nature research

Corresponding author(s): Robert Wechsler-Reya

Last updated by author(s): Feb 3, 2020

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	Software used to collect data include Living Image (Perkin Elmer) for collection of bioluminescence imaging data, Image Lab Software version 5 (BioRad) for acquisition of Western blot data, CFX manager software version 2.0 (BioRad) for acquisition of qPCR data, and BD FACSDIVA software version 8 (BD Bioscience) for acquisition of flow cytometric data.
Data analysis	Software used to analyze data are ContraV3 to identify binding sites for p53, RelA and p50, FlowJo version 10 (TreeStar) for FACS analysis, GraphPad PRISM software version 7 for all graphing and statistical analysis, STAR - ENCODE version 2.5.1b for RNAseq analysis, Living Image (Perkin Elmer) for analysis of bioluminescence images, CFX manager software version 2.0 (BioRad) for analysis of qPCR data, and Image Lab Software version 5 (BioRad) for analysis of Western blots.

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

ERAP1 and TAP1 expression levels in human p53 mutant and p53 WT medulloblastomas (Figure 3f-g) were determined from RNAseq data. The sequencing data are deposited in the European Genome-Phenome Archive (EGA) as EGAD00001001899, and EGAD00001004958. ERAP1 and TAP1 expression in other human tumors (Extended Data Figure 4a-d) was determined by analyzing data from TCGA, downloaded from cBioPortal. All other data are available in the main paper or the supplementary materials.

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

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Based on experience with studies of this type, we performed power analysis, and determined that with 8 mice per group we will have a power of 90% to detect an average survival difference of 14 days with a significance of p=0.05. Thus survival experiments include at least 8 mice/ group and are repeated at least 3 times.
Data exclusions	No data were excluded from analyses.
Replication	All experiments were done at least three times. All attempts at replication were successful.
Randomization	Randomization is not relevant for in vitro studies, since experiments were done on pools of cells isolated from three distinct tumors. At the beginning of each in vivo experiment, tumor-bearing mice were subjected to bioluminescence imaging and animals with comparable signals were randomized into treatment groups; this prevents outcomes from being influenced by initial differences in tumor burden.
Blinding	Blinding was not necessary for the study because quantitative bioluminescent imaging and standard software analysis were used. No subjective analysis of tumor burden was carried out.

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

For Western-Blotting
TAP1 : Tap1 Polyclonal Antibody, rabbit, Bioss Antibodies (bs-2789R) 1/500
ERAP1 : ARTS1 Polyclonal Antibody, rabbit, ThermoFisher (PA5-36218) 1/1000
MHC-I : Anti-MHC Class I H2 Kb/Db antibody, rabbit, AbCam (ab93364) 1/500
RelA : Human/Mouse RelA/NFkB p65 Antibody, mouse, R&D system (MAB5078) 1/500
RelB : RelB Monoclonal Antibody (F.576.6), rabbit, ThermoFisher (MA5-14852) 1/1000
Actin : beta-Actin (13E5) Rabbit mAb, rabbit, Cell signaling (4970S) 1/1000
GAPDH : GAPDH (14C10) Rabbit mAb rabbit, Cell signaling (2118S) 1/2000
HistoneH3 : Histone H3 Antibody, rabbit, Cell signaling (9715S) 1/1000
secondary rabbit : Anti-rabbit IgG HRP-linked Antibody, Cell signaling (7074S) 1/1000
secondary mouse : Anti-mouse IgG HRP-linked Antibody, Cell signaling (7076S) 1/1000

For Flow cytometry
MHC-I : Anti-MHC Class I H2 Kb/Db antibody-PE, eBioscience (12-5998-81) 1/500
Isotype Ctl for MHC-I : Mouse IgG1 kappa Isotype Control-PE, eBioscience (12-4724-81) 1/500
HLA A/B/C Anti-human : HLA-A,B,C [W6/32]-FITC, Biolegend (311403) 1/500
Isotype Ctl for HLA A/B/C : Mouse IgG2a, κ Isotype Ctrl Antibody-FITC, Biolegend (400207) 1/500
CD3 : CD3 Monoclonal Antibody (17A2)-APC/cy7, Biolegend (100221) 1/250
Isotype Ctl for CD3 : Rat IgG2b kappa Isotype Control -APC, Biolegend (400623) 1/250
CD8 : anti-mouse CD8a Antibody-Pe-cy5, Biolegend (100709) 1/250
Isotype Ctl for CD8 : PE/Cy5 Rat IgG2a, κ Isotype Ctrl Antibody, Biolegend (400509) 1/250

