The Open Pediatric Cancer Project

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In Brief

Highlights

Summary

Keywords

Introduction

Results

Discussion

Acknowledgments

Author Contributions

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Eric Wafula	Formal analysis, Software
Krutika S. Gaonkar	Data curation, Formal analysis, Investigation, Methodology, Software, Writing – Original draft, Writing - Review and editing
Run Jin	Data curation, Formal analysis, Visualization, Writing – Original draft, Writing - Review and editing
Komal S. Rathi	Formal analysis, Investigation, Methodology, Writing – Original draft
Yuankun Zhu	Data curation, Formal analysis, Investigation, Methodology, Supervision
Bailey K. Farrow	Data curation, Software
Daniel P. Miller	Formal analysis
Mariarita Santi	Investigation, Validation, Writing - Review and editing
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Nicholas Van Kuren	Data curation, Software
Noel Coleman	Data curation
Christopher Blackden	Resources
Jennifer L. Mason	Supervision
Saksham Phul	Data curation, Methodology, Formal analysis
Miguel A. Brown	Data curation, Methodology, Formal analysis
Alex Sickler	Methodology, Formal analysis
Adam C. Resnick	Conceptualization, Funding acquisition, Resources, Supervision
Jo Lynne Rokita^	Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Software, Supervision, Writing – Original draft, Writing - Review and editing

Declarations of Interest

Figure Titles and Legends

Table Titles and Legends

OPENPEDCAN METHODS

RESOURCE AVAILABILITY

Lead contact

Requests for access to OpenPedCan raw data and/or specimens may be directed to, and will be fulfilled by Jo Lynne Rokita (rokita@chop.edu).

Materials availability

This study did not create new, unique reagents.

Data and code availability

Merged summary files for OpenPedCan v12 are openly accessible in CAVATICA or via download script in the https://github.com/PediatricOpenTargets/OpenPedCan-analysis repository. Cancer group summary data are visible within the NCI's pediatric Molecular Targets Platform and cohort, cancer group, and individual data are visible within PedcBioPortal

OpenPedCan analysis modules were developed within OpenPBTA [1], modified based on OpenPBTA, or newly created and can be found within the following publicly available repositories. OpenPBTA module analyses can be found at https://github.com/AlexsLemonade/OpenPBTA-analysis. OpenPedCan module analyses can be found at https://github.com/PediatricOpenTargets/OpenPedCan-analysis. OpenPedCan api code can be found at https://github.com/PediatricOpenTargets/OpenPedCan-api.

Software versions are documented in **Table XX**.

Data releases

EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

METHOD DETAILS

Nucleic acids extraction and library preparation

Data generation

DNA WGS Alignment

Please refer to the OpenPBTA manuscript for details [1].

Quality Control of Sequencing Data

Please refer to the OpenPBTA manuscript for details [1].

SNP calling for B-allele Frequency (BAF) generation

Please refer to the OpenPBTA manuscript for details [1].

Somatic Mutation Calling

SNV and indel calling

Please refer to the OpenPBTA manuscript for details [1].

VCF annotation and MAF creation

Gather SNV and INDEL Hotspots

Consensus SNV Calling

Somatic Copy Number Variant Calling (WGS samples only)

Consensus CNV Calling

Somatic Structural Variant Calling (WGS samples only)

Please refer to the OpenPBTA manuscript for details [1].

Methylation Analysis

Gene Expression

Abundance Estimation

Gene Expression Matrices with Unique HUGO Symbols

Gene fusion detection

QUANTIFICATION AND STATISTICAL ANALYSIS

Focal Copy Number Calling (`focal-cn-file-preparation` analysis module)

Please refer to the OpenPBTA manuscript for details on assignment of copy number status values to CNV segments, cytobands, and genes [1]. We applied criteria to resolve instances of multiple conflicting status calls for the same gene and sample, which are described in detail in the focal-cn-file-preparation module. Briefly, we prioritized 1) non-neutral status calls, 2) calls made from dominant segments with respect to gene overlap, and 3) amplification and deep deletion status calls over gain and loss calls, respectively, when selecting a dominant status call per gene and sample. These methods resolved >99% of duplicated gene-level status calls.

Gene Set Variation Analysis (`gene-set-enrichment-analysis` analysis module)

Please refer to the OpenPBTA manuscript for details [1].

Fusion prioritization (`fusion_filtering` analysis module)

Mutational Signatures (`mutational-signatures` analysis module)

Tumor Mutation Burden (`snv-callers` analysis module)

Clinical Data Harmonization

WHO Classification of Disease Types

Molecular Subtyping

Here, we build upon the molecular subtyping performed in OpenPBTA [1].

High-grade gliomas..

Atypical teratoid rhabdoid tumors..

Neuroblastoma tumors...

Integration of brain tumor methylation classifications

TP53 Alteration Annotation (`tp53_nf1_score` analysis module)

Please refer to the OpenPBTA manuscript for details [1].

Prediction of participants' genetic sex

Please refer to the OpenPBTA manuscript for details [1].

Selection of independent samples (`independent-samples` analysis module)

For analyses that require all input biospecimens to be independent, we use the OpenPedCan-analysis independent-samples module to select only one biospecimen from each input participant. For each input participant of an analysis, the independent biospecimen is selected based on the analysis-specific filters and preferences for the biospecimen metadata, such as experimental strategy, cancer group, and tumor descriptor.

Supplemental Information Titles and Legends

Consortia

References

1. **OpenPBTA: The Open Pediatric Brain Tumor Atlas**
Joshua A Shapiro, Krutika S Gaonkar, Stephanie J Spielman, Candace L Savonen, Chante J Bethell, Run Jin, Komal S Rathi, Yuankun Zhu, Laura E Egolf, Bailey K Farrow, ... Jaclyn N Taroni
Cell Genomics (2023-05) https://doi.org/gr92p6
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