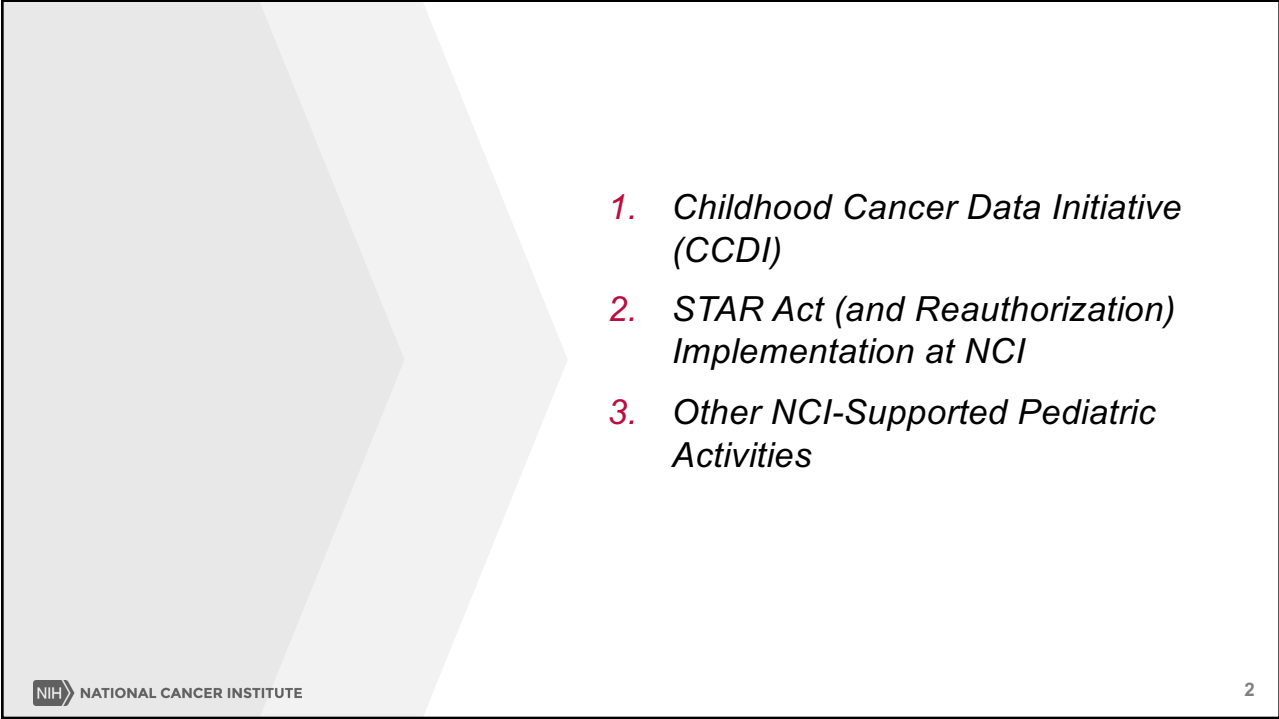# NCI Childhood Cancer Overview

Coalition Against Childhood Cancer (CAC2)

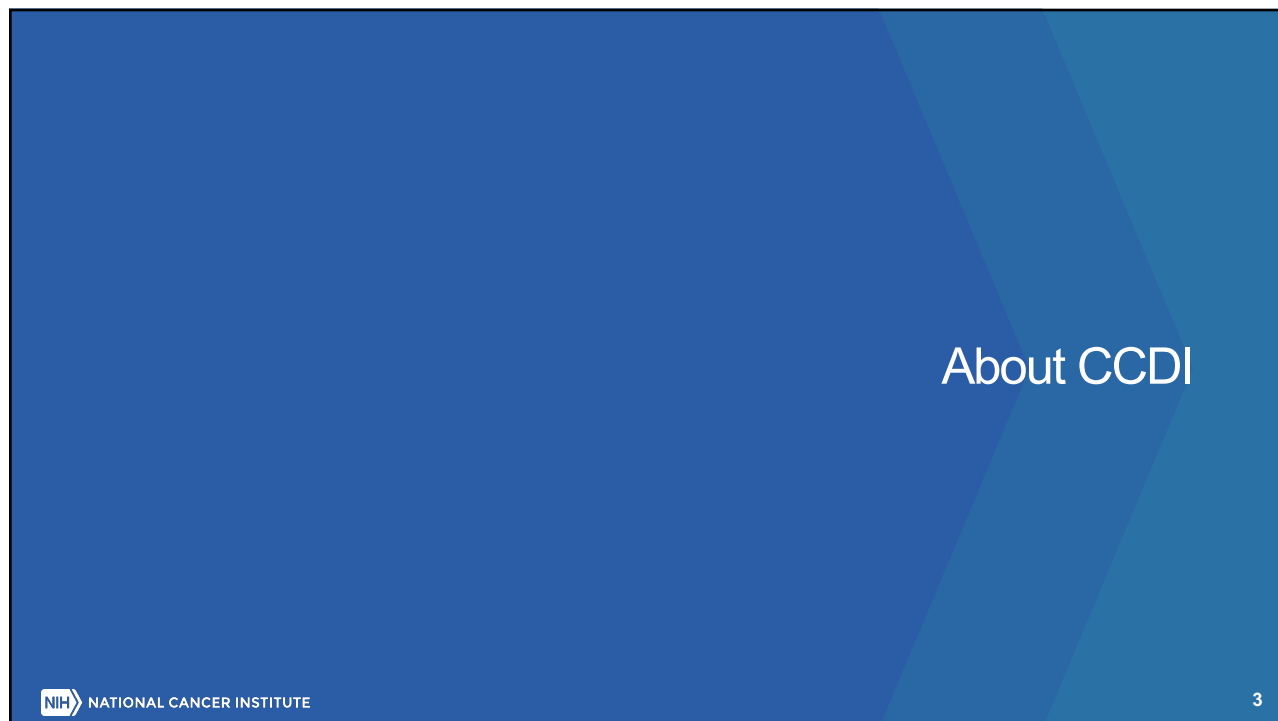**NIH⟩ NATIONAL CANCER INSTITUTE**

June 20, 2023

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1. *Childhood Cancer Data Initiative (CCDI)*
2. *STAR Act (and Reauthorization) Implementation at NCI*
3. *Other NCI-Supported Pediatric Activities*

