

# Using the CCDI Molecular Targets Platform

*CCDI Webinar Series*

1. *CCDI Hub*
2. *Overview of the Molecular Targets Platform (MTP)*
3. *Demonstration of MTP Pediatric Cancer Data Navigation*
4. *MTP Use Cases*

# CCDI Hub: [ccdi.cancer.gov](https://ccdi.cancer.gov)

Entry point to use and connect with CCDI applications, data, tools, and other resources

The screenshot shows the top navigation bar with the NIH logo and 'NATIONAL CANCER INSTITUTE Childhood Cancer Data Initiative Hub'. Below the navigation are sections for 'Discover CCDI Resources' and a grid of application cards including 'Molecular Characterization Initiative for Childhood Cancer', 'Molecular Targets Platform', 'National Childhood Cancer Registry Explorer', 'Cancer Genomics Cloud', and 'Childhood Cancer Data Catalog'.

## CCDI Stats At a Glance

**223**  
Cataloged Datasets  
Childhood Cancer  
Data Catalog

**1,303**  
Participants  
Molecular  
Characterization  
Initiative for  
Childhood Cancer

**58,867**  
Potential Pediatric  
Molecular Targets  
Molecular Targets  
Platform

**1,496,577**  
Reported Cases  
Under Age 40  
(1995-2020)  
National Childhood  
Cancer Registry  
Explorer

## Latest Updates

**Childhood Cancer Data Catalog April Update**  
The update includes one new resource, eight new datasets, and many other changes. [Read More >](#)

**Molecular Characterization Initiative releases initial data**  
Genomics and clinical data for MCI participants is housed in NCI's Cancer Data Service and accessible through CGC. [Read More >](#)

**CCDI Symposium features Data Ecosystem Progress**  
More than 800 people came together to discuss CCDI progress, including in the Data Ecosystem. [Read More >](#)

## CCDI APPLICATIONS

**CCDC** Childhood Cancer Data Catalog (ccdc) [🔗](#)  
A searchable inventory of childhood cancer resources.

**CIViC** Clinical Interpretation of Variants in Cancer (civic) [🔗](#)  
An open access, open source, community-driven web resource for clinical interpretations of mutations related to cancer.

**MCI** Molecular Characterization Initiative for Childhood Cancers (mci) [🔗](#)  
A program providing molecular testing for children, adolescents, and young adults with certain cancer types.

**MTP** Molecular Targets Platform (mtp) [🔗](#)  
An instance of the Open Targets Platform with a focus on childhood cancer data that allows users to browse and identify associations between molecular targets, diseases, and drugs.

**NCCR Explorer** National Childhood Cancer Registry Explorer (nccr Explorer) [🔗](#)  
A tool to browse demographic, incidence, and survival statistics for cancers in children, adolescent, and young adults.

## OTHER RESOURCES

**CGC** Cancer Genomics Cloud (cgc) [🔗](#)  
A cloud-based platform to access and analyze cancer research data.

**dbGaP** Database of Genotypes and Phenotypes (dbgap) [🔗](#)  
A database to store and distribute data and results from studies examining the interaction of genotypes and phenotypes.

# Overview of CCDI Molecular Targets Platform

*Big Data Approach to Provide Evidence*

# Thank You to Everyone Who Helped Build the MTP!

## National Cancer Institute, Food and Drug Administration, and Frederick National Laboratory

Alemayehu Akalu	Tony Kerlavage
Yizhen Chen	Rena Kingery
Rosane Charlab Orbach	Shea Buckman Manley
Sisley Chung	Anna Mencarelli
Mark Cunningham	Gayathri Radhakrishnan
Cole Devries	Gregory Reaman
Zachary Dorman	Bonny Sheppard
Valentina Epishina	Malcolm Smith
Samantha Gonzalez	Hannah Stogsdill
Jaime Guidry Auvil	Nahom Tesfatsion
Sarah Hunter	Natavia Vineyard
Subhashini Jagu	Megan Walsh
Anita Johnson	Shawn Wang
Sowmya Karavadi	Cindy Winter

## Foundation for the National Institutes of Health

Stacey Adam  
Tetyana Murza

## Children's Hospital of Philadelphia

Christopher Blackden	Matthew Lueder
Miguel Brown	John Maris
Asif Chinwalla	Daniel Miller
Ryan Corbett	Saksham Phul
Sharon Diskin	Komal Rathi
Brian Ennis	Adam Resnick
Alvin Farrel	Jo Lynne Rokita
Bailey Farrow	Sangeeta Shukla
Krutika Gaonkar	Alex Sickler
Zhuangzhuang Geng	Sarah Tasian
Dave Hill	<b>Deanne Taylor</b>
Xiaoyan Huang	Nicholas Van Kuren
Run Jin	Eric Wafula
Kelsey Keith	Yuanchao Zhang
Adam Kraya	Bo Zhang
Aditya Lahiri	Yuankun Zhu

## European Molecular Biology Laboratory

Annalisa Buniello  
Miguel Carmona  
Helena Comu  
Andrew Hercules  
Manuel Bernal Llinares  
Ellen McDonagh



# CCDI Working Group Report

24 specific recommendations



Landscape of Pediatric/AYA Cancer Research Data & Needs Analysis



Types of Data for Collection and Aggregation



Potential Barriers to Progress



Generating New Data



Distinction Between Research & Clinical Data



Engaging Diverse Array of Stakeholders for Input



Potential Opportunities for Transformative Discoveries

# Strategic Plan

- Established a collaborative working group of multi-disciplinary investigators from the National Cancer Institute (NCI), US Food and Drug Administration (FDA), Foundation for the National Institutes of Health (FNIH), and Children's Hospital of Philadelphia (CHOP).
- Adopted the open source Open Targets Portal ([opentargets.org](https://opentargets.org)) for pediatric cancer drug development in collaboration with European Molecular Biology Laboratory.
- Developed a node within the CCDI Data Ecosystem to provide the computational infrastructure for academics, industry partners, and advocates to support pediatric cancer drug development.



# Open Targets Platform

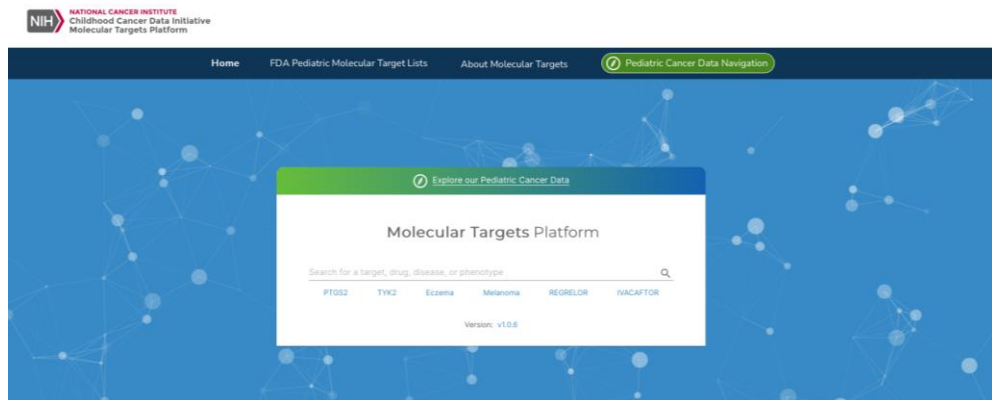
- A knowledgebase and prioritization tool sourced from numerous public datasets.
- Reduces time spent monitoring and organizing scientific literature.
- A public-private partnership with several large pharmaceutical and biomedical research institutions.
- Includes a broad range of harmonized targets, diseases, and drugs.





# CCDI Molecular Targets Platform

- NCI's instance of the Open Targets Platform with a focus on pediatric cancers (launched Aug 2022).
- Allows users to browse and identify associations between molecular targets, diseases, and drugs.
  - 58,867 molecular targets and 64 diseases within the childhood cancer data.
- Includes a computable interpretation of 215 targets from the FDA Relevant Molecular Target List (Sep 2022 release).

