Supplemental Materials

A novel mechanism underlying inflammatory smooth muscle phenotype in abdominal aortic aneurysm

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Materials and Methods

Cytokines and reagents

Angiotensin II was purchased from Bachem Americas, Inc (Torrance, CA). The following antibodies were used in Western blotting and immunofluorescent staining: ADAR1 (D-8), HuR (6A97) and VCAM-1 (E-10) antibodies were obtained from Santa Cruz Biotechnology. MMP2 (ab97779) and smooth muscle myosin heavy chain 11 (ab82541) antibodies were purchased from Abcam. IL-1β (3A6), smooth muscle α-actin (ACTA2, D4K9N), and calponin 1 (D8L2T) antibodies were from Cell Signaling Technology. α-Tubulin (T5168) antibody was purchased from Sigma. Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) and MMP9 (10375-2-AP) antibodies were from Proteintech. Nuclei were stained with 4, 6-diamidino-2-phenylindole (DAPI, Vector Laboratories, Inc.). IRDye® 680RD goat anti-rabbit and goat anti-Mouse secondary antibodies were from LI-COR Biosciences. Recombinant Human IL-1 beta (201-LB-010) was from R&D Systems, Inc. ADAR1 editing inhibitor 8-azaadenosine (8-aza, 6868/10) was obtained from Bio-Techne Corporation. 8-aza dissolved in water was added to the cell culture medium at a final concentration of 25 nM.

Animals

Male ADAR1 heterozygous knockout mice (ADAR+/-, B6.129(Cg)-Adartm1.1Phs/ KnkMmjax), ADAR1fl/fl mice (B6.129-Adartm1Knk/Mmjax), and ApoE-/- mice (B6;129-Apobtm2Sgy Apoetm1Unc/J) were purchased from the Jackson Laboratory (Bar Harbor, ME). Myh11-CreERT2;ApoE-/- mice were obtained from Dr. Gary K. Owens [22]. We used only male mice in this study by following the ATVB Council's recommendation that identifying mechanisms of reduced AAA formation focus on males because ADAR1 deficiency reduces AAA formation [31]. All mice are in C57BL6 genetic background. Animals were housed under conventional conditions in the animal care facilities and received humane care in compliance with the Principles of Laboratory Animal Care formulated by the National Society for Medical Research and the Guide for the Care and Use of Laboratory Animals. All animal procedures were approved by the Institutional Animal Care and Use Committee of the University of Missouri. Animals were randomly grouped, and all operators were blinded to the grouping. The number of animals (sample size) was determined by power calculation based on the prior experience.

Ang II-induced murine model of AAA

Eight-week-old ApoE-/- or ADAR1+/-;ApoE-/- mice were infused with phosphate buffered saline (PBS) or Ang II (1000 ng/kg/min) via osmotic minipumps (AP-2004, Alzet, CA, USA) for 28 days, as described previously [32]. Briefly, mice were anesthetized with inhaled isoflurane (5% for induction and 2% for maintenance) and the minipumps were surgically implanted into the subcutaneous space of the mice in the back of the neck. 28 days later, mice were anesthetized using 2.0% isoflurane, and hair was removed from the abdomen by using depilatory cream (Nair; Church & Dwight Co, Inc; Princeton, NJ). Mice were then laid supine on a heated table, and warmed ultrasound transmission gel was placed on the abdomen. Aortic diameters were measured using a doppler ultrasound Vevo 1100 Imaging System (VisualSonics) with a real-time microvisualization scan head in B mode. The B-Mode is a two-dimensional ultrasound image display composed of bright dots representing the ultrasound echoes. The brightness of each dot was determined by the amplitude of the returned echo signal. The abdominal aortas were then harvested for RNA, protein, and morphological or histological analyses. AAA incidence was defined by an increase of external aorta diameter by 50% or greater as compared to aortas from saline-infused mice. For ADAR1f/+;Myh11 Cre-ERT2;ApoE-/- and Myh11 Cre-ERT2; ApoE-/- male mice, prior to saline or Ang II infusion, the mice were pre-treated with tamoxifen (1 mg/day, i.p.) for 5 days to induce Cre activity and generate ADAR1-SMC heterozygous knockout in the ApoE-/- background.

Heterotopic allograft aortic transplantation

Aortic transplantation procedures were performed as described previously with some modifications [21, 33]. Donor or recipient mice were anesthetized with inhaled isoflurane (5% for induction and 2% for maintenance). Carprofen was used for analgesia prior to the surgery and during the 72 hours post-operation. For donor mice, abdominal aorta from just below the left renal vein to the iliac bifurcation was identified, ligated, transected between the proximal and distal ligation, and stored in sterile saline containing heparin (100 U/mL) at 4 ^{o}C until transplantation. Recipient mice were anesthetized with inhaled isoflurane, laparotomy was performed, and the retro-peritoneum exposed. The infrarenal aorta was dissected between the left renal artery and the iliac bifurcation. The aortic branches were exposed and ligated with 9-0 sutures, and the donor aorta was end-to-side anastomosed to the recipient aorta with interrupted 11-0 suture. After the distal anastomosis was completed, the distal ligature was removed, followed by removal of the proximal ligature. Fluid (1 ml of warm saline) was administered to assure adequate volume resuscitation, and the laparotomy was closed with 4-0 Vicryl sutures. The skin incision was sealed with Vetbond tissue adhesive. One ml of warm saline was injected subcutaneously to maintain fluid homeostasis. After the surgery, the mice were kept on a Far Infrared Warming Pad (Kent Scientific) until fully recovered from anesthesia and monitored every two hours for the first day and then once daily. Two weeks after the operation, mice were infused with Ang II (1000 ng/kg/min) via osmotic minipumps (Alzet osmotic pump Model 2004, Durect Corporation) for 28 days. Animals were then anesthetized, and abdominal aorta ultrasound images were taken to measure the maximal aortic diameters followed by perfusion with PBS. The abdominal aortas were harvested for RNA, protein, morphological or histological analyses.

Human AAA specimens

Human healthy abdominal aorta and AAA specimens were obtained from Mizzou OneHealth Biorepository and surgical operations of patients with abdominal aortic aneurysms in the Department of Surgery, School of Medicine, University of Missouri. All participants gave written informed consent before the specimens were collected. The patient information was de-identified and is included in Online Table I. All specimens were collected under a protocol approved by the Institutional Review Board of University of Missouri (IRB # 2026026). The aortic specimens were fixed overnight in formalin, embedded in paraffin, sectioned, and subsequently used for immunostaining. Aorta proteins were extracted from formalin-fixed tissues by following the published protocol [34, 35].

Histopathology and immunofluorescent staining

Abdominal aortic tissues were fixed in 4% paraformaldehyde (PFA) and embedded in paraffin. Tissue sections (5 µm thick) were processed for hematoxylin-eosin (H&E) or Verhoeff's elastic staining (EVG) using commercial kits (DAKO) according to the manufacturer’s protocol. Elastin degradation index was calculated based on the published elastin degradation grading keys [17]. For immunofluorescent staining, serial sections (10 µm) of OCT-embedded frozen tissues or primary cultured cells were fixed in cold acetone. After blocking with 1% goat serum, sections were incubated with primary antibodies at room temperature for 2 hours and then with fluorescent dye-conjugated secondary antibodies for 1 hour. Images were acquired with a fluorescence microscope (Keyence Corporation of Americ.).

Western blotting

Abdominal aorta or SMCs were lysed in RIPA lysis buffer (1% Nonidet P-40, 0.1% sodium dodecyl sulfate (SDS), 0.5% sodium deoxycholate, 1 mM sodium orthovanadate, and protease inhibitors) to extract total proteins. Samples were separated on SDS-polyacrylamide gels and electro-transferred onto nitrocellulose membranes (Amersham Biosciences). After blocking with 5% BSA, the membranes were incubated with a primary antibody at 4 °C overnight. The membranes were then incubated with IRDye secondary antibodies

(LI-COR Biosciences) at room temperature for 1 hour. The protein expression was detected and quantified by Odyssey CLx Imaging System (LI-COR Biosciences).

Construction of adenoviral vector

Adenovirus expressing ADAR1 shRNA (Ad-shADAR1) was generated and purified as described previously [15]. cDNA fragment encoding the full length of human ADAR1 was amplified from ADAR1 plasmid (DNASU, HsCD00076320) by PCR, and then inserted into the pShuttle-IRES-hrGPF-1 vector (Agilent) through XhoI site. ADAR1 cDNA in the vector was verified by sequencing. Green fluorescent protein (GFP)-expressing adenovirus (Ad-GFP) was used as a control.

Cell culture and transient transfection

Mouse SMCs were cultured by enzymatic digestion method from mouse abdominal aorta as described [36,37]. Briefly, 2-month-old male mouse was euthanized with CO_2 and then perfused with 10 ml PBS from the apex of the left ventricle. Abdominal aorta was then identified and collected. The adventitial layer of the aorta was removed by straining the aorta oppositely with straight and angled forceps. The remaining aorta was cut into 3 pieces and incubated in 1 ml digestion cocktail (collagenase type I 675U/ml, Collagenase type XI 18.75U/ml and Hyaluronidase type I-s 90U/ml) at 37 °C for 30-40 min with rotation until no visible pieces were present. 0.5 mL DMEM containing 10% fetal bovine serum (FBS, Hyclone) was then added to stop the enzymatic reaction. The digested aorta was passed through a 70-μm strainer and washed with 5 ml of DMEM (10% FBS). Endothelial cells were then removed by incubating with CD31 magnetic beads following the manufacture's instruction (Invitrogen, 11155D). The media SMC was plated onto a 60mm dish and cultured with DMEM containing 20% FBS and 5% L-glutamine (Corning) at 37°C in a humidified atmosphere with 5% CO_2. One hour later, the medium with SMCs was moved to a new 60mm dish to discard fibroblasts attached to the original dish. After 5 days of incubation, the primary SMCs were passaged, and the phenotype of the cells was confirmed by examining ACTA2 and SM22α expression. Control vector or HuR expression plasmid (OHu23723, GenScript) was transiently transfected into SMC using JetPrime® transfection reagent following the manufacturer's instruction.

