Data S1.

Supplemental Methods

Human aortic samples

Human AAA tissue was obtained from 5 patients undergoing open AAA repair, and the control samples were trimmed from the nondilating aorta surrounding the lesions from the same patients. Written informed consent was obtained from all subjects before participation. All the studies involving human samples were approved by the Ethics Committee of Ren Ji Hospital (KY2020-151), School of Medicine, Shanghai Jiao Tong University, and conformed to the principles outlined in the Declaration of Helsinki.

Nur77−/− mice construction

CRISPR/Cas9 technology was used to introduce the mutation by non-homologous end joining (NHEJ), resulting in a frameshift of the Nur77 protein reading frame and loss of function. The brief process is as follows: The transcript of Nur77 was obtained from the Ensemble database(ENSMUST00000023779.7). The gRNAs were constructed through the website (http://crispr.mit.edu/), and gRNAs with the highest score were selected (The sequence is provided in Table S2). Then Cas9 mRNA and gRNAs were obtained by vitro transcription. Cas9 mRNA and gRNAs were microinjected into the fertilized eggs of C57BL/6J mice. The injected fertilized eggs were transplanted into pseudo-pregnant female mice, and the born mice were F0 generation mice. Since the early cleavage rate of fertilized eggs is very fast, the F0 generation mice obtained were chimeras and may not have the ability to stabilize heredity. The F0 generation mice identified by PCR (primer information is provided in Table S2) were mated with wild-type C57BL/6J mice to obtain F1 generation heterozygous mice (Nur77+/−). Nur77+/− mice were
inbred to obtain Nur77−/− mice. The baseline date of Nur77−/− mice is presented in Figure S1.

**Blood Pressure Measurement**

The blood pressure was measured by a noninvasive blood pressure system for mice (BP-2010A, Softron Biotechnology). Briefly, mice’s blood pressure was measured by putting the mice tail into the tail-cuff system in a dark quiet room and waiting for the mice to calm down to read the meter. The measurements were carried out in conscious mice without anesthesia. To avoid variations in blood pressure due to day cycle, all measurements were performed between 2 and 6 pm. Systolic blood pressure values were derived from an average of five measurements per animal.

**Tissue collection**

After 4 weeks, mice were euthanized with an inhalation overdose of isoflurane (3%). Then, left cardiac ventricles were immediately perfused with ice-cold isotonic saline (10ml) with an exit through the severed right atrium. After aortic tissues were isolated, the aorta’s morphology was photographed. And the maximum diameters of the abdominal aortas were measured using calipers. An aneurysm was defined as a >50% increase in suprarenal aorta diameter compared with aortas from saline-infused mice. Then the abdominal aortic was dissected into two sections. One section was stored at -80°C for molecular analysis and the other section was fixed overnight in 10% formalin and then embedded in paraffin or optimal cutting temperature (OCT) embedding compound (Tissue-Tek). Serial sections (8-10 mm) of the aortas were prepared for morphometric analysis and immunofluorescence staining.

**Histomorphology analysis**

After the serial 8μm sections were cut, the paraffin-embedded abdominal aorta sections were stained with hematoxylin and eosin for general morphology, Masson’s Trichrome for fibrosis detection, or Verhoeff-van Gieson staining (EVG) for elastin. Serial sections of aneurysm were processed with hematoxylin and eosin staining. Section levels with lesions severity ranked among the top
three were chosen to undergo further histomorphology analysis and immunohistochemistry processes to acquire the averages of indicated parameters. All samples were processed with the same protocol. Images were captured under the identical microscope (Leica DM3000B, Germany), and were analyzed using Image-Pro Plus 6.0 (Media Cybernetics Inc). Determination of elastin degradation was performed by semiquantitative grading as described previously\(^3\). The grades were defined as follows: grade 1, no degradation; grade 2, mild elastin degradation; grade 3, severe elastin degradation; and grade 4, aortic rupture.

