# nature research

Corresponding author(s):	David T.W Jones, Stefan M. Pfister
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## **Reporting Summary**

Nature Research 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 Research policies, see our Editorial Policies and the Editorial Policy Checklist.

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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
x	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. <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 P values as exact values whenever suitable.</i>
×	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
X	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 <i>d</i> , Pearson's <i>r</i> ), indicating how they were calculated
	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.

### Software and code

Policy information about <u>availability of computer code</u>

Data collection No software was used to collect the data.

140 Software was asea to concertific data.

Data analysis

R version 3.4.4 (R Development Core Team, 2019): conumee Bioconductor package version 1.12.0; minfi Bioconductor package version 1.24.0.; Rtsne package version 0.13; limma package version 3.34.5.

MAS5.0 algorithm

R2: Genomics Analysis and Visualization Platform (http://r2.amc.nl)

Integrative Genomic Viewer (IGV\_2.7.2 version)

The 1000 Genomes phase 2 human reference assembly (NCBI build 37.1) Burrow-Wheeler Aligner (BWA version 0.6.2)

deFuse algorithm

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 Research guidelines for submitting code & software for further information.

#### Data

Policy information about availability of data

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

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

Methylation data were deposited in GEO: GSE131482

Gene expression data are available in GEO: GSE168457

Remaining data are available directly from the corresponding authors upon request.

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Please select the one below that is the best fit for t	our research. If yo	u are not sure, re	ead the appropriate s	sections before mak	ing your selection.

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

For a reference copy of the document with all sections, see  $\underline{\mathsf{nature.com/documents/nr-reporting-summary-flat.pdf}}$ 

### Life sciences study design

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

Sample size	No sample-size calculation was performed. Samples were retrospectively collected, depending on their availability.
Data exclusions	No data was excluded from the analyses.
Replication	Not relevant. Genomic sequencing data were not reproduced due to the limited amount of patient tumor material. Replication of sequencing data was not performed if sequencing quality was considered adequate.
Randomization	Not relevant due to the (retrospective) nature of the study.
Blinding	Not relevant due to the (retrospective) nature of the study.

### 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.

Materia	ls & 6	experimental	systems

n/a Involved in the study

Antibodies

**x** Eukaryotic cell lines

Palaeontology and archaeology
Animals and other organisms

Human research participants

Clinical data

Dual use research of concern

#### Methods

n/a Involved in the study

ChIP-seq

Flow cytometry

MRI-based neuroimaging