Reverse transcription PCR (RT-PCR) and mRNA stability assay

SMC were lysed in 1 ml of Trizol Reagent, and RNA was extracted. Following DNase I treatment to remove potential genomic DNA contamination, reverse transcription was performed using the iScript™ cDNA Synthesis Kit (Biorad, 17088941). Semi-quantitative PCR was performed to detect the pre- and mature MMP2 and MMP9 mRNA levels. The primers used in this study are listed in Major Resource Table. For MMP2 and MMP9 mRNA stability assay, SMC were treated with 10 μg/ml Actinomycin D (Sigma-Aldrich, A9415) to inhibit gene transcription. The cells were collected at 0, 0.5, 1, 2, 4, 6 hours following the treatment for RNA extraction. MMP2 and MMP9 mRNA levels were detected by semi-quantitative PCR.

Gelatin zymography

Gelatin zymography was carried out following the published protocol [38]. Control or AAA tissues were lysed in RIPA buffer and mixed with non-reducing sample buffer (Thermo Scientific™, 84788). 10% acrylamide gel containing gelatin (Invitrogen™, ZY00100BOX) was used to run the samples. Gels were then stained with Coomassie brilliant blue and washed with de-staining solution containing 45% methanol and 10% acetic acid. Regions of protease activity appeared as clear bands against a dark background where the proteases have digested the substrate.

In situ zymography

In situ zymography was performed using EnzChek® gelatinase/collagenase assay kit (Thermo Fisher Scientific Inc.) according to manufacturer's instruction. Briefly, 14 days after Ang II infusion, animals were anesthetized, and abdominal aorta were collected and mounted in O.C.T. mounting medium. cryosections (10 um) were cut and rinsed once with reaction buffer (50 mM Tris-HCl, 150 mM NaCl, 5 mM CaCl2, and 0.2 mM sodium azide, pH 7.7), and then incubated in a humidified chamber at RT for 30 min in reaction buffer containing 1 mg/ml DQ-gelatin with or without 1 mM 1,10-phenanthroline (Sigma) as negative controls. Then the sections were rinsed three times with PBS followed by mounting with Prolong Gold Antifade reagent containing DAPI. Stained tissue sections were imaged using a Nikon fluorescent microscope.

Co-immunoprecipitation (Co-IP)

The protein A/G-agarose beads (Santa Cruz, CA) were incubated with IgG or ADAR1 antibody at 4°C for 2 hours. SMCs were lysed in 500 µl Co-IP lysis buffer (Pierce) on ice for 5 min, and the supernatants were incubated with antibody-conjugated beads at 4°C overnight. After washing with the Co-IP buffer, proteins were eluted from the beads and boiled in SDS loading buffer. Western blotting was performed to detect the precipitation of proteins.

RNA immunoprecipitation (RIP)

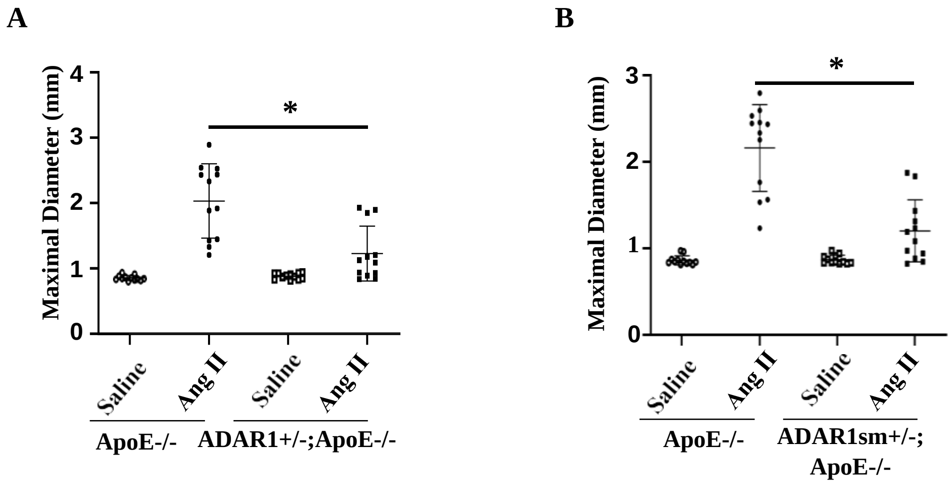
RNA immunoprecipitation experiments were performed with mouse aorta tissues. Tissue lysates were cross-linked by 1% formaldehyde, lysed by sonication, incubated with HuR antibody at 4°C overnight. Protein A/G magnetic beads (Thermo Scientific, Cat: 88802) were then added and incubated for 1 h at 4°C with gentle rotation to pull down HuR-interacting molecules. Following DNase I treatment to remove potential genomic DNA contamination, RNAs were isolated and reversely transcribed using the iScript™ cDNA Synthesis Kit (Biorad, 17088941). Semi-quantitative PCR was performed to detect the pre- and mature MMP2 and MMP9 mRNA levels using specific primers (Major Resource Table).

Proximity Ligation Assay (PLA)

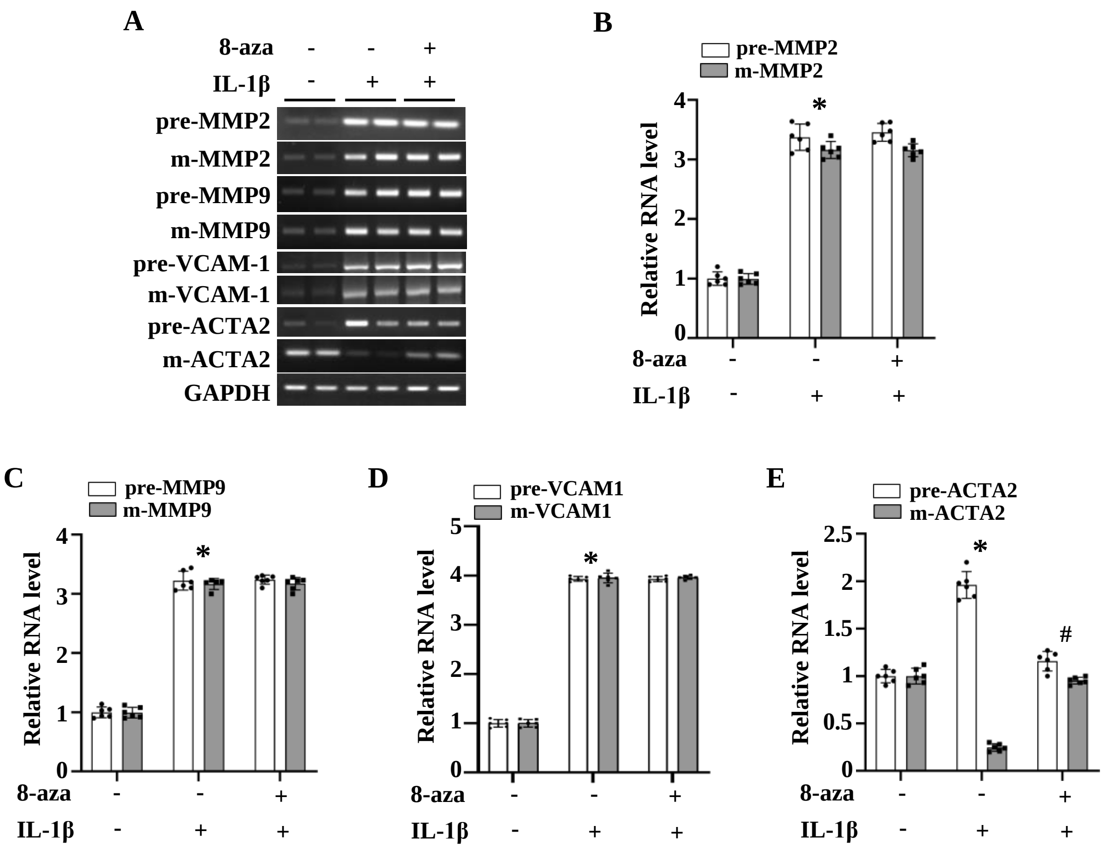
PLA was performed by using reagents provided in the Duo-link PLA kit (Sigma-Aldrich) according to the manufacturer instructions with minor modifications. Briefly, human and mouse control aorta or AAA sections (5 um) were deparaffinized, re-hydrated, permeabilized with Triton 0.3% (in PBS), and then incubated with blocking solution for 45 min followed by incubation with mouse anti-HuR (Santa Cruz) and rabbit anti-ADAR1 (Cell Signaling) at 4 °C overnight. After washing with Buffer A for three times, the sections were incubated with secondary antibodies conjugated with PLA DNA probes at 37 °C for 1 h. Following 4 ×10 min washing and a rinse at 37 °C with Buffer A, sections were incubated with ligation buffer containing oligonucleotides that can hybridize to the PLA probe to form a rolling circle DNA strandby DNA ligase, which was incubated at 37 °C for 30 min. Subsequently, the sections were washed with Buffer A at 37 °C and incubated with the amplification-detection solution containing DNA polymerase for rolling circle amplification at 37 °C for 100 min. Then, the sections were washed with Buffer B for four times followed by four times of washing with 0.01× Buffer B. Finally, the sections were mounted with mounting buffer containing DAPI under coverslips and observed with a fluorescence microscope (Keyence Corporation of America). The PLA spots were counted with ImageJ, and the mean spot number/cell was calculated for each sample. Rabbit and mouse IgG antibody were used as negative controls.