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About CCDI

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DATA TYPES:

CCDI
BUILDING A COMMUNITY CENTERED AROUND CHILDHOOD CANCER CARE AND RESEARCH DATA

LEARN FROM EVERY CHILD

- CLINICAL
- TREATMENT
- OUTCOME
- MOLECULAR
- BIOSPECIMEN
- LONGITUDINAL
- POPULATION

Improving the quality, consistency, and accessibility of data to make it easier for researchers to develop new and better treatments for children with cancer.

Build a strong base: Progress requires data from many sources that is connected and easy to access.

Assemble better data: Complete data sets are needed to understand each type of cancer.

Make data easy to use: More thoughtful tools for analyzing data will help answer important questions.

Improve treatments and outcomes: Data is the foundation that informs new treatments and improves lives faster.
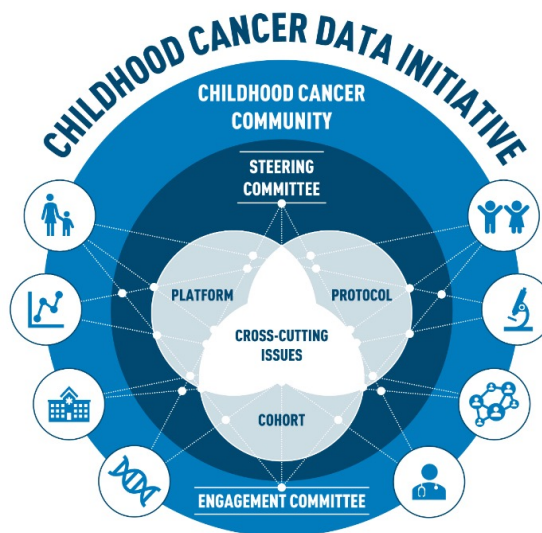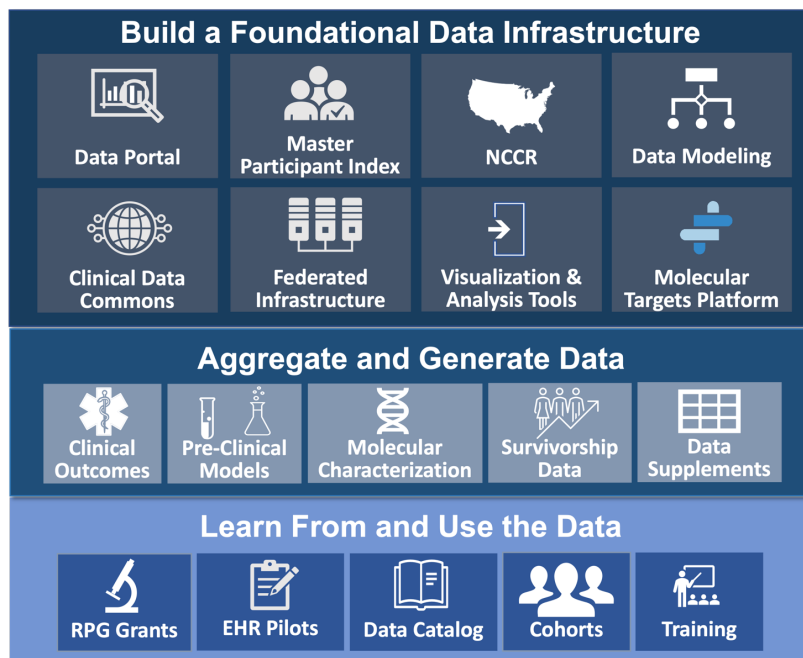
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CCDI's Structure

- CCDI is organized into committees and working groups that include diverse representation from the childhood cancer community
- Members include advocates, pediatric oncologists, researchers, data scientists, and others
- Scientific Director:
  - Dr. Gregory Reaman

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CCDI Publication

- Learn more about CCDI's progress and opportunities for the future of the initiative in a new *Journal of Clinical Oncology* paper
- "The Childhood Cancer Data Initiative: Using the Power of Data to Learn From and Improve Outcomes for Every Child and Young Adult with Pediatric Cancer" is available on open access:

  https://ascopubs.org/doi/10.1200/JCO.22.02208

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CCDI Events

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CCDI Events

NCI hosts several events that bring together the childhood cancer care and research community and:

- Feature presentations by subject matter experts
- Provide updates on CCDI progress and next steps
- Foster discussion around community data sharing needs

Event recordings, presentations, and summaries are on **cancer.gov/CCDI**

Thank you to everyone who has participated!

