

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

Provide a description of all commercial, open source and custom code used to collect the data in this study, specifying the version used OR state that no software was used.

Data analysis

Provide a description of all commercial, open source and custom code used to analyse the data in this study, specifying the version used OR state that no software was used.

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

The data that support the findings of this study are available within the article and its supplementary materials.

The authors declare that the gene expression RNA microarrays, ChIP-seq, RNA-seq, sc-RNA-seq, PRO-seq and spatial transcriptomics are available in the Gene Expression Omnibus (GEO) repository under accession code GSE148321 and are accessible within the link <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE148321>.

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 all the animal experiments, adequate sample size was determined based on results of pilot studies. No statistical method was used to determine sample size.
Data exclusions	All animals that fulfilled proper experimental conditions during the experimental procedures were included in the analysis. For all the experiments no data was excluded from any of the analysis.
Replication	Measures were taken individually from each animal within the experiment. Each animal was considered as a biological replicate. For SCC-25 and VDH-15, PLKO and shCD36 control and Palm diet, experiments were reproduced at least 2 times. For Microarray analysis, each in vivo experiment was considered as a biological replicate.
Randomization	No previously described randomization method was used for the experimental design.
Blinding	No blinding method was used for the experimental design.

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	CD36-APC (clone 5-271, ref. 336208, BioLegend), CD44-PeCy7 (clone GG-26, ref. 560533, BD Pharmigen), anti-CD31 clone MEC13.3 (ref. 553371, BD Pharmigen), anti-CD45 clone 30-F11 (ref. 13-045-81, eBioscience), H2Kd, clone SF1-1.1.1 (ref. 553564, eBioscience), anti-mouse CD45, clone 30-F11, (ref. 103113, BioLegend), anti-mouse CD326, clone G8.8 (RUO), (ref. 563477, BD Pharmigen), Anti-CD184; Clone 2B11/CXCR4 (RUO) (Ref.558644, BD Biosciences), Anti-CD15 (SSEA-1), clone # MC-480 (ref. FAB2155A-100, RD Systems), Anti-CD29 Clone HMβ1-1 (ref. 102215, BioLegend), anti-CD171 (L1CAM) clone 555 (ref.130-102-221, Miltenyi Biotec), anti-CD24, Clone M1/69 (RUO) (ref.562349, BD Biosciences), anti-GLAST clone ACSA-1 (ref.130-095-814, Miltenyi Biotec), anti-A2B5 Clone 105HB29 (ref.130-093-582 Miltenyi Biotec), anti-NCAM-1/CD56 Clone # 809220 (ref.FAB7820A, RD Systems), anti-s100 (ref. ab868, Abcam), anti-NEF-L (ref. AB9568, Chemicon), anti-Gap43 (ref. ab16053, Abcam), anti-CK14 (ref. 906001, BioLegend).
Validation	Antibody validation has been demonstrated by suppliers and is well documented at respectively website.

Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)	Oral squamous cell carcinoma cell lines: SCC-25 (ATCCR CRL-168TM) was purchased from ATCC, VDH-15 (primary patient-derived cell line) was patient-derived from a biopsy from Hospital Vall d'Hebron (Barcelona, Spain) with informed consent
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and approval of the Bank of Tumor Committees of the hospital according to Spanish ethical regulations.; Melanoma cell line (501-mel) was provided by Dr. Claudia Wellbrock, Manchester Cancer Research Centre, The University of Manchester, UK.

Authentication

None of the cell lines were authenticated

Mycoplasma contamination

All cell lines tested negative for mycoplasma contamination.

Commonly misidentified lines
(See [ICLAC](#) register)

Name any commonly misidentified cell lines used in the study and provide a rationale for their use.

Palaeontology

Specimen provenance

Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information).

Specimen deposition

Indicate where the specimens have been deposited to permit free access by other researchers.

Dating methods

If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.

☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Animals and other organisms

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

Laboratory animals

NOD scid gamma (NSG) (NOD.Cg-Prkdcscid Il2rgtm1Wjl/SzJ) mice were purchased from Charles River and crossed in-house.

Wild animals

Provide details on animals observed in or captured in the field; report species, sex and age where possible. Describe how animals were caught and transported and what happened to captive animals after the study (if killed, explain why and describe method; if released, say where and when) OR state that the study did not involve wild animals.

Field-collected samples

All mice (a mix of male and female) were housed under a regimen of 12 h light/12 h dark cycles and SPF conditions. All tissue samples were collected before ethical final point.

