

# Childhood Cancer Data Initiative Virtual Symposium Series

*Logan Spector and Yi Xing*

# Today's Speakers



## Logan G. Spector, Ph.D., University of Minnesota

- Professor, Division Director, Division of Pediatric Epidemiology & Clinical Research
- Faculty, Department of Pediatrics and Brain Tumor Program
- Suzanne Holmes Hodder Chair in Pediatric Cancer Research, Children's Cancer Research Fund

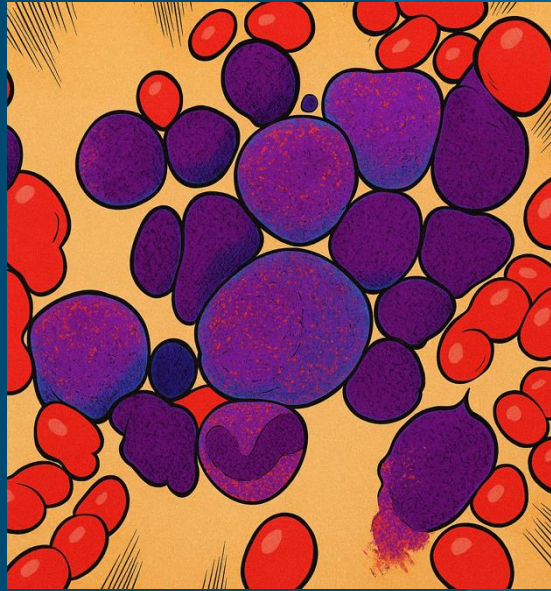


## Yi Xing, Ph.D., Children's Hospital of Philadelphia

- Associate Chief Scientific Officer for Omics, Technology & Engineering
- Executive Director, Department of Biomedical and Health Informatics
- Director, Center for Computational and Genomic Medicine

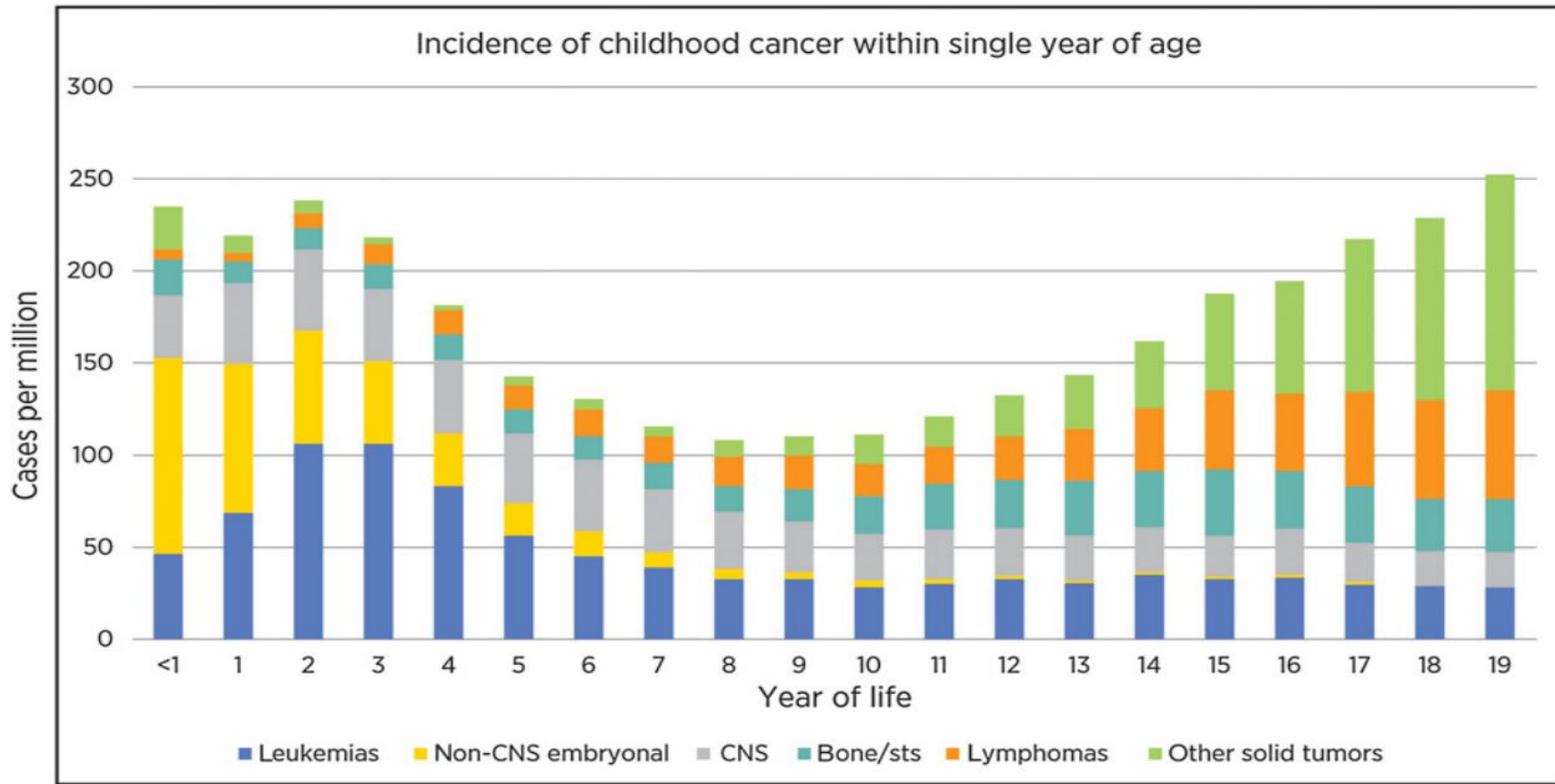
# Agenda

1. *The Emerging Genetic Architecture of B-Cell Acute Lymphoblastic Leukemia in African-American Children*
  - Q&A
2. *Illuminating Dark Antigens for Childhood Cancer Immunotherapy*
  - Q&A



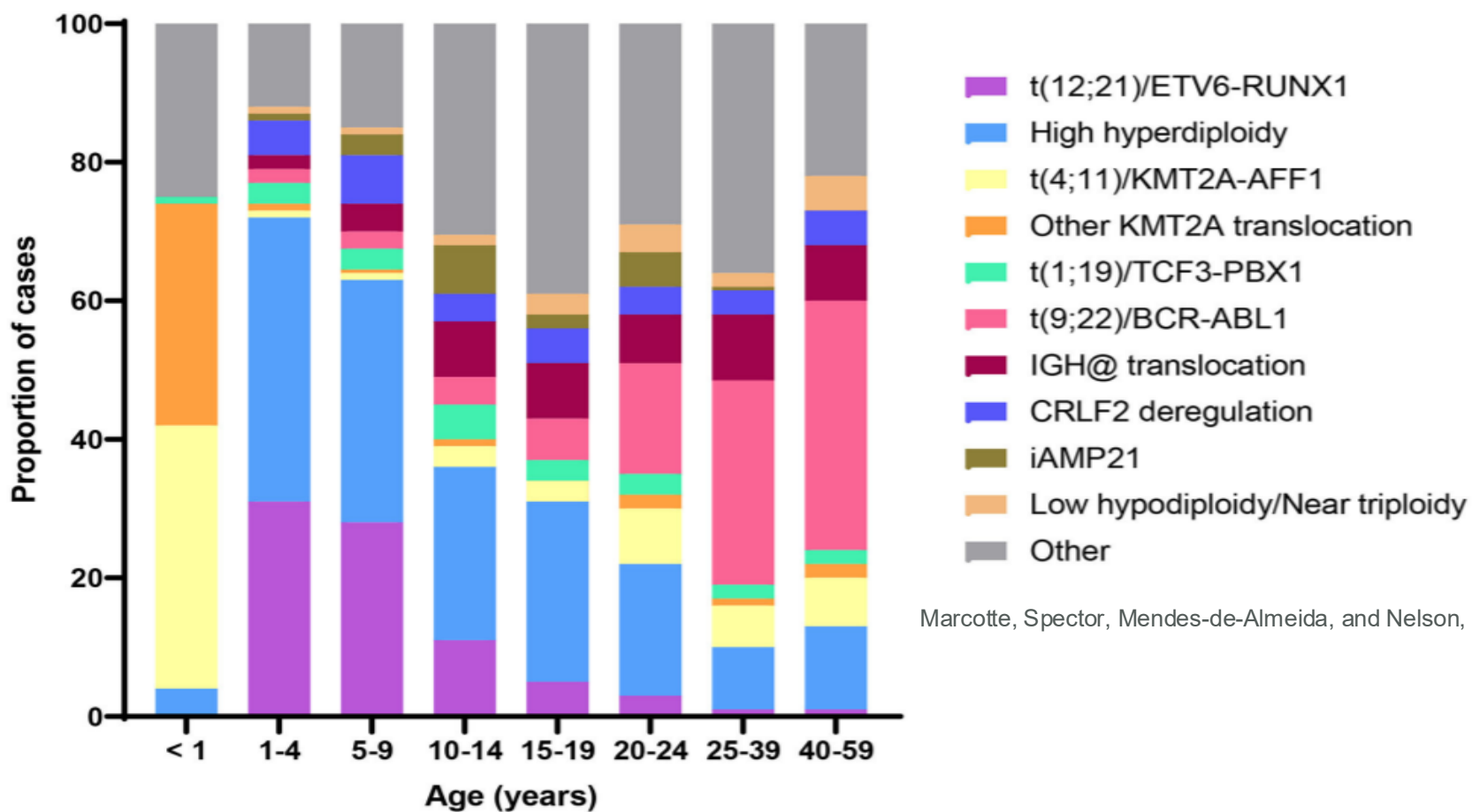
# The Emerging Genetic Architecture of B-Cell Acute Lymphoblastic Leukemia in African-American Children

*Logan G. Spector, Ph.D.*



Spector and Lupu, 2020

**Figure 2.** Distribution of tumors across the pediatric age spectrum.



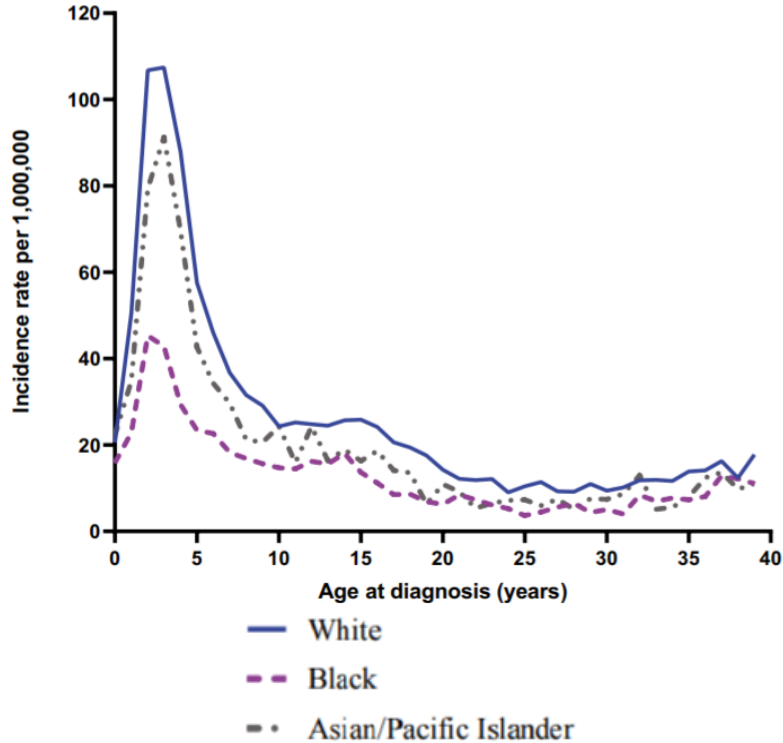
Marcotte, Spector, Mendes-de-Almeida, and Nelson, 2021

**FIGURE 2** | Distribution of B-cell acute lymphoblastic leukemia (ALL) cytogenetic subtypes by age at diagnosis. Data adapted from (6).

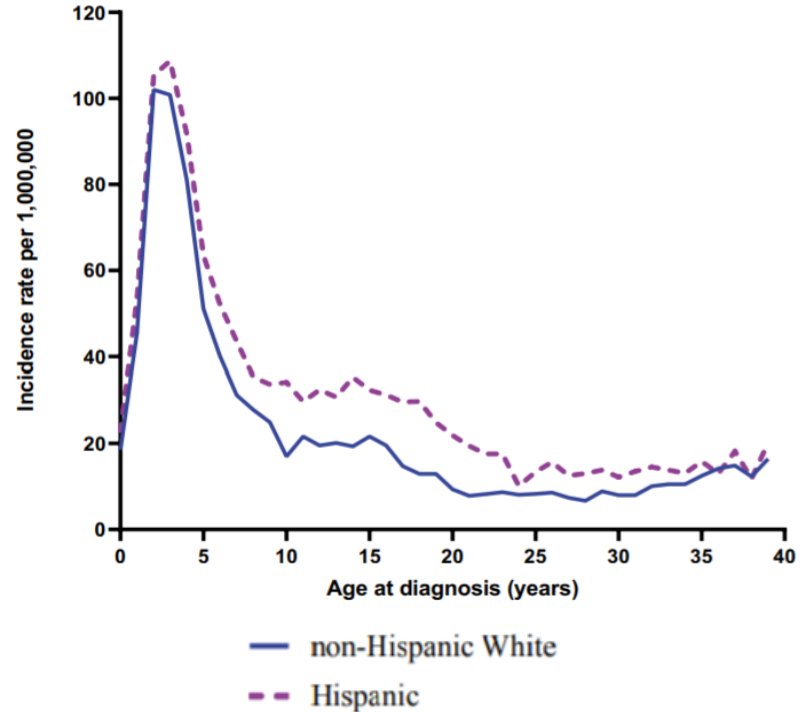
# Racial and Ethnic Disparities in Pediatric Cancer Incidence Among Children and Young Adults in the United States by Single Year of Age

Erin L. Marcotte, PhD <sup>1,2</sup>; Allison M. Domingues, MS<sup>1</sup>; Jeannette M. Sample, MPH <sup>1</sup>; Michaela R. Richardson, MPH<sup>1</sup>; and Logan G. Spector, PhD<sup>1,2</sup>

**A** la Acute lymphoid leukemia



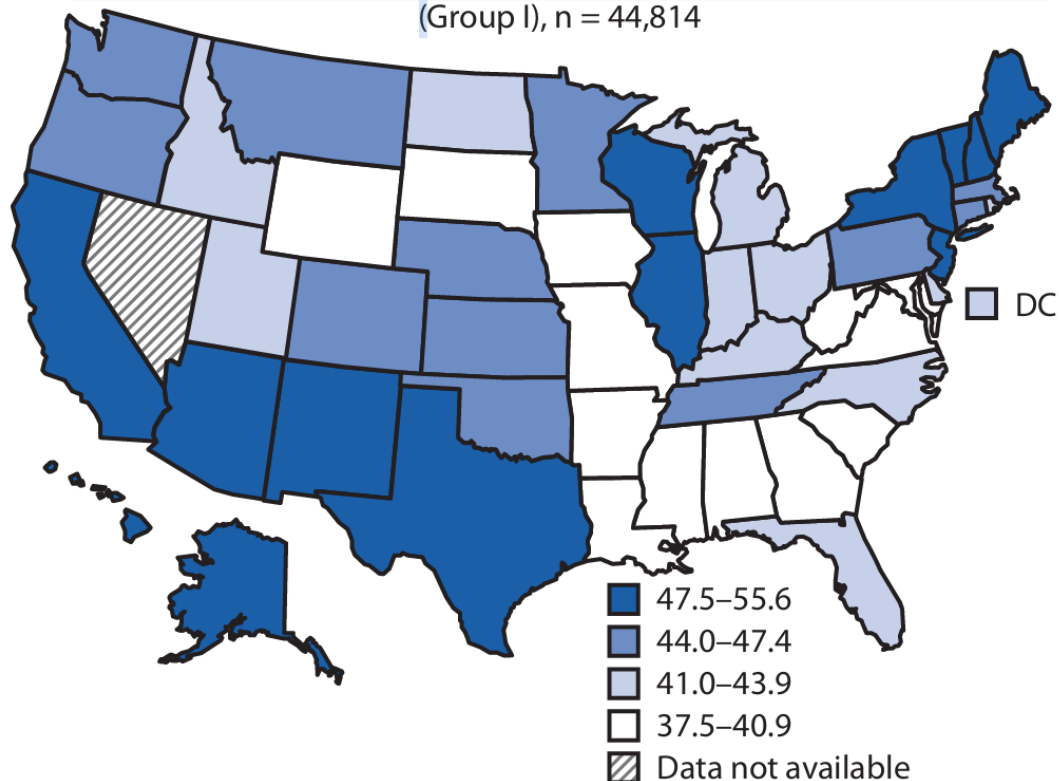
**A** la Acute lymphoid leukemia



## Geographic Variation in Pediatric Cancer Incidence — United States, 2003–2014

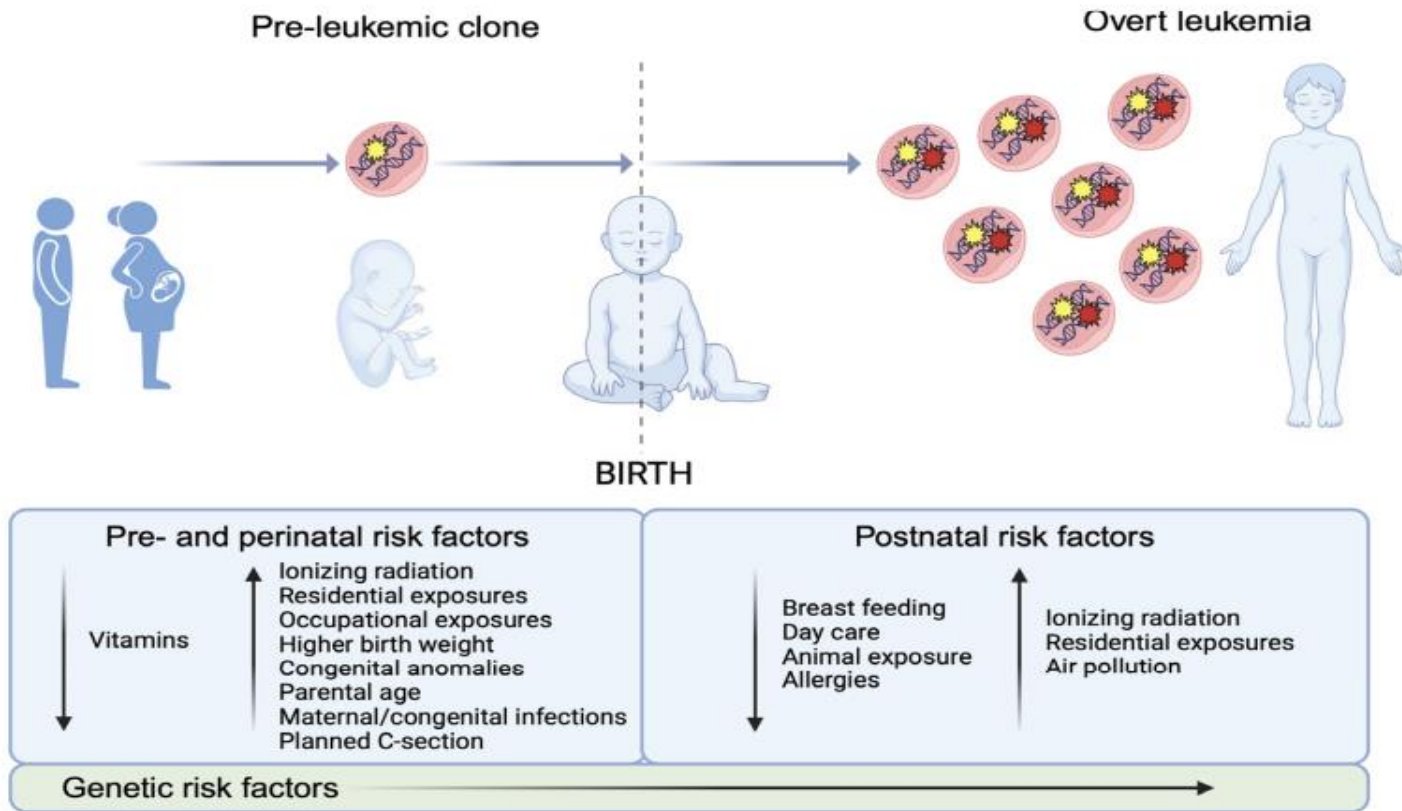
David A. Siegel, MD<sup>1,2</sup>; Jun Li, MD, PhD<sup>2</sup>; S. Jane Henley, MSPH<sup>2</sup>; Reda J. Wilson, MPH<sup>2</sup>; Natasha Buchanan Lunsford, PhD<sup>2</sup>;  
Eric Tai, MD<sup>2</sup>; Elizabeth A. Van Dyne, MD<sup>1,2</sup>

