Corresponding	author/sl.	Careban Done
corresponding	author(s).	Stephen burge

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>.

Sta	atistical parameters
	en statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main , 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
	An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
\boxtimes	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.
\boxtimes	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 <u>central tendency</u> (e.g. means) or other basic estimates (e.g. regression coefficient) AND <u>variation</u> (e.g. standard deviation) or associated <u>estimates of uncertainty</u> (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.
	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
\boxtimes	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
\boxtimes	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)

State explicitly what error bars represent (e.g. SU, SE, LI)			
	Our web collection on <u>statistics for biologists</u> may be useful.		
Software and	l code		
Policy information a	bout <u>availability of computer code</u>		
Data collection	R version 3.4.2 (2017-09-28) "Short Summer" Copyright () 2017 The R Foundation for Statistical Computing Platform: x86, 64-apple-drawin15.6.0 (64-bit) Python 2.7.10		
Data analysis	R version 3.4.2 (2017-09-28) "Short Summer" Copyright () 2017 The R Foundation for Statistical Computing Platform: 266, 44-apped-arima*15.6 (04-bit) MR-BMA and jubilely available curmany data on AMD and NMR metabolites as presented in the applied example is public on https://github.com/verens-auber/demon AMD		

Data

- 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
- Our study is based on publicly available summarized data. We reference first the publications that describe in full detail the data generation and second the web resources we used to obtain the data. In particular, this is:
- Summarized data on genetic associations with IMMR metabolites http://computationalmedicine.fl/dataHNMR_GWMS
 Summarized data on genetic associations with age-related macular degeneration: http://ag.sph.umich.edu/abecasic/public/amx2015/
 Summarized data on genetic associations with blood traits https://www.ebi.ac.ul/gwas/

Field-specific reporting

All data used in our study is in the public domain.

	ne document were as to more, see <u>particular symmetry particular and a</u>
	nces study design close on these points even when the disclosure is negative.
Sample size	Sample size was obtained from the original studies (Kettunen, J. et al. Nature Communications 7 (2016) and Fritsche, L. G. et al. Nature Genetics 48, 134 EP – (2015)) that produced the data.
Data exclusions	A detailed description of which metabolites are included into the study is given in the manuscript, section: Data pre-processing and analysis for applied example of age-related manufactured. The selection of genetic instruments is detailed in the manuscript section: Simulation results on MRR metabolities data. We used generative aromans associated with blood lipsis, in particular trightenders, LDI and HDL inhoisterol, as reported by the Global Lipsi Genetic Consortium Nature Genetics 45, 1274 EP – (2013). Exclusion of genetic variants is idetailed in the manuscript, section Metabolities as risk factors for age-related metabolities declared in the manuscript.
Replication	N/A
Barrier Control	11/2

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Reporting for specific materials, systems and methods

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