Figure S1. Confirmation of transfection efficiency. (A) Western blots and quantification to evaluate the expression of Ablim1 in the VSMCs transfected with si*Ablim1* or siControl (n=3 per group). (B) The mRNA expression of *Ablim1* in the VSMCs transfected with si*Ablim1* or siControl (n=3 per group). (C) Western blots and quantification to evaluate the expression of Ablim1 in the VSMCs transfected with pcDNA3.1-*Ablim1* or pc-DNA3.1-Flag (n=3 per group). (D) The mRNA expression of *Ablim1* in the VSMCs transfected with pcDNA3.1-*Ablim1* or pc-DNA3.1-Flag (n=3 per group). (E) Western blots and quantification to evaluate the expression of c-Myc in the VSMCs transfected with si*c-Myc* or siControl (n=3 per group). (F) The mRNA expression of *c-Myc* in the VSMCs transfected with si*c-Myc* or siControl (n=3 per group). (G) Western blots and quantification to evaluate the expression of c-Myc in the VSMCs transfected with pcDNA3.1-*c-Myc* or pc-DNA3.1-Flag (n=3 per group). (H) The mRNA expression of *c-Myc* in the VSMCs transfected with pcDNA3.1-*c-Myc* or pc-DNA3.1-Flag (n=3 per group). (I) Western blots and quantification to evaluate the expression of Mkl1 in the VSMCs transfected with si*Mkl1* or siControl (n=3 per group). (J) The mRNA expression of *Mkl1* in the VSMCs transfected with si*Mkl1*or siControl (n=3 per group). (K) Western blots and quantification to evaluate the expression of Mkl1 in the VSMCs transfected with pcDNA3.1-*Mkl1* or pc-DNA3.1-His (n=3 per group). (L) The mRNA expression of *Mkl1* in the VSMCs transfected with pcDNA3.1-*Mkl1* or pc-DNA3.1-His (n=3 per group). Data are presented as the mean ± SEM. P-values were calculated by Student's t test. ***P<0.001 vs. siControl, pc-DNA3.1-Flag or pc-DNA3.1-His. Ablim1, actin-binding LIM protein 1; VSMCs, vascular smooth muscle cells; si, small interfering.

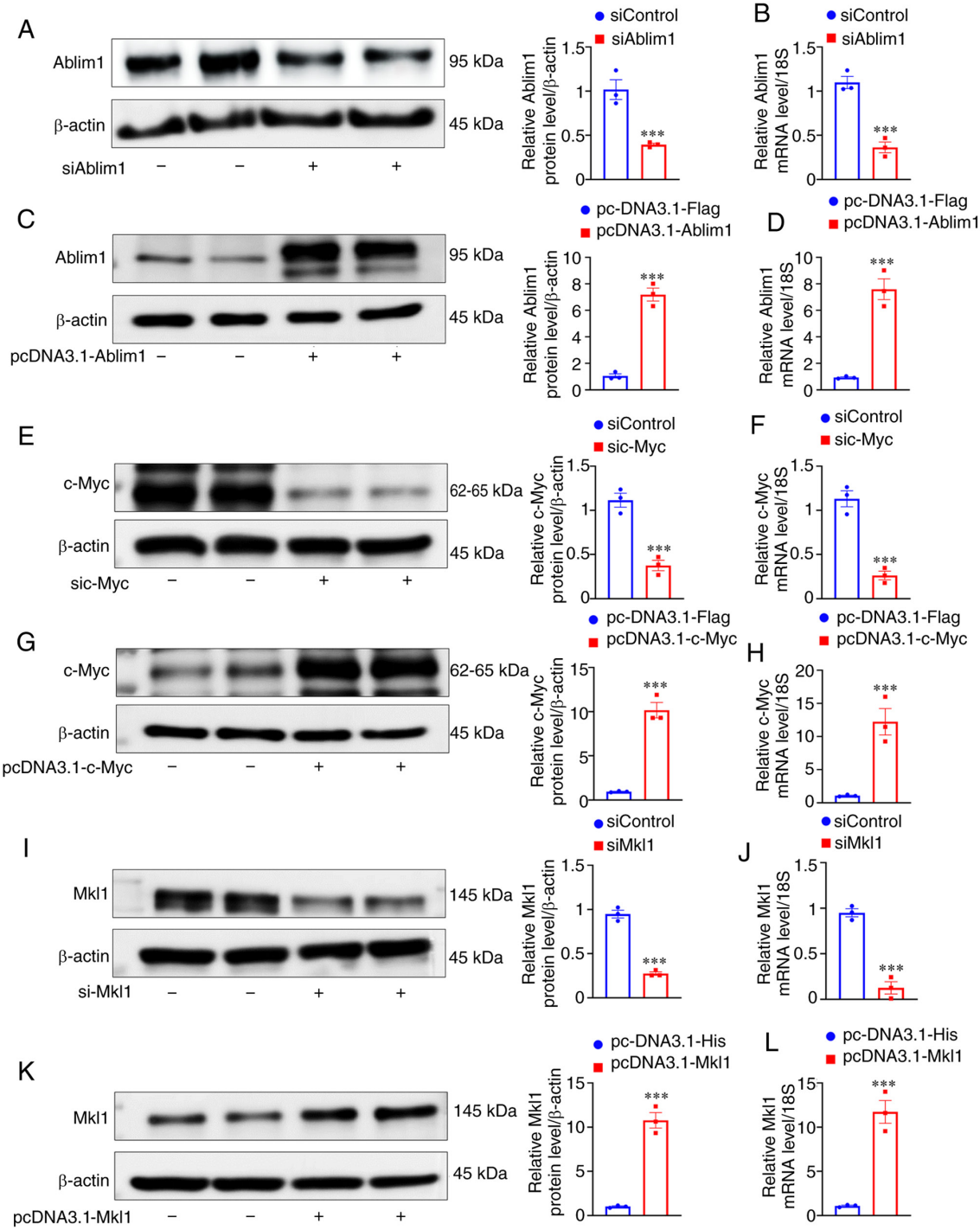

Figure S2. C-Myc is a transcription factor of miR-378a. (A) Homology analysis of miRNA. Sequences of miR-149-5p, miR-200b-3p, miR-200c-3p, miR-342-5p, miR-150-3p, miR-378a-5p in human and mice. (B) Immunofluorescence images of VSMCs markers including α-SMA and SM22-α. (C and D) Western blots and quantification analysis of the protein expression levels of MMP2, CNN1, α-SMA and SM22-α in the different concentrations of TNFα-treated VSMCs (n=3 per group). (E) The prediction of the intersection transcription factors of miR-378a in human and mice using two databases, respectively. (F) Western blots and quantification of the protein expression levels of c-MYC and MYOD1 in the different concentrations of TNFα-treated VSMCs (n=3 per group). (G) Western blots and quantification of the protein expression levels of c-MYC in human aorta tissues (n=4 per group). (H) Relative luciferase activity in 293T cells of luciferase reporter constructs containing miR-378a promoter or its mutants transfected along with pRL-TK (internal control plasmid) followed by transfection with c-MYC encoding plasmid (n=8 per group). (I) Expression of *c-Myc* and miR-378a-5p were determined by RT-qPCR (n=3 per group). (J) Expression of *c-Myc* and miR-378a-5p were determined by RT-qPCR (n=3 per group). Data are presented as the mean ± SEM. Two-way ANOVA followed by Bonferroni post hoc test. ***P<0.001 vs. TNFα (0 ng/ml) or Normal or pcDNA-3.1-Flag or siControl. miR or miRNA, microRNA; VSMCs, vascular smooth muscle cells; α-SMA, α-smooth muscle actin; SM22α, smooth muscle 22α; MMP2, matrix metalloproteinase 2; CNN1, calponin 1; RT-qPCR, reverse transcription-quantitative PCR.

