

Corresponding author(s):	Junjeong Choi
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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 <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

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For	statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.				
n/a	a Confirmed				
	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement				
\boxtimes	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.				
\boxtimes	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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>				
\boxtimes	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 <i>d</i> , Pearson's <i>r</i>), indicating how they were calculated					
,	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.				
Sof	ware and code				
Polic	nformation about <u>availability of computer code</u>				
Da	The Cancer Genome Atlas Database, rVista (http://rvista.dcode.org), CONTRA v2 (http://www.dmbr.ugent.be/prx/bioit2-public/contrav2/index.php), NCBI sequence finder tool, Morpheus online tool (https://software.broadinstitute.org/morpheus/), The molecular signature database (MsigDB) website (http://software.broadinstitute.org/gsea/msigdb/genesets.jsp?collection=C5).				

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 analysis

Data
Policy information about <u>availability of data</u>

All manuscripts must include a <u>data availability statement</u>. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets

GraphPad Prism 6.0 (GraphPad Software Inc.)

- A list of figures that have associated raw data
- A description of any restrictions on data availability

The uncropped blots presented in this study are available in Supplementary Figure 7. All additional data is available from the corresponding author upon reasonable request.

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.

Field-spe	ecific reporting		
Please select the o	ne 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 scier	nces study design		
All studies must dis	close on these points even when the disclosure is negative.		
Sample size	The in vitro cell culture experiments, we used 2-3 biological samples in each experiment.		
Data exclusions	No data were excluded.		
Replication	All attempts at replication were successful.		
Randomization	N/A		
Blinding	Investigators were blinded to grade tumour staining		
Reportin	g for specific materials, systems and methods		
	on from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material,		
	ed 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.		
	perimental systems Methods		
n/a Involved in th	·		
Palaeontol	☐ Palaeontology ☐ MRI-based neuroimaging		
	Animals and other organisms		
	Human research participants		
Clinical dat	a		
Antibodies			
Antibodies used	CD36 - Proteintech (Cat. no. 18836-1-AP), Vimentin - Proteintech (Cat. no. 60330-1-Ig), ZEB1 - Sigma-Aldrich (Cat. no. HPA027524), E-cadherin - Cell Signalling (cat. no. 3195), CD44 - Cell Signalling (Cat. no. 3570), CD133- Abcam (Cat. no. Ab19898), ALDH - BD (Cat. no. 611195), AKT- Cell Signalling (cat. no. 9272), pAKT (ser473) - Cell Signalling (Cat. no. 9271), pAKT (Thr308) - cell Signalling (cat. no. 5106), ERK1/2 - Cell Signalling (cat. no. 9102), pERK1/2 (Thr202/Tyr204) - Cell Signalling (cat. no. 9191), P38-MAPK - Santa cruz (cat. no. Sc-728), pP38-MAPK - Cell Signalling (Cat. no. 9211), SMAD 2/3 - Cell Signalling (cat. no. 3102), pSMAD2/3 - Cell Signalling (Cat. no. 8828), STAT3 - Cell Signalling (Cat. no. 9139), pSTAT3 (Y705) - Abcam (Cat. no. Ab76315), AMPK - ThermoFisher (Cat. no. MA5-15815), pAMPK (Thr172) - ThermoFisher (Cat. no. 44-1150G), ACC - Abcam (Cat. no. Ab70246), pACC (Ser79) - Cell Signalling (Cat. no. 11818), ATGL - Abcam (Cat. no. Ab207799), FASN - Abcam (Cat. no. Ab128856), PPAR-a - Santa Cruz (Cat. no. Sc-398394), PPAR-b - Santa Cruz (Cat. no. Sc-74440), PPAR-g - Cell Signalling (Cat. no. 2435), FABP4 - Santa Cruz (Cat. no. Sc-271529), BAX - Cell Signalling (Cat. no. 2772), BCL-xL - Cell Signalling BCL-xL Cell Signalling (Cat. no. 2762), Caspase 3 - Cell Signalling (Cat. no. 9662), CL-Cas3 - Cell Signalling (Cat. no. 9661), PUMA - Santa Cruz (Cat. no. Ab150077), IgG (Mouse) - Santa cruz (Cat. no. Sc-2005), IgG (Rabbit) - Santa cruz (Cat. no. Sc-2004), a-lamin - Santa Cruz (Cat. no. Sc-518013), Actin - Santa Cruz (Cat. no. Sc-47778).		
Validation	Each antibody was validated by data sheet from the manufacturer, literature's citations and previously published articles from the same group.		
Eukaryotic c	ell lines		

Policy information about <u>cell lines</u>

Cell line source(s)

Cell lines were purchased from ATCC.

Authentication	ATCC authenticated, and observation of morphology.		
Mycoplasma contamination	Cell lines were negative for mycoplasma contamination.		
Commonly misidentified lines (See <u>ICLAC</u> register)	No cell lines listed by ICLAC were used.		
Animals and other o	organisms		
olicy information about studie	es involving animals; ARRIVE guidelines recommended for reporting animal research		
Laboratory animals	The study did not involve laboratory animals		
Wild animals	The study did not involve wild animals.		
Field-collected samples	The study did not involve samples collected from the field.		
Ethics oversight	N/A		
lote that full information on the ap	oproval of the study protocol must also be provided in the manuscript.		
Clinical data			
Policy information about clinica	ıl studies		
ll manuscripts should comply with	the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submission		
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.		
Flow Cytometry			
Plots			
Confirm that:			
The axis labels state the m	narker 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 num	nber of cells or percentage (with statistics) is provided.		
Methodology			
Sample preparation	To determine the proportion of CD36/CD44 expressing cells, cells co-cultured and control cells were harvested and resuspended to approximately 1-5x106 cells /ml in ice cold PBS. Cells are fixed with 4% formaldehyde for 15 mins at room temperature. Cells are resuspended in 100ul BSA/PBS and incubated with primary antibodies against CD36 and CD44 and for 1hr at room temperature. Cells are rinsed 3X and resuspended in ice cold PBS. Cells are incubated with Alexa Fluor 488 and Alexa Fluor 647-conjugated secondary antibody for another 30 minutes, rinsed and analysed.		
Instrument	BD FACSAria™ III (BD Biosciences, San Jose, USA)		
Software	Flowing software 2		
Cell population abundance	Followed the manufacturer's instruction		

Gating boundaries were designed equally in all of analyses.

Gating strategy