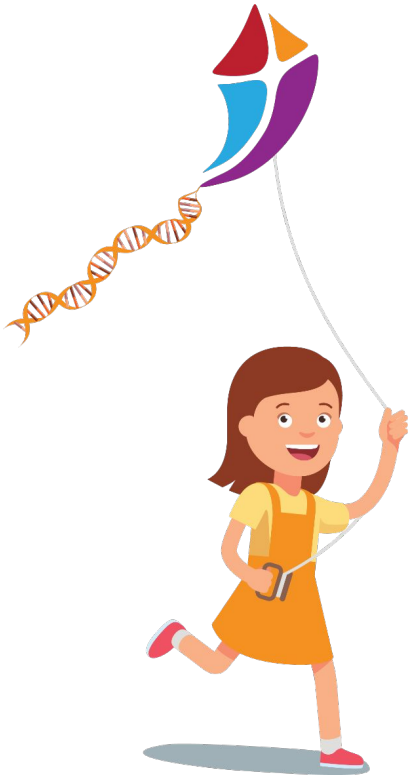
Gabriella Miller Kids First
PEDIATRIC RESEARCH PROGRAM
Data Resource Center



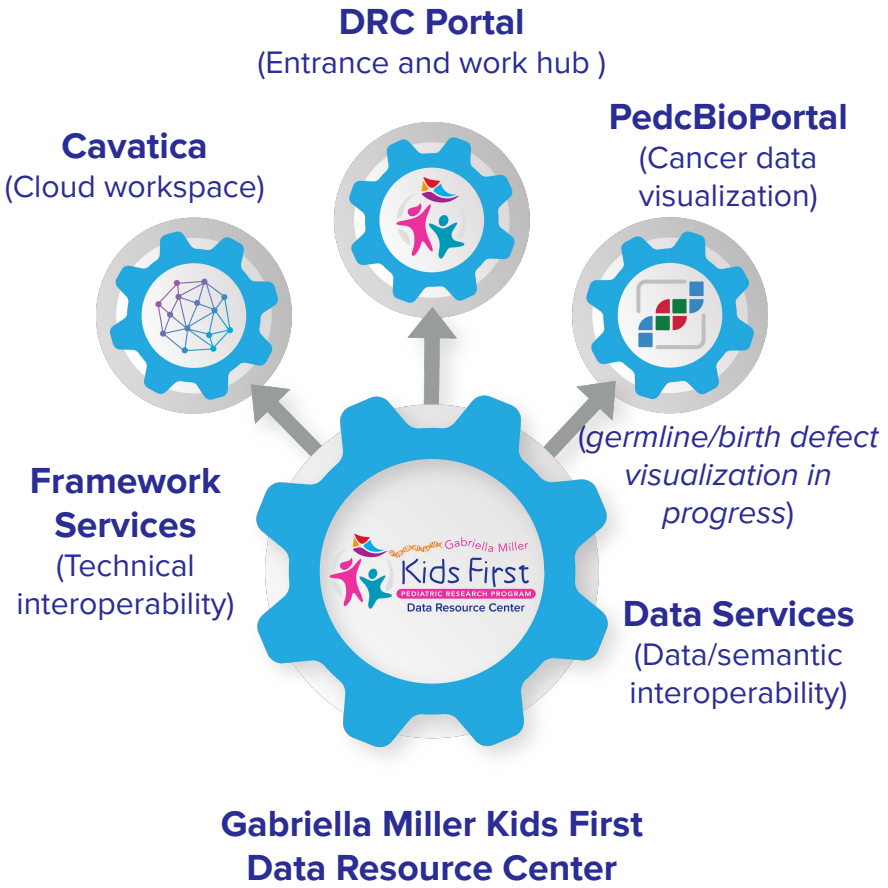
Kids First DRC

Features and Workflows for Team-based Discovery

Kids First 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.

Kids First DRC Platform Status

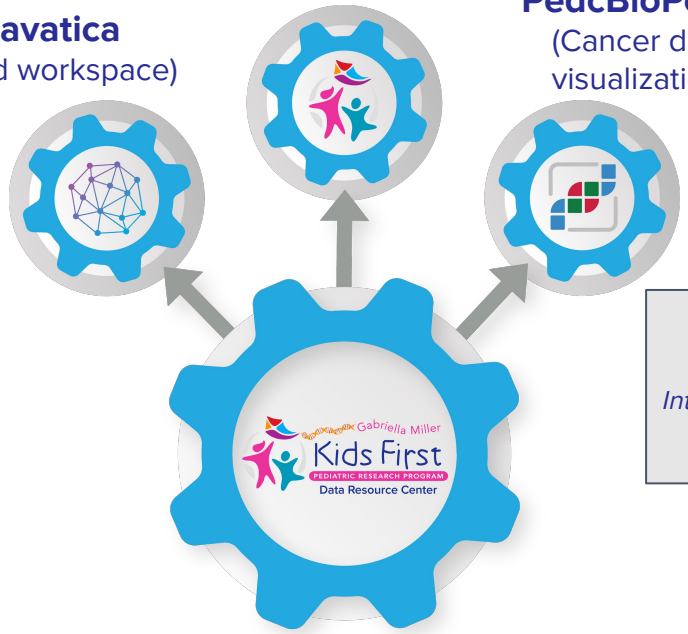
- **8,000+** participants from **3,000+** families for a total of **900+ TB** of released data
  (double by the end of the year)
- **1,000+** diagnoses harmonized over **30+** studies
- **600+** portal users with a 50% return user rate
- **1,000+** Cavatica users with over **250,000+** analysis pipelines completed and **13** cloud pilot projects underway
- **90,000+** somatic mutations from more than **900+** tumor samples available on PedcBioPortal