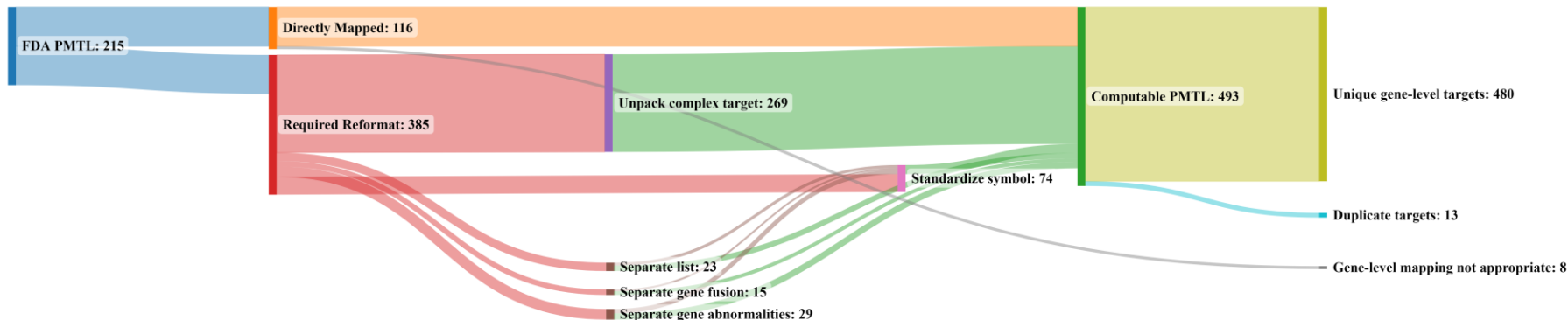


[moleculartargets.ccdi.cancer.gov](https://moleculartargets.ccdi.cancer.gov)

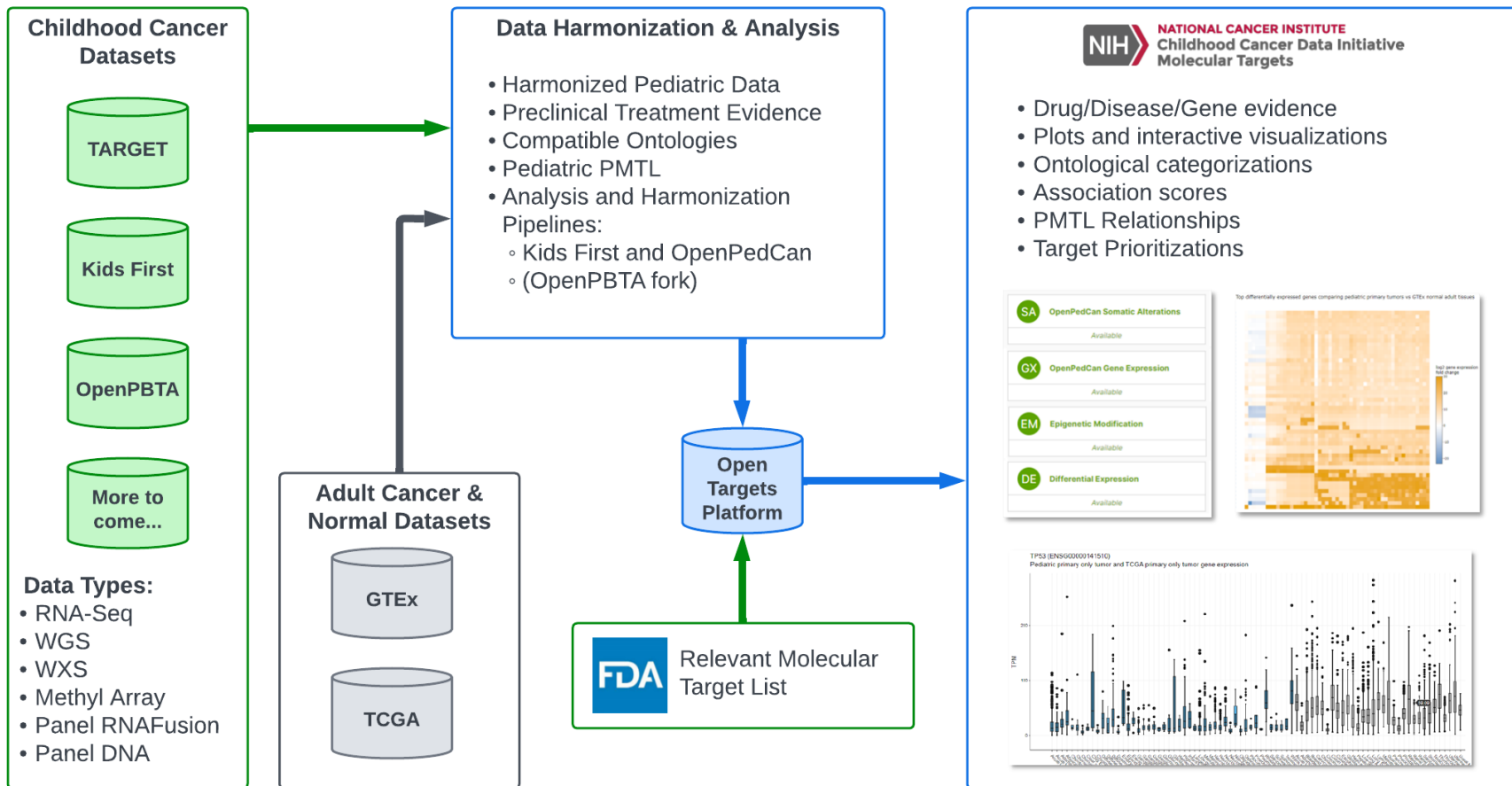
# Computable Pediatric Molecular Target Lists (PMTL)