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CCDI Webinar Series: Upcoming Event

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CHILDHOOD CANCER DATA INITIATIVE WEBINAR

Using the CCDI Hub & Childhood Cancer Data Catalog

June 29, 2023
2:00 p.m.–3:00 p.m. ET

REGISTER TODAY
CANCER.GOV/CCDI

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Progress on the CCDI Data Ecosystem

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CCDI Data Ecosystem

- The CCDI Data Ecosystem is a connected network of tools and resources that will bring together clinical, research, and registry data on children, adolescents, and young adults (AYAs) with cancer from separate collections of data

- It will also provide tools to use the data in new ways

- Launched this year: The CCDI Hub, an entry point for user to access the resources in the Data Ecosystem

CCDI Hub

API Query Federation & Aggregation

Pediatric Cancer Data Commons (PCDC)
University of Chicago
API

St. Jude Cloud
St. Jude Children's Research Hospital
API

The Center for Data Driven Discovery in Biomedicine (D³b)
Children's Hospital of Philadelphia (CHOP)
API

Treehouse Child Cancer Initiative
UC Santa Cruz
API

Cancer Research Data Commons (CRDC)
National Cancer Institute
API

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CCDI Hub

- The CCDI Hub is an entry point for researchers, data scientists, and citizen scientists looking to use and connect with CCDI-related data

- It provides information and direct links to CCDI platforms, tools, and resources, along with additional technical information

- CCDI platforms and tools (discussed in upcoming slides) bring together data and allow us to use these data in new ways

ccdi.cancer.gov

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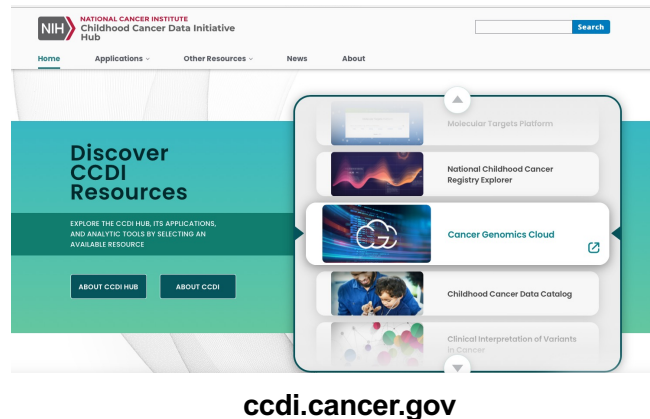
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Molecular Targets Platform (MTP)

- NCI's instance of the Open Targets Platform, specific to childhood cancers

- Allows users to find data from multiple sources on molecular targets (molecules involved in the growth and spread of cancer cells)

- Identifies targets, how they affect cancers, and how they interact with drugs, which can improve how childhood cancers are treated

- 40,929 molecular targets and 63 diseases

- Launched August 2022

moleculartargets.ccdi.cancer.gov

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National Childhood Cancer Registry (NCCR)

Leverage and link data from registries and other sources:

- Long-term data on treatment, procedures, outcomes, social determinants of health
- Clinical trials, survivorship studies, biospecimen, or tissue location
- Tumor and germline molecular characterization

All childhood cases from state registries

Reach consensus on pediatric cancer definitions and data standards

Share data from multiple, heterogenous data sources for analysis

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NCCR*Explorer

- Visualize statistics in dynamic tables and plots based on user criteria for patients diagnosed under age 40
- Sort data by sex, race and ethnicity, age, and type of cancer
- In the past year, >7,700 unique visitors produced >10,000 graphs
- Launched November 2021

nccrexplorer.ccdi.cancer.gov

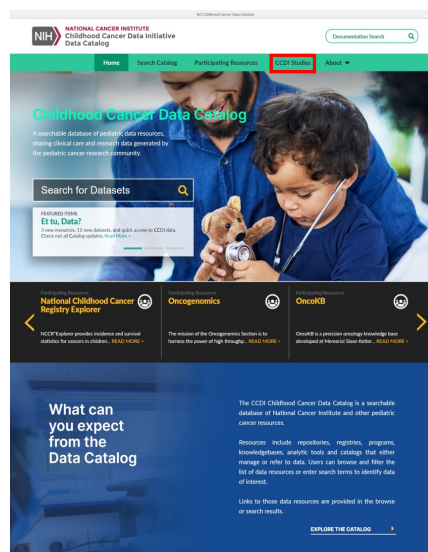NIH⟩ NATIONAL CANCER INSTITUTE

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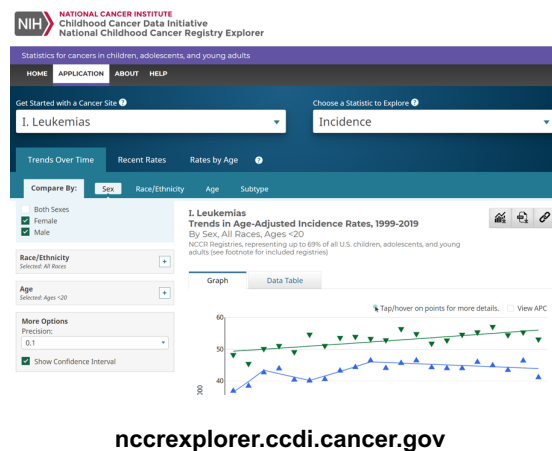
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Childhood Cancer Data Catalog

- An inventory of childhood cancer data resources
  - Repositories
  - Registries
  - Knowledge bases
  - Catalogs
- 41 resources, 203 datasets
- Launched April 2022

datacatalog.ccdi.cancer.gov

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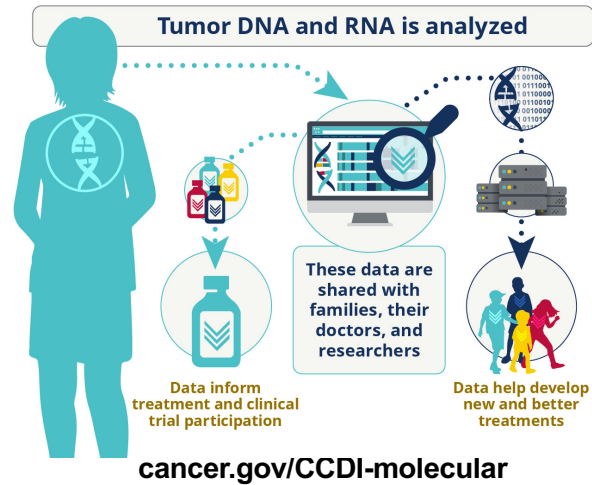
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CCDI Molecular Characterization Initiative