Statistical analysis

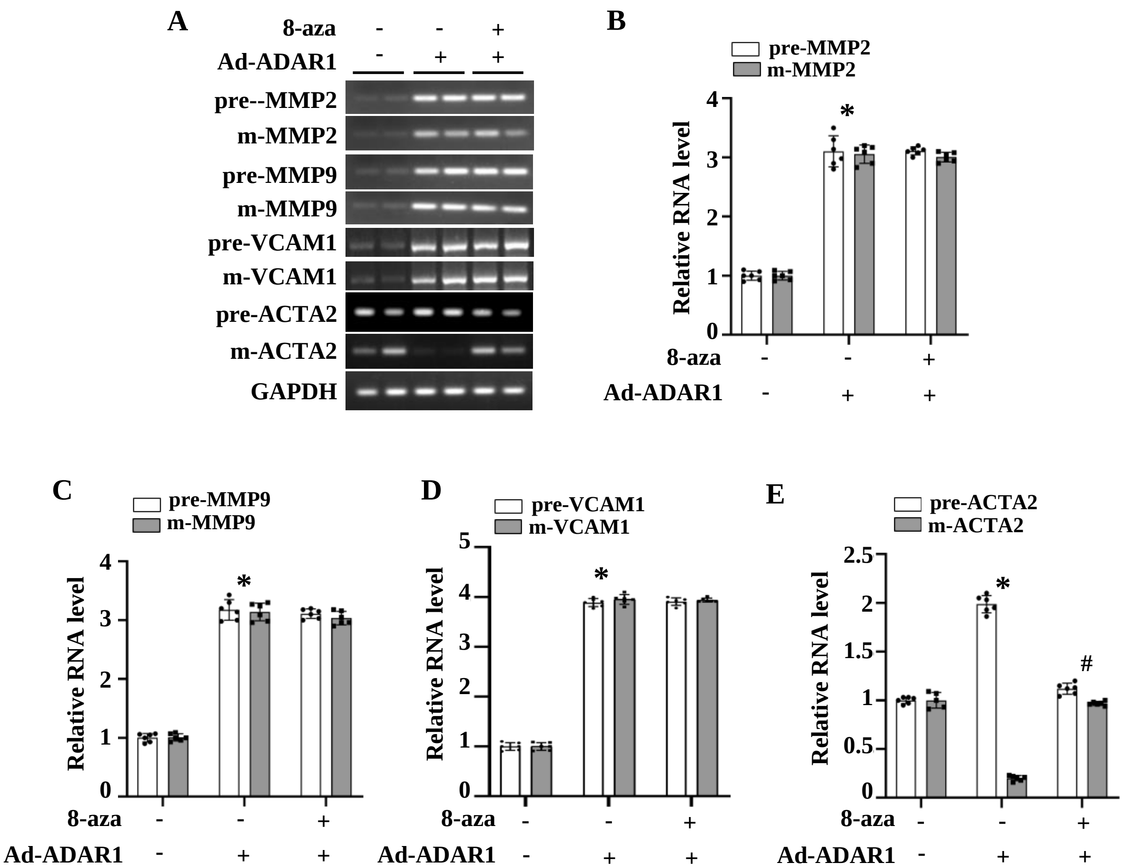
All experiments were repeated at least for three times. All data represent independent data points but not technical replicates. Data are presented as the mean ± SD. Normality of data was assessed by the D'Agostino & Pearson normality test with alpha=0.05 (Online Table II). For comparisons of two groups, student's unpaired two-tailed t test was used for normally distributed data, and Mann-Whitney two tailed test was used for non-normally distributed data or for groups with n less than 7. For more than 2 groups, 1-way ANOVA with Tukey post-test analysis was used for normally distributed data and Kruskal-Wallis test with Dunn's multiple comparisons test was used for non-normally distributed data. Fisher's exact test was used for test of proportions for Figures 1B, 1F and 4G. All p-values and corresponding statistical test was provided (Online Table III). Prism 9.0 (GraphPad Software, CA) or RStudio (Desktop 1.4.1717) was used for statistical analyses, and differences considered statistically significant when nominal $P<0.05$ or adjusted $P<0.05$ in case of multiple testing. However, the correcting for multiple testing across the entire body of the studies was not performed because both *in vitro* and *in vivo* experiments were performed, and various approaches were used in this study.



Online Figure I: Ex vivo maximal diameters of AAA lesions. A. ApoE-/- and ADAR1+/-;ApoE-/- mice were infused with saline or Ang II (1000 ng/kg/min) for 28 days. Aorta maximal external diameters were measured ex vivo. *P = 5.03E-03, n=12. **B.** ApoE-/- and ADAR1sm+/-;ApoE-/- mice were infused with saline or Ang II (1000ng/kg/min)for 28 days. Aorta maximal external diameters were measured ex vivo. *P = 6.11E-03, n=12. One-way ANOVA with Tukey's multiple comparison test was performed to determine statistical difference for both A and B.



Online Figure II: RNA editing inhibitor altered ACTA2, but not MMP2, MMP9, or VCAM-1 pre-mRNA splicing. Mouse aortic SMCs treated with vehicle (-) or 10 ng/ml of IL-1β for 24 h with or without 25 nM (8-aza). Semi-quantitative RT-PCR was performed to detect mature (m-) and precursor (pre-) mRNA levels of MMP2, MMP9,VCAM1, and ACTA2 genes (A). Their pre- and m-mRNA levels were quantified by normalizing to GAPDH, respectively (B-E). *P = 8.96E-04 for pre-MMP2 and 3.49E-03 for m-MMP2 (B), 1.90E-03 for pre-MMP9 and 3.49E-03 for m-MMP9 (C), 3.23E-03 for pre-VCAM1 and 1.23E-02 for m-VCAM1 (D), 3.36E-03 for pre-MMP2 and 1.20E-04 for m-MMP2 (E) vs. vehicle-treated cells, respectively (n=6). #P = 2.04E-02 for pre-ACTA2 and 3.40E-03 for m-ACTA2 vs. 8-aza-untreated cells (-) with IL-1β treatment, n=6. Kruskal-Wallis test with Dunn's multiple comparisons test were performed to determine statistical difference for Panels B-E.



Online Figure III: RNA editing inhibitor attenuated ADAR1-mediated pre-mRNA accumulation of ACTA2, but not MMP2, MMP9, or VCAM-1 genes. Mouse aortic SMCs were transduced with control (-) or ADAR1 adenoviral vector (Ad-ADAR1) and treated with vehicle (-) or 25 nM of 8-azaadenosine for 24 h. Semi-quantitative RT-PCR was performed to detect the mature (m-) and precursor (pre-) mRNA levels of ACTA2, MMP2, MMP9, and VCAM1 genes(A). Their pre- and m-mRNA levels were quantified by normalizing to GAPDH, respectively (B-E). *P = 4.56E-04 for pre-MMP2 and 5.60E-04 for m-MMP2 (B), 3.30E-04 for pre-MMP9 and 4.30E-04 for m-MMP9 (C), 2.71E-04 for pre-VCAM1 and 3.10E-04 for m-VCAM1 (D), 4.03E-03 for pre-MMP2 and 7.50E-03 for m-MMP2 (E) vs. vehicle-treated cells, respectively (n=6). #P = 1.71E-02 for pre-ACTA2 and 4.30E-03 for m-ACTA2 vs. 8-aza-untreated cells (-) with IL-1β treatment, n=6. Kruskal-Wallis test with Dunn’s multiple comparisons test were performed to determine statistical difference for panels B-E.

Online Table I: Healthy individual and aneurysm patients' information.

AAA or Control	Gender	Race	DIAGNOSIS/PROCEDURE
Control	M	White	Healthy abdominal aorta near aorta-aneurysmal wall.
Control	M	n/a	Healthy abdominal aorta near aorta-aneurysmal wall
Control	M	White	Healthy abdominal aorta near aorta-aneurysmal wall
Control	M	White	Healthy abdominal aorta near aorta-aneurysmal wall
Control	M	Asian	Healthy abdominal aorta of an individual died from road traffic crash
Control	M	Asian	Healthy abdominal aorta of an individual died from road traffic crash
Control	M	Asian	Healthy abdominal aorta of an individual died from road traffic crash
Control	F	Asian	Healthy abdominal aorta of an individual died from road traffic crash
AAA	M	White	Aorta-aneurysmal wall, changes compatible with dissecting aneurysm; myxoid change; sclerosis; calcification
AAA	M	White	Aortic aneurysm wall; resection; vascular aneurysm with atherosclerosis and calcification
AAA	M	White	Aorta aneurysm repair; atherosclerosis; unorganized thrombus
AAA	F	White	Abdominal aorta-aneurysm repair. changes with aneurysm wall atherosclerosis
AAA	M	n/a	Dissecting aneurysm repair: consistent with aortic dissection
AAA	M	White	Abdominal aorta; plaque; aneurysm repair; atherosclerotic plaque
AAA	M	n/a	Abdominal aortic aneurysm; complicated atherosclerosis
AAA	M	White	Abdominal aortic aneurysm; sclerosis with focal calcification and organizing thrombus

Online Table II: Sample size and normality tests for data presented in all Figures.

