Childhood Cancer Data Initiative Virtual Symposium Series

Philip Lupo, Brenda Weigel, and Michael Cox

NIH NATIONAL CANCER INSTITUTE

April 7, 2026

Today's Speakers

Philip Lupo, Ph.D., M.P.H.

- Professor, Pediatrics, Emory University
- Co-Director, REACH Center, Pediatric Children's Alliance
- Chair, Epidemiology Committee, Children's Oncology Group

Brenda Weigel, M.Sc., M.D.

- Vice President, Clinical Research Industry Engagement, St. Jude Children's Research Hospital

Michael Cox, Pharm.D., M.H.Sc., BCOP

- Principal, Martian Clinical Consulting

Agenda

1. *Strategies for Follow Up and Potential Interventions for Patients with Pathological or Likely Pathological Germline Variants*
   - *Q&A*
2. *Genomic and Epigenomic Characterization of Childhood Cancer: Clinical Trials and New Drug Discovery and Development – Academic and Industry Perspectives*
   - *Q&A*
3. *Abstract Awards and Lightning Oral Presentations*

Childhood Cancer Data Initiative Virtual Symposium Series

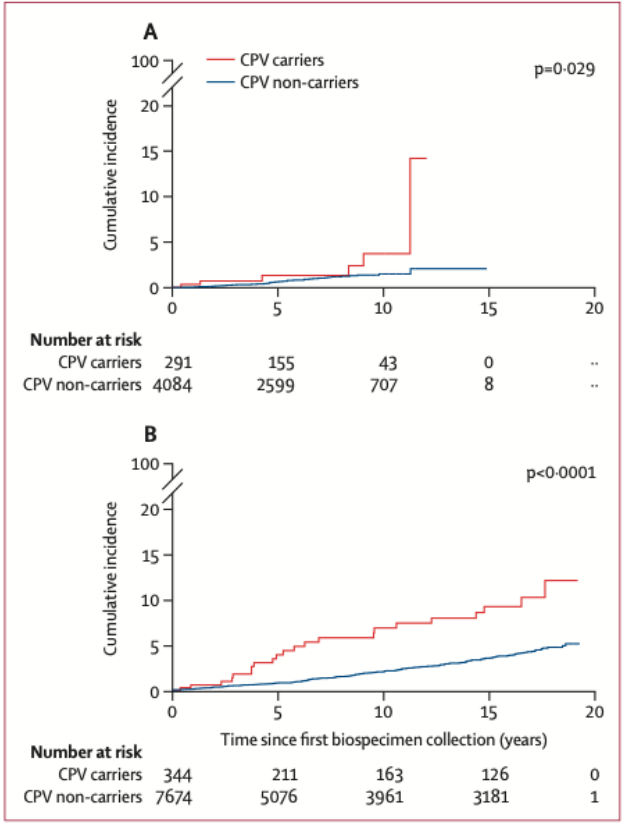
Strategies for Follow-up and Potential Interventions for Patients with Pathogenic or Likely Pathogenic Germline Variants

Philip J. Lupo, Ph.D.

NIH NATIONAL CANCER INSTITUTE

Childhood Cancer Predisposition

- **~10-15% of children with cancer have a cancer predisposition variant (CPV)**
  - Zhang et al, *NEJM*, 2015: **8.5%** (95/1,120)
  - Parsons et al, *JAMA Onc*, 2016: **10%** (15/150)
  - Akhavanfard et al, *Nature Comm*, 2020: **12%** (182/1,507)
  - Villani et al, *Nature Cancer*, 2022: **15%** (46/300)
  - Many more
- **~5% of childhood cancer survivors have a cancer predisposition variant (CPV)**
  - Kim et al, *JNCI Cancer Spectrum*, 2021: 4.1% (211/5,105)
  - Chen et al, *Lancet Oncol*, 2023: 5.1% (641/12,469)
  - Stoltze et al, *Clin Cancer Res*, 2025: 4.4% (15/344)

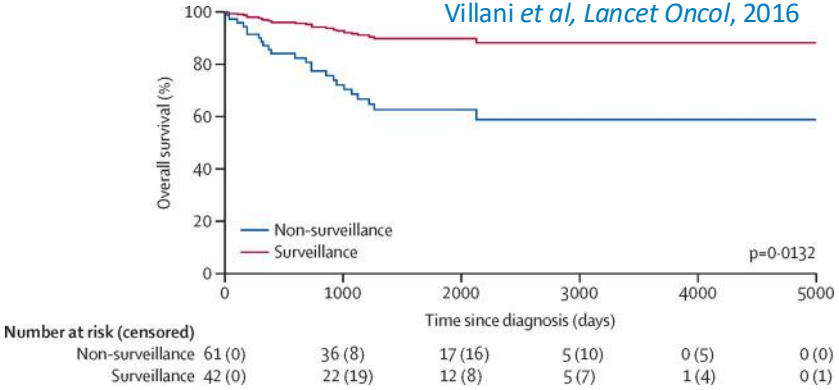


Chen et al, Lancet Oncol, 2023

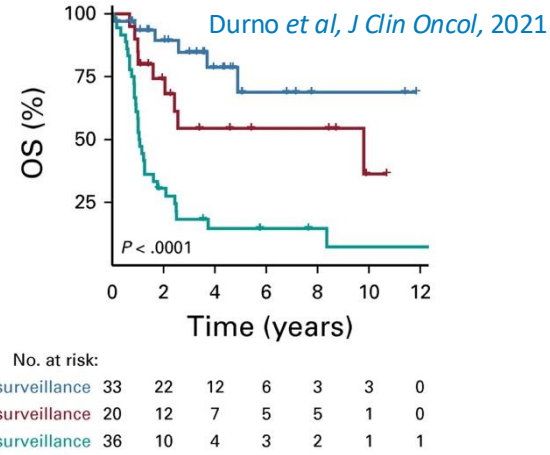
Implications for Treatment and Prevention

- Cancer prevention strategies
- Cancer treatment may be influenced by diagnosis of cancer predisposition syndrome (CPS)
  - Down syndrome
  - Fanconi anemia
- Cascade testing may identify additional family members
- Diagnosis of CPS may influence family planning
- Tumor surveillance may improve outcomes

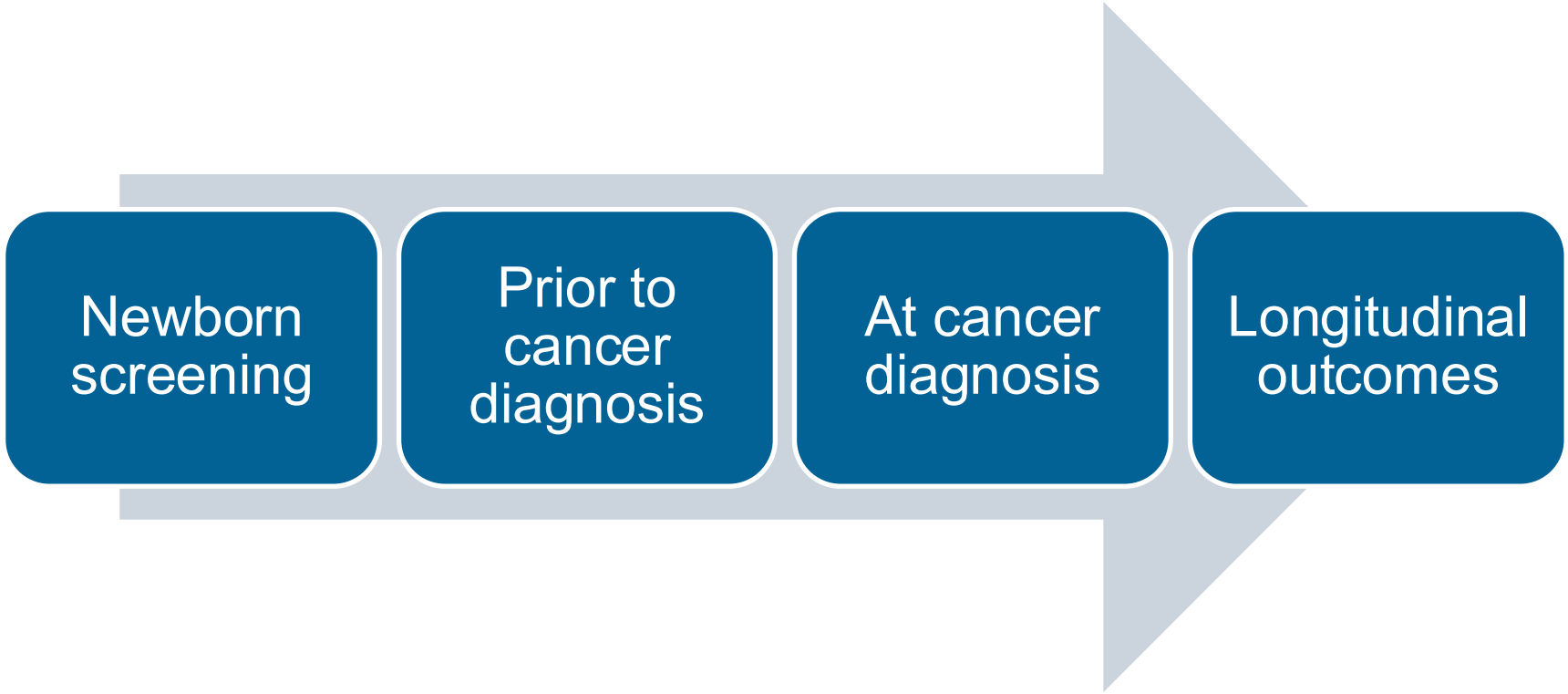
Villani *et al, Lancet Oncol*, 2016



Durno *et al, J Clin Oncol*, 2021



Cancer Predisposition Across the Continuum



Studies to Address Issues Across the Continuum

- ***Newborn screening (NBS)***
  - Implementing Newborn Screening for Pediatric Cancer Predisposition Syndromes in Texas: **INSPECT**
  - Newborn Cancer Risk Evaluation: **N-CARE**
- ***Prior to cancer diagnosis***
  - Consortium for Childhood Cancer Predisposition: **C3P**
  - Childhood Cancer Predisposition Study: **CCPS**
- ***At cancer diagnosis and beyond: Molecular Characterization Initiative (MCI)***
  - Outcomes and Health Risks among Individuals with Genetic Predispositions to Cancer: **ORIGen**
  - Genetic Information for Families after Tumor Testing: **GIFTT**

N-CARE Aims

How can population-based targeted sequencing be done cost-effectively at scale?

What is the penetrance for early childhood cancer in carriers of pathogenic or likely pathogenic variants in genes on panel?

What are the most effective ways to describe cancer-risk NBS to parents and primary care physicians?

How do mothers of newborns experience limited versus full panel cancer-risk NBS across diverse populations in the US?