DRC Portal
(Entrance and work hub)

Cavatica
(Cloud workspace)

PedcBioPortal
(Cancer data visualization)



Gabriella Miller Kids First Data Resource Center

FAIR
(Findability, Accessibility, Interoperability, and Reusability)

Interdisciplinary Team

PLATFORM DEMO

Resources

Contacting the DRC:

- Email support@kidsfirstdrc.org

Kids First DRC Website & Information Materials

- www.kidsfirstdrc.org

Kids First Data Resource Portal

- Accessible through the website above or at https://portal.kidsfirstdrc.org

Cavatica: Cloud-based Analysis Portal & Data Delivery mechanism

- https://cavatica.sbgenomics.com/

Kids First DRC Genomic Processing pipelines are open source and open for feedback:

- Alignment workflow: https://github.com/kids-first/kf-alignment-workflow
- Joint genotyping workflow: https://github.com/kids-first/kf-jointgenotyping-workflow
- Genotype refinement workflow: https://github.com/kids-first/kf-genotype-refinement-workflow
- Somatic workflows: https://github.com/kids-first/kf-somatic-workflow
- RNA-Seq workflows: https://github.com/kids-first/kf-rnaseq-workflow

Webinar Instructions

Welcome to the Gabriella Miller Kids First Pediatric Research Program's Fall Public Webinar!

- Every participant is muted upon entry.
- To ask public questions, use the **Q&A** bar (right side of your screen). We encourage you to save these for the question periods.
- You can ask also use the "chat"  service to send private messages to the host or presenters throughout the webinar.
- After the webinar, additional program-related questions can be emailed to: KidsFirst@od.nih.gov.

This webinar will be recorded.
We will start at noon (EDT)

Gabriella Miller Kids First Pediatric Research Program

Public Webinar

September 26, 2019
12:00 pm EDT

Webinar Agenda

- Introduction by NIH Kids First staff (~5min)
- New Kids First Data Resource Portal Features – DRC (~30min)
- Kids First X01 Neuroblastoma Project Findings – Sharon Diskin, PhD (~30min)
- Kids First Program Updates – NIH (~15min)
- Kids First Second Chance: Community Engagement for Kids First Research – NIH (~10min)
- Questions from the Attendees (~15min)

This webinar is being recorded.

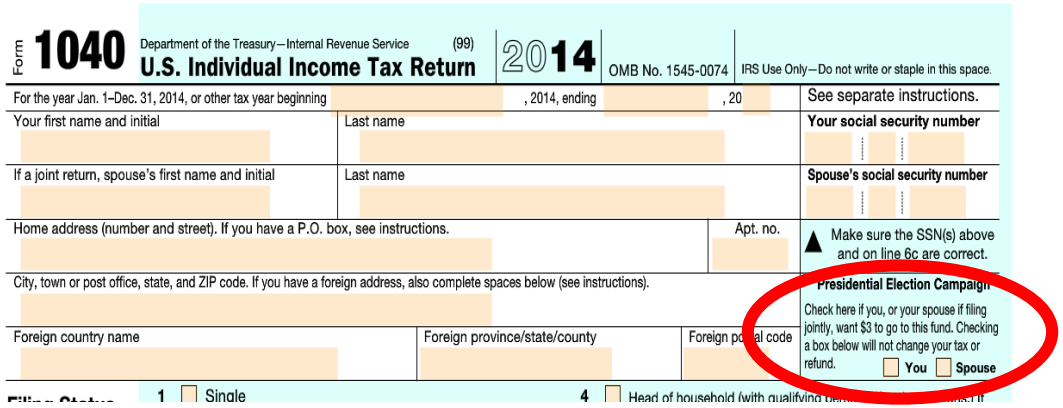
NIH
The Common Fund

Gabriella Miller Kids First
PEDIATRIC RESEARCH PROGRAM

Valerie Cotton [C]
Kids First Program Manager
Eunice Kennedy Shriver National Institute of
Child Health and Human Development (NICHD)

How did Kids First get started?

- Initiated in response to the 2014 Gabriella Miller Kids First Research Act:
  - Signed into law on April 3, 2014
  - Ended taxpayer contribution to presidential nominating conventions
  - Transferred $126 million into the Pediatric Research Initiative Fund
  - Authorized appropriation of $12.6 million per year for 10 years to the NIH Common Fund for pediatric research; first appropriation was for FY2015


Form **1040** Department of the Treasury—Internal Revenue Service (99) **U.S. Individual Income Tax Return** 2014 OMB No. 1545-0074 IRS Use Only—Do not write or staple in this space.

For the year Jan. 1–Dec. 31, 2014, or other tax year beginning , 2014, ending , 20 See separate instructions.

Your first name and initial | Last name | Your social security number

If a joint return, spouse's first name and initial | Last name | Spouse's social security number

Home address (number and street). If you have a P.O. box, see instructions. | Apt. no. | Make sure the SSN(s) above and on line 6c are correct.