Figure	Sample Group	Sample Size	D'Agostino & Pearson normality test P value	Passed normality test
Figure 1D	Saline ADAR1 110 kd	9	0.53	Yes
	Ang II ADAR1 110 kd	9	0.17	
	Saline ADAR1 150 kd	9	0.52	
	Ang II ADAR1 150 kd	9	0.28	
Figure 1H	Normal Aorta ADAR1 110 kd	9	0.46	Yes
	Human AAA ADAR1 110 kd	9	0.12	
	Normal Aorta ADAR1 150 kd	9	0.33	
	Human AAA ADAR1 150 kd	9	0.07	
Figure 2D	ApoE-/- Saline	9	12	Yes
	ApoE-/- Ang II	9	14	
	ADAR1+/- ApoE-/- Saline	9	12	
	ADAR1+/- ApoE-/- Ang II	9	12	
Figure 2F	ApoE-/- Saline	8	N/A (discontinuous measurement)	No
	ApoE-/- Ang II	8		
	ADAR1+/- ApoE-/- Saline	8		
	ADAR1+/- ApoE-/- Ang II	8		
Figure 3B	ApoE-/- Saline Pre-MMP2	6	N too small	No
	ApoE-/- Saline Cleaved-MMP2	6		
	ADAR1+/- ApoE-/- Saline Pre-MMP2	6		
	ADAR1+/- ApoE-/- Saline Cleaved-MMP2	6		
	ApoE-/- Ang II Pre-MMP2	6		
	ApoE-/- Ang II Cleaved-MMP2	6		
	ADAR1+/- ApoE-/- Ang II Pre-MMP2	6		
	ADAR1+/- ApoE-/- Ang II Cleaved-MMP2	6		
Figure 3C	ApoE-/- Saline Pre-MMP9	6	N too small	No
	ApoE-/- Saline Cleaved-MMP9	6		
	ADAR1+/- ApoE-/- Saline Pre-MMP9	6		
	ADAR1+/- ApoE-/- Saline Cleaved-MMP9	6		
	ApoE-/- Ang II Pre-MMP9	6		
	ApoE-/- Ang II Cleaved-MMP9	6		
	ADAR1+/- ApoE-/- Ang II Pre-MMP9	6		
	ADAR1+/- ApoE-/- Ang II Cleaved-MMP9	6		
Figure 3D	ApoE-/- Saline VCAM-1	6	N too small	No
	ADAR1+/- ApoE-/- Saline VCAM-1	6		
	ApoE-/- Ang II VCAM-1	6		
	ADAR1+/- ApoE-/- Ang II VCAM-1	6		
Figure 3E	ApoE-/- Saline ACTA2	6	N too small	No
	ApoE-/- Saline Calponin	6		
	ADAR1+/- ApoE-/- Saline ACTA2	6		
	ADAR1+/- ApoE-/- Saline Calponin	6		
	ApoE-/- Ang II ACTA2	6		
	ApoE-/- Ang II Calponin	6		
	ADAR1+/- ApoE-/- Ang II ACTA2	6		
	ADAR1+/- ApoE-/- Ang II Calponin	6		
Figure 3G	ApoE-/- Saline	6	N too small	No
	ApoE-/- Ang II	6		
	ADAR1+/- ApoE-/- Ang II	6		
Figure 3I	ApoE-/- Saline	6	N too small	No
	ApoE-/- Ang II	6		
	ADAR1+/- ApoE-/- Ang II	6		

Figure 3J	ApoE-/- Saline ApoE-/- Ang II ADAR1+/- ApoE-/- Ang II	6 6 6	N too small	No
Figure 4C	Donor: ApoE-/- Donor: ADAR1+/- ApoE-/-	6	N too small	No
Figure 4F	Donor: ApoE-/- Donor: ADAR1+/- ApoE-/-	6 6	N/A (discontinuous measurement)	No
Figure 5D	ApoE-/- Saline ApoE-/- Ang II ADAR1sm+/- ApoE-/- Saline ADAR1sm+/- ApoE-/- Ang II	12 12 12 12	0.87 0.22 0.74 0.18	Yes
Figure 5F	ApoE-/- Saline ApoE-/- Ang II ADAR1sm+/- ApoE-/- Saline ADAR1sm+/- ApoE-/- Ang II	6 6 6 6	N/A (discontinuous measurement)	No
Figure 6B	IL-1β- + shADAR1- ADAR1 110kD IL-1β- + shADAR1- ADAR1 150kD IL-1β- + shADAR1+ ADAR1 110kD IL-1β- + shADAR1+ ADAR1 150kD IL-1β+ + shADAR1- ADAR1 110kD IL-1β+ + shADAR1- ADAR1 150kD IL-1β+ + shADAR1+ ADAR1 110kD IL-1β+ + shADAR1+ ADAR1 150kD	6 6 6 6 6 6 6 6	N too small	No
Figure 6C	IL-1β- + shADAR1- ADAR1 IL-1β- + shADAR1+ ADAR1 IL-1β+ + shADAR1- ADAR1 IL-1β+ + shADAR1+ ADAR1	6 6 6 6	N too small	No
Figure 6D	IL-1β- + shADAR1- ADAR1 Pre-MMP2 IL-1β- + shADAR1- ADAR1 Cleaved-MMP2 IL-1β- + shADAR1+ ADAR1 Pre-MMP2 IL-1β- + shADAR1+ ADAR1 Cleaved-MMP2 IL-1β+ + shADAR1- ADAR1 Pre-MMP2 IL-1β+ + shADAR1- ADAR1 Cleaved-MMP2 IL-1β+ + shADAR1+ ADAR1 Pre-MMP2 IL-1β+ + shADAR1+ ADAR1 Cleaved-MMP2	6 6 6 6 6 6 6 6	N too small	No
Figure 6E	IL-1β- + shADAR1- ADAR1 Pre-MMP9 IL-1β- + shADAR1- ADAR1 Cleaved-MMP9 IL-1β- + shADAR1+ ADAR1 Pre-MMP9 IL-1β- + shADAR1+ ADAR1 Cleaved-MMP9 IL-1β+ + shADAR1- ADAR1 Pre-MMP9 IL-1β+ + shADAR1- ADAR1 Cleaved-MMP9 IL-1β+ + shADAR1+ ADAR1 Pre-MMP9 IL-1β+ + shADAR1+ ADAR1 Cleaved-MMP9	6 6 6 6 6 6 6 6	N too small	No
Figure 6F	IL-1β-+shADAR1- ADAR1 IL-1β-+shADAR1+ ADAR1 IL-1β+ + shADAR1- ADAR1 IL-1β+ + shADAR1+ ADAR1	6 6 6 6	N too small	No
Figure 6G	IL-1β- + shADAR1- ADAR1 IL-1β- + shADAR1+ ADAR1 IL-1β+ + shADAR1- ADAR1 IL-1β+ + shADAR1+ ADAR1	6 6 6 6	N too small	No
Figure 6H	IL-1β- + shADAR1- ADAR1 IL-1β- + shADAR1+ ADAR1 IL-1β+ + shADAR1- ADAR1 IL-1β+ + shADAR1+ ADAR1	6 6 6 6	N too small	No

Figure 6I	IL-1β- + shADAR1- ADAR1 IL-1β- + shADAR1+ ADAR1 IL-1β+ + shADAR1- ADAR1 IL-1β+ + shADAR1+ ADAR1	6 6 6 6	N too small	No
Figure 6K	IL-1β- + shADAR1- ADAR1 Pre-MMP2 IL-1β- + shADAR1- ADAR1 Cleaved-MMP2 IL-1β- + shADAR1+ ADAR1 Pre-MMP2 IL-1β- + shADAR1+ ADAR1 Cleaved-MMP2 IL-1β+ + shADAR1- ADAR1 Pre-MMP2 IL-1β+ + shADAR1- ADAR1 Cleaved-MMP2 IL-1β+ + shADAR1+ ADAR1 Pre-MMP2 IL-1β+ + shADAR1+ ADAR1 Cleaved-MMP2	6 6 6 6 6 6 6 6	N too small	No
Figure 6L	IL-1β- + shADAR1- ADAR1 Pre-MMP9 IL-1β- + shADAR1- ADAR1 Cleaved-MMP9 IL-1β- + shADAR1+ ADAR1 Pre-MMP9 IL-1β- + shADAR1+ ADAR1 Cleaved-MMP9 IL-1β+ + shADAR1- ADAR1 Pre-MMP9 IL-1β+ + shADAR1- ADAR1 Cleaved-MMP9 IL-1β+ + shADAR1+ ADAR1 Pre-MMP9 IL-1β+ + shADAR1+ ADAR1 Cleaved-MMP9	6 6 6 6 6 6 6 6	N too small	No
Figure 7B	shGFP 0 hour shGFP 0.5 hour shGFP 1 hour shGFP 2 hours shGFP 4 hour shGFP 6 hours shADAR1 0 hour shADAR1 0.5 hour shADAR1 1 hour shADAR1 2 hours shADAR1 4 hour shADAR1 6 hours	6 6 6 6 6 6 6 6 6 6 6 6	N too small	No
Figure 7C	shGFP 0 hour shGFP 0.5 hour shGFP 1 hour shGFP 2 hours shGFP 4 hour shGFP 6 hours shADAR1 0 hour shADAR1 0.5 hour shADAR1 1 hour shADAR1 2 hours shADAR1 4 hour shADAR1 6 hours	6 6 6 6 6 6 6 6 6 6 6 6	N too small	No
Figure 7E	IP: IgG + IL-1β- IP: IgG + IL-1β+ IP: ADAR1 + IL-1β- IP: ADAR1 + IL-1β+	6 6 6 6	N too small	No
Figure 7G	shGFP + Ctrl 0 hour shGFP + Ctrl 2 hour shGFP + Ctrl 4 hour shGFP + Ctrl 6 hour shGFP + HuR 0 hour shGFP + HuR 2 hour shGFP + HuR 4 hour	6 6 6 6 6 6 6	N too small	No