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CCDI Molecular Characterization Initiative (MCI)

- A partnership between NCI and COG Project:EveryChild; supports implementation of the STAR Act

- Provides state-of-the-art molecular characterization, which includes looking for fusions, at the time of diagnosis to inform the best and most appropriate treatment

- Results returned to participants and treating physicians within 21 days

- Remaining samples will be stored in a biobank for future research

Tumor DNA and RNA is analyzed

These data are shared with families, their doctors, and researchers

Data inform treatment and clinical trial participation

Data help develop new and better treatments

cancer.gov/CCDI-molecular

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Participation in the Molecular Characterization Initiative
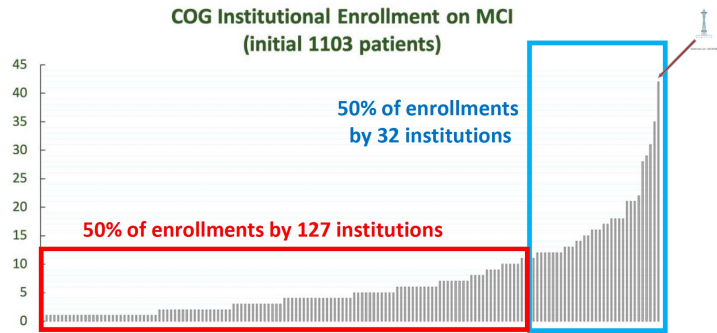
- **Participants must be:**
  - Child or AYA 25 years old or younger
  - Newly diagnosed
  - Diagnosed with a central nervous system tumor (tumors of the brain and spine), a soft tissue sarcoma, or a rare tumor
  - Obtaining care at Children's Oncology Group-affiliated hospital
  - Enroll on Project:EveryChild

In its first year, MCI enrolled more than 1,000 participants from 47 states, Canada, Australia, and New Zealand.

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Future Molecular Characterization Initiative Expansions

- Other cancer types:
  - High risk neuroblastoma (ANBL2131 enrollment scheduled to open fall 2023)
  - Proposed in concept for newly diagnosed metastatic Ewing sarcoma patients
  - Relapsed cancers
- Additional hospitals / centers
- Longitudinal cohort studies

COG Institutional Enrollment on MCI
(initial 1103 patients)

50% of enrollments
by 32 institutions

50% of enrollments by 127 institutions

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A National Initiative for Rare Cancers in Children, Adolescents, and Young Adults

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CCDI Coordinated National Study of Rare Childhood Cancers
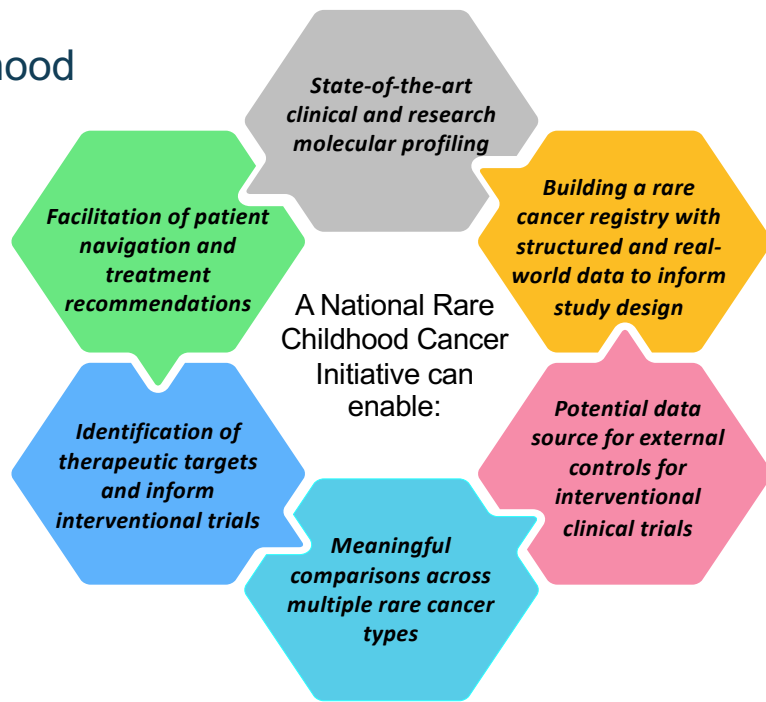
- **Background:**
  - Rare cancer is defined as less than 150 cases per million per year
  - Very rare pediatric cancer is defined as less than 2 cases per million per year (11% of all pediatric cancers)
- **Challenges:**
  - Accurate and timely diagnosis
  - Poor understanding of natural history and biology
  - Lack of standard therapy and treatment trials
  - Identification of centers with treatment expertise
- *A national effort will allow enrolling adequate numbers of participants to more rapidly, efficiently, and consistently study multiple rare cancers.*

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National Rare Childhood Cancer Initiative

A National Rare Childhood Cancer Initiative can enable:

- State-of-the-art clinical and research molecular profiling
- Building a rare cancer registry with structured and real-world data to inform study design
- Facilitation of patient navigation and treatment recommendations
- Potential data source for external controls for interventional clinical trials
- Identification of therapeutic targets and inform interventional trials
- Meaningful comparisons across multiple rare cancer types

