The Gabriella Miller Kids First Research Program

Marie Nierras, PhD
Lorette Javois, PhD
Malcolm Smith, MD, PhD

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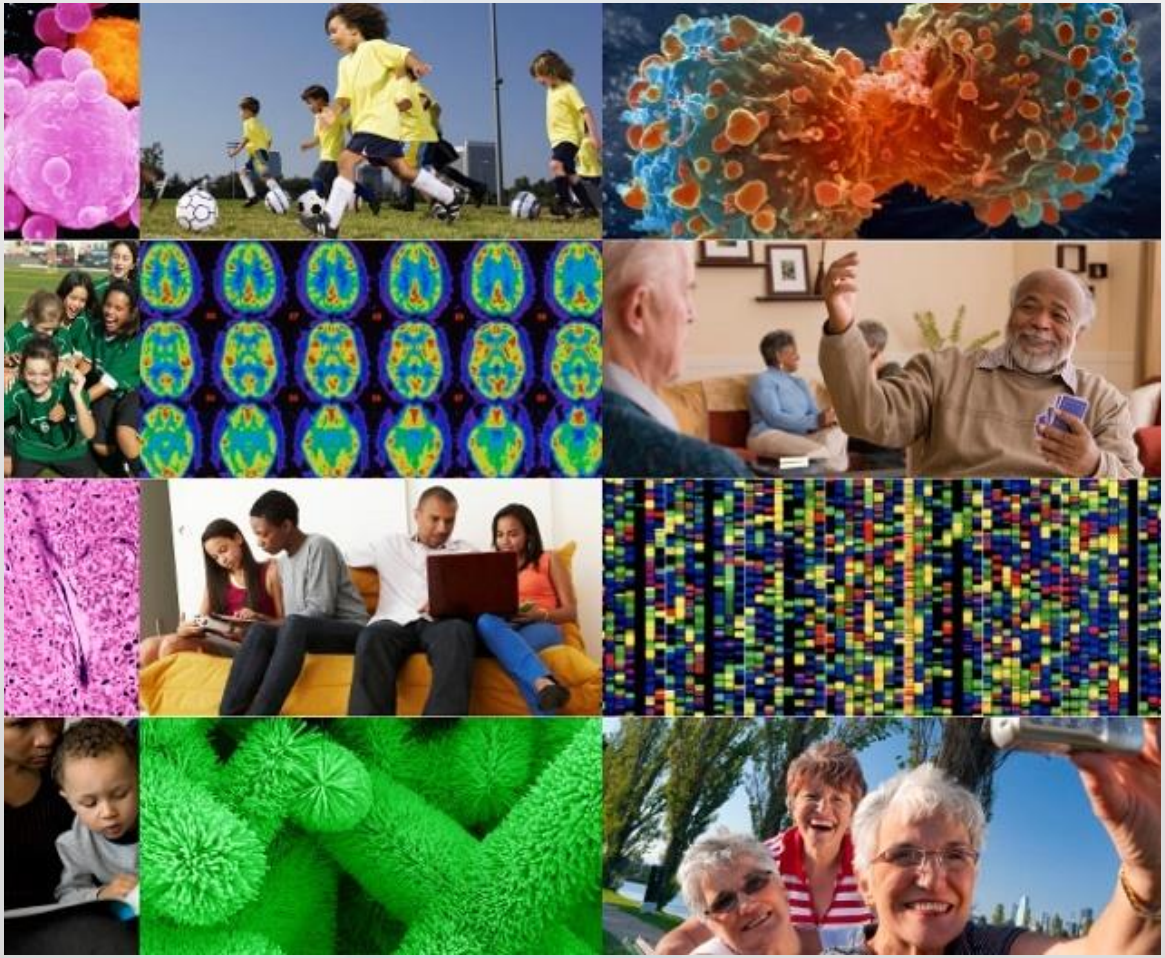
National Institutes of Health
Office of Strategic Coordination - The Common Fund

