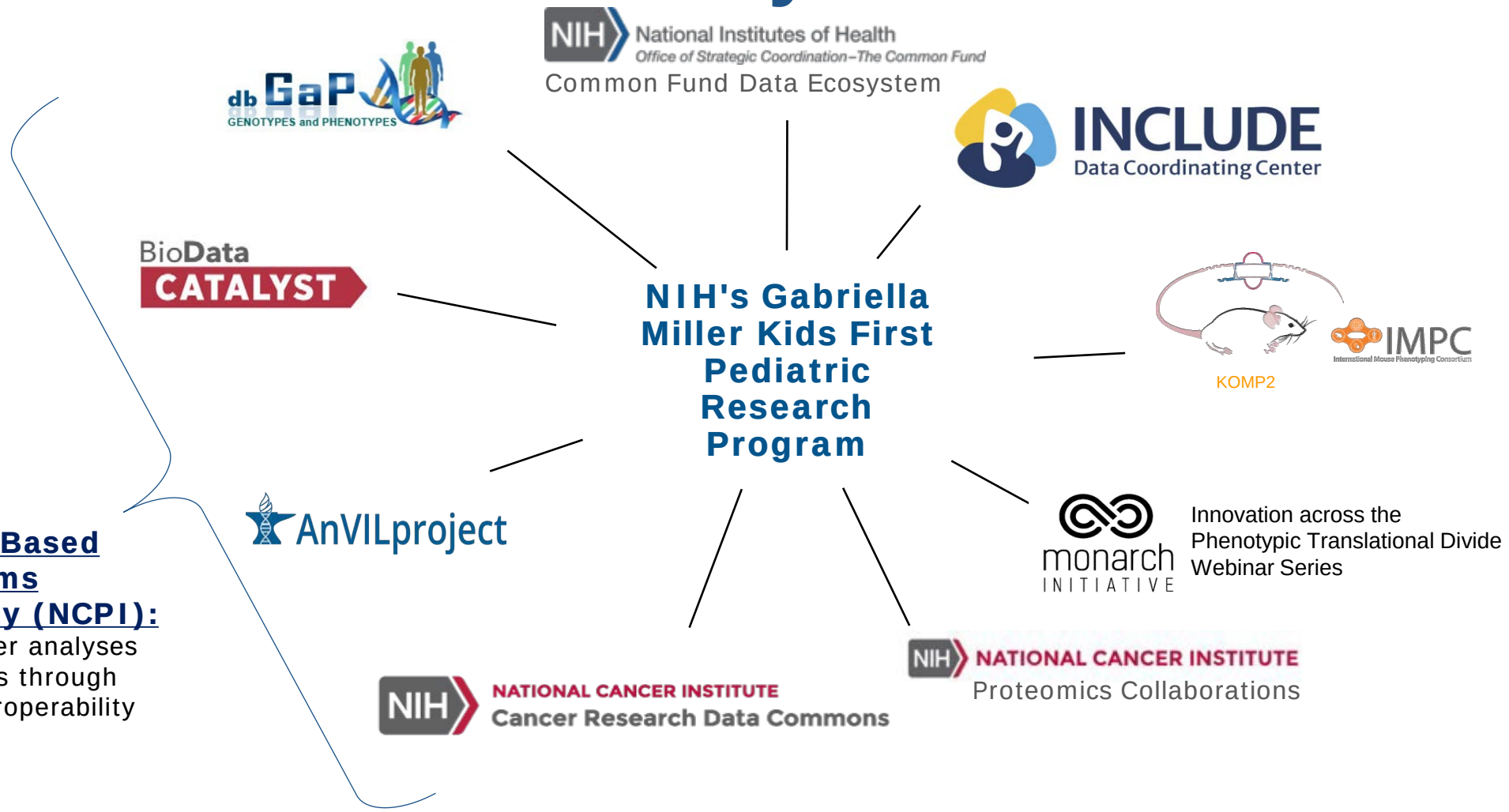
Index and point to files in the cloud (for approved users)