Leukemias, myeloproliferative diseases, and myelodysplastic diseases  
(Group I), n = 44,814



# In utero origins of childhood leukemia

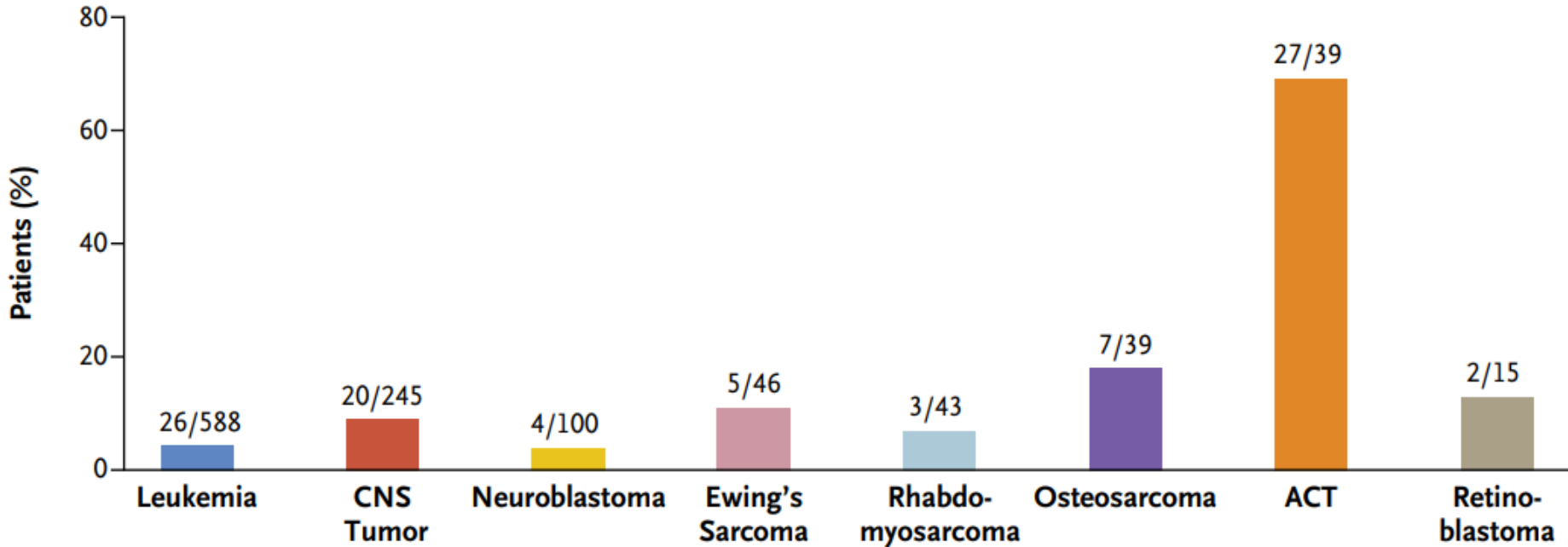
☀ Initiating lesion  
☀ Second-hit mutations



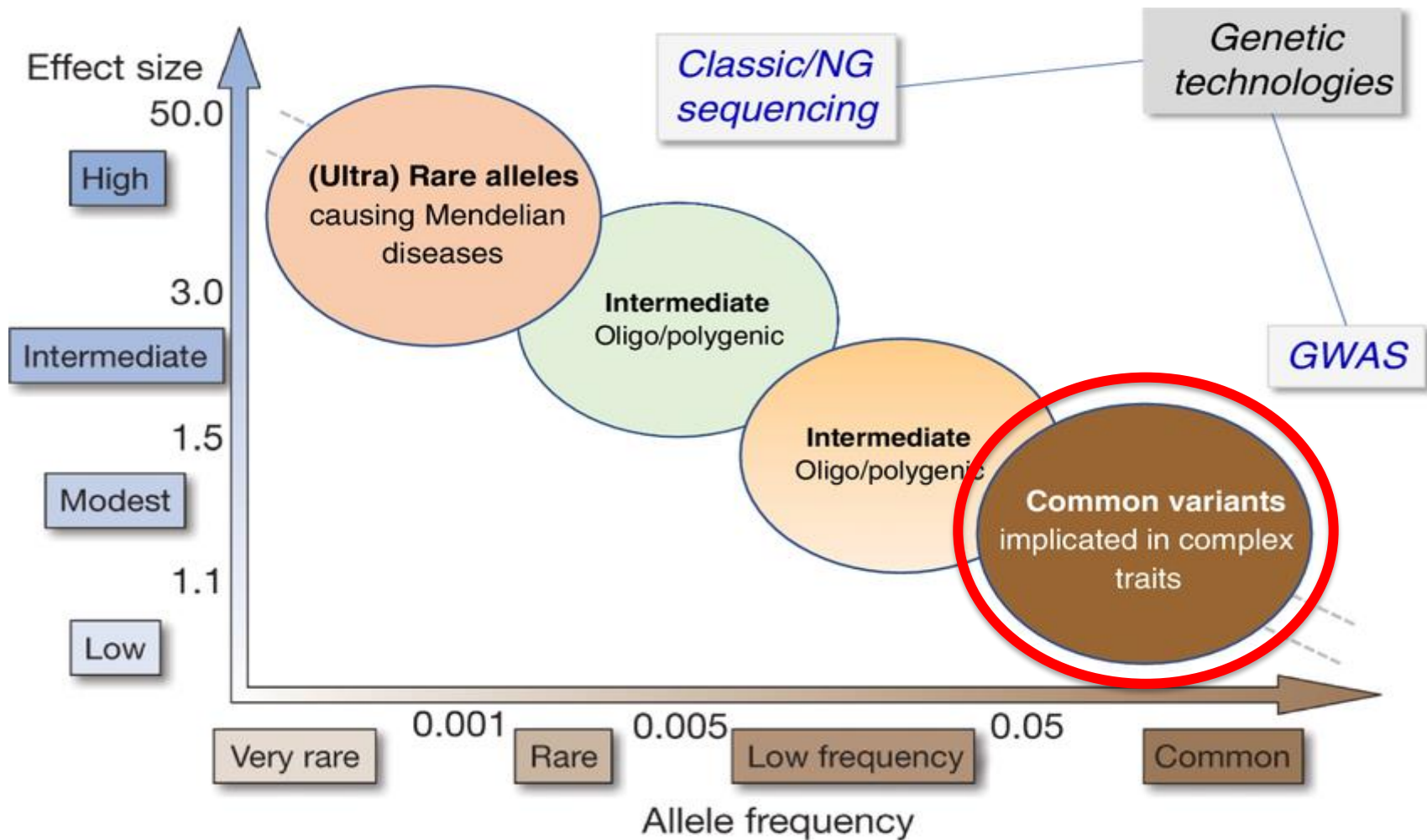
De Smith and Spector, 2024

# Germline Mutations in Predisposition Genes in Pediatric Cancer

## B Mutation Frequency in 21 Genes, According to Cancer Subtype

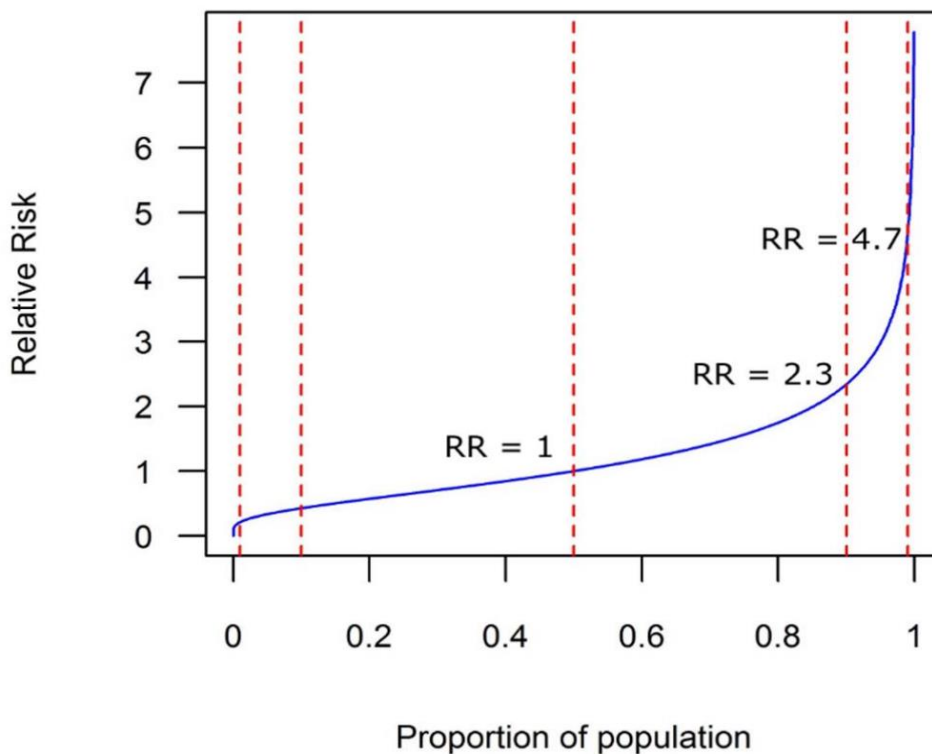


Zhang et al, 2015

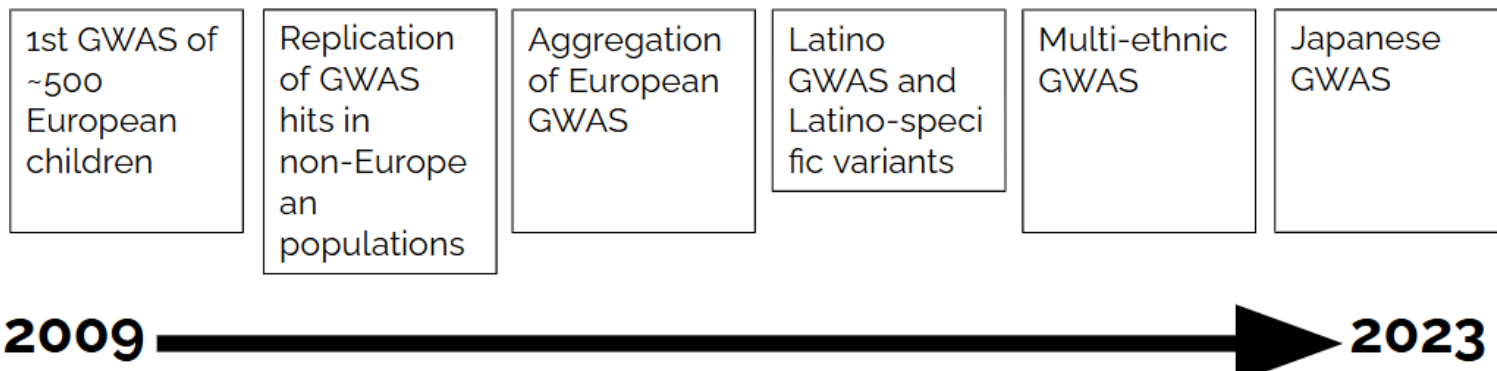


# Identification of four novel associations for B-cell acute lymphoblastic leukaemia risk

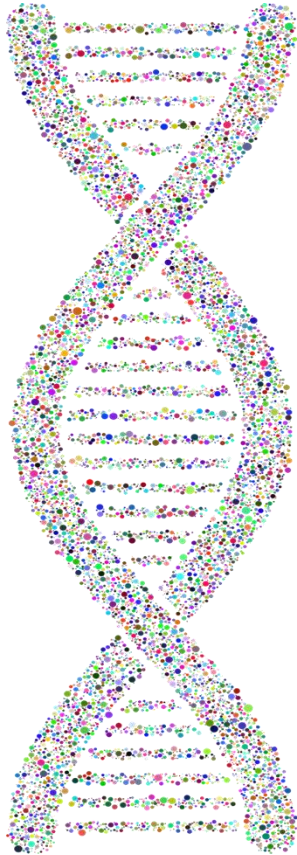
Jayaram Vijayakrishnan<sup>1,19</sup>, Maoxiang Qian<sup>2,3,19</sup>, James B. Studd<sup>1</sup>, Wenjian Yang<sup>2</sup>, Ben Kinnersley<sup>1</sup>, Philip J. Law<sup>1</sup>, Peter Broderick<sup>1</sup>, Elizabeth A. Raetz<sup>4</sup>, James Allan<sup>5</sup>, Ching-Hon Pui<sup>6,7</sup>, Ajay Vora<sup>8</sup>, William E. Evans<sup>2,7</sup>, Anthony Moorman<sup>9</sup>, Allen Yeoh<sup>10,11</sup>, Wentao Yang<sup>2</sup>, Chunliang Li<sup>12</sup>, Claus R. Bartram<sup>13</sup>, Charles G. Mullighan<sup>6,7,14</sup>, Martin Zimmerman<sup>15</sup>, Stephen P. Hunger<sup>16</sup>, Martin Schrappe<sup>17</sup>, Mary V. Relling<sup>2,7</sup>, Martin Stanulla<sup>15</sup>, Mignon L. Loh<sup>18</sup>, Richard S. Houlston<sup>1\*</sup> & Jun J. Yang<sup>2,6,7\*</sup>



# History of GWAS in ALL



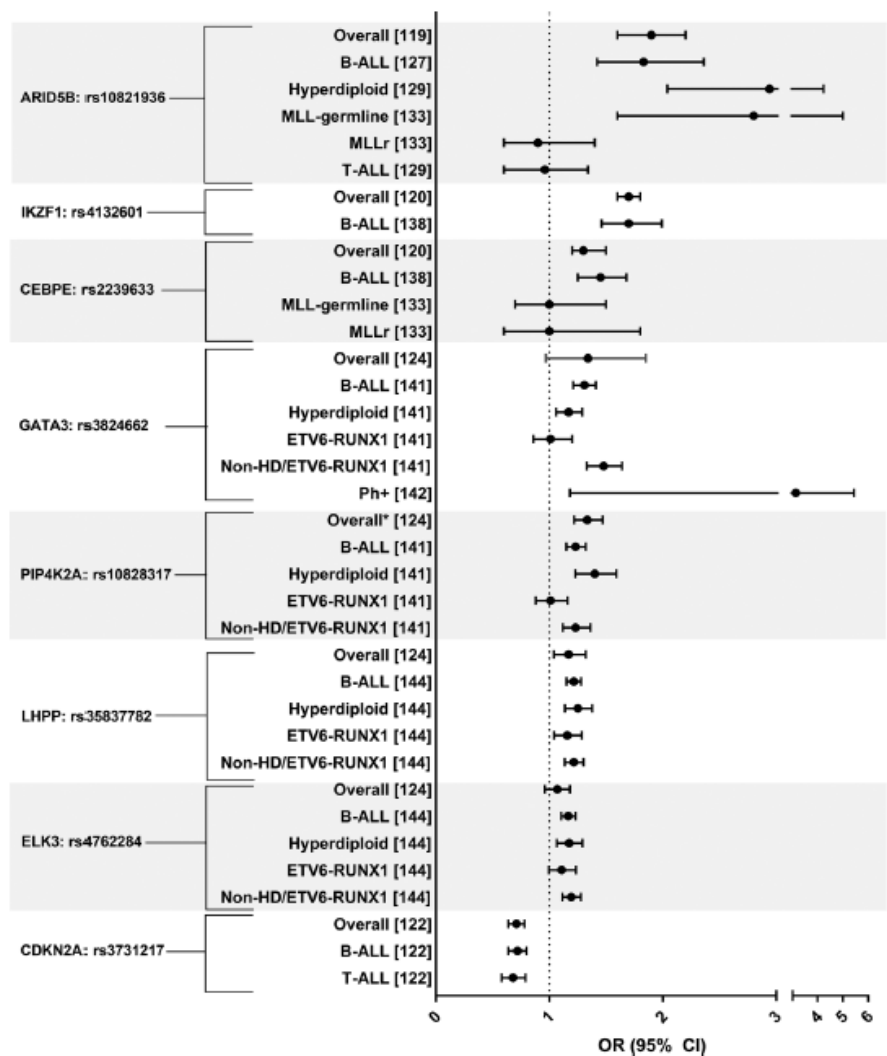
# Themes in the Genetic Architecture of ALL



- Rare, high penetrance variation < 10% of patients
- Several moderately rare germline variants with OR's of 2-5 in genes of somatic interest (e.g. PAX5, ETV6)
- High common-SNP heritability (~24%)
- Strong per-allele OR's
- Most SNPs involved in lymphocyte development
- Most SNPs replicate transethnically with similar effect sizes despite differing allele frequencies
- Many variants have differing associations with molecularly-defined subtypes
- **Population-specific variants have also emerged**

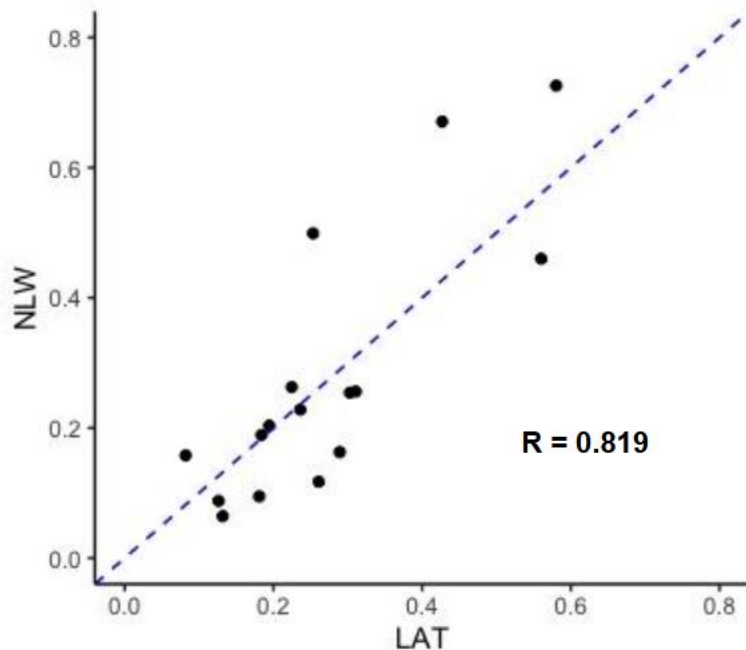
# Is There Etiologic Heterogeneity between Subtypes of Childhood Acute Lymphoblastic Leukemia? A Review of Variation in Risk by Subtype

Lindsay A. Williams<sup>1</sup>, Jun J. Yang<sup>2,3</sup>, Betsy A. Hirsch<sup>4,5</sup>, Erin L. Marcotte<sup>1,5</sup>, and Logan G. Spector<sup>1,5</sup>

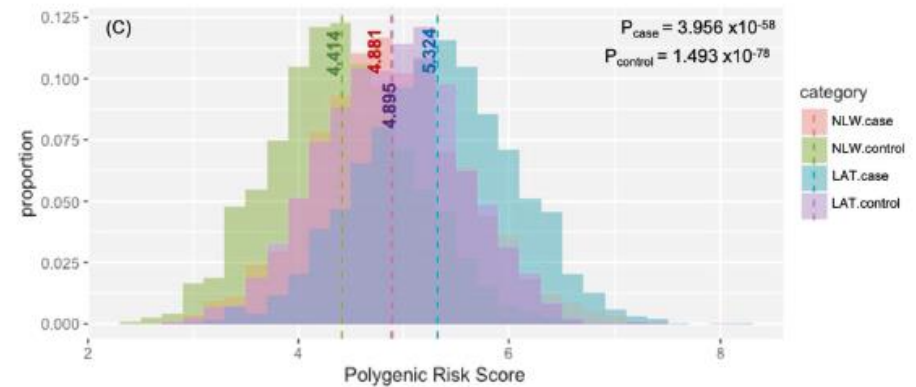
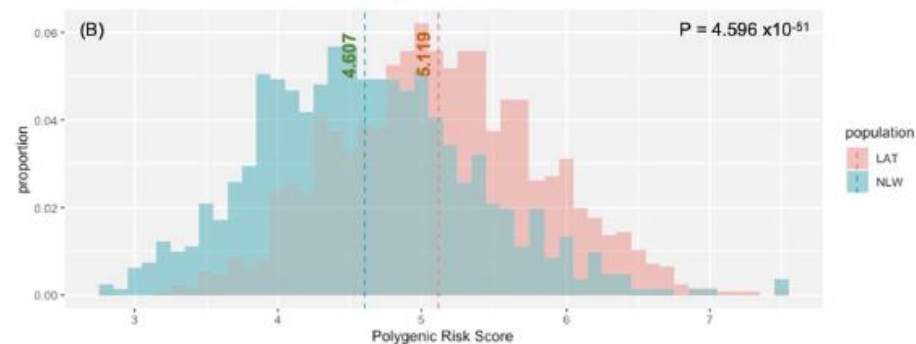
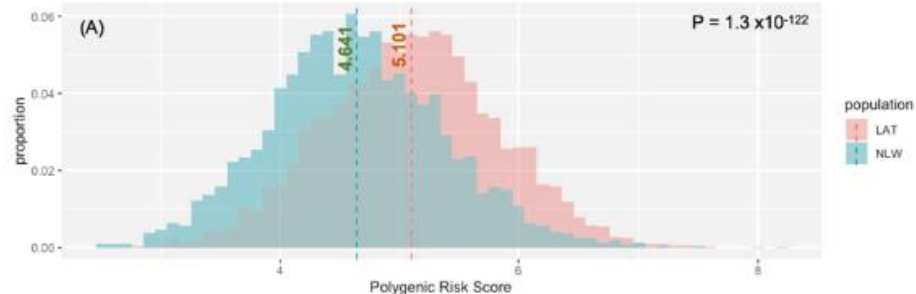