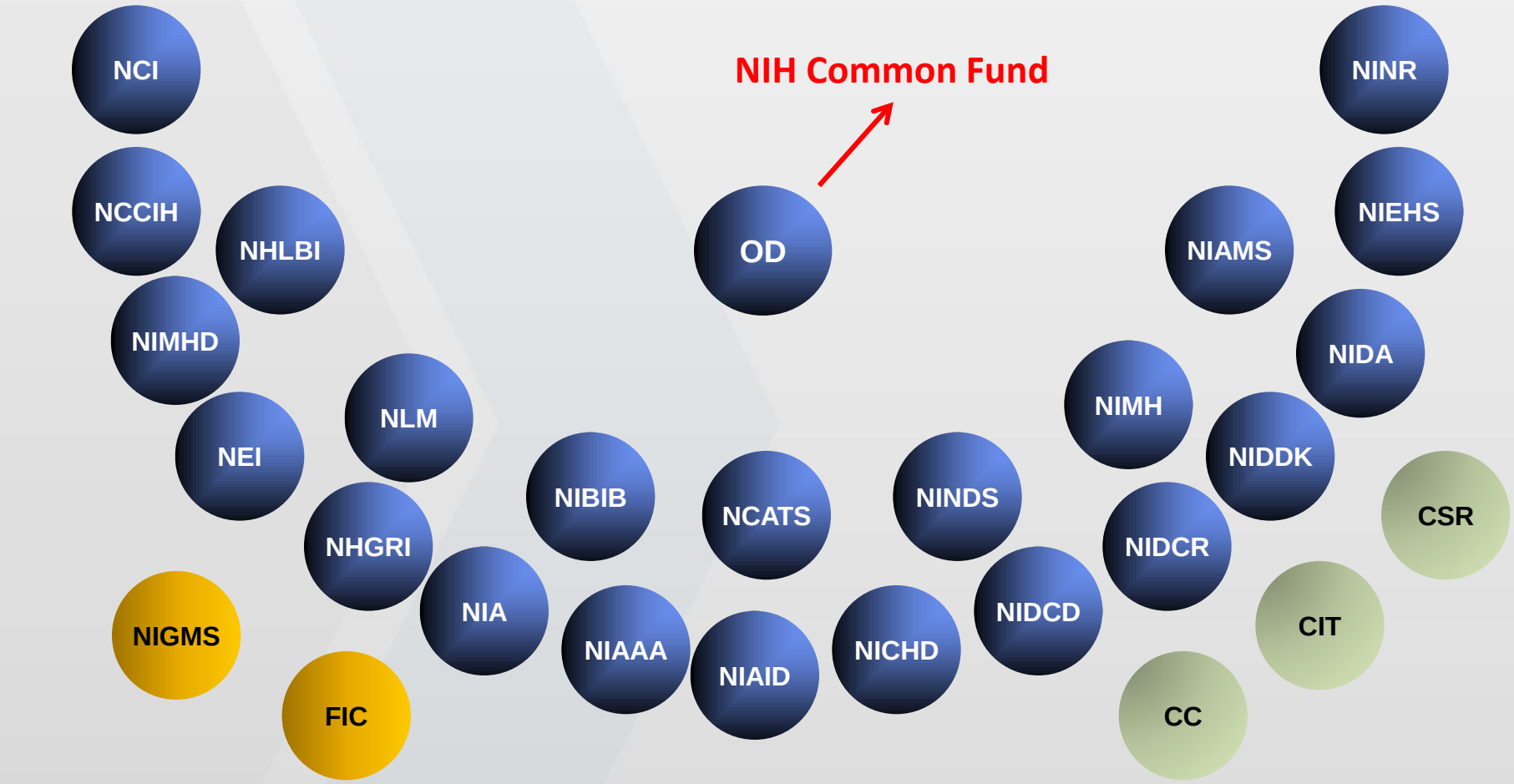
NIH Overview



"Science in pursuit of **fundamental knowledge** about the nature and behavior of living systems….

and the **application of that knowledge** to enhance health, lengthen life, and reduce illness and disability."

NIH Institutes and Centers



Pediatric Research is an NIH Priority

- In fiscal year 2014, the NIH funded research grants and projects directed specifically at pediatric research for a total of approximately $3.5 billion.

- The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) funds the largest portion of pediatric research

- NICHD alone accounts for only 20 percent of the total NIH support for pediatric research. This reflects the breadth of the research portfolio at the NIH dedicated to improving the health of children everywhere. 25 ICs support pediatric research.

Pediatric Research in the Common Fund:

How did we get here?

Gabriella Miller Kids First Research Act: Signed into law April 3, 2014

- Named for Gabriella Miller, a 10 year old who died of cancer; prior to her death, she called on Congress to take action on pediatric research.
- Ends taxpayer contribution to presidential nominating conventions.
- Transfers this money into the 10 year Pediatric Research Initiative Fund; **authorizes** $12.6 million out of the Fund each year for pediatric research through the Common Fund.

FY 2015 Funding Bill: Signed into law December 16, 2014

- Appropriated $12.6 million to the Common Fund for pediatric research, as authorized in the Gabriella Miller Kids First Research Act.
- Although the Act **authorizes** funds for 10 years, funds must be **appropriated** every year. NIH has received funds for FY 2015 only. We are developing plans for a 10 year program, in the event that appropriations continue.
- Must meet Common Fund criteria, align with Common Fund vision/purpose.

Origins of the Common Fund

One Hundred Ninth Congress
of the
United States of America

AT THE SECOND SESSION

Begun and held at the City of Washington on Tuesday, the third day of January, two thousand and six

An Act

To amend title IV of the Public Health Service Act to revise and extend the authorities of the National Institutes of Health, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the "National Institutes of Health Reform Act of 2006".

TITLE I—NIH REFORM

2004: NIH Roadmap is launched

December 2006: Congress passes a reauthorization bill affirming importance of NIH and its vital role in advancing biomedical research to improve the health of the Nation

Establishes the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) within Office of the Director and the NIH Common Fund to provide a dedicated source of funding to enable goal driven, *trans*-NIH research

What do we look for in a Common Fund program?

Transformative: Programs are expected to have **exceptionally high and broadly applicable impact**. They should be relevant to many diseases and many ICs. They should create entirely new approaches to research or clinical care, or establish new biological paradigms.

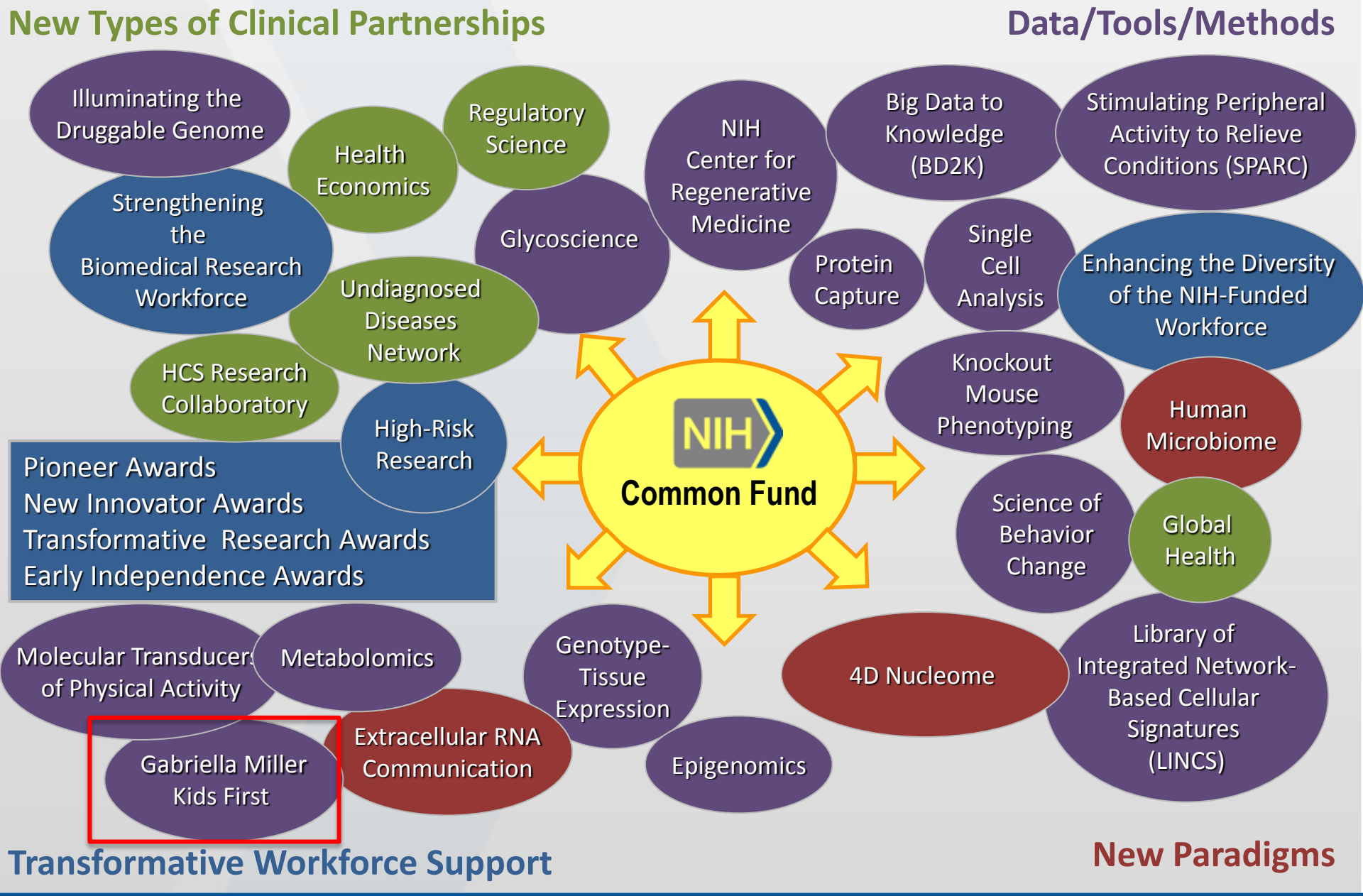
Catalytic, Short Term and Goal-driven: Programs must achieve – not just work toward – a goal. They have **deliverables** – data sets, tools, technologies, approaches, or fundamental principles of biology, etc – that can be achieved within **5-10 years**. If the deliverable is expected to have ongoing maintenance costs, a vision for transition and sustainment must be articulated.

