

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

No software was used for data collection

Data analysis

R (v4.1.3), fastp (v0.20.0), bwa-mem (v0.7.17-r1188), samtools (v1.7), MetaPhlAn (v2.7.7), Humann2 (v2.8.1), LEfSe (v1.0.8), Cytoscape (v3.8.0), MMuphin (v1.8.1), MaAsLin2 (v1.10.0), vegan (v2.6-4), CCREPE (v1.0), MEGAHIT (v1.2.9), MetaBAT2 (v2.15), minimap2 (v2.26), CheckM2 (v1.0.2), barrnap (v0.9), tRNAScan-SE (v2.0.12), GUNC (v1.0.5), GTDB-Tk (v2.3.2), GTDB version r214, Prokka (v1.14.6), MinPath (v1.6), MetQuest (v0.1.33), ggplot(v3.5.1), curatedMetagenomicData (v3.8.0), curatedMetagenomicData (v1.16.0), HUMAnN2 (v2.8.1), eggNOG-mapper (v2.1.9), DIAMOND (v2.0.15.153)

Custom code used in this manuscript are available here - <https://github.com/CSB5/SG90>

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](#)

Shotgun metagenomic sequencing data are available from the European Nucleotide Archive (ENA – <https://www.ebi.ac.uk/ena/browser/home>) under project accession number PRJEB49124.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender

Sex (biological attribute) was obtained from the subjects involved in this study. Sex was not considered in this study design and all our findings are applicable to both sexes across different age groups since we accounted for sex bias using our machine-learning model. The complete characteristics of the cohort can be obtained from Table 1. Disaggregated sex and gender data were not obtained in this study.

Reporting on race, ethnicity, or other socially relevant groupings

The ethnicity of participants of SG90 cohort were self-reported. For all our analysis, we restricted to participants of ethnic Chinese group and hence ethnicity was not a confounding factor.

Population characteristics

The complete characteristics of the cohort can be obtained from Table 1.

Recruitment

The SG90 cohort is based on a longitudinal population health study that was set up in the 1990s which involved routine measurement of metabolic and other health variables. 234 elderly individuals (77-97 years old) who are community-living participants (not living in a nursing home, no diagnosis of dementia and not physically unfit) and consented to providing their stool and blood samples were recruited under the SLAS-3 protocol.

Ethics oversight

The participants in the SG90 cohort were recruited under the SLAS-3 protocol approved by the Institutional Review Board (IRB) at National University of Singapore (reference number: B-15-081). This study was also approved by an IRB for the Singapore Chinese Health Study at National University of Singapore (reference number: H-17-027).

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](https://www.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

Sample size was determined based on the number of subjects recruited for the study and the availability of resources. Sample sizes were not predetermined using any statistical tests.

Data exclusions

For the analyses, only the subjects with Chinese ethnicity were used since the data available for cross-comparison were based on Chinese ethnic groups.

Replication

Our dataset comprises healthy individuals over the age of 70 and our findings are generalizable across the age groups in our study.

Randomization

Randomization was not essential since this study is observational.

Blinding

Blinding was not essential because this study is observational.

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
☒	☐ Plants

Methods

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

Animals and other research organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals	Two independent groups of male and female 18 month old C57BL6/J mice (RRID:IMSR JAX:000664, Jackson Laboratories), with n=20 mice per group each (regular chow diet) were housed separately (maximum of four mice per cage). All the mice were kept at 25°C, 50% humidity and were on a 12h light/dark cycle.
Wild animals	NA
Reporting on sex	Both male and female mice were used for all our analyses (n=10 male, n=10 female for each group).
Field-collected samples	NA
Ethics oversight	All the mouse experiments were carried out with the approval of the Institutional Animal Care and Use Committee (IACUC) of National University of Singapore (NUS) under the R21-0135 protocol.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Plants

Seed stocks	NA
Novel plant genotypes	NA
Authentication	NA