## Genome-wide trans-ethnic meta-analysis identifies novel susceptibility loci for childhood acute lymphoblastic leukemia

Soyoung Jeon<sup>1,2</sup>, Adam J. de Smith<sup>1</sup>, Shaobo Li<sup>1,2</sup>, Minhui Chen<sup>1</sup>, Tsz Fung Chan<sup>1</sup>, Ivo S. Muskens<sup>1</sup>, Libby M. Morimoto<sup>3</sup>, Andrew T. DeWan<sup>4,5</sup>, Nicholas Mancuso<sup>1,6,7</sup>, Catherine Metayer<sup>8</sup>, Xiaomei Ma<sup>9</sup>, Joseph L. Wiemels<sup>1,10</sup> and Charleston W. K. Chiang<sup>1,6,10</sup>

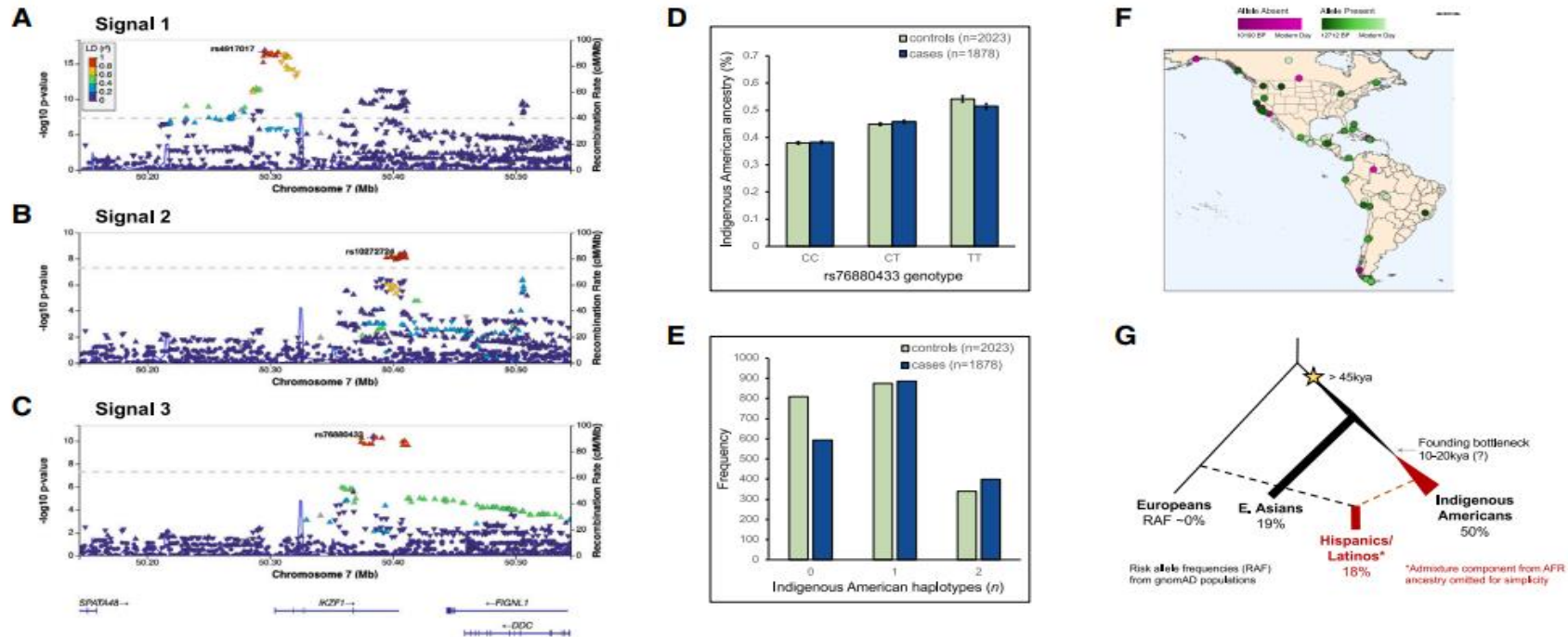


Effect sizes for lead SNPs in each of the 16 known loci



# A noncoding regulatory variant in *IKZF1* increases acute lymphoblastic leukemia risk in Hispanic/Latino children

Adam J. de Smith,<sup>1,2,13,\*</sup> Lara Wahlester,<sup>3,4,13</sup> Soyung Jeon,<sup>1,2,13</sup> Linda Kachuri,<sup>5</sup> Susan Black,<sup>3,4</sup> Jalen Langie,<sup>1,2</sup> Liam D. Cato,<sup>3,4</sup> Nathan Nakatsuka,<sup>6</sup> Tsz-Fung Chan,<sup>1,2</sup> Guangze Xia,<sup>7</sup> Soumyaa Mazumder,<sup>3,4</sup> Wenjian Yang,<sup>8</sup> Steven Gazal,<sup>1,2</sup> Celeste Eng,<sup>9,10</sup> Donglei Hu,<sup>9</sup> Esteban González Burchard,<sup>9,10</sup> Elad Ziv,<sup>9</sup> Catherine Metayer,<sup>11</sup> Nicholas Mancuso,<sup>1,2</sup> Jun J. Yang,<sup>8</sup> Xiaomei Ma,<sup>12</sup> Joseph L. Wiemels,<sup>1,2</sup> Fulong Yu,<sup>3,4,7,14</sup> Charleston W.K. Chiang,<sup>1,2,14</sup> and Vijay G. Sankaran<sup>3,4,14,15,\*</sup>

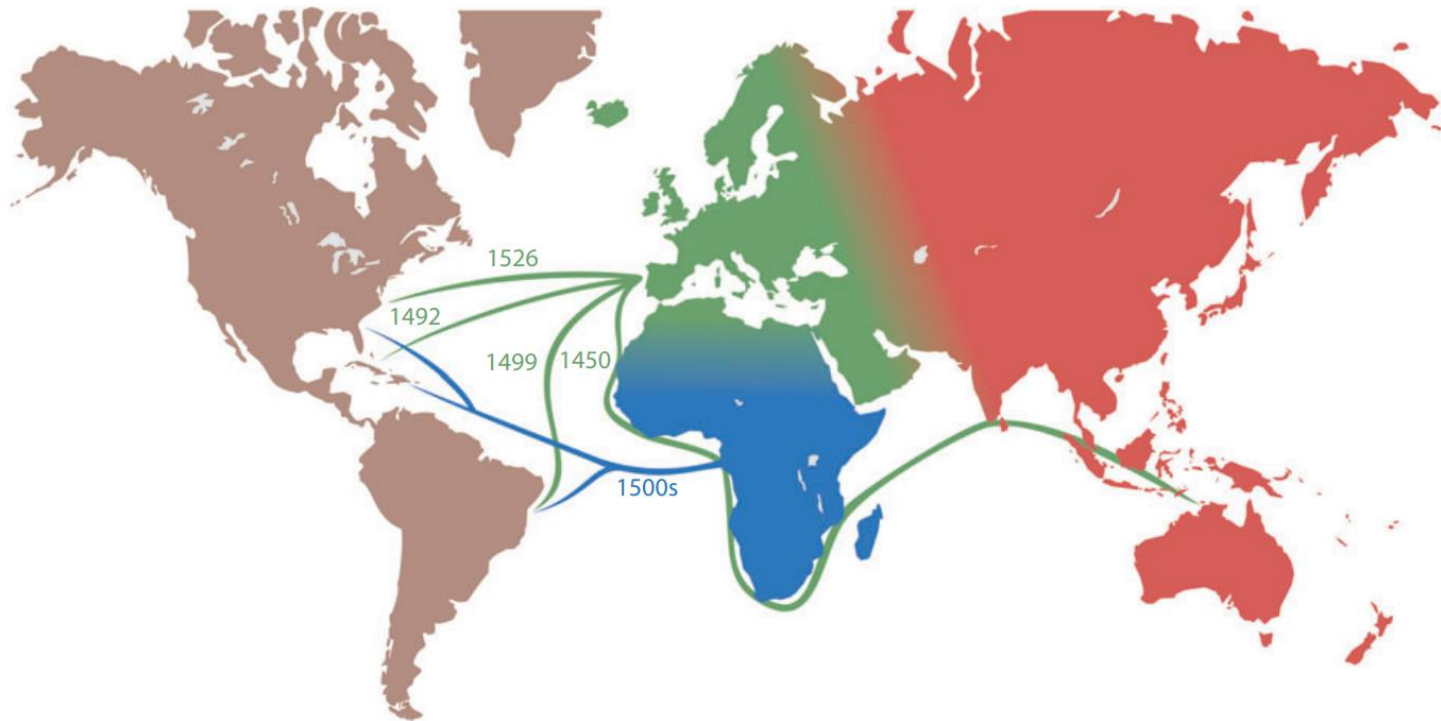


**Figure 1. Novel childhood ALL risk locus at *IKZF1* is associated with Indigenous American ancestry and demonstrates ancient origins and positive selection in Hispanic/Latino populations**



# The ADMIRAL Study

Admixture analysis of acute lymphoblastic leukemia in African American children





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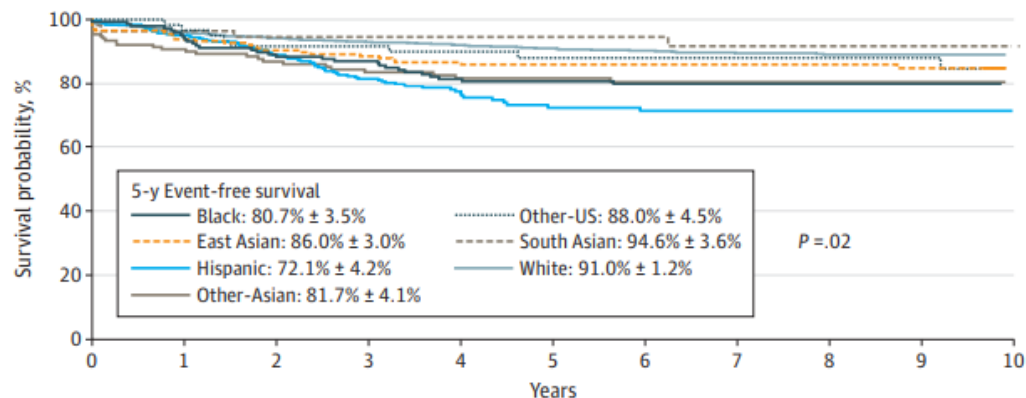


- Markedly lower risk in both sub-Saharan Africa and African diaspora
- Lower risk robust to control for SES and perinatal risk factors
- Burden of putative risk factors for ALL mostly fall more heavily on AA children
- Blood cell parameters differ widely in AA and have known genetic influences (e.g. Duffy allele)

# Association of Genetic Ancestry With the Molecular Subtypes and Prognosis of Childhood Acute Lymphoblastic Leukemia

Shawn H. R. Lee, MBBS; Federico Antillon-Klussmann, MD; Deqing Pei, MS; Wenjian Yang, PhD; Kathryn G. Roberts, PhD; Zhenhua Li, PhD; Meenakshi Devidas, PhD; Wentao Yang, PhD; Cesar Najera, BS; Hai Peng Lin, MBBS; Ah Moy Tan, MBBS; Hany Ariffin, MBBS; Cheng Cheng, PhD; William E. Evans, PharmD; Stephen P. Hunger, MD; Sima Jeha, MD; Charles G. Mullighan, MD; Mignon L. Loh, MD; Allen E. J. Yeoh, MBBS; Ching-Hon Pui, MD; Jun J. Yang, PhD

**A** Event-free survival



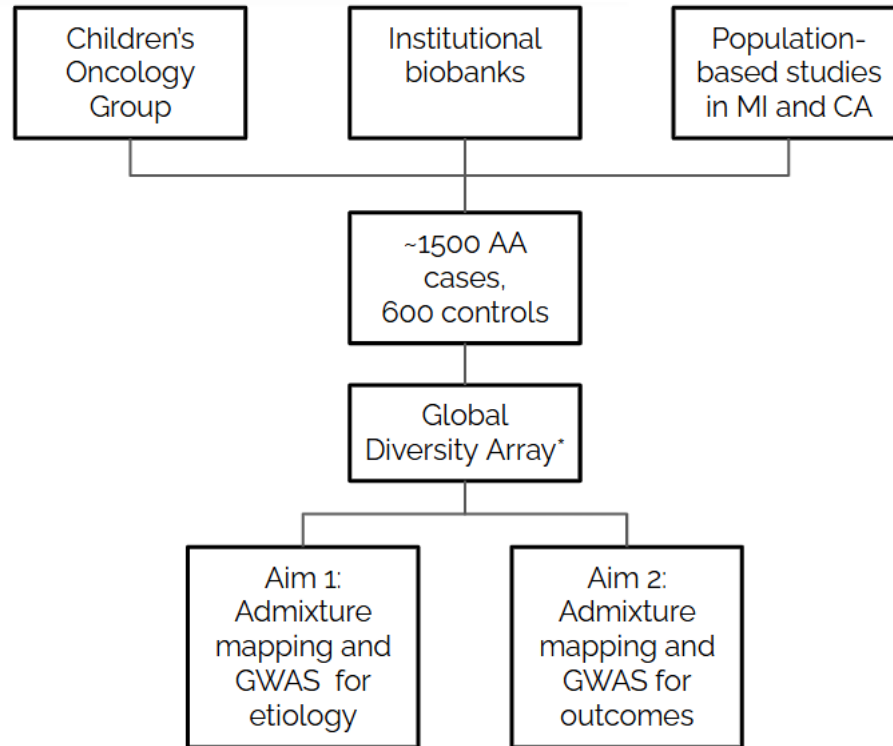
No. at risk	0	1	2	3	4	5	6	7	8	9	10
Black	147	139	129	127	112	99	93	83	79	64	58
East Asian	202	170	155	143	128	117	110	98	83	70	57
Hispanic	305	289	232	196	120	82	75	69	65	58	49
Other-Asian	152	128	107	97	84	72	66	58	49	42	35
Other-US	61	58	55	55	50	44	40	34	29	26	21
South Asian	56	53	50	45	39	36	34	29	25	22	18
White	673	647	633	611	562	514	471	427	391	355	309

Prognostic factor	Event-free survival	
	HR (95% CI)	P value <sup>a</sup>
Age at diagnosis, y		
<1	2.4 (1.1-5.0)	.06
≥1 to <10	1 [Reference]	
≥10	1.2 (0.9-1.6)	
Leukocyte count at diagnosis, cells/μL		
<50 000	1 [Reference]	.006
≥50 000	1.5 (1.1-2.1)	
Biological subtypes <sup>b</sup>		
<i>ETV6-RUNX1</i>	1 [Reference]	<.001
<i>DUX4</i>	1.8 (0.7-4.4)	
Hyperdiploid	2.0 (1.0-3.8)	
<i>ZNF384</i>	2.9 (0.9-8.9)	
B other	3.4 (1.7-6.8)	
<i>CRLF2</i>	7.2 (3.4-15.0)	
<i>ETV6-RUNX1</i> -like	6.3 (2.7-14.9)	
<i>KMT2A</i>	6.5 (2.9-14.7)	
Low hypodiploid	10.0 (3.7-27.5)	
<i>MEF2D</i>	4.5 (1.3-15.8)	
Near haploid	12.2 (3.9-38.1)	
<i>PAX5alt</i>	3.5 (1.6-7.5)	
<i>BCR-ABL1</i>	7.4 (3.3-16.5)	
<i>BCR-ABL1</i> -like	6.9 (3.1-15.4)	
T-ALL	4.8 (2.5-9.0)	
<i>TCF3-PBX1</i>	2.3 (1.0-5.3)	
Percentage genetic ancestry <sup>c</sup>		
European	1 [Reference]	.005
African (every 25% increase)	1.2 (1.1-1.4)	
Native American (every 25% increase)	1.3 (1.01-1.6)	
East Asian (every 25% increase)	1.0 (0.7-1.4)	
South Asian (every 25% increase)	0.9 (0.7-1.3)	



