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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 & Reference</u> and the <u>Editorial Policy Checklist</u>.

Statistical narameters

Statistical parameters					
When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, 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				
\boxtimes	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 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 statistics 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)				
\boxtimes	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.				
\boxtimes	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings				
M	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes				

Software and code						
Policy information about <u>availability of computer code</u>						
	Data collection	no specific software was used				
	Data analysis	R version 3.5				
For manuscripts utilizing custom algorithms or reflected that are central to the research but not use discribed in published literature, reflected must be made available to edited						

Policy information about <u>availability of data</u>

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

Estimates of effect sizes (e.g. Cohen's d, Pearson's r), indicating how they were calculated

Clearly defined error bars
State explicitly what error bars represent (e.g. SD, SE, CI)

Summary data of all significant associations is provided in the supplementary tables. The informed consent given by the study participants does not cover posting of participant level phenotype and genotype data in splic databases. However, data are available upon request from KORA-gen [http://epi.helmholtz-muenchen.de/korz-gen/Request are submitted online and are subject to approval by the KORA-board.

Field-specific reporting

Recruitment

Please select 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/authors/policies/ReportingSummary-flat.pdf						
Life sciences study design						
All studies must disclose on these points even when the disclosure is negative.						
Sample size	Sample size was determined by the available financial resources. A-posteriori power calculations we conducted to estimate replication power					
Data exclusions	All samples that passed standard platform QC for methylation, genotyping, and proteomics were used.					
Replication	An independent replication cohort was used. The fraction of replicated pQTMs is reported (Table 1) and discussed.					
Randomization	As this study only involves participants from the general population, no randomization was required.					
Blinding	Blinding was not relevant as no groups were defined.					
Reporting for specific materials, systems and methods						

Materials & experimental sy	stems Methods	
n/a Involved in the study	n/a Involved in	the study
Unique biological materia	ls ChIP-se	1
Antibodies	⊠ Flow cyt	ometry
Eukaryotic cell lines	MRI-bas	ed neuroimaging
Palaeontology		
Animals and other organ	ms	
Human research particip	nts	
Human research par	icipants	
Policy information about studie	involving human research participant	<u>s</u>
Population characteristics	ecruited between 2006 and 2008 compris Diabetes (QMDiab) is a cross-sectional case	ohort of 3,080 subjects living in the southern Germany. Study participants were ing individuals with age ranging from 32 to 81. The Qatar Metabolomics Study on -control study that was carried out in 2012 at the Dermatology Department in Hama

No recruitment was conducted for this study. Here we only analyze anonymized data from previous studies, deemed non-human subject research