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CCDI Coordinated National Study of Pediatric/AYA Rare Cancers

- Key elements of the proposed national rare cancer study will be synergistic with CCDI and other rare tumor efforts:

  - CCDI:
    - Conduct of longitudinal epidemiological cohort studies
      - Genetic tumor predisposition
    - Collect core clinical information on the Molecular Characterization Initiative (MCI)

  - Other efforts:
    - Support data collection and connection
    - Patient navigation
    - Portable patient owned medical record
    - Ability to follow patients longitudinally and facilitate data for survivorship studies

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STAR Act (and Reauthorization) Implementation at NCI

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STAR Act (and Reauthorization) Implementation at NCI

Examples below focus on **research provisions** within the STAR Act

NCI also continues to include pediatric expertise across advisory boards, steering committees, and other relevant groups, and continues to report to Congress and the public on childhood cancer research activities.

- Sec. 101. Children's cancer **biorepositories and biospecimen research** (including collaboration with CCDI)

- Sec. 202. Grants to improve care for **pediatric cancer survivors**

- Sec. 203. **Best practices** in survivorship care (AHRQ Evidence Reports supported by NCI)

- Through the **Childhood Cancer STAR Reauthorization Act** (FY2024-2028), NCI also plans to implement **Sec. 201 (a)**, focused on research to evaluate model systems of care for pediatric cancer survivors, including transition to adult care and care coordination

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NCI STAR Act Implementation Webinar *(September 12, 2022)*
*Available at: www.cancer.gov/star-act*

Malcolm Smith, MD, PhD
Associate Branch Chief,
Pediatrics in the Clinical Investigations Branch,
Division of Cancer Treatment and Diagnosis (DCTD)

Nita Seibel, MD
Head,
Pediatric Solid Tumor Therapeutics in the Clinical
Investigations Branch, Cancer Therapy and
Evaluation Program, DCTD

Emily Tonorezos, MD, MPH
Director,
Office of Cancer Survivorship, Division of Cancer
Control and Population Sciences (DCCPS)
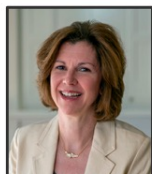
Sandra Mitchell, PhD, CRNP
Senior Scientist and Program Director,
Outcomes Research Branch in the Healthcare
Delivery Research Program, DCCPS

Danielle Daee, PhD
Program Director,
Genomic Epidemiology Branch, Epidemiology and
Genomics Research Program, DCCPS

Paul Jacobsen, PhD
Associate Director,
Healthcare Delivery Research Program, DCCPS

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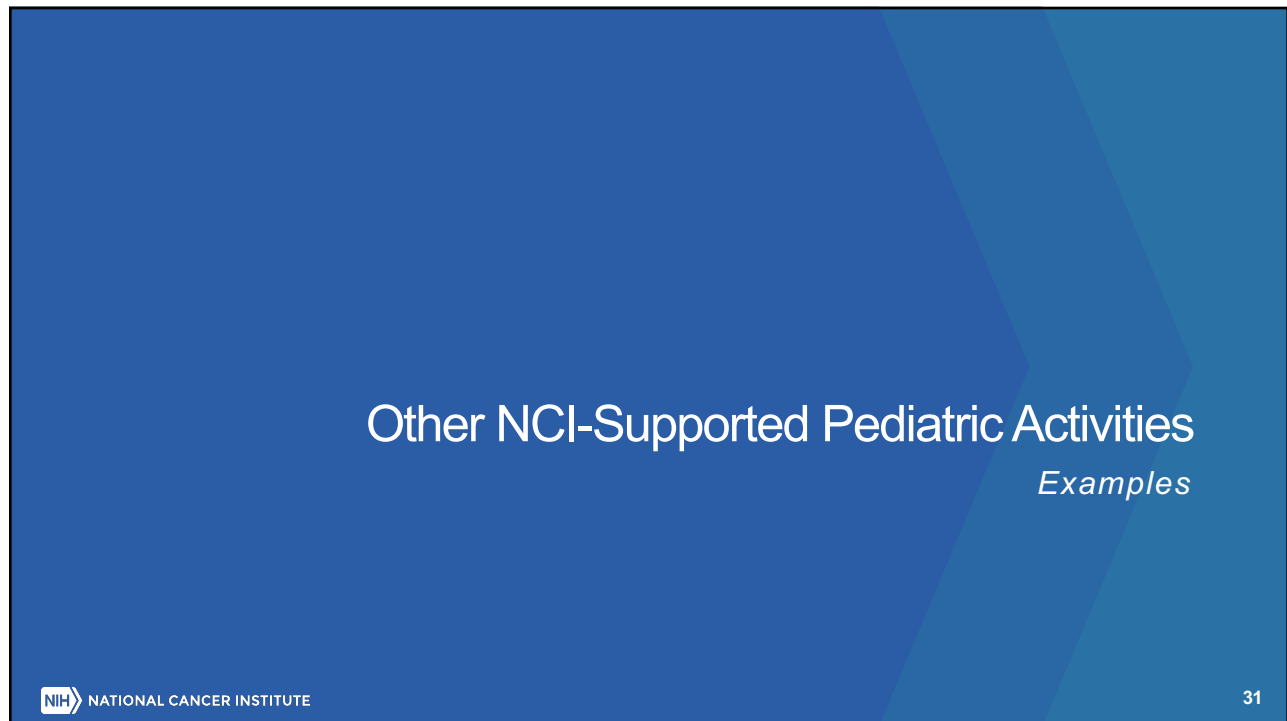## Childhood and AYA Survivorship Research (Sec. 202)

