

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 (<i>n</i>) 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 <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☒	☐ 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
☒	☐ 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 <i>d</i> , Pearson's <i>r</i>), 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 custom computer code was used in analysis of the data.
Data analysis	Enzyme activity data was analyzed in Prism 10. Mass spectrometry data was analyzed in Thermo BioPharma Finder 5.3, RStudio Version 2024.12.0+467, and Prism 10. Thermo BioPharma Finder 5.3 (Thermo Scientific BioPharma Finder 5.3, San Jose, California) was used to process data in peptide mapping experiments, as previously described

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](#)

All data are available in the manuscript or the supplementary materials. The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium via the PRIDE partner46 repository with the dataset identifier PXD070124.

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	Use of human tissues. Human tissue samples used in this study were obtained in accordance with the Declaration of Helsinki and approved ethical guidelines. Human tissue samples were purchased from NDRI (National Disease Research Interchange), which certifies that all samples were collected with appropriate ethical approval and donor consent.

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	No formal statistical power analysis was performed to predetermine sample sizes. Sample sizes of n=3 (or greater) were selected based on established standards for evaluating enzyme kinetics and activity. Because these specific biochemical assays exhibit low intra-experimental variance, n=3 was sufficient to reliably capture the large effect sizes and pronounced activity differences observed with the CMLase enzyme. All statistical analyses, including any non-significant results, are appropriately noted within the text and corresponding figure legends
Data exclusions	No data was excluded in the study results.
Replication	To verify the reproducibility of the experimental findings, all assays were independently repeated on different days. We confirm that all attempts at replication were successful and yielded highly consistent results.
Randomization	Sample randomization was not relevant to this study. The experiments performed are highly controlled in vitro biochemical assays.
Blinding	For the experiments shown in Figure 4 and Supplementary Figures 15-20, investigators were blinded to the identity of the tissues and enzymes during both data collection and analysis. For the remaining in vitro experiments in this study, blinding was not possible because the investigators required knowledge of group allocation to correctly execute the assays and perform the appropriate biochemical treatments. However, observer bias was mitigated for these unblinded experiments because data collection relied on objective, automated quantitative readouts.

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

Antibodies

Antibodies used	ELISA primary antibody: Anti-CML antibody from Abcam, catalog number: abcam27684, lot number: 1086871-1 ELISA secondary antibody: HRP-conjugated anti-rabbit antibody from Abcam, catalog number: abcam6721, lot number: 1094269-4 IHC primary antibody: Anti-CML antibody provided by Dr. Nagai Ryoji, clone name: 6D12 IHC secondary antibody: biotinylated anti-mouse antibody from Abcam, catalog number: ab64259
Validation	ELISA primary antibody was validated using unmodified BSA and CML modified BSA generated in house. IHC primary antibody was validated by Dr. Nagai Ryoji and additionally as shown in Figure 4C and Supplementary Figure 15.

Plants

Seed stocks	Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.
Novel plant genotypes	Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.
Authentication	Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosaicism, off-target gene editing) were examined.