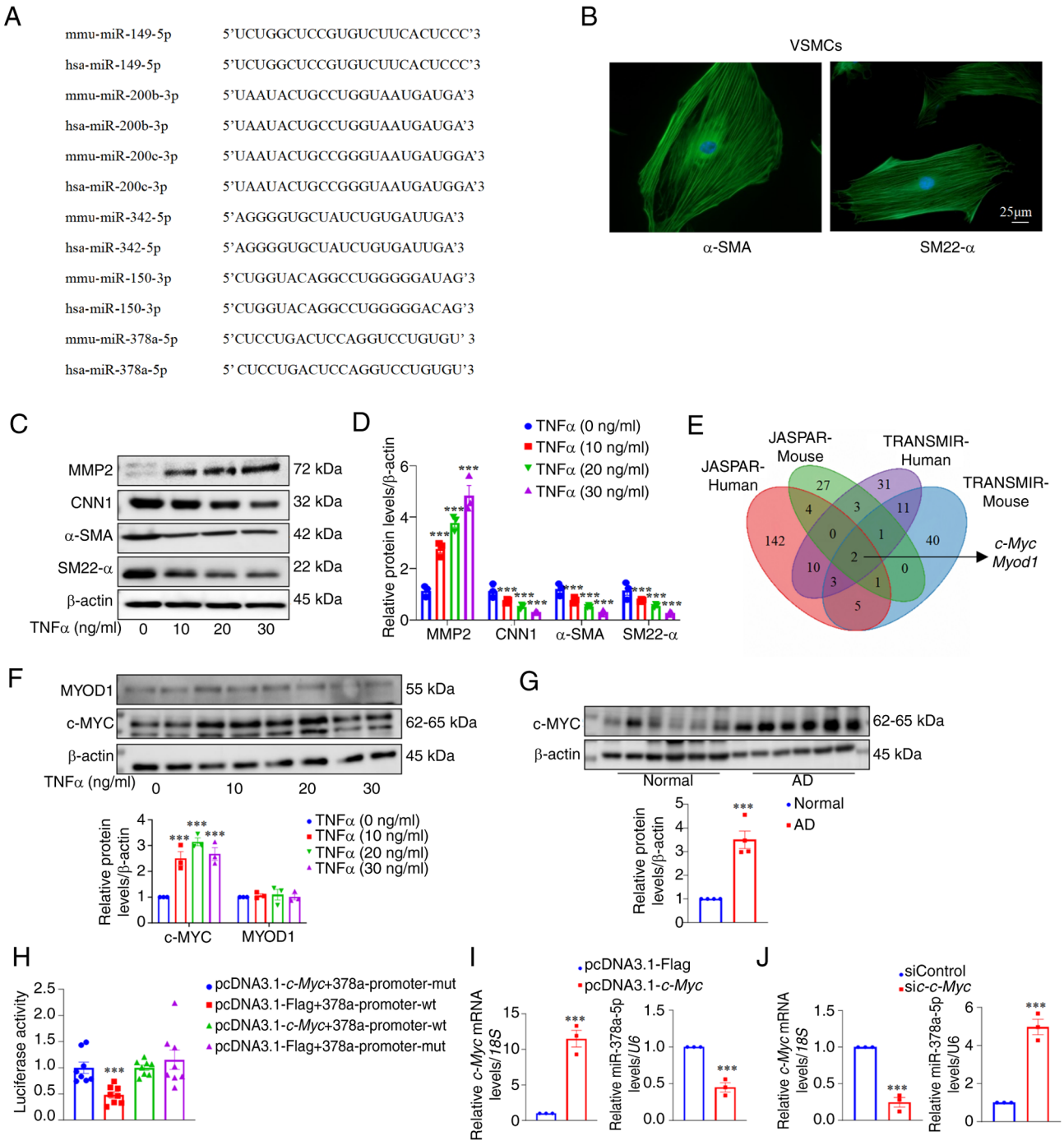

Figure S3. Overexpression of miR-378a-5p prevents Ang II-induced abdominal aortic aneurysm formation. (A) The flowchart of experimental design. 8-week-old ApoE$^{-/-}$ mice were injected with angomir-NC or angomir-378a-5p through tail venous injection. After successful overexpression of miR-378a-5p, all mice were infused with Ang II for 28 days. (B) Body weight of four groups of mice treated with Ang II for 28 days (n=10 in Ang II groups and n=5 in saline groups). (C and D) Blood pressure of four groups of mice (n=5 per group). (E) RT-qPCR analysis of miR-378a-5p in the aortas of mice treated with angomir-NC and angomir-378a-5p (n=6 per group). (F) Survival curves in four groups. n=10 in Ang II groups and n=5 in saline groups. (G) All gross specimen image of aortas in four groups of mice. Red represented aortic aneurysm formation, yellow represented death, the representative image in the figure was outlined in red (n=10 in Ang II groups and n=5 in saline groups). Data are presented as the mean±SEM. P-values were calculated by Student's t test (for E), two-way ANOVA with Holm-Sidak multiple comparisons test (for B, C and D). Kaplan-Meier survival curves were analyzed with the log-rank (Mantel-Cox) test (for F). ***P<0.001 vs. angomir-NC. miR or miRNA, microRNA; Ang II, angiotensin-II; *ApoE*$^{-/-}$, apolipoprotein E-deficient; SBP, systolic blood pressure; DBP, diastolic blood pressure; NC, negative control.

