nature portfolio

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Last updated by author(s): Sep 26, 2021

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	Gene Set Enrichment Analysis (GSEA): https://www.gsea-msigdb.org/gsea/index.jsp Database for Annotation,Visualization and Integrated Discovery (DAVID): https://david.ncifcrf.gov/ Loupe browser 5: https://www.10xgenomics.com/products/loupe-browser Partek Flow: https://www.partek.com/partek-flow/ CIPR: https://aekiz.shinyapps.io/CIPR/ XENA: https://xenabrowser.net/ cBioPortal: https://www.cbioportal.org/ ImageJ: https://imagej.nih.gov/ij/ Prism8: https://www.graphpad.com/scientific-software/prism/
Data analysis	Gene Set Enrichment Analysis (GSEA) was used to identify classes of genes that are over-represented in a large set of genes. Database for Annotation,Visualization and Integrated Discovery (DAVID) was used to analysis gene ontology (GO) between clusters in single cell sequencing. Loupe browser 5 was used to analysis Visium Spatial Gene Expression. Partek Flow was used to analysis single cell sequencing and output gene expression data. CIPR was used to annotate cell clusters in single cell RNA sequencing. XENA and cBioPortal were used to collect The Cancer Genome Atlas Program (TCGA) data. ImageJ software was used for quantification of multiplex immunofluorescence staining. Prism software was used for statistical 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 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 small RNA sequencing data were deposited in the Gene Expression Omnibus (GEO) with the accession number GSE99474.
The TVGH RNA sequencing data were deposited in the GEO with the accession number GSE178537 (review token: mnytwiwedxkfvsf).
The single cell RNA sequencing data were deposited in the GEO with the accession number GSE172326 (review token: mxqtioykdbebtip).
The Visium Spatial Gene Expression data were deposited in the GEO with the accession number GSE181300 (review token: wjuhsswmvnylxub).

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	We performed at least three biologically independent experiments for all key data presented, and each experiments included multiple technical replicates.
Data exclusions	There was no exclusion from the experiments.
Replication	All attempts at replication were successful.
Randomization	Experiments were all randomized.
Blinding	Analysis was performed blindly.

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 and archaeology
☐	☒	Animals and other organisms
☐	☒	Human research participants
☒	☐	Clinical data
☒	☐	Dual use research of concern

Methods

n/a	Involved in the study	
☒	☐	ChIP-seq
☐	☒	Flow cytometry
☒	☐	MRI-based neuroimaging

Antibodies

Antibodies used

Anti-CD63 Antibody, clone RFAC4, Merck KGaA, CBL553
Anti-CD81 antibody,GeneTex, GTX101766
Alix (3A9) Mouse mAb, Cell Signaling Technology, #2171
Snail (L70G2) Mouse mAb, for WB, Cell Signaling Technology, #3895
Snail polyclonal antibody, for IHC, Abnova Corporation, PAB1924
Monoclonal ANTI-FLAG® M2 antibody, Merck KGaA, F1804
Purified anti-HA.11 Epitope Tag Antibody,BioLegend, 901502
Anti-Caspase-1 antibody, Abcam plc, ab17820
IL-1β Antibody (H-153), Santa Cruz Biotechnology, sc-7884

Anti-IL-6 antibody [B-E8], Abcam plc, ab11449
Human IL-8/CXCL8 Antibody, R&D Systems, AF-208-NA
Human CCL2/JE/MCP-1 Antibody, R&D Systems, AF-279-NA
Human CCL5/RANTES Antibody, R&D Systems, AF-278-NA
ASC Antibody (N-15), for WB and IP, Santa Cruz Biotechnology, sc-22514-R
ASC/TMS1 Antibody, for PLA, Novus Biologicals, NBP1-78977
anti-NLRP3/NALP3, mAb antibody (Cryo-2), Adipogen Life Sciences, AG-20B-0014
K63-linkage Specific Polyubiquitin (D7A11) Rabbit mAb, Cell Signaling Technology, #5621
CD14 MicroBeads human, Miltenyi Biotec, 130-050-201
IFN gamma Monoclonal Antibody (XMG1.2), Thermo Fisher Scientific Inc, 17-7311
CD8a Antibody, anti-mouse, PE, Miltenyi Biotec, 130-102-595
PE/Cyanine7 anti-mouse CD45 Antibody, BioLegend, 103114
APC anti-mouse F4/80 Antibody, BioLegend, 123116
PE/Cyanine7 Rat IgG2b, κ Isotype Ctrl Antibody, BioLegend, 400617
APC Rat IgG2a, κ Isotype Ctrl Antibody, BioLegend, 400511
CD68 Ab, Agilent Technologies, M0876
Goat anti-Mouse IgG, Thermo Fisher Scientific Inc, F2761
Anti-Actin Antibody, Thermo Fisher Scientific Inc, MAB1501
GAPDH (14C10) Rabbit mAb, Thermo Fisher Scientific Inc, #2118
normal mouse IgG, Santa Cruz Biotechnology, sc-2025
BRCC3 (D5E5H) Rabbit mAb, Cell Signaling Technology, #18215
PTEN (D4.3) XP® Rabbit mAb, Cell Signaling Technology, #9188
Anti-CD9 antibody, Abcam plc, ab92726
Anti-CD81 antibody, GeneTex, GTX101766
Anti-Calreticulin antibody, Abcam plc, ab39897
CD45 MicroBeads for mouse, Miltenyi Biotec, 130-052-301
PerCP anti-mouse F4/80 Antibody, BioLegend, 123126
CD4 for multiplex IHC, Thermo Fisher Scientific Inc, Clone: 4B12
CD8a, for multiplex IHC, Thermo Fisher Scientific Inc, Clone: C8/144B
CD163, for multiplex IHC, Thermo Fisher Scientific Inc, Clone: 10D6
CD68, for multiplex IHC, Abcam plc, Clone: KPI
CD66b, for multiplex IHC, BD, Clone: G10F5
PanCK, for multiplex IHC, Abcam plc, Clone: AE1/AE3+5D3