Immunohistochemistry staining of F4/80 and MMP9 was used to observe the macrophage infiltration, as well as expression of MMP9 in the mice aorta, as previously described\(^4\). In brief, primary antibody against F4/80 (1:200) or MMP-9 (1:200) were used. Specific labeling was detected with an HRP-conjugated goat anti-rabbit secondary antibody (1:200), and then were incubated with DAB substrate (cat#ab64238, Abcam) for 10 min. Representative images were captured by light microscopy.

**Immunofluorescence staining**

Frozen sections were fixed by 4% paraformaldehyde for 15 min and permeabilized in cold methanol for 10 min at room temperature. After blocking with 5% BSA for 1 h, the sections were incubated with primary antibodies against Nur77(1:200), CD68(1:200), LOX-1(1:200), overnight at 4°C, followed by incubation with Secondary antibodies, an Alexa Fluor 488 goat anti-mouse secondary antibody (1:200) or an Alexa Fluor 555 goat anti-rabbit secondary antibody (1:200), for 1 h at room temperature. DAPI (S36973, Thermo Scientific) was used to identify nuclei. The stained sections were viewed using fluorescence microscopy.

**In situ MMP zymography**

In situ MMP zymography was performed using Gelatinase Assay Kit following the manufacturer's instruction (GMS80062.1, Genmed Scientifics Inc). In brief, abdominal aortas were OCT embedded and freshly cut into 8 μm
sections using a freezing microtome. Gelatinolytic activity was analyzed in unfixed frozen sections using FITC-labeled gelatin as a substrate. Slides were incubated at room temperature, protected from light for 2h. Proteolytic activity was detected as green fluorescence (530 nm) by fluorescence microscopy (Leica DM3000B, Germany).

Cell culture and treatment

Ang II was used to induce AAA in vitro model. Raw264.7 cells (murine macrophage cell line) and Movas (mouse aorta smooth muscle cell line) from the Cell Bank of the Chinese Academy of Sciences (Shanghai, China) were cultured in Dulbecco's Modified Eagle's Medium (DMEM, Gibco) supplemented with 10% fetal bovine serum (FBS, Gibco), 100U/mL of penicillin and 100μg/mL of streptomycin at 37°C in a humidified 5% CO₂ atmosphere. Cells were collected after incubating with Ang II (1μmol/L) for the selected time (0, 0.5, 1, 3, 6, 12h). In a separate experiment, the Cells were pretreated with or without celastrol (0.3μM) for 2h, followed by treatment with Ang II (1μmol/L) for 12h. Cells were treated with serum-free DMEM for 12h before drug treatment.

Bone marrow-derived macrophage (BMDM) isolation and culture

Bone marrow cells were prepared from femurs and tibiae of 6- to 8-week-old WT and Nur77⁻/⁻ mice as previously described\(^{15}\). Briefly, mice were euthanized with an inhalation overdose of isoflurane (3%). Next, surgically removed cleaned bones were transferred into a sterile Petri dish containing ice-cold, sterile 1x PBS (10 ml), and the marrow was flushed with PBS in a syringe with a 27-gauge needle. Simultaneously, the needle was moved up and down while scraping the inside of the bone to dissociate the cells until the bone appears clear. Cell suspension was centrifuged at 150g for 5 minutes at 4°C. The supernatant was discarded and the cells were resuspended and seeded in 6-well plates with complete DMEM containing 10% FBS, 2 mM glutamine, 100 U/ml penicillin, 100μg/ml streptomycin, and supplement with 30 ng/ml recombinant M-CSF (416-ML-050, R&D Systems). The plate was incubate at 37 °C and 5% CO₂. Fresh BMDM growth medium was changed on day 3. On
day 7, the mature BMDM can be used for subsequent experiments.

**Lentiviral transduction, LOX-1 overexpression and knockdown**

To overexpress Nur77, lentivirus was purchased from Genomeditech Co, Ltd. (Shanghai, China) and stable cell lines were constructed by the lentivirus infection. A similar lentiviral vector encoding the green fluorescent protein (GFP) gene (LentiGFP) was used as a control. Raw264.7 cells were transduced with lentiviral in diluted media at a multiplicity of transduction of 100 for 48h and then cultured in DMEM media containing 10% bovine serum.