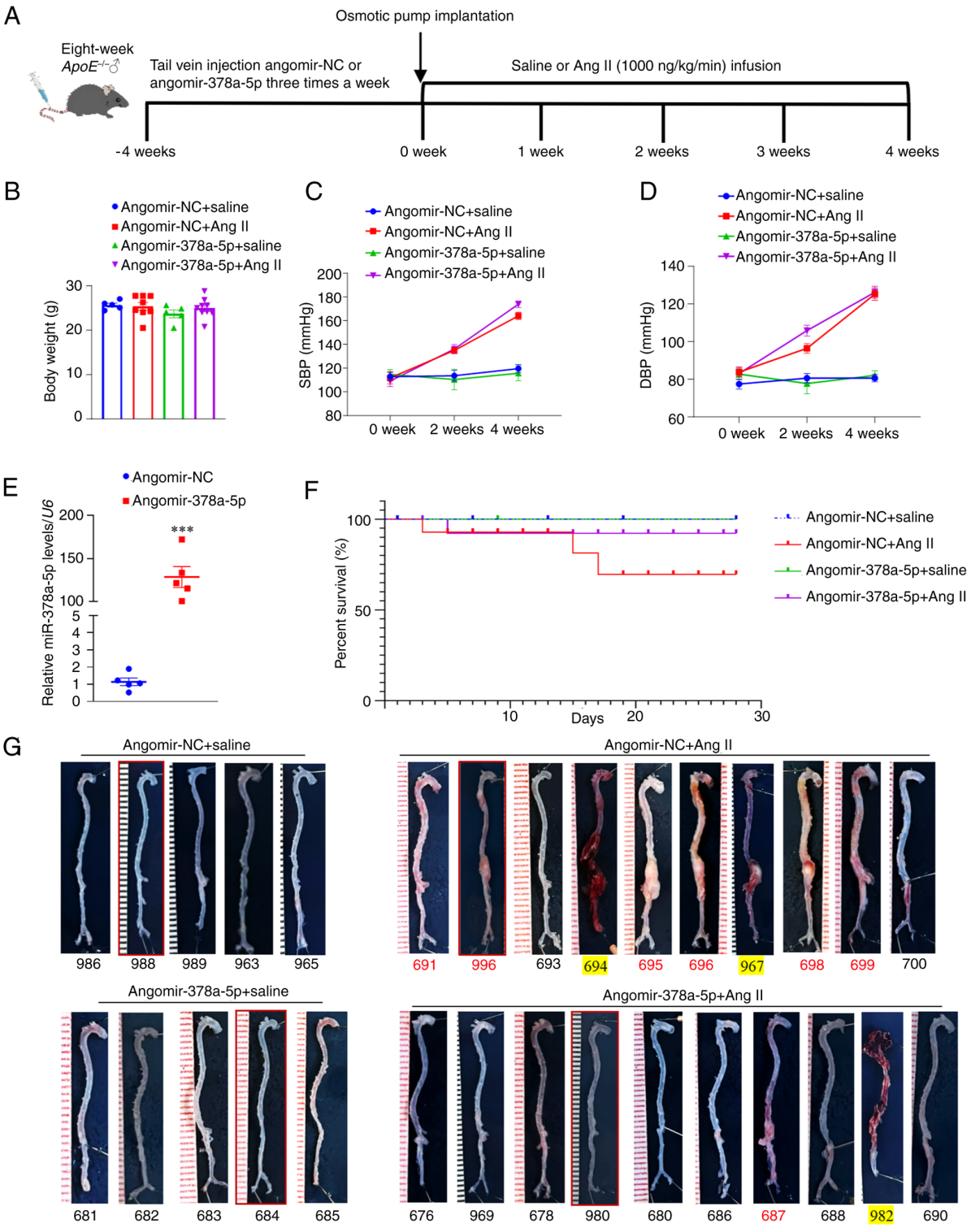

Figure S4. miR-378a-5p inhibitor aggravates abdominal aortic aneurysm development in *ApoE*$^{-/-}$ mice. (A) The flowchart of experimental design. 8-week-old *ApoE*$^{-/-}$ mice were injected with antagomir-NC or antagomir-378a-5p through tail venous injection. After successful knockdown of miR-378a-5p, all mice were infused with Ang II for 28 days. (B) Body weight of four groups of mice treated with Ang II for 28 days (n=15 in Ang II groups and n=5 in saline groups). (C and D) Blood pressure of four groups of mice (n=5 per group). (E) Reverse transcription-quantitative PCR of miR-378a-5p in the aortas of mice treated with antagomir-NC and antagomir-378a-5p (n=6 per group). (F) The incidence of aortic aneurysm in Ang II-infused mice (n=15 in Ang II groups and n=5 in saline groups). (G) Survival curves in four groups (n=15 in Ang II groups and n=5 in saline groups). (H) All gross specimen image of aortas in four groups of mice. Red represented aortic aneurysm formation, yellow represented death, the representative image in the figure was outlined in red (n=15 in Ang II groups and n=5 in saline groups). Data are presented as the mean ± SEM. P values were calculated by Student's t test (for E), two-way ANOVA with Holm-Sidak multiple comparisons test (for B-D). Kaplan-Meier survival curves were analyzed with the log-rank (Mantel-Cox) test (for G). ***P<0.001 vs. antagomir-NC. miR or miRNA, microRNA; Ang II, angiotensin-II; *ApoE*$^{-/-}$, apolipoprotein E-deficient; NC, negative control; SBP, systolic blood pressure; DBP, diastolic blood pressure.

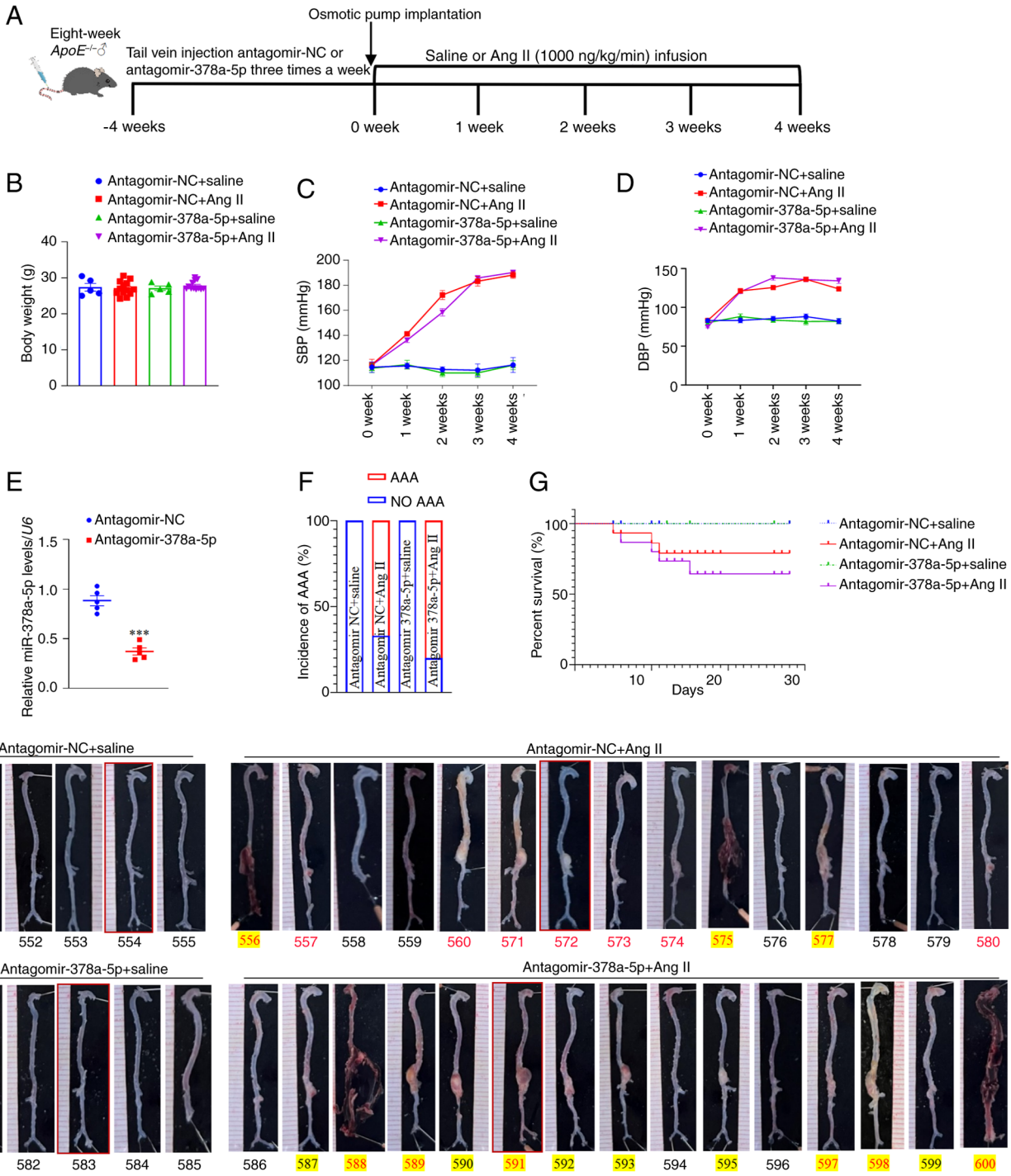

Figure S5. miR-378a-5p overexpression inhibits the migration of VSMCs, and miR-378a-5p knockdown increases the migration of VSMCs. (A) RT-qPCR analysis of miR-378a-5p in the VSMCs transfected with mimics-miR-378a-5p or inhibitor-miR-378a-5p, n=6 per group. (B) VSMCs' migration was assessed using a wounding healing assay in VSMCs' transfected with mimics-miR-378a-5p or mimics-NC (n=3 per group). (C) VSMCs' migration was assessed using a wounding healing assay in VSMCs transfected with inhibitor-miR-378a-5p or inhibitor-NC (n=3 per group). Data are presented as the mean ± SEM. P values were calculated by two-way ANOVA with Holm-Sidak multiple comparisons test. ***P<0.001 vs. mimics-NC or inhibitor-NC; $^{\#\#}$P<0.01 vs. mimics-NC + TNFα or Inhibitor-NC + TNFα; $^{\&\&}$P<0.01 vs. mimics-miR-378a-5p or inhibitor-miR-378a-5p. miR or miRNA, microRNA; VSMCs, vascular smooth muscle cells; NC, negative control.

