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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒ A description of all covariates tested
☐	☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	1. WES data was produced via illumina WES sequencing. 2. TARGET neuroblastoma WES data files from dbGaP under accession number phs000467. 3. Germline variants of 10,389 patients included in the TCGA corresponding to 33 cancer types generated by Huang, et al. Cell 2018. 4. The somatic mutations were obtained from the TCGA PanCancer Altlas MC3 set.
Data analysis	For variant calling, we used Picards v 2.17.5 and GATK v 4.0.2. For variant annotation, we used Annovar for the germline variants annotation which included REVEL score and VEP for somatic mutations. For statistical analysis and visualization, we used R (v 4.2).

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The datasets generated and analyzed during the present study are available in the NCBI Sequence Read Archive repository under accession number PRJNA592880 (https://www.ncbi.nlm.nih.gov/sra/PRJNA592880). The TARGET neuroblastoma WES data files were downloaded from dbGaP under accession number phs000467. The TCGA pan-cancer data are available in the Genomic Data Commons (GDC, https://gdc.cancer.gov/about-data/publications/PanCancerAtlas-Germline-AWG) of the National Cancer Institute. KOREA1K data available through http://koreangenome.org/.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	The distribution of sex (determined based on biological attributes) in our study cohort was reported within the paper. The study sample had almost equal distribution of male (49%) and female (51%). Sex-based analysis was not performed. Our study population was among young children with an average age of 4 years, where sex was not associated with mortality outcome and it is not likely to be associated with our exposures of interest. We do not have information on gender.
Reporting on race, ethnicity, or other socially relevant groupings	For the analysis of race in our study using TARGET data, we relied on self-reported racial information and inferred racial categories from genotype analysis using EthSEQ. However, the study did not include a detailed report on other socially relevant groupings of the participants.
Population characteristics	We analyzed blood and tissue DNA from 125 neuroblastoma patients at the Samsung Medical Center (SMC). Most patients (82%) underwent prospective clinical sequencing. However, 23 patients (18%) were also included in this study using samples deposited at the SMC Bio Bank. Detailed patient characteristics are reported in Supplementary Table 1.
Recruitment	Selection was based on tumor sample availability. The cohort consists of all neuroblastoma risk-groups.
Ethics oversight	The present study was approved by the SMC Institutional Review Board (IRB No. 2015-11-053-014), and all patients provided written informed consent from parents or legal guardians for tumor sequencing and review of medical records for demographic, clinical, and pathological information.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	No statistical methods were used to pre-determine sample sizes. Sample size was therefore determined by availability of patient samples. Further sample size was given by the sample size of the public data analyzed.
Data exclusions	SMC: Among initially identifying 145 patients with peripheral neuroblastoma tumors, we excluded ganglioneuroma cases (n=6), tumors obtained post-relapse (n=9), patients with unmatched DNA pairs confirmed by NGSCheckMate (n=1), and non-primary site tumors (n=4), our analysis focused on the remaining 125 cases. TARGET: We excluded two patients whose tumor tissue was obtained from metastatic sites. TCGA: We excluded non-European ethnic patients for TCGA. We also excluded non-solid tumor patients.
Replication	None
Randomization	None
Blinding	None

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	Among all 125 patients in this study, 54 high-risk patients were enrolled in the NB-2014 clinical trial (NCT02771743), which was designed to evaluate the potential benefits of response-adapted strategies in consolidation therapy.
Study protocol	https://onlinelibrary.wiley.com/doi/10.1002/pbc.31173
Data collection	Regardless of trial participation, all specimens and clinical data were archived and made available by Samsung Medical Center.
Outcomes	The outcomes used in this study include overall survival and progression-free survival. Among the patients in this study, 54 overlap with those enrolled in the NB-2014 clinical trial. In this analysis, we incorporated extended follow-up and survival data, which differs from the original trial that initiated follow-up after the induction period, as the original trial focused on the effects of consolidation treatment. Here, we calculated survival time starting from the time of diagnosis. Therefore, the outcome analysis used here includes non-prespecified exploratory outcomes for NCT02771743.

Plants

Seed stocks	*Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*
Novel plant genotypes	*Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*
Authentication	*Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*