Synergistic /Enabling: Programs should be **value-added to the ICs**, with the output enabling the mission of multiple ICs.

Requires a High Level of Trans-NIH Coordination: CF programs should address complex issues that require trans-NIH teams, insights and perspectives to design and manage. There must be a **reason why strategic coordination is required**.

Novel: Programs should provide **new solutions to specific challenges**. If similar efforts exist, the CF program should be tightly coordinated to prevent duplication of effort. Programs should not be something another entity would be likely to support.

Current Common Fund Programs (FY16)



Kids First Program Timeline

January 2015: NIH leaders and pediatric research experts meet to discuss Kids First and approve the idea of a data resource

February/March 2015: Kids First Trans-NIH Working Group develops program proposal focusing data resource on structural birth defects and childhood cancer.

April 20, 2015: Kids First Program proposal presented to IC Directors

Early May 2015: Kids First program announced and website launched

May 15, 2015: First Funding Opportunity posted (identify cohorts for sequencing)

June 27, 2015 – July 27, 2015: Open dates for researchers to apply for funding

Mid-late September 2015: Final funding decisions made

October 26, 2015: Seven awards announced; 2 for childhood cancer and 5 for structural birth defects

2016: Identify additional cohorts for sequencing (FOA similar to that in 2015) and issue FOA for a dedicated sequencing center. Pending availability of funds.

2016-2017: Plans to issue an FOA in fiscal year 2016 or 2017 to build the pediatric data resource. Pending availability of funds.

Kids First Program

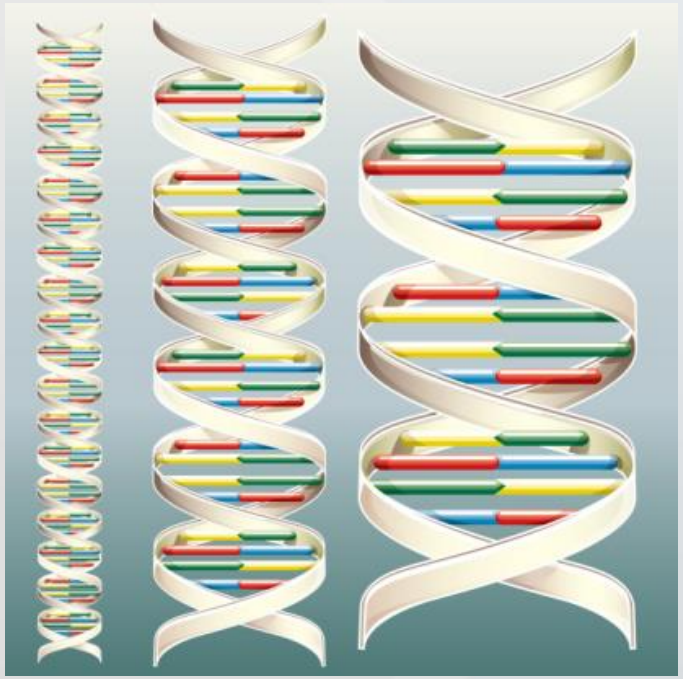
Overall Goal

Develop a data resource
for the pediatric research community incorporating
both structural birth defects and childhood cancer data.

- This program will support DNA sequencing of patients with structural birth defects or childhood cancers. These data will be combined with clinical information to provide researchers with a rich resource to link genes and diseases/conditions.
- This data set will be integrated and made widely available to researchers, so that they can have access to large data sets to enable their own research studies into pediatric conditions.
- The program will also support a limited number of projects that use this data set, to demonstrate its value to the research community.

What Do Genes Have to Do With disease?

Linking Genotype and Phenotype



Environment

Genotype = the genetic information of an individual

Phenotype = an individual's observed properties

- Hair color/eye color
- Height
- Disease/condition

Sequencing the DNA of Pediatric Research Cohorts

Cohort: a group of people who share a common characteristic

Pediatric research cohort: a group of pediatric patients with a common characteristic, disease, or condition who have been recruited for a research study (childhood cancer or structural birth defects)

Researchers can apply to the Kids First program to have the DNA of a cohort they have assembled for research to be sequenced.

An Opportunity for Pediatric Research

- Critical research questions for **structural birth defects**
  - What is the genetic basis of specific structural birth defects?
  - What genetic overlaps exists between different birth defects and how does that overlap influence phenotypic expression?
  - How can an improved genetic understanding of birth defects be translated into improved prevention, diagnosis, and treatment for patients?
- Critical research questions for **childhood cancer**
  - What is the genetic basis for treatment failure for pediatric cancers?
    - In future years this will be a focus of the Precision Medicine Initiative
  - What is the genetic basis for childhood cancers – either inherited or new mutations – not identified to date?