To overexpress and knockdown LOX-1. Plasmids including overexpression negative control plasmid (oe-NC), LOX-1 overexpression plasmid (oe-LOX-1), small interfering RNA targeting LOX-1 (si-LOX-1), and si-NC were all purchased from Shanghai Genomeditech (Shanghai, China). Cells in 6-well plates were transfected with plasmid or siRNA using Lipofectamine™3000 (L3000150, Invitrogen) according to the manufacturer's instructions. After transfection for 24h, the mRNA and protein expression of the cells were detected, respectively.

**MRI screening assay**

Magnetic resonance imaging (MRI) was performed at weeks 4 after surgery. All scanning was carried out with a 7.0-T small animal, Superconducting magnet and BioSpec spectrometer (BioSpec 70/20 USR: Bruker, Bruker Biospin, Ettlingen, Germany). All mice were induced and maintained under isoflurane anesthesia (1.5% to 2%) in medical-grade and monitored simultaneously via a sensor positioned on the abdomen for respiration rate (30-50 breath/min). All MRI images were acquired according to the manufacturer’s instruction. RadiAnt DICOM Viewer (Poznan, Poland) software was used to delineate an ROI to determine the abdominal aorta cross-sectional area.

**Vascular ultrasound imaging**

Micro-ultrasound images were obtained using the Vevo770 system (Visual Sonics) 4 weeks after surgery. Mice were anesthetized using 1.5%-2.0% isoflurane, the abdominal hair was removed using depilatory cream and
ultrasound transmission gel was added onto the abdomen area to acquire optimal images. Heart rate and respiration were monitored throughout the procedure. An ultrasonic probe was first applied on the transverse plane to locate the abdominal aorta, the “Portal Triad” (hepatic artery, hepatic vein, and bile duct) was used as anatomic markers to confirm the location of the aorta. The aorta was centered and the probe was moved down to find the kidney. Color mode Doppler was activated to help localize the two renal arteries, and the probe then switched to the long axis. The probe was placed parallel to the aorta to obtain a longitudinal axis view of the abdominal aorta. Images were recorded to acquire measurements of the aortic diameter.

**Quantitative real-time PCR**

Total RNA was extracted from AAA and sham control tissues or cells using RNAiso Plus (Takara). cDNA was synthesized using PrimeScript RT Master Mix kit (Takara). qRT-PCR of mRNAs was performed using TB Green® Premix Ex Taq™ (Takara) and real-time PCR experiments were carried on a LightCycler® 480 System (Roche). Quantitative results were normalized against GAPDH and presented by the \(2^{-\Delta\Delta Ct}\) method. The primers used for q-PCR are listed in Table S3.

**Western blot analysis**

Total proteins were extracted from cells or from abdominal aortas of the mice and lysed in lysis buffer (Roche, USA) with the protease and phosphatase inhibitor (Thermo Scientific) for 30 min on the ice. The supernatant fluid was then collected after centrifugation. Proteins were separated by 7%-12.5% SDS-PAGE gels and transferred onto PVDF membranes (Millipore, Bedford, MA). Membranes were blocked with 5% non-fat dry milk in TBST for 1h at room temperature and incubated overnight at 4°C with different primary antibodies. Membranes were washed and incubated with horseradish peroxidase-conjugated anti-rabbit IgG (cat#111-035-003, Jackson ImmunoResearch) for 1h at room temperature. GAPDH, β-actin, or tubulin acted as the control. Protein bands were detected with LAS-4000 mini system (Fujifilm, Japan).
Chromatin immunoprecipitation (ChIP) analysis

