nature portfolio

Corresponding author(s): Leah E. Cowen

Last updated by author(s): Dec 9, 2024

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	Molecular Devices/TECAN infinite M NANO+/F200 Pro/SPARK plate readers were used for OD600, fluorescence, and luminescence measurements. Agilent 6538 Ultra High Accuracy TOF MS was used to quantify compound concentration in metabolic stability assays. IncuCyte S3 Live-Cell Analysis System qas used to visualize and quantify mammalian and fungal growth in co-culture.
Data analysis	Java TreeView 1.1.6r4 was used to plot heat maps for fungal growth. IncuCyte Base Analysis Software was used to quantify mammalian and fungal growth in co-culture. Phoenix 64 WinNonlin 8.3.3.333 was used to calculate PK parameters. PyMol (Schrodinger) were used for structural analyses/visualization.

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

The datasets generated during and/or analyzed during the current study are available from corresponding author upon reasonable request.

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	N/A
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	N/A
Recruitment	N/A
Ethics oversight	N/A

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	Sample size was always n=3 or greater when statistical analysis was required. All experiments were performed in biological duplicate or greater with little deviation between replicates. Selection of these sample sizes was sufficient to observe statistically significant and reproducible results in all experiments.
Data exclusions	No data was excluded.
Replication	In cases of fungal growth, assays were performed in technical duplicate which were averaged. In all other cases experiments were performed in technical triplicates as indicated in figure legends. Each experiment was performed in at least biological duplicate with both replicates showing similar results. All attempts at replication were successful.
Randomization	Randomization was not relevant to the type of experimentation reported. All assays had quantitative output where statistical analysis was performed, rather that qualitative observations, and therefore, randomization was not required to eliminate user bias.
Blinding	Blinding was not relevant to the type of experimentation reported. All assays had quantitative output where statistical analysis was performed, rather that qualitative observations, and therefore, randomization was not required to eliminate user bias.

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

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	HepG2 cells (ATCC, male, CAT# HB-8065) infectd with lentiviral vector expressing firefly luciferase from a CMV promoter. J774A.1 cells (ATCC, Cat# TIB-67)
Authentication	None
Mycoplasma contamination	All cell lines tested negative for mycoplasma contamination by PCR-based detection.
Commonly misidentified lines (See ICLAC register)	No common misidentified cell lines were used.

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	For PK, female CD1 mice from Charles River (Wilmington, MA) were used. For compound efficacy studies, six-week-old, specific pathogen-free, female ICR/Swiss mice weighing 23 g–27 g were used for all studies (Harlan Sprague-Dawley, Indianapolis, IN, USA).
Wild animals	No wild animals were used.
Reporting on sex	Female mice were used in the study given their overall smaller size, which has been optimized for the C. albicans inocuaslum used. Female mice were also used as they are easier to handle and do not fight when caged together, enabling adequate optimization of inoculum dose (PMID: 35366989).
Field-collected samples	No field-collected samples were used.
Ethics oversight	All mouse PK experiments were conducted under Protocol 2015-100840-CORE approved by UT Southwestern Medical Center IACUC. All animal procedures for compound efficacy studies were approved by the Institutional Animal Care and Use Committee at the University of Wisconsin-Madison according to the guidelines of the Animal Welfare Act, The Institute of Laboratory Animals Resources Guide for the Care and Use of Laboratory Animals, and Public Health Service Policy. The approved animal protocol number is DA0042.

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

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A