City, town or post office, state, and ZIP code. If you have a foreign address, also complete spaces below (see instructions). | **Presidential Election Campaign**

Check here if you, or your spouse if filing jointly, want $3 to go to this fund. Checking a box below will not change your tax or refund. You Spouse

Foreign country name | Foreign province/state/county | Foreign postal code

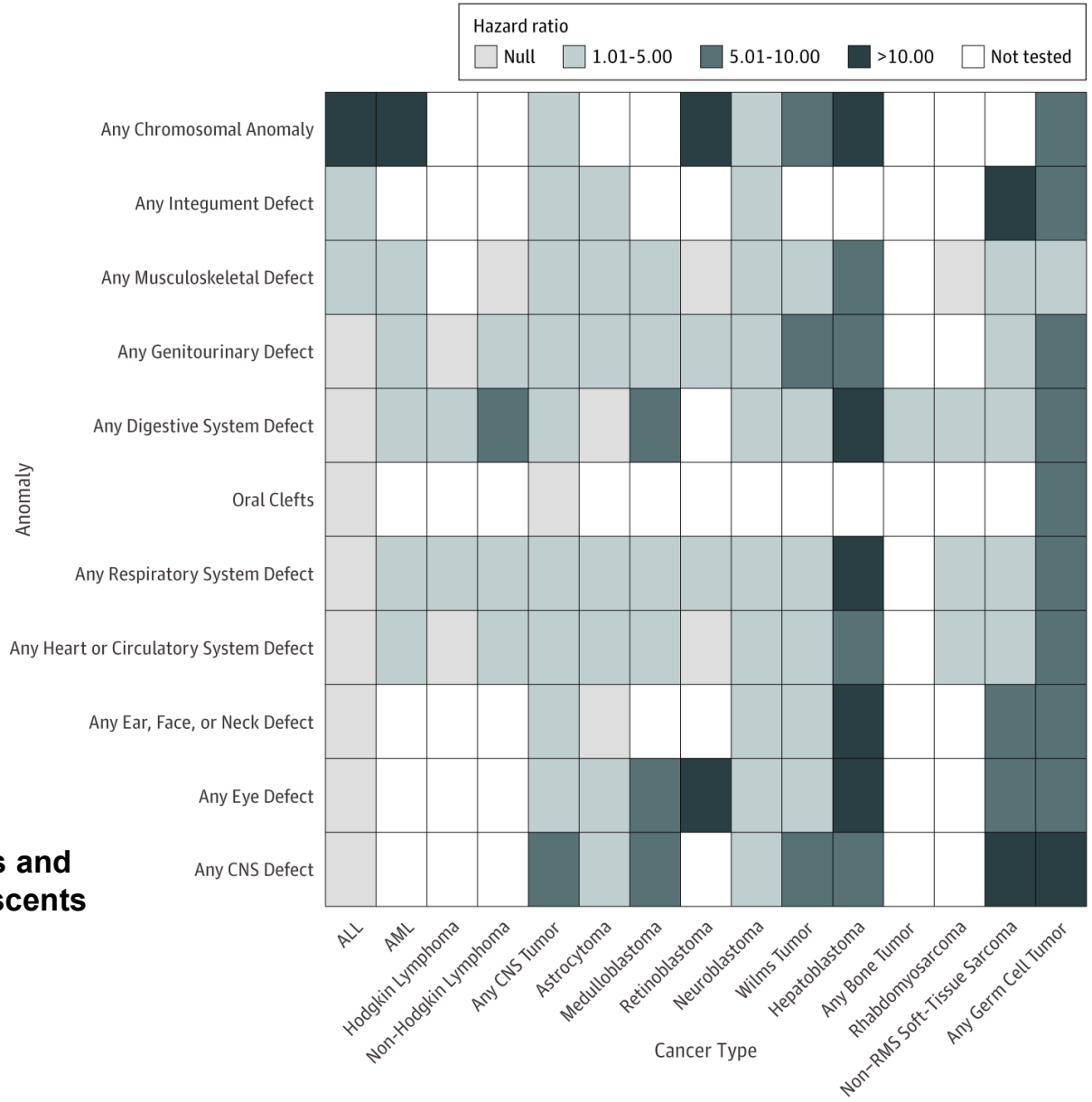
Filing Status 1 Single 4 Head of household (with qualifying

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.

Why study childhood cancer & structural birth defects together?

Birth defects associated with increased risk of cancer among children



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

Lupo et al, JAMA Oncol. 2019;5(8):1150-1158. doi:10.1001/jamaoncol.2019.1215

NIH Kids First Working Group

Kids First is an NIH Common Fund program coordinated by a **trans-NIH Working Group**, which is chaired by four institutes:

Eunice Kennedy Shriver National Institute of Child Health and Human Development (**NICHD**)

National Human Genome Research Institute (**NHGRI**)

National Heart, Lung, and Blood Institute (**NHLBI**)

National Cancer Institute (**NCI**)

Other Working Group Representation:

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

Kids First Major Initiatives

1. **Identify cohorts of children with childhood cancer and/or structural birth defects, and their families, for whole genome (DNA) sequencing**