	shGFP + HuR 6 hour shADAR1 + Ctrl 0 hour shADAR1 + Ctrl 2 hour shADAR1 + Ctrl 4 hour shADAR1 + Ctrl 6 hour shADAR1 + HuR 0 hour shADAR1 + HuR 2 hour shADAR1 + HuR 4 hour shADAR1 + HuR 6 hour	6 6 6 6 6 6 6 6 6		
Figure 7H	shGFP + Ctrl 0 hour shGFP + Ctrl 2 hour shGFP + Ctrl 4 hour shGFP + Ctrl 6 hour shGFP + HuR 0 hour shGFP + HuR 2 hour shGFP + HuR 4 hour shGFP + HuR 6 hour shADAR1 + Ctrl 0 hour shADAR1 + Ctrl 2 hour shADAR1 + Ctrl 4 hour shADAR1 + Ctrl 6 hour shADAR1 + HuR 0 hour shADAR1 + HuR 2 hour shADAR1 + HuR 4 hour shADAR1 + HuR 6 hour	6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6	N too small	No
Figure 8B	ApoE-/- Saline ADAR1+/- ApoE-/- Saline ApoE-/- Ang II ADAR1+/- ApoE-/- Ang II	6 6 6 6	N too small	No
Figure 8C	ApoE-/- Saline ADAR1+/- ApoE-/- Saline ApoE-/- Ang II ADAR1+/- ApoE-/- Ang II	6 6 6 6	N too small	No
Online Figure 1A	ApoE-/- Saline ApoE-/- Ang II ADAR1+/- ApoE-/- Saline ADAR1+/- ApoE-/- Ang II	12 12 12 12	0.73 0.09 0.64 0.11	Yes
Online Figure 1B	ApoE-/- Saline ApoE-/- Ang II ADAR1sm+/- ApoE-/- Saline ADAR1sm+/- ApoE-/- Ang II	12 12 12 12	0.30 0.07 0.34 0.09	Yes
Online Figure 2B	8-aza- + IL-1β- pre-MMP2 8-aza- + IL-1β- m-MMP2 8-aza- + IL-1β+ pre-MMP2 8-aza- + IL-1β+ m-MMP2 8-aza+ + IL-1β+ pre-MMP2 8-aza+ + IL-1β+ m-MMP2	6 6 6 6 6 6	N too small	No
Online Figure 2C	8-aza- + IL-1β- pre-MMP9 8-aza- + IL-1β- m-MMP9 8-aza- + IL-1β+ pre-MMP9 8-aza- + IL-1β+ m-MMP9 8-aza+ + IL-1β+ pre-MMP9 8-aza+ + IL-1β+ m-MMP9	6 6 6 6 6 6	N too small	No
Online Figure	8-aza- + IL-1β- pre-VCAM1 8-aza- + IL-1β- m-VCAM1	6 6	N too small	No

2D	8-aza- + IL-1β+ pre-VCAM1 8-aza- + IL-1β+ m-VCAM1 8-aza+ + IL-1β+ pre-VCAM1 8-aza+ + IL-1β+ m-VCAM1	6 6 6 6		
Online Figure 2E	8-aza- + IL-1β- pre-ACTA2 8-aza- + IL-1β- m-ACTA2 8-aza- + IL-1β+ pre-ACTA2 8-aza- + IL-1β+ m-ACTA2 8-aza+ + IL-1β+ pre-ACTA2 8-aza+ + IL-1β+ m-ACTA2	6 6 6 6 6 6	N too small	No
Online Figure 3B	8-aza- + Ad-ADAR1- pre-MMP2 8-aza- + Ad-ADAR1- m-MMP2 8-aza- + Ad-ADAR1+ pre-MMP2 8-aza- + Ad-ADAR1+ m-MMP2 8-aza+ + Ad-ADAR1+ pre-MMP2 8-aza+ + Ad-ADAR1+ m-MMP2	6 6 6 6 6 6	N too small	No
Online Figure 3C	8-aza- + Ad-ADAR1- pre-MMP9 8-aza- + Ad-ADAR1- m-MMP9 8-aza- + Ad-ADAR1+ pre-MMP9 8-aza- + Ad-ADAR1+ m-MMP9 8-aza+ + Ad-ADAR1+ pre-MMP9 8-aza+ + Ad-ADAR1+ m-MMP9	6 6 6 6 6 6	N too small	No
Online Figure 3D	8-aza- + Ad-ADAR1- pre-VCAM1 8-aza- + Ad-ADAR1- m-VCAM1 8-aza- + Ad-ADAR1+ pre-VCAM1 8-aza- + Ad-ADAR1+ m-VCAM1 8-aza+ + Ad-ADAR1+ pre-VCAM1 8-aza+ + Ad-ADAR1+ m-VCAM1	6 6 6 6 6 6	N too small	No
Online Figure 3E	8-aza- + Ad-ADAR1- pre-ACTA2 8-aza- + Ad-ADAR1- m-ACTA2 8-aza- + Ad-ADAR1+ pre-ACTA2 8-aza- + Ad-ADAR1+ m-ACTA2 8-aza+ + Ad-ADAR1+ pre-ACTA2 8-aza+ + Ad-ADAR1+ m-ACTA2	6 6 6 6 6 6	N too small	No

Online Table III: Statistical tests and P values for data presented in all Figures.

Figures	Statistical Test	Sample group	P Value	Statistically significant (P < 0.05)?
Figure 1B	Fisher's exact test (two-tailed)	Saline vs Ang II	4.4e-5	Yes
Figure 1F	Fisher's exact test (two-tailed)	Normal Aorta vs Human AAA	3e-6	Yes
Figure 1D	Unpaired t test (two-tailed)	Saline ADAR1 110 kd vs Ang II ADAR1 110 kd Saline ADAR1 150 kd vs Ang II ADAR1 150 kd	1.9423e-2 1.7e-5	Yes Yes
Figure 1H	Unpaired t test (two-tailed)	Normal Aorta ADAR1 110 kd vs Human AAA ADAR1 110 kd	<1e-6	Yes

		Normal Aorta ADAR1 150 kd vs Human AAA ADAR1 150 kd	<1e-6	Yes
Figure 2D	One-way Anova with Tukey's multiple comparison test	ApoE-/- Saline vs ApoE-/- Ang II	2.28E-02	Yes
		ApoE-/- Saline vs ADAR1+/- ApoE-/- Saline	1.00E+00	No
		ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II	3.71E-01	No
		ApoE-/- Ang II vs ADAR1+/- ApoE-/- Saline	2.68E-02	Yes
		ApoE-/- Ang II vs ADAR1+/- ApoE-/- Ang II	2.71E-02	Yes
		ADAR1+/- ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II	3.71E-01	No
Figure 2F	Kruskal-Wallis test with Dunn’s multiple comparisons test	ApoE-/- Saline vs ApoE-/- Ang II	8.51E-04	Yes
		ApoE-/- Saline vs ADAR1+/- ApoE-/- Saline	>1.00E+00	No
		ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II	>1.00E+00	No
		ApoE-/- Ang II vs ADAR1+/- ApoE-/- Ang II	2.05E-02	Yes
		ApoE-/- Ang II vs ADAR1+/- ApoE-/- Saline	8.51E-04	Yes
		ADAR1+/- ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II	>1.00E+00	No
Figure 3B	Kruskal-Wallis test with Dunn’s multiple comparisons test	ApoE-/- Saline Pre-MMP2 vs ADAR1+/- ApoE-/- Saline Pre-MMP2	>1.00E+00	No
		ApoE-/- Saline Pre-MMP2 vs ApoE-/- Ang II Pre-MMP2	2.34E-02	Yes
		ApoE-/- Saline Pre-MMP2 vs ADAR1+/- ApoE-/- Ang II Pre-MMP2	>1.00E+00	No
		ADAR1+/- ApoE-/- Saline Pre-MMP2 vs ApoE-/- Ang II Pre-MMP2	1.46E-02	Yes
		ADAR1+/- ApoE-/- Saline Pre-MMP2 vs ADAR1+/- ApoE-/- Ang II Pre-MMP2	8.38E-01	No
		ApoE-/- Ang II Pre-MMP2 vs ADAR1+/- ApoE-/- Ang II Pre-MMP2	3.31E-02	Yes
		ApoE-/- Saline Cleaved-MMP2 vs ADAR1+/- ApoE-/- Saline Cleaved-MMP2	>1.00E+00	No
		ApoE-/- Saline Cleaved-MMP2 vs ApoE-/- Ang II Cleaved-MMP2	2.70E-02	Yes
		ApoE-/- Saline Cleaved-MMP2 vs ADAR1+/- ApoE-/- Ang II Cleaved-MMP2	>1.00E+00	No
		ADAR1+/- ApoE-/- Saline Cleaved-MMP2 vs ApoE-/- Ang II Cleaved-MMP2	2.10E-02	Yes
		ADAR1+/- ApoE-/- Saline Cleaved-MMP2 vs ADAR1+/- ApoE-/- Ang II Cleaved-MMP2	7.50E-01	No
		ApoE-/- Ang II Cleaved-MMP2 vs ADAR1+/- ApoE-/- Ang II Cleaved-MMP2	2.40E-02	Yes
Figure 3C	Kruskal-Wallis test with Dunn’s multiple comparisons test	ApoE-/- Saline Pre-MMP9 vs ADAR1+/- ApoE-/- Saline Pre-MMP9	>1.00E+00	No
		ApoE-/- Saline Pre-MMP9 vs ApoE-/- Ang II Pre-MMP9	1.87E-02	Yes
		ApoE-/- Saline Pre-MMP9 vs ADAR1+/- ApoE-/- Ang II Pre-MMP9	>1.00E+00	No
		ADAR1+/- ApoE-/- Saline Pre-MMP9 vs ApoE-/- Ang II Pre-MMP9	1.58E-02	Yes
		ADAR1+/- ApoE-/- Saline Pre-MMP9 vs ADAR1+/- ApoE-/- Ang II Pre-MMP9	1.00E-01	No
		ApoE-/- Ang II Pre-MMP9 vs ADAR1+/- ApoE-/- Ang II Pre-MMP9	8.70E-02	Yes
		ApoE-/- Saline Cleaved-MMP9 vs ADAR1+/- ApoE-/- Saline Cleaved-MMP9	>1.00E+00	No
		ApoE-/- Saline Cleaved-MMP9 vs ApoE-/- Ang II	2.87E-02	Yes