ChIP assay was performed with SimpleChIP® Enzymatic Chromatin IP Kit (Cat#9003, Cell Signaling Technology) according to manufacturer’s instructions. Raw 264.7 cells were treated with PBS or Ang II (1 μmol/L) for 12h. Crosslinking of chromatin was performed by treatment with 1% formaldehyde for exactly 10 minutes at room temperature. Then, glycine was added into the culture medium to terminate the crosslinking reaction. After termination of crosslinking, nuclear extraction from cell pellets was performed with SimpleChIP® Enzymatic Chromatin IP Kit. Crosslinked chromatin was sheared to 150-900 bp with micrococcal nuclease. Then the lysate was treated with 3 sets of 20-sec pulse using an Ultrasonic Sonicator. Immunoprecipitation was performed with 2μg anti-IgG antibody (CST) and 10ul anti-Histone H3 Rabbit antibody (CST) as negative and positive control of ChIP, respectively. As a target antibody, 10μg polyclonal anti-Nur77 antibody was used. ChIP PCR was performed with primers encompassing the following loci of the LOX-1 promoter in mice: forward:5’-TGGACTGGATGGTTCGACTTG-3’ reverse:5’-ACTCAGGAGCCAGGAATGGAA-3’. Then LOX-1 promoter-specific PCR products were subjected to agarose gel electrophoresis analysis.

RNA sequencing

Total RNA was extracted using the mirVana miRNA Isolation Kit (Ambion) following the manufacturer’s protocol. RNA quality was verified using the Agilent 2100 Bioanalyzer (Agilent Technologies, Santa Clara, CA, USA). Then the libraries were constructed using TruSeq Stranded mRNA LT Sample Prep Kit (Illumina, San Diego, CA, USA) according to the manufacturer’s instructions. Then, these libraries were sequenced on the Illumina sequencing platform (Illumina HiSeq X Ten) and 125 bp/150 bp paired-end reads were generated. Differentially expressed genes (DEGs) were identified using the DESeq R package functions to estimate Size Factors and nbinomTest. P-value < 0.05 and foldchange>2 or foldchange<0.5 was set as the threshold for significantly differential expression. KEGG pathway enrichment analysis of DEGs was
performed respectively using R based on the hypergeometric distribution. RNA-Seq Data had been submitted to GEO (GSE174768). Principal component analysis (PCA) is presented in Figure S4. QC metrics for the RNA-seq data are shown in Table S4.

**ChIP-sequencing analysis**

The data downloaded from the GEO database (GSE102393) were, respectively, SRR5914767.1, SRR988407.2, SRR988408.2, SRR1694053.1. The quality control of clean data was performed by FastQC. All reads were mapped to the mm10 mouse genome using bwa program, and uniquely mapped reads were processed further for peak identification. MACS14 was used to identify significant peaks with input DNA (ChIP-seq) as the control, and -p 10^{-7} was used as the threshold for peak calibration. Then R package ChIPseeker was used to annotate the peak identification results. The consensus binding motif analysis for Nur77 was performed by MEME.

**Supplemental statistical analysis**

Blinding was used in the study. According to our randomization and blinding strategy, animals were grouped by Dr. Che, and the surgery was operated by Dr. Zhang. The color Doppler ultrasound and MRI scans were carried out by Dr. Geng. Slide scoring and follow-up study were performed by Dr. Sun, assisted by Dr. Chen. The researchers except Dr. Che were unaware of the treatment group assignment or genotype.
### Table S1. Key Resource Table.