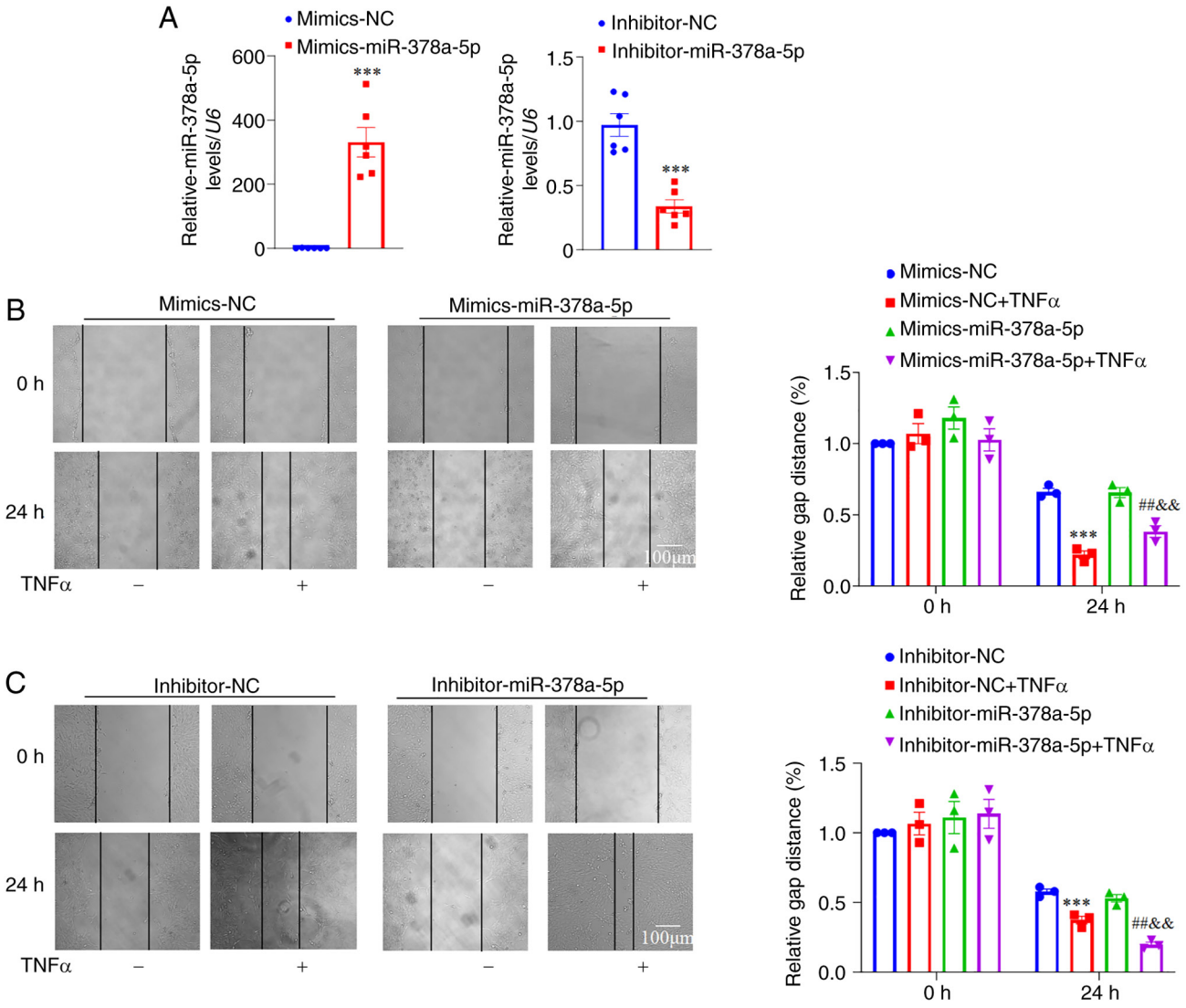

Figure S6. ABLIM1 is a target gene of miR-378a-5p and is involved in abdominal aortic aneurysm. (A) Representative images and quantification of immunofluorescence staining identified ABLIM1 protein in human aortic tissues and normal aortas. (B) Western blots and quantification to evaluate the expression of ABLIM1 in human aortic tissues compared with normal aortas. (C) Representative images and quantification of immunofluorescence staining identified *ABLIM1* protein in mice aneurysm and normal aortas. (D) Western blots and quantification to evaluate the expression of ABLIM1 in the aortas of mice aneurysm compared with normal aortas. (E) Representative images and quantification of immunofluorescence staining identified α-SMA and Ablim1 protein in VSMCs treated with or without TNFα. (F) Western blots and quantification to evaluate the expression of ABLIM1 in VSMCs treated with or without TNFα. (G) Western blots and quantification to evaluate the expression of ABLIM1 in the aortas of mice between antagomir-NC and antagomir-378a-5p groups. (H) Western blots and quantification to evaluate the expression of ABLIM1 in the aortas of mice between angomir-NC and angomir-378a-5p groups. (I) Western blots and quantification analysis of ABLIM1 in the VSMCs transfected with mimics-miR-378a-5p or mimics-NC. (J) RT-qPCR analysis of *Ablim1* in the VSMCs transfected with mimics-miR-378a-5p or mimics-NC. (K) Western blots and quantification analysis of Ablim1 in the VSMCs transfected with inhibitor-miR-378a-5p or inhibitor-NC. (L) RT-qPCR analysis of *Ablim1* in the VSMCs transfected with inhibitor-miR-378a-5p or inhibitor-NC. Data are presented as the mean ± SEM (n=3 per group). P-values were calculated by Student's t test (for B). **P<0.01 and ***P<0.001 vs. normal or saline or control or antagomir-NC or angomir-NC or mimics-NC or inhibitor-NC. miR, microRNA; ABLIM1, actin-binding LIM protein 1; VSMCs, vascular smooth muscle cells; α-SMA, α-smooth muscle actin; NC, negative control; RT-qPCR, reverse transcription-quantitative PCR.