# The ADMIRAL Study

Admixture analysis of acute lymphoblastic leukemia in African American children

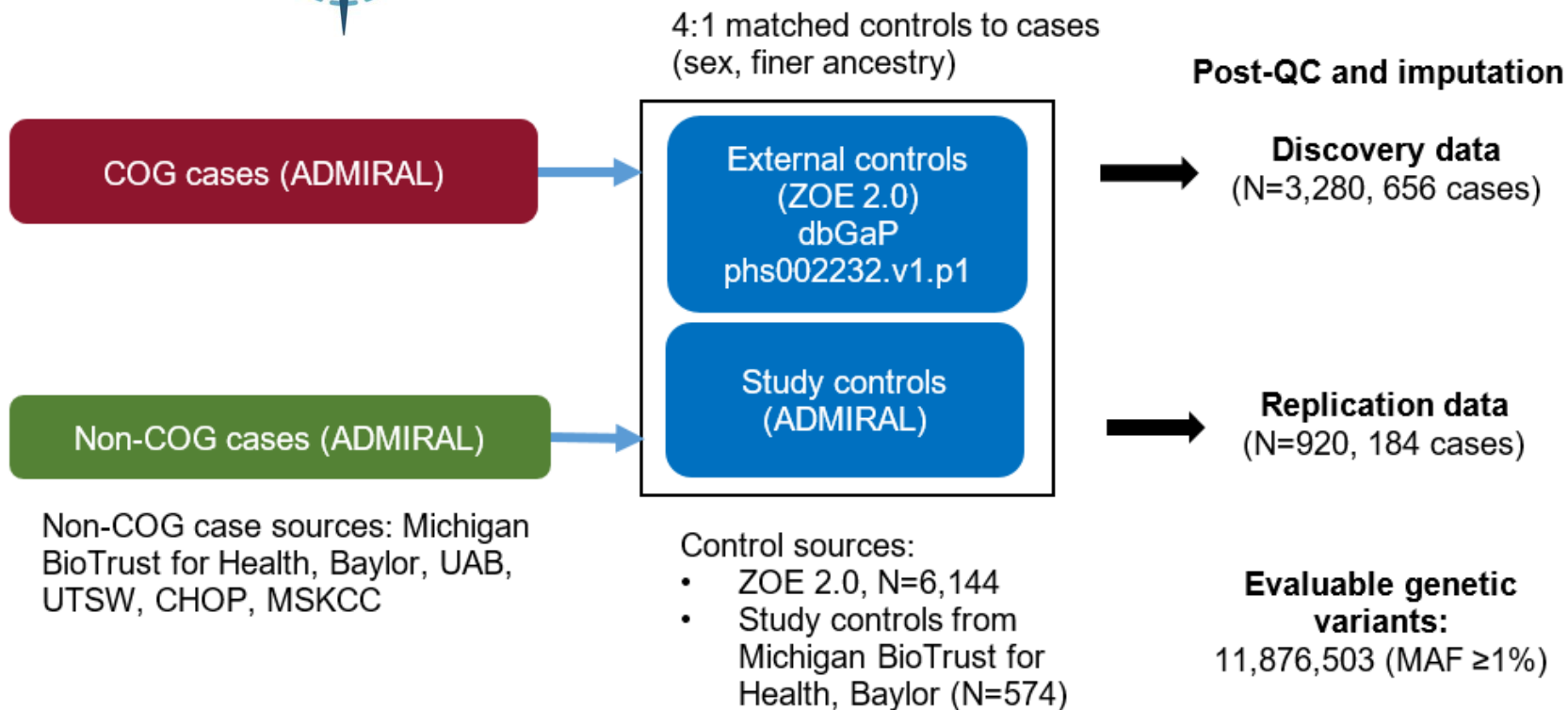


NIH R01 CA239701

\*Affymetrix Axiom World Array in CA study

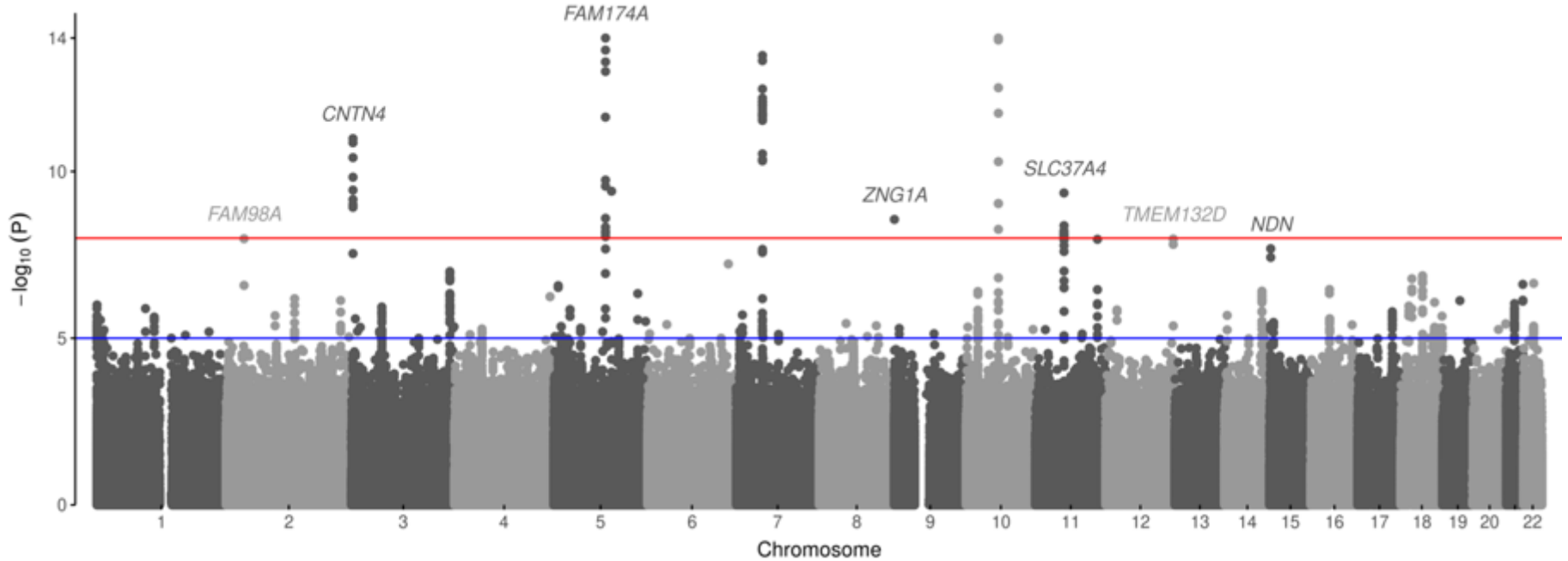


# History of GWAS in ALL



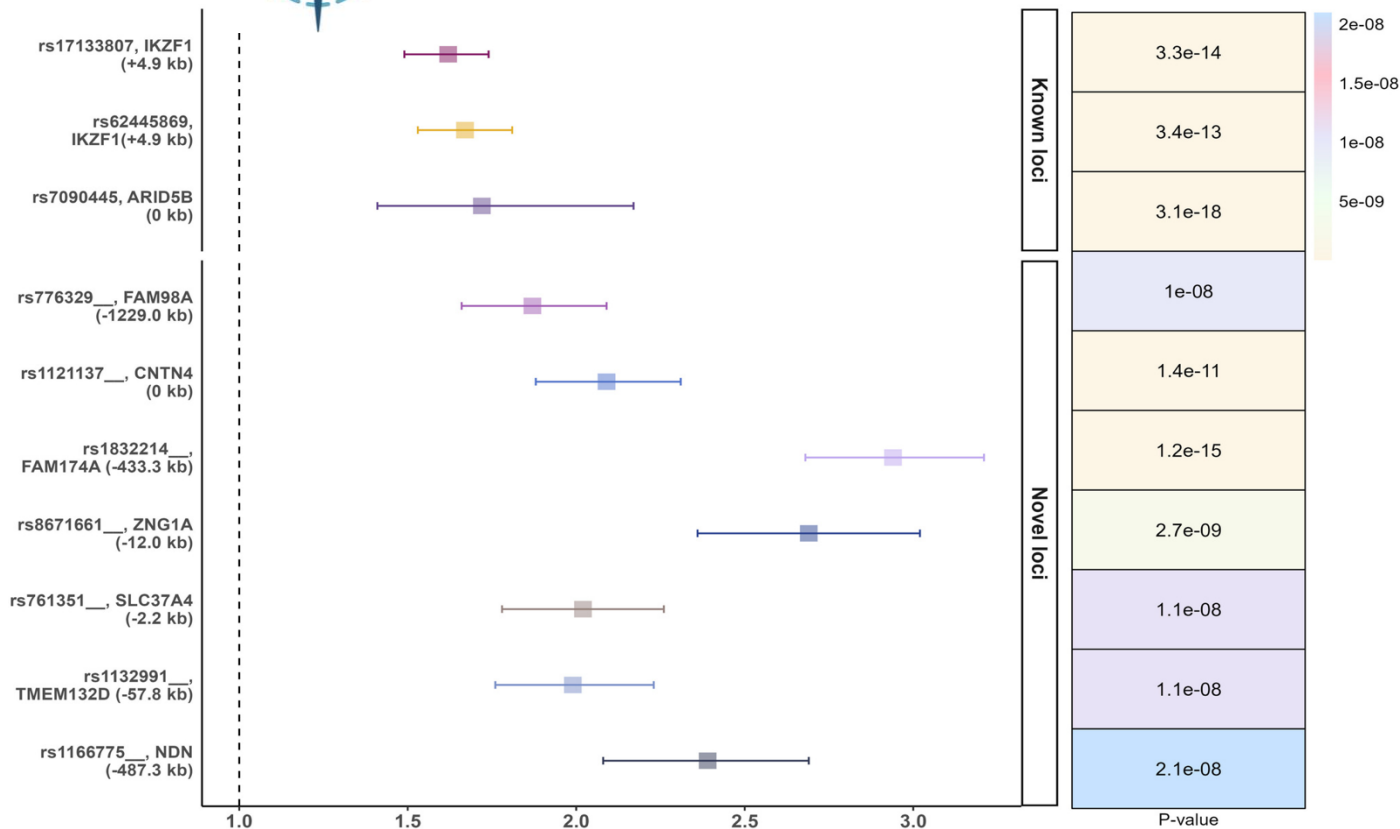


# ADMIRAL GWAS



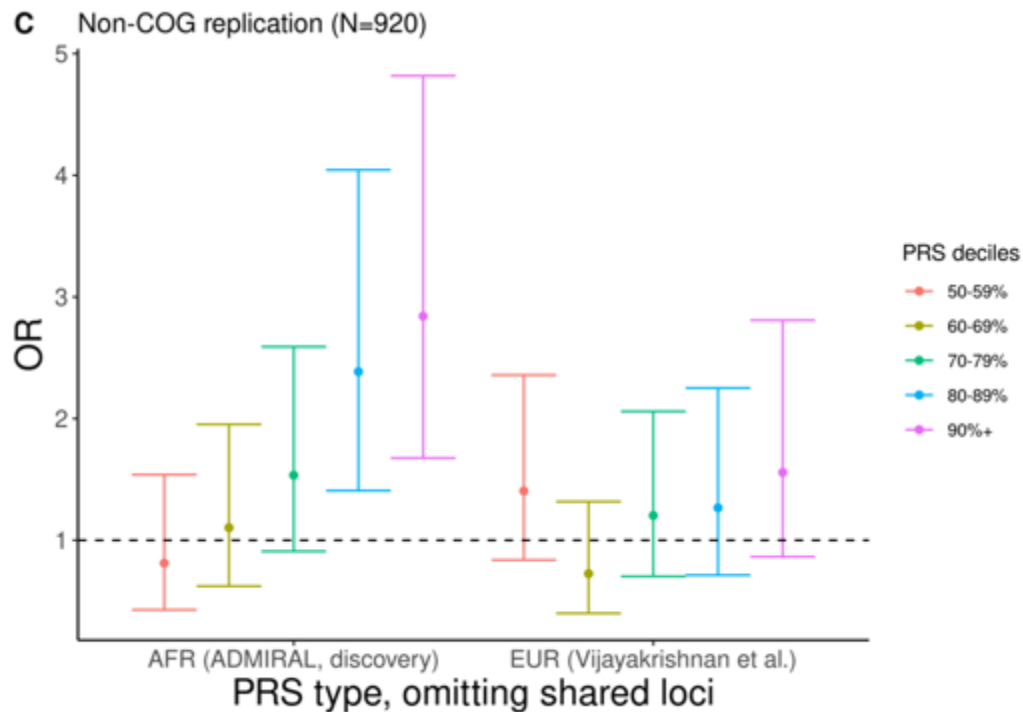
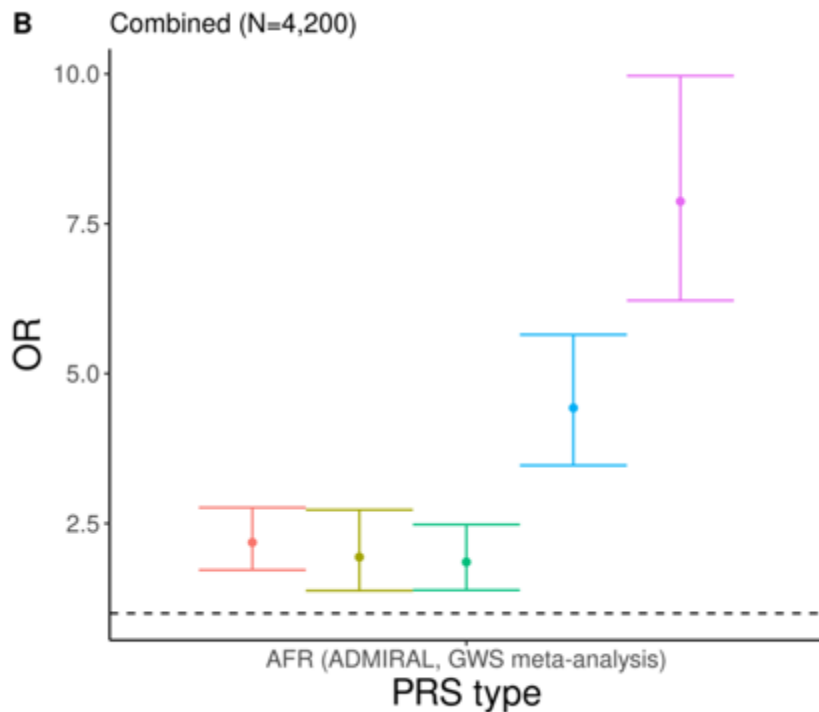


# ADMIRAL GWAS



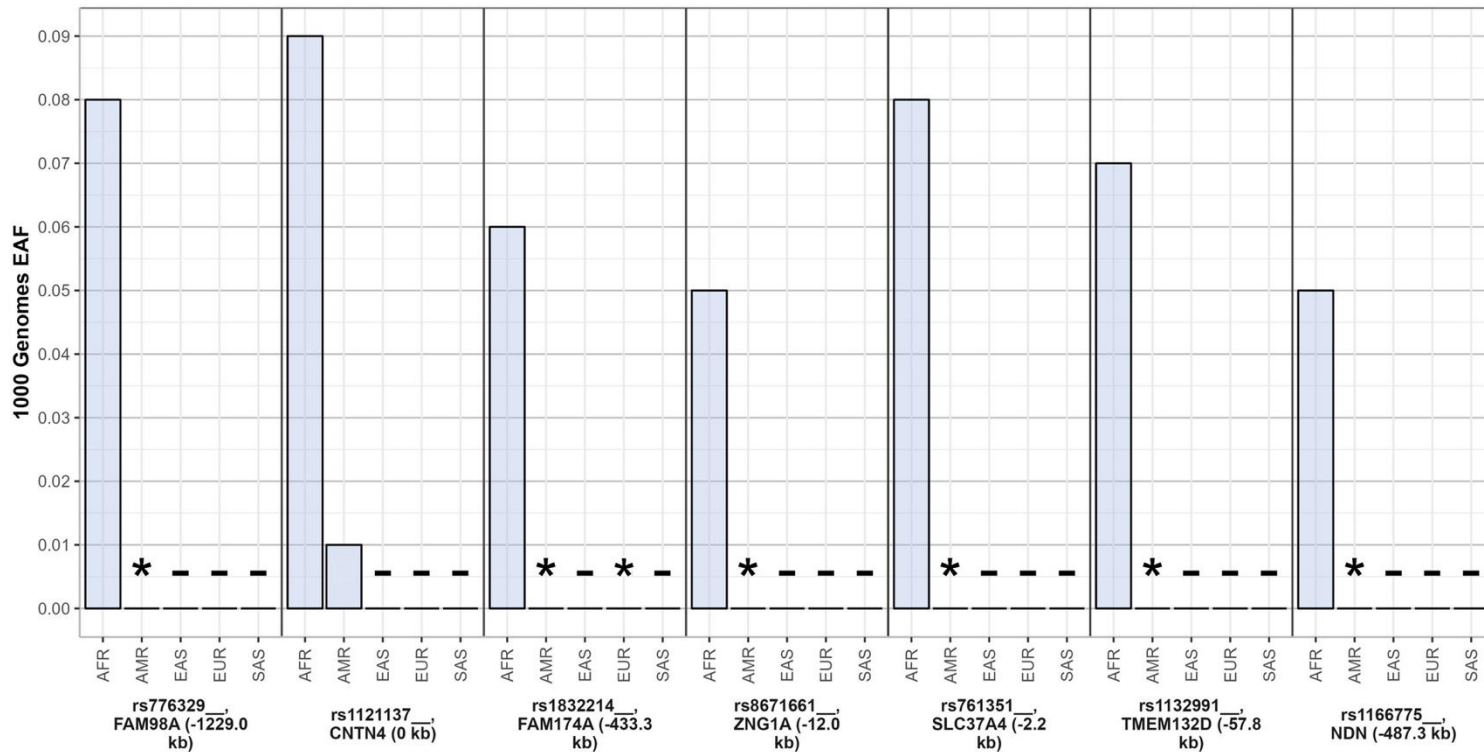


# ADMIRAL Polygenic Risk Scores(s)





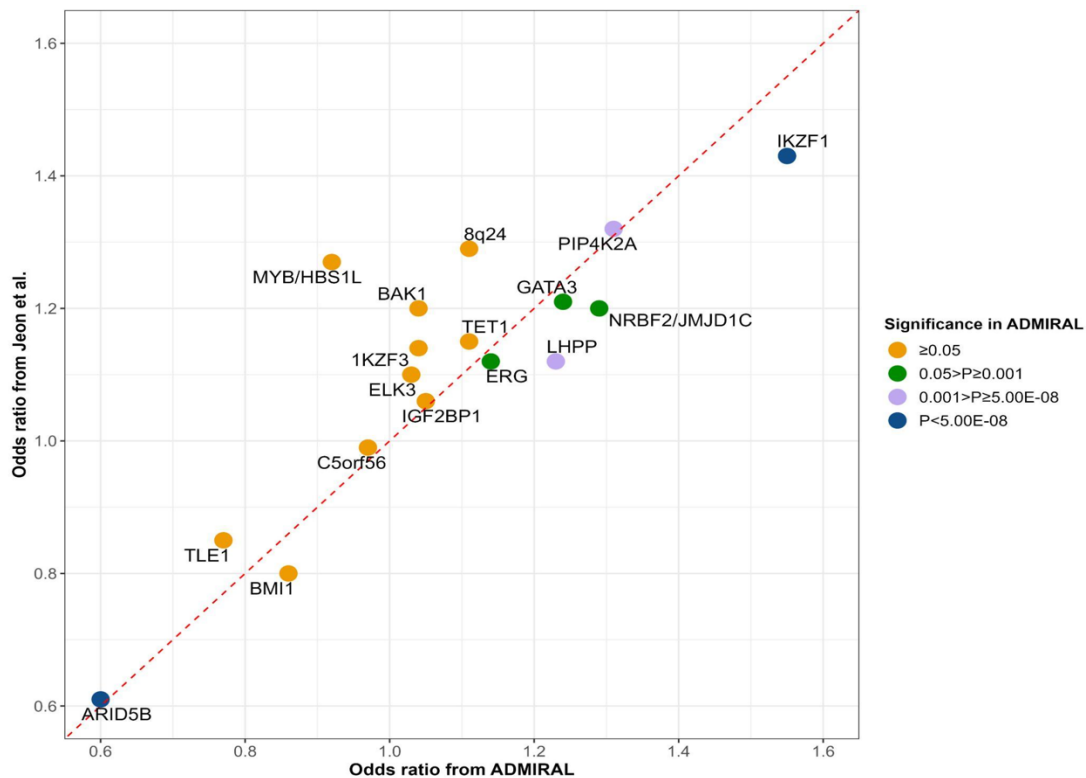
# Effect Allele Frequency of Novel Loci in 1000 Genomes



Asterisks (\*) represent EAFs  $\geq 0.001$  and  $< 0.01$  and dashes (-) represent EAFs  $< 0.001$

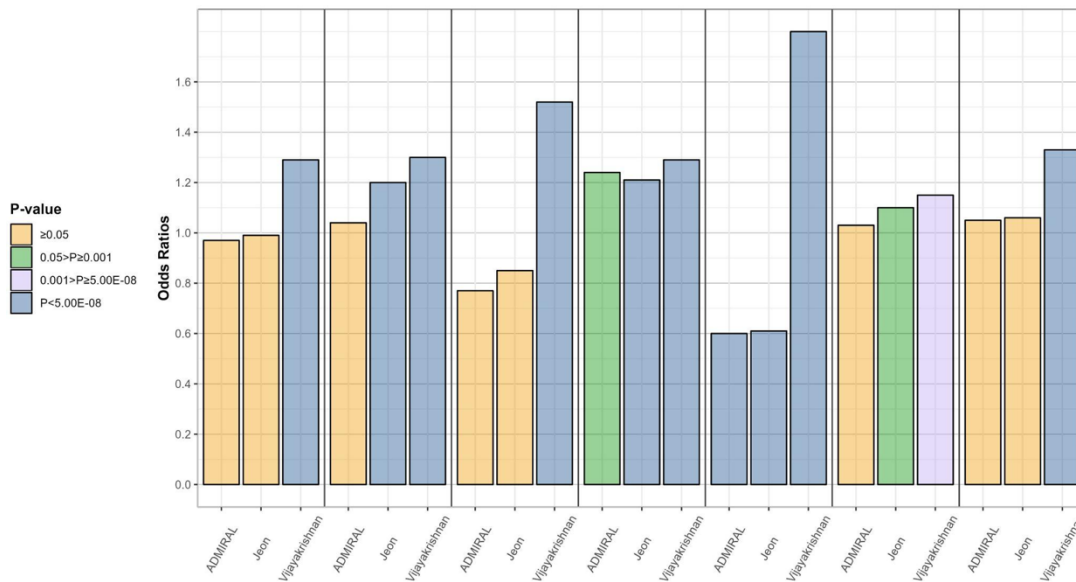


# Correlation of OR of Known Loci in Jeon et al with ADMIRAL





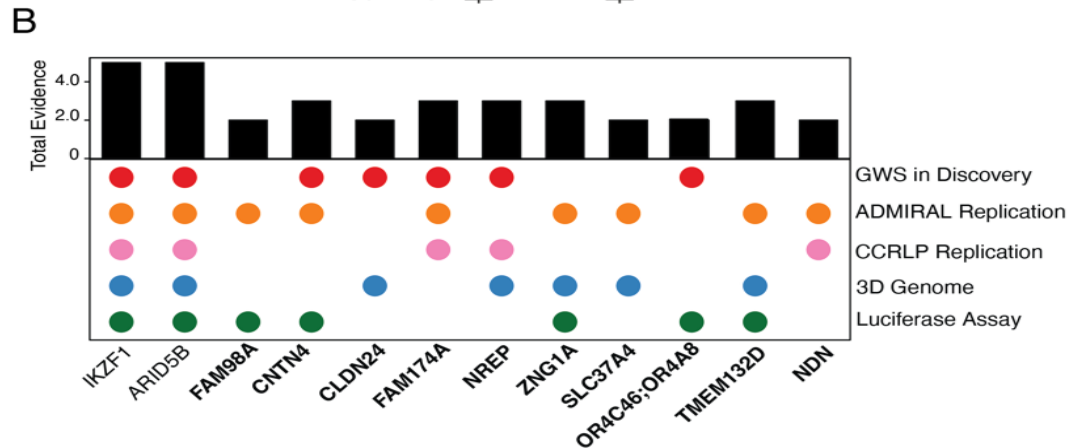
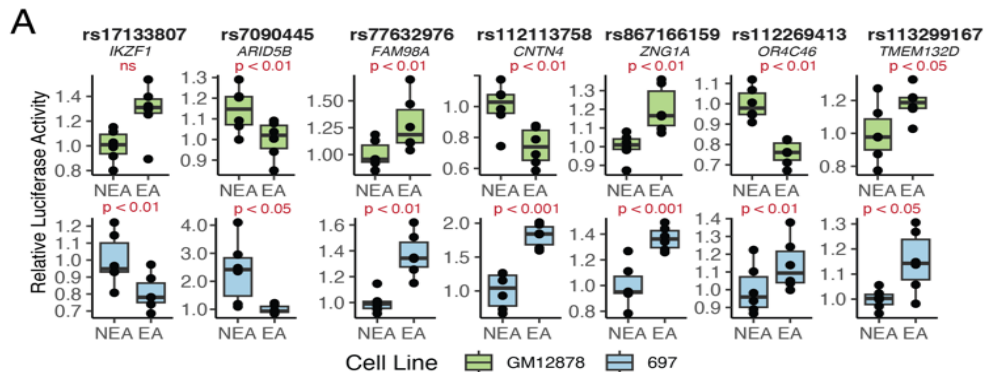
# ORs in 3 GWAS and Effect Allele Frequencies in 1000 Genomes



	rs886285, C5orf56	rs210143, BAK1	rs76925697, TLE1	rs3824662, GATA3	rs10821936, ARID5B	rs4762284, ELK3	rs10853104, IGF2BP1
AFR -	0.28	0.76	0.03	0.08	0.80	0.45	0.69
AMR -	0.70	0.76	0.03	0.37	0.53	0.49	0.42
EAS -	0.35	0.83	0.00	0.27	0.64	0.60	0.12
EUR -	0.66	0.73	0.04	0.19	0.67	0.30	0.47
SAS -	0.48	0.87	0.02	0.17	0.49	0.31	0.40

