

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

Imaging data were collected on a Leica DMI8 microscope using LAS X software.

Data analysis

We used MetaMorph (Molecular Devices), Fiji (open source), GraphPad Prism version 8 (GraphPad software), Excel (Microsoft) and Illustrator (Adobe) to analyse the data in this study.

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 data are available in the main text, Extended Data figures or the Supplementary Information. Proteomics data is available at ProteomeXchange (PXD018563). The MetaMorph journals are freely available at <https://cloudstor.aarnet.edu.au/plus/s/8XGL750dlgwLYDn>.

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	Sample size was determined based on previous experience and was large enough to detect differences between samples with biological significance.
Data exclusions	Animals that failed to reach pre-defined human endpoints were excluded from the analysis.
Replication	Results were verified by independent biological repeats as described in the figure legends.
Randomization	Animals were not randomized, and assigned to treatment groups by the investigator. In some cases animal identification (ie genotypes of litter mates) was obtained after the treatment and at the end of the experiment. Gender and age were matched across groups.
Blinding	No blinding was used as the investigator performed all experiments.

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

Antibodies

Antibodies used	anti-Cleaved Caspase-3 (CST #9964), anti-BCL-XL antibody (CST #2746), anti-MCL-1 antibody (CST #5453), anti-Tubulin antibody (CST #2144), anti-IL-1 β antibody (AF-401-NA, R&D Systems), anti-GSDMD anti-BAX antibody (D3R2M-14796), anti-BAK antibody (in house)
Validation	Antibodies were validated based on the manufacturer's website, which includes relevant literature, and by using gene-specific knock out cells.

Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

Laboratory animals	Mus musculus, C57BL/6 Jackson Laboratory Stock sourced from the Monash Animal Research Platform, Bcl-xL fl/fl, LysMCre, housed at WEHI, Australia (Speir et al, 2016) Mcl-1fl/fl, housed at WEHI, Australia (Okamoto et al, 2014) Mcl-1fl/fl, ERCre, housed at WEHI, Australia (Glaser et al, 2012) Casp11-/-, housed at WEHI, from Vishva Dixit (Genentech) Casp1/11-/-, housed at WEHI, from Vishva Dixit (Genentech) Casp8/Ripk3-/-, housed at WEHI, Australia (Lawlor et al, 2015)
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Bak^{-/-}, housed at WEHI, Australia (Knudson et al, 1995)
Bax^{-/-} housed at WEHI, Australia (Ke et al, 2018)
Bak^{-/-}/Bax^{fl/fl}, LysM^{Cre}, housed at WEHI, Australia (this study)
Males and females, 6-8 week old mice.

Wild animals

No wild animals were used in this study.

Field-collected samples

The study did not involve samples collected from the field.

Ethics oversight

Animal experiments were performed in accordance with the National Health and Medical Research Council Australian Code of Practice for the Care and Use of Animals and were approved by the Monash University Animal Ethics Committee (approval number MARP2/099), and by the Walter and Eliza Hall Institute Animal Ethics Committee.

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