- NCI continues to support and conduct childhood and AYA cancer survivorship research through funding opportunity announcements and notices of special interest, as well as long-standing NCI-supported investments like the Childhood Cancer Survivor Study

- New STAR Act initiatives in survivorship through **2** funding announcements, with **31 awards issued** from FY 2019 – 2022 (**RFA CA-19-033** and **RFAs CA-20-027/028**), focused on developing effective interventions for childhood and AYA survivors

- **Notices of Special Interest (NOSI)** focusing on transitions in care, and on disparities affecting healthcare utilization and health outcomes (**NOT-HD-21-027** and **NOT-CA-22-029**)

Evidence Reviews in partnership with AHRQ Agency for Healthcare Research and Quality (Sec. 203)

- **Transitions of Care From Pediatric to Adult Services for Children With Special Healthcare Needs**

- **Models of Care That Include Primary Care for Adult Survivors of Childhood Cancer**

- **Disparities and Barriers for Pediatric Cancer Survivorship Care**

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Biobanking Progress (Sec. 101)

- New Biobanking Projects: supplement awards to the Childhood Cancer Survivor Study (CCSS)
  - Childhood Cancer Survivor Study: Somatic and Germline Sequencing
  - Banking of Blood on Childhood Cancer Survivors with Chronic Health Conditions
  - Gene Expression analyses of biospecimens CCSS with grade 3 and 4 health conditions
  - Whole genome/whole exome sequencing for additional specimens from CCSS Cohort

- New Biobanking Projects: supplement awards to the Children's Oncology Group (COG) Biobank
  - NCI-COG Pediatric MATCH Diagnostic Tumor Specimens
  - Postmortem Tumor Tissue Collection at Autopsy
  - Tumor Specimens from Patients at Relapse
  - Rare and Under-Represented Cancer Tissue Banking in partnership with the CCDI Molecular Characterization Initiative

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Other NCI-Supported Pediatric Activities

Examples
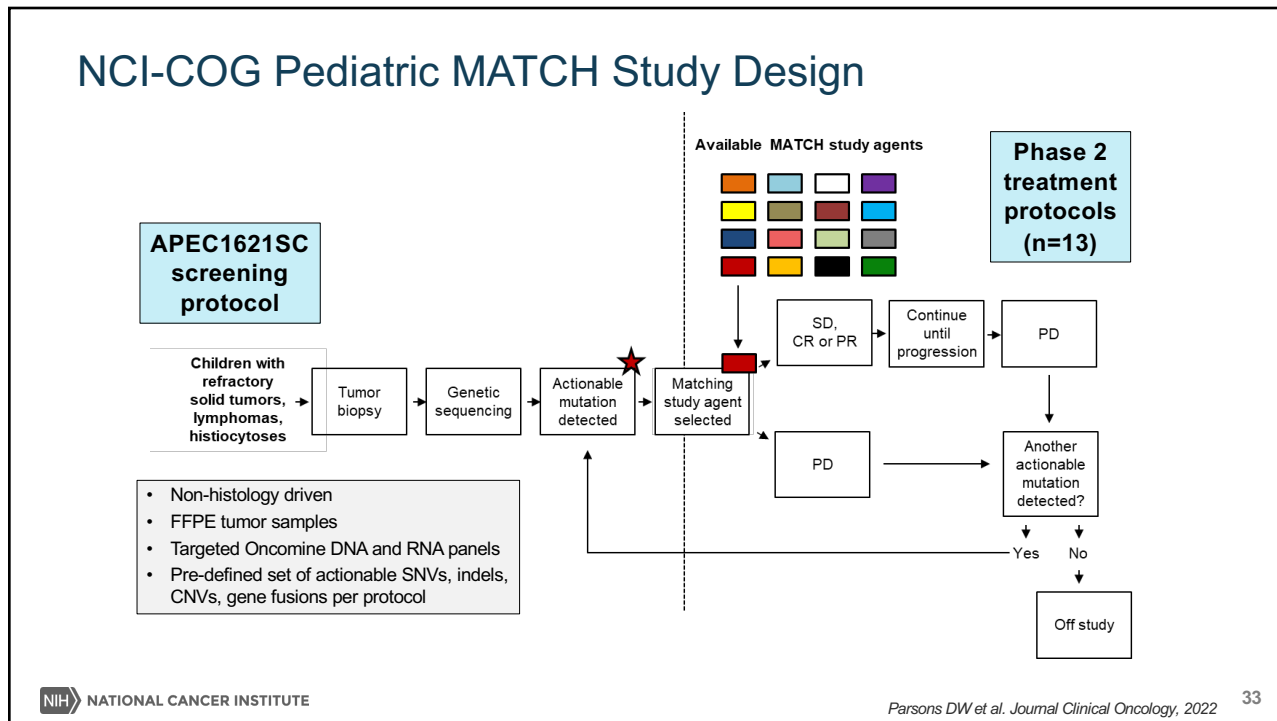
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Activities to be Covered

- Precision Medicine

- Adolescents and Young Adults (AYA)

- Childhood Cancer Survivorship

- Funding Opportunities -Pediatric Immunotherapy Network (PIN); Can-ACT; Fusion oncoproteins; Kids First

