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Corresponding author(s): Davide Ruggero

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.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	FACSuite Software to collect the flow cytometry data; ZEN lite to collect the immunofluorescence data; Logger Pro to collect the sucrose gradient fractionation data; GLOMAX to collect the reporter assay data. ChemiDoc™ Imaging Systems (BIO-RAD) to develop Western blots.
Data analysis	FlowJo v10.2 for flow cytometry analysis; ImageJ for immunofluorescence intensity quantification; Excel and Prism 6 for data analysis; Burrows-Wheeler Aligner (BWA), RSEM, Bowtie2, limma package, Integrative Genomics Viewer (IGV), ClueGO, and STRING v10.0 were used for RNA-seq and ribosome profiling analysis.

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 upon request. 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 generated during this study are included in this paper and its figures and Supplementary Information. In addition, publicly available data were analyzed in this study and are cited wherever relevant. The sequencing data of the manuscript can be accessed using the following accession number: GSE105147.

Field-specific reporting

Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences

For a reference copy of the document with all sections, see nature.com/authors/policies/ReportingSummary-flat.pdf

Life sciences

Study design

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

Sample size	Sample sizes were chosen based on previous literature, or decided by using a power analysis (Power/Sample Size Calculator) based on pilot experiments that provided an estimate of effect size.
Data exclusions	No data exclusions were performed.
Replication	All replications were successful.
Randomization	Mice used for immunohistochemical analysis were selected randomly from a set of genotyped animals. For preclinical animal experiments, animals were randomized into different experimental groups.
Blinding	For animal experiments in this study, the investigators collecting data and performing analyses were blinded as they were not involved in executing the experiments.

Materials & experimental systems

Policy information about availability of materials

n/a	Involved in the study
☒	☐ Unique materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☐	☒ Research animals
☐	☒ Human research participants

Antibodies

Antibodies used	Antibodies below are available commercially. Western blot and Immunofluorescence: GFP (Abcam no. ab290, 1:2000 for Western blot, 1:500 for immunofluorescence), MYC (Cell Signaling no. 5605, 1:1000 for Western blot, 1:500 for immunofluorescence), β-actin (Sigma no. A5316, 1:10000), ARG1 (Sigma no. HPA024006, 0.4μg/ml for Western blot, 1:1000 for immunofluorescence), RASG12D (Cell Signaling no. 14429, 1:1000), p-eIF2α Ser51 (Cell Signaling no. 3597, 1:500), eIF2α (Cell Signaling no. 9722, 1:1000), p-eIF4E Ser209 (Cell Signaling no. 9721, 1:1000), eIF4E (BD no. 610270, 1:1000), GAPDH (Cell Signaling no. 2118, 1:1000), Anti-mouse CD274 Biotin (eBioscience, 13-5982-81, 1: 200), p-ERK1/2 (Cell Signaling no. 4370, 1:1000), SNAIL (Proteintech, 13099-1-AP, 1:500), CDC20 (Proteintech, 10252-1-AP, 1:1000), PLK1 (Proteintech,10305-1-AP, 1:1000), ADAM8 (Proteintech, 23778-1-AP, 1:1000), RPS2 (Abcam, ab58341, 1:1000), HA-HRP (Cell Signaling no. 2999, 1:1000), HSP90 (Cell Signaling, no. 4877, 1:1000) and PD-L1 (Cell Signaling, no. 13684, 1:1000). Flow cytometry: Mouse anti-PD-L1 (BioLegend, 124314, 1:200), mouse anti-CXCR6 PE (R&D systems, FAB2145P, 1:200), APC-CD45 (eBioscience, 17-0451-82, 1:200), PECy7-CD3 (eBioscience, 25-0031-82, 1:200), PE-CD19 (eBioscience, 16-0193-81, 1:200), PE-CD4 (eBioscience, 12-0042-82, 1:200), PerCPCy5.5-CD8 (eBioscience, 45-0081-80, 1:200), PECy7-Ly6G/C (eBioscience, 25-5931-81, 1:200), PE-CD11c (eBioscience, 12-0114-81, 1:200), and CD11b eFluor450 (eBioscience, 48-0112-82, 1:200). IHC: NIMP-R14 (Abcam, ab2557, 1:100), CD68 (Abcam, ab955, 1:100).

Validation	These antibodies were validated by the vendor or published studies using either knockout or knockdown/overexpression immunofluorescence, flow cytometry and immunoblot assays.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	We used mouse hepatocarcinoma cell lines generated from genetically engineered mouse (GEM) models and SNU-449 liver cancer cell line (ATCC® CRL-2234™) in this study.
Authentication	The SNU-449 have not been authenticated by our lab independently of ATCC's authentication. We authenticated the mouse HCC cell lines generated from GEMs by genotyping using both PCR, Western Blot and Immunofluorescence assays to detect the expression of MYC, KRASG12D, GFP and HA, etc. PD-L1 5'UTR CRISPR mutation cell lines were genotyped by PCR followed by sequencing.
Mycoplasma contamination	All cell lines were tested and are free of mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.

Research animals

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

Animals/animal-derived materials	In this study, we developed genetically engineered mouse (GEM) models in C57/BL6 mouse strain. Data were generated from both male and female mice. For the orthotopic mouse model, male C57/BL6 mice and male athymic nude mice aged between 4-6 weeks, weight between 18-25g (median weight: 22g) were used.

Human research participants

Policy information about studies involving human research participants

Population characteristics	The patients' median age was 67.5 (17-84). The gender distribution was 8 female and 28 male. Viral status: Hep B (11 patients); Hep C (3 patients) and 1 patient with both Hep B and Hep C. T stage: T1: 18 (50%); T2: 8 (22.2%); and T3 10 (27.8%).

Method-specific reporting

n/a	Involved in the study
☒	☐ ChIP-seq
☐	☒ Flow cytometry
☒	☐ Magnetic resonance imaging

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	Cultured cell lines were detached and harvested with 1X citric saline. Primary hepatocytes were harvested from mice and prepared with a liver dissociation kit (Miltenyi Biotech, 130-105-807) according to the manufacturer's instructions.
Instrument	BD FACSverse was used for PD-L1 expression measurement and BD LSRII for immune profiling analysis.
Software	FACSuite Software and FlowJo version 10.2.
Cell population abundance	After antibody staining of single cells, FSC - SSC gating was used to determine pure live cell population to be analyzed.
Gating strategy	After live cell gating, PD-L1 positive cell populations were determined based on PD-L1 FMO control. The detailed gating strategy of immune profiling is described in Supplementary Figure 1.

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