

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 (<i>n</i>) 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 <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☐	☒ 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>
☒	☐ 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 [statistics for biologists](#) contains articles on many of the points above.

Software and code

Policy information about [availability of computer code](#)

Data collection	n/a
Data analysis	n/a

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 data supporting the findings from this study are available within the manuscript and its supplementary information. Source data are provided with this paper. The single cell RNA sequencing data generated and analyzed during the current study are available in the National Center for Biotechnology Information Gene Expression Omnibus (GEO) repository under accession code GSE307653 [https://ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE30753]. In brief, FASTQ files and matrices of the normalized expression values are listed for each sample of this project along with a description of the analysis. All single cell sequencing raw data are

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender	N/A
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	N/A
Recruitment	N/A
Ethics oversight	N/A

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

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	Sample sizes were determined based on prior studies in the field (ours and other's) and designed to ensure adequate statistical power to detect biologically meaningful differences in atherosclerosis-related outcomes.
Data exclusions	Animals with cholesterol levels below 100mg/dL after 12 weeks on western diet were excluded
Replication	To verify the reproducibility of our findings, all experiments were performed using at least three biological replicates. All attempts at replication were successful.
Randomization	All mice were allocated randomly into experimental groups.
Blinding	All imaging analysis and quantification of atherosclerotic lesions were performed by researchers blinded to the experimental groups to which each sample belonged.

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
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

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

Antibodies used

The following antibodies were used in this study:

Cedarlane Lab:

1. Mac-2 antibody (Catalog CL8942AP)
2. Rat IgG2a isotype control antibody (catalog CLCR2A00)

Invitrogen:

1. CD115-APC (Invitrogen, cat# 17-1152-82)
2. Ly6G-eFluor450 (Invitrogen, cat# 48-9668-82)
3. CD3e-FITC (Invitrogen, cat# 11-0031-82)

Biolegend:

1. CD19-PE (cat# 152407)
2. CD45-PerCP-Cy5.5 (cat# 103132)
3. CD45R/B220 (Biolegend, cat#103251)
4. CD3-APC (Biolegend, cat# 100236)
5. CD11b-BV605 (Biolegend, cat# 101237)
6. TotalSeq™-A0301 anti-mouse Hashtag 1 Antibody (cat# 155801)
7. TotalSeq™-A0302 anti-mouse Hashtag 2 Antibody (cat# 155803)
8. TotalSeq™-A0303 anti-mouse Hashtag 3 Antibody (cat# 155805)
9. TotalSeq™-A0304 anti-mouse Hashtag 4 Antibody (cat# 155807)

BD Biosciences:

1. CD45-AF700 (BD Biosciences, cat# 560510)
2. Siglec-F-APC-Cy7 (BD Biosciences, cat#565527)
3. Ly-6G-PE (BD Biosciences, cat# 561104)

Southern Biotech:

Biotinylated secondary antibody Goat-anti-Rat f(cat. 3050-08)

Validation

Validation statements for all the antibodies listed above can be found through the following links to the manufacturer's websites.

Cedarlane Lab:

1. <https://www.cedarlanelabs.com/Products/Detail/CL8942AP?lob=AllProducts>
2. <https://www.cedarlanelabs.com/Products/Detail/CLCR2A00?lob=AllProducts>

Invitrogen:

1. <https://www.thermofisher.com/antibody/product/CD115-c-fms-Antibody-clone-AFS98-Monoclonal/17-1152-82>
2. <https://www.thermofisher.com/antibody/product/Ly-6G-Ly-6C-Antibody-clone-RB6-8C5-Monoclonal/11-5931-82>
3. <https://www.thermofisher.com/antibody/product/CD3e-Antibody-clone-145-2C11-Monoclonal/11-0031-82>

Biolegend:

1. <https://www.biolegend.com/en-gb/products/pe-anti-mouse-cd19-antibody-13641?GroupID=BLG15527>
2. <https://www.biolegend.com/fr-lu/products/percp-cyanine5-5-anti-mouse-cd45-antibody-4264>
3. <https://www.biolegend.com/fr-lu/products/brilliant-violet-421-anti-mouse-human-cd45r-b220-antibody-7158>
4. <https://www.biolegend.com/fr-lu/products/apc-anti-mouse-cd3-antibody-8055>
5. <https://www.biolegend.com/fr-lu/products/brilliant-violet-605-anti-mouse-human-cd11b-antibody-7637>
6. <https://www.biolegend.com/fr-lu/products/totalseq-a0301-anti-mouse-hashtag-1-antibody-16103>
7. <https://www.biolegend.com/fr-lu/products/totalseq-a0302-anti-mouse-hashtag-2-antibody-16104>
8. <https://www.biolegend.com/fr-lu/products/totalseq-a0303-anti-mouse-hashtag-3-antibody-16105>
9. <https://www.biolegend.com/fr-lu/products/totalseq-a0304-anti-mouse-hashtag-4-antibody-16106>