- The FDA [released two lists](#) to address the needs of the RACE Act, which were processed into the PMTL for MTP.
  - **Relevant Molecular Target List:** targets have evidence indicating their relevance in the growth or progression of pediatric cancers. Any new drugs developed for these targets in adult cancers must also be studied for use in pediatric cancers.
  - **Non-Relevant Molecular Target List:** targets have evidence indicating that they are not relevant in the growth or progression of pediatric cancers. Any new drugs developed for these targets in adult cancers will receive an automatic waiver from also studying them in pediatric cancers.

215 targets in FDA Relevant and Non-Relevant Lists → 480 unique, gene-level targets in Computable PMTL (501 including duplicates and non-gene targets)



# MTP: Data Flow



# MTP Pediatric Cancer Data Navigation



*Demonstration*

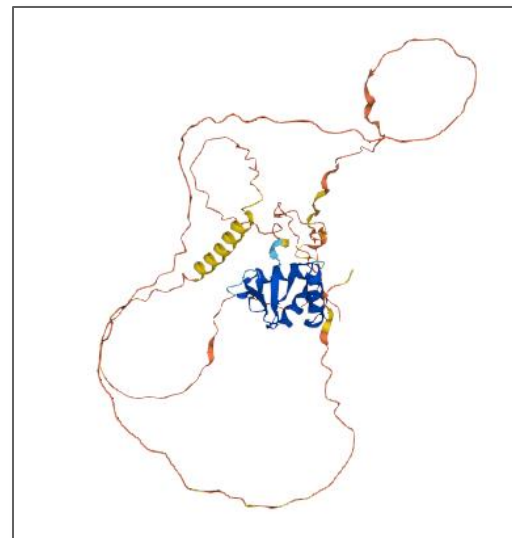
# CCDI Molecular Targets Platform Use Cases

*Demonstration*

# Use Case #1: Using MTP to Explore Drug Development

- A lead researcher in a drug company is interested in a particular gene (ETS1) found on the FDA's PMTL list.
- In MTP, the PMTL list has been curated and expanded to include gene family members which are not on the FDA's website (in particular, ETV3L, a member of the ETS transcription factor family).
- If we have an effective treatment for adults with ETV3L mutations, then finding pediatric data for ETV3L mutations could lend support to justify setting up a pediatric cancer clinical trial for this drug.

 **ETV3L** ETS variant transcription factor 3 like  
Ensembl: [ENSG00000253831](#) | UniProt: [Q6ZN32](#) | GeneCards: [ETV3L](#) | HGNC: [ETV3L](#)  
FDA PMTL: **Relevant Molecular Target** 



# Use Case #2: Using MTP to Explore Mutations


- What is the landscape of FGFR3 mutations in all pediatric cancers?
- Do they exist with a frequency useful for development, and are there specific histologies where they are enriched?
- Investigators may want to know about any somatic alterations (SNVs, CNVs, Fusions), including splice variants, to understand protein-domain specific drugs.
- We can explore the MTP to determine if there are splice variants present in a particular pediatric cancer.

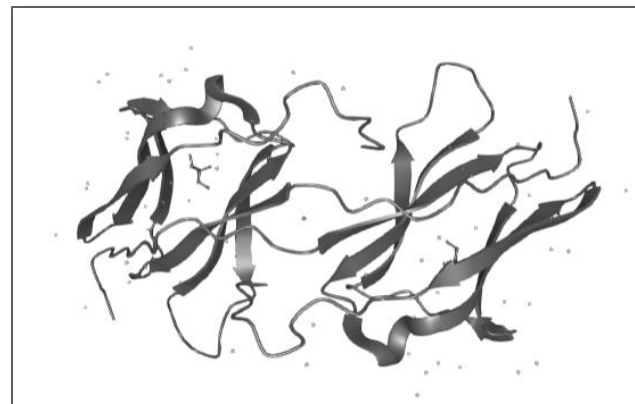
 **FGFR3** fibroblast growth factor receptor 3  
Ensembl: [ENSG00000068078](#) | UniProt: [P22607](#) | GeneCards: [FGFR3](#)  
FDA PMTL: [Relevant Molecular Target](#) 



# Use Case #3: Using MTP to Explore Clinical Trial Opportunity

- A drug company has a new pan-TRK inhibitor that crosses the blood-brain barrier and would like to develop this drug for pediatric brain tumors.
- To set up a clinical trial, we need to know what types of brain tumor histologies have TRK fusions and in what frequency.
- We also want to see expression levels of NTRK1-3 across pediatric brain tumor histologies.