X01 Childhood Cancer & Structural Birth Defects Cohorts

→

Kids First Sequencing Centers

2. **Build the Gabriella Miller Kids First Data Resource to empower discovery**

Gabriella Miller Kids First PEDIATRIC RESEARCH PROGRAM Data Resource Center

The Kids First Community

X01 Childhood Cancer & Structural Birth Defects Cohorts

Kids First Sequencing Centers

Gabriella Miller Kids First
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Data Resource Center

Gabriella Miller Kids First
PEDIATRIC RESEARCH PROGRAM
Data Resource Center

Adam Resnick, PhD
Children's Hospital of Philadelphia
Principal Investigator, Gabriella Miller Kids First Data Resource Center

Allison Heath, PhD
Children's Hospital of Philadelphia
Co-Principal Investigator, Gabriella Miller Kids First Data Resource Center

Vincent Ferretti, PhD
Sainte-Justine University Hospital
Principal Investigator, Gabriella Miller Kids First Data Resource Portal

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Gabriella Miller Kids First
PEDIATRIC RESEARCH PROGRAM

Charlene Schramm, PhD

Program Officer
Division of Cardiovascular Sciences/Heart Development and Structural Diseases Branch (HDSD)
National Heart, Lung, and Blood Institute (NHLBI)

Gabriella Miller Kids First Pediatric Research Program

Program Updates

Kids First X01 Cohorts (Years 1-4)

Disorders of Sex Development (FY15)
Congenital Diaphragmatic Hernia (FY15, 16, 17)
Ewing Sarcoma (FY15, 17)
Orofacial Clefts; Caucasian (FY15), Latin American (FY16), Asian & African (FY17)
Osteosarcoma (FY15)
Structural Heart & Other Defects (FY15, 16, 18)
Syndromic Cranial Dysinnervation Disorders (FY15)
Cancer Susceptibility (FY16)
Adolescent Idiopathic Scoliosis (FY16)
Familial Leukemia (FY16)
Hearing Loss (FY16)
Neuroblastomas (FY16)
Craniofacial Microsomia (FY17)
Enchondromatoses (FY17)
Hemangiomas, Vascular Anomalies & Overgrowth (FY17, 18)
Nonsyndromic Craniosynostosis (FY17)
Patients with both childhood cancer and birth defects (FY17)
Bladder Exstrophy (FY18)
Cornelia de Lange Syndrome (FY18)
Esophageal Atresia and Tracheoesophageal Fistulas (FY18)
Kidney and Urinary Tract Defects (FY18)
Intracranial Germ Cell Tumors (FY18)
Microtia (FY18)
Fetal Alcohol Spectrum Disorders (FY18)
Myeloid Malignancies + overlap with Down syndrome (FY18)
Congenital Heart Defects and Acute Lymphoblastic Leukemia in Children with Down Syndrome (FY18)

- **26 projects**
- **~10,000 patients** (+ family members and tumors)
- **4 X01 cycles**
- **8 released datasets**

2019 X01 Cohorts (Year 5)

Structural Brain Defects
Structural Defects of the Neural Tube (Spina Bifida: Myelomeningocele)
Orofacial Clefts in the Philippines
CHARGE Syndrome
Laterality Birth Defects
Kidney and Urinary Tract Defects
Esophageal Atresia & Tracheoesophageal Fistulas
Congenital Anomalies of the Kidney & Urinary tract
T-cell Acute Lymphoblastic Leukemia
Pediatric Rhabdomyosarcoma
Extracranial Germ Cell Tumors

> 10,000 genomes

BROAD INSTITUTE

HUDSONALPHA INSTITUTE FOR BIOTECHNOLOGY

St. Jude Children's Research Hospital

Abstracts & Contact PIs listed on: https://commonfund.nih.gov/kidsfirst/x01projects

Collaborations increase the impact of the Kids First program

In collaboration with…

The **INCLUDE Project** (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE), increase sequencing of:

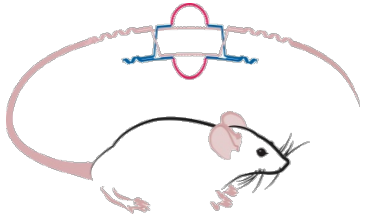
- Myeloid Malignancies + overlap with Down syndrome
- Congenital Heart Defects and Acute Lymphoblastic Leukemia in Children with Down Syndrome

NIAAA, increase sequencing of:

- Fetal Alcohol Spectrum Disorders

The Knockout Mouse Phenotyping Project (KOMP2), creating models to validate variants identified in Kids First datasets including:

- Congenital Diaphragmatic Hernia
- Structural Heart & Other Defects
- Syndromic Cranial Dysinnervation Disorders
- Enchondromatoses
- Adolescent Idiopathic Scoliosis