BD Biosciences:

1. https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/alexa-fluor-700-rat-anti-mouse-cd45.560510?tab=antibody_details
2. https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/apc-cy-7-rat-anti-mouse-siglec-f.565527?tab=product_details
3. https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/pe-rat-anti-mouse-ly-6g.561104?tab=product_details

Southern Biotech:

<https://www.southernbiotech.com/goat-anti-rat-igg-h-l-mouse-ads-biot-3050-08>

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)	Mouse microvascular endothelial cells were obtained from Angiocrine Bioscience (mVera-hrt-01) Primary human coronary artery endothelial cells (HCAEC) were obtained PromoCell (Heidelberg, Germany)
Authentication	Positive for endothelial cell markers and receptors
Mycoplasma contamination	All cell lines tested negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified lines were used.

Animals and other research organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals	12-18-week-old, male and female mice were maintained in a temperature controlled (25°C) facility with a 12-h light/dark cycle. Mice were given free access to water and food, except when fasting blood specimens were obtained. Strains used were C57BL/6 and Global inducible LpL-knockout mice generated by crossing floxed Lpl (Lplfl/fl) mice ⁴⁸ with β -actin driven tamoxifen-inducible Cre (MerCreMer) transgenic mice (Jackson Laboratory) to obtain the β -actin-MerCreMer/LpLfl/fl offspring designated as iLpL ^{-/-} mice. During the progress of this study we also crossed the inducible LpL knockout line onto the Ldlr ^{-/-} background and used these mice for studies or the effects of LpL deficiency on aortic gene expression. Control and diabetic rabbits were obtained from Charles River Laboratories (Wilmington, MA) and were specific pathogen-free.
Wild animals	No wild animals were used or observed in this study.
Reporting on sex	All studies were performed in both male and female mice, data are shown disaggregated for sex.
Field-collected samples	No field collected samples were utilized in this study.
Ethics oversight	All procedures were approved by the Institutional Animal Care and Use Committees at New York University Langone Health (animal protocol #160907 "Lipoprotein Lipase and ApoB").

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

Plants

Seed stocks	n/a
Novel plant genotypes	n/a
Authentication	n/a

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	NOTE: FC PLOTS ARE NOT SHOWN IN THIS STUDY. We used flow cytometry to assess circulating and arterial WBCs. Results are expressed as a percentage of CD45+ cells. For blood leukocytes, an aliquot of whole blood obtained from retro-orbital
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plexus of mice was placed into EDTA-coated tubes to prevent coagulation and kept on ice to prevent leukocyte activation. A 30 µl aliquot was used for automated cell counting with remaining cells subjected to red blood cell (RBC) lysis. A portion of white blood cells (WBCs) were then washed and stained with an antibody cocktail containing CD45-AF700 (BD Biosciences, cat# 560510), CD115-APC (Invitrogen, cat# 17-1152-82), Ly6G-eFluor450 (Invitrogen, cat# 48-9668-82), CD3e-FITC (Invitrogen, cat# 11-0031-82) and CD19-PE (Biolegend, cat# 152407) for 30 min in the dark on ice. Antibodies were diluted 1:200. Gated from the CD45+ leukocytes, monocytes were identified as CD115+ and includes the Ly6G low subset. Neutrophils were identified as CD115- and Ly6-G high. T- and B-lymphocytes were identified as CD3+CD19- and CD19+CD3- respectively.

To obtain vascular WBCs, aortic arches were isolated from the mouse and digested in liberase (5 mg/ml; Roche, 273582), DNase I (58 µg/ml; Sigma, DN25) and hyaluronidase (99 µg/ml; Sigma, 3506) for 15min at 37C° using the gentleMacs dissociator (Miltenyi Biotec). Aortic cell suspensions were live/dead stained with Fixable Green Dead Cell Stain Kit (Invitrogen, cat# L34970) and incubated with following antibodies Siglec-F-APC-Cy7 (BD Biosciences, cat#565527), CD45-PerCP-Cy5.5 (Biolegend, cat# 103132), CD45R/B220 (Biolegend, cat#103251), Ly-6G-PE (BD Biosciences, cat# 561104), CD3-APC (Biolegend, cat# 100236), CD11b-BV605 (Biolegend, cat# 101237).

Instrument	For blood leukocytes, samples were run on a MoFlo XDP sorter (Beckman Coulter). For vascular WBCs, samples were run on a MACSQuant Analyzer 16 (Miltenyi Biotec).
Software	All samples were analyzed using FlowJo V10 (Tree-Star).
Cell population abundance	Purity of the samples was assessed as described above.
Gating strategy	Unstained cells and FMO controls were used as negative controls to set gates. Compensation beads (01-1111-42, ThermoFisher) were used to set compensation.

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