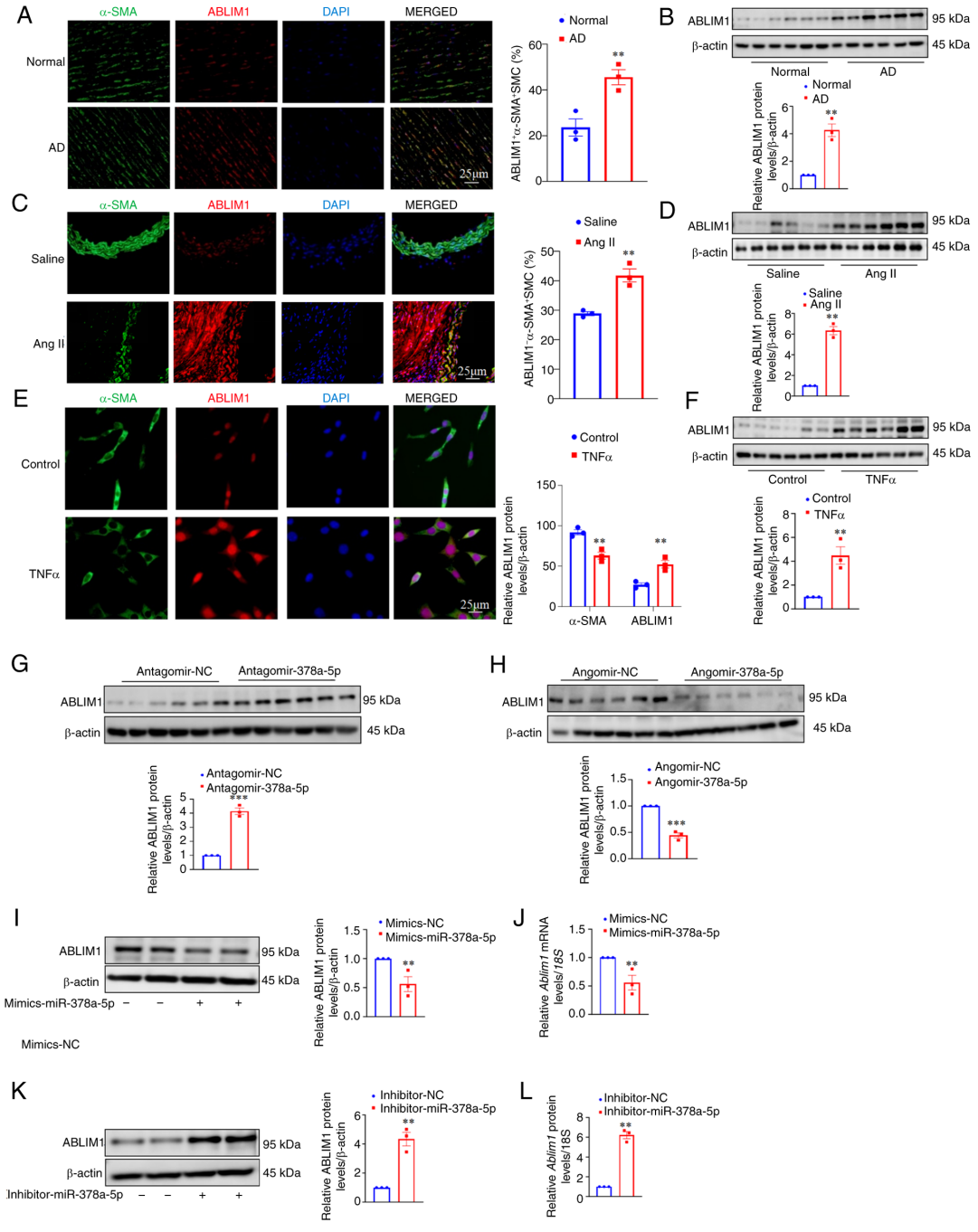

Figure S7. Identification of ABLIM1 as a target gene of miR-378a-5p. (A) The binding sites for miR-378a-5p and *Ablim1* were shown. (B) Schematic diagram of plasmids construction for the wild-type and mutant 3'UTR region of *Ablim1*. ABLIM1, actin-binding LIM protein 1; miR, microRNA; UTR, untranslated region; MUT, mutated; WT, wild-type.

A

Position 21-27 of *Ablim1* 3'UTR	5' UCGAGUAAACGACAAUCAGGAAA 3' UGUGUCCUGGACCUCAGUCCUC
Position 1403-1409 of *Ablim1* 3'UTR	5' AGGGUCCCCAGAGUCUCAGGAAA 3' UGUGUCCUGGACCUCAGUCCUC
Position 2502-2508 of *Ablim1* 3'UTR	5' GGAAAUUGAAGUAUUCAGGAAA 3' UGUGUCCUGGACCUCAGUCCUC

