## nature research

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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 <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

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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
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 Give <i>P</i> 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 <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 GenomeSTRiP v2.00

Data analysis Perl 5, R (3.5.0, 3.6.1), fastQTL v2.0, TRUFFLE v1.38, CAVIAR v2.0, MATLAB, IMPUTE2 v2.3.2, bwa v0.7.13, Picard Tools (v2.9.0), GATK

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 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

Data of hESC and iPSC lines sequenced in this study were desposited in dbGaP (accession number: phs001957). (https://www.ncbi.nlm.nih.gov/projects/gapprev/gap/cgi-bin/study.cgi?study\_id=phs001957.v1.p1) and are available under restricted access.

Field-sne	ecific reporting	
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Life sciences	Behavioural & social sciences Ecological, evolutionary & environmental sciences	
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Life scier	nces study design	
All studies must dis	sclose on these points even when the disclosure is negative.	
Sample size	No statistical method was used to predetermine sample size. To maximize statistical power, we used all cell lines with available replication timing information in rtQTL mapping, except for samples used for validation. Our sample sizes are appropriate because they are comparable with human eQTL mapping studies.	
Data exclusions	For rtQTL mapping in hESCs, we removed eight samples because of non-European ancestry. This exclusion criterion was pre-established.	
Replication	We mapped rtQTLs in two similar cell types - hESCs and iPSCs. We successfully replicated rtQTLs between these two datasets. Furthermore, we successfully replicated hESC rtQTLs using three additional datasets (totaling 17 iPSCs and 32 hESCs). A locus-specific single-molecule assay was used also to validate an rtQTL in hESC.	
Randomization	This is not relevant because our study did not require allocation of samples to experimental groups.	
Blinding	This is not relevant because this is a cohort study.	
We require information	g for specific materials, systems and methods on 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 & exp	perimental systems Methods	
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	nd other organisms	
	search participants	
Clinical dat		
MI Dual use re	esearch of concern	
Eukaryotic c	ell lines	
Policy information	about <u>cell lines</u>	
Cell line source(s	CHB1, CHB2, CHB3 (Lerou et al. 2008); CuFS1, CuFS2, CuFS3, CuFS6, MR14, MR15, MR16, MR18, MR20, 1016B, 1078.	

1106-4, 1128A, 1135B, 1141-1, 1224B, 1225A, C9012, FA0003 (unpublished); CuES4 (Sagi et al. 2019); HuES48 (Chen et al. 2009); HuES6 (Cowan et al. 2004); 1018A, 1018E, BJiPSM, BJiPSO (Johannesson et al. 2014, Sui et al. 2017); 1158F, 1159B (Sui

et al. 2017); C2A (Si-Tayeb et al. 2010).

All cell lines have been authenticated by whole-genome sequencing and SNP genotyping.

Mycoplasma contamination All cell lines tested negative for mycoplasma.

Commonly misidentified lines (See <u>ICLAC</u> register)

Authentication

No commonly misidentified lines (version 10, Mar 25, 2020) were used in this study.