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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	No software was used to collect data
Data analysis	Statistical analyisis was performed in GraphPad Prism 9, Version 9.5.0 (525). For pathology and spatial analysis the following softwares were used: HALO image Analysis platform and AI version 3.5.3577 and version 3.6.4134 (Indica Labs, Inc.). Design and Analysis Software Version 2.6 (Applied Biosystems) were used for RT-PCR analysis. Single-cell RNAseq, bulk RNAseq and Luminex were analyzed with Seurat package (v4.0.3), CellRanger (10X Genomics v3.1.0), FastQC2 (v.0.11.7), STAR (v.2.6.1d), R (v.4.0.3), R package DESeq2 (v1.30.1), pheatmap package (v1.0.12). Pathway analysis was performed with Enrichr v3 hosted at https://maayanlab.cloud/Enrichr/. Code used for data analysis is available on GitHub at https://github.com/giannarelli-lab/SARS-CoV-2-infection-triggers-pro-atherogenic-inflammatory-responses-in-human-coronary-vessels.

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

Single cell RNA sequencing data from the 6 human carotid arteries were previously published and are available in Gene Expression Omnibus (GEO) NCBI (GSE224273). Four additional carotid plaques were processed to obtain sc-RNAseq data deposited in GEO NCBI (GSE235437). scRNA-seq data coronary lesions were obtained from GEO NCBI (GSE131780). Bulk RNA sequencing data from macrophages and foam cell experiments and the plaque tissues infected with SARS-CoV-2 are deposited in GEO repository (GEO:GSE235437). All other data supporting the findings in this study are included in the main article and associated files. Source data files are available on GitHub at https://github.com/giannarelli-lab/SARS-CoV-2-infection-triggers-pro-atherogenic-inflammatory-responses-in-human-coronary-vessels.
GTEx data used in Extended Data Figure 6 is available at the GTEx Portal (https://www.gtexportal.org/home) For this manuscript the data used was version V8, dbGaP Accession phs000424.v8.p2.
Murine single-cell RNA-seq data used in Extended Figure 2 from from Wang et al. (2020) was extracted from BioProject Accession: PRJNA626450 (https://www.ncbi.nlm.nih.gov/bioproject/626450).
Human (Homo sapiens) genome assembly GRCh38 (hg38) was obtained from Genome Reference Consortium [GCA_000001405.15 GCF_000001405.26])
SARS-CoV-2 Washington isolate (WA1/2020) genome (GeneBank: MN985325.1) was obtained from the NIH repository https://www.ncbi.nlm.nih.gov/nuccore/MN985325

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	We refer to biological sex in the manuscript, although we did not investigate sex differences in the current manuscript. We did not actively select the sex or gender of the enrolled patients.
Population characteristics	Supplementary Table S1 and S2 describe demographics and clinical history of cohort of COVID-19 patients. Patient cohort consisted in 8 patients (75% male), ethnicity 62.5% non-hispanic or latino, 37.5% unknown or not reported, race 37.5% black or african american, 37.5% unknown or not reported, 12.5% white and 12.5% more than one race. Supplementary Table S4 describes the clinical history and demographics of patients enrolled in the study for single cell RNAseq analysis. Patient cohort in 10 patients (90% male), ethnicity 90% non-hispanic or latino, 10% not reported, race 50% white, 20 % african american, 20% asian and 10% more than one race or not reported, median age 68.5 years old (range 62-93).
Recruitment	All adult patients are recruited that meet the study by the responsible research coordinators priot to carotid endarterectomy surgery. Patients included in the study get a study ID and remain anonymous for the rest of the study. The recruitment process for participants in this study is designed to minimize bias and ensure a comprehensive representation of eligible individuals. All patients who meet the predetermined enrolling criteria and have provided informed consent are enrolled, without any form of bias.
Ethics oversight	Post-mortem coronary artery specimens from 8 patients diagnosed with COVID-19 were obtained from the NYU Langone Health and NYU School of Medicine's Center for Biospecimen Research and Development (CBRD), with approval by the Institutional Review Board of NYU Langone Health for (IRB i21-01587). Patients undergoing carotid endarterectomy (CEA) were enrolled in the ATHERO-IN study, an observational clinical study approved by the Institutional Review Boards of the Icahn School of Medicine at Mount Sinai (IRB 11–01427) and the NYULH (IRB i21-00429).