		Cleaved-MMP9 ApoE-/- Saline Cleaved-MMP9 vs ADAR1+/- ApoE-/- Ang II Cleaved-MMP9 ADAR1+/- ApoE-/- Saline Cleaved-MMP9 vs ApoE-/- Ang II Cleaved-MMP9 ADAR1+/- ApoE-/- Saline Cleaved-MMP9 vs ADAR1+/- ApoE-/- Ang II Cleaved-MMP9 ApoE-/- Ang II Cleaved-MMP9 vs ADAR1+/- ApoE-/- Ang II Cleaved-MMP9	>1.00E+00 2.58E-02 8.00E-02 7.60E-02	No Yes No Yes
Figure 3D	Kruskal-Wallis test with Dunn's multiple comparisons test	ApoE-/- Saline vs ADAR1+/- ApoE-/- Saline ApoE-/- Saline vs ApoE-/- Ang II ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II ADAR1+/- ApoE-/- Saline vs ApoE-/- Ang II ADAR1+/- ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II ApoE-/- Ang II vs ADAR1+/- ApoE-/- Ang II	>1.00E+00 1.80E-02 >1.00E+00 1.70E-02 >1.00E+00 2.10E-02	No Yes No Yes No Yes
Figure 3E	Kruskal-Wallis test with Dunn's multiple comparisons test	ApoE-/- Saline ACTA2 vs ADAR1+/- ApoE-/- Saline ACTA2 ApoE-/- Saline ACTA2 vs ApoE-/- Ang II ACTA2 ApoE-/- Saline ACTA2 vs ADAR1+/- ApoE-/- Ang II ACTA2 ADAR1+/- ApoE-/- Saline ACTA2 vs ApoE-/- Ang II ACTA2 ADAR1+/- ApoE-/- Saline ACTA2 vs ADAR1+/- ApoE-/- Ang II ACTA2 ApoE-/- Ang II ACTA2 vs ADAR1+/- ApoE-/- Ang II ACTA2 ApoE-/- Saline Calponin vs ADAR1+/- ApoE-/- Saline Calponin ApoE-/- Saline Calponin vs ApoE-/- Ang II Calponin ApoE-/- Saline Calponin vs ADAR1+/- ApoE-/- Ang II Calponin ADAR1+/- ApoE-/- Saline Calponin vs ApoE-/- Ang II Calponin ADAR1+/- ApoE-/- Saline Calponin vs ADAR1+/- ApoE-/- Ang II Calponin ApoE-/- Ang II Calponin vs ADAR1+/- ApoE-/- Ang II Calponin	>1.00E+00 2.40E-05 >1.00E+00 1.30E-05 4.60E-01 3.20E-05 >1.00E+00 4.40E-05 >1.00E+00 2.50E-05 6.50E-01 4.20E-05	No Yes No Yes No Yes No Yes No Yes No Yes
Figure 3G	Kruskal-Wallis test with Dunn's multiple comparisons test	ApoE-/- Saline vs ApoE-/- Ang II ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II ApoE-/- Ang II vs ADAR1+/- ApoE-/- Ang II	2.80E-04 1.50E-01 2.40E-02	Yes No Yes
Figure 3I	Kruskal-Wallis test with Dunn's multiple comparisons test	ApoE-/- Saline vs ApoE-/- Ang II ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II ApoE-/- Ang II vs ADAR1+/- ApoE-/- Ang II	3.60E-03 2.50E-01 3.30E-02	Yes No Yes
Figure 3J	Kruskal-Wallis test with Dunn's multiple comparisons test	ApoE-/- Saline vs ApoE-/- Ang II ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II ApoE-/- Ang II vs ADAR1+/- ApoE-/- Ang II	2.90E-03 1.70E-01 1.30E-02	Yes No Yes
Figure 4C	Mann-Whitney test (two-sided)	Donor: ApoE-/- vs ADAR1+/- ApoE-/-	2.17E-03	Yes
Figure	Mann-Whitney	Donor: ApoE-/- vs ADAR1+/- ApoE-/-	2.165e-3	Yes

4F	test (two-sided)			
Figure 4G	Fisher's exact test (two-sided)	Donor: ApoE-/- vs ADAR1+/- ApoE-/-	1.72e-4	Yes
Figure 5D	One-way Anova with Tukey's multiple comparison test	ApoE-/- Saline vs ApoE-/- Ang II ApoE-/- Saline vs ADAR1sm+/- ApoE-/- Saline ApoE-/- Saline vs ADAR1sm+/- ApoE-/- Ang II ApoE-/- Ang II vs ADAR1sm+/- ApoE-/- Saline ApoE-/- Ang II vs ADAR1sm+/- ApoE-/- Ang II ADAR1sm+/- ApoE-/- Saline vs ADAR1sm+/- ApoE-/- Ang II	2.70E-02 1.00E+00 8.70E-01 7.70E-02 2.50E-02 7.70E-01	Yes No No Yes Yes No
Figure 5F	Kruskal-Wallis test with Dunn's multiple comparisons test	ApoE-/- Saline vs ApoE-/- Ang II ApoE-/- Saline vs ADAR1sm+/- ApoE-/- Saline ApoE-/- Saline vs ADAR1sm+/- ApoE-/- Ang II ADAR1sm+/- ApoE-/- Saline vs ADAR1sm+/- ApoE-/- Ang II ApoE-/- Ang II vs ADAR1sm+/- ApoE-/- Saline ApoE-/- Ang II vs ADAR1sm+/- ApoE-/- Ang II	7.81E-04 >1.00E+00 >1.00E+00 >1.00E+00 7.81E-04 4.56E-03	Yes No No No Yes Yes
Figure 6B	Kruskal-Wallis test with Dunn's multiple comparisons test	IL-1β- + shADAR1- ADAR1 110kD vs IL-1β- + shADAR1+ ADAR1 110kD IL-1β- + shADAR1- ADAR1 110kD vs IL-1β+ + shADAR1- ADAR1 110kD IL-1β- + shADAR1- ADAR1 110kD vs IL-1β+ + shADAR1+ ADAR1 110kD IL-1β- + shADAR1+ ADAR1 110kD vs IL-1β+ + shADAR1- ADAR1 110kD IL-1β- + shADAR1+ ADAR1 110kD vs IL-1β+ + shADAR1+ ADAR1 110kD IL-1β+ + shADAR1- ADAR1 110kD vs IL-1β+ + shADAR1+ ADAR1 110kD IL-1β- + shADAR1- ADAR1 150kD vs IL-1β- + shADAR1+ ADAR1 150kD IL-1β- + shADAR1- ADAR1 150kD vs IL-1β+ + shADAR1- ADAR1 150kD IL-1β- + shADAR1- ADAR1 150kD vs IL-1β+ + shADAR1+ ADAR1 150kD IL-1β- + shADAR1+ ADAR1 150kD vs IL-1β+ + shADAR1- ADAR1 150kD IL-1β- + shADAR1+ ADAR1 150kD vs IL-1β+ + shADAR1+ ADAR1 150kD IL-1β+ + shADAR1- ADAR1 150kD vs IL-1β+ + shADAR1+ ADAR1 150kD	>1.00E+00 1.45E-02 >1.00E+00 1.78E-02 >1.00E+00 1.98E-02 >1.00E+00 2.05E-02 >1.00E+00 1.88E-02 >1.00E+00 2.48E-02	No Yes No Yes No Yes No Yes No Yes No Yes
Figure 6C	Kruskal-Wallis test with Dunn's multiple comparisons test	IL-1β- + shADAR1- vs IL-1β- + shADAR1+ IL-1β- + shADAR1- vs IL-1β+ + shADAR1- IL-1β- + shADAR1- vs IL-1β+ + shADAR1+ IL-1β- + shADAR1+ vs IL-1β+ + shADAR1- IL-1β- + shADAR1+ vs IL-1β+ + shADAR1+ IL-1β+ + shADAR1- vs IL-1β+ + shADAR1+	1.00E+00 2.08E-03 6.14E-01 3.86E-03 8.52E-01 3.11E-02	No Yes No Yes No Yes
Figure 6D	Kruskal-Wallis test with Dunn's multiple comparisons test	IL-1β- + shADAR1- Pre-MMP2 vs IL-1β- + shADAR1+ Pre-MMP2 IL-1β- + shADAR1- Pre-MMP2 vs IL-1β+ + shADAR1- Pre-MMP2 IL-1β- + shADAR1- Pre-MMP2 vs IL-1β+ + shADAR1+ Pre-MMP2 IL-1β- + shADAR1+ Pre-MMP2 vs IL-1β+ +	>1.00E+00 2.85E-03 6.70E-01 7.43E-03	No Yes No Yes

