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Original Article

BASP1, targeted by miR-185-5p, promotes atherosclerosis via VSMC proliferation and inflammation

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Abstract: Objective: To investigate the functional role and regulatory mechanisms of brain acid-soluble protein 1 (BASP1) in atherosclerosis (AS). Methods: qRT-PCR was performed to detect BASP1 and miR-185-5p expression in the serum of healthy subjects and AS patients. Human umbilical artery smooth muscle cells (HUASMCs) were exposed to oxidized low-density lipoprotein (ox-LDL) to induce an AS cell model. The target binding relationship between BASP1 and miR-185-5p was verified by luciferase reporter gene assay and qRT-PCR. The effects of BASP1 on ox-LDL-induced proliferation, apoptosis and inflammation were evaluated through a series of in vitro assays. Rescue experiments were conducted to analyze the functional regulation of miR-185-5p by BASP1. Results: BASP1 expression was significantly elevated in the serum of AS patient and in ox-LDL-treated HUASMCs. Silencing BASP1 or overexpressing miR-185-5p reduced cell proliferation, apoptosis, inflammation, and adhesion molecule expression (vascular cellular adhesion molecule-1 (VCAM-1) and Intercellular adhesion molecule 1 (ICAM-1)). miR-185-5p directly targeted and negatively regulated BASP1. BASP1 overexpression partially reversed the effects of miR-185-5p mimics on ox-LDL-induced proliferation, apoptosis, inflammation, and adhesion molecule expression. Conclusion: BASP1 may promote ox-LDL-induced proliferation and apoptosis in HUASMCs. The miR-185-5p/BASP1 molecular axis represents a promising target for the prevention and treatment of AS.

Keywords: Atherosclerosis, BASP1, miR-185-5p, apoptosis, inflammation

Introduction

Atherosclerosis (AS) is a chronic inflammatory disorder characterized by arterial plaque formation, leading to severe cardiovascular events such as myocardial infarction and stroke, posing a significant threat to global public health [1]. AS is typically manifested as deposition of extracellular lipids and fibrous tissue, the accumulation of various inflammatory cells alongside vascular smooth muscle cells (VSMCs), and persistent endothelial damage [2]. Its pathogenesis is complex, primarily involving lipid accumulation, the infiltration of inflammatory cells, the uncontrolled proliferation of VSMCs, and significant endothelial dysfunction that drives disease progression [3, 4]. Despite widespread use of lifestyle interventions and medications, clinical outcomes for AS remain unsatisfactory [5]. Despite extensive research efforts, the complex molecular mechanisms underlying AS, including the signaling pathways and cellular interactions, are not yet fully understood. This underscores the urgent need to identify novel biomarkers and new therapeutic targets to improve clinical management.

Brain acid soluble protein 1 (BASP1) is a highly conserved, cysteine-rich protein found in various cellular membranes. While originally identified in the brain, BASP1 is also present in non-neuronal tissues, including the heart, kidneys, and various tumor types. Due to its N-terminal myristoylation, BASP1 is anchored to the cell membrane, where it plays a role in cytoskeletal regulation and membrane dynam-

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ics. Recent studies suggest that BASP1 exhibits abnormal expression in aortic tissue, raising the possibility of its potential as a diagnostic marker or even a therapeutic target for AS [6]. However, its specific role in AS remains poorly defined.

MicroRNAs (miRNAs) are key post-transcriptional regulators for gene expression and play a crucial role in the progression of AS. miRNAs primarily function by binding to the 3'UTR of target mRNAs, leading to either transcript degradation or inhibition of translation, effectively repressing gene expression [7]. Specifically, miR-185 has been shown, through knockdown experiments, to promote the production of vascular endothelial growth factor (VEGF) and matrix metalloproteinase-9 (MMP-9), which exacerbates arterial tissue damage in vitro, highlighting its potential therapeutic significance [8]. However, it remains unclear whether miR-185-5p influences AS progression by targeting BASP1.

In this study, we focused on the regulatory relationship between BASP1 and miR-185-5p in AS. Our findings provide new insights into the molecular mechanisms of AS and suggest that the miR-185-5p/BASP1 axis may serve as a potential therapeutic target for the treatment of AS, warranting further investigation in future studies.

Materials and methods

Clinical samples

Sixty individuals diagnosed with coronary atherosclerosis at The Second Affiliated Hospital of Jiaxing University were enrolled as the observation cohort (AS group). Eligible participants exhibited at least one coronary artery with >50% stenosis confirmed by angiography and had not received prior treatment. Exclusion criteria comprised comorbidities such as hypertension, diabetes mellitus, renal or hepatic impairment, and malignancies. Additionally, 30 healthy volunteers were recruited as controls. Serum samples were obtained from all participants and cryopreserved at -80°C. The study was approved by the Ethics Committee of The Second Affiliated Hospital of Jiaxing University (Approval No. 2022JX031-02), and written informed consent was obtained from each subject upon enrollment.

