

## 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

- |                                     |                                     |                                                                                                                                                                                                                                                            |
|-------------------------------------|-------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input 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 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 type="checkbox"/>            | <input checked="" type="checkbox"/> | The statistical test(s) used AND whether they are one- or two-sided<br><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 type="checkbox"/>            | <input checked="" 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 type="checkbox"/>            | <input checked="" 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<br><i>Give <math>P</math> 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** MetaFluor 6.2 (Universal Imaging), Living Image 3.0 (PerkinElmer), BD Accuri C6 Analysis Software, SONY SH800 Analysis Software, Thermoguide (Image Guided Therapy)

**Data analysis** Prism 8, ImageJ/Fiji, FlowJo 10.6.1, Living Image 3.0 (PerkinElmer), BD Accuri C6 Analysis Software, SONY SH800 Analysis Software, Thermoguide (Image Guided Therapy)

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 main data supporting the results in this study are available within the paper and its Supplementary Information. Tumour-growth-related source data are provided with this paper. Other raw data generated in this study are available from the corresponding author upon request.

# 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     | For in vitro experiments, sample sizes of $n \geq 3$ for each group were chosen for reasonable statistical analyses. For in vivo experiments, due to the larger variation than in vitro experiments, sample sizes of $n \geq 4$ for each group were chosen for reasonable statistical analyses. These samples sizes were sufficient based on prior experience and published literature. |
| Data exclusions | For FUS stimulation experiment in vivo in mice, data of mice with unsuccessful (interrupted) FUS stimulation due to the malfunction of the FUS system were discarded. These were pre-established criteria.                                                                                                                                                                              |
| Replication     | Independent biological replicates were performed to ensure the reproducibility of the results. All attempts at replication were successful.                                                                                                                                                                                                                                             |
| Randomization   | Mice were randomly divided into different treatment groups. In bilateral tumor model mice where only one side received FUS or T cell treatment, that side was randomly determined to be the left side.                                                                                                                                                                                  |
| Blinding        | The experimenters were not blinded during the experiments or analysis. Blinding was not feasible in cases when the person performing the experiment and analyzing data was the same person.                                                                                                                                                                                             |

## 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    |                                                                 | Methods                             |                                                    |
|-------------------------------------|-----------------------------------------------------------------|-------------------------------------|----------------------------------------------------|
| n/a                                 | Involved in the study                                           | n/a                                 | Involved in the study                              |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> Antibodies                  | <input checked="" type="checkbox"/> | <input type="checkbox"/> ChIP-seq                  |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> Eukaryotic cell lines       | <input type="checkbox"/>            | <input checked="" type="checkbox"/> Flow cytometry |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Palaeontology and archaeology          | <input checked="" type="checkbox"/> | <input type="checkbox"/> MRI-based neuroimaging    |
| <input type="checkbox"/>            | <input checked="" 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           |                                     |                                                    |

## Antibodies

|                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Antibodies used | Myc-Tag (9B11) Mouse mAb (Alexa Fluor® 647 Conjugate), catalogue number:2233S (Cell signaling Technology).<br>Goat Anti-Mouse IgG Fab (Alexa Fluor® 647 conjugated), catalogue number: 115-606-072 (Jackson ImmunoResearch Laboratories).<br>APC anti-human CD69 Antibody (Clone FN50), catalogue number:310910 (BioLegend).<br>FITC anti-human HLA-A,B,C Antibody, catalogue number: 311404 (Biolegend).<br>Alexa Fluor® 647 anti-human CD3 Antibody, catalogue number: 300322 (Biolegend).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Validation      | Myc-tag antibody: Certificate of analysis and relevant citations can be found on <a href="https://www.cellsignal.com/products/antibody-conjugates/myc-tag-9b11-mouse-mab-alexa-fluor-647-conjugate/2233">https://www.cellsignal.com/products/antibody-conjugates/myc-tag-9b11-mouse-mab-alexa-fluor-647-conjugate/2233</a> .<br>Goat anti-mouse IgG (Fab) antibody: Certificate of analysis and antibody profile can be found on <a href="https://www.jacksonimmuno.com/catalog/products/115-606-072">https://www.jacksonimmuno.com/catalog/products/115-606-072</a> . This antibody has been used in publications such as:<br>Eyquem, J., Mansilla-Soto, J., Giavridis, T., van der Stegen, S. J., Hamieh, M., Cunanan, K. M., Odak, A., Gönen, M., & Sadelain, M. (2017). Targeting a CAR to the TRAC locus with CRISPR/Cas9 enhances tumour rejection. <i>Nature</i> , 543(7643), 113–117. <a href="https://doi.org/10.1038/nature21405">https://doi.org/10.1038/nature21405</a><br>CD69 antibody: Certificate of analysis and relevant citations can be found on <a href="https://www.biolegend.com/en-us/products/apc-anti-human-cd69-antibody-1674">https://www.biolegend.com/en-us/products/apc-anti-human-cd69-antibody-1674</a> .<br>HLA-A,B,C antibody: <a href="https://www.biolegend.com/en-us/products/fic-anti-human-hla-a-b-c-antibody-1871?GroupID=GROUP28">https://www.biolegend.com/en-us/products/fic-anti-human-hla-a-b-c-antibody-1871?GroupID=GROUP28</a><br>CD3 antibody: <a href="https://www.biolegend.com/it-it/products/alexa-fluor-647-anti-human-cd3-antibody-3416">https://www.biolegend.com/it-it/products/alexa-fluor-647-anti-human-cd3-antibody-3416</a><br>Specificity of all antibodies used in this study were tested using cells not expressing the target antigens (based on literatures, negative control), as well as cells known to be expressing the target antigens (based on literatures, positive control). |