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

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	No a-priori sample size calculation was performed for the study. We have included all possible samples that were available at the time of

Sample size	experiments.
Data exclusions	No samples were excluded from the analysis
Replication	Experiments were replicated at least once for the immunohistochemical, immunofluorescence and RNAscope and in-vitro studies involving NRP1 inhibitor and NRP1 siRNA analysis. For bulk-RNA and Luminex, a minimum of two/three samples per group or condition were used. All attempts at experimental replication were successful.
Randomization	Randomization was not employed in this study due to the unique characteristics of our target population and the specific nature of the interventions being investigated. The nature of our study design involved a specific target population with unique characteristics that could not be easily randomized. For COVID-19 patients' post-mortem samples, samples were obtained from NYU Center for Biospecimen Research and Development (CBRD) based on availability. For CEA studies we did not actively randomize our patients, as the samples were processed from prospectively enrolled patients.
Blinding	For the studies using human specimens, we used unbiased computational approaches to analyze the data. Bioinformatitians and investigators are blinded to the study conditions and experimental designs for the analysis.

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

Methods

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

Antibodies

Antibodies used	The following antibodies were used: Mouse anti-human CD68 (KP1) 760-2037 Ventana Medical Systems (pre-diluted. Cat# 760-2931, Lot#'s H354244, H15799, RRID AB_2335972); human Neuropilin-1 Antibody Cat. #AF3870 R&D Systems (1:100); CD68 Monoclonal Antibody (KP1), eBioscience Cat. #14-0688-82 Invitrogen (1:100); Goat anti-Mouse IgG (H+L) Highly Cross-Adsorbed Secondary Antibody, Alexa Fluor 594 Cat. #A11032 Invitrogen (2:400); Goat anti-Rabbit IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor Cat. #488 A-11008 Invitrogen (1:400); Goat anti-Mouse IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor 488 Cat. #A-11001 Invitrogen (1:400); anti-SARS-CoV-2 Nucleocapsid Antibody clone 1C7 Cat. # 10-605 ProScience (1:100); goat anti-mouse Alexa Fluor 488 A11001 Invitrogen (1:400); anti-NRP1 rabbit monoclonal antibody 3725 Cell Signaling (1:50); anti-β-actin mouse monoclonal antibody A2228 Sigma Aldrich (1:500); anti-rabbit HRP conjugated antibody Cat. #042-206 Protein Simple; anti-mouse HRP conjugated antibody Cat. #031-108 Protein Simple.
Validation	All antibodies were validated for the applications in this manuscript by the correspondent manufacturer and the information is located in their website. Our usage was described in the Methods section of the manuscript.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	Cells used in this study are the following: Vero E6 (American Type Culture Collection; Cercopithecus aethiops Kidney Epithelial Cells) obtained from ATC, Cat #CRL-1586. Vero E6 Expressing Transmembrane Protease, Serine 2 and Human Angiotensin-Converting Enzyme 2 (Vero E6-TMPRSS2-T2A-ACE2) obtained from Biodefense and Emerging Infections Research Resources Repository (BEI Resources), Cat. #NR-54970 Human Peripheral Blood Monocytes obtained from StemCell Technologies , Cat. #200-0167 Human Aortic Smooth Muscle Cells (HAoSMC) obtained from PromoCell, Cat. #C-12533
Authentication	All cell lines were recently purchased from vendors. We did not do in-house authentication of cell lines.
Mycoplasma contamination	Cell lines were confirmed to be negative for Mycoplasma contamination with MycoAlert Detection kit (Lonza).

Commonly misidentified lines (See ICLAC register)	No commonly misidentifed cell lines were used in this study according to ICLAC register of misidentified cell lines.