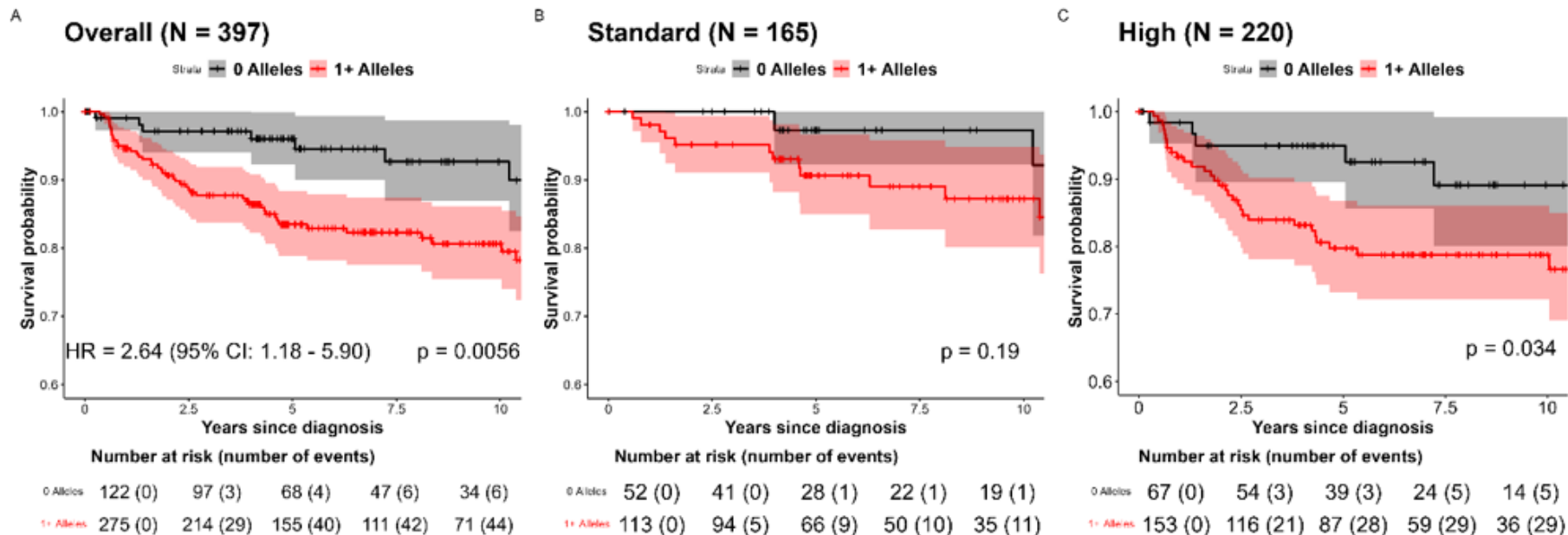


# Functional Evidence from Luciferase Reporter Assays (A), Statistical Replication (B), and 3D Genome Data (B)





# Novel Alleles and Overall Survival for B-ALL in ADMIRAL



Hazard ratio (HR) adjusted for sex, genetic ancestry, and trial treatment risk stratification



# ADMIRAL Conclusions

- **Known transethnic variants replicate in AA children**
  - Remarkably similar magnitudes of association
  - PRS less in AA children due to lower allele freqs
  - Partial explanation for lower risk in AA
- **Novel loci fit profile**
  - Low allele frequency (<10%)  
Spelling out all acronyms during the first instance
  - Large OR's
  - African-ancestry specific
  - High evidence of function
- **Novel variants appear associated with survival**

# Thank you!

## University of Minnesota

Cindy Im  
Erin Marcotte  
Jen Poynter  
Andy Raduski  
Zhanni Lu  
Tianzhong Yang  
Nathan Pankratz  
Saonli Basu

## Emory University

Philip Lupo  
Michael Scheurer  
Sharon Castellino

## Children's Oncology Group

Meenakashi Devidas  
Karen Rabin  
Sarah Vargas

## USC

Adam de Smith  
Joe Wiemels

## UC Berkeley

Catherine Metayer  
Alice Kang

## St Jude

Dan Savic  
Jun Yang



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United**



**St. Baldrick's  
FOUNDATION**  
Conquer Childhood Cancers



**National Institutes  
of Health**



[cancer.gov](http://cancer.gov)



[cancer.gov/espanol](http://cancer.gov/espanol)

# Q&A

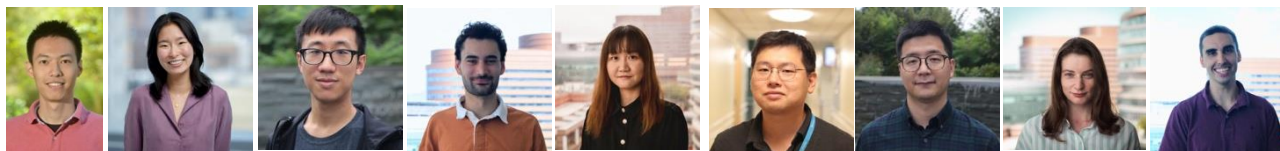
Childhood Cancer Data Initiative Virtual Symposium Series

# ILLUMINATING DARK ANTIGENS FOR CHILDHOOD CANCER IMMUNOTHERAPY

*Yi Xing, Ph.D.*

# Acknowledgments

## Xing Lab



## CHOP



Lan Lin

Richard  
Aplenc

Jessica  
Foster

## UCLA



Owen  
Witte

Gay  
Crooks

Chris  
Seet

## Penn



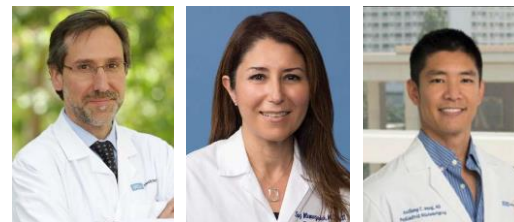
Carl June

Avery  
Posey

## Roswell Park



Song Liu

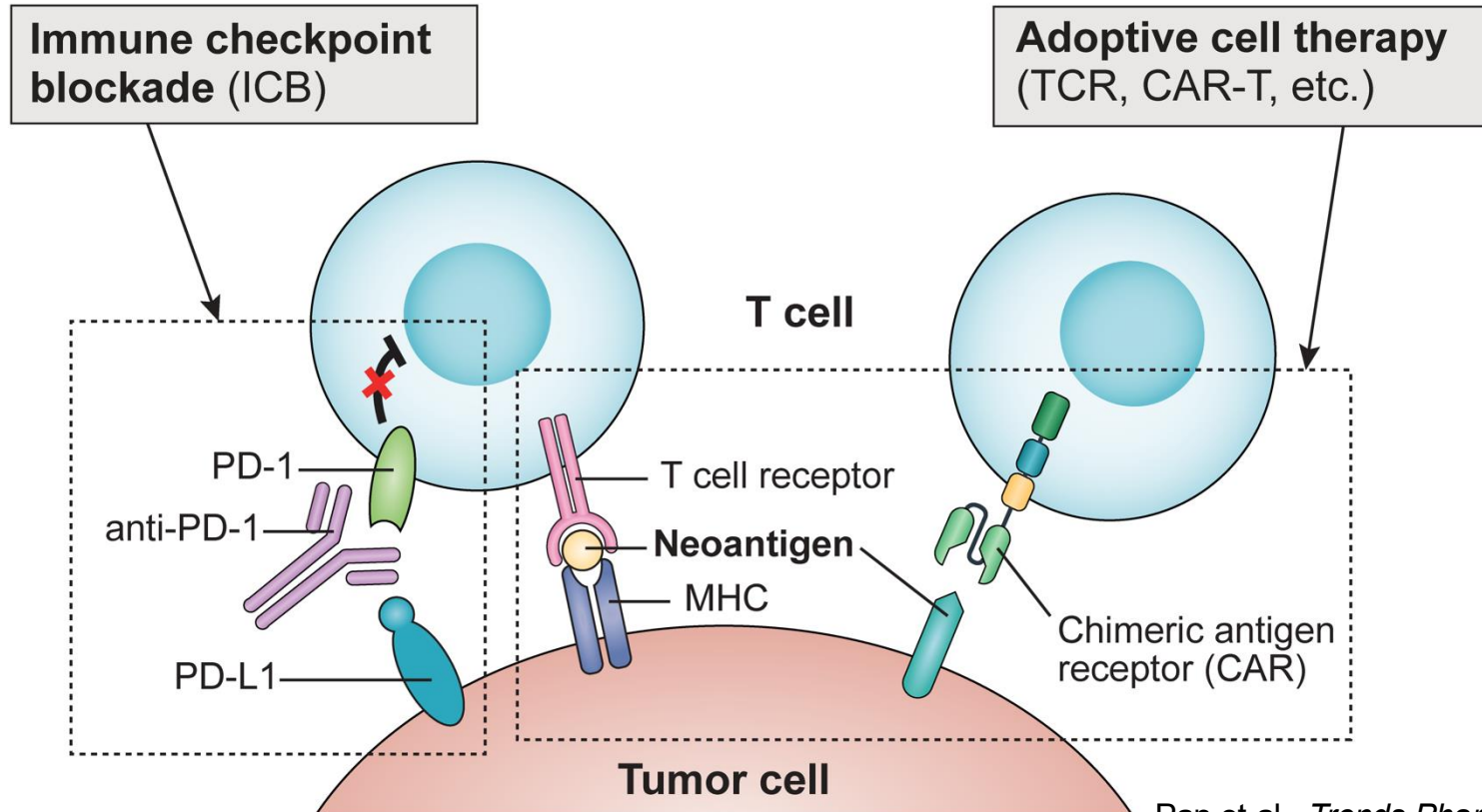


Antoni  
Ribas

Sanaz  
Memarzadeh

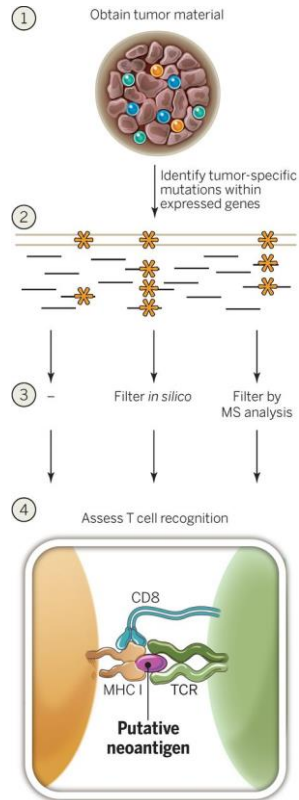
Anthony  
Wang

# Targeting Tumor Antigens for Cancer Immunotherapies



Pan et al., *Trends Pharmacol Sci*, 2021

# Immunotherapy & Tumor Antigen Discovery



Schumacher & Schreiber, *Science*, 2015

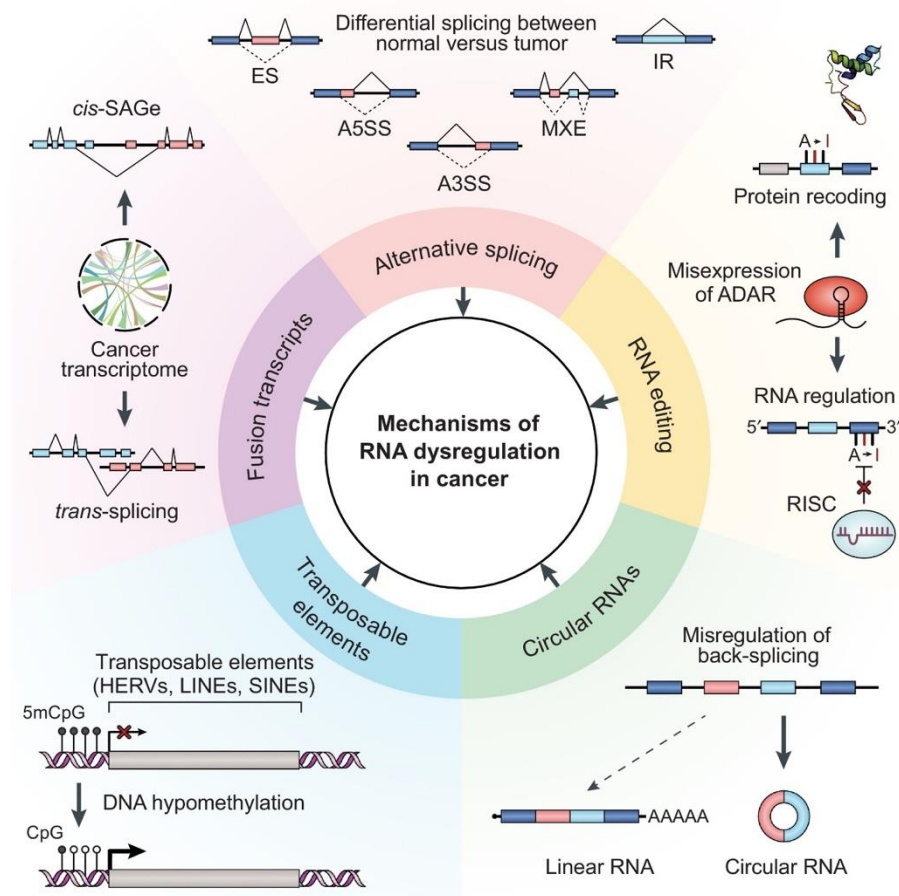
## First-generation tumor antigen discovery tools

- Focus on somatic mutations
- Use RNA-seq and/or MS proteomics to confirm expression

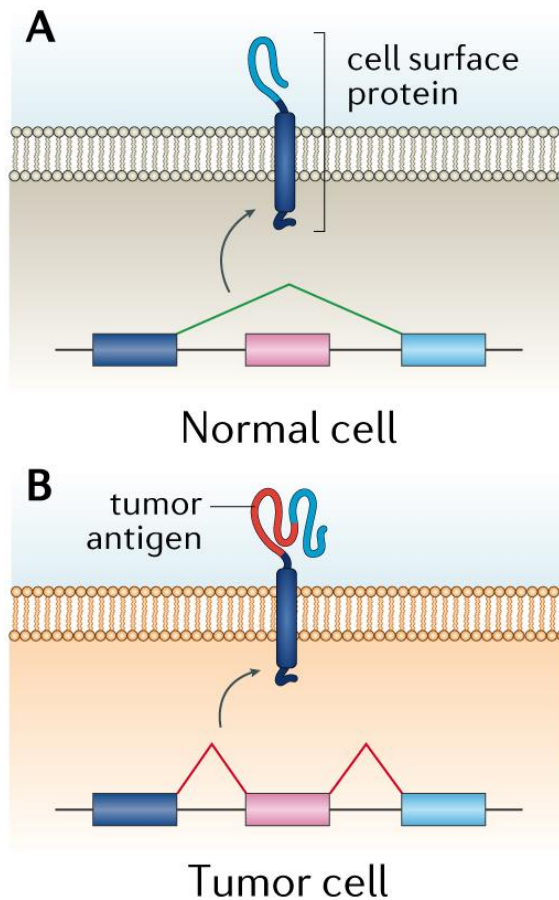
## Limitations

- Ignore other sources of transcriptomic and proteomic alterations in cancer cells (e.g., alternative splicing, RNA editing, fusion transcripts)

# RNA Dysregulation in Cancer

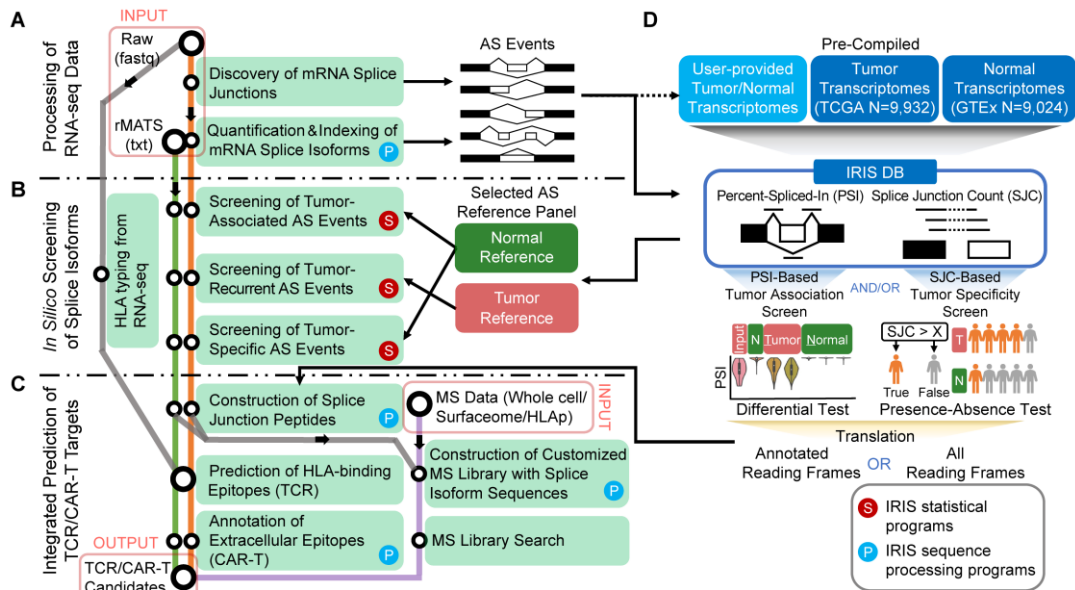


# RNA Dysregulation May Create Tumor Antigens



# IRIS: Discovery of Splicing-Derived Immunotherapy Targets Using Short-Read RNA-seq Data

Isoform peptides from RNA splicing for Immunotherapy target Screening



Targets for TCR-T/CAR-T

rMATS (Shen et al., PNAS, 2014)



DARTS (Zhang et al., Nature Methods, 2019)



IRIS (Yang et al., bioRxiv, 2019)




IRIS 2.0 (Yang et al., PNAS, 2023)


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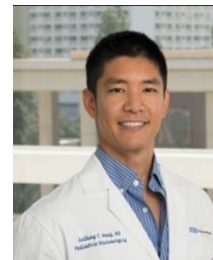
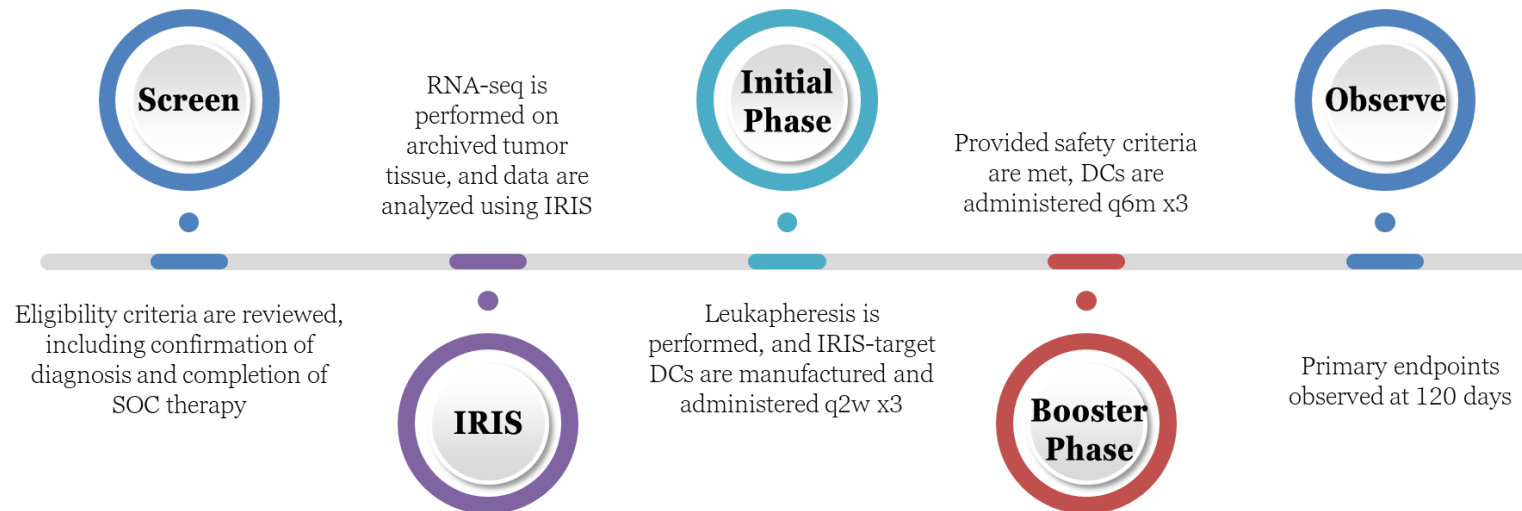
## A Vaccine (Neoantigen-Targeted ppDC) for the Treatment of H3 G34-mutant Diffuse Hemispheric Glioma

ClinicalTrials.gov ID  NCT06342908

Sponsor  Jonsson Comprehensive Cancer Center

Information provided by  Jonsson Comprehensive Cancer Center (Responsible Party)

Last Update Posted  2024-12-09



Anthony Wang, M.D.

