nature portfolio

Corresponding author(s): Arne Sahm

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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	base calling - bcl2fastq v1.8.4 (Illumina HiSeq 2500) and v2.20.0.422 (NovaSeq 6000)
Data analysis	Single cell analysis: read trimming - Trim Galore read mapping - bwa mem duplicate removal - samtools indel realignment and base quality recalibration - GATK variant calling - VarScan2, MuTect, UnifiedGenotyper statistical tests - R Pedigree analysis: read trimming - Trimmomatic read mapping - bwa mem duplicate removal, indel realignment and base quality recalibration - GATK clipping of second mate overlaps - bamUtil variant calling - bcftools, freebayes, Mutect2, Platypus, VarDict, Varscan2 additional filters: custom scripts following the Bcbio-nextgen pipeline

statistical tests: R

whole workflow available at: https://github.com/Hoffmann-Lab/muvac

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

Raw read data were deposited as ENA study with the accession PRJEB50344. The identified variants are available as browser accessible track hub at http://genome.ucsc.edu/cgi-bin/hgTracks?genome=Hm105_Dovetail_Assembly_1.0&hubUrl=https://genome.leibniz-fli.de/paras/hydra/hub.txt.

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	Does not apply.
Population characteristics	Does not apply.
Recruitment	Does not apply.
Ethics oversight	Does not apply.

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	9 for the comparison mother vs buds (1st comparison), 3 vs 3 for the single-cell lines examined (2nd comparison), 10 for the comparison against the reference genome (
Data exclusions	We excluded one single-cell sequencing run that we assessed as failed due to extreme high duplication rates (>65 and >90% respectively).
Replication	Regarding the single-cell analysis, we first downloaded the raw data of Milholland et al (https://www.nature.com/articles/ncomms15183) and ensured that we could replicate their results by using their methodology of single cell variant detection. Then, we applied the same methods to our data and compared our results (somatic mutation rate in Hydra) against that of Milholland et al (somatic mutation rates in human and mouse). Regarding, the pedigree analysis, we first performed an in-depth analysis based on variant caller results and initial filter criteria. Based on this analysis described in detail in Supplement Text S1, we defined even more strict filter criteria to ensure reliability of results.
Randomization	Single-cell samples are categorized by their belonging to the interstitial or epithelial cell line (I-cells and E-cells). The Pedigree samples cover an age gradient from a few weeks to 12 years.
Blinding	The persons performing DNA extraction, library preparation and sequencing were ignorant regarding group allocation.

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

Methods

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