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Corresponding author(s): Michael G Surette

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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 Authors & Referees 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	16S rRNA gene sequencing data was collexcted via Illumina MiSeq v2 chemistry, and processed using sl1p v3.9 (default settings). Metagenomic shotgun sequencing data was colleted via Illumina HiSeq 1500 rapid v2 chemistry, and processed using the following softwares: cutadapt v1.9.1, sickle v1.33, DeconSeq v0.4.3, Megahit v1.1.1-2-g02102e1, Maxbin v2.2.1, checkM v1.0.9, KrakenUniq v0.5, bowtie2 v2.2.6
Data analysis	Data analyses were performed using the following software (and packages): GraPhlAn v0.9.7, R v3.4.3 (ggplot2, pheatmap, phyloseq), QIIME v1.8.0 (rarefaction, taxa summaries), Hansel v0.0.81 & Gretel v0.0.81, minCED v0.2.0, eggnog-mapper v1, CARD v2.0.2/RGI v4.1.0, Phaster (https://phaster.ca/), PRISM3. Additionally, computer code generated for this project is publicly available at the following Github repositories: https://github.com/shekas3/BinTaxaAssigner, https://github.com/fwhelan/PLCA.

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/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

All sequencing results are publically available (BioProject IDL PRJNA503799).

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	20 samples were used in this study: no sample size calculations were performed. The number of samples included were dependent on participant availability/consent in the study. This sample size was sufficient to answer our hypothesis of whether this human microbial community was culturable, and whether culture-enriched metagenomics could more readily identify low abundant organisms in these samples.
Data exclusions	Low abundant operational taxonomic units (OTUs) were excluded from this study. The rationale for this was to remove any possible contaminants, PCR errors, and/or any sequences which were erroneously assigned in silico.
Replication	All bioinformatic processing and analysis of this data was performed in order to make these results reproducible. Biological and technical replicates included in the manuscript show the reproducibility of sequencing sputum samples in short succession and of culturing these samples on various media types.
Randomization	Randomization was not relevant to this study. The only "groups" analyzed were in comparisons of cultured and not cultured samples, in which randomization does not apply.
Blinding	Blinding is not relevant to this study as all analyses were performed automatically with bioinformatic software i.e. there were no opportunities for human judgment to interfere with results.

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
☒	☐ Animals and other organisms
☐	☒ Human research participants
☒	☐ Clinical data

Methods

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

Human research participants

Policy information about studies involving human research participants

Population characteristics	All patients were adult (>18yrs) with cystic fibrosis. As within patient variability was the primary interest, no specific age, sex, or gender was used as a recruitment criteria. Clinical status (cftr genotype), FEV1, or other clinical indicators were also not used as requirement criteria.
Recruitment	Patients were approached at the onset of exacerbation as to whether they would like to be participants in this study. Willing patients were recruited that met the criteria for a pulmonary exacerbation during (using established criteria as defined by Fuchs et al.). Two samples were collected from each patient (with the noted exceptions): one at the onset of pulmonary exacerbation and a second during a follow up appointment (1week-4months) following the resolution of symptoms and antibiotic discontinuation.
Ethics oversight	Ethical approval granted by the Calgary Health Region Ethics Board, REB-24123.

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