Prior to Cancer Diagnosis: C3P and CCPS

- Establish a framework for recruitment, participation, and surveillance of children with a CPS
- Define the natural history of disease in children with CPS
- Evaluate clinical impact and effectiveness of standard and emerging tumor surveillance strategies

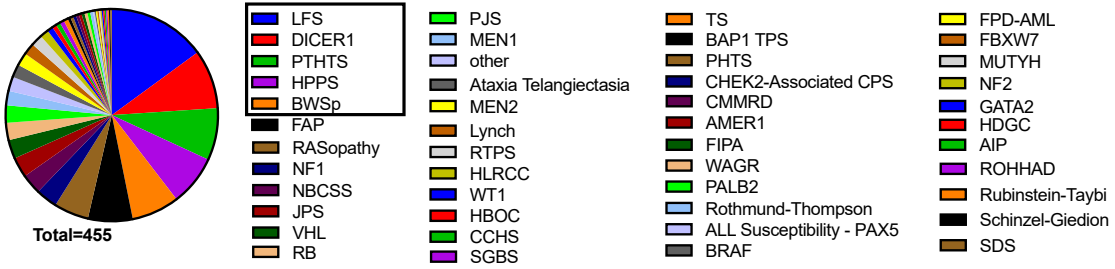
C3P Consortium for Childhood Cancer Predisposition

St. Baldrick's FOUNDATION
Conquer Childhood Cancers

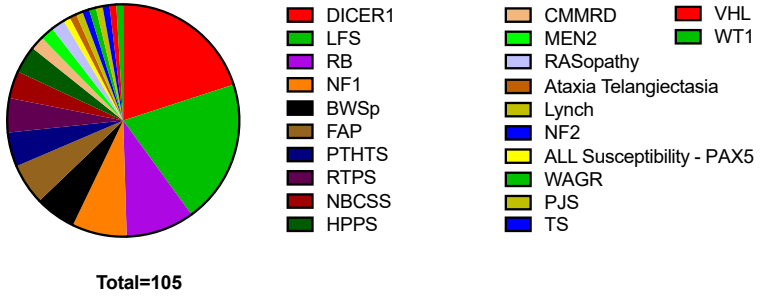
CCPS: By the Numbers

Primary Subjects	
Total	455 (100)
Male	214 (47%)
Female	241 (53%)
Age (Median)	9 years
No. of syndromes	>50
History of Cancer	
Yes	105 (23.1)
No	350 (76.9)

All Primary Subjects



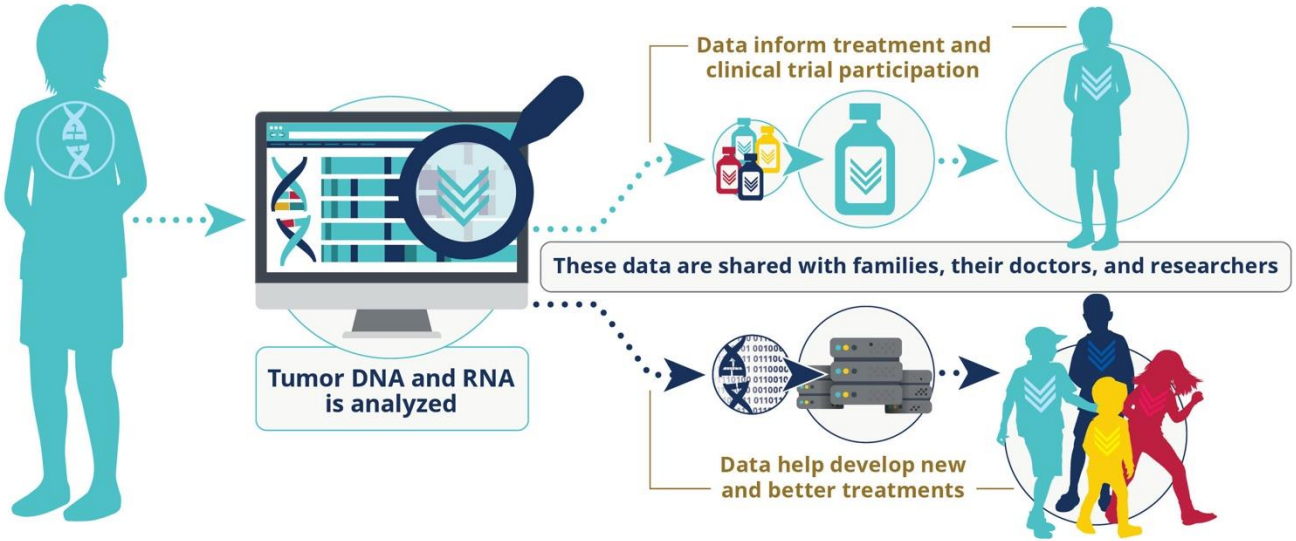
Primary Subjects with Tumors



At Cancer Diagnosis and Beyond

Building from the MCI

WHAT IS THE CCDI Molecular Characterization Initiative?



cancer.gov/CCDI-molecular

Germline Reporting: Key Takeaways

- For germline analysis, the report is focused on pathogenic or likely pathogenic variation in cancer-associated genes
- Variants of uncertain significance in genes with a clear association to the cancer type under study may be reported
- Germline variants are classified using the ACMG/AMP guidelines (PMID: 25741868)
- Secondary or incidental findings are not reported

Summary of Germline Exome Results

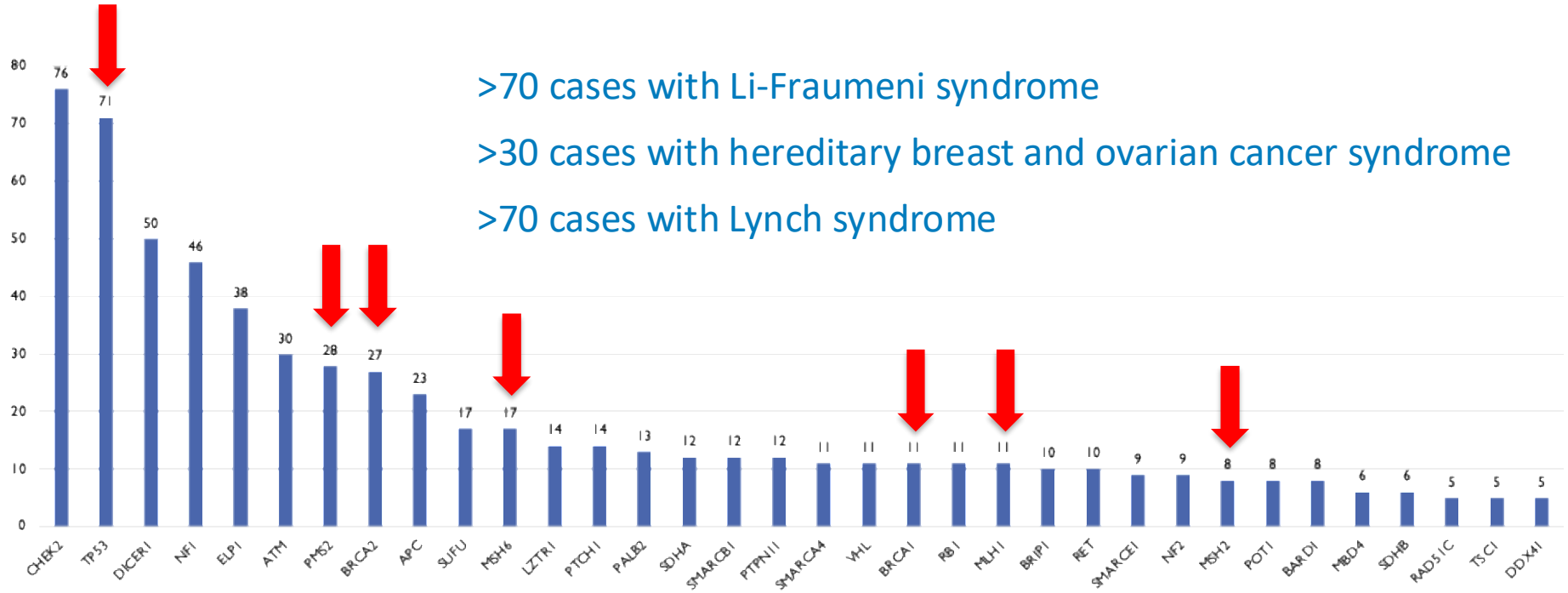
Disease group	Total individuals	Germline SNV	Germline CNV	Total with finding
CNS	3,465	447 (12.9%)	43 (1.2%)	489 (14.1%)
STS	983	87 (8.9%)	14 (1.4%)	99 (10.1%)
RAR	533	122 (22.9%)	10 (1.9%)	130 (24.4%)
NBL	375	34 (9.1%)	0 (0%)	34 (9.1%)

CNS, central nervous system; STS, soft tissue sarcoma; RAR, rare; NBL, neuroblastoma; SNV, single nucleotide variant; CNV, copy number variant

Among 5,356 patients, 14% have a reportable germline finding

Data from 3/31/22-7/31/25 courtesy of Catherine Cottrell, Ph.D. and Kareesma Parbhoo

CPGs in MCI



>70 cases with Li-Fraumeni syndrome

>30 cases with hereditary breast and ovarian cancer syndrome

>70 cases with Lynch syndrome

SNVs found in at least 5 patients

Data from 3/31/22-7/31/25 courtesy of Catherine Cottrell, PhD and Kareesma Parbhoo

Challenges, Opportunities, and Premise

- Currently no systematic assessment of outcomes among those with positive germline findings or their family members
- Assumption: family members receive genetic testing; however, there are potential barriers
- There is a need to understand outcomes in children with a CPS and to assess the uptake of genetic testing among family members

Genetic Delivery Innovations Could Address Barriers to Cascade Testing

- Telehealth and digital tools could address barriers to cascade testing
- Penn Telegenetics can provide services in the home and across the US[1-3]
  - In two RCTs, offering remote telehealth services increased uptake of genetic testing in patients who meet criteria for testing[1]
  - Studies show similar patient-reported outcomes with digital pre-test interventions as an alternative to traditional genetic counseling[3]

[1]Cacioppo *Ca Med* 2021; Henderson ASCO 2024. [2]R01 CA284748; R01 CA237369, U01 243702. [3]Kilbride JCO 2023. Bradbury et al. ASCO 2025

ORIGen/GIFTT Aims

- Assess genetics-related healthcare utilization and outcomes in children and their family members: **ORIGen cohort**
- Develop a patient-informed digital chatbot to increase uptake of and reduce barriers to cascade testing in parents of children found to have a pathogenic variant in a CPG
- Evaluate uptake and longitudinal outcomes of offering remote genetic services for cascade testing in first-degree relatives of children with cancer found to have a pathogenic variant in a CPG: **GIFTT study**