Children's Hospital of Philadelphia · CHU Sainte-Justine Research Center, Mother and Child University Hospital Center · VELSERA · The University of Chicago · University of Colorado Anschutz Medical Campus · Vanderbilt University

Kids First Genetic Variant Browser



Kids First in the Data Ecosystem



NIH Cloud-Based Platforms Interoperability (NCPI):
Empower end-user analyses across platforms through federation & interoperability

Kids First Data Resource Portal Metrics

ABOUT THE DATA

22
Birth defect cohorts

11
Cancer cohorts

27,000+
Study participants

192,000+
Data files available

ABOUT THE PORTAL

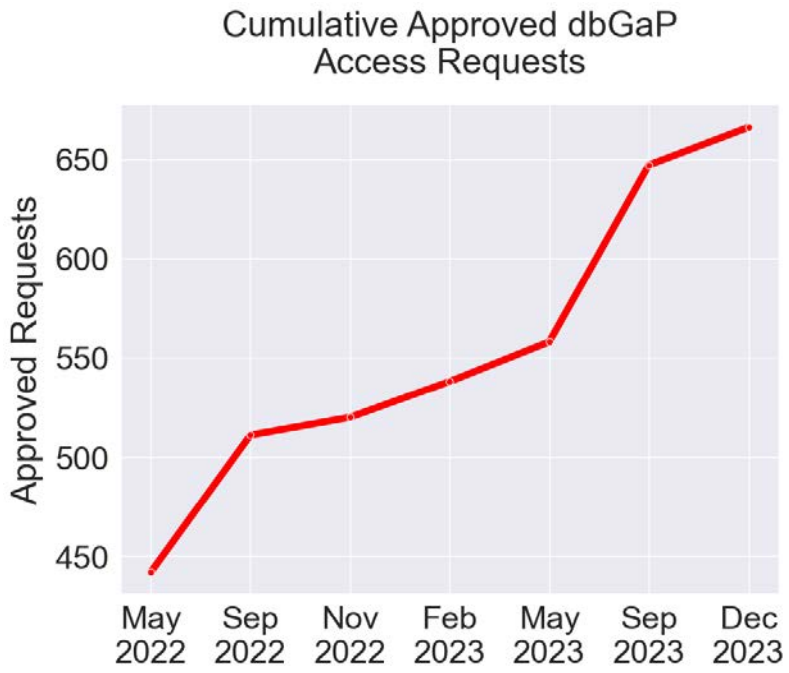
50
Unique countries represented by portal users

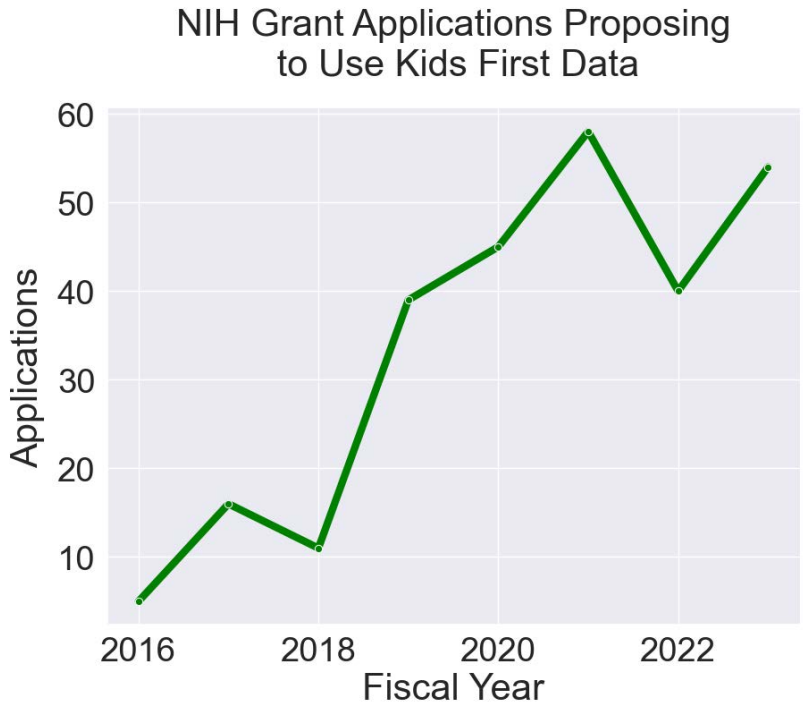
650+
Approved access requests for secondary data use