IMPC
International Mouse Phenotyping Consortium

https://commonfund.nih.gov/kidsfirst/collaboration

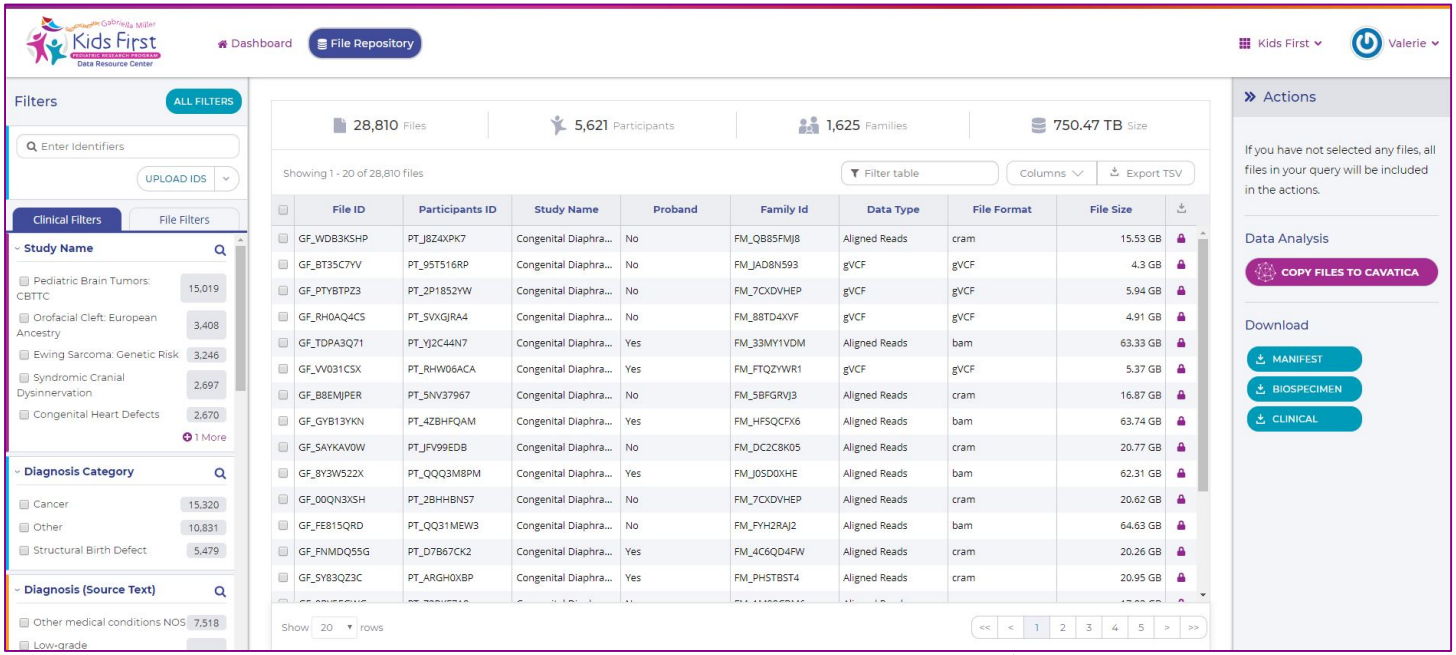
8 Released Datasets

➢ Disorders of Sex Development.	PI: Eric Vilain
➢ Congenital Diaphragmatic Hernia	PI: Wendy Chung
➢ Ewing Sarcoma	PI: Joshua Schiffman
➢ Orofacial Clefts: Caucasian families	PI: Mary Marazita
➢ Orofacial Clefts: Latin American families	PI: Mary Marazita
➢ Structural Heart & Other Defects	PI: Christine Seidman (PCGC)
➢ Cranial Dysinnervation Disorders	PI: Elizabeth Engle
➢ Adolescent Idiopathic Scoliosis	PI: Jonathan Rios

- **Kids First DRC website:** https://kidsfirstdrc.org/support/studies-and-access/
- **NIH Kids First Umbrella BioProject:** https://www.ncbi.nlm.nih.gov/bioproject/338775 > dbGaP links
- **X01 Abstracts**: https://commonfund.nih.gov/kidsfirst/x01projects

How do I access data?

Anyone can register & login to the portal to filter, search, visualize datasets



Individual-level sequence data

Investigators must submit dbGaP Data Access Requests (DARs) and receive approval from the **Kids First Data Access Committee**, before datasets can be accessed through the portal

NIH Kids First Data Access Committee

dbGaP GENOTYPES and PHENOTYPES

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Gabriella Miller Kids First
PEDIATRIC RESEARCH PROGRAM

Danyelle Winchester, PhD

Health Specialist
Office of Strategic Coordination
Division of Program Coordination, Planning, and Strategic Initiatives
Office of the Director, National Institutes of Health (NIH)

What is next for Kids First?

Strategic Planning

Year	15 ✓	16 ✓	17 ✓	18 ✓	19 ✓	20	21	22	23	24

Gabriella Miller Kids First
PEDIATRIC RESEARCH PROGRAM
Data Resource Center

?

What is next for Kids First?

2018 Strategic (Re-)Planning Exercise:

- **2018 Program Survey launched at ASHG**
- **Kids First Steering Committee**
- **Kids First Program Consultants**
- **DRC Admin & Outreach Core** (feedback from the public, patients, foundations)
- **NIH Kids First Working Group**

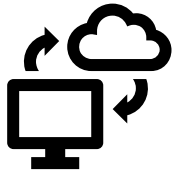
7 Consensus Recommendation Themes Emerged

1. **Innovation: Resource, infrastructure, or tool development.**
   Activities: Data Visualization tools; other tools for clinical/phenotypic data

2. **Clinical/phenotypic data extraction, harmonization, & curation.**
   Activities: Collect, extract, organize, curate, harmonize, and submit deep clinical and phenotypic data; annotate variants with pathogenicity, ClinGen scores.