Why a Pediatric Data Resource?

- Birth defects and pediatric cancers are **critical pediatric conditions**
  - Birth defects are common (1 in 33 US infants) with high mortality and pediatric cancers are the leading cause of disease-related death beyond the first year of life
  - Both have profound lifelong effects on survivors and their families with society bearing the socioeconomic costs

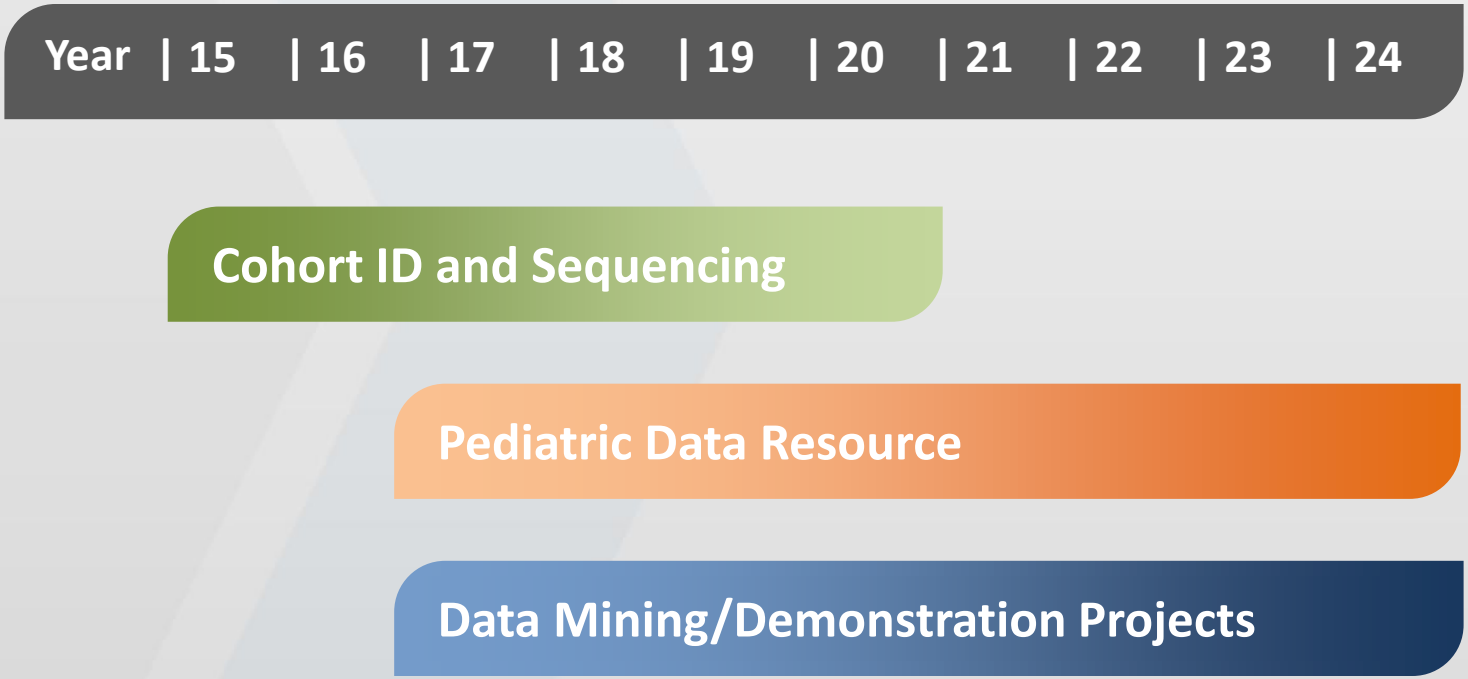
- **Catalytic investment** to drive discovery
  - Genome sequencing has potential to uncover genetic basis of pediatric conditions
  - Data resource will enable assembly of larger populations
  - Data resource will facilitate cross cutting, collaborative research

- **Transformative resource** for pediatric research community by democratizing access to genomic data and reducing storage and analysis costs

- **Accelerate the science towards improving diagnosis, risk stratification, intervention, and identification of new targets for therapy**
  - Positive impact for patients and families

Kids First Program Activities

Activities and Timeline



Kids First Program Activities

Cohort Identification and Enrichment will identify appropriate samples with phenotype data and provide genome sequence for them

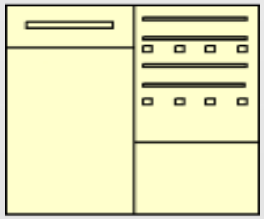
Deliverables

- Cohort data sets that will enrich the data resource
- Data sets with common data elements including whole genome sequence

Pediatric Data Resource will store, integrate, and provide views of data for the pediatric research community.

Deliverables

- Virtual environment to store, catalogue, search, share, and aggregate data
- Policies and procedures that guide operation of the data resource