		shADAR1- Pre-MMP2		
		IL-1β- + shADAR1+ Pre-MMP2 vs IL-1β+ + shADAR1+ Pre-MMP2	>1.00E+00	No
		IL-1β+ + shADAR1- Pre-MMP2 vs IL-1β+ + shADAR1+ Pre-MMP2	2.53E-02	Yes
		IL-1β- + shADAR1- Cleaved-MMP2 vs IL-1β- + shADAR1+ Cleaved-MMP2	1.00E+00	No
		IL-1β- + shADAR1- Cleaved-MMP2 vs IL-1β+ + shADAR1- Cleaved-MMP2	1.45E-03	Yes
		IL-1β- + shADAR1- Cleaved-MMP2 vs IL-1β+ + shADAR1+ Cleaved-MMP2	7.77E-01	No
		IL-1β- + shADAR1+ Cleaved-MMP2 vs IL-1β+ + shADAR1- Cleaved-MMP2	3.43E-03	Yes
		IL-1β- + shADAR1+ Cleaved-MMP2 vs IL-1β+ + shADAR1+ Cleaved-MMP2	1.00E+00	No
		IL-1β+ + shADAR1- Cleaved-MMP2 vs IL-1β+ + shADAR1+ Cleaved-MMP2	1.83E-02	Yes
Figure 6E	Kruskal-Wallis test with Dunn's multiple comparisons test	IL-1β- + shADAR1- Pre-MMP9 vs IL-1β- + shADAR1+ Pre-MMP9	1.00E+00	No
		IL-1β- + shADAR1- Pre-MMP9 vs IL-1β+ + shADAR1- Pre-MMP9	1.85E-03	Yes
		IL-1β- + shADAR1- Pre-MMP9 vs IL-1β+ + shADAR1+ Pre-MMP9	6.50E-01	No
		IL-1β- + shADAR1+ Pre-MMP9 vs IL-1β+ + shADAR1- Pre-MMP9	5.43E-03	Yes
		IL-1β- + shADAR1+ Pre-MMP9 vs IL-1β+ + shADAR1+ Pre-MMP9	1.00E+00	No
		IL-1β+ + shADAR1- Pre-MMP9 vs IL-1β+ + shADAR1+ Pre-MMP9	2.53E-02	Yes
		IL-1β- + shADAR1- Cleaved-MMP9 vs IL-1β- + shADAR1+ Cleaved-MMP9	1.00E+00	No
		IL-1β- + shADAR1- Cleaved-MMP9 vs IL-1β+ + shADAR1- Cleaved-MMP9	2.35E-03	Yes
		IL-1β- + shADAR1- Cleaved-MMP9 vs IL-1β+ + shADAR1+ Cleaved-MMP9	5.60E-01	No
		IL-1β- + shADAR1+ Cleaved-MMP9 vs IL-1β+ + shADAR1- Cleaved-MMP9	4.33E-03	Yes
		IL-1β- + shADAR1+ Cleaved-MMP9 vs IL-1β+ + shADAR1+ Cleaved-MMP9	1.00E+00	No
		IL-1β+ + shADAR1- Cleaved-MMP9 vs IL-1β+ + shADAR1+ Cleaved-MMP9	3.23E-02	Yes
Figure 6F	Kruskal-Wallis test with Dunn's multiple comparisons test	IL-1β- + shADAR1- vs IL-1β- + shADAR1+	1.00E+00	No
		IL-1β- + shADAR1- vs IL-1β+ + shADAR1-	2.11E-02	Yes
		IL-1β- + shADAR1- vs IL-1β+ + shADAR1+	6.90E-01	No
		IL-1β- + shADAR1+ vs IL-1β+ + shADAR1-	3.76E-02	Yes
		IL-1β- + shADAR1+ vs IL-1β+ + shADAR1+	1.00E+00	No
		IL-1β+ + shADAR1- vs IL-1β+ + shADAR1+	4.05E-02	Yes
Figure 6G	Kruskal-Wallis test with Dunn's multiple comparisons test	IL-1β- + shADAR1- vs IL-1β- + shADAR1+	1.00E+00	No
		IL-1β- + shADAR1- vs IL-1β+ + shADAR1-	1.41E-02	Yes
		IL-1β- + shADAR1- vs IL-1β+ + shADAR1+	7.50E-01	No
		IL-1β- + shADAR1+ vs IL-1β+ + shADAR1-	2.26E-02	Yes
		IL-1β- + shADAR1+ vs IL-1β+ + shADAR1+	1.00E+00	No
		IL-1β+ + shADAR1- vs IL-1β+ + shADAR1+	2.05E-02	Yes
Figure 6H	Kruskal-Wallis test with Dunn's	IL-1β- + shADAR1- vs IL-1β- + shADAR1+	1.00E+00	No
		IL-1β- + shADAR1- vs IL-1β+ + shADAR1-	8.41E-03	Yes

	multiple comparisons test	IL-1β- + shADAR1- vs IL-1β+ + shADAR1+ IL-1β- + shADAR1+ vs IL-1β+ + shADAR1- IL-1β- + shADAR1+ vs IL-1β+ + shADAR1+ IL-1β+ + shADAR1- vs IL-1β+ + shADAR1+	6.70E-01 6.26E-03 1.00E+00 1.35E-02	No Yes No Yes
Figure 6I	Kruskal-Wallis test with Dunn's multiple comparisons test	IL-1β- + shADAR1- vs IL-1β- + shADAR1+ IL-1β- + shADAR1- vs IL-1β+ + shADAR1- IL-1β- + shADAR1- vs IL-1β+ + shADAR1+ IL-1β- + shADAR1+ vs IL-1β+ + shADAR1- IL-1β- + shADAR1+ vs IL-1β+ + shADAR1+ IL-1β+ + shADAR1- vs IL-1β+ + shADAR1+	1.00E+00 1.85E-03 6.90E-01 5.43E-03 1.00E+00 2.53E-02	No Yes No Yes No Yes
Figure 6K	Kruskal-Wallis test with Dunn's multiple comparisons test	IL-1β- + shADAR1- Pre-MMP2 vs IL-1β- + shADAR1+ Pre-MMP2 IL-1β- + shADAR1- Pre-MMP2 vs IL-1β+ + shADAR1- Pre-MMP2 IL-1β- + shADAR1- Pre-MMP2 vs IL-1β+ + shADAR1+ Pre-MMP2 IL-1β- + shADAR1+ Pre-MMP2 vs IL-1β+ + shADAR1- Pre-MMP2 IL-1β- + shADAR1+ Pre-MMP2 vs IL-1β+ + shADAR1+ Pre-MMP2 IL-1β+ + shADAR1- Pre-MMP2 vs IL-1β+ + shADAR1+ Pre-MMP2 IL-1β- + shADAR1- m-MMP2 vs IL-1β- + shADAR1+ m-MMP2 IL-1β- + shADAR1- m-MMP2 vs IL-1β+ + shADAR1- m-MMP2 IL-1β- + shADAR1- m-MMP2 vs IL-1β+ + shADAR1+ m-MMP2 IL-1β- + shADAR1+ m-MMP2 vs IL-1β+ + shADAR1- m-MMP2 IL-1β- + shADAR1+ m-MMP2 vs IL-1β+ + shADAR1+ m-MMP2 IL-1β+ + shADAR1- m-MMP2 vs IL-1β+ + shADAR1+ m-MMP2	1.00E+00 4.92E-03 1.00E+00 1.35E-02 1.00E+00 5.98E-03 1.00E+00 1.99E-02 1.00E+00 1.45E-02 1.00E+00 3.40E-02	No Yes No Yes No Yes No Yes No Yes No Yes
Figure 6L	Kruskal-Wallis test with Dunn's multiple comparisons test	IL-1β- + shADAR1- Pre-MMP9 vs IL-1β- + shADAR1+ Pre-MMP9 IL-1β- + shADAR1- Pre-MMP9 vs IL-1β+ + shADAR1- Pre-MMP9 IL-1β- + shADAR1- Pre-MMP9 vs IL-1β+ + shADAR1+ Pre-MMP9 IL-1β- + shADAR1+ Pre-MMP9 vs IL-1β+ + shADAR1- Pre-MMP9 IL-1β- + shADAR1+ Pre-MMP9 vs IL-1β+ + shADAR1+ Pre-MMP9 IL-1β+ + shADAR1- Pre-MMP9 vs IL-1β+ + shADAR1+ Pre-MMP9 IL-1β- + shADAR1- m-MMP9 vs IL-1β- + shADAR1+ m-MMP9 IL-1β- + shADAR1- m-MMP9 vs IL-1β+ + shADAR1- m-MMP9 IL-1β- + shADAR1- m-MMP9 vs IL-1β+ + shADAR1+ m-MMP9 IL-1β- + shADAR1+ m-MMP9 vs IL-1β+ + shADAR1- m-MMP9 IL-1β- + shADAR1+ m-MMP9 vs IL-1β+ +	1.00E+00 4.92E-03 1.00E+00 1.35E-02 1.00E+00 2.98E-02 1.00E+00 9.22E-03 1.00E+00 1.15E-02 1.00E+00	No Yes No Yes No Yes No Yes No Yes No

		shADAR1+ m-MMP9 IL-1β+ + shADAR1- m-MMP9 vs IL-1β+ + shADAR1+ m-MMP9	3.18E-02	Yes
Figure 7B	Mann-Whitney test (two-sided)	shGFP 0-hour vs shADAR1 0 hour shGFP 0.5-hour vs shADAR1 0.5-hour shGFP 1 hour vs shADAR1 1-hour shGFP 2 hours vs shADAR1 2 hours shGFP 4 hours vs shADAR1 4 hour shGFP 6 hours vs shADAR1 6 hours	>1.00E+00 >1.00E+00 2.17E-03 1.50E-03 2.21E-01 6.40E-01	No No Yes Yes Yes No
Figure 7C	Mann-Whitney test (two-sided)	shGFP 0-hour vs shADAR1 0 hour shGFP 0.5-hour vs shADAR1 0.5-hour shGFP 1 hour vs shADAR1 1-hour shGFP 2 hours vs shADAR1 2 hours shGFP 4 hours vs shADAR1 4 hour shGFP 6 hours vs shADAR1 6 hours	>1.00E+00 1.40E-02 2.30E-03 1.40E-04 1.10E-02 6.60E-01	No Yes Yes Yes Yes No
Figure 7E	Kruskal-Wallis test with Dunn's multiple comparisons test	IP: IgG + IL-1β- vs IP: IgG + IL-1β+ IP: IgG + IL-1β- vs IP: ADAR1 + IL-1β- IP: IgG + IL-1β- vs IP: ADAR1 + IL-1β+ IP: IgG + IL-1β+ vs IP: ADAR1 + IL-1β- IP: IgG + IL-1β+ vs ADAR1 + IL-1β+ IP: ADAR1 + IL-1β- vs IP: ADAR1 + IL-1β+	>1.00E+00 5.64E-03 1.35E-03 1.56E-02 1.35E-03 2.24E-02	No Yes Yes Yes Yes Yes
Figure 7G	Mann-Whitney test (two-sided)	shADAR1 + HuR 0 hour vs shGFP + HuR 0 hour shADAR1 + HuR 2 hour vs shGFP + HuR 2 hour shADAR1 + HuR 4 hour vs shGFP + HuR 4 hour shADAR1 + HuR 6 hour vs shGFP + HuR 6 hour	>1.00E+00 2.17E-02 1.10E-02 2.50E-02	No Yes Yes Yes
Figure 7H	Mann-Whitney test (two-sided)	shADAR1 + HuR 0 hour vs shGFP + HuR 0 hour shADAR1 + HuR 2 hour vs shGFP + HuR 2 hour shADAR1 + HuR 4 hour vs shGFP + HuR 4 hour shADAR1 + HuR 6 hour vs shGFP + HuR 6 hour	>1.00E+00 1.40E-02 2.20E-02 3.80E-02	No Yes Yes Yes
Figure 8B	Kruskal-Wallis test with Dunn's multiple comparisons test	ApoE-/- Saline vs ADAR1+/- ApoE-/- Saline ApoE-/- Saline vs ApoE-/- Ang II ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II ADAR1+/- ApoE-/- Saline vs ApoE-/- Ang II ADAR1+/- ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II ADAR1+/- ApoE-/- Ang II vs ApoE-/- Ang II	1.00E+00 4.92E-03 1.00E+00 3.51E-03 1.00E+00 5.98E-03	No Yes No Yes No Yes
Figure 8C	Kruskal-Wallis test with Dunn's multiple comparisons test	ApoE-/- Saline vs ADAR1+/- ApoE-/- Saline ApoE-/- Saline vs ApoE-/- Ang II ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II ADAR1+/- ApoE-/- Saline vs ApoE-/- Ang II ADAR1+/- ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II ADAR1+/- ApoE-/- Ang II vs ApoE-/- Ang II	1.00E+00 1.92E-02 1.00E+00 1.35E-02 1.00E+00 3.98E-02	No Yes No Yes No Yes
Online Figure 1A	One-way Anova with Tukey's multiple comparison test	ApoE-/- Saline vs ApoE-/- Ang II ApoE-/- Saline vs ADAR1+/- ApoE-/- Saline ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II ApoE-/- Ang II vs ADAR1+/- ApoE-/- Saline ApoE-/- Ang II vs ADAR1+/- ApoE-/- Ang II ADAR1+/- ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II	2.78E-03 1.00E+00 1.57E-01 5.03E-03 1.00E+00 1.00E+00	Yes No No Yes Yes No
Online Figure 1B	One-way Anova with Tukey's multiple comparison test	ApoE-/- Saline vs ApoE-/- Ang II ApoE-/- Saline vs ADAR1sm+/- ApoE-/- Saline ApoE-/- Saline vs ADAR1sm+/- ApoE-/- Ang II ApoE-/- Ang II vs ADAR1sm+/- ApoE-/- Saline ApoE-/- Ang II vs ADAR1sm+/- ApoE-/- Ang II	2.78E-03 1.00E+00 1.57E-01 6.11E-03 4.00E-02	Yes No No Yes Yes