B

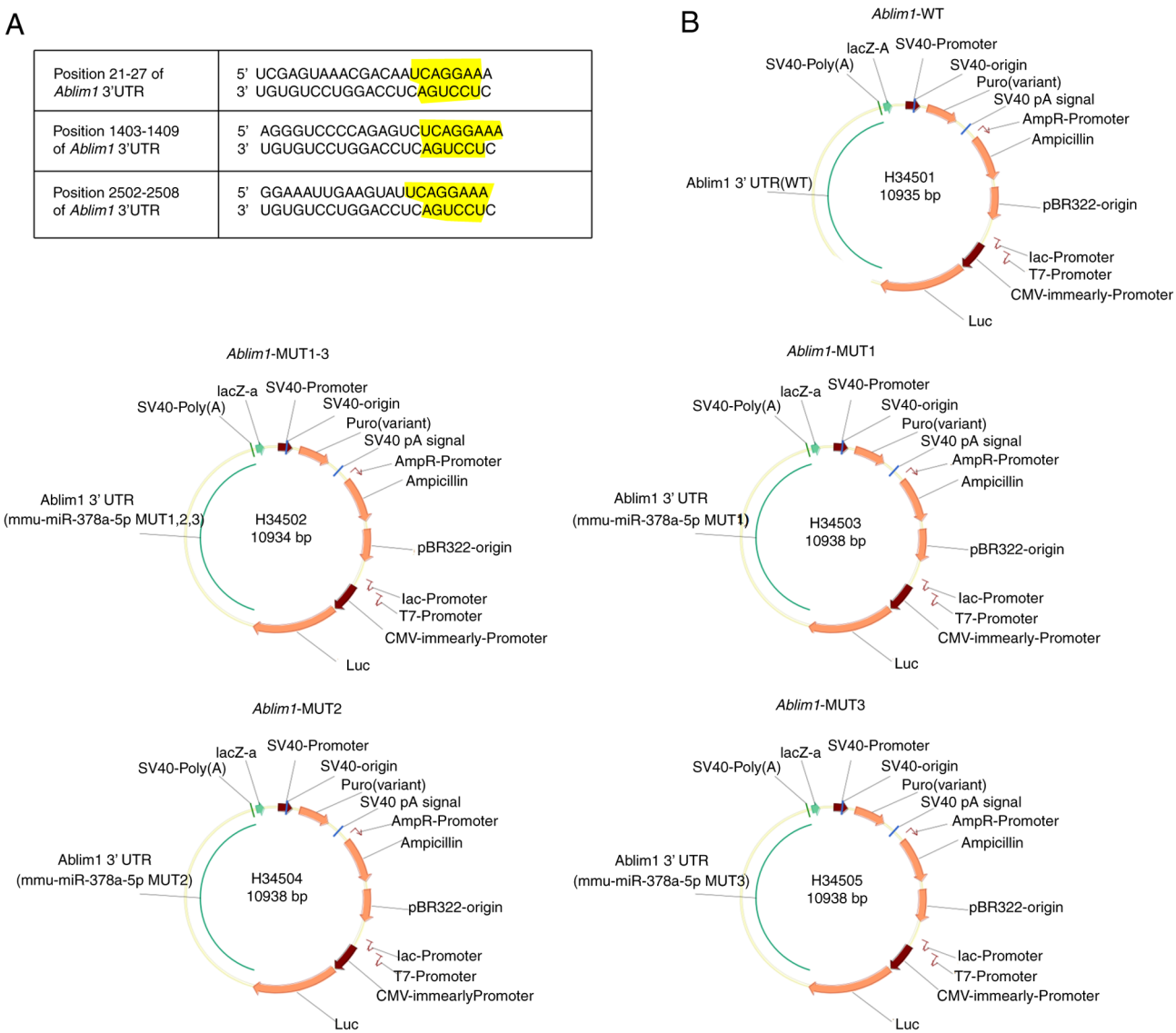

Figure S8. Reanalysis of GSE155468 single-cell RNA sequencing. (A) tSNE plot of cells from eight patients with thoracic aortic aneurysm and three healthy donor thoracic aortas. Colors denote different conditions. (B) tSNE plot of cells showing all cells colored according to cell types between the two groups. (C) Dot plot of selected marker genes for each cluster and lineage in aggregate cell clusters. Dot size indicated the percentage of cells expressing each gene, and dot color indicated expression level. (D) tSNE plot showing all cells colored according to the 7 major cell types in merged samples. (E) Single cells annotated as VSMCs on the tSNE displayed were *in silico* extracted, reanalyzed with tSNE, and clustered identifying 8 major populations. (F) tSNE plot of cells showing VSMCs colored according to cell types between the two groups. (G) Expression of *ABLIM1* transcript in the VSMCs' population. (H) tSNE plot of cells showing VSMCs colored according to the expression of *ABLIM1*. (I) Classical VSMCs contractile phenotype biomarkers (*CNN1*, *MTH11*, *TAGLN*, *MYL9* and *ACTA2*) were highly expressed in the *ABLIM1*$^{-}$ group. (J) Dot plot of Gene Ontology analysis of different expression genes between *ABLIM1*$^{+}$ and *ABLIM1*$^{-}$ groups. (K) Dot plot of Kyoto Encyclopedia of Genes and Genomes' analysis of different expression genes between *ABLIM1*$^{+}$ and *ABLIM1*$^{-}$ groups. tSNE, T-distributed Stochastic Neighbor Embedding; VSMCs, vascular smooth muscle cells.

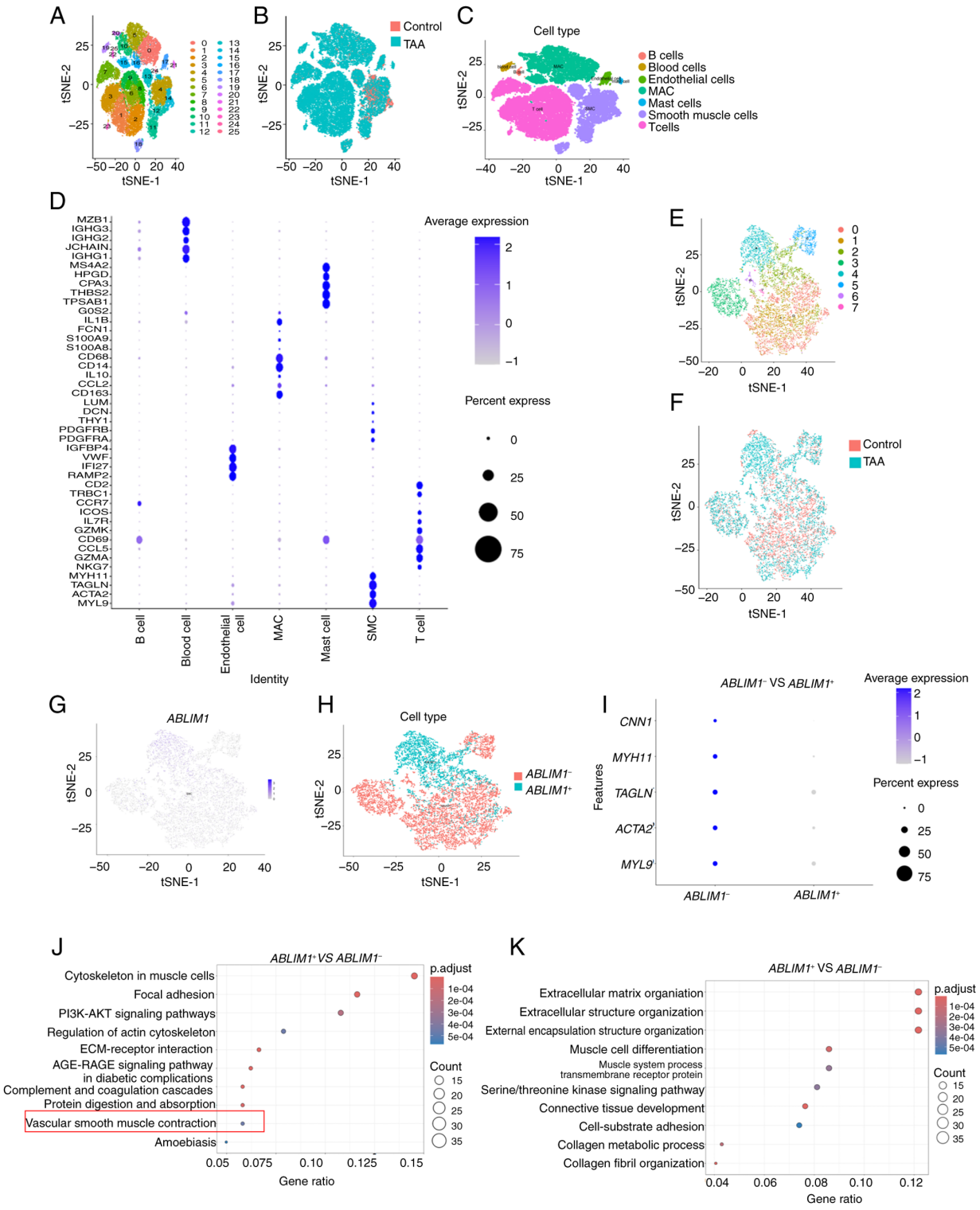

Figure S9. Knockdown of *Ablim1* prevents Ang II-induced abdominal aortic aneurysm formation. (A) Experimental design. 8-week-old *ApoE*$^{-/-}$ mice were injected with AAV-SM22-shNC or AAV-SM22-sh*Ablim1* through tail venous injection. After successful knockdown of *Ablim1*, all mice were infused with Ang II for 28 days. (B and C) Western blots and quantification analysis of ABLIM1 in the heart, liver, spleen, kidney and aortas of mice treated with AAV-SM22-shNC or AAV-SM22-sh*Ablim1*-1-3 (n=3 per group). (D) Reverse transcription-quantitative PCR analysis of *Ablim1* in the heart, liver, spleen, kidney and aortas of mice treated with AAV-SM22-shNC or AAV-SM22-sh*Ablim1*-3 (n=3 per group). Data are presented as the mean±SEM. P-values were calculated by Student's t test. **P<0.01 vs. AAV-SM22-shNC. ABLIM1, actin-binding LIM protein 1; Ang II, angiotensin-II; *ApoE*$^{-/-}$, apolipoprotein E-deficient; sh-, short hairpin; NC, negative control.