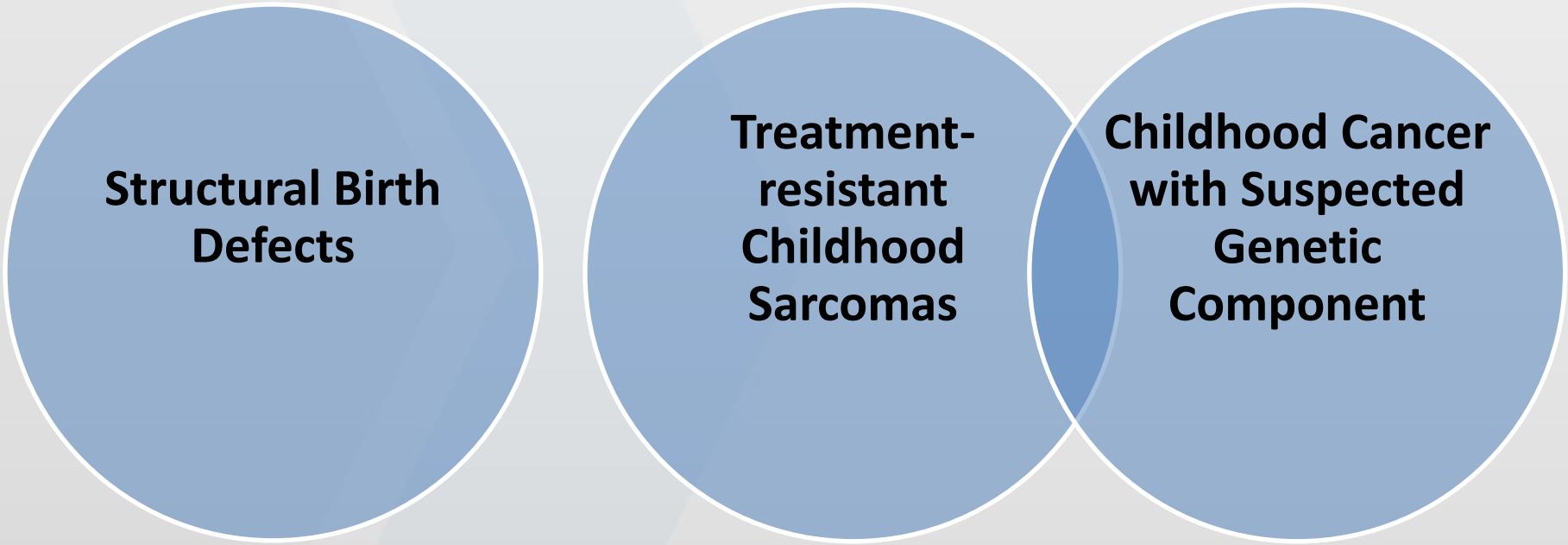


Data Mining and Development Projects will support investigators to leverage data within the data resource

Deliverables

- Pilot projects that use the data resource including data mining, and bioinformatics tools with the goal of developing new insights into the biology of pediatric disease
- Identify and develop new targets for intervention

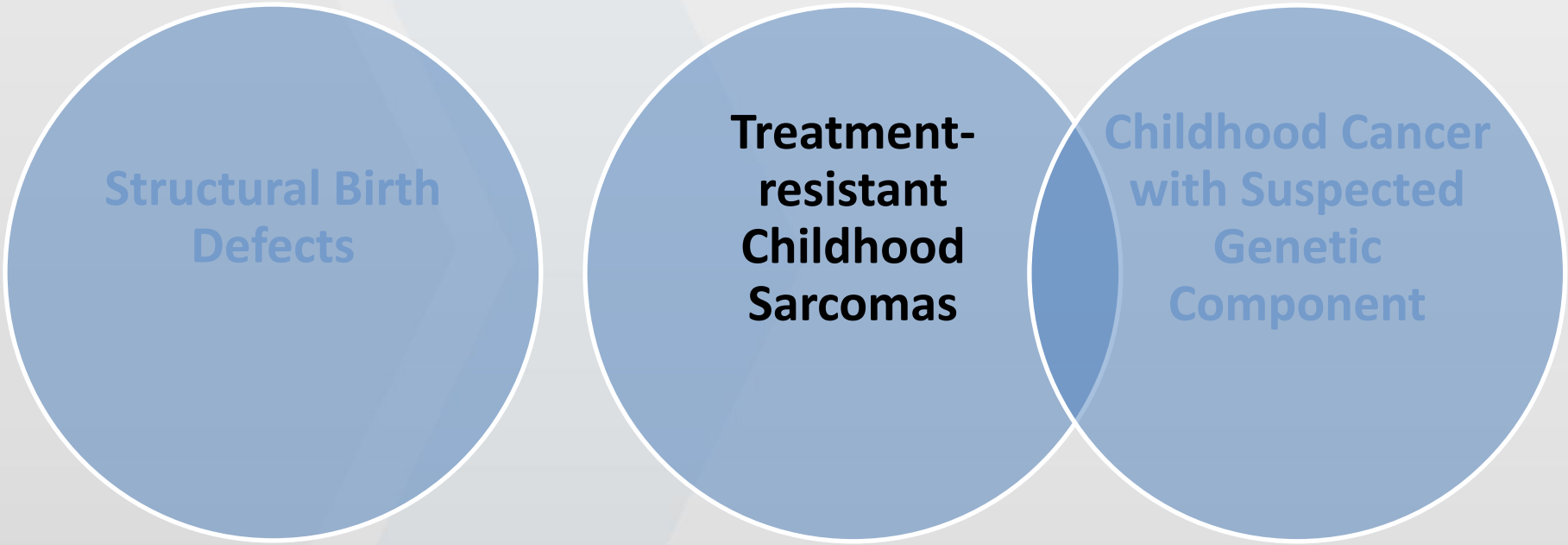
Types of Research Cohorts Eligible for DNA Sequencing in Fiscal Year 2015



Types of Research Cohorts Eligible for DNA Sequencing in Fiscal Year 2015

Cohorts will consist of trios (affected child and parents) to identify genetic variants contributing towards the condition.

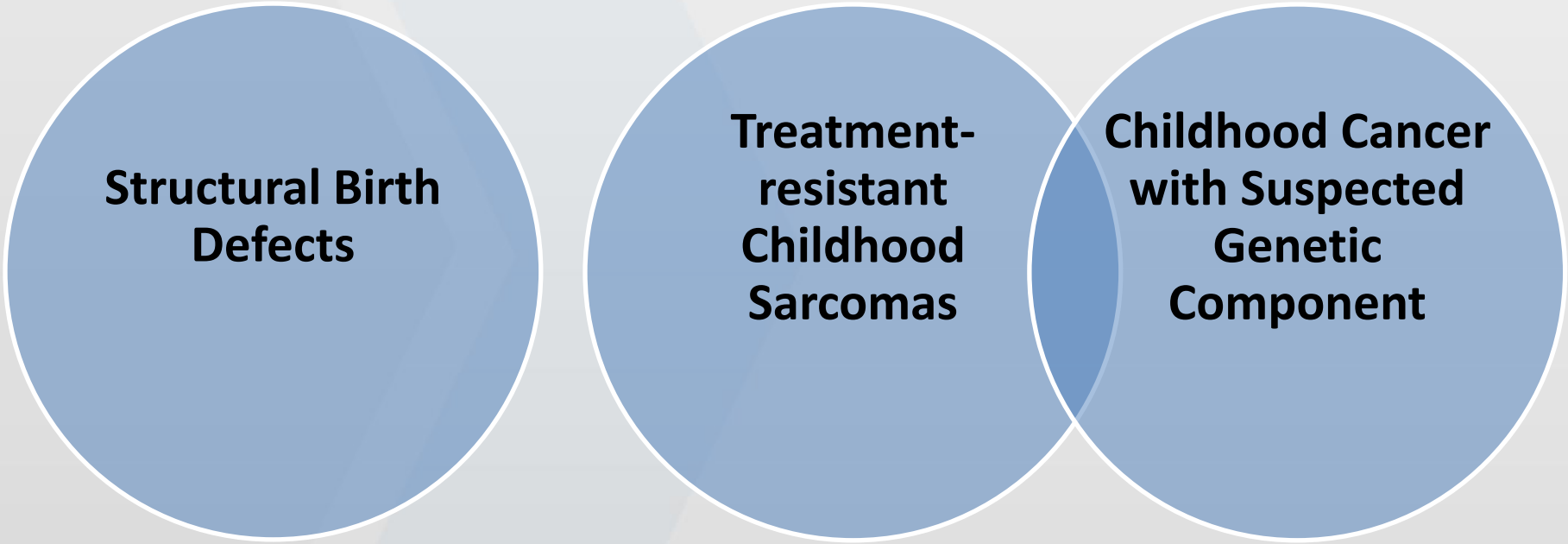
Types of Research Cohorts Eligible for DNA Sequencing in Fiscal Year 2015