| Regents or Resources                | Source               | Identity       |
|-------------------------------------|----------------------|----------------|
| Angiotensin-II                      | Sigma-Aldrich        | A9525          |
| Celastrol                           | MedChemExpress       | HY-13067       |
| Isoflurane                          | RWD                  | R510-22        |
| OCT embedding compound              | Sakura               | 4583           |
| H&E kit                             | Servicebio           | G1005-500ML    |
| Masson’s Trichrome kit              | Servicebio           | G1006-100ML    |
| EVG dye solution set                | Servicebio           | G1042          |
| DAPI                                | Thermo Scientific    | S36973         |
| Gelatinase Assay Kit                | Genmed Sciences       | GMS80062.1     |
| DMEM                                | Gibco                | 10569-010      |
| Fetal bovine serum                  | Gibco                | 10099-141      |
| M-CSF                               | R&D Systems          | 416-ML-050     |
| Cell Counting Kit-8 assay           | Beyotime             | C0041          |
| Lipofectamine™3000                  | Invitrogen           | L3000150       |
| RNaIso Plus                         | Takara               | 9108           |
| PrimeScript RT Master Mix kit       | Takara               | RR036A         |
| TB Green® Premix Ex Taq™            | Takara               | RR420A         |
| Complete lysis-M                    | Roche                | 04719964001    |
| Protease and phosphatase inhibitor  | Thermo Scientific    | 78443          |
| SimpleChIP®Enzymatic                | Cell Signaling       | 9003           |
| Chromatin IP Kit                    | Technology           |                |
| Osmotic Pumps                       | Alzet                | 2004           |
| DAB substrate                       | Abcam                | ab64238        |
| Mouse anti-CD68                      | Abcam                | ab31630        |
| Mouse anti-CD68                      | Abcam                | ab955          |
| Rabbit anti-Nur77                   | Abcam                | ab13851        |
| Antibody                                      | Supplier                | Catalogue Number |
|-----------------------------------------------|-------------------------|------------------|
| Mouse anti-alpha smooth muscle Actin          | Abcam                   | Ab7817           |
| Rabbit anti-LOX-1                            | Abcam                   | ab60178          |
| Rabbit anti-GAPDH                            | Abcam                   | ab371668         |
| Rabbit anti-β-actin                          | Cell Signaling Technology | 4970             |
| Rabbit anti-MMP-2                            | Abcam                   | ab37150          |
| Rabbit anti-MMP-9                            | Abcam                   | ab38898          |
| Rabbit anti-F4/80                            | Abcam                   | ab111101         |
| Goat anti-rabbit (HRP)                       | Jackson ImmunoResearch   | 111-035-003      |
| Alexa Fluor 488 goat anti-Mouse              | Cell Signaling Technology | A-11001          |
| Alexa Fluor 555 goat anti-Rabbit             | Cell Signaling Technology | A-21428          |
| Goat Anti-Rabbit IgG H&L (HRP polymer)       | Abcam                   | ab214880         |
| Raw264.7 cell                                | Cell Bank of the Chinese Academy of Sciences (Shanghai, China) |
| Movas cell                                   | Cell Bank of the Chinese Academy of Sciences (Shanghai, China) |
| ApoE<sup>−/−</sup> mice on a C57BL/6 background | Shanghai Model Organisms Center | NM-KO-190565    |
| C57BL/6 mice                                 | Beijing SPF Biotechnology Co., Ltd. | SPF-A04-001     |
Table S2. gRNAs sequence.

| gRNAs   | Sequence (5’-3’)          |
|---------|---------------------------|
| gRNA1   | CCTTCCTCTACCAGCTGCCGGGG   |
| gRNA2   | ACCAGCCACCCACCAGCTTGGGG   |

Primer information

| Primer Type | Sequence (5’-3’)          |
|-------------|---------------------------|
| Forward     | CCCTCCCCGGCCTACCAAGTT     |
| Reverse     | TGTGCCCTGCTGAATAAAAAGTCC  |

The primer information for F0 generation mice identification
### Supplemental Table S3

