nature portfolio

Corresponding author(s): Michael P. Snyder

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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	Lipidomics Workflow Manager (LWM, v1.0.5.0), Progenesis QI software (v2.3), OlinkAnalyze R package, HUMAnN3 (3.0.1), and bowtie2 (2.5.2). The Insulin SECretion (ISEC) software was used to calculate insulin secretion rate from plasma C-peptide measurements (PMID: 8894385).

Data analysis	R version 4.2.1 (2022-06-23), R packages: Rcpm_1.0.4,masscleaner_1.0.6,lipidr_2.12.0,SummarizedExperiment_1.28.0,GenomicRanges_1.50.1,GenomeInfoDb_1.34.2,MatrixGenerics_1.10.0,matrixStats_0.62.0,pathview_1.38.0,ggfortify_0.4.15,ComplexUpset_1.3.3,Rodin_0.1.43,visNetwork_2.1.2,gridExtra_2.3,mediation_4.5.0,sandwich_3.0-2,mvtnorm_1.1-3,Matrix_1.5-3,doSNOW_1.0.20,snow_0.4-4,iterators_1.0.14,KEGG.db_2.7.1,MSnbase_2.24.0,ProtGenerics_1.30.0,mzR_2.32.0,Rcpp_1.0.9,massdataset_1.0.19,masstools_1.0.8,metid_1.2.25,metid_0.2.0,metpath_1.0.5,ReactomePA_1.42.0,org.Hs.eg.db_3.16.0,AnnotationDbi_1.60.0,IRanges_2.32.0,S4Vectors_0.36.0,Biobase_2.58.0,BiocGenerics_0.44.0,clusterProfiler_4.6.0,ppcor_1.1,MASS_7.3-57,igraph_1.3.5,psych_2.2.9,reshape2_1.4.4,lsr_0.5.2,circlize_0.4.15,ggpubr_0.6.0,ComplexHeatmap_2.14.0,data.table_1.14.4,dplyr_1.0.10,readxl_1.4.1,npreg_1.0-9,Hmisc_5.1-0,tidyr_1.3.0,ggplot2_3.4.0,magrittr_2.0.3,foreach_1.5.2,stringr_1.5.0, caret_4.4.0, glmnet_4.4.0 Python 3.9.12 packages: pandas 2.0.3, matplotlib 3.5.1, seaborn 0.11.2, numpy 1.22.3, scipy 1.7.3 MATLAB R2022a Code for the analysis are publicly available at https://github.com/mikeaalv/cgm_meal_manuscript

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

Data is shared through supplementary tables, public repositories, and an integrated web interface. This paper focused on participants with CGM and, particularly, with complete metabolic testing, a subset of the whole cohort. Only patient data with consent to data sharing were shared. The subject participant ids were also reassigned to prevent identification. Metabolomics and lipidomics data were deposited into Metabolomics Workbench with id ST003630 and ST0036365367. Microbiome data were deposited into NCBI SRA under PRJNA1189566. The affinity proteomics Olink data have been deposited to the PRIDE repository with the dataset identifier PAD0000015468, which will be open after publication. Clinical data, CGM data, and omics data were also shared in integration through a web interface for the whole cohort (NCT03919877) when consent for data sharing was obtained from the participants. The link is https://cgmdb.stanford.edu/. New types of data will be shared through the web interface when finalized. This manuscript used datasets/databases including human genome GRCh38 (https://benlangmead.github.io/aws-indexes/bowtie), and metid based database-mapping.

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	We have reported the sex information on the enrolled patients, which is determined by self-reporting. We have not collected gender information. The conclusion apply to male and female.
Population characteristics	The information is detailed in Table 1
Recruitment	Participants provided written informed consent. Participants were recruited from the San Francisco Bay Area via locally placed advertisements online, in local newspapers, and during faculty lectures to the community. Detailed in recruitment is described in the methods. The population tends to come locally from the bay area which might not represent patterns in other populations in demographic, socioeconomic, lifestyle, and environmental factors. Individuals who join the study are self selected and may not represent the general population
Ethics oversight	The study protocol was approved by the institutional review board at Stanford University (protocols IRB-43883).

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

Life sciences study design

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

Sample size	104 participants were enrolled in total among which 55 had the necessary data and were used for this analysis. We hypothesized that individuals with different clinical measurements had significantly different PPGRs. As the focus, participants were planned to be classified into insulin resistant and sensitive groups by Steady State Plasma Glucose from the insulin suppression test. The delta glucose peak is defined as the difference between the peak and the baseline. The main approach is planned to be the Mann-Whitney test (two-sided). Significant results is planned to be validated by linear regression with covariates including BMI and age. The power analysis is based on the published result in the Zeevi 2015 paper, where PPGR to bread is 44 ± 31 mg/dL*h (mean ± SD) by AUC in a population without type 2 diabetes, the required sample size is 11 (alpha=0.05 and Power=80%) in each group for Mann-Whitney test (two-sided) for detecting a group difference of 40 mg/dL*h.
Data exclusions	A small part of data were excluded for the reasons of noncompliance in CGM data and failure of QC in omics data
Replication	Participants were instructed to repeat the standardized meal test at least two times and more than 70% of tests were conducted at least two times after removal of low quality data. Routine clinical and omics (metabolomics, lipidomics, microbiome) data were collected at multiple time points and the quantification were averaged. Olink data and metabolic testing (SSPG, IIGI, OGTT) has few replicates for the same participant.
Randomization	Samples were assigned randomly to acquire omics data.
Blinding	CGM data was collected in blinded mode, meaning that participants did not see the real-time glucose values. At the stage of acquisition and preprocessing of omics, the scientists were blinded of the groups. This is a Basic Experimental Studies in Humans (BESH) studies not an RCT study. The investigator was not blinded regarding CGM patterns or metabolic subtypes during analysis. The goal of this study is to test the relationship between the two. There is no specific treatment vs control groups in this study.

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

Methods

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

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	NCT03919877
Study protocol	https://clinicaltrials.gov/study/NCT03919877
Data collection	Details are listed in methods and previous publications. The first participant consented on 05/24/2018 and the last one on 02/15/2023. Samples were collected at Stanford hospital and at home of the participants. CGM and omics data were collected at Stanford. Omics data collection started after the sample collection and run until 2024 spring.
Outcomes	Primary outcomes: 1. Change in glycemic control as measured by change blood sugar values 2. Classification of metabolic subphenotype Secondary outcomes: Change in area under the curve (AUC) of blood glucose level by continuous glucose monitoring