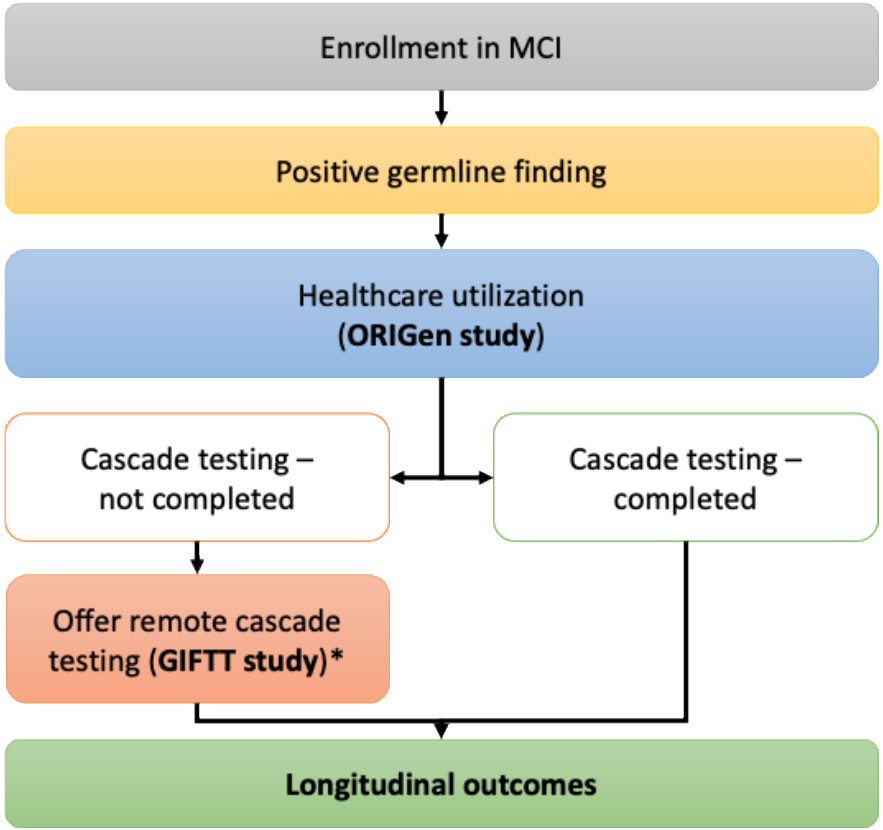
Methods

Recruitment, Follow-Up, and Intervention

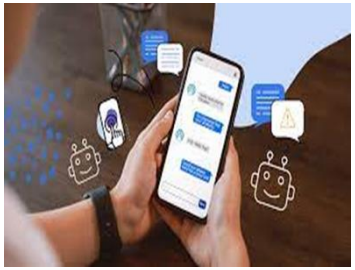
Recruitment to ORIGen/GIFTT

- Project:EveryChild (APEC14B1)
  - “Registry, Eligibility Screening, Biology and Outcome Study” for the Children’s Oncology Group (COG)
  - On-study mechanism for the MCI, enabling rapid implementation under established consent protocols
  - *Aim 1.4: To **allow the use of registry data for permission to be contacted in the future** to consider participating in non-therapeutic and prevention research studies involving the child or their parents*
- Build on recruitment and engagement infrastructure at Emory University, Baylor College of Medicine, and Penn Telegenetics Program

Study Schema and Eligibility



*Option for patient-informed chatbot as an alternative to pre-test counseling; Disclosure by telehealth in the home.



Surveys and Questionnaires

- Family history of cancer
- Previous genetic testing
- Other medical conditions
- Measures of healthcare utilization
- Patient-reported outcomes
- Other outcomes

Parent Survey Domains, Outcomes, Measures, and Timepoints by Objective

Objective	Domain	Outcome	Measure/Source	Survey Timepoint		
				RoR	6mo	1yr
Objective: Healthcare Utilization	Healthcare Utilization for *patient*	Medical actions[a] prompted by germline finding	Parent reported	x	x	x
	Healthcare Utilization for *family*	Medical actions[a] prompted by germline finding	Parent reported	x	x	x
Objective: Patient-reported Outcomes (PROs)	Perceived Utility/Disutility	Perceived Utility/Disutility	Gene-U	x	x	x
		Risk/Benefit Assessment	Novel, open ended	x	x	x
		Results Sharing	Adapted from U01HG006485	x	x	x
		Decision Regret	Decision Regret Scale, Brehaut et al.	x	x	x
	Results Experience	Subjective Understanding	Adapted from U19HD077671	x		
		Satisfaction with Results	Adapted from U01HG006485	x		
		Satisfaction with Communication	Adapted from U01HG006485	x		
	Psychosocial Impact	Impact of Results	FACToR, Li et al.	x	x	x
	Parent and Family Characteristics	Perception of Child's Prognosis	Novel	x	x	x
		Access to Care	Medical Expenditure Panel Survey, Agency for Healthcare Research and Quality	x	x	x
		Locus of Control	IE-4, Nießen et al.	x		
		Genetics Knowledge	Cancer Genetics Knowledge, Underhill-Blazey et al.	x		
		Trust in Medicine	Trust in the Medical Profession, Hall et al.	x		
		Religiosity/Spirituality	Daily Spiritual Experiences Scale, Underwood & Teresi	x		
		Sociodemographics, Geographic Location, Insurance Status	CSER harmonized items	x		

RoR=Return of Results: administered after germline result is disclosed
6mo=Six months after result disclosure
1yr=One year after result disclosure
[a]: Medical actions include, but are not limited to: follow-up tests, surveillance, genetic counseling, etc.

Cascade Testing: Institute of Genomic Medicine

gnomAD
Genome Aggregation Database

STEVE AND CINDY RASMUSSEN INSTITUTE FOR GENOMIC MEDICINE
Optimizing Patient Care Through Translational Genomics

ARCHER™ Quiver
Fusion Database

International Agency for Research on Cancer
World Health Organization

varsome

50 YEARS OMIM
Human Genetics Knowledge for the World

NCCN National Comprehensive Cancer Network®

St. Jude Cloud PeCan

PubMed®

FDA U.S. FOOD & DRUG ADMINISTRATION

ClinVar

cBioPortal FOR CANCER GENOMICS

UNIVERSITY OF CALIFORNIA SANTA CRUZ Genomics Institute

UCSC Genome Browser

Conclusion and Goals

- ~10-15% of children diagnosed with cancer also have a cancer predisposition syndrome (CPS)
- Far-reaching implications for patients and their families
- Develop a national cohort of children with a CPS who **have not** developed cancer
- Develop a national cohort of children, adolescents, and young adults enrolled in the MCI with positive germline findings
  - Implement remote genetic services for cascade testing
  - Prospectively follow participants to evaluate short- and long-term outcomes

Acknowledgements

- University of Pennsylvania
  - Angela Bradbury, M.D.
- Emory University
  - Christopher Porter, M.D.
  - Michael Scheurer, Ph.D.
  - Olga Taylor, M.P.H
- Dana-Farber Cancer Institute
  - Lisa Diller, M.D.
  - Junne Kamihara, M.D., Ph.D.
  - Kayla Hamilton, M.S., C.G.C.
- Hospital for Sick Children
  - Anita Villani, M.D.
- Children's Oncology Group
  - Douglas Hawkins, M.D.
  - Todd Alonzo, Ph.D.
- Baylor College of Medicine
  - Sarah Scollon, M.S., C.G.C.
  - Stacey Pereira, Ph.D.
  - Sharon Plon, M.D., Ph.D.
- Nationwide Children's Hospital
  - Catherine Cottrell, Ph.D.
  - Claire Hou, Ph.D.
  - Elaine Mardis, Ph.D.
  - Kareesma Parbhoo, B.S.
- Lurie Children's Hospital
  - Tara Henderson, M.D., M.P.H.
- National Cancer Institute
  - Gregory Reaman, M.D.
  - Subhashini Jagu, Ph.D.
- Many others…

Q&A

Childhood Cancer Data Initiative Virtual Symposium Series

Genomic and Epigenomic Characterization of Childhood Cancer: Clinical Trials and New Drug Discovery and Development – Academic and Industry Perspectives

Brenda Weigel, M.Sc., M.D.
Michael Craig Cox, Pharm.D., M.H.Sc., BCOP

NIH NATIONAL CANCER INSTITUTE

Disclosures

- Brenda Weigel
  - I may discuss off-label, or investigational uses of FDA approved medicines

- Michael Cox
  - I hold patents which have been assigned to Day One Biopharmaceuticals, Inc. and Loxo Oncology, Inc.
  - I am a stockholder of Circle Pharma, Inc.
  - I may discuss off-label, or investigational uses of FDA approved medicines

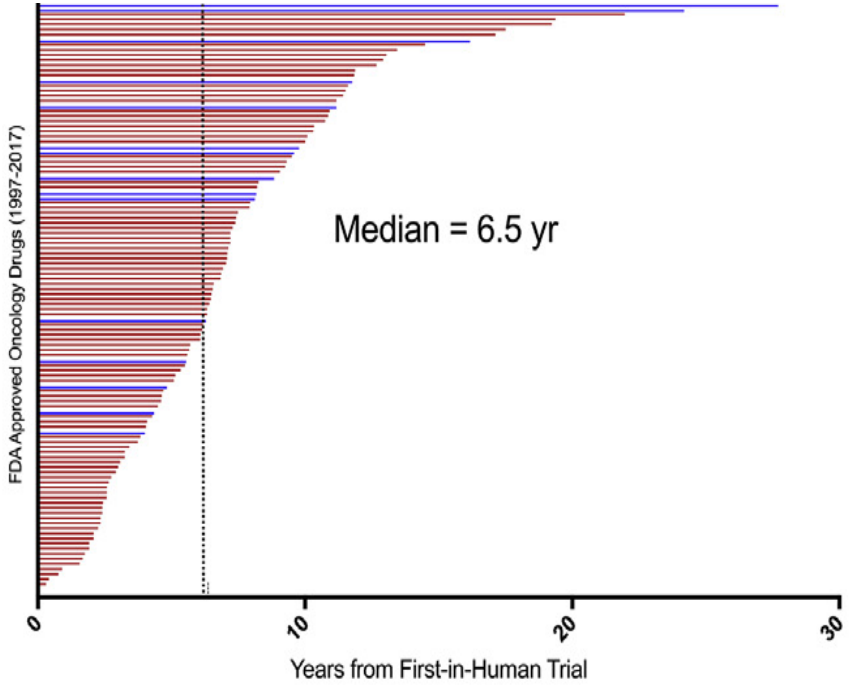
Pediatric Oncology Drug Development: Challenges and Opportunities in the Genomic Era

Brenda Weigel, M.Sc., M.D.