		ADAR1sm+/- ApoE-/- Saline vs ADAR1+/- ApoE-/- Ang II	1.00E+00	No
Online Figure 2B	Kruskal-Wallis test with Dunn's multiple comparisons test	8-aza- + IL-1β- pre-MMP2 vs 8-aza- + IL-1β+ pre-MMP2	8.96E-04	Yes
		8-aza- + IL-1β- pre-MMP2 vs 8-aza+ + IL-1β+ pre-MMP2	7.20E-02	Yes
		8-aza- + IL-1β+ pre-MMP2 vs 8-aza+ + IL-1β+ pre-MMP2	5.22E-01	No
		8-aza- + IL-1β- m-MMP2 vs 8-aza- + IL-1β+ m-MMP2	3.49E-03	Yes
		8-aza- + IL-1β- m-MMP2 vs 8-aza+ + IL-1β+ m-MMP2	2.43E-02	Yes
		8-aza- + IL-1β+ m-MMP2 vs 8-aza+ + IL-1β+ m-MMP2	1.00E+00	No
Online Figure 2C	Kruskal-Wallis test with Dunn's multiple comparisons test	8-aza- + IL-1β- pre-MMP9 vs 8-aza- + IL-1β+ pre-MMP9	1.90E-03	Yes
		8-aza- + IL-1β- pre-MMP9 vs 8-aza+ + IL-1β+ pre-MMP9	2.20E-02	Yes
		8-aza- + IL-1β+ pre-MMP9 vs 8-aza+ + IL-1β+ pre-MMP9	7.22E-01	No
		8-aza- + IL-1β- m-MMP9 vs 8-aza- + IL-1β+ m-MMP9	3.49E-03	Yes
		8-aza- + IL-1β- m-MMP9 vs 8-aza+ + IL-1β+ m-MMP9	2.43E-02	Yes
		8-aza- + IL-1β+ m-MMP9 vs 8-aza+ + IL-1β+ m-MMP9	9.00E-01	No
Online Figure 2D	Kruskal-Wallis test with Dunn's multiple comparisons test	8-aza- + IL-1β- pre-VCAM1vs 8-aza- + IL-1β+pre-VCAM1	3.23E-03	Yes
		8-aza- + IL-1β- pre-VCAM1vs 8-aza+ + IL-1β+pre-VCAM1	2.67E-02	Yes
		8-aza- + IL-1β+ pre-VCAM1vs 8-aza+ + IL-1β+pre-VCAM1	1.00E+00	No
		8-aza- + IL-1β- m-VCAM1 vs 8-aza- + IL-1β+ m-VCAM1	1.23E-02	Yes
		8-aza- + IL-1β- m-VCAM1 vs 8-aza+ + IL-1β+ m-VCAM1	1.67E-02	Yes
		8-aza- + IL-1β+ m-VCAM1 vs 8-aza+ + IL-1β+ m-VCAM1	1.00E+00	No
Online Figure 2E	Kruskal-Wallis test with Dunn's multiple comparisons test	8-aza- + IL-1β- pre-ACTA2 vs 8-aza- + IL-1β+ pre-ACTA2	3.36E-03	Yes
		8-aza- + IL-1β- pre-ACTA2 vs 8-aza+ + IL-1β+ pre-ACTA2	1.00E+00	No
		8-aza- + IL-1β+ pre-ACTA2 vs 8-aza+ + IL-1β+ pre-ACTA2	2.04E-02	Yes
		8-aza- + IL-1β- m-ACTA2 vs 8-aza- + IL-1β+ m-ACTA2	1.20E-04	Yes
		8-aza- + IL-1β- m-ACTA2 vs 8-aza+ + IL-1β+ m-ACTA2	9.00E-01	No
		8-aza- + IL-1β+ m-ACTA2 vs 8-aza+ + IL-1β+ m-ACTA2	3.40E-03	Yes
Online Figure 3B	Kruskal-Wallis test with Dunn's multiple comparisons test	8-aza- + Ad-ADAR1- pre-MMP2 vs 8-aza- + Ad-ADAR1+ pre-MMP2	4.56E-04	Yes
		8-aza- + Ad-ADAR1- pre-MMP2 vs 8-aza+ + Ad-ADAR1+ pre-MMP2	1.08E-02	Yes
		8-aza- + Ad-ADAR1+ pre-MMP2 vs 8-aza+ + Ad-	2.73E-01	No

		ADAR1+ pre-MMP2		
		8-aza- + Ad-ADAR1- m-MMP2 vs 8-aza- + Ad-ADAR1+ m-MMP2	5.60E-04	Yes
		8-aza- + Ad-ADAR1- m-MMP2 vs 8-aza+ + Ad-ADAR1+ m-MMP2	1.77E-02	Yes
		8-aza- + Ad-ADAR1+ m-MMP2 vs 8-aza+ + Ad-ADAR1+ m-MMP2	2.47E-01	No
Online Figure 3C	Kruskal-Wallis test with Dunn's multiple comparisons test	8-aza- + Ad-ADAR1- pre-MMP9 vs 8-aza- + Ad-ADAR1+ pre-MMP9	3.30E-04	Yes
		8-aza- + Ad-ADAR1- pre-MMP9 vs 8-aza+ + Ad-ADAR1+ pre-MMP9	1.32E-02	Yes
		8-aza- + Ad-ADAR1+ pre-MMP9 vs 8-aza+ + Ad-ADAR1+ pre-MMP9	1.92E-01	No
		8-aza- + Ad-ADAR1- m-MMP9 vs 8-aza- + Ad-ADAR1+ m-MMP9	4.30E-04	Yes
		8-aza- + Ad-ADAR1- m-MMP9 vs 8-aza+ + Ad-ADAR1+ m-MMP9	2.16E-02	Yes
		8-aza- + Ad-ADAR1+ m-MMP9 vs 8-aza+ + Ad-ADAR1+ m-MMP9	3.21E-01	No
Online Figure 3D	Kruskal-Wallis test with Dunn's multiple comparisons test	8-aza- + Ad-ADAR1- pre-VCAM1 vs 8-aza- + Ad-ADAR1+pre-VCAM1	2.71E-04	Yes
		8-aza- + Ad-ADAR1- pre-VCAM1 vs 8-aza+ + Ad-ADAR1+pre-VCAM1	1.51E-03	Yes
		8-aza- + Ad-ADAR1+ pre-VCAM1 vs 8-aza+ + Ad-ADAR1+pre-VCAM1	3.51E-01	No
		8-aza- + Ad-ADAR1- m-VCAM1 vs 8-aza- + Ad-ADAR1+ m-VCAM1	3.10E-04	Yes
		8-aza- + Ad-ADAR1- m-VCAM1 vs 8-aza+ + Ad-ADAR1+ m-VCAM1	4.41E-03	Yes
		8-aza- + Ad-ADAR1+ m-VCAM1 vs 8-aza+ + Ad-ADAR1+ m-VCAM1	6.31E-01	No
Online Figure 3E	Kruskal-Wallis test with Dunn's multiple comparisons test	8-aza- + Ad-ADAR1- pre-ACTA2 vs 8-aza- + Ad-ADAR1+ pre-ACTA2	4.03E-03	Yes
		8-aza- + Ad-ADAR1- pre-ACTA2 vs 8-aza+ + Ad-ADAR1+ pre-ACTA2	1.00E+00	No
		8-aza- + Ad-ADAR1+ pre-ACTA2 vs 8-aza+ + Ad-ADAR1+ pre-ACTA2	1.71E-02	Yes
		8-aza- + Ad-ADAR1- m-ACTA2 vs 8-aza- + Ad-ADAR1+ m-ACTA2	7.50E-03	Yes
		8-aza- + Ad-ADAR1- m-ACTA2 vs 8-aza+ + Ad-ADAR1+ m-ACTA2	8.66E-01	No
		8-aza- + Ad-ADAR1+ m-ACTA2 vs 8-aza+ + Ad-ADAR1+ m-ACTA2	4.30E-03	Yes