# Cancer-Specific Alternative Splicing Creates Tumor Antigens

2023

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RESEARCH ARTICLE | IMMUNOLOGY AND INFLAMMATION

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## IRIS: Discovery of cancer immunotherapy targets arising from pre-mRNA alternative splicing

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2024

nature communications



Article

<https://doi.org/10.1038/s41586-024-47649-y>

## Discovery of immunotherapy targets for pediatric solid and brain tumors by exon-level expression

Received: 13 November 2023

Accepted: 9 April 2024

Published online: 03 May 2024

Check for updates

Timothy I. Shaw<sup>1,2,11</sup>, Jessica Wagner<sup>3,11</sup>, Lijing Tian<sup>1,3,11</sup>, Elizabeth Wickman<sup>3,4</sup>, Suresh Poudel<sup>5</sup>, Jian Wang<sup>1</sup>, Robin Paul<sup>1</sup>, Selene C. Koo<sup>6</sup>, Meifen Lu<sup>6</sup>, Heather Sheppard<sup>6</sup>, Yiping Fan<sup>7</sup>, Francis H. O'Neill<sup>8</sup>, Ching C. Lau<sup>8,9,10</sup>, Xin Zhou<sup>1</sup>, Jinghui Zhang<sup>1,12</sup> & Stephen Gottschalk<sup>3,12</sup>

2024

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CANCER

## Splicing neoantigen discovery with SNAF reveals shared targets for cancer immunotherapy

Guangyuan Li<sup>1,2,\*</sup>, Shweta Mahajan<sup>3,†</sup>, Siyuan Ma<sup>3</sup>, Erin D. Jeffery<sup>4</sup>, Xuan Zhang<sup>3</sup>, Anukana Bhattacharjee<sup>1</sup>, Meenakshi Venkatasubramanian<sup>1,5</sup>, Matthew T. Weirauch<sup>1,6,7,8</sup>, Emily R. Miraldi<sup>1,3,8</sup>, H. Leighton Grimes<sup>3,8</sup>, Gloria M. Sheynkman<sup>4</sup>, Tamara Tilburgs<sup>3,8,\*</sup>, Nathan Salomonis<sup>1,2,8,\*</sup>

2025

Article

## Tumour-wide RNA splicing aberrations generate actionable public neoantigens

<https://doi.org/10.1038/s41586-024-08552-0>

Received: 26 October 2023

Accepted: 19 December 2024

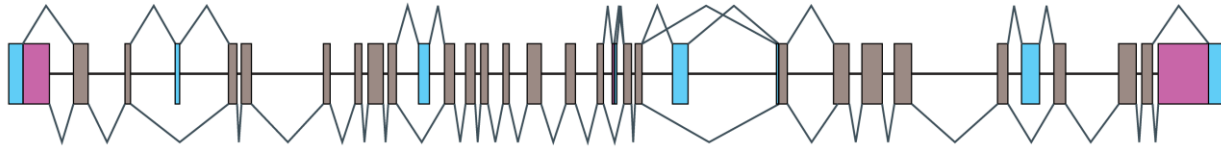
Published online: 19 February 2025

Open access

Darwin W. Kwok<sup>1</sup>, Nicholas O. Stevers<sup>1</sup>, Iñaki Etxeberria<sup>2,3</sup>, Takahide Nejo<sup>1</sup>, Maggie Colton Cove<sup>1</sup>, Lee H. Chen<sup>1</sup>, Jangham Jung<sup>1</sup>, Kaori Okada<sup>1</sup>, Senthilnath Lakshmanachetty<sup>1</sup>, Marco Gallus<sup>1,4</sup>, Abhilash Barpanda<sup>5</sup>, Chibo Hong<sup>1</sup>, Gary K. L. Chan<sup>1</sup>, Jerry Liu<sup>1</sup>, Samuel H. Wu<sup>1</sup>, Emilio Ramos<sup>5</sup>, Akane Yamamichi<sup>1</sup>, Payal B. Watchmaker<sup>1</sup>, Hirokazu Ogino<sup>1</sup>, Atsuro Saijo<sup>1</sup>, Aidan Du<sup>1</sup>, Nadia R. Grishanina<sup>1</sup>, James Woo<sup>1</sup>, Aaron Diaz<sup>1</sup>, Shawn L. Hervey-Jumper<sup>1</sup>, Susan M. Chang<sup>1</sup>, Joanna J. Phillips<sup>1,6</sup>, Arun P. Wiita<sup>5,7,8</sup>, Christopher A. Klebanoff<sup>2,3,9</sup>, Joseph F. Costello<sup>1,10</sup> & Hideho Okada<sup>1,10</sup>

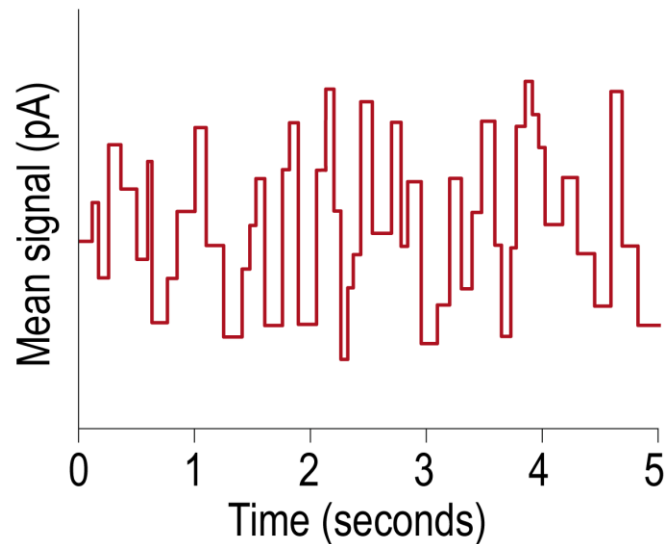
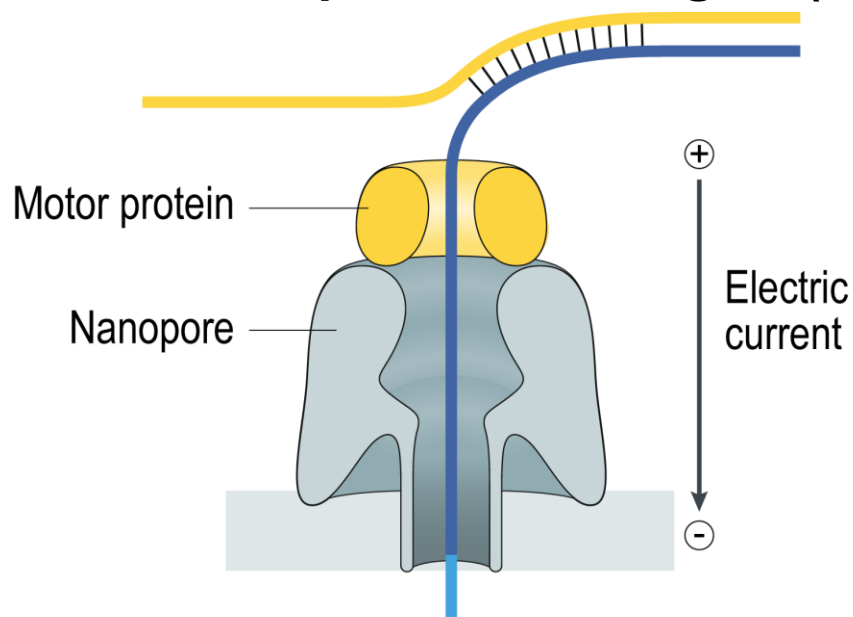
# Traditional RNA Sequencing

*KCNMA1* pre-mRNA



# Long-Read Sequencing: Seeing the Whole Picture

- Pacific Biosciences (PacBio)
- **Oxford Nanopore Technologies (ONT)**



- Generate reads  $> 10$  kb
- Directly sequence entire transcript molecules

Logsdon et al., *Nat. Rev. Genet.* 2020

# Robust and Low-Cost Technologies for Long-Read RNA-seq

SCIENCE ADVANCES | RESEARCH ARTICLE

GENETICS

## ESPRESSO: Robust discovery and quantification of transcript isoforms from error-prone long-read RNA-seq data

Yuan Gao<sup>1\*†‡</sup>, Feng Wang<sup>1†</sup>, Robert Wang<sup>1,2†</sup>, Eric Kutschera<sup>1</sup>, Yang Xu<sup>1,2</sup>, Stephan Xie<sup>1</sup>, Yuanyuan Wang<sup>1§</sup>, Kathryn E. Kadash-Edmondson<sup>1</sup>, Lan Lin<sup>3,4</sup>, Yi Xing<sup>1,3,5\*</sup>

Gao et al.  
*Science Advances* (2023)

nature communications



Article

<https://doi.org/10.1038/s41467-023-40083-6>

## TEQUILA-seq: a versatile and low-cost method for targeted long-read RNA sequencing

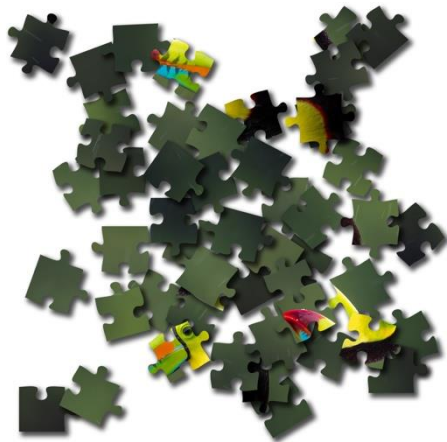
Received: 3 December 2022

Accepted: 11 July 2023

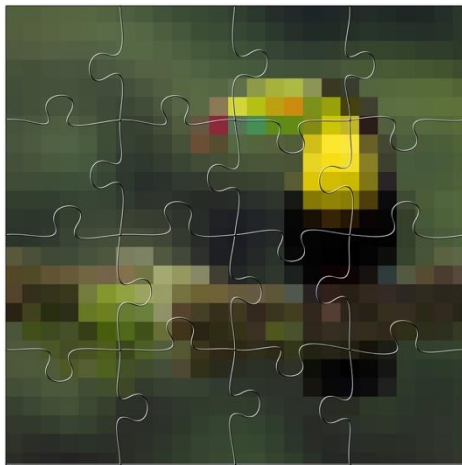
Feng Wang<sup>1,6</sup>, Yang Xu<sup>1,2,6</sup>, Robert Wang<sup>1,2,6</sup>, Beatrice Zhang<sup>①</sup><sup>1</sup>, Noah Smith<sup>1</sup>, Amber Notaro<sup>1</sup>, Samantha Gaerlan<sup>1</sup>, Eric Kutschera<sup>①</sup><sup>1</sup>, Kathryn E. Kadash-Edmondson<sup>1</sup>, Yi Xing<sup>①</sup><sup>1,3,4</sup> ✉ & Lan Lin<sup>①</sup><sup>3,5</sup> ✉

Wang et al.  
*Nature Communications* (2023)

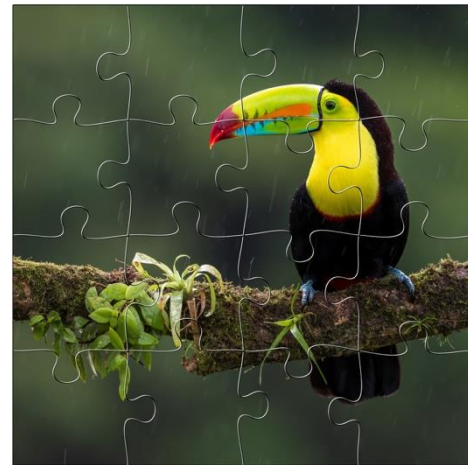
## Short-read transcriptome



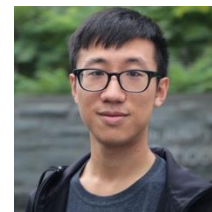
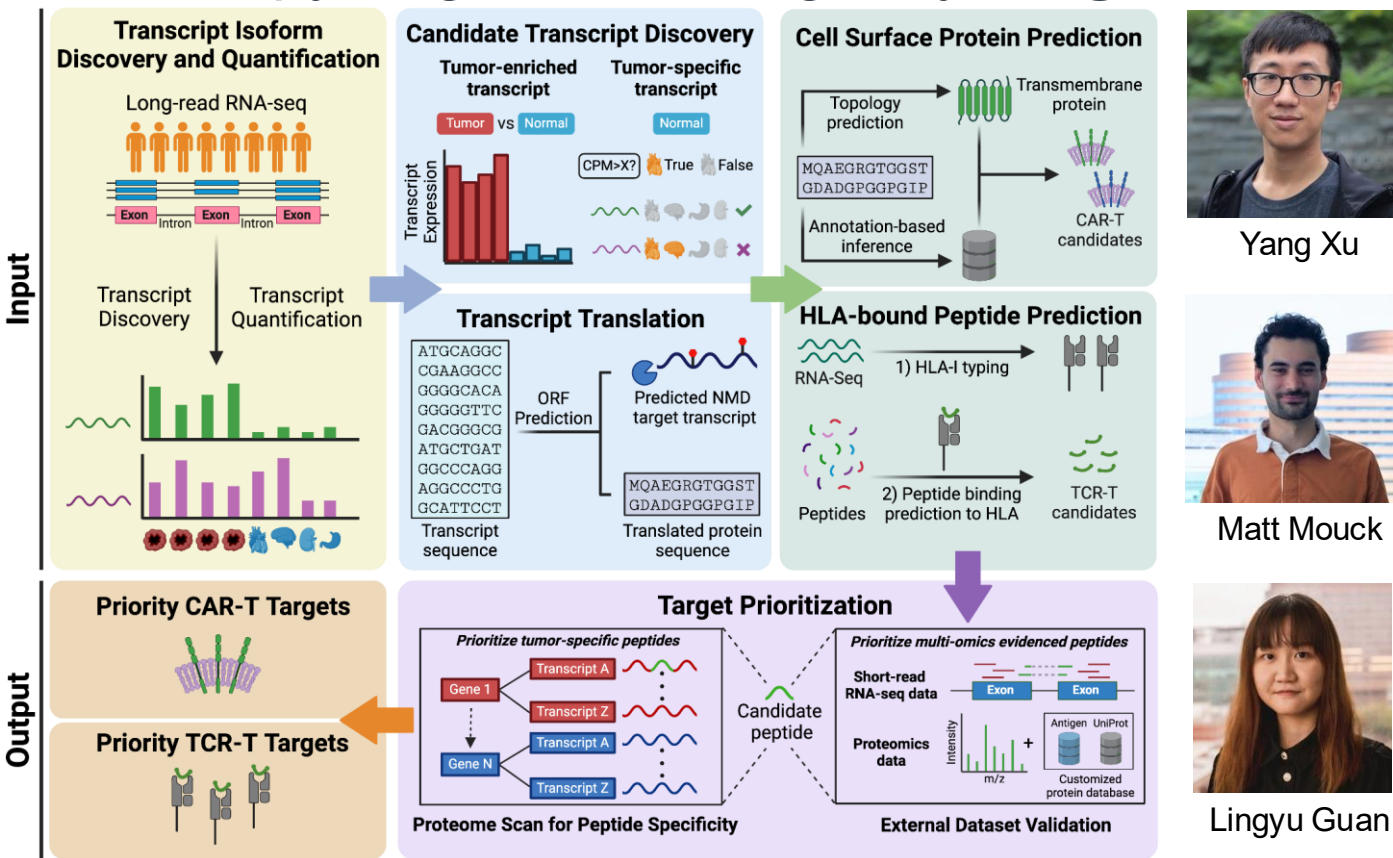
## Long-read transcriptome



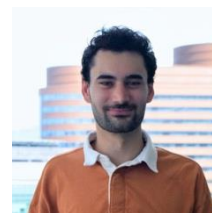
## High-definition long-read transcriptome



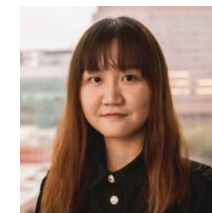
# IRIS-long: Isoform peptides from RNA dysregulation for Immunotherapy target Screening – by long-read RNA-seq



Yang Xu

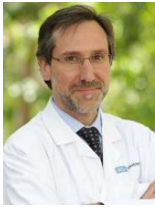
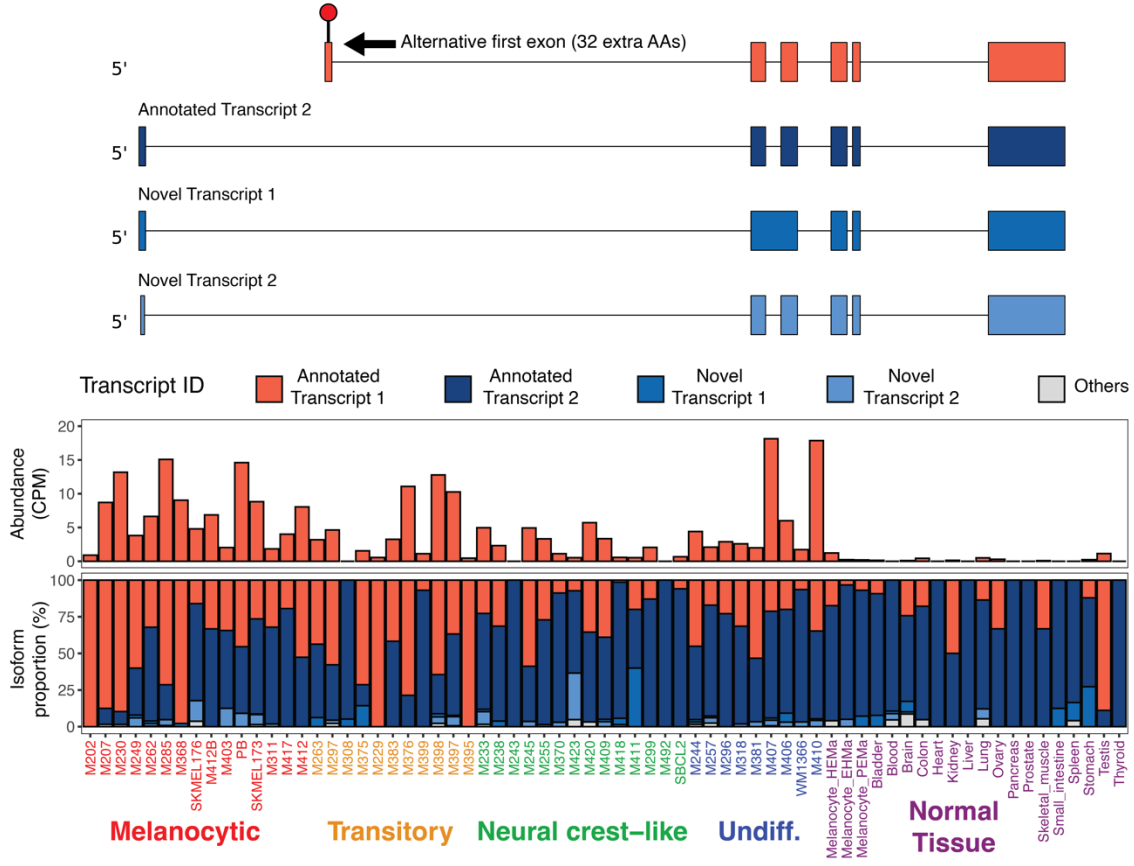


