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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 <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

Statistical parameters

	en statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main s, or Methods section).
n/a	Confirmed
	The <u>exact sample size</u> (n) for each experimental group/condition, given as a discrete number and unit of measurement
	An indication of 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

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1	A full description of the statistics including <u>central tendency</u> (e.g. means) or other basic estimates (e.g. regression coefficient) AND
1	variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)

\square	For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) witl	n confidence intervals,	effect sizes,	degrees of freedom	and P va	alue noted
\triangle	Give P values as exact values whenever suitable.					

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		Estimates of effect sizes	leg Cohen's d	Pearson's r	indicating	how they	were calculated
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\neg	\square	Clearly defined error bars State explicitly what error bars represent (e.a. SD. SE.	
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Our web collection on <u>statistics for biologists</u> may be useful.

Software and code

Policy information about availability of computer code

Data collection no software was used. Data are publicly available.

Data analysis R version 3.4.3

PLINK 1.9 samtools 1.3.1 bedtools 2.27.1 ADMIXTURE 1.3.0 vcftools 0.1.14

Code is available on https://github.com/makovalab-psu/Mito_nuclear_incompatibility

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/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

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Policy information about availability of data

 $All\ manuscripts\ must\ include\ a\ \underline{data\ availability\ statement}.\ This\ statement\ should\ provide\ the\ following\ information,\ where\ applicable:$

- 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

All analyses were conducted using publicly available data. The 1000 Genomes Project data are available on their ftp site. Intermediate files and code have also been made publicly available on github:
(https://github.com/makovalab-psu/Mito_nuclear_incompatibility).

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☐ Life sciences	Behavioural & social sciences	Ecological, evolutionary & environmental sciences					
For a reference copy of the document with all sections, see <u>nature.com/authors/policies/ReportingSummary-flat.pdf</u>							

Life sciences study design

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

Sample size

No sample size calculations were carried out. We analyzed publicly available data. As a result, we were restricted to the sample size of this dataset. We carried out simulations to test whether the available sample sizes provide sufficient power for analyses. These are detailed in the paper.

Data exclusions Some of the data points were excluded. Specifically, we removed samples which were sequenced from blood samples, as opposed to lymphoblastoid cell lines, to limit heterogeneity in tissue type. This is described in more detail in the manuscript.

Replication

This is an exploratory study and was limited by the sample size available. Thus, no explicit replication experiments were carried out. However, there are implicit replications in our experimental setup. For example, the association between ancestry and mtDNA copy number is independently reproducible across mtDNA haplotypes.

Randomization As this is an observational study, experimental randomization is not applicable.

Blinding As this is an observational study, blinding (w.r.t treatment) is not applicable.

Reporting for specific materials, systems and methods

Materials & experimental systems			Methods			
n/a	Involved in the study	n/a	Involved in the study			
\boxtimes	Unique biological materials	\boxtimes	ChIP-seq			
\boxtimes	Antibodies	\boxtimes	Flow cytometry			
\boxtimes	Eukaryotic cell lines	\boxtimes	MRI-based neuroimaging			
\boxtimes	Palaeontology					
\boxtimes	Animals and other organisms					
	Human research participants					

Human research participants

Policy information about studies involving human research participants

Population characteristics

Our analyses are based on samples of admixed ancestry, which are part of the 1,000 Genomes Project Dataset. The samples derive their ancestry from Native American, European, and African source populations.

Recruitment

These samples were collected by the 1,000 Genomes Project Group. The data are publicly available.