CCDI Has Three Foundational Goals:

- Gather data from every child, adolescent, and young adult (AYA) diagnosed with a childhood cancer, regardless of where they receive their care
- Create a national strategy of appropriate clinical and molecular characterization to speed diagnosis and inform treatment for all types of childhood cancers
- Develop a platform and tools to bring together clinical care and research data that will improve preventive measures, treatment, quality of life, and survivorship for childhood cancers

Realities of Clinical Research in Children with Cancer



Interval From First in Human to First in Child Trials for Oncology Drugs

- Relatively low incidence study population, sub-classification and risk groups mandate **multi-center** and **multi-disciplinary** clinical trials
- Improved outcome, accrual rates, **integration of biology** -evidence of success of NCI Cooperative Groups
- Lag time to initiation trials in children and formulation constraints **impact trial design**

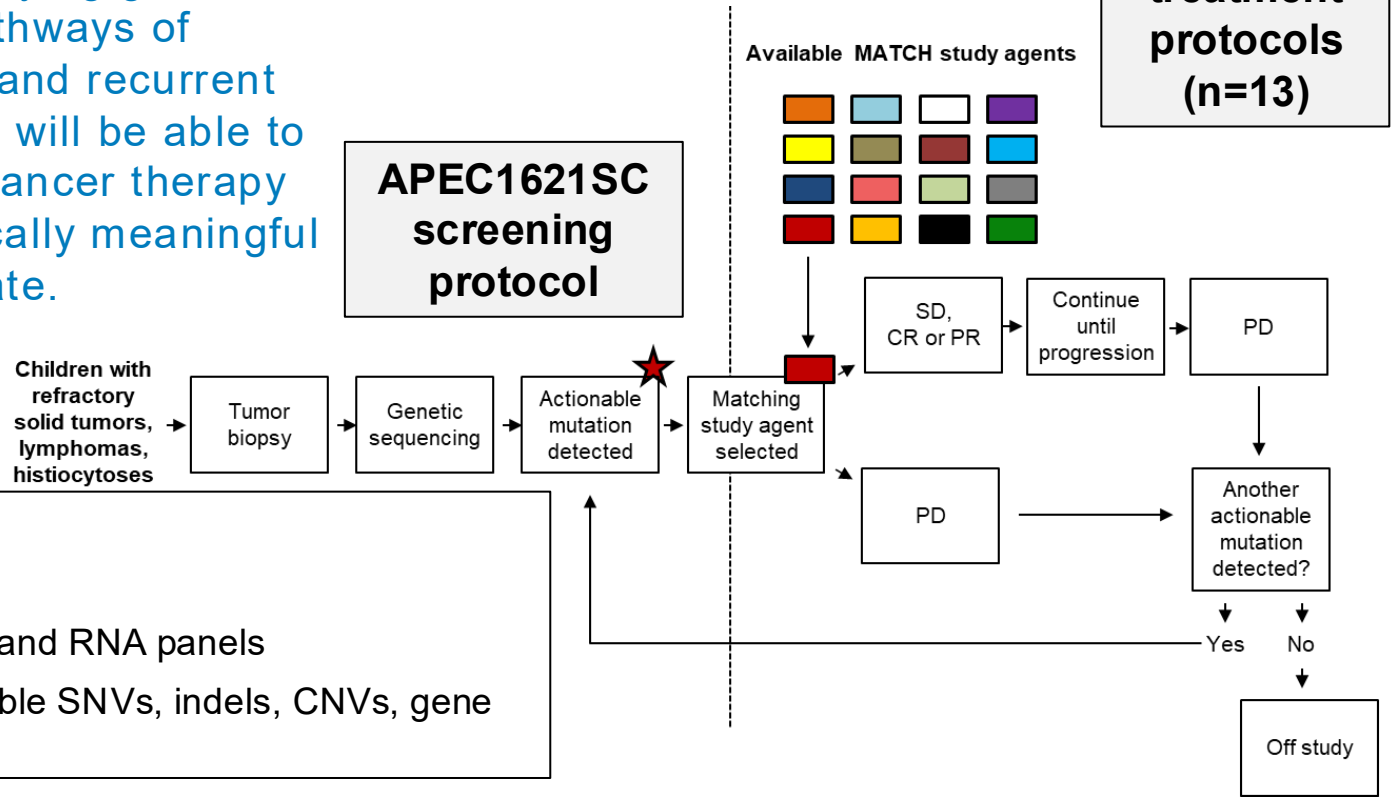
Neel DV et al. *Eur J Cancer*. 2019

Strategies to Prioritize Drugs For Pediatric Development

- Biology: Molecular target identification, micro-environment
- Drug availability and formulation
- Pre-clinical data: Cell lines, validated in vivo models
- Clinical data: Relevant adult trials

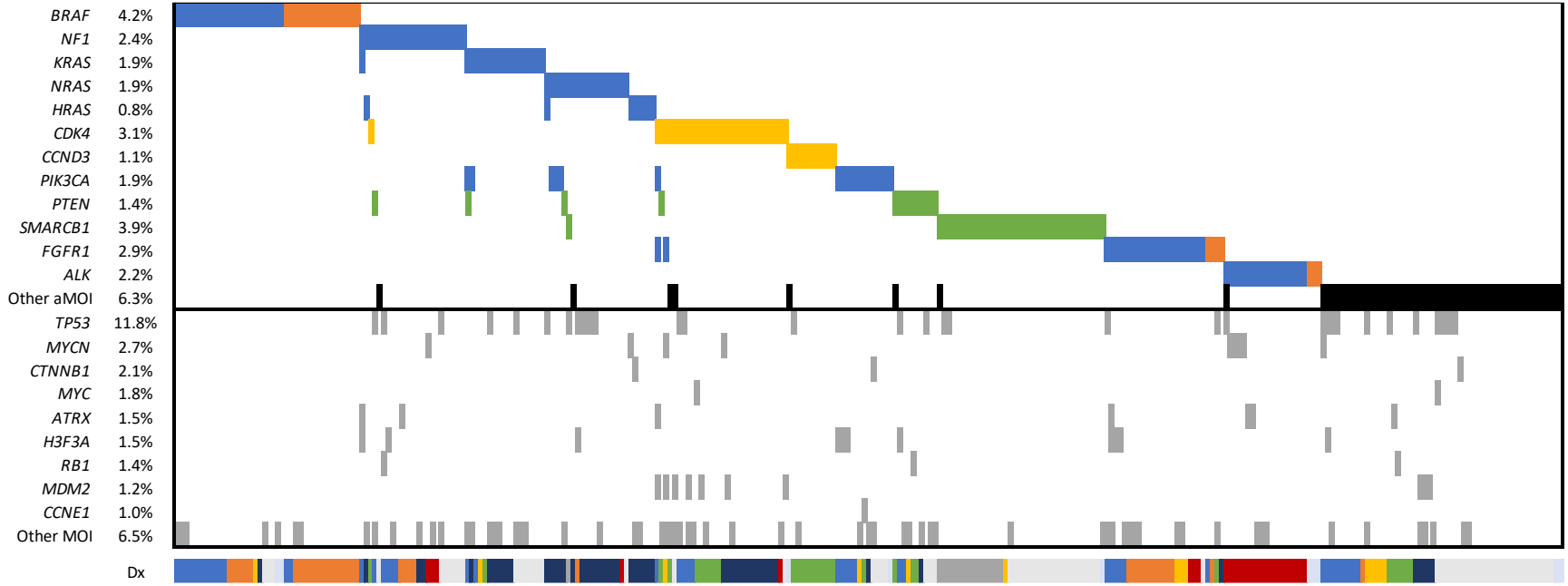
Pediatric MATCH Trial

Hypothesis: By identifying genetic changes affecting pathways of interest in refractory and recurrent pediatric cancers, we will be able to deliver targeted anticancer therapy that produces a clinically meaningful objective response rate.



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

Tumor Alterations Detected



Alteration type

- Mutation
- Loss/mutation
- Fusion
- Amplification
- Not specified (aMOI)
- Not specified (MOI)

Tumor diagnosis

- High-grade glioma
- Low-grade glioma
- AT/RT
- Other CNS tumor
- Osteosarcoma
- Rhabdomyosarcoma
- Neuroblastoma
- Other non-CNS solid tumor
- Lymphoma/histiocytosis

Parsons DW et al. *JCO* 2022

Match Sub-Protocol Results (enrollment closed Dec. 31, 2023)

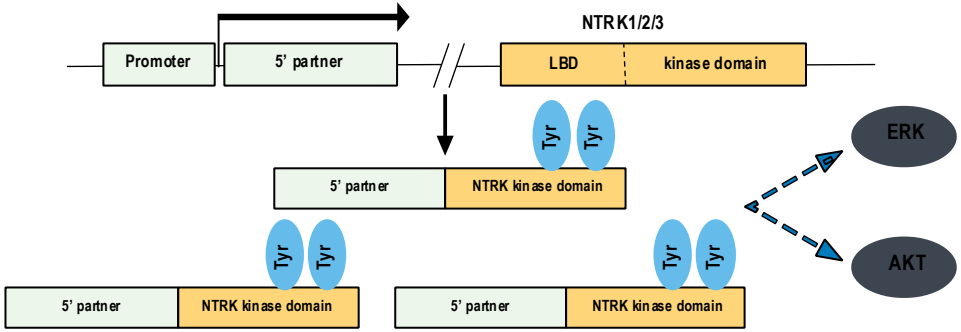
MATCH Trial	Agent	Actionable alterations	Number Enrolled	Response	Reference
APEC1621 A	Larotrectinib	*NTRK1, NTRK2, NTRK3* fusion	9	pending	TBD
APEC1621 B	Erdafitinib	*FGFR1, FGFR2, FGFR3* mutation/fusion; *FGFR4* mutation	20	2 PR, 6 SD (median 6.5 cycles), 6 mon PFS 45%	*J Clin Oncol 41, 2023 (suppl 16; abstr 10007)*
APEC1621 C	Tazemetostat	*SMARCB1, SMARCA4* mutation/loss, *EZH2* mutation	20	1 PR, 4 SD: 6 mon PFS 35%	*J Natl Cancer Inst 115(11); 2023*
APEC1621 D	Samotolisib	*TSC1, TSC2, MTOR, PIK3CA, PIK3R1* mutation; *PTEN* mutation/loss	17	No responses: 3 mon PFS 13%	*JCO Precis Oncol: e2400258, 2024*
APEC1621 E	Selumetinib	*BRAF* mutation/fusion; *NRAS, KRAS, HRAS, NF1, ARAF, GNAQ, GNA11* mutation	20	3 SD: 6 mon PFS 15%	*J Clin Oncol 40(2); 2022*
APEC1621 F	Ensartinib	*ALK* mutation/fusion; *ROS1* fusion	7	pending	TBD
APEC1621 G	Vemurafenib	*BRAF V600* mutation	4	1 PR	*Oncologist 29(8); 2024*
APEC1621 H	Olaparib	*BRCA1, BRCA2, ATM, RAD51C, RAD51D* mutation	6	No responses	*Oncologist 29(8); 2024*
APEC1621 I	Palbociclib	*CDK4, CDK6, CCND1, CCND2, CCND3* amplification	23	2 SD: 6 cycles and 3 cycles: 6 mon PFS 10%	*JCO Precis Oncol; e2400418, 2024*
APEC1621 J	Ulixertinib	*BRAF* mutation/fusion; *NRAS, KRAS, HRAS, NF1, ARAF, GNAQ, GNA11, MAP2K1* mutation	20	3 SD > 6 mon	*JCO Precis Oncol; e2400103, 2024*
APEC1621 K	Ivosidenib	*IDH1 R132* mutation	3	pending	TBD
APEC1621 M	Tipifarnib	*HRAS* mutation	5	pending	TBD
APEC1621 N	Selpercatinib	*RET* mutation/fusion	1	pending	TBD