Cell culture and treatment

Human umbilical artery smooth muscle cells (HUASMCs) were purchased from Ningbo Mingzhou Biotechnology Co., Ltd. (China). To establish the model, cells in stable growth phase were treated for 24 hours with oxidized low-density lipoprotein (ox-LDL) at varying concentrations (25, 50, and 100 μg/mL). Besides, BASP1 small interfering RNA (si-BASP1; 5'-GCAAGCTCAGCAAGAAGAAGA-3'), negative control siRNA (si-NC; 5'-GGAGGCACAAGCGAGCATAAA-3'), pcDNA3.1-BASP1 overexpression plasmids (OE-BASP1), and pCDNA3.1-HA-C empty vector (OE-NC) were all purchased from GenePharma. miR-185-5p mimics (#miR-10000455-1-5), miR-185-5p inhibitors (#miR-20000455-1-5), and their respective negative control (#miR1N0000001-1-5 or #miR2N0000001-1-5) were all purchased from Ribobio (Guangzhou, China). All transfections were performed using Lipofectamine 3000.

qRT-PCR

Total RNA extraction was performed using Trizol reagent. RNA concentration and purity were quantified on a NanoDrop spectrophotometer. First-strand cDNA was synthesized using a commercial cDNA synthesis kit according to the manufacturer's instructions. Subsequent quantitative real-time PCR for BASP1 and miR-185-5p was conducted with SYBR® Green Master Mix under manufacturer-recommended conditions. For normalization, U6 and GAPDH served as endogenous controls for miR-185-5p and BASP1, respectively. Relative expression levels were determined using the $2^{-\Delta\Delta Ct}$ method. The primer sequences used for qRT-PCR are listed below: BASP1: forward, 5'-CTTAAAAACCCCAGCATCTC-3'; reverse: 5'-TCTGAAAGTTGGCATTCATC-3'; GAPDH forward: 5'-ACAGTCAGCCGCATCTTCTT-3'; reverse: 5'-ACGACCAAATCCGTTGACTC-3'; miR-185-5p: forward, 5'-CGCGTGGAGAGAAAGGCAGT-3', reverse 5'-AGTGCAGGGTCCGAGGTATT-3'; U6: forward 5'-CTCGCTTCGGCAGCACA-3', reverse 5'-AACGCTTCACGAATTTGCGT-3'.

CCK-8 assay

After treatment, HUASMCs were inoculated in 96-well plates for 24, 48 and 72 hours. After incubation, 10 μL of CCK-8 reagent was introduced into each well. After 2 hours of reaction,

optical density (OD) values of each well were detected using a microplate reader.

Flow cytometry

Following treatment, HUASMCs were collected and resuspended in 100 μL of binding buffer. Annexin V-FITC (5 μL) was introduced to the cell suspension for a 10-minute incubation, followed by the addition of 5 μL of PI and a further 15-minute incubation. Apoptosis was quantified by flow cytometry.

Western blot assay

Total proteins were extracted using RIPA lysis buffer. Protein concentration and purity were determined by the BCA method. Protein samples were separated by SDS-PAGE and transferred to a PVDF membrane. The membrane was blocked for 2 h and then incubated overnight with primary antibodies: BASP1 (1:1000, #96510, Cell Signaling Technology), Bax (1:1000, #2772, Cell Signaling Technology), Bcl-2 (1:1000, #3498, Cell Signaling Technology), caspase-3 (1:1000, #9664, Cell Signaling Technology), VCAM-1 (1:1000, #39036, Cell Signaling Technology), ICAM-1 (1:1000, #67836, Cell Signaling Technology) and GAPDH (1:2000, ab9485, Abcam). The membrane was washed and then incubated with secondary antibodies (1:3000, #7074, Cell Signaling Technology) for 1 h. Protein bands were visualized using an ECL chemiluminescence kit.

ELISA

ELISA (Beyotime, Shanghai, China) was employed to determine the extracellular levels of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) in cultured HUASMCs.

Dual luciferase reporter gene assay

A dual-luciferase reporter gene assay was performed to verify the binding relationship between BASP1 and miR-185-5p. Two constructs were used: one carrying the wild-type BASP1 3'UTR sequence (BASP1-WT) and the other containing a mutated miR-185-5p binding site (BASP1-MUT), both synthesized by Genechem (Shanghai, China). HUASMCs were co-transfected with either the wild-type or mutant reporter plasmid alongside miR-185-5p mimics or negative control (miR-NC). After 24 h of culture, luciferase activity was measured to assess the regulatory relationship.

Statistical analysis

Data were analyzed using SPSS (v.26.0; IBM). Results were summarized as means ± SD. The significance of differences between groups was evaluated using the t-test. Multiple group comparisons were analyzed by one-way ANOVA followed by Tukey's post-hoc test. A *P*-value <0.05 was considered statistically significant.