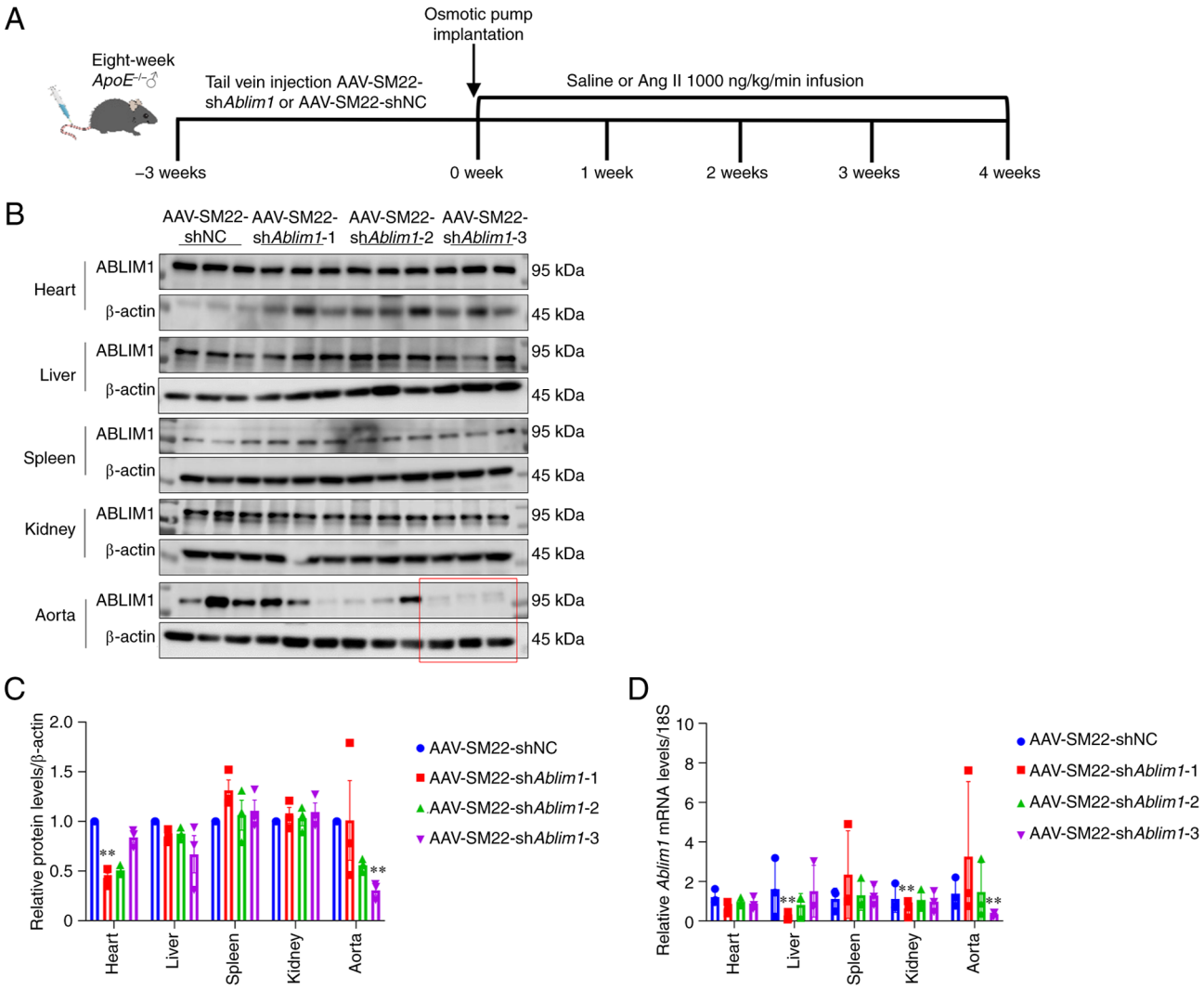

Figure S10. Knockdown of *Ablim1* prevents Ang II-induced abdominal aortic aneurysm formation. (A) Body weight of four groups of mice treated with Ang II for 28 days (n=25 in Ang II groups and n=5 in saline groups). (B) Blood pressure of four groups of mice (n=5 per group). (C) Survival curves in four groups (n=25 in Ang II groups and n=5 in saline groups). (D) Quantification of fibrosis in aorta tissues (n=3 per group). (E) Quantification of the degree of elastic fiber degradation levels in the abdominal aortic wall (n=3 per group). Data are presented as the mean ± SEM. P-values were calculated by two-way ANOVA with Holm-Sidak multiple comparisons test (for A, B, D and E). Kaplan-Meier survival curves were analyzed with the log-rank (Mantel-Cox) test (for C). *P<0.005 vs. AAV-SM22-shNC + saline; $^{\#}$P<0.005 vs. AAV-SM22-sh*Ablim1* + saline; $^{\&}$P<0.005 vs. AAV-SM22-shNC + Ang II. ABLIM1, actin-binding LIM protein 1; Ang II, angiotensin-II; *ApoE*$^{-/-}$, apolipoprotein E-deficient; sh-, short hairpin; NC, negative control; SBP, systolic blood pressure; DBP, diastolic blood pressure.

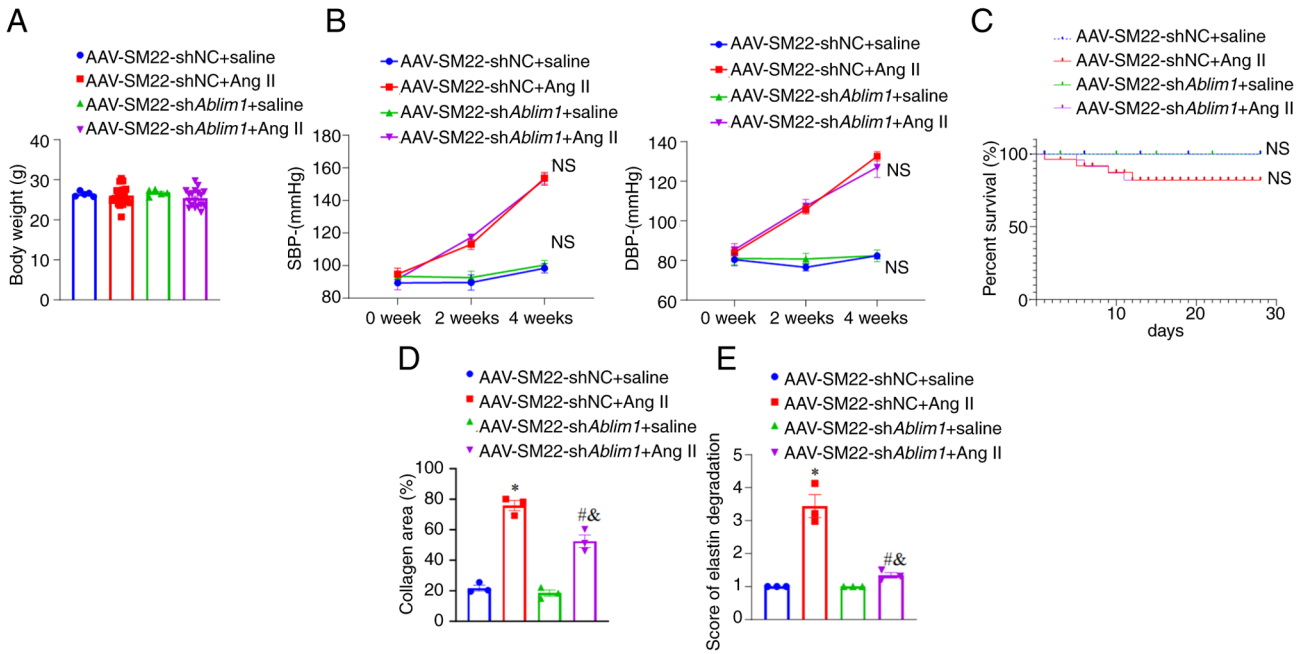

Figure S11. Knockdown of Ablim1 prevents Ang II-induced AAA formation. All gross specimen image of aortas in four groups of mice. Red represented aortic aneurysm formation, yellow represented death, the representative image in the figure was outlined in red (n=25 in Ang II groups and n=5 in saline groups). ABLIM1, actin-binding LIM protein 1; Ang II, angiotensin-II; AAA, abdominal aortic aneurysm; sh-, short hairpin; NC, negative control.

