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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 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	Atherosclerosis lesion area data were collected by Photoshop CS2 (Adobe), western blot densitometry data by Epson Scan ver.3.9.2.1 (Seiko Epson Corp.), flow cytometry data by BD FACSDiva software, confocal microscopy data by ZEN Black Edition software, leukocyte adhesion and rolling by NIS-Elements Advanced Research software, and fluorescence intensity by Omega software (BMG Labtech).
Data analysis	Flow cytometry data analysis was performed using FlowJo software (Treestar), confocal microscopy data analysis using ZEN Black Edition software, and leukocyte adhesion and rolling data analysis using Image-Pro v.6.2 (Media Cybernetics). All other data analyses were performed using Graphpad Prism vers. 7.03.

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

The following figures have associated raw data: Figure 1e,g, Figure 4a,b,c,f, Extended Data Figure 1b,d,h,j, Extended Data Figure 6b,d,f, Extended Data Figure 7a, Extended Data Figure 8a,b,d, and Extended Data Figure 9a,c. There are no restrictions on data availability.

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 ☐ Ecological, evolutionary & environmental 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	When evaluating changes in atherosclerotic lesion development with the manipulation of SR-B1 in apoE null mice, we observed a difference in percent lesion area of 8.7%, with a standard deviation of 5.7%. Using these values and a Type I error of 5% and a Type II error of 10%, the number of mice needed per group is 9. No power calculations were performed for the other types of experiments pursued. Sample sizes were chosen based on standard practice for that type of experiment. For studies performed in mice, the number of independent mice employed is either apparent in the data or listed in the figure legend.
Data exclusions	No data were excluded for data analysis.
Replication	Findings in in vivo mouse studies were replicated in 2-3 separate cohorts. Findings from cell culture studies were replicated at least 3 independent experiments.
Randomization	Within all genotype groups, age- and sex-matched animals were randomly assigned to the experimental groups.
Blinding	The investigators were not blinded to experimental group assignment.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☒	☐ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☒	☐ Human research participants

Methods

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

Antibodies

Antibodies used	Anti-SR-B1 (NB400-104, NB400-113 and NB400-134,Novus; ab52629, Abcam), anti-PDZK1 (ab64856, Abcam), anti-LOX-1(MAB1798, R&D Systems), anti-LDLR (AF2148,R&D Systems), anti-CD36 (NB400-144,Novus; MA-5-14112, Invitrogen), anti-GAPDH (sc-365062, Santa Cruz), anti-DOCK4 (ab85723, Abcam)a anti-HIS tag (ab18184, Abcam), anti-CD45 (103101, clone 30-F11, biolegend), anti-F4/80 (clone BM8, biolegend), anti-human apoB (MA5-15851, ThermoFisher), anti-calnexin (ADI-SPA-860-F, Enzo Life Sciences), anti-Rac1 (clone 23A8 , Cat.# 05-389, Millipore), and anti-transferrin receptor (ab84036, Abcam).
Validation	In addition to the validation provided by the commercial sources, we independently validated the specificity of the antibodies

used in western blotting by RNAi deletion of the protein being detected. For immunofluorescence, we validated the specificity by performing control studies omitting the primary antibody or deleting the antigen protein by shRNA.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	Primary human aortic endothelial cells (HAEC) were purchased from Lonza (cat#: CC-2535).
Authentication	HAEC express endothelial markers CD31/105 and von Williebrand Factor VIII. HAEC used in the studies are also positive for acetylated low density lipoprotein uptake.
Mycoplasma contamination	The cells were tested negative for mycoplasma, bacteria, yeast, and fungi.
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	ApoE null mice with or without SR-B1 or PDZK1 expression in endothelial cells were placed on an atherogenic diet beginning at age 4-5 weeks for 1 week or 8 weeks. LDLR null mice or wild-type mice administered AAV8-PCSK9, with or without SR-B1 in endothelial cells, were placed on an atherogenic diet beginning at age 4-5 weeks for 1 to 12 weeks.
Wild animals	Wild animals were not used.
Field-collected samples	Field-collected samples were not used.

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	In the studies of aorta macrophages, the aortas were digested with liberase TH (4 U/ml,Roche), deoxyribonuclease (DNase) I (0.1 mg/ml, Sigma), and hyaluronidase (60 U/ml, Sigma) at 37C for 2h. In the studies of human aortic endothelial cells expressing reconstituted wild-type SR-B1 or mutant forms of SR-B1, cells were fixed in formalin and then incubated with primary and secondary antibodies on ice.
Instrument	BD LSR II
Software	BD FACSDiva software or FlowJo 10.4.2 software (Tree star)
Cell population abundance	Abundance of aorta CD45+,F4/80+ macrophages was approximately 20,000.
Gating strategy	Compensation was performed with single antibody-stained cells. Unstained cells were used as gating controls. All cells were first gated in FSC/SSC according to cell size and granularity. The resulting population (100,000 events) was then gated according to cell viability using DAPI (Sigma). Subsequently the cells were gated according to positivity or negativity for the specific surface markers being interrogated.

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