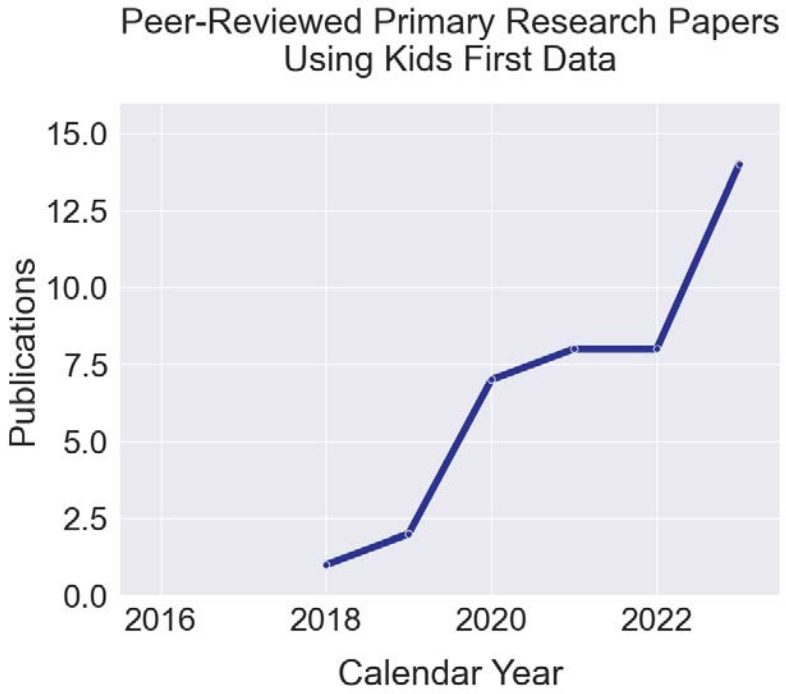
3,389+
Total portal users

6,500+
Total portal logins in 2022

Use of Kids First Data is Growing

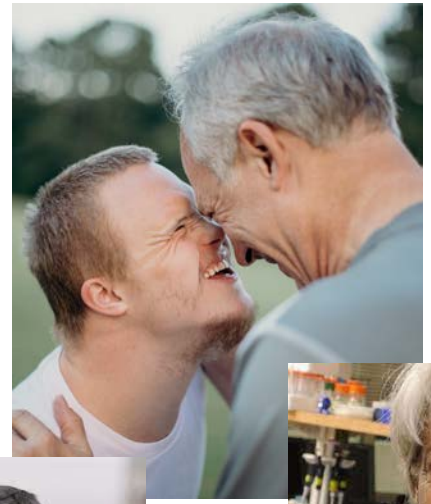


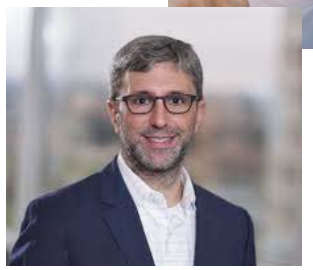




Kids First Collaborations for Data Release Across Pediatric Conditions

- July 10, 2023 "Kids First and INCLUDE: Down Syndrome, Heart Defects, and Acute Lymphoblastic Leukemia".
- Children with Down Syndrome (DS) have a 2000-fold increased risk of atrioventricular septal defects (AVSD) and a 20-fold increased risk of acute lymphoblastic leukemia (ALL).
- The objectives of this study are to determine the genetic variants underlying AVSD and ALL risk in children with Down Syndrome. WGS data for children with DS-AVSD was compared to data from children with DS who have structurally normal hearts. WGS data for children with DS-ALL was compared with children with DS without history of ALL.
- Data available from 2489 participants along with phenotypes and clinical information