 **NTRK1** neurotrophic receptor tyrosine kinase 1  
Ensembl: [ENSG00000198400](#) | UniProt: [P04629](#) | GeneCards: [NTRK1](#)  
FDA PMTL: [Relevant Molecular Target](#) **R**

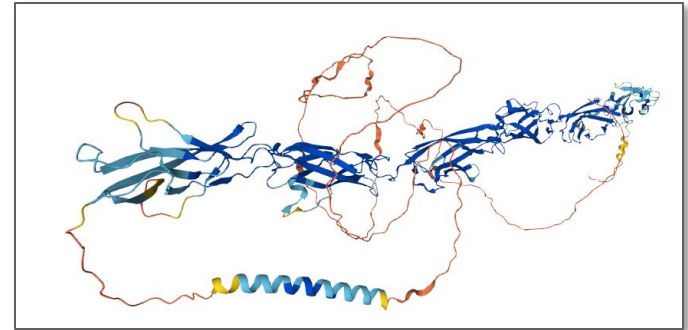




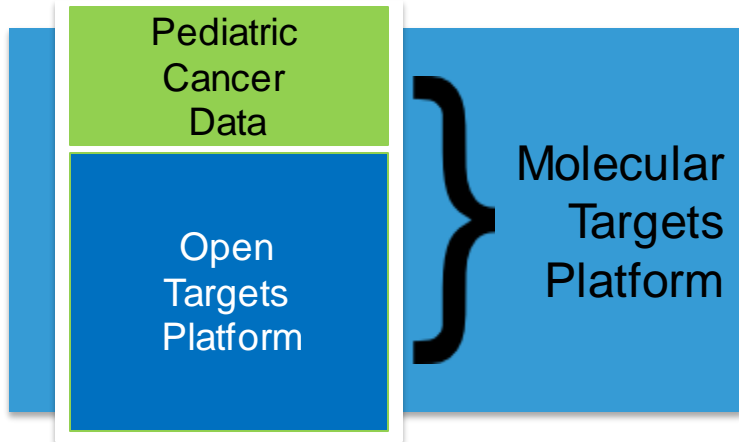
# Use Case #4: Using MTP to Help Researchers Plan Additional Experiments

- As a researcher, my experiments have shown incidentally that a gene has little known function in cancer but is associated with HLHS cardiac syndrome and neurodevelopmental impairment.
- PCDHA9 has very high mRNA expression in adult oligodendroglioma cancer cell lines.
- I'm wondering if any pediatric brain cancer patients from various data sets represented in MTP also show this trend of high mRNA expression?

 **PCDHA9** protocadherin alpha 9  
Ensembl: [ENSG00000204961](#) | UniProt: [Q9Y5H5](#) |  
FDA PMTL: **Unspecified Target** ?



# Summary



Allows users to identify associations between molecular targets, diseases, and drugs

Uses FAIR and Computable Pediatric Molecular Target Lists to allow the research community to explore molecular targets relevant to the growth or progression of childhood cancers

The addition of childhood cancer data within MTP has yielded childhood-cancer specific views and utility to the research community

\*September 2022 release

# Soliciting Feedback!

## Gene/Target-Centric Platform:

- Should we develop a gene/target-centric platform that leverages the Computable PMTL, incorporates the necessary genomics data, and enriches the platform with relevant evidence for each gene?

## Incorporate New Data Sets:

- Should we include new data sets and if so, what is your feedback on introducing these new data sets without undergoing a complete harmonization process with the existing data sets?

## Ideal Home Page:

- Should we keep the main search home page inherited from Open Targets as-is, or should we allow users to land directly on the Pediatric Cancer Data Navigation page as the site entry point?

## Find Out More About CCDI

**Visit the CCDI Hub and access the  
CCDI Data Ecosystem.**

[ccdi.cancer.gov](https://ccdi.cancer.gov)

**Subscribe to our monthly newsletter.**

[cancer.gov/CCDI](https://cancer.gov/CCDI)

**Questions? Email us.**

[NCIChildhoodCancerDataInitiative@mail.nih.gov](mailto:NCIChildhoodCancerDataInitiative@mail.nih.gov)



*Thank you for attending!*

U.S. Department of Health & Human Services  
National Institutes of Health | National Cancer Institute

cancer.gov  
1-800-4-CANCER