| PCR production | Oligoes for mutations (forward/reverse) |
|----------------|-----------------------------------------|
| **Human GAPDH** | 5'-ACAACTTTGGTATCGTGGAAGG-3' |
| **Human Nur77** | 5'-GCCATCACGCCACAGTTTC-3' |
| **Mouse GAPDH** | 5'-TGTCGAGTTGGATCTCAGTTGGAACAG-3' |
| **Mouse Nur77** | 5'-TGGCTGAGGACGAGGATGTGG-3' |
| **Mouse MMP9**  | 5'-GCACCTTCATGGACCGCTACAC-3' |
| **Mouse IL-1β** | 5'-GATGGCTGCACATCTCTCTATGAC-3' |
| **Mouse TNF-α** | 5'-ATGGCTCTGAGAGAGTGGTGATGAGAGGAG-3' |
| **Mouse CCL2**  | 5'-ATGGCTCTGAGAGAGTGGTGATGAGAGGAG-3' |
| **Mouse IL-6**  | 5'-GCCTCTTGGGACTGATGCT-3' |
| **Mouse LOX-1** | 5'-CAAAACAGCACAGGAGATGAC-3' |
| **Mouse FATP2** | 5'-AACAGAGCAGAGATGAC-3' |
| **Mouse BMAL1** | 5'-TGACTCGGATGTTGCTTATG-3' |
| **Mouse Lipe**  | 5'-AACAGGAGCAGAGATGAC-3' |
| **Mouse LOX-1 promoter** | 5'-ACTCAGGGCCAGGGATGAGA-3' |
Table S4. QC metrics for the RNA-seq data.

| Sample | raw_reads | raw_bases | clean_reads | clean_bases | valid_bases | Q30  | GC   | Total mapped reads | Uniquely mapped |
|--------|-----------|-----------|-------------|-------------|-------------|------|------|-------------------|-----------------|
| ApoE1  | 57.57M    | 8.64G     | 56.77M      | 8.06G       | 93.3%       | 95.54| 50.42| 56008857(98.65%)  | 50792134(89.46%)|
| ApoE2  | 55.88M    | 8.38G     | 55.12M      | 7.84G       | 93.59%      | 95.59| 50.9%| 54379283(98.65%)  | 50108049(90.90%)|
| ApoE3  | 54.41M    | 8.16G     | 52.80M      | 7.35G       | 90.04%      | 91.14| 50.82| 51996454(98.47%)  | 46979689(88.97%)|
| KO1    | 53.01M    | 7.95G     | 52.20M      | 7.47G       | 93.9%       | 95.28| 50.13| 51471056(98.61%)  | 47573941(91.15%)|
| KO2    | 54.09M    | 8.11G     | 53.34M      | 7.61G       | 93.81%      | 95.58| 50.95| 52631363(98.66%)  | 48959442(91.78%)|
| KO3    | 57.08M    | 8.56G     | 56.30M      | 8.08G       | 94.38%      | 95.44| 50.61| 55510843(98.59%)  | 51602334(91.65%)|
| KO4    | 53.11M    | 7.97G     | 52.32M      | 7.45G       | 93.51%      | 95.48| 51.05| 51553451(98.53%)  | 47854627(91.46%)|

raw_reads: Number of original reads  
raw_bases: Number of bases  
clean_reads: Number of clean reads obtained after pretreatment  
clean_bases: Number of bases obtained after pretreatment  
valid_bases: Percentage of effective bases  
Q30: The percentage of bases with a Qphred value more than 30 in raw_bases to the total bases  
GC: The percentage of the total number of G and C in clean bases to the total number of bases  
Total mapped reads: Number of sequences that can be mapped to the genome  
Uniquely mapped: Number of sequences with unique alignment positions on the reference sequence
### Table S5. Blood pressure and heart rate in Ang II-infused mice.

| Groups               | sBP (mmHg) | dBP (mmHg) | HR (Beats/min) |
|----------------------|------------|------------|----------------|
| ApoE<sup>−/−</sup>   | 105.1 ± 1.6| 57.9 ± 3.3 | 457.1 ± 15.6   |
| ApoE<sup>−/−</sup> + Ang II | 141.3 ± 3.3* | 91.3 ± 3.6* | 440.8 ± 16.6   |
| ApoE<sup>−/−</sup>Nur77<sup>−/−</sup> | 106.5 ± 1.6 | 63.0 ± 2.9 | 449.5 ± 23.5   |
| ApoE<sup>−/−</sup>Nur77<sup>−/−</sup> + Ang II | 145.7 ± 4.1# | 91.2 ± 2.5# | 463.1 ± 21.5   |

N is 4-5 in each group. Data are expressed by mean ± SD.