Philip Lupo
Baylor College of Medicine
Houston, TX, USA

Stephanie Sherman
Emory University
Atlanta, GA, USA

Planning for the Future of Kids First

Kids First 1.0 ends:
Program will end with the FY2024 appropriation with work extending into 2025

Kids First 2.0 is passed into law:

H.R. 3391 and **S. 1624** currently on legislative calendars

- **H.R. 3391** 37 Co-sponsors - authorizes Kids First for 5 years
- **S. 1624** 14 Co-sponsors - authorizes Kids First for 10 years

Key Program Priorities

User Experience

De-identified data available for research

NIH Data Governance

NIH maintains control and authority

Cloud Computing

Workspace supporting large-data, tools, and workflow development

Interoperability

Kids First data is part of the NIH data ecosystem

Data Sharing

Allow broad data sharing

Kids First Phase 3 Proposal Builds Upon Prior Success. What is New.

1. Enable Data Generation

Sequencing Centers generate clinical-grade genomic data

2. Enhance Development of Data Resources

Collect clinical data from EHRs via FHIR server with deidentification and longitudinal follow-up

3. Support Expert-Driven Activities to Increase the Value of Kids First Data

Prioritize tool development for biomedical research

1. Enable Data Generation

Sequencing Centers generate clinical –grade genomic

- Collaborate with networks of hospitals and patient registries.
- Create a state-of-the-art genetic variant curation center.
- Return results to doctors, patients, and families.
- Deidentified genomic and clinical data added to the data resource.

Enhance cohort-based genomic data

- Emphasize diversity of conditions and participants
- Addition of data types such as long-read, proteomics, methylation, single cell, spatial analyses, imaging, and other relevant technologies

2. Enhance Development of Data Resources

Enhance Data Sharing and Discovery

- Develop pediatric FHIR implementation and data sharing standards
- Collect clinical data from EHRs via FHIR server with deidentification and longitudinal follow-up
- Enhance and facilitate interoperability with NIH data-system resources
- Expand integration of pediatric data from other NIH-funded research

Support Portal and Analysis Tool Development and Maintenance

- Further develop genetic variant browser with user-friendly interface for non-bioinformaticians
- Provide improved annotation and analysis of genetic variants using state-of-the-art information sources
- Expand capabilities to facilitate cloud computing, tools and workflows for data discovery, data analysis, and data visualization

3. Support Expert-Driven Activities to Increase the Value of Kids First Data

Prioritize scientific discovery for biomedical research

- Support new analysis tool development using Kids First data
- Support submission of additional data and longitudinal data, and extensive clinical and phenotypic data
- Develop functional modeling centers and collaborative cross-disciplinary programs

Develop training, education, and outreach activities

- Support development of online or in-person short courses for researchers, students, and other professionals using the Kids First data resources and portal
- Support development of fellowships for data analysis
- Publicize publication of relevant data releases, data sharing, and data resources

Enhance user support for analyses and cloud computing resources

- Develop communication strategies to enhance research collaborations
- Develop user support tools for the portal and data usage
- Support cloud computing offerings to stimulate analysis using cloud resources

Kids First is Catalyzing a Collaborative Pediatric Research Community

"Kids First is an amazing opportunity to sequence our patients and identify genes that might cause diseases" _ Mustafa Khokha MD, Yale

"If Kids First wasn't there it would have to be invented. It is important because pediatrics always come last, and it is really important to have a program where kids come first – and we can ask questions that we usually would not have a space for." – Ingo Helbig MD, Children Hospital of Philadelphia

"I am excited to discuss how useful Kids First cohort have been, the need for more sequencing, and better phenotyping, and discuss what we can do as a community moving ahead" – Soumya Rao PhD, U. of Missouri Kansas City

"The best part of this network is the opportunity to learn from each other" – Emmanuel Aladenika, U. Iowa

Council Action:
Vote for approval of the concept for The Gabriella Miller Kids First Pediatric Research Program