B220 CD45R : B220 Monoclonal Antibody (RA3-6B2) PE-cyanine 7, eBioscience (25-0452-82) 1/250
Isotype Ctl for B220 : Rat IgG2a kappa Isotype Control PE-cyanine 7, eBioscience (25-4321-82) 1/250
CD11b : Anti-mouse/human CD11b Antibody (M1/70)-APC, eBioscience (17-0112-8) 1/500
Isotype Ctl for CD11b : Rat IgG2b, κ Isotype Ctrl-APC, eBioscience (17-4031-82) 1/500
NK1.1 : NK1.1 Monoclonal Antibody (PK136)-PE, eBioscience (12-5941-82) 1/200
Isotype Ctl for NK1.1 : Mouse IgG2a kappa Isotype Control-PE, eBioscience (12-4724-81) 1/200
TNFR2 : Mouse TNF RII/TNFRSF1B APC-conjugated Antibody-APC, R&D systems (FAB426A) 1/500
Isotype Ctl for TNFR2 : Hamster IgG Allophycocyanin Control Antibody-APC, R&D systems (F0121) 1/500
TNFR1 : TNFR1 Monoclonal Antibody (HM104)-PE, ThermoFisher (MA5-17899) 1/500
LTβR : anti-mouse lymphotoxin beta receptor (LTβR) Antibody-PE, Biolegend (134403) 1/500
Isotype Ctl for LTβR and TNFR1 PE : Rat IgG2a, κ Isotype Ctrl Antibody-PE, Biolegend (400507) 1/500
viability dye : 7-AAD Staining Solution, BD pharmingen (559925) 1/1000

For ChIP

p53 : p53 (1C12) Mouse mAb, Cell signaling (2524) 7.5µg
Isotype Ctl for p53 : Normal Rabbit IgG Control, Cell signaling (2729) 7.5µg
RelA : Human/Mouse RelA/NFkB p65 Antibody, R&D system (AF5078) 10µg
Isotype Ctl for RelA : Normal Sheep IgG Control, R&D system (5-001-A) 10µg
p50 : Human / Mouse NFkB1 Antibody, R&D system (AF2697) 10µg
Isotype Ctl for p50 : Normal Goat IgG Control, R&D system (AB-108-C) 10µg

Validation

Commercial antibodies used in Western-Blot (ERAP1, TAP1, MHC-I, RelA, RelB and p50) were tested on cells known to lack the corresponding transcript. Bands observed were at the predicted size. For FACS analysis, mouse MHC-I, NK1.1, CD11b and CD3 antibodies were validated on mouse splenocytes; human MHC-I (HLA A/B/C) was validated on 2 cell types known to express HLA A/B/C. For ChIP experiments, p53, RelA and p50 antiobodies were validated by looking at a published positive control in cell lines.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)

Medulloblastoma lines:
RCMB18, RCMB40,DMB006, RCMB56, RCMB58 were established in R. Wechsler-Reya's laboratory (Sandford Burnham Prebys Medical Discovery Institute, La Jolla, CA)
ICb984 and Icb1487 were obtained from Xiao-Nan Li's laboratory (Baylor College of Medicine, Houston, TX)
BT-084 and HDMB03 were established by T.Milde (DKFZ, Germany)
MB002 was established by J. Cho's laboratory (Oregon Health & Science University, Portland, OR)
Med211 was obtained from J. Olson's laboratory (Fred Hutchinson Cancer Research Center, Seattle, WA)

DIPG lines
SF 8628 was established by N. Gupta's laboratory (University of California San Francisco, CA)
SU-DIPG was established by M. Monje's laboratory (Stanford Medicine, Stanford, CA)
PKC and PDGF-B; H3.3K27M murine DIPG lines were generated by O. Becher's laboratory (Northwestern University,Chicago, IL)

AML cell lines
MV4-11, MOLM-13, THP1, U937, P31, HL60 and ML-2 were provided by A. Deshpande (Sanford Burnham Prebys Medical Discovery Institute)

Authentication

Lines were authenticated using STR with the Geneprint 10 system from Promega

Mycoplasma contamination

Cell lines used were not tested for mycoplasma contamination.

Commonly misidentified lines
(See ICLAC register)

No commonly misidentified lines were used

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals

Animal strains used for the study are described in methods section. Male and Female NSG and albino-BL/6 mice were used at 6-7 weeks old. For most experiments, 5-7 day-old C57BL/6 pups were used to generate primary mouse medulloblastoma. For some experiments p53 knockout (KO), MHC-I KO, TNFR1 KO, TNFR2 KO, TNFR1/R2 KO and LTbR KO pups were used.

Wild animals

No wild animals were used

Field-collected samples

This study did not involve samples collected from the field.

Ethics oversight

Animal studies were overseen by the Institutional Animal Care and Use Committees (IACUC) at Sanford Burnham Prebys and University of California San Diego.

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	Sample preparation is detailed in the Methods section.
Instrument	Data were acquired on BD LSRFortessa (cat#647177, year 2012) and BD FACSAriaIII (cat#648282-01, year 2010).
Software	Data were acquired using DIVA software and then analyzed using FlowJo software.
Cell population abundance	Cell sorting was performed to purify neural stem cells from the neonatal cerebellum. Dissociated cells from P5-P7 cerebellum were stained with antibodies against Prominin1 and sorted for Prominin1+ cells (as described in Pei et al., Cancer Cell 2012). These cells represent approximately 2% of the total population. After sorting, cells were re-analyzed by FACS and found to be >95% Prominin1+.
Gating strategy	Gating strategy is depicted in Extended Data 9. Cells isolated from tumors were first gated based on FSC/SSC to select intact cells (and not debris or clumps), and then based on FSCH/FSCA to enrich for single cells (as opposed to doublets). Cells were then selected for viability based on lack of staining with 7-AAD. Finally, cells were stained with isotype control to identify the negative population, which was used to determined "negative" or "positive" populations in cells stained with the specific antibody.

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