*P<0.05 compared to control ApoE<sup>−/−</sup> mice

#P<0.05 compared to ApoE<sup>−/−</sup>+Ang II mice
Table S6. Blood pressure and heart rate in Celastrol-treated mice.

| Groups       | sBP (mmHg) | dBP (mmHg) | HR (Beats/min) |
|--------------|------------|------------|----------------|
| Sham + Veh   | 104.3±3.6  | 53.7±4.9   | 446.1±18.9     |
| Sham + Cel   | 104.8±2.7  | 60.3±7.1   | 441.8±29.5     |
| AAA + Veh    | 147.3±5.8* | 92.1±3.4*  | 463.9±29.8     |
| AAA + Cel    | 146.7±3.2# | 92.3±1.9#  | 438.1±24.0     |

N is 4-5 in each group. Data are expressed by mean ± SD.

*P<0.05 compared to control Sham+ Veh mice

#P<0.05 compared to control AAA+ Veh mice
**Figure S1. Physiological condition of different groups.**

**A and B,** The relative mRNA and protein levels of Nur77 in WT and Nur77⁻/⁻ group (n=3 mice per group). **C,** SBP, DBP, and Heart rate in the indicated groups (n=5 mice per group). **D,** The external diameter of abdominal aortas measured with vernier calipers in the indicated groups (n=5 mice per group). **E,** The internal diameter of abdominal aortas measured with ultrasonography (n=5 mice per group). **F,** Representative images of suprarenal aortic sections stained with hematoxylin and eosin (H&E), Masson Trichrome (collagen) and Van Gieson (elastin). Data are presented as mean± SEM. Student's two-tailed t test for A, B; one way-ANOVA followed by Tukey's multiple comparisons test for C, D. ns, nonsignificant; WT, wild type; SBP, systolic blood pressure; DBP, diastolic blood pressure.
Figure S2. Representative immunofluorescence and immunohistochemical images.

A, Representative images of dual immunofluorescence staining of Nur77 (red) and CD68 (green) in the abdominal aorta tissue from mice with AAA and sham control. B, Representative immunohistochemical staining images showing macrophages (F4/80) and MMP-9 in mouse abdominal aortas. AAA, abdominal aortic aneurysm; MMP, matrix metalloproteinase.
Figure S3. Full blots of the Western data
Figure S4. Principal component analysis of the RNA-seq data

ApoE:ApoE\(^{-/-}\) mice; DKO: ApoE\(^{-/-}\)Nur77\(^{-/-}\) mice
Figure S5. Characteristics of abdominal aortic aneurysm in ApoE<sup>−/−</sup> Nur77<sup>+/−</sup> mice.

ApoE<sup>−/−</sup> and ApoE<sup>−/−</sup>-Nur77<sup>+/−</sup> mice were subjected to AAA surgery. A, Representative photographs showing mouse aortas infused with saline or Ang II at 4 Weeks. Scale bar indicates 5mm. B, The incidence of AAA of the Ang II-infused mice compared with their sham controls. n=10 in each group of ApoE<sup>−/−</sup>, ApoE<sup>−/−</sup>-Nur77<sup>+/−</sup> mice infused with saline, n=15 each for ApoE<sup>−/−</sup>, ApoE<sup>−/−</sup>-Nur77<sup>+/−</sup> mice infused with Ang II. C, Maximal abdominal aortic diameter, total aortic weight-to-BW ratio of the indicated groups (n=7). D, Representative views of the internal diameter of the abdominal aorta measured with ultrasonography and the quantification of the maximal abdominal aortic diameter (n=5). Data are presented as mean± SEM. Fisher's exact test for B. Two-way ANOVA followed by Tukey's multiple comparisons test for C and D. ns, nonsignificant; AAA, abdominal aortic aneurysm; BW, body weight.
**Figure S6. Celastrol attenuated the macrophages infiltration and MMP-9 expression.**