3. **Collaborative validation and discovery.**
   Activities: Building synthetic cohorts; identify structural variants; test pipelines.
   *Engage trainees in data analysis projects**Bring users to the platform*

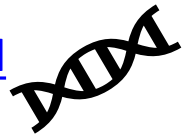
4. **Integration and interoperability of external pediatric datasets.**
   Activities: Using DRC workflow and best practices to harmonize external pediatric datasets; Building tools that can operate across multiple spaces



5. **Consent and data sharing.**
   Activities: Re-consenting cohorts in line with our data sharing expectations

6. **Validation with model organisms.**
   Activities: validating KF findings/variants, deep phenotyping of animal models

7. **Continue WGS & data generation**, invest in long-read, consider other –omics. Reissues of: https://grants.nih.gov/grants/guide/pa-files/PAR-19-104.html

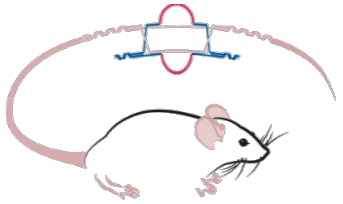


Get involved with Kids First!

- **Connect with and provide feedback to the DRC:** support@kidsfirstdrc.org
- **Contact the program for questions or feedback:** kidsfirst@od.nih.gov
- **Learn more about the program:** https://commonfund.nih.gov/kidsfirst
- **Search data available through the Kids First Data Resource Portal:** https://portal.kidsfirstdrc.org/

What funding opportunities are available?

- **Kids First cohort sequencing opportunity (X01):**
  - 2 more reissues of **PAR-19-104** **for 2020 and 2021**
- **Analyze Kids First data with support from:**
  - **"Kids First R03":** https://grants.nih.gov/grants/guide/pa-files/PAR-19-375.html
  - **NIH Parent R03**: https://grants.nih.gov/grants/guide/pa-files/PA-19-052.html
  - **NIH "Parent" R01**: https://grants.nih.gov/grants/guide/pa-files/PA-19-056.html
- **Validate variants with support from**:
  - ORIP's Development of Animal Models and Related Biological Materials for Research (R21): https://grants.nih.gov/grants/guide/pa-files/PA-16-141.html
  - Mechanistic Studies of Gene-Environment Interplay in Dental, Oral, Craniofacial, and Other Diseases and Conditions (R01) (PAR-19-292).
  - Development of Novel and Robust Systems for Mechanistic Studies of Gene-Environment Interplay in Dental, Oral, Craniofacial, and Other Diseases and Conditions (R21) (PAR-19-293).
  - To pursue collaborations with the Knockout Mouse Phenotyping Program (KOMP2), contact: KidsFirstKOMP@nih.gov



- **To receive updates about future Kids First opportunities, sign up for the listserv:**
  - https://commonfund.nih.gov/kidsfirst/register

Small Research Grants for Analyses of Gabriella Miller Kids First Pediatric Research Data

(R03 - Clinical Trial Not Allowed)

PAR-19-375

Purpose: support analyses of Kids First X01 datasets and appropriate tools development

- NICHD, NCI, NHLBI, NIAAA, and NIDCR
- Standard Receipt Dates (after Open Date): Feb 2020
- Combined direct cost budget for the two-year project period may not exceed $200,000
- Contact IC representative or James Coulombe (coulombej@mail.nih.gov)

Small Research Grants for Analyses of Gabriella Miller Kids First Pediatric Research Data

(R03 - Clinical Trial Not Allowed)

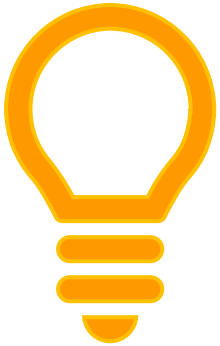
PAR-19-375

FOA Updates

- Data and Resource Sharing Plans:
  - "data…, tools, workflows, and/or pipelines ***created*** or ***used*** …will be provided to the Kids First Data Resource Center to be shared with the wider scientific community… in ***a timely manner*** that would enable other researchers to replicate and build on the analyses for future research efforts."
  - For applications that aim to co-analyze Kids First X01 data with non-Kids First genomic datasets, describe:
    - the database through which the non-KF data are accessible, or
    - ability & willingness to submit the non-KF sequence data to an NIH-approved repository (e.g., dbGaP)