The Larotrectinib Story: A Reminder

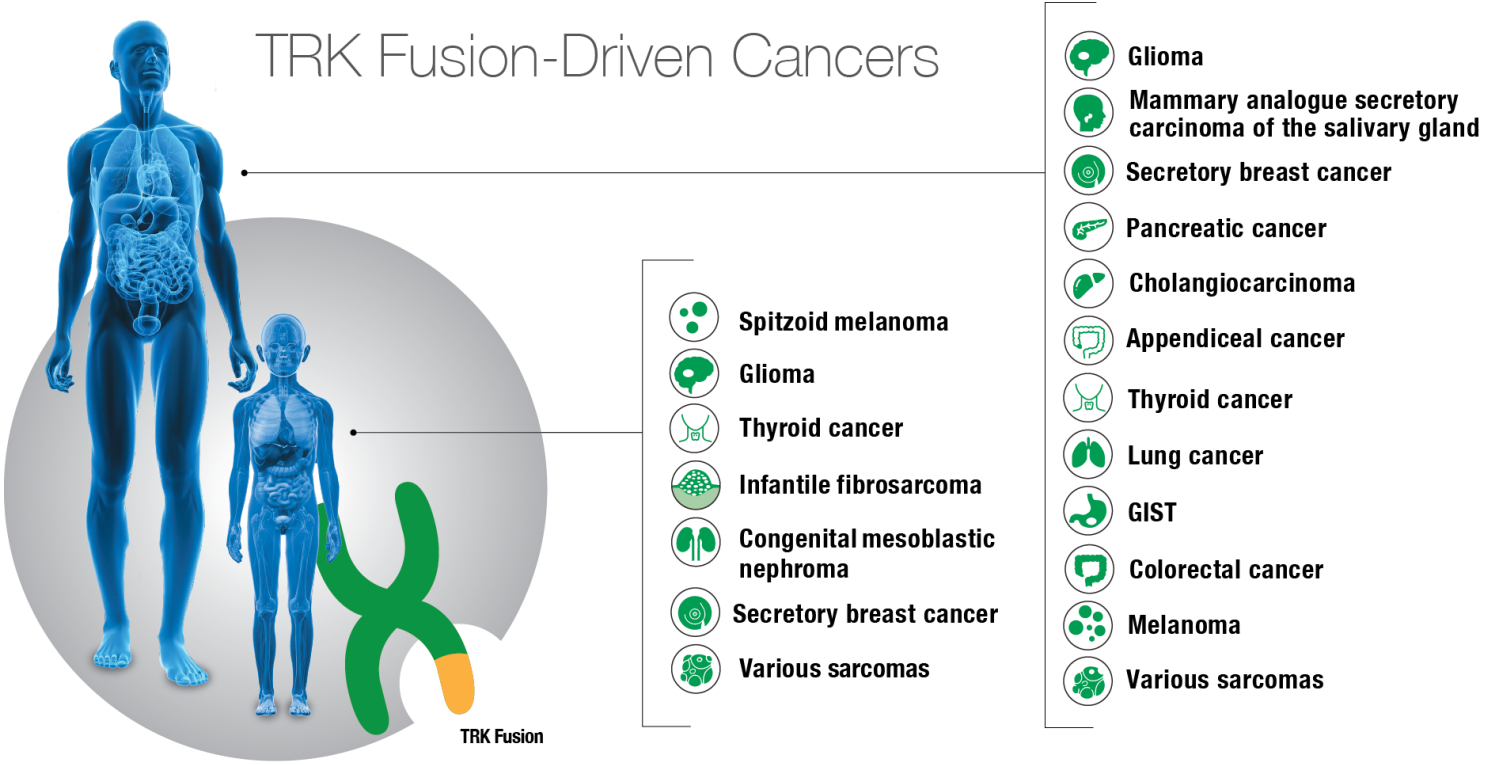
Michael Craig Cox, Pharm.D., M.H.Sc., BCOP

TRK Fusions Are Rare but Recurrent Oncogenic Drivers

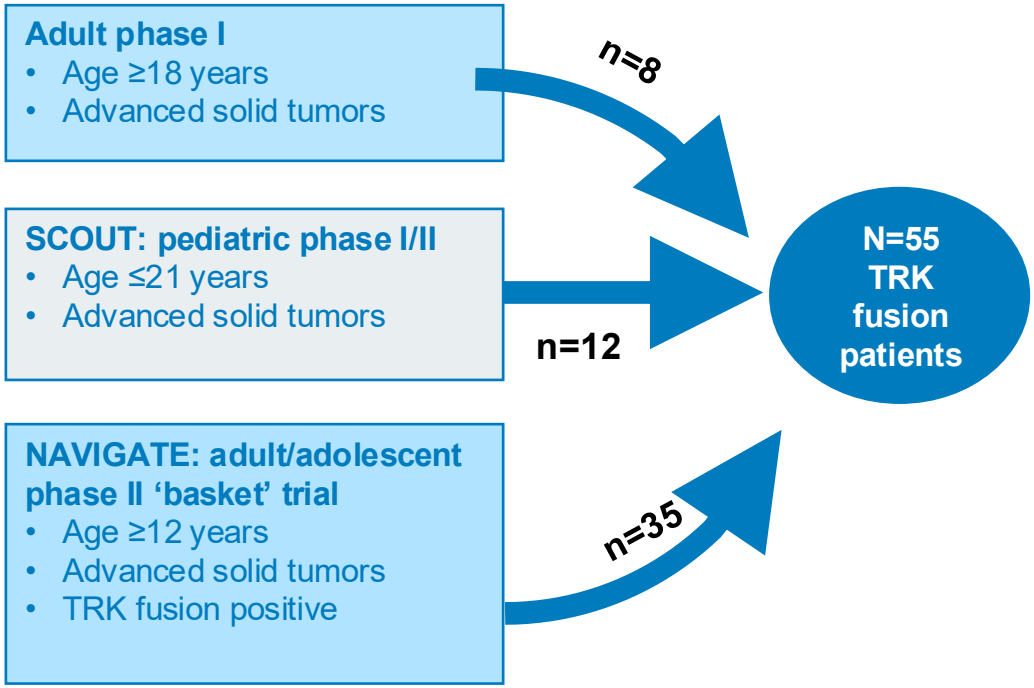
- Beyond the embryo, tropomyosin receptor kinase (TRK) proteins are primarily limited to the nervous system[1]
- 3 neurotrophin receptors encoded by 3 distinct genes that regulate specific normal functions[2-6]
  - *NTRK1* → TRKA → Pain, thermoregulation
  - *NTRK2* → TRKB → Movement, memory, mood, appetite, body weight
  - *NTRK3* → TRKC → Proprioception
- Recurrent chromosomal fusion events have been identified across diverse pediatric and adult cancers[7-13]



TRK Fusions Are Found in Diverse Cancer Histologies

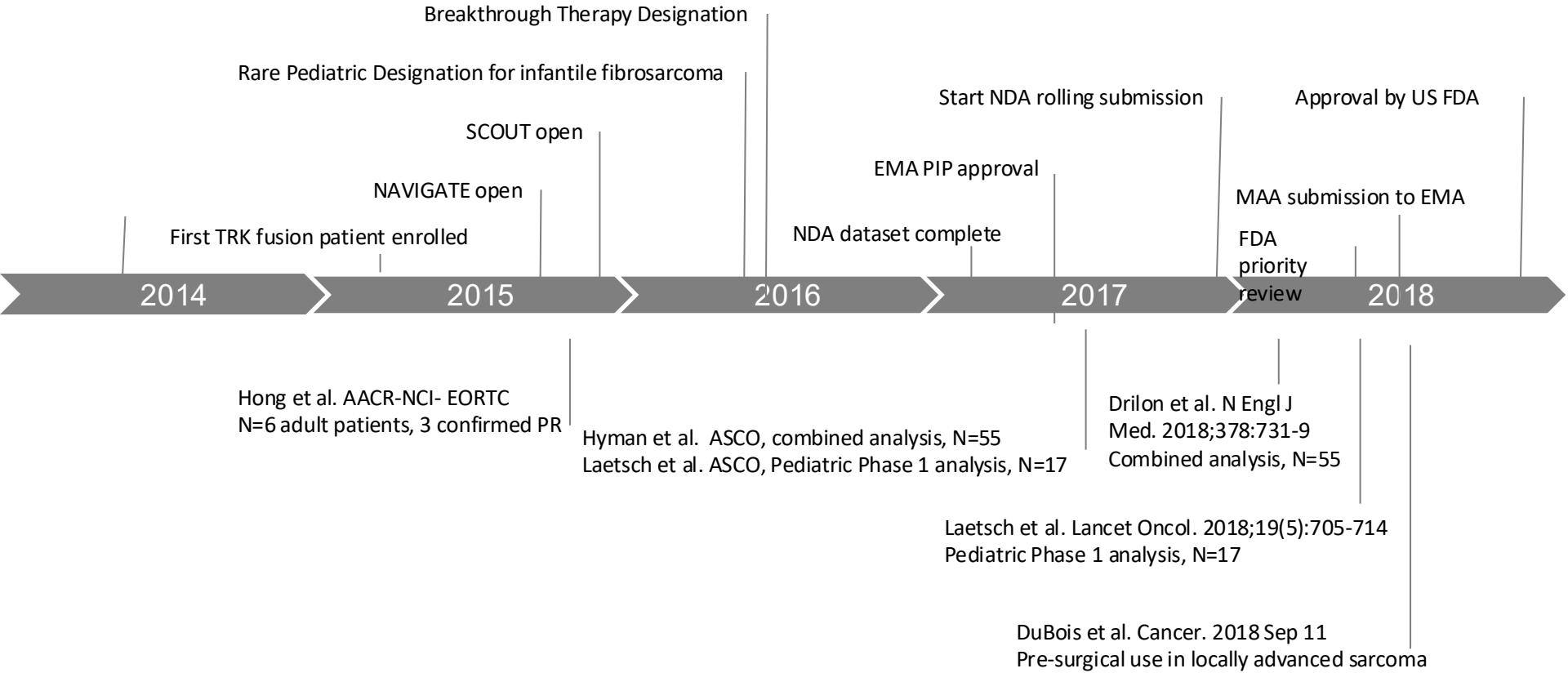


Larotrectinib Clinical Development in Adult and Pediatric TRK Fusion Cancers



- **TRK fusion status** determined by local CLIA (or similarly accredited) laboratories
- **Primary endpoint**
  - Best objective response rate (ORR)
  - RECIST v1.1 per investigator assessment
- **Secondary endpoints**
  - Duration of response (DOR)
  - Progression-free survival (PFS)
  - Safety
- **Dosing**
  - Single-agent larotrectinib, administered predominantly at 100 mg BID continuously
  - Treatment beyond progression permitted if patient continuing to benefit

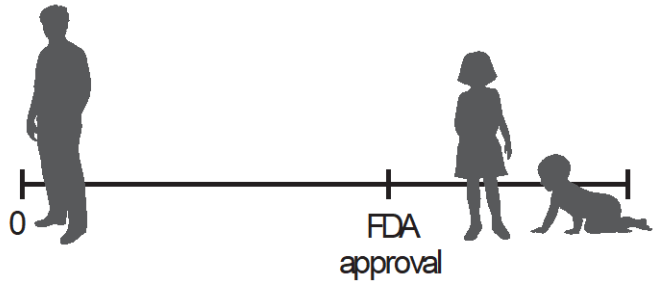
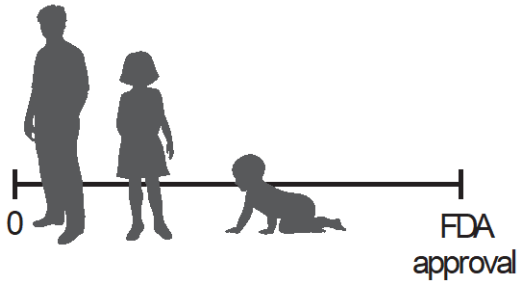
Could the Larotrectinib Program Have Moved Faster Today?