Matt Mouck



Lingyu Guan

# IRIS-long Predicts an MT1 Isoform as a Melanoma-Specific Antigen

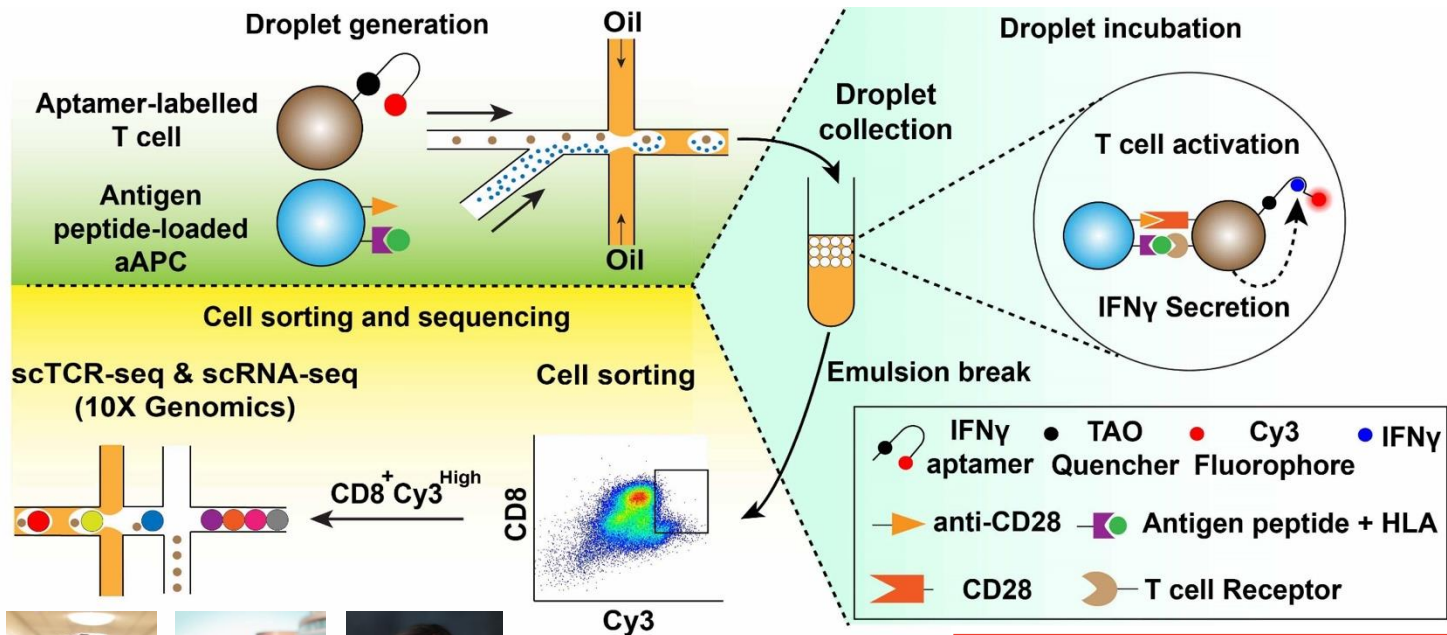


Antoni Ribas (UCLA)

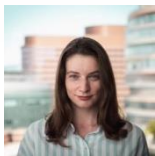
Unpublished/Confidential

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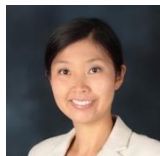
# ATLAS-seq: Aptamer-Based T Lymphocyte Activity Screening and Sequencing



Siwei Luo



Amber Notaro



Lan Lin

nature communications



Article

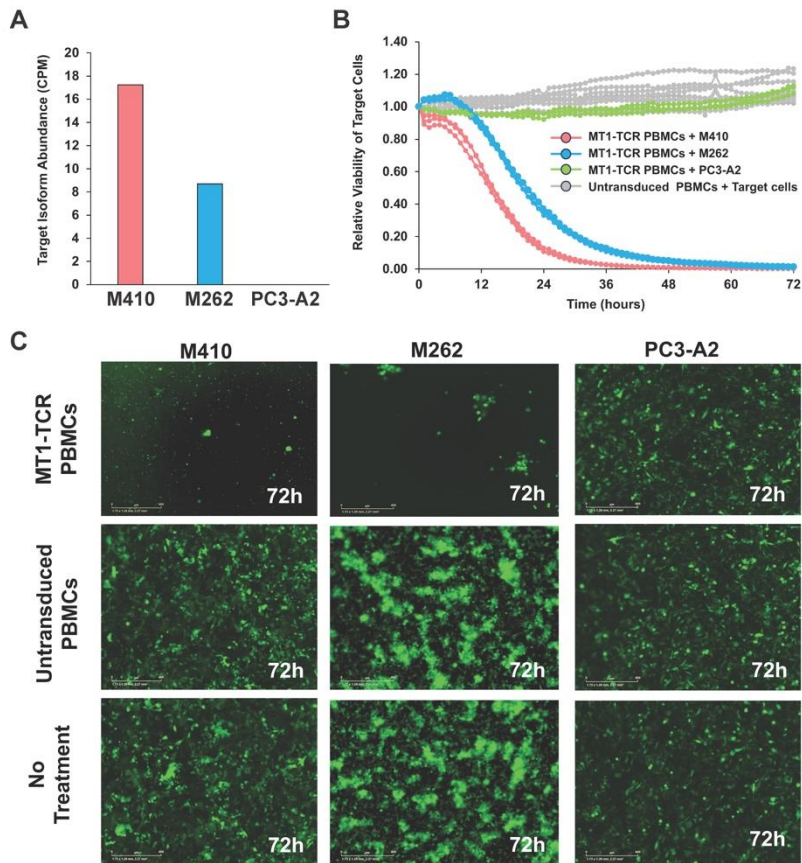
<https://doi.org/10.1038/s41467-024-54675-3>

ATLAS-seq as a microfluidic single-cell TCR screen for antigen-reactive TCRs

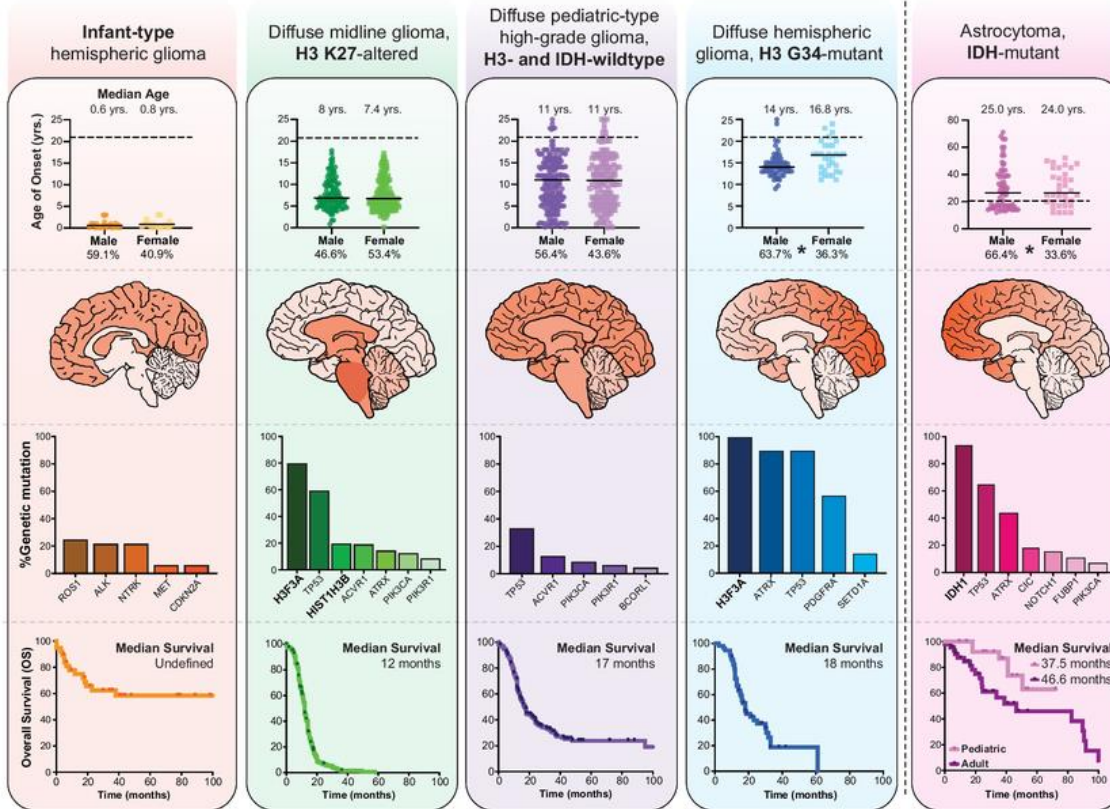
Luo et al., *Nat. Commun.*, 2025

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# MT1 Isoform Specific TCR Kills Melanoma Cells



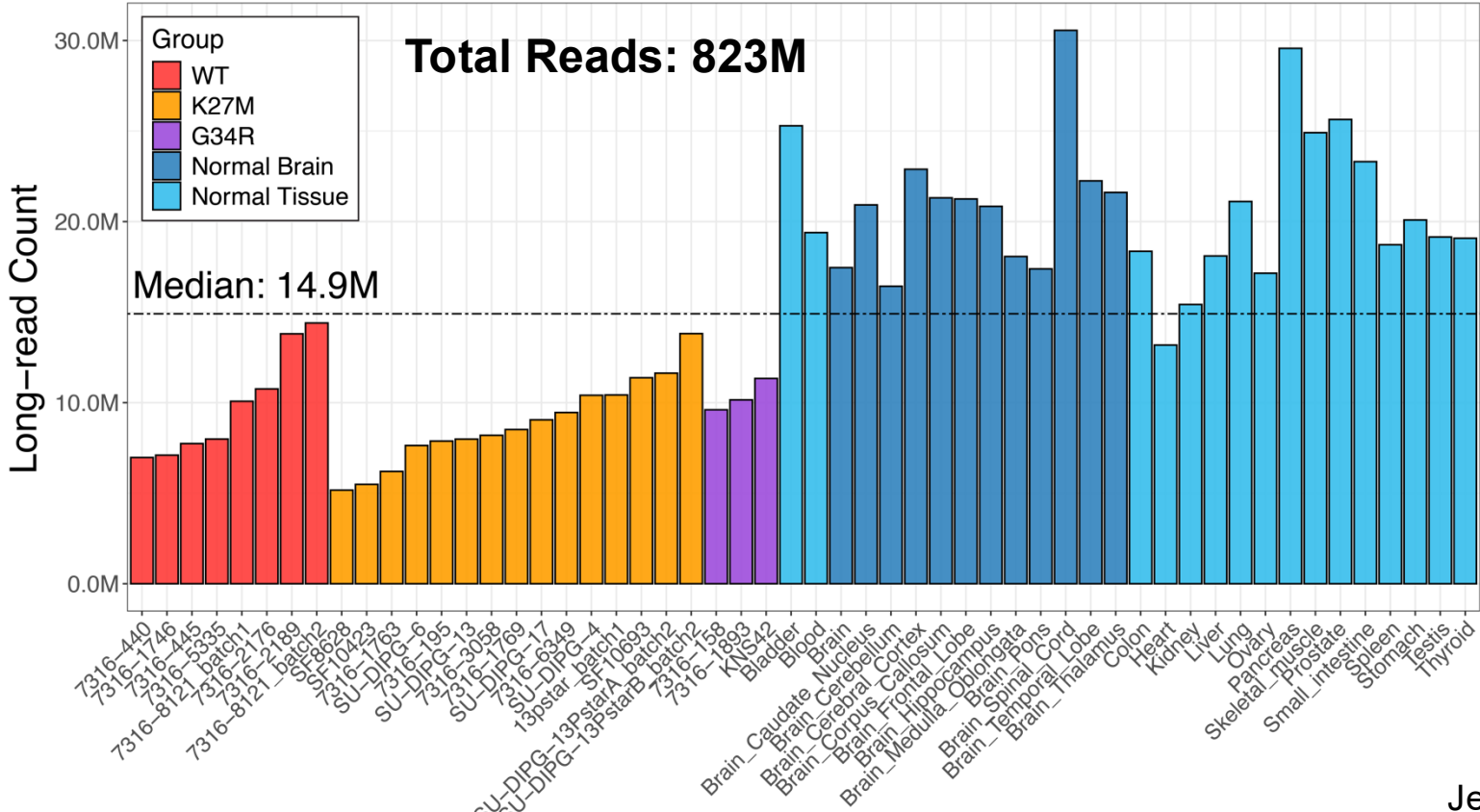
# Pediatric High-Grade Gliomas Are Aggressive Brain and Spinal Cord Tumors



Ocasio, 2023

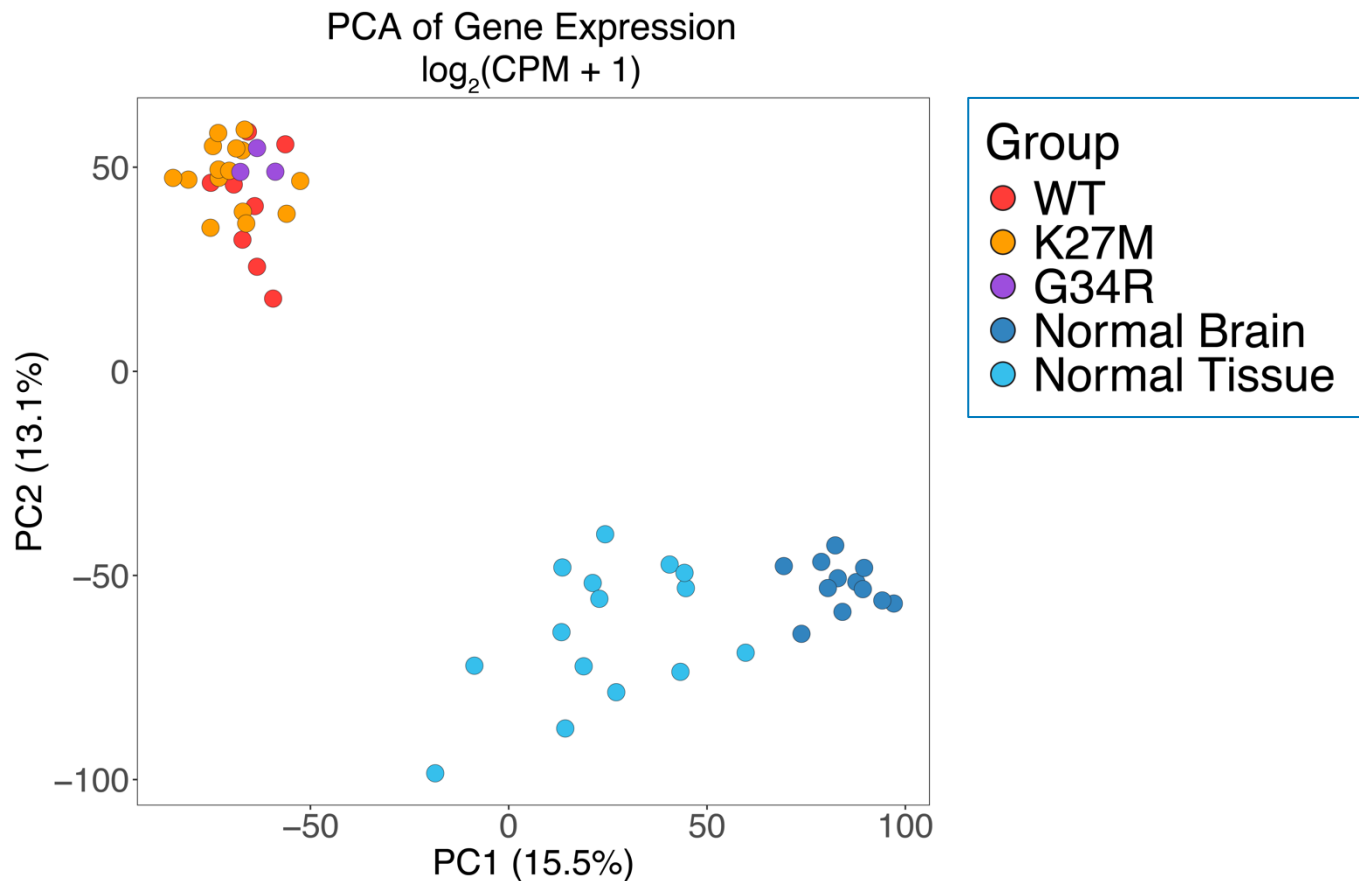
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# Long-Read RNA-seq of pHGG Subtypes and Diverse Normal Tissues

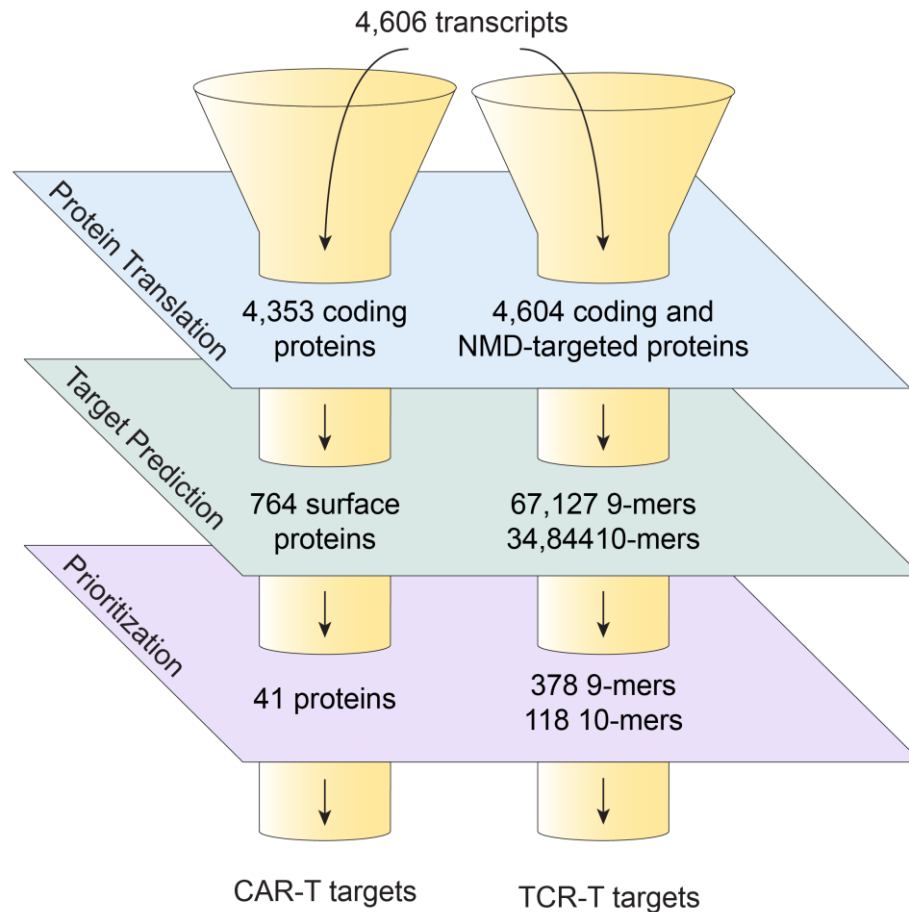


Jessica Foster (CHOP)