Kids First
Second Chance

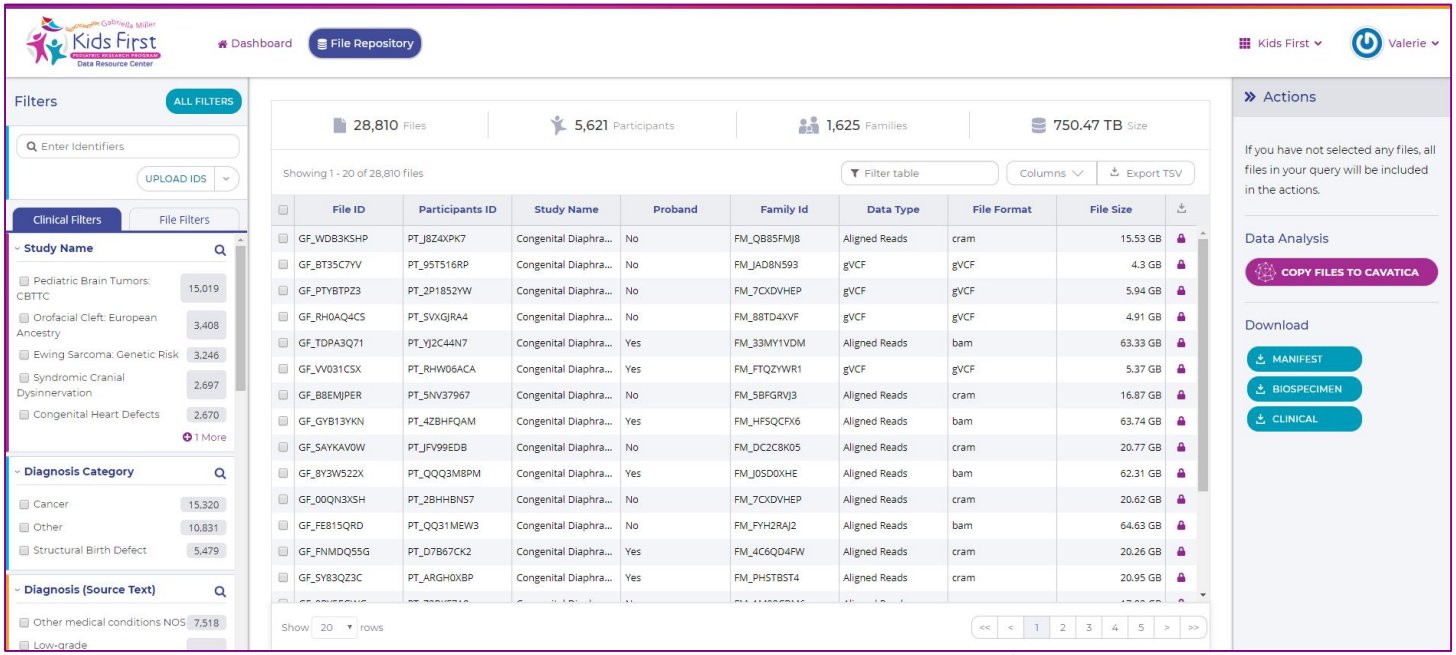
Community Engagement for Analysis of
Data Generated by the
Gabriella Miller Kids First Pediatric Research Program



The value of Kids First datasets will be amplified when researchers use and analyze these data to make discoveries that will ultimately improve prevention, diagnostics, and therapeutic interventions for these conditions

Researchers are accessing Kids First data!