## Eukaryotic cell lines

Policy information about [cell lines](#)

|                                                                      |                                                                                                                                                                                                                                                                                                    |
|----------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Cell line source(s)                                                  | Cell lines HEK 293T, Jurkat and Toledo were from American Tissue Culture Collection (ATCC, Manassas, VA), with the authentication and verification of the absence of mycoplasma contamination. Nalm-6 cell line was a gift from Michel Sadelain Lab. PC3 cell line was a gift from Kirk Shung Lab. |
| Authentication                                                       | Authentications were performed for all the cell lines listed above via morphology check under microscope and growth rate analyses.                                                                                                                                                                 |
| Mycoplasma contamination                                             | All cell lines were negative for mycoplasma contamination.                                                                                                                                                                                                                                         |
| Commonly misidentified lines<br>(See <a href="#">ICLAC</a> register) | No misidentified lines were used.                                                                                                                                                                                                                                                                  |

## Animals and other organisms

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

|                         |                                                                                                                                                                                                                                                                               |
|-------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Laboratory animals      | Six-to-eight weeks old male NOD.Cg-Prkdcscid Il2rgtm1Wjl/SzJ (NSG) mice obtained from Jackson Laboratories or UCSD ACP.                                                                                                                                                       |
| Wild animals            | This study did not involve wild animals.                                                                                                                                                                                                                                      |
| Field-collected samples | This study did not involve samples collected from the field.                                                                                                                                                                                                                  |
| Ethics oversight        | Animal experiments were performed following Protocol S15285 approved by UCSD Institutional Animal Care and Use Committee (IACUC). All researchers involved in animal experiments have complied with relevant animal-use guidelines and ethical regulations during this study. |

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

## Flow Cytometry

### Plots

Confirm that:

- ☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- ☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- ☒ All plots are contour plots with outliers or pseudocolor plots.
- ☒ A numerical value for number of cells or percentage (with statistics) is provided.

### Methodology

|                           |                                                                                                                                                                                                                                                                                                                                                                                  |
|---------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Sample preparation        | Cells were washed twice and resuspended in 100 $\mu$ L wash buffer (PBS + 0.5% BSA) containing the suggested amounts of antibodies, incubated in dark at room temperature for 30 min (or under manufacturers' suggested conditions), and washed three times before being analyzed by flow cytometry. Primary human T cells were purified from buffy coat (San Diego Blood Bank). |
| Instrument                | BD Accuri C6, SONY SH800                                                                                                                                                                                                                                                                                                                                                         |
| Software                  | BD Accuri C6 Analysis Software. SONY SH800 Analysis Software. FlowJo 10.6.1                                                                                                                                                                                                                                                                                                      |
| Cell population abundance | For FACS, positive cells were gated, and typically the top 70% of the cells in the positive gate were sorted and collected to ensure the purity.                                                                                                                                                                                                                                 |
| Gating strategy           | Gating was based on non-engineered cells. For flow cytometry on stained cells, gating was based on non-engineered cells with the same staining.                                                                                                                                                                                                                                  |

- ☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.