Cohorts will consist of patients whose cancer failed to respond to therapy. Researchers will submit both normal patient and tumor DNA.

Types of Research Cohorts Eligible for DNA Sequencing in Fiscal Year 2015

All cohorts must:



- Be large enough to discover something meaningful about the disease or condition (a minimum of 100 trios for structural birth defects).
- Have approval for sharing sequencing results through a controlled access database.

Selection of Research Cohorts for DNA Sequencing in Fiscal Year 2015

All applications have undergone peer review.

After peer review, applications received a second level of review by Common Fund and other NIH staff.

To be considered in making selection decisions:

- Scientific and technical merit of the proposed project as determined by scientific peer review.
- Availability of capacity for DNA sequencing.
- Compliance with resource sharing policies as appropriate.
- Program balance, including making available DNA sequence data for a diverse set of disorders.
- Available funds.

Selection of Research Cohorts for DNA Sequencing in Fiscal Year 2015

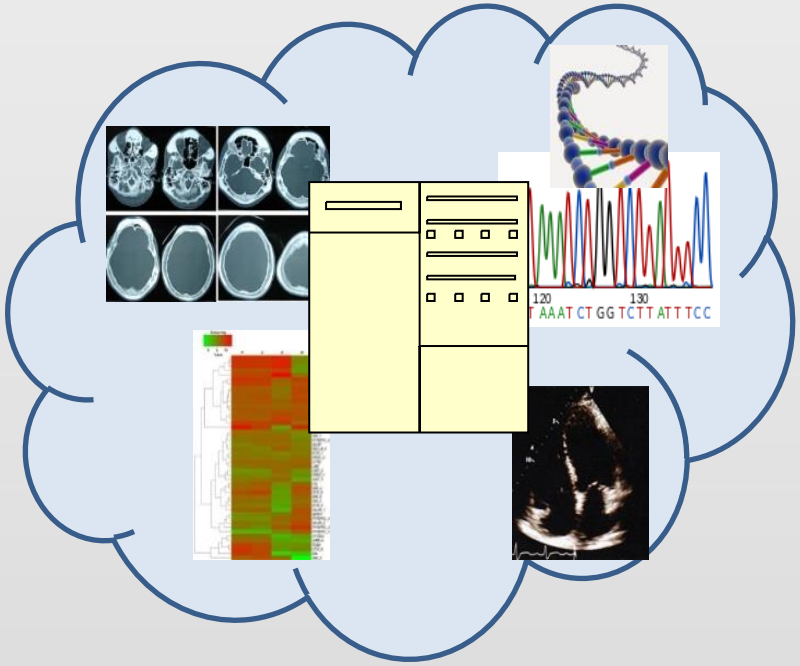
Applications selected for funding in 2015 covered the following diseases:

Ewing Sarcoma
Pediatric Osteosarcoma
Orofacial Cleft Birth Defects
Syndromic Cranial Dysinnervation Disorders
Congenital Heart Defects
Congenital Diaphragmatic Hernia
Disorders of Sex Development

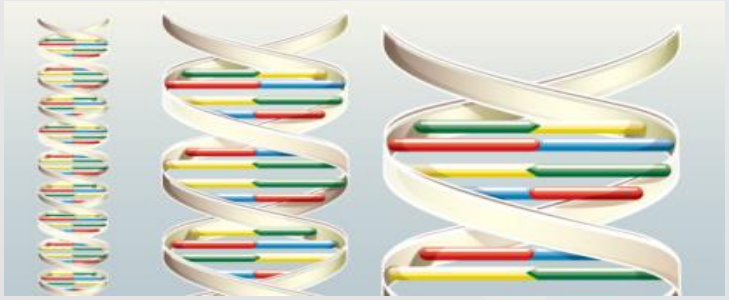
Opportunity to sequence additional structural birth defect cohorts and childhood cancer cohorts will be announced in FY16 pending the availability of funds

Fiscal Year 2015 Data = Foundation of the Data Resource

- DNA sequences will be returned to researchers and deposited in dbGaP.
  - Cancer data also submitted to NCI's Genomic Data Commons to leverage Kids First results with NCI's investment in adult and childhood cancer genomics
- Researchers will provide phenotype data obtained from their cohorts.
- DNA sequence and phenotype data from Fiscal Year 2015 will form the foundation of the Kids First Data Resource