~800 users since launch last September 2018

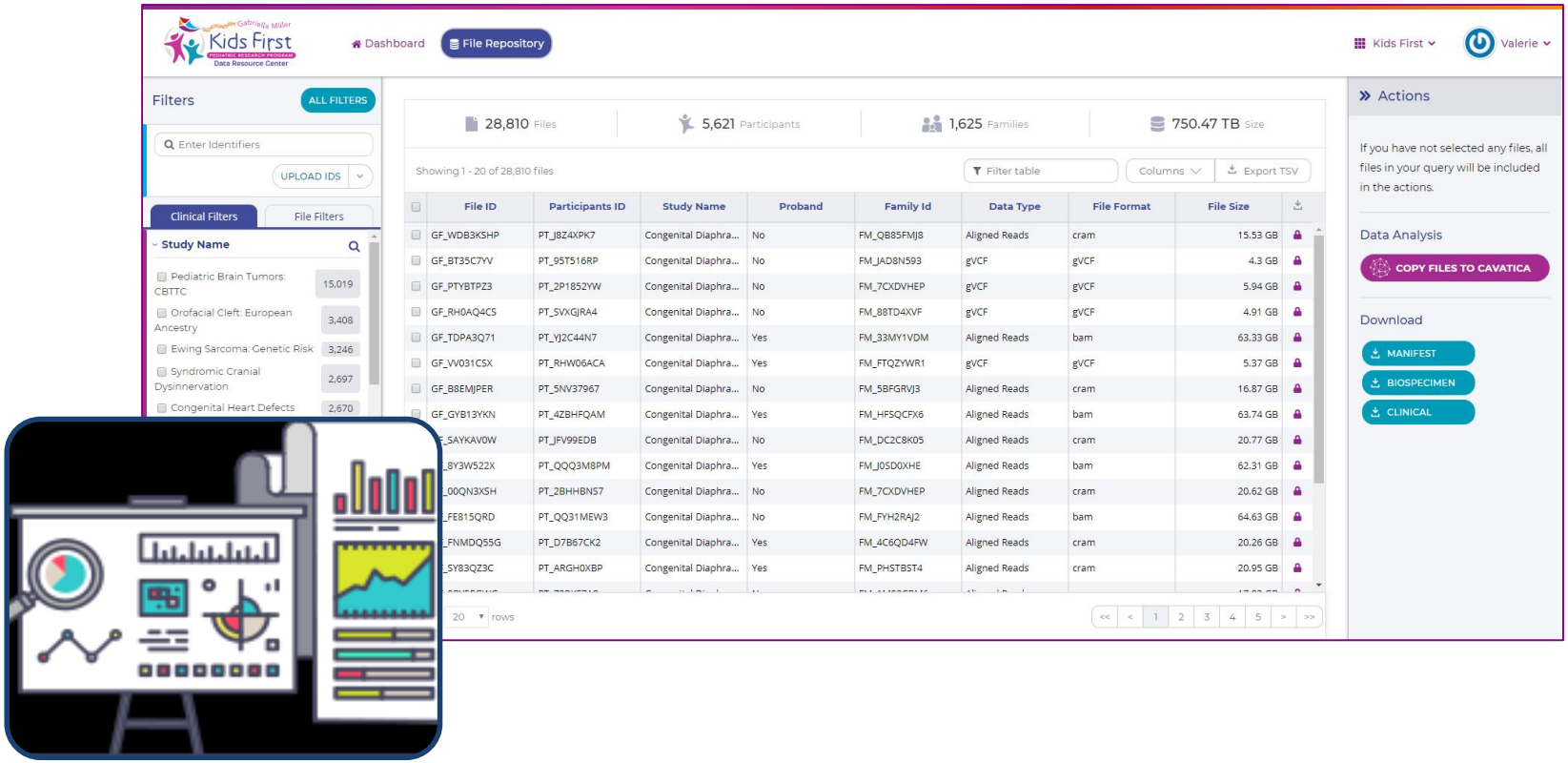


Individual-level sequence data

>70 Data Access Requests approved by the Kids First Data Access Committee across 8 Kids First genomic datasets available

NIH Kids First Data Access Committee

dbGaP GENOTYPES and PHENOTYPES



Researchers can analyze Kids First data with support from:

- NICHD-led “Kids First” R03 (PAR)
- Other NIH R03s
- NIH R01s
- Other NIH grant mechanisms

many excellent applications go unfunded

Small Research Grants for Analyses of Data for the Gabriella Miller Kids First Data Resource

(R03 - Clinical Trial Not Allowed)

Past: ***PAR-16-348 ; PAR-18-733; PAR-19-069***

Purpose: support analyses of Kids First X01 datasets

- Since 2016 through FY2019
  - **37 R03 applications**
    - 11 have been funded
    - 26 were not funded
      - –of these 10 were discussed/scored, but missed payline

X01 Cohorts → Whole Genome & Phenotypic Datasets

➢ Disorders of Sex Development.	PI: Eric Vilain
➢ Congenital Diaphragmatic Hernia	PI: Wendy Chung
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➢ Adolescent Idiopathic Scoliosis	PI: Jonathan Rios

….25+ more datasets in the pipeline!

→

→

Gabriella Miller Kids First
PEDIATRIC RESEARCH PROGRAM
Data Resource Center

Community Engagement

Foundations and other organizations have expressed interest in working with the NIH to support pediatric research, particularly in areas that coincide with the mission and goals of the organization(s).

Additionally, foundations are strongly supportive of the Kids First program's emphasis on **data sharing** and **collaboration.**

Connecting Community Organizations & Researchers

NIH

Gabriella Miller Kids First PEDIATRIC RESEARCH PROGRAM

1. **Organizations** agree to be contacted by **researchers** seeking an additional chance for funding to analyze Kids First data

2. **Researchers** apply for NIH grant(s) to analyze Kids First datasets

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5. **Organizations & researchers** follow normal procedures to establish agreements

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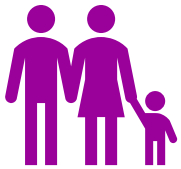
6. Data are shared with the research community
7. Together, we accelerate research & discovery and improve the lives of children and families



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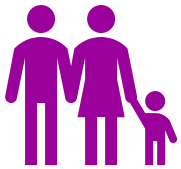

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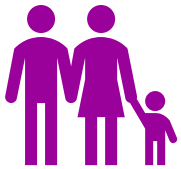
6. Data are shared with the research community
7. Together, we accelerate research & discovery and improve the lives of children and families



Kids First
Second Chance

https://commonfund.nih.gov/kidsfirst/secondchance

Q & A

- To ask public questions, use the **Q&A** bar (right side of your screen).
- You can ask also use the “chat”  service to send private messages to the host or presenters throughout the webinar.

"How do I join the program?"

- **Apply to have DNA (and RNA) samples from childhood cancer and/or structural birth defects cohorts sequenced and shared by Kids First:** https://grants.nih.gov/grants/guide/pa-files/PAR-19-104.html
- **Search data available through the Kids First Data Resource Portal:** https://portal.kidsfirstdrc.org/
- **Apply for dbGaP access and analyze Kids First sequence data.**
- **Attend events and webinars**
- **To receive updates about future Kids First opportunities, sign up for the listserv:** https://commonfund.nih.gov/kidsfirst/register

Upcoming Event

Kids First Poster Session at ASHG in Houston:
Accelerating Pediatric Genomics Research through Collaboration

- October 15th, 6-9pm CT
- Free and open to the public
- 40+ posters are planned representing Kids First X01 cohort projects, sequencing centers, and the DRC, as well as a variety of current and new collaborators, including other NIH programs.
- Registration and details: https://www.eventbrite.com/e/kids-first-poster-session-accelerating-pediatric-genomics-research-through-collaboration-tickets-65121015711

Thank You!

Email Additional Questions and Comments to the Kids First Mailbox: **kidsfirst@od.nih.gov**

Individual-level sequence data

- To learn more about submitting dbGaP Data Access Requests (DARs) watch: https://www.youtube.com/watch?v=39cba0gF2tw&index=3&t=503s&list=PLoXwgZflAe4aMwWpVQU_WVeWHzyhI3BCu