How Could the Next Iteration of CCDI Speed Pediatric Drug Development?

Brenda Weigel, M.D. and Michael Cox, Pharm.D.

Changing the Landscape of Oncology Drug Development

TRIAL ASPECT	PAST	FUTURE
Timeline for trials in pediatrics		
	First-in-child occurs several years after first-in-human	Adolescents enrolled in trials concurrent with adults Plan for trials in children in place early in drug development

Dubois S et al. *Science*. 2019

CCDI to Foster Pre-Clinical Studies in Pediatric Oncology

- Who are the key labs (disease state, oncogenic fusion, etc)?
- What models exist (cell lines, PDX, etc)?
- Access to PDX sequencing for relevance to pediatric tumor types.
- How can CCDI be enhanced to foster pediatric oncology drug development: shift the paradigm especially for fusion oncoproteins which are more likely oncogenic drivers in pediatric oncology?

Can CCDI Be the Access Point of the Global Databases (INFORM, MappyActs, Zero, EveryChild, etc.)?

- A one-stop shop (or at least a roadmap of how to access).
- A place for industry to understand prevalence data to inform iPSP and PIP development.
- Knowing who to call is half the battle.
- Need to move from risk stratification to therapy development: develop methods to link MCI to clinical trials.

Accessing Data to Inform Trial Development

- Pre-clinical
  - Abstracts and publications
  - PIVOT
- Clinical
  - CT.gov
  - Abstracts and publications

All are delayed in accessing data: CCDI could speed access

Key Questions

- Enhanced access and input from industry to CCDI data.
- Enhanced ways to clinically annotate the CCDI data; outcomes, clinical features etc.
- Strategies to utilize CCDI to drive novel combination strategies for pediatric oncology.

Enhanced Utilization of CCDI Data for Regulatory Requirements

- Molecular data
- Clinical data
- Outcomes data (wearables, others?)
- Radiology scans (central reading)
- Can CCDI lead the push for FDA (and EMA, others if we could) BUY IN

How Do We Build Industry Knowledge about CCDI?

- CCDI–Industry roundtables/advisory boards.
- Development of a CCDI “elevator speech” when industry comes knocking on your door.
- CCDI representation to PhRMA, BIO
- Influence FDA to refer industry to CCDI during iPSP discussions
- CCDI work with FoCR

Q&A

Abstract Awards

Abstract Award Winners

Jaclyn N. Taroni

Adam Thiesen

Lukas Chavez

Lightning Oral Presentations

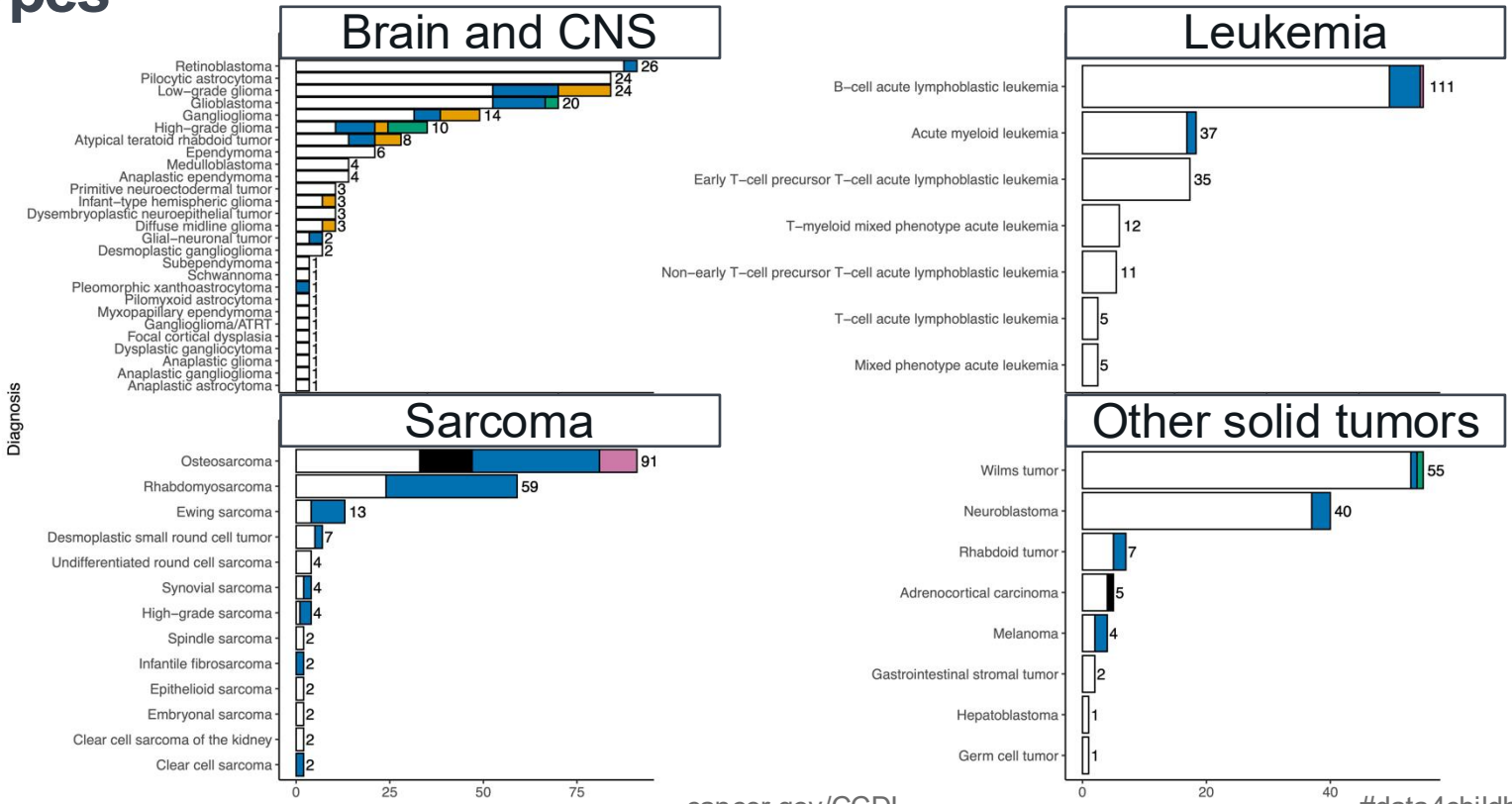
Childhood Cancer Data Initiative Virtual Symposium Series

The Open Single-cell Pediatric Cancer Atlas Project: Collaborative Analysis of Pediatric Tumor Data

Jaclyn N. Taroni, Ph.D.

NIH NATIONAL CANCER INSTITUTE

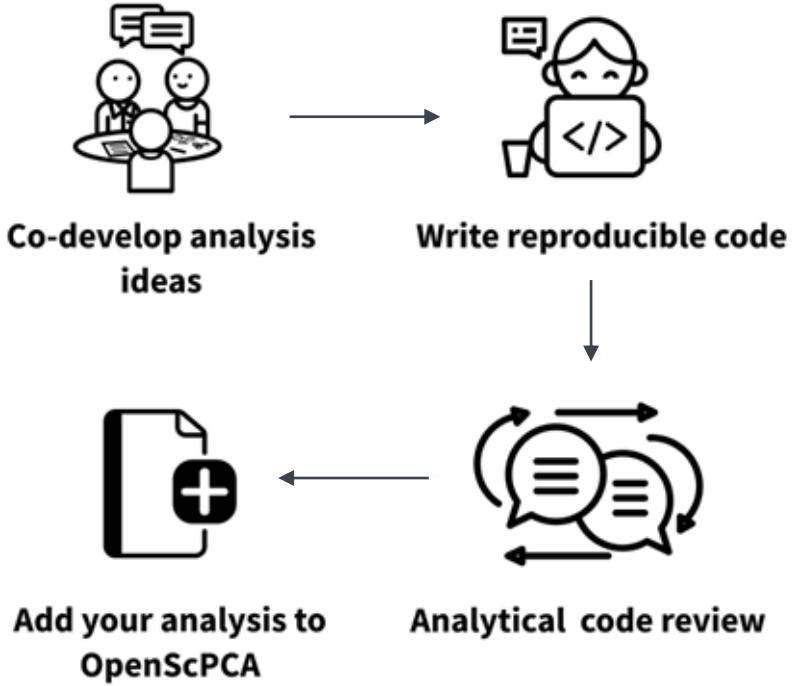
The Single-cell Pediatric Cancer Atlas (ScPCA) Contains Uniformly Processed scRNA-seq Data From Over 50 Cancer Types



OpenScPCA Is a Project to Collaboratively Analyze ScPCA Data Openly on GitHub

Project goals include:

- Characterizing samples with analyses such as cell type identification
- Building consensus around usage, strengths, and pitfalls of methods and their application to pediatric cancer data
- Improving the utility of ScPCA data for the community



We Invite You to Participate in OpenScPCA

Get started at our docs

Visit the repositories

AlexsLemonade/OpenScPCA-analysis

AlexsLemonade/OpenScPCA-nf

Browse the data

https://scpca.alexslemonade.org

Childhood Cancer Data Initiative Virtual Symposium Series

Generalizable Pediatric Sarcoma Histopathology Classification with Multi-Institutional Machine Learning

Adam Thiesen

NIH NATIONAL CANCER INSTITUTE

Sarcomas Are Challenging to Diagnose

- Accurate diagnosis is critical for guiding disease management
- Over 70 different subtypes, with high heterogeneity
  - Genetic fusion status, protein markers, cell of origin, anatomical location
- Often require genetic and molecular panels, as well as guidance from expert pathologists and clinical team
- Machine learning and AI can be used to standardize this process globally, allowing for more equitable access to care
  - However, these models come with caveats

Multi-Institutional Image Library Allows Training of Generalizable Deep Learning Models

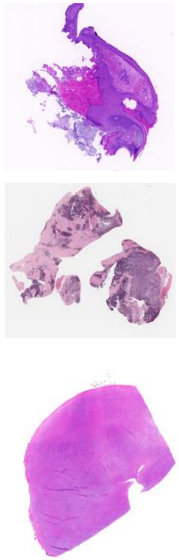
Institution Table	Total # of images*
Children's Oncology Group	582
Yale	153
St. Jude Children's	71
MGH	63
Total	**869**

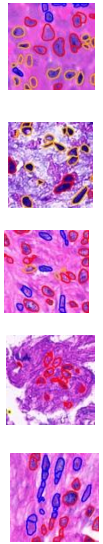
*Individual patients can have multiple images within the data set