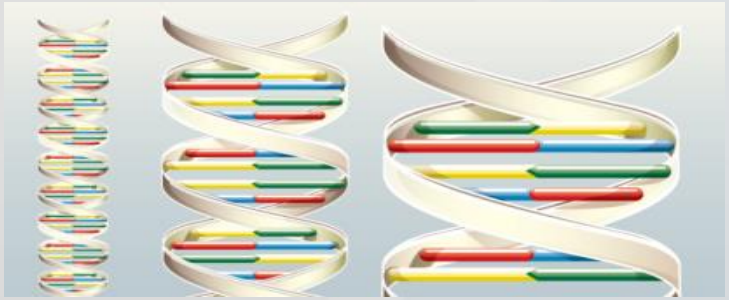


Using the Data Resource to Link DNA Sequence and Diseases/Conditions



Environment

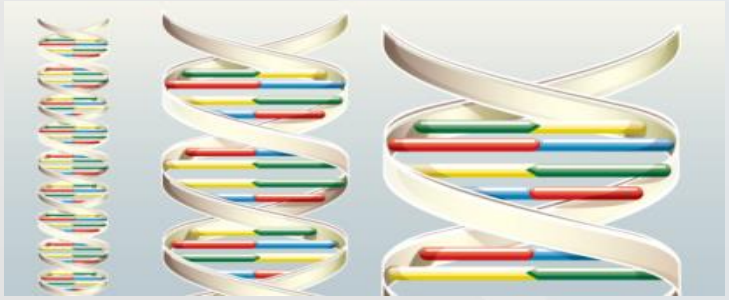
Li Fraumeni Syndrome



Genetic Component ???

Predisposition to multiple cancer types observed in family members (particularly childhood and adolescent cancers)

Using the Data Resource to Link DNA Sequence and Diseases/Conditions



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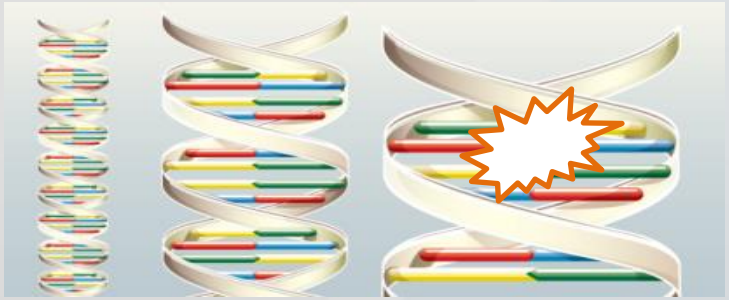


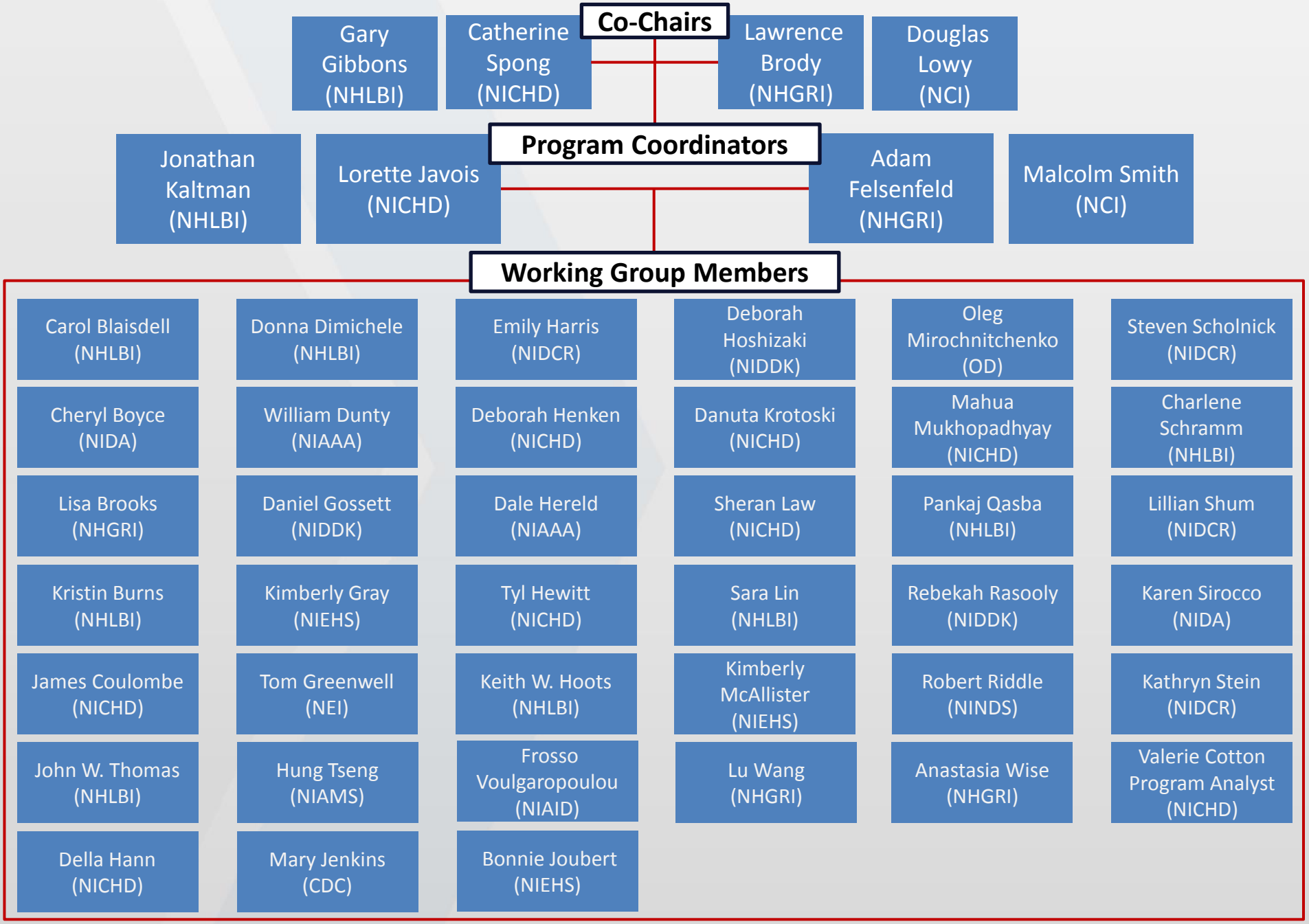
Mutated Gene in Affected People

Predisposition to multiple cancer types observed in family members

People with mutated gene now know to receive early screening procedures.

What Do We Expect from the Data Resource?

- This resource will be made widely available to the research community to stimulate research supported by other mechanisms, broadening the impact of the Kids First program.
- The combination of many cohorts into one data resource will enable researchers to have access to much larger samples than they would otherwise have access to, strengthening their studies and enabling studies of rare pediatric conditions.
- This resource will lay the foundation for an improved understanding of various pediatric conditions, and may provide new avenues for the development of therapies.
- Not all pediatric conditions will have a genetic basis, and not all genetic findings will result in new therapies. Patients may not be able to directly benefit from participating in this study.
- Development of therapies, if they occur, may be many years in the future. However, this program will build a strong foundation to accelerate the development of therapies that might otherwise not be possible.