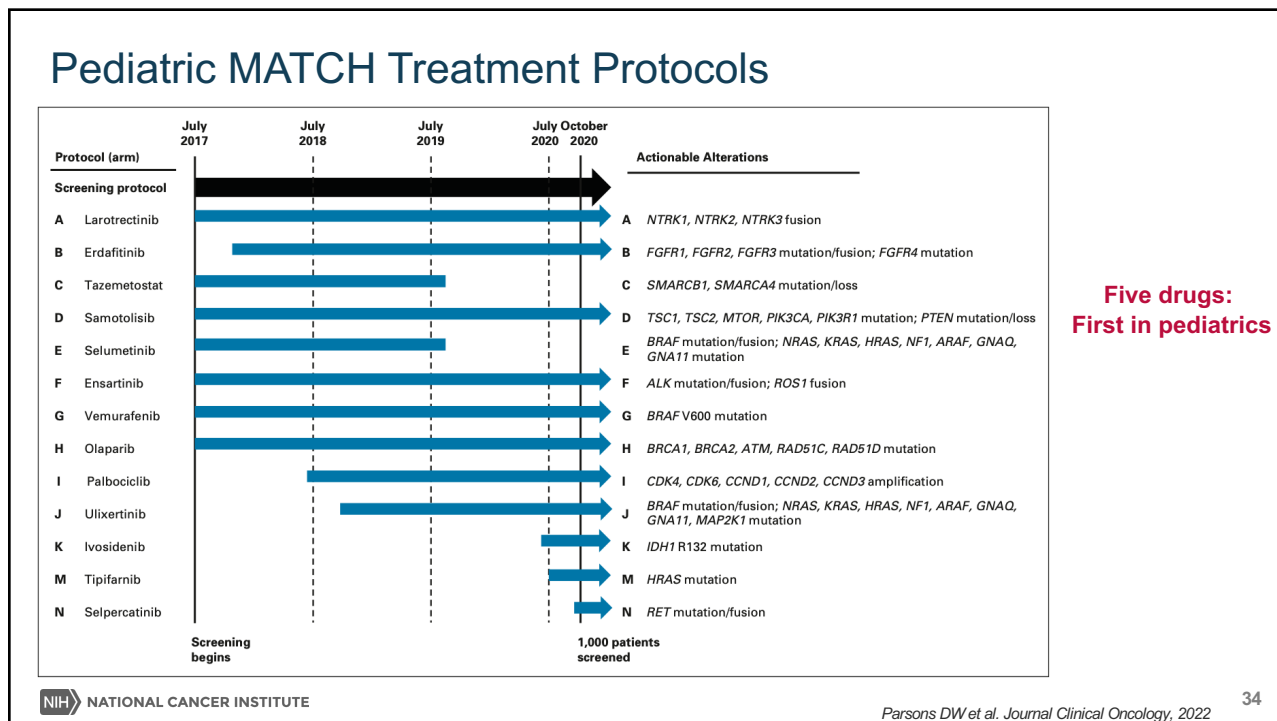- Cancer Grand Challenge (CGC)-Next Generation T Cells for Childhood Cancer; 2023 question

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NCI-COG Pediatric MATCH Study Design
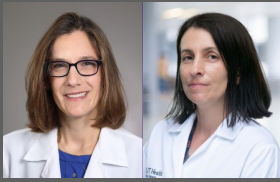
Available MATCH study agents

Phase 2 treatment protocols (n=13)

APEC1621SC screening protocol

Children with refractory solid tumors, lymphomas, histiocytoses → Tumor biopsy → Genetic sequencing → Actionable mutation detected → Matching study agent selected → SD, CR or PR → Continue until progression → PD

PD → Another actionable mutation detected? → Yes / No → Off study

- Non-histology driven
- FFPE tumor samples
- Targeted Oncomine DNA and RNA panels
- Pre-defined set of actionable SNVs, indels, CNVs, gene fusions per protocol

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Parsons DW et al. Journal Clinical Oncology, 2022   33

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Pediatric MATCH Treatment Protocols

Protocol (arm)		Actionable Alterations
	Screening protocol	
A	Larotrectinib	A *NTRK1, NTRK2, NTRK3* fusion
B	Erdafitinib	B *FGFR1, FGFR2, FGFR3* mutation/fusion; *FGFR4* mutation
C	Tazemetostat	C *SMARCB1, SMARCA4* mutation/loss
D	Samotolisib	D *TSC1, TSC2, MTOR, PIK3CA, PIK3R1* mutation; *PTEN* mutation/loss
E	Selumetinib	E *BRAF* mutation/fusion; *NRAS, KRAS, HRAS, NF1, ARAF, GNAQ, GNA11* mutation
F	Ensartinib	F *ALK* mutation/fusion; *ROS1* fusion
G	Vemurafenib	G *BRAF* V600 mutation
H	Olaparib	H *BRCA1, BRCA2, ATM, RAD51C, RAD51D* mutation
I	Palbociclib	I *CDK4, CDK6, CCND1, CCND2, CCND3* amplification
J	Ulixertinib	J *BRAF* mutation/fusion; *NRAS, KRAS, HRAS, NF1, ARAF, GNAQ, GNA11, MAP2K1* mutation
K	Ivosidenib	K *IDH1* R132 mutation
M	Tipifarnib	M *HRAS* mutation
N	Selpercatinib	N *RET* mutation/fusion

July 2017 — July 2018 — July 2019 — July 2020 October 2020

Screening begins — 1,000 patients screened

Five drugs: First in pediatrics

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Parsons DW et al. Journal Clinical Oncology, 2022   34

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Childhood Cancer Survivor Study (CCSS): Expanding Resources

Specific causes of excess late mortality and association with modifiable risk factors among survivors of childhood cancer: a report from the Childhood Cancer Survivor Study cohort

Stephanie B Dixon, Qi Liu, Eric J Chow, Kevin C Oeffinger, Paul C Nathan, Rebecca M Howell, Wendy M Leisenring, Matthew J Ehrhardt, Kirsten K Ness, Kevin R Krull, Ann C Mertens, Melissa M Hudson, Leslie L Robison, Yutaka Yasui, Gregory T Armstrong

