

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

Ion Reporter Software (v. 5.10.5.0)
Illumina Local App v.2
NanoString nSolver v.4.0

Data analysis

HaTSPiL framework35.
Novoalign (<http://www.novocraft.com/>)
Picard Markduplicates tool (<https://broadinstitute.github.io/picard/>)
GATK RealignerTargetCreator and IndelRealigner tools (<https://gatk.broadinstitute.org/hc/en-us>).
MuTect v.1.1.17 (<https://software.broadinstitute.org/cancer/cga/mutect>)
Strelka v.1.0.1436
Varscan2 v.2.3.6 (<http://varscan.sourceforge.net/>) RefSeq v.64
InterVar tool 2.1.3
ClinVar (<https://www.ncbi.nlm.nih.gov/clinvar/>)
Ensembl (<https://www.ensembl.org/index.html>),
Varsome (<https://varsome.com/>)
InSIGHT (<https://www.insight-group.org/variants/databases/>)
LOVD (<https://databases.lovd.nl/shared/genes>)
Human Genome Mutations Database (HGMD, <http://www.hgmd.cf.ac.uk/ac/index.php>)
Alamut software
Phyre2 software
Maftools R packages (<https://github.com/PoisonAlien/maftools>).
Python tool :ncokb/ncokb-annotator.
Ion Reporter Software (v. 5.10.5.0)
OncoPrint OCAV3 w3.0 - DNA -Single Sample (v. 5.10)

Novoalign (<http://www.novocraft.com/>)
 Picard MarkDuplicates tool (<https://broadinstitute.github.io/picard/>)
 GATK RealignerTargetCreator and IndelRealigner tools (<https://gatk.broadinstitute.org/hc/en-us>)
 MuTect v.1.1.17 (<https://software.broadinstitute.org/cancer/cga/mutect>)
 Varscan2 v.2.3.6 (<http://varscan.sourceforge.net/>)

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](#)

This statement has been included 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](https://www.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	n/a (case report)
Data exclusions	n/a (case report)
Replication	Technical replicates have been provided when needed.
Randomization	n/a
Blinding	n/a

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	Involvement in the study
☐	☒ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Human research participants
☐	☒ Clinical data
☒	☐ Dual use research of concern

Methods

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

Antibodies

Antibodies used	Anti- MSH2, MSH6, MLH1, PMS2 antibodies.
Validation	Validation performed on clinical samples with known MSH2, MSH6, MLH1, PMS2 gene status.

Human research participants

Policy information about [studies involving human research participants](#)

Population characteristics	A single patient with multiple neoplasms has been studied. Due to germline findings, the two parents have been investigated for specific germline pathogenic variants.
Recruitment	n/a
Ethics oversight	n/a

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	not a clinical trial
Study protocol	n/a
Data collection	n/a
Outcomes	Descriptive outcome of the single patient has been included.