Co-Chairs
Gary Gibbons (NHLBI)
Catherine Spong (NICHD)
Lawrence Brody (NHGRI)
Douglas Lowy (NCI)
Program Coordinators
Jonathan Kaltman (NHLBI)
Lorette Javois (NICHD)
Adam Felsenfeld (NHGRI)
Malcolm Smith (NCI)
Working Group Members
Carol Blaisdell (NHLBI)
Donna Dimichele (NHLBI)
Emily Harris (NIDCR)
Deborah Hoshizaki (NIDDK)
Oleg Mirochnitchenko (OD)
Steven Scholnick (NIDCR)
Cheryl Boyce (NIDA)
William Dunty (NIAAA)
Deborah Henken (NICHD)
Danuta Krotoski (NICHD)
Mahua Mukhopadhyay (NICHD)
Charlene Schramm (NHLBI)
Lisa Brooks (NHGRI)
Daniel Gossett (NIDDK)
Dale Hereld (NIAAA)
Sheran Law (NICHD)
Pankaj Qasba (NHLBI)
Lillian Shum (NIDCR)
Kristin Burns (NHLBI)
Kimberly Gray (NIEHS)
Tyl Hewitt (NICHD)
Sara Lin (NHLBI)
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Karen Sirocco (NIDA)
James Coulombe (NICHD)
Tom Greenwell (NEI)
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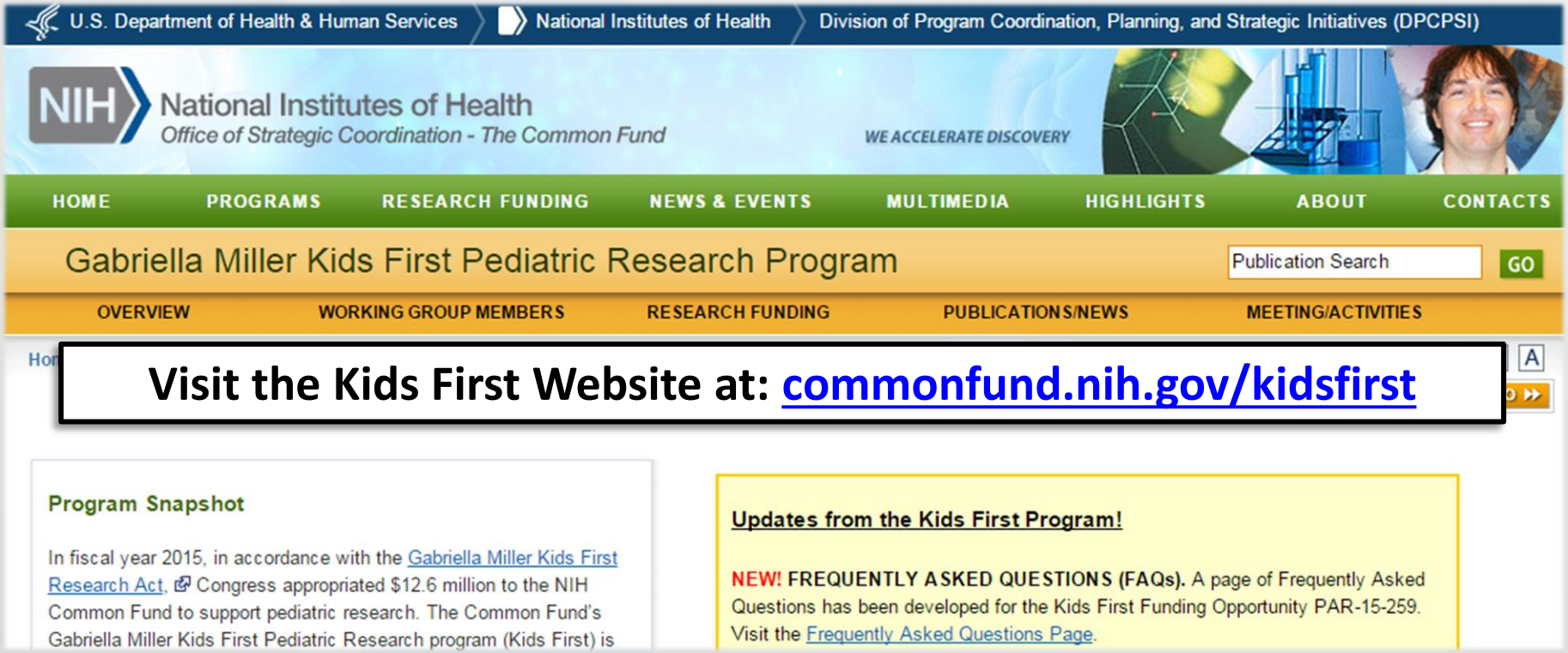
Kimberly McAllister (NIEHS)
Robert Riddle (NINDS)
Kathryn Stein (NIDCR)
John W. Thomas (NHLBI)
Hung Tseng (NIAMS)
Frosso Voulgaropoulou (NIAID)
Lu Wang (NHGRI)
Anastasia Wise (NHGRI)
Valerie Cotton Program Analyst (NICHD)
Della Hann (NICHD)
Mary Jenkins (CDC)
Bonnie Joubert (NIEHS)

Stay Up-To-Date on Kids First Activities



Get Updates through the Kids First Listserv
commonfund.nih.gov/kidsfirst/register

Receive Kids First Program Updates and Help to Spread the News

kidsfirst@od.nih.gov

Does your organization have connections with scientists in the research community who could be made aware of this program? If so, please let them know about this opportunity!

We Want to Know

- How do you anticipate that your organization would benefit from this program?
- What would success look like for this program? What are some short-term (3 year, 5 year, 10 year) metrics to measure success?
- If we are able to include additional activities in future years, what types of studies do you think would be most helpful?
- What sorts of information would you like to know as the data resource is being developed and about its use once it is established?
- How best can NIH keep the advocacy community apprised of the progress and activities of the Kids First program?

Submit Questions and Comments to the Kids First Mailbox

kidsfirst@od.nih.gov