**A,** Representative immunohistochemical staining images showing macrophages (F4/80) and MMP-9 in mouse abdominal aortas, with the quantification results in the right panels (n=3 mice per group). **B,** The q-PCR analysis of inflammatory cytokines (IL-1β, TNF-α, CCL2, and IL-6) in the aortic wall. Results were normalized against GAPDH and converted to fold induction relative to their respective controls (n=3 mice per group). **C,** Gene expression of MMP9 in AAA lesioned tissues. Results were normalized against GAPDH and converted to fold induction relative to their respective controls (n=3 mice per group). **D,** Western blot analysis and quantitative results of MMP9. Results were normalized against tubulin and converted to fold induction relative to their respective controls (n=4 mice per group). **E,** In situ zymography for gelatinase activity (n=3 per group). *P<0.05 vs Sham-vehicle mice, **P<0.01 vs Sham-vehicle mice.
vehicle mice; #P<0.05 vs AAA-vehicle mice, ##P<0.01 vs AAA-vehicle mice. Data are presented as mean± SEM. Two-way ANOVA followed by Tukey's multiple comparisons test for A-D. Student's two-tailed t test for E. ns, nonsignificant; Veh, vehicle; Cel, celastrol; IL-1β, Interleukin-1β; TNFα, tumor necrosis factor-α; CCL2, chemokine (C-C motif) ligand 2; IL-6, Interleukin-6; MMP, matrix metalloproteinase.
Figure S7. The expression level of Nur77.

A and B, The expression of Nur77 in Raw264.7 cells transduced with LentiGFP or LentiNur77 to overexpress Nur77. The mRNA level (A) or the protein level (B) of Nur77 (n=3 independent experiments per group). C and D, The expression of Nur77 in bone marrow-derived macrophages (BMDMs) from WT or Nur77⁻/⁻ mice. The mRNA level (C) or the protein level (D) of Nur77 (n=3 independent experiments per group). Data are presented as mean± SEM. Student's two-tailed t test for A-D. Lenti, lentiviral; GFP, green fluorescent protein; WT, wild type.
**Figure S8. The expression level of LOX-1.**

**A and B,** The expression of LOX-1 in Raw264.7 cells transduced with LOX-1 overexpression plasmid (oe-LOX-1) to overexpress LOX-1. The mRNA level (A) or the protein level (B) of LOX-1 (n=3 independent experiments per group). **C and D,** The expression of LOX-1 in BMDMs transfected with control siRNA(si-NC) or LOX-1 siRNA(si-LOX-1). The mRNA level (C) or the protein level (D) of Nur77 (n=3 independent experiments per group). Data are presented as mean±SEM. Student’s two-tailed t test for A-D. BMDM, bone marrow-derived macrophage; LOX-1, lectin like Ox-LDL receptor-1; oe, overexpression; si, small interfering RNA.
Figure S9. Expression of Nur77 in vascular smooth muscle cells in AAA.

A, Representative images of dual immunofluorescence staining of Nur77 (red) and α-SMA (green) in the abdominal aorta tissue from mice with AAA and sham control (n=3 per group). Scale bar indicates 200μm. B, Quantification of the relative Nur77 fluorescence intensity in aortas from mice with AAA and sham control. C, The relative mRNA level of Nur77 in Movas cells after stimulated with Ang II (1μM) for the indicated time (n=3 per group, *P<0.05 vs PBS, **P<0.01 vs PBS). D, Representative images of dual immunofluorescence staining of Nur77 (red) and α-SMA (green) in Movas cells, and quantification of the relative Nur77 fluorescence intensity. Scale bar indicates 200μm. Data are presented as mean± SEM. Student's two-tailed t test for B and D. One way-ANOVA followed by Dunnett’s T3 multiple comparisons test for C. AAA, abdominal aortic aneurysm; Ang II, angiotensin II; α-SMA, alpha smooth muscle actin.