Figure S12. Overexpression of *Ablim1* aggravates Ang II-induced AAA formation. (A) Experimental design. 8-week-old *ApoE*$^{-/-}$ mice were injected with AAV-SM22-NC or AAV-SM22-*Ablim1* through tail venous injection. After successful overexpression of *Ablim1*, all mice were infused with Ang II for 28 days. (B) Body weight of four groups of mice treated with Ang II for 28 days (n=25 in Ang II groups and n=9 in saline groups). (C) Blood pressure of four groups of mice (n=5 per group). (D) Survival curves in four groups (n=25 in Ang II groups and n=9 in saline groups). (E) Quantification of fibrosis in aorta tissues (n=3 per group). (F) Quantification of the degree of elastic fiber degradation levels in the abdominal aortic wall (n=3 per group). Data are presented as the mean ± SEM. P values were calculated by two-way ANOVA with Holm-Sidak multiple comparisons test (for A, B, E and F). Kaplan-Meier survival curves were analyzed with the log-rank (Mantel-Cox) test (for D). *P<0.05 vs. AAV-SM22-NC + saline; $^{\#}$P<0.05 vs. AAV-SM22-*Ablim1* + saline; $^{\&}$P<0.05 vs. AAV-SM22-NC + Ang II. ABLIM1, actin-binding LIM protein 1; Ang II, angiotensin-II; AAA, abdominal aortic aneurysm; *ApoE*$^{-/-}$, apolipoprotein E-deficient; NC, negative control; SM22, smooth muscle 22; SBP, systolic blood pressure; DBP, diastolic blood pressure.

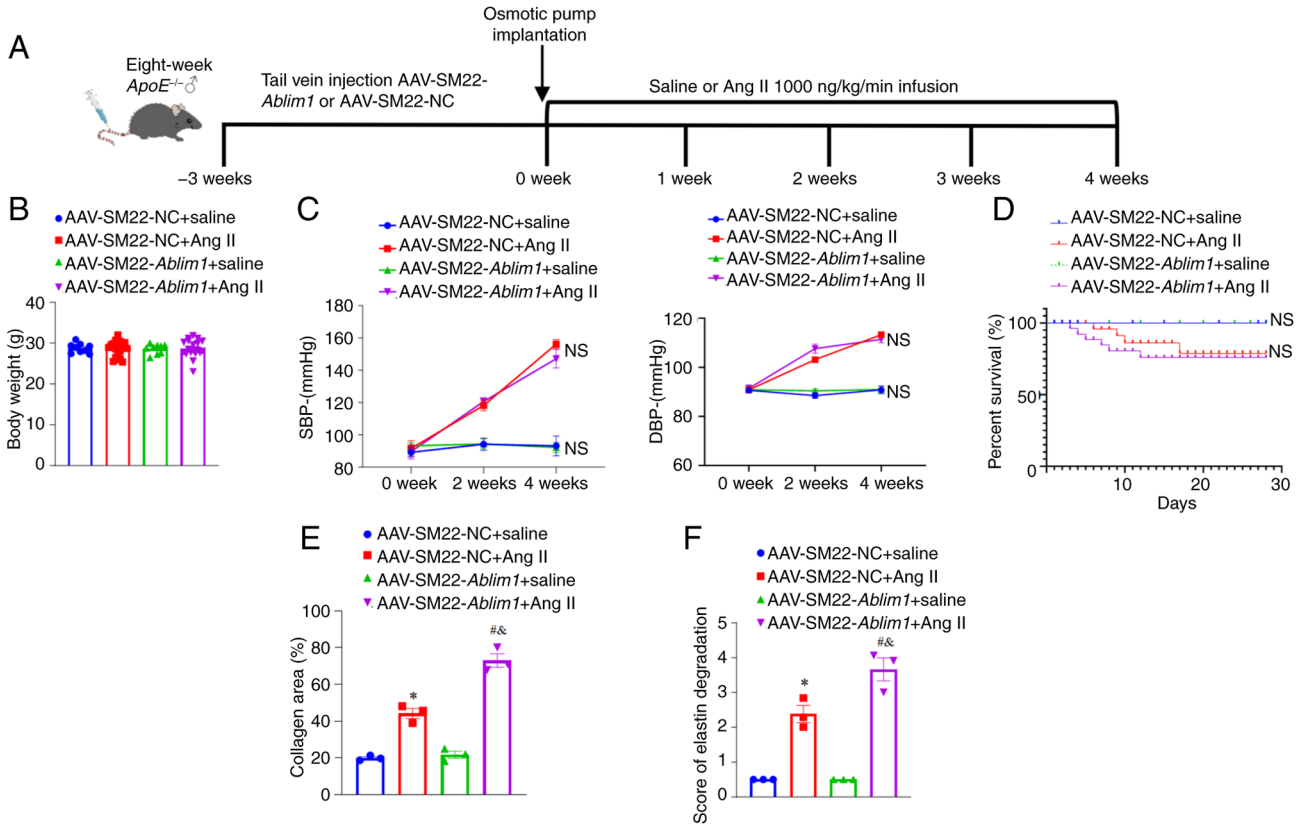

Figure S13. Overexpression of Ablim1 aggravates Ang II-induced AAA represented death, the representative image in the figure was outlined in red (n=25 in Ang II groups and n=9 in saline groups). ABLIM1, actin-binding LIM protein 1; Ang II, angiotensin-II; AAA, abdominal aortic aneurysm; NC, negative control.

Figure S14. ABLIM1 aggravates contractile phenotype of vascular smooth muscle cells through the MKL1/SRF signaling pathway. 293T cells were transfected with pcDNA3.1-Flag-*Ablim1* lysates were immunoprecipitated with anti-Flag magnetic beads, and blotted with anti-Flag, LMOD1, ADM and PRKCD antibodies (n=3 per group). ABLIM1, actin-binding LIM protein 1; MKL1, megakaryoblastic leukemia 1; SRF, serum response factor; ADM, adrenomedullin; PRKCD, protein kinase C delta.

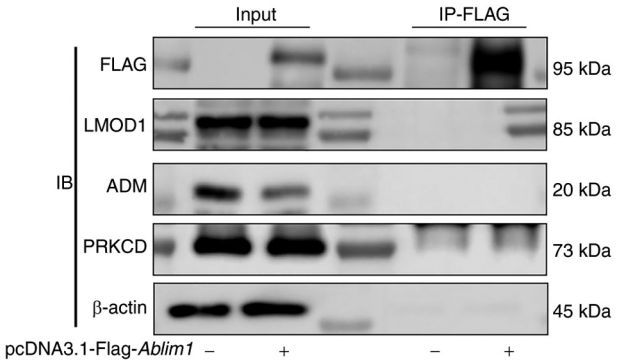

Figure S15. Mechanism diagram of miR-378a-5p in the development of AAA. (A) Under physiological conditions, miR-378a-5p functions as endogenous silencer of the ABLIM1 and MKL1 binds to SRF to activate the expression of VSMCs' marker genes, and VSMCs maintained a fractional contractile phenotype. (B) In the case of injury, miR-378a-5p downregulated which is regulated by the transcription factor of c-MYC. MiR-378a-5p targets the 3'-UTR of ABLIM1 to inhibit MKL1/SRF pathway and inhibited the expression of VSMCs marker genes, VSMCs dedifferentiation and triggering (AAA). miR, microRNA; AAA, abdominal aortic aneurysm; ABLIM1, actin-binding LIM protein 1; MKL1, megakaryoblastic leukemia; SRF, serum response factor; VSMCs, vascular smooth muscle cells; UTR, untranslated region; Ang II, angiotensin-II.