Ethics oversight

All procedures were evaluated and approved by the CEEA (Ethical Committee for Animal Experimentation) from the Government of Catalunya.

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

Biological samples were obtained from patients of the Hospital Vall d'Hebron (Barcelona, Spain) with informed consent and approval of the Bank of Tumor Committees of the hospital according to Spanish ethical regulations.

Recruitment

Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.

Ethics oversight

The study followed the guidelines of the Declaration of Helsinki, and patient identity and pathological specimens remained anonymous (in the study and elsewhere).

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

Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

Clinical trial registration

Provide the trial registration number from ClinicalTrials.gov or an equivalent agency.

Study protocol

Note where the full trial protocol can be accessed OR if not available, explain why.

Data collection

Describe the settings and locales of data collection, noting the time periods of recruitment and data collection.

Outcomes

Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures.

ChIP-seq

Data deposition

- ☐ Confirm that both raw and final processed data have been deposited in a public database such as [GEO](#).
- ☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links

May remain private before publication.

For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.

Files in database submission

Provide a list of all files available in the database submission.

Genome browser session

(e.g. [UCSC](#))

Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.

Methodology

Replicates

Describe the experimental replicates, specifying number, type and replicate agreement.

Sequencing depth

Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.

Antibodies

Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.

Peak calling parameters

Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files used.

Data quality

Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.

Software

Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.

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

Tumours were isolated from mice, and connective tissue was removed to the largest extent possible. Tissue was chopped in 0.5% trypsin 1-300 (MP Biomedical) in KSFM media (GIBCO) in a McIlwain Tissue Chopper. After complete homogenization, samples were incubated at 37°C for 90 min with shaking. Homogenates were filtered and centrifuged at 1000 rpm for 10 min at 4°C. Supernatant was discarded, and each pellet was resuspended in 1x PBS/4% calcium-chelated FBS for antibody staining and subsequent FACS analysis.

Instrument

Samples were analysed in a BD FACS ARIA FUSION Instrument- BD Biosciences

Software

BD FACS Diva Software was used to collect and analyse sorted cells.

Cell population abundance

For microarray analysis: CD36brightCD44+population constituted 3-5% of total GFP+ in VDH-15 and 5-10% of total GFP+ in SCC-25; CD36dimCD44bright population constituted 60-70% of total GFP+ in VDH-15 and SCC-25. Purity was determined by CD36 expression level analysis of sorted population. For neural-enriched fraction isolation, Neu-Mixbright population constituted 5-12% of total GFP-CD31-population in VDH-15 and SCC-25 and no analytical method to determine purity was used.

Gating strategy

For microarray analysis: Cells were selected on the basis of their Forward and Side scatter excluding cellular debris. Doublets and dead cells were eliminated by DAPI. GFP-positive cells were gated excluding lineage-BV+ positive cells. This population was selected for further CD36 human analysis. GFP-negative cells were gated excluding endothelial (CD31+), macrophages (CD45+) and epithelial (CD326+) cells. This population was selected for further mouse neural analysis.

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

Magnetic resonance imaging

Experimental design

Design type	<i>Indicate task or resting state; event-related or block design.</i>
Design specifications	<i>Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.</i>
Behavioral performance measures	<i>State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).</i>

Acquisition

Imaging type(s)	<i>Specify: functional, structural, diffusion, perfusion.</i>
Field strength	<i>Specify in Tesla</i>
Sequence & imaging parameters	<i>Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.</i>
Area of acquisition	<i>State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.</i>
Diffusion MRI	☐ Used ☐ Not used

Preprocessing

Preprocessing software	<i>Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).</i>
Normalization	<i>If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization.</i>
Normalization template	<i>Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized.</i>
Noise and artifact removal	<i>Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).</i>
Volume censoring	<i>Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.</i>

Statistical modeling & inference

Model type and settings	<i>Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).</i>
Effect(s) tested	<i>Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.</i>
Specify type of analysis:	☐ Whole brain ☐ ROI-based ☐ Both
Statistic type for inference (See Eklund et al. 2016)	<i>Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.</i>
Correction	<i>Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).</i>

Models & analysis

n/a	Involvement in the study
☐	☐ Functional and/or effective connectivity
☐	☐ Graph analysis
☐	☐ Multivariate modeling or predictive analysis
Functional and/or effective connectivity	<i>Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).</i>
Graph analysis	<i>Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).</i>