Subtype Diagnosis	Count
Embryonal RMS	442
Alveolar RMS	135
Spindle Cell RMS	33
Alv. + Embr. RMS	2
RMS NOS	69
Ewing Sarcoma	41
Synovial Sarcoma	12
Infantile Fibrosarcoma	9
Clear Cell Sarcoma	4
Other Sarcoma	73
Sarcoma NOS	36

Computational Pipeline: From Raw Images to Trained Classifiers

*Normalize images, split into tiles, extract morphology information**

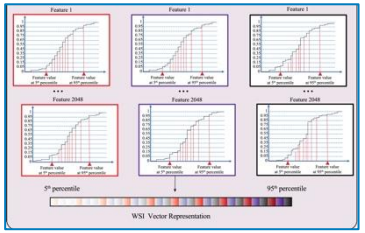




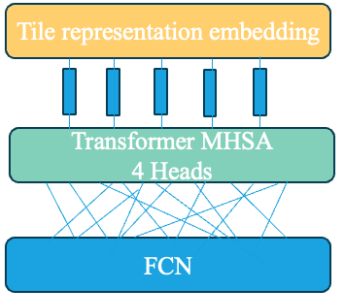
$$\begin{bmatrix} x_{i1} \\ \vdots \\ x_{in} \end{bmatrix} \quad \begin{bmatrix} x_{j1} \\ \vdots \\ x_{jn} \end{bmatrix} \quad \begin{bmatrix} x_{k1} \\ \vdots \\ x_{kn} \end{bmatrix}$$

Train deep learning models on features

SAMPLER



Transformer

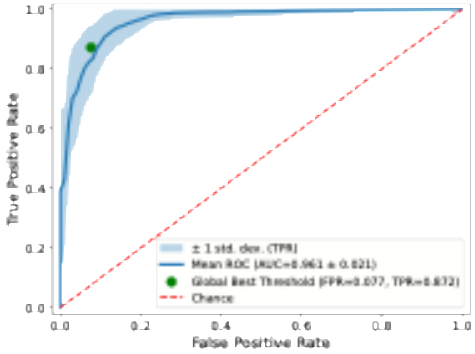


Prediction

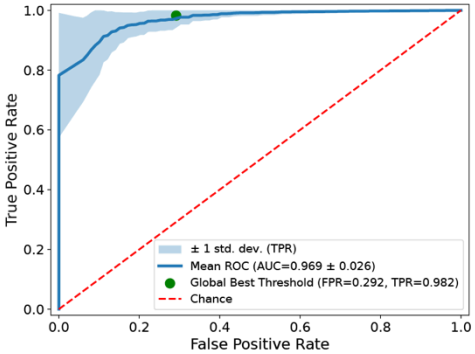
**Using STQ Pipeline, developed by JAX computational scientist Sergii Domanskyi*

When We Train Across Our Data Set, We Achieve Strong Results

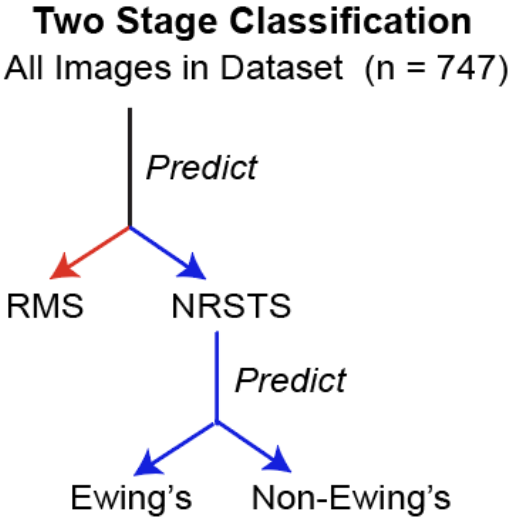
Embryonal vs Alveolar

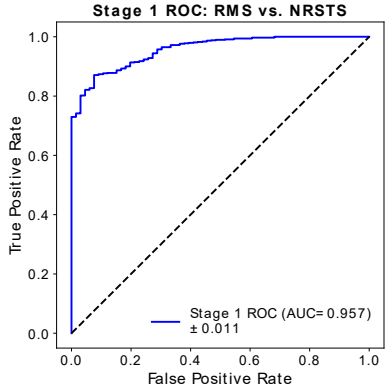


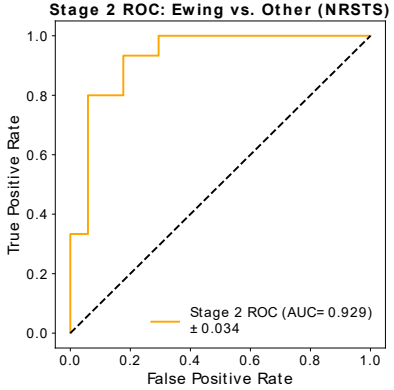
Rhabdo vs Non-Rhabdo Sarcoma



Ewing Sarcoma







Acknowledgements

The Jackson Laboratory:

Jill C. Rubinstein, M.D., Ph.D., FACS

Jeffrey Chuang, Ph.D.

Carol J. Bult, Ph.D.

Steven B. Neuhauser, Ph.D.

Sergii Domanskyi, Ph.D.

Ali Foroughi-Pour, Ph.D.

Todd Sheridan, M.D.

Jingyan Zhang

Brian White, Ph.D.

Patience Mukashyaka, Ph.D.

Jie Zhou, Ph.D.

Sam Liu

Massachussetts General Hospital:

Danielle B. Cameron, M.D., M.P.H.

Katelynn Dannheim, M.D.

Alyssa Stetson, M.D.

Yale New Haven Children's Hospital:

Emily R. Christison-Lagay, M.D.

Hao Wu, M.D., Ph.D.

The University of Pennsylvania

Shawn Ahn, M.D., Ph.D.

The University of Washington

Eleanor Y. Chen, M.D.

Jonathan Henriksen

Centers/Consortia:

Children's Oncology Group

Massachusetts General Hospital

St. Jude Children's Research Hospital

Yale New Haven Children's Hospital

University of Washington

Grant support:

NIH: P30CA034196 – CCDI Supplement Funding

JAX: DIF Program (Rubinstein, Chuang)

Hartford Hospital (Rubinstein)

Childhood Cancer Data Initiative Virtual Symposium Series

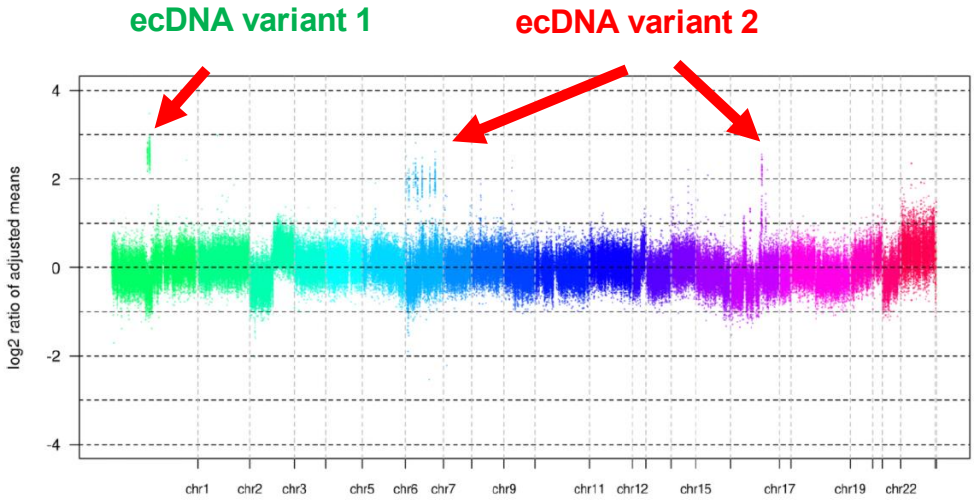
Exploring Extrachromosomal DNA's (ecDNA's) Impact on Childhood Cancers

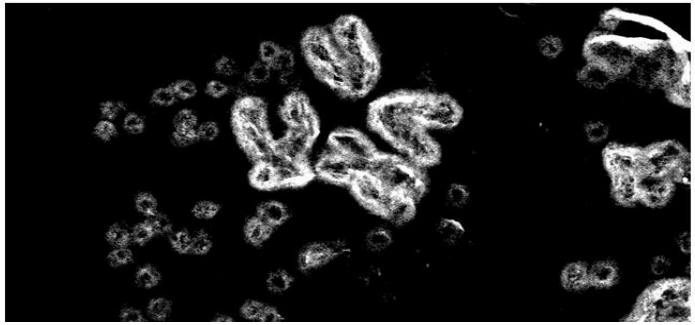
Sunita Sridhar

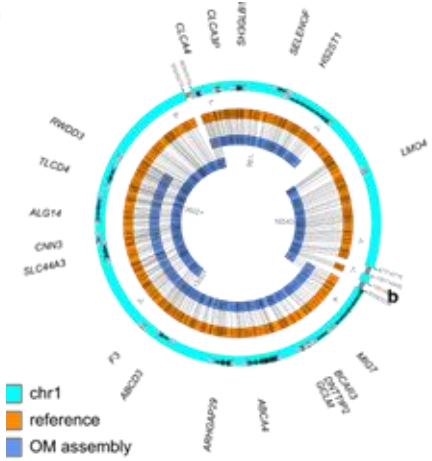
(presented on behalf of Lukas Chavez)

NIH NATIONAL CANCER INSTITUTE

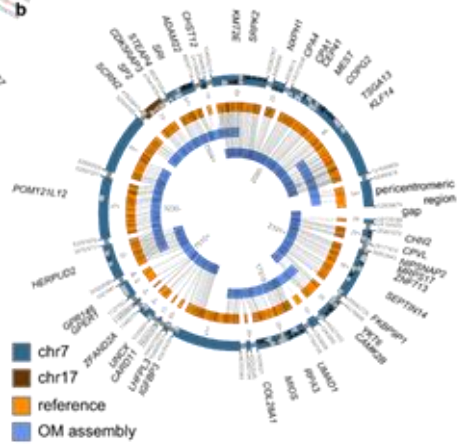
Anaplastic Medulloblastoma Tumor With Two Distinct ecDNA Variants







