

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
<input type="checkbox"/>	<input checked="" type="checkbox"/> The exact sample size (<i>n</i>) for each experimental group/condition, given as a discrete number and unit of measurement
<input type="checkbox"/>	<input checked="" type="checkbox"/> A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
<input type="checkbox"/>	<input checked="" type="checkbox"/> The statistical test(s) used AND whether they are one- or two-sided <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
<input type="checkbox"/>	<input checked="" type="checkbox"/> A description of all covariates tested
<input type="checkbox"/>	<input checked="" type="checkbox"/> A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
<input type="checkbox"/>	<input checked="" type="checkbox"/> 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)
<input type="checkbox"/>	<input checked="" type="checkbox"/> For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give <i>P</i> values as exact values whenever suitable.</i>
<input checked="" type="checkbox"/>	<input type="checkbox"/> For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
<input checked="" type="checkbox"/>	<input type="checkbox"/> For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
<input checked="" type="checkbox"/>	<input type="checkbox"/> Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i>), 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	<p>The following standard software were used to analyze whole genome copy number profiling and sequencing data. References are given in Online Methods:</p> <p>CytoScan HD SNP array (Thermo Fisher/Affymetrix) was used and the copy number profiles were visualized with Chromosome Analysis Suite (version 3.3.0.139; Thermo Fisher/Affymetrix) to analyze DNA from fresh frozen samples and cell culture experiments. CEL files were normalized by the R package Rawcopy, and scatter plots whose x-axis and y-axis denotes log2 ratio and allelic imbalance, respectively, were generated through the R package TAPS (Tumor Aberration Prediction Suite). CEL-files were converted to OSCHP-files with the OncoScan Console (version 1.3.0.39; Affymetrix). The Nexus Express software for OncoScan (version 3.1) was used for visual inspection of the OSCHP-files. Aberration plots were generated with BioCircos (v0.3.4) in R (v4.1).</p> <p>For patient derived xenograft analyses, paired end reads were mapped to the human reference genome (GRCh37 with decoys from the 1000 Genomes' Project) using BWA-MEM 0.7.1513. Duplicate reads were marked using sambamba 0.6.714. Somatic variant calling was performed using freebayes (with the --pooled-continuous, --pooled-discrete and -F 0.03 flags; https://arxiv.org/abs/1207.3907v2) and strelka2 (using the --exome flag). The Polyphen-2 tool, was used to predict the impact of mutations on protein function.</p> <p>For WES of FFPE tumor material paired-end reads were aligned to the human reference genome hg19 by BWA-MEM (https://arxiv.org/abs/1303.3997v2). Duplicate reads marking and local realignment were performed by GATK (version 4.0.11.0)18. Mutect (version 1.1.7), GATK Mutect2 (version 4.0.11.0), and MuSE (version v1.0rc) were used to identify somatic single nucleotide variants (SNVs) and small insertions/deletions (indels). The SNVs and indels called by Mutect2 were further filtered with the GATK FilterMutectCalls. The variant vcf files were converted into maf files by the vcf2maf package (https://github.com/mskcc/vcf2maf).</p>
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For targeted resequencing of FFPE tumor material, raw reads were processed through the Sentieon[®] unique molecular indices (UMI) aware pipeline (<https://support.sentieon.com/appnotes/umi/>). Briefly, UMIs were extracted from raw fastqs and raw reads were aligned to the reference genome (GRCh37) using the sentieon implementation of bwa mem (<https://arxiv.org/abs/1303.3997v2>), followed by consensus fastq generation using the sentieon consensus tool (<https://www.sentieon.com/products/>). The consensus reads were then mapped to the reference genome (again using the sentieon implementation of bwa mem) and the resulting bam-files were processed through freebayes (<https://arxiv.org/abs/1207.3907>)

All variants were annotated using the VEP tool (https://grch37.ensembl.org/Homo_sapiens/Tools/VEP).

Data analysis

The in-house software DEVOLUTION was used for clustering and phylogenetic analyses of bulk sequencing data. The full software including access links is published in Andersson et al. Commun Biol 4,1103 (2021). After clustering phylogenetic trees were constructed using standard R packages phangorn (v2.8.1) and visualized using the ggplot2 (v.3.3.5) package. Another in-house software was used to construct phylogenies from single cell WGS and this is published online at <https://github.com/NatalieKAndersson/SCem>.

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 during and/or analysed during the current study are available in curated raw data format in Supplementary Table 1. Revision of Swedish regulations regarding publication of human genome data currently makes it legally questionable to deposit raw SNP or sequencing data in a public archive, forcing us to postpone this until a national system has been put in place.

Human research participants

Policy information about [studies involving human research participants and Sex and Gender in Research](#).

Reporting on sex and gender

No analyses of sex and gender were performed as this was not within the scope of the study.

Population characteristics

Children diagnosed with cancer in Sweden.

Recruitment

Patients selected from a consecutive regional cohort based on availability of tumor material for analysis.

Ethics oversight

The study was approved by the regional ethics review board under permit numbers L289-11 (genomic analyses; updated as L796-2017) and L605-05 (biobanking; updated as L883-2018).

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

This is an explorative study where all patients (n=12) from a consecutive cohort were enrolled based on availability of material for analysis.

Data exclusions

Patients having scarce material in biobanks/pathology archives were excluded, creating a bias towards patients with disease remaining after treatment. However, these patients are the ones most relevant from a clinical perspective and they were the ones that the study was in fact focused on.

Replication

Because the present study would take many years to reproduce in a clinical prospective study, we chose to use patient-derived xenografts (PDXs) as well as cell cultures to evaluate whether the data could be reproduced in prospective, controlled setting.

Randomization

Not applicable.

Blinding

Not applicable.

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
<input checked="" type="checkbox"/>	<input type="checkbox"/> Antibodies
<input type="checkbox"/>	<input checked="" type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input type="checkbox"/>	<input checked="" type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern

Methods

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s) The IMR-32 neuroblastoma cell line was from ATCC (CCL-127)

Authentication SNP array

Mycoplasma contamination Tested negative.

Commonly misidentified lines
(See [ICLAC](#) register) Not applicable

Animals and other research organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals NMRI nude mice were purchased from Taconic.

Wild animals Not applicable.

Reporting on sex Not collected.

Field-collected samples Not applicable.

Ethics oversight All procedures were conducted according to the guidelines from the regional Ethics Committee for Animal Research (permit no. M11-15, 19012-19 and 289-2011).

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

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 This was not clinical trial.

Study protocol This was not clinical trial.

Data collection We reviewed pathology files of all patients <18 years of age diagnosed with and treated for a histopathologically verified neuroblastoma in the Southern Healthcare Region of Sweden from 1998-2018. From this cohort of 50 patients, we selected those from whom there were samples with >50% viable tumor cells available for DNA-analysis, material from at least two different disease time points, and samples from at least two intratumoral locations from at least one of these time points. This resulted in totally 12 patients.

Outcomes This was not clinical trial.