- Pilot study: Feasibility and validity of automated electronic health record (EHR)-based data collection of multi-institutional, cumulative dose chemotherapy data on childhood cancer survivors treated between 2020 and 2022 (CCDI)

- Pilot study: Feasibility of collecting multi-institutional, multi-modality contemporary radiotherapy data and generation of organ- and body-region dosimetry for childhood cancer survivors treated between 2000 and 2022 (STAR Act)

- Whole genome/whole exome sequencing of additional germline specimens from CCSS Cohort an additional 1,470 survivors not previously sequenced (CCDI)

- Contacting participants with grade 3 and 4 chronic health conditions to collect blood specimens that will be banked and made available for researchers (STAR Act)

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Dixon S et al. Lancet, 2023 36

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Pediatric Immunotherapy Network (PIN)

Background

- Building on the success of Cancer Moonshot-funded Pediatric Immunotherapy Discovery and Development Network (PI-DDN)

Structure

- U01 Research Projects

  - "U" funding mechanism: Cooperative agreement with substantive NCI scientific and programmatic involvement


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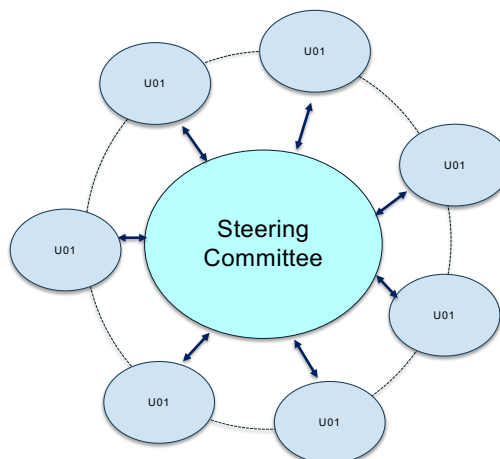
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Cancer Adoptive Cellular Therapy Network (Can-ACT)

Purpose: Foster innovation, promote early-stage clinical testing of novel cell-based immunotherapies for solid tumors

Structure:

- Separate **UG3/UH3** for adult and pediatric cancers (7 total)

- Each two-phased UG3/UH3 will conduct

  - UG3: preclinical, IND-enabling studies of ACT (2yr)

  - UH3: early phase clinical trials of ACT (3yr)

NCI Resource: Immune Cell Network Core at FNLCR can be used for multi-center trials

NCI/FNLCR Resources
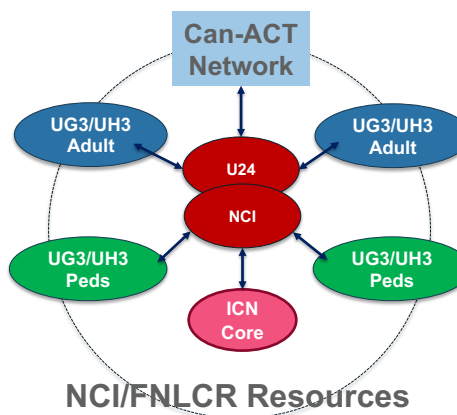
Can-ACT for **Adult** Cancers (RFA-CA-22-028)

Can-ACT for **Pediatric** Cancers (RFA-CA-22-029)

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Fusion-Driven Oncogenesis in Childhood Cancers

- Intensify research on major drivers of childhood cancers
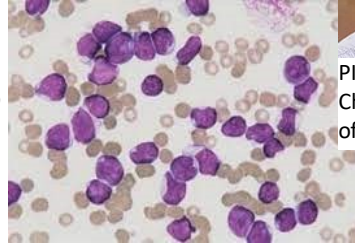- Fusion Oncoproteins in Childhood Cancers Consortium

- New initiative, the Targeting Fusion Oncoproteins in Childhood Cancers (TFCC) Network
  - Identifying and developing novel treatment strategies for childhood cancer fusion oncoproteins
  - Mechanisms of Fusion-Driven Oncogenesis in Childhood Cancers (NOT-CA-23-058) to be published June 29, 2023-UM1 Next Generation Chemistry Centers for Fusion Oncoproteins
  - Mechanisms of Fusion-Driven Oncogenesis in Childhood Cancers (NOT-CA-23-057); to be published June 29, 2023-UO1
    - Goal is to identify potential drug targets

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Gabriella Miller Kids First Research Act

- Transfers 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
- **Focus on genetics of childhood cancers & structural birth defects**
- X01 "grants" provide sequencing services for informative cohorts (germline and tumor; options for WGS/WES/RNA-seq)
- PAR-23-035: X01 solicitation for FY2023, Applications were due in March 2023

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New Childhood Cancer Public Data Releases

- September 26, 2022, Gabriella Miller Kids First Pediatric Research Program in Pediatric T-Cell Acute Lymphoblastic Leukemia

- Outcome for patients with relapsed T-ALL is dismal: 3-year event free survival of <15%

- Primary treatment goal of T-ALL is to prevent relapse, which requires accurate risk stratification. No genetic alterations have been identified to date that are reproducibly prognostic independent of minimal residual disease, making it difficult at diagnosis to identify patients likely to relapse

PI: David T. Teachey, Children's Hospital of Philadelphia

- ~1,350 cases of T-ALL from children and young adults treated on AALL0434 were selected for whole genome sequencing, whole exome sequencing, and transcriptome profiling (RNA-Seq) of tumor DNA/RNA and whole genome sequencing of germline DNA

- Clinical Trial: NCT00408005

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Cancer Grand Challenges
Next Generation T-Cells for Childhood Cancers

NGTC

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and move it forward!

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cancer.gov/CCDI

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