Validation

Describe the validation of each primary antibody for the species and application, noting any validation statements on the manufacturer's website, relevant citations, antibody profiles in online databases, or data provided in the manuscript.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	FaDu cells, ATCC, HTB-43 OECM1 cells, Dr. Kuo-Wei Chang's lab, SCC180 (Merck KGaA) THP-1 cells, ATCC, TIB-202 HEK 293T cells, ATCC, CRL-3216 MTC-Q1,Dr. Kuo-Wei Chang's lab, DOI: 10.1016/j.oraloncology.2019.06.026 LLC1, ATCC, CRL-1642 4T1, ATCC, CRL-2539
Authentication	Cells lines are authenticated at GeneLabs Life Science Corp. using short tandem repeat DNA profiling.
Mycoplasma contamination	Mycoplasma contamination were tested by PCR, all cell lines were tasted negative.
Commonly misidentified lines (See ICLAC register)	N/A

Animals and other organisms

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

Laboratory animals	6-8 weeks old wild type C57BL/6JNarl female mice and Nlrp3 Knockout C57BL/6JNarl female mice
Wild animals	N/A
Field-collected samples	N/A
Ethics oversight	The animal study was approved by the Institutional Animal Care and Utilization Committee of National Yang Ming Chiao Tung University (IACUC certificate No. 1090514) and Taipei Veterans General Hospital (IACUC certificate No. 2013-169)

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

Human research participants

Policy information about studies involving human research participants

Population characteristics	Peripheral blood mononuclear cell collection from healthy donors was approved by the Institutional Review Board of both Taipei Veterans General Hospital. For HNSCC patients RNA-seq analysis, total of 44 tumor samples and 21 normal oral epithelia from 21 HNSCC patients (21 males with a mean age=58) were collected. For multiplex immunofluorescent analysis, total of 9 tumor samples form HNSCC patients include 9 males, mean age=58 were collected. For RT-qPCR analysis, total of 50 tumor samples form HNSCC patients include 45 males and 5 females, 26T=1-2 & 24T=3-4, 20N=0 & 30N=1-3, mean age=61 were collected. For serum collection and related tumor samples, total of 19 tumor samples form HNSCC patients include 17 males & 2 females, 6T=1-2 & 13T=3-4, 3N=0 & 16N=1-3, mean age=55 were collected. For immunofluorescence and PLA staining, total of 5 tumor samples form HNSCC patients include 5 males, 2T=2 & 3T=3-4, 2N<2 & 3N=2 were collected.
Recruitment	The patients who received treatment at Taipei Veterans General Hospital were recruited with signed inform consents.
Ethics oversight	The study were approved bythe Institutional Review Board of both Taipei Veterans General Hospital with the numbers bellow: TVGH-IRB certificate No. 2014-03-004AC TVGH-IRB certificate No.2017-05-013AC TVGH-IRB certificate No.2018-06-001BC

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	Tumor tissue were digest with type IV collagenase and wash with 10% FBS contained PBS to harvest cells. than cell were stained with fluorescent conjugated antibody for 30 min, if staining with intracellular cytokine, Perm/Wash Buffer (BD) were used.
Instrument	Beckman Coulter CytoFLEX were used as flow analysis, BD FACSAria was used to sorted cells.
Software	CytExpert (v2.3)
Cell population abundance	Cells were counted and analysis at least 10000 cells of the main target (e.g. TAM)
Gating strategy	For flow analysis, gating of FSC/SSC were avoid doublets. F4/80+ FLICA+ cells were gated as Caspase1 activated macrophages. CD45+ CD8+ IFN-γ+ cells were gated as cytotoxic T cell.

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