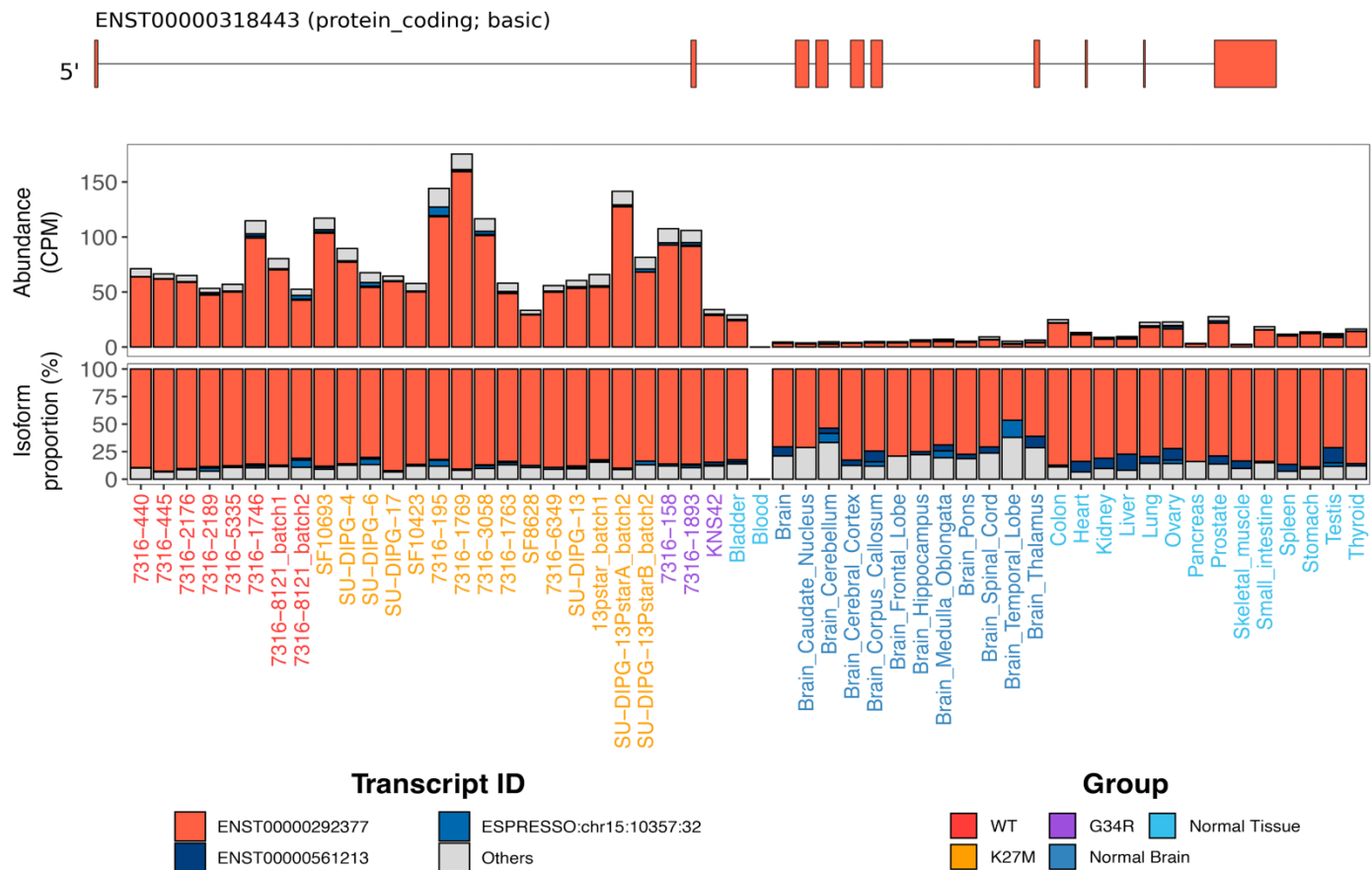
# pHGG Samples Are Transcriptionally Distinct from Normal Tissues



# IRIS-long Identifies and Prioritizes pHGG CAR-T and TCR-T Targets

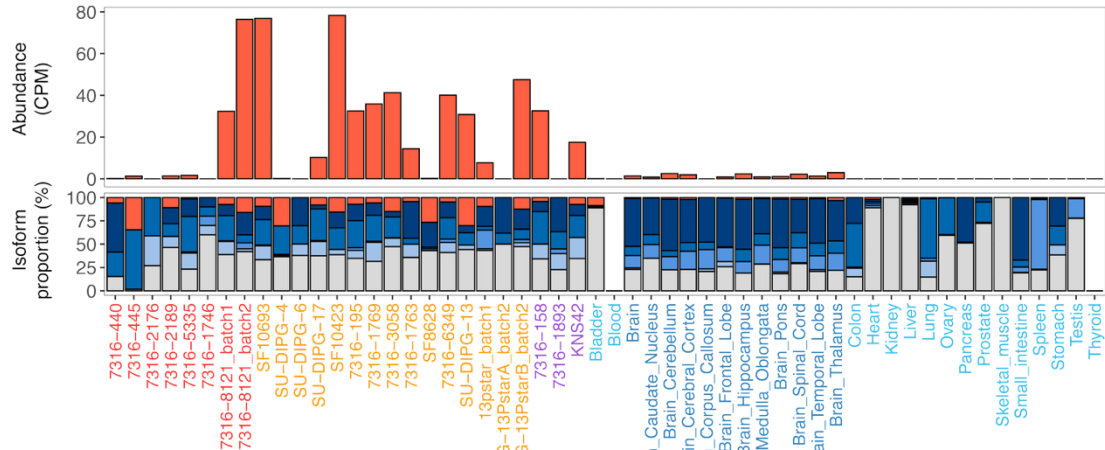


# IRIS-long Recaptures B7-H3: A CAR-T Target in Clinical Trials

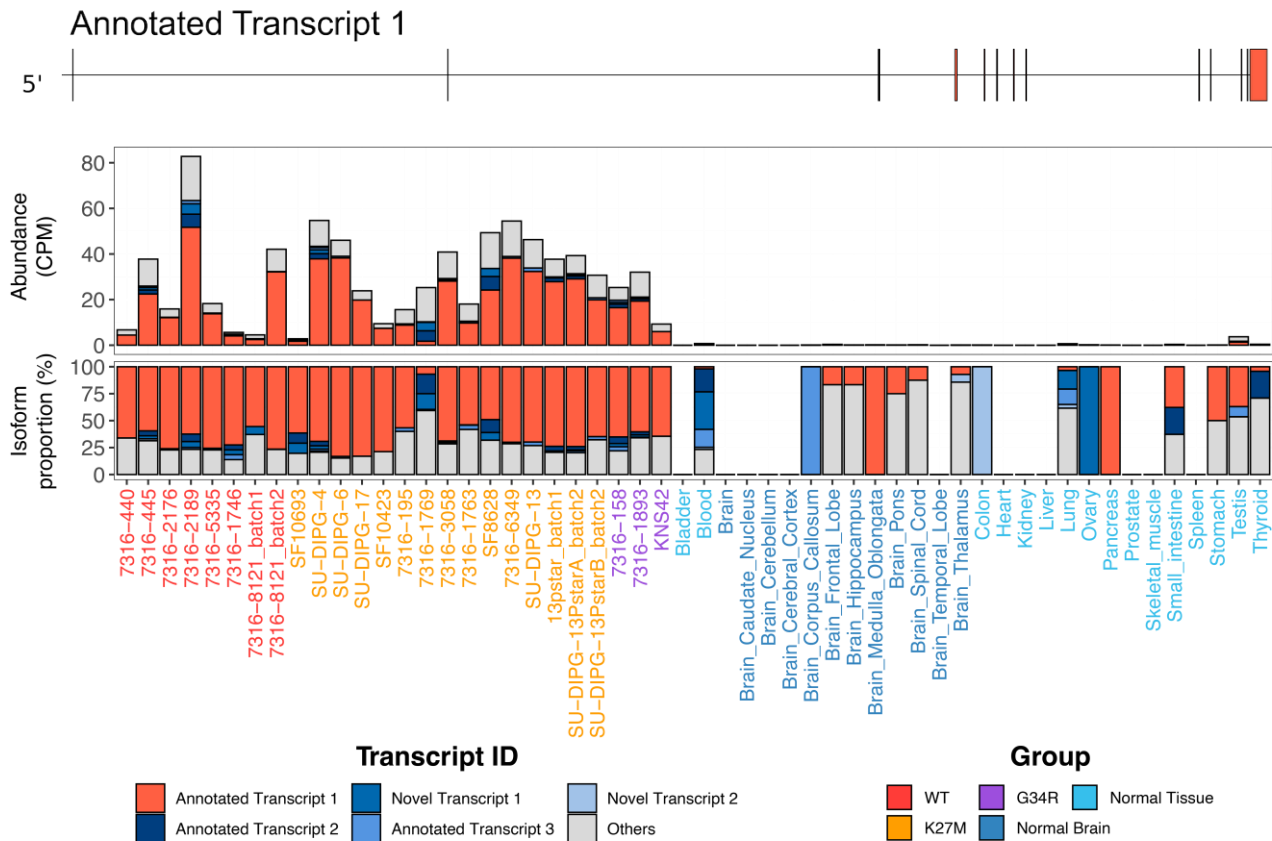


# PGT1 Tumor-Specific Alternative Splicing Generates an A\*02:01 Compatible Antigen

 A\*02:01 Epitope

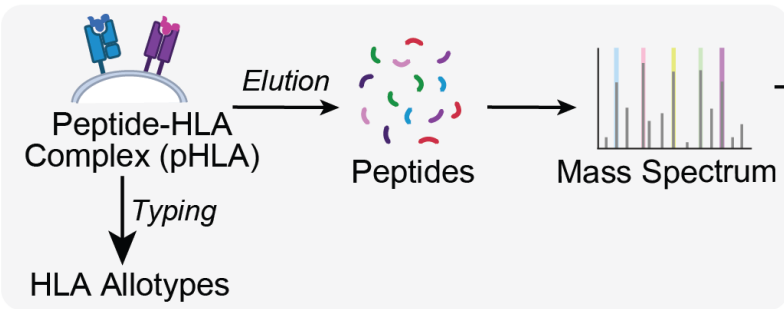


# PGT2 Tumor-Specific Gene Expression Generates Multiple A\*02:01 Compatible Antigens

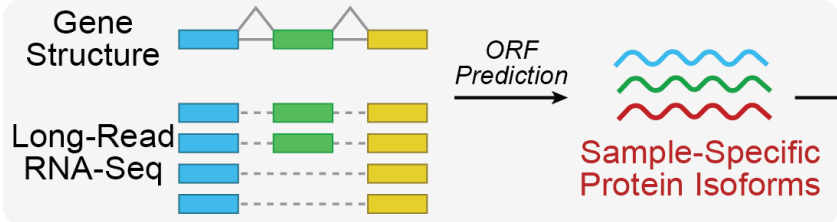


# Long-Read RNA-seq Based Analysis of Immunopeptidomes

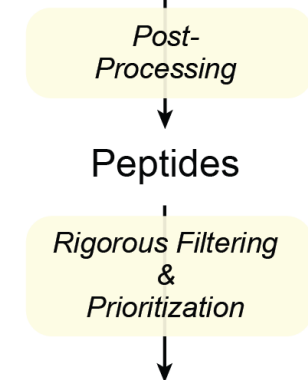
## HLA Immunopeptidomics



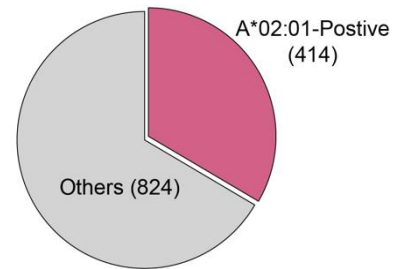
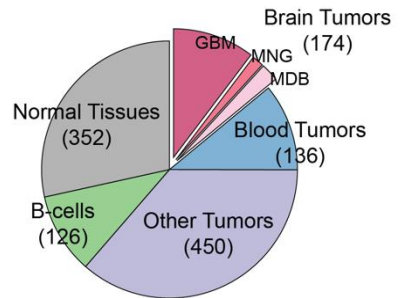
## Long-Read RNA-Seq Based Proteotranscriptomics Analysis



## Peptide Spectrum Matches (PSMs)

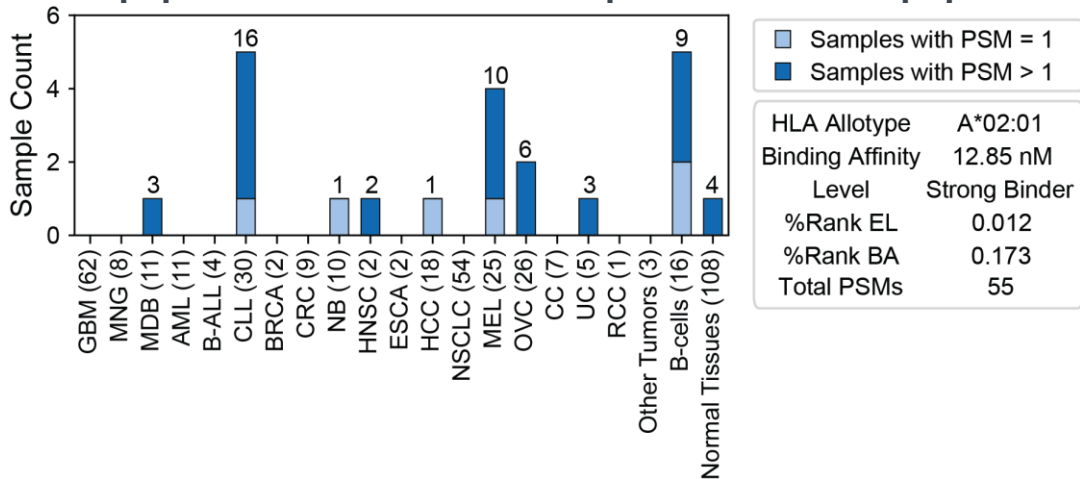


**1,238 Samples**  
**160.4 Million Mass Spectra**

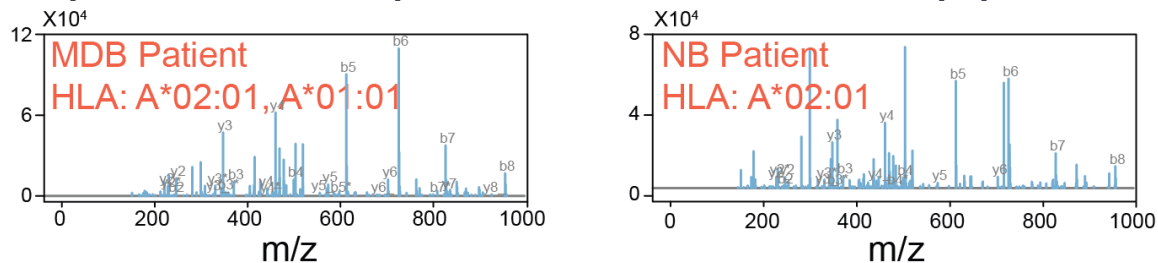


# PGT2 A\*02:01 Epitope Is Expressed Across Multiple Cancers

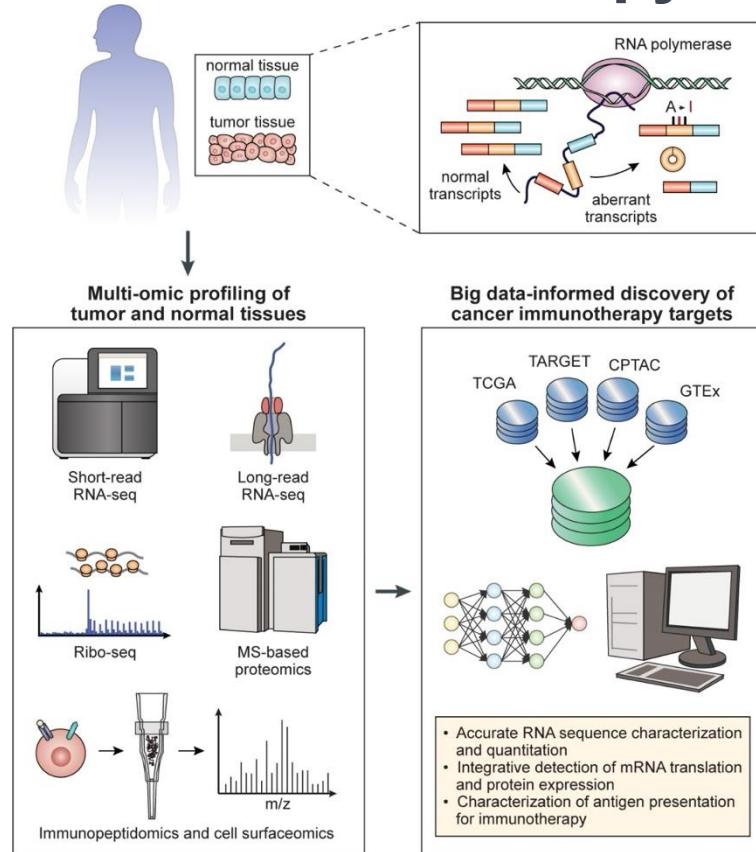
A\*02:01 peptide of PGT2 in A\*02:01-positive immunopeptidomes



Two experimental mass spectra matched to the A\*02:01 peptide of PGT2



# Multimomic and Big Data Strategies to Discover Immunotherapy Targets



cancer.gov/CCDI

Pan et al., *Trends Pharmacol Sci*, 2021

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# Advanced Personalized Therapeutics and Precision Surgery Program for Childhood Cancers



Theodore Laetsch, M.D.



Marilyn Li, M.D., M.S.



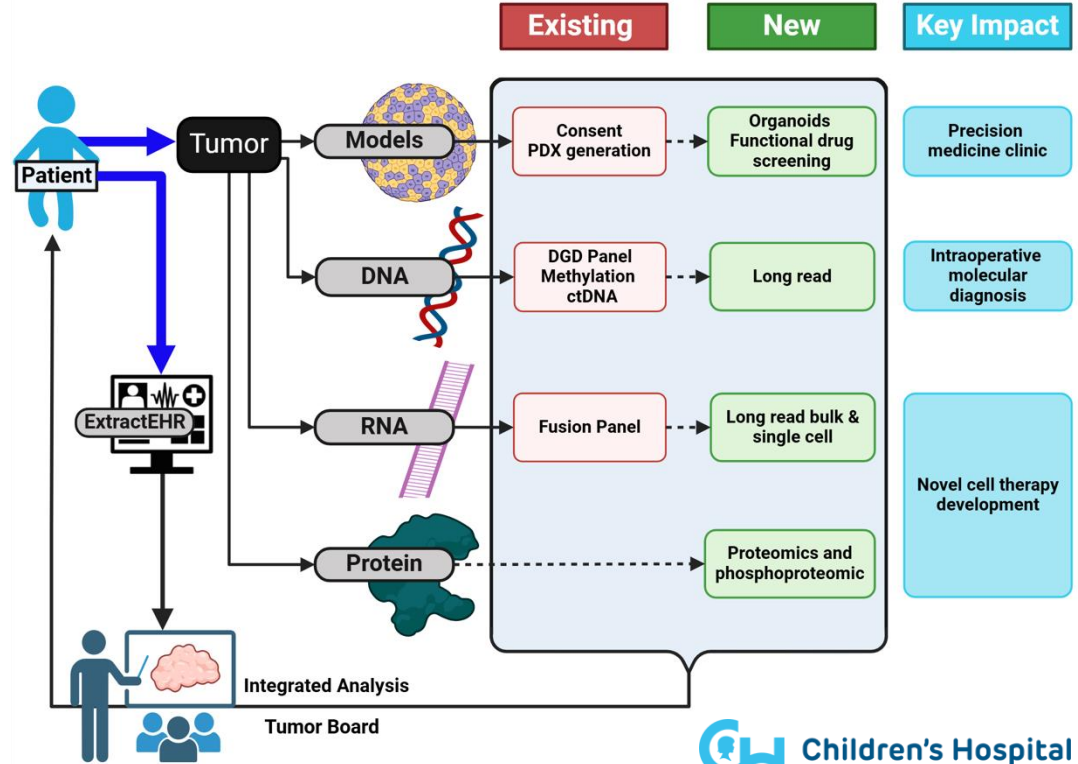
Phillip Jay Storm, M.D.



Adam Resnick, Ph.D.



Yi Xing, Ph.D.



# Acknowledgements

## Xing Lab



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Richard Aplenc

Jessica Foster

Andrei Thomas-Tikhonenko

Theodore Laetsch

Song Liu

Carl June

Avery Posey

Owen Witte

Antoni Ribas

Sanaz Memarzadeh

Anthony Wang

## Funding



Prostate Cancer  
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MEDICAL RESEARCH PROGRAMS



# Q&A

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

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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](https://events.cancer.gov/ccdi/webinar)

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# Thank you for attending!



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