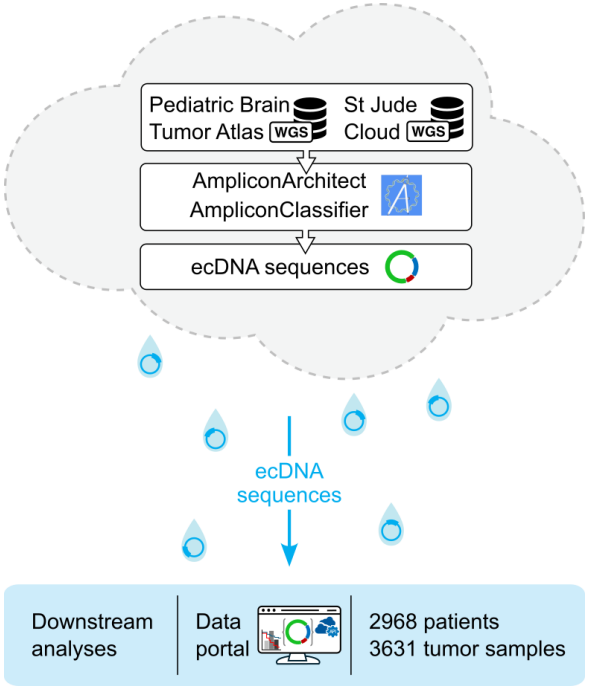
ecDNA variant 1



ecDNA variant 2

AmpliconArchitect (Desphande et al., Nature Communications 2019)

ecDNA in Childhood Cancers



Owen Chapman

Sunita Sridhar

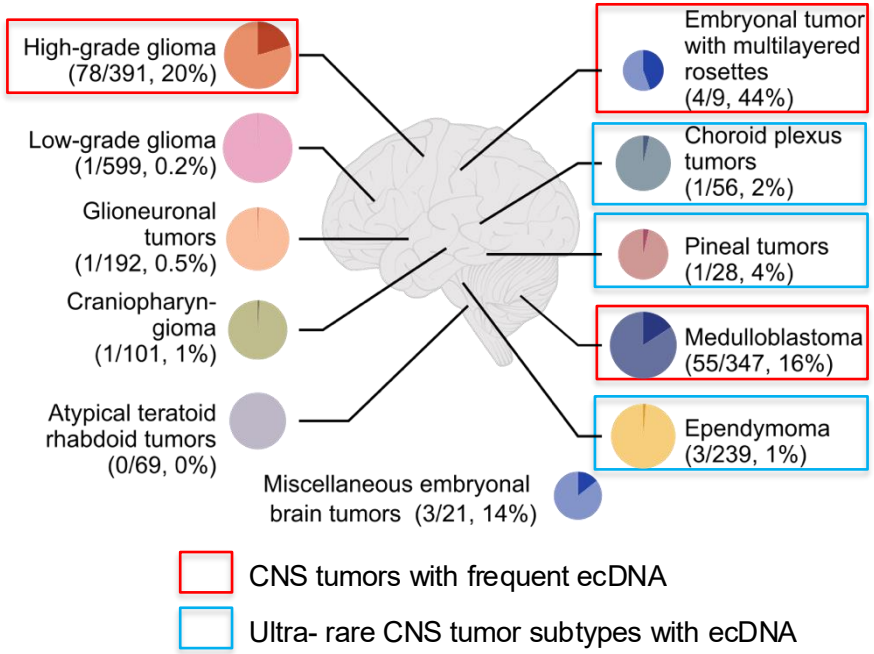
Key Questions:

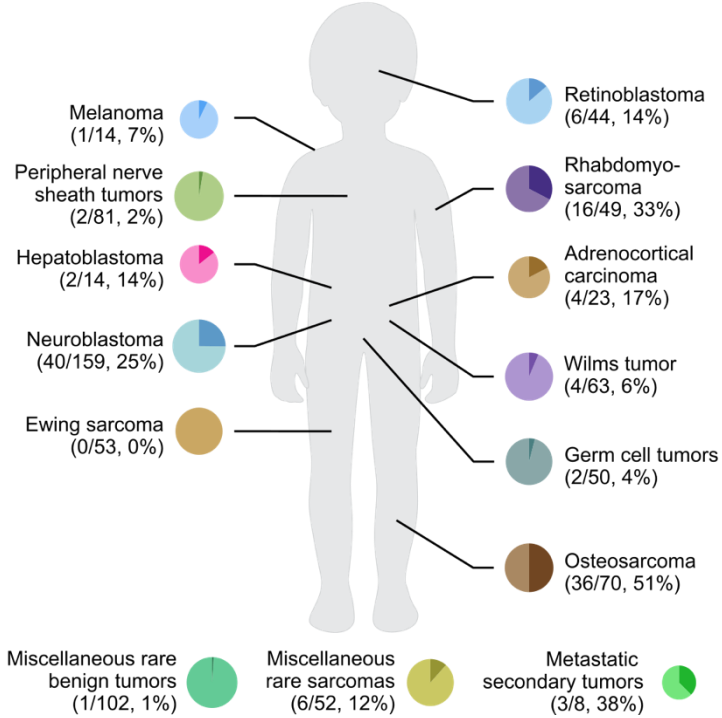
- Which pediatric tumor types have ecDNA?
- Which parts of the genome are amplified?
- ecDNA as an independent prognostic biomarker?
- Molecular evolution of ecDNA during disease progression?

Chapman, Sridhar et al., *Extrachromosomal DNA associates with poor survival across a broad spectrum of childhood solid tumors*, medRxiv 2025

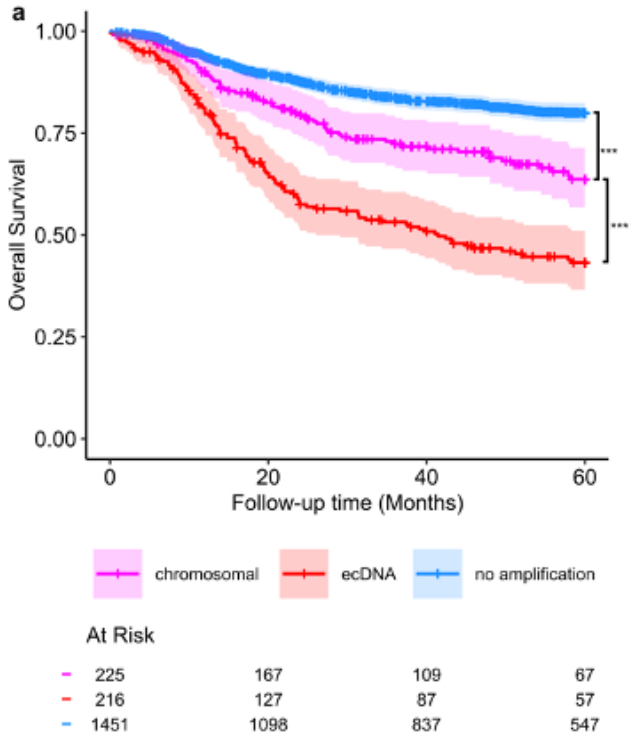
ecDNA in Childhood Cancers

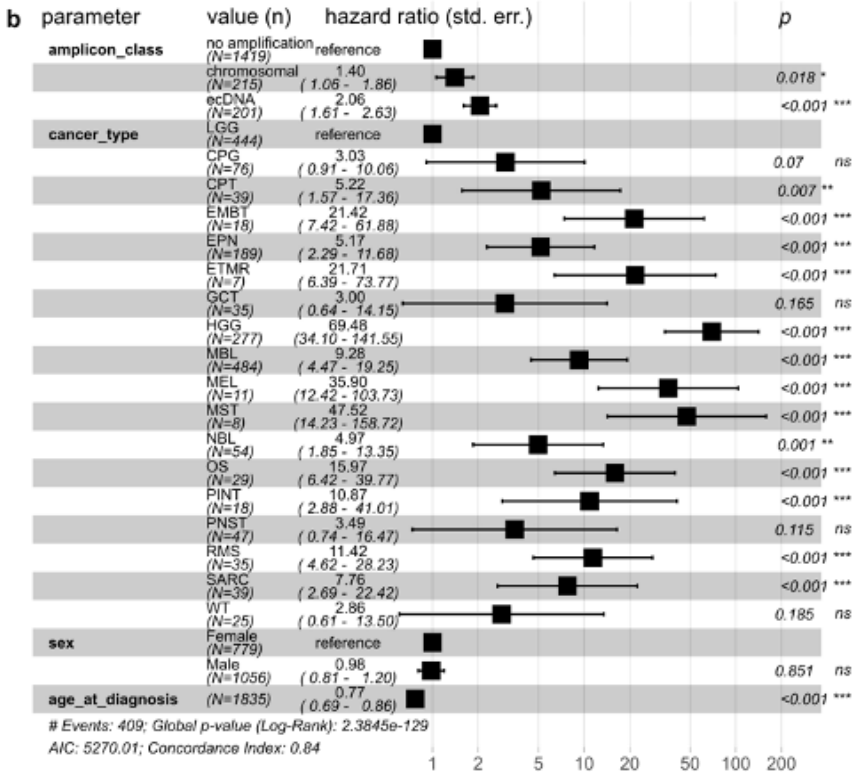
Overall fraction of ecDNA+ tumors: 9% vs. 14-17% in adult cancers



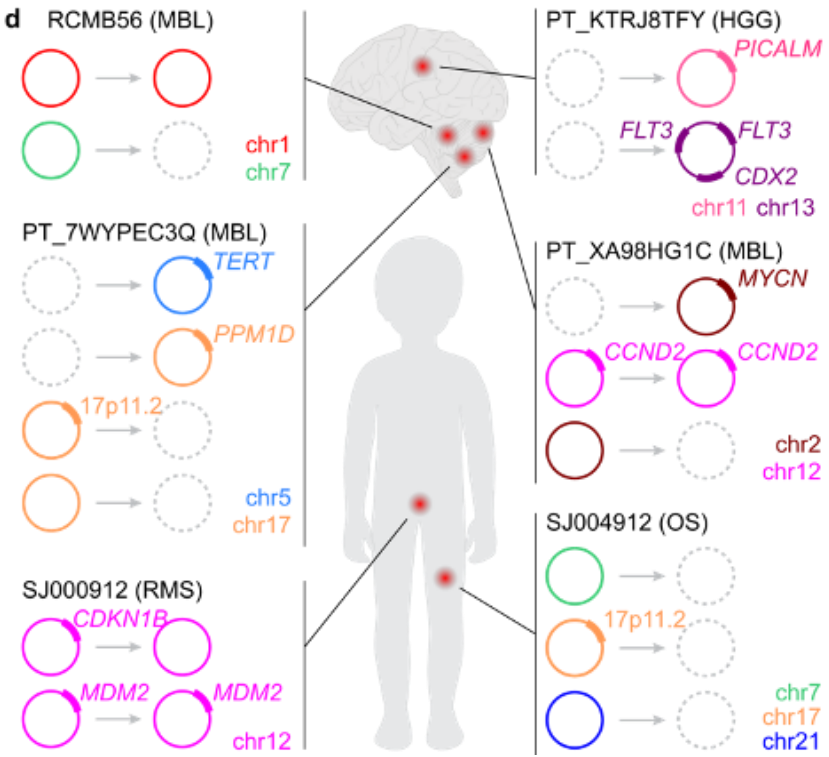


Survival is poorer in patients with ecDNA





ecDNA can change over time



Thank you!

cancer.gov

cancer.gov/espanol

Join Us For Our Upcoming Events!

Molecular Targeted Therapies Reveal Glioma Cell Plasticity Linked to Immune Evasion in BRAF-Mutant Brain Tumors

Tuesday, April 14 at 1:00–2:00 p.m. ET

CCDI Pediatric, Adolescent, and Young Adult Rare Cancer Study

Monday, April 27 at 12:00–1:00 p.m. ET

Learn more and register at **events.cancer.gov/ccdi/webinar**

How You Can Engage with CCDI

Learn about CCDI and subscribe to our monthly newsletter:
cancer.gov/CCDI

Access CCDI data and resources:
ccdi.cancer.gov

Questions? Email us at:
NCIChildhoodCancerDataInitiative@mail.nih.gov

Thank you for attending!

cancer.gov

cancer.gov/espanol