

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 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 |
| <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement |
| <input checked="" type="checkbox"/> | <input checked="" type="checkbox"/> A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> The statistical test(s) used AND whether they are one- or two-sided
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> A description of all covariates tested |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> 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) |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For null hypothesis testing, the test statistic (e.g. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P value noted
<i>Give P values as exact values whenever suitable.</i> |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> 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 RRE-containing Uniprot identifiers were previously gathered by RRE-Finder. RRE families with precursor peptide families were paired using a custom algorithm available in the supplementary information and on GitHub. Daptide BGC family was expanded by PSI-BLAST and hmmsearch. The structure of MpaA1-MpaB-MpaC complex was predicted by AlphaFold-Multimer.

Data analysis The pHMMs for daptide precursor peptides and RRE domains was generated by MAFFT and HMMER3, and visualized by Skylign. Aminotransferase phylogenetic tree was generated by MAFFT and FastTree (version 2.1.10), and visualized on Interactive Tree of Life (iTOL) website. BGCs DNA sequence were analyzed by SnapGene viewer software (version 5.0). MALDI-MS results were analyzed by flexAnalysis (version 3.4). High-resolution mass spectrometry data was analyzed by the Qualbrowser application of Xcalibur (version 4.1.31.9). NMR (nuclear magnetic resonance) data were analyzed by MestReNova (version 11.0.3). The protein-protein interaction was visualized and analyzed using PyMOL (version 2.5.4) and Chimera (version 1.16). Chemical structures were drawn using ChemBioDraw (version 14.0).

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 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

We declare that all data supporting the findings of this study are presented in the main text, supplementary data, and supplementary information. All custom

pHMMs are provided on Github (<https://github.com/the-mitchell-lab/rodeo2>). NCBI accessions used in this paper were obtained from NCBI (<https://www.ncbi.nlm.nih.gov/>) and include KZD28690.1 [<https://www.ncbi.nlm.nih.gov/protein/1017038289>]. PDB accessions were obtained from RCSB PDB (<https://www.rcsb.org/>) and include 6C76 [<https://www.rcsb.org/structure/6C76>]. Additional NCBI, PDB, and Uniprot (<https://www.uniprot.org/>) accessions are referenced in the supplementary information and supplementary data, and these accessions are publicly accessible on the respective NCBI, RCSB PDB, and Uniprot websites. Data is available from the corresponding authors upon request. Source data are provided with this paper.

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	No statistical methods were used to predetermine sample size. Bioactivity assays were performed with at least three biological replicates. The results obtained suggest the chosen sample size was appropriate because clear distinctions can be seen with the current sample size.
Data exclusions	No data was excluded from analysis. All the experimental/analysis results are included in the manuscript or Supplementary Information.
Replication	Each data point in all experiments has been repeated successfully. For the bioactivity assay, three biological replicates were conducted in addition to 2-3 technical replicates.
Randomization	No randomization was performed as none of the experiments involved allocation of samples to test groups.
Blinding	Not relevant because no group allocation was involved 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	Involvement in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> Antibodies
<input checked="" type="checkbox"/>	<input type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input checked="" type="checkbox"/>	<input type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Human research participants
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern

Methods

n/a	Involvement in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging