

## 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

Not applicable

## Data analysis

DeepSeek-R1  
 XGBoost v3.0.5  
 GraphPad Prism v8  
 PyMOL v2.1  
 RDKit v2024.09.5  
 scikit-learn v1.6.1  
 pandas v2.2.3  
 NumPy v2.1.3  
 SciPy v1.15.2  
 NetworkX v3.6.1  
 Biopython v1.86  
 lifelines v0.30.1  
 OpenAI Python SDK v1.71.0  
 Matplotlib v3.10.8  
 SHAP v0.51.0  
 AutoGluon-Tabular v1.3.1

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 associated with this work are available at the GitHub repository: <https://github.com/GRIT621/KnowMol>.

## 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

Reporting on race, ethnicity, or other socially relevant groupings

Population characteristics

Recruitment

Ethics oversight

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://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

Data exclusions

Replication

Randomization	Rats were randomly assigned to treatment groups using a computer-generated randomization list, with stratification by sex to ensure balanced distribution of males and females across groups. For in vitro experiments, cell culture wells were randomly allocated to treatment conditions.
Blinding	There was no blinding since all datasets are publicly available.

## 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
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input type="checkbox"/>	<input checked="" type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern
<input checked="" type="checkbox"/>	<input type="checkbox"/> Plants

### Methods

n/a	Involved 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

## Antibodies

Antibodies used	All antibodies were purchased from Cell Signaling Technology. PRMT3 (E9R7B) Rabbit mAb, LRP6 Rabbit Monoclonal Antibody, Cat. #13418, ASC (D2W8U) Rabbit Monoclonal Antibody, and Cleaved Caspase-1 (p20) (D57A2) Rabbit Monoclonal Antibody.
Validation	For all antibodies, validation data are publicly available on the manufacturers' official websites. No custom validation was performed in this study beyond standard positive and negative controls (e.g., knockout/knockdown cell lines, known activating stimuli) included in the experimental design.

## Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)	Human primary hepatocytes (lot HU8391) were purchased from Thermo Fisher Scientific (Catalog No. HMCPSM).
Authentication	HU8391 primary human hepatocytes were authenticated by the manufacturer via STR profiling and viability assays, confirming human origin and purity. No additional authentication was performed in this study.
Mycoplasma contamination	No mycoplasma contamination was detected in this study.
Commonly misidentified lines (See <a href="#">ICLAC</a> register)	No commonly misidentified cell lines were used in this study.

## 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	Twenty-four Sprague-Dawley (SD) rats (12 males, 12 females, weighing 200–250 g, 6–8 weeks old) were obtained from the Laboratory Animal Center of Army Medical University. All animals were housed under standard specific pathogen-free conditions with a 12-hour light/dark cycle, controlled temperature ( $22 \pm 2^\circ\text{C}$ ) and humidity (50–60%), with ad libitum access to food and water.
Wild animals	This study did not involve wild animals.
Reporting on sex	Both male and female rats were included in the study (1:1 ratio). Sex was assigned by visual inspection prior to the experiment. Data were analyzed with stratification by sex where appropriate; no significant sex-related differences were observed in the measured outcomes, and thus sex-specific subgroup analyses are not presented separately.
Field-collected samples	This study did not involve samples collected from the field.
Ethics oversight	All animal experiments conducted in this study were performed in strict compliance with institutional animal care and use guidelines, fully aligned with the internationally recognized standards set forth in the Scientific Basis for Regulation of Animal Care and Use published by the American Association for Laboratory Animal Science (AALAS) and the Animal Research: Reporting of In Vivo Experiments (ARRIVE) 2.0 guidelines. All animal procedures were carried out in strict adherence to the ethical principles, welfare

standards and regulatory requirements stipulated by this committee. Additionally, all animal husbandry, handling and surgical interventions were independently reviewed and approved by the Research Council and Institutional Animal Care and Use Committee (IACUC) of Army Medical University (Approval No. GZR2021022325).

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## Plants

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Seed stocks

N/A

Novel plant genotypes

N/A

Authentication

N/A