Results

Increased BASP1 expression and decreased miR-185 expression in AS patients

To investigate the potential role of BASP1 in AS, we first measured BASP1 expression in serum samples from AS patients and healthy controls. qRT-PCR revealed significantly higher BASP1 expression in the AS patient group compared to the control group (**Figure 1A**). In addition, the ox-LDL-induced AS cell model showed that BASP1 expression in HUASMCs increased in a dose-dependent manner with higher concentrations of ox-LDL (**Figure 1B**). A potential binding site between miR-185-5p and BASP1 was identified using starBase online analysis tool (https://rnasysu.com/encori/) (**Figure 1C**).

Compared to normal controls, serum miR-185-5p expression was downregulated in the AS samples (**Figure 1D**). Similarly, miR-185-5p expression was lower in HUASMC in a dose-dependent manner with increasing concentrations of ox-LDL (**Figure 1E**).

To confirm the regulatory relationship between BASP1 and miR-185-5p, we manipulated BASP1 expression in HUASMCs. Specifically, overexpression of miR-185-5p significantly suppressed BASP1 expression, whereas knockdown of miR-185-5p markedly elevated BASP1 levels in HUASMCs (**Figure 1F**). Additionally, we constructed luciferase reporter plasmids containing either BASP1-WT or BASP1-MUT to verify whether miR-185-5p directly targets BASP1. Co-transfection of HUASMCs with miR-185-5p mimics and BASP1-WT resulted in a pronounced inhibition of luciferase activity, whereas the same mimics failed to alter luminescence when co-introduced with the BASP1-MUT plasmid (**Figure 1G**).

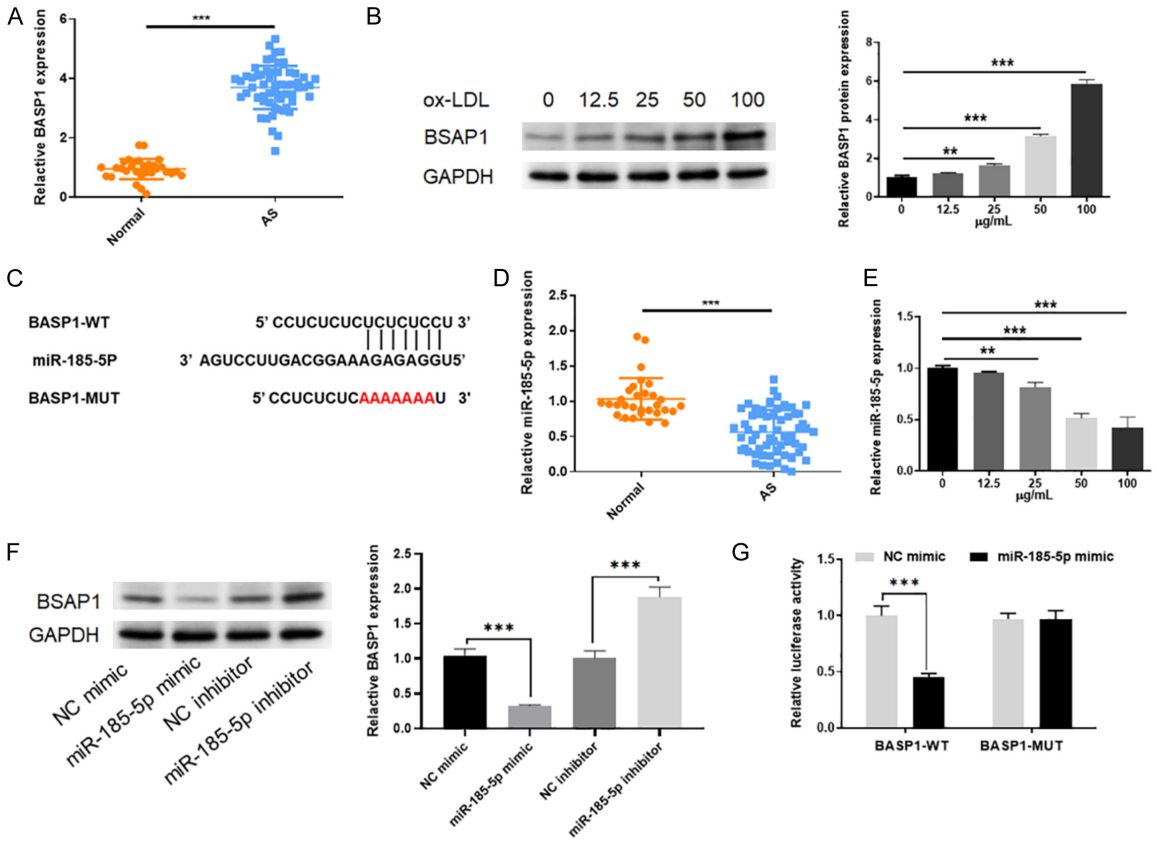

Figure 1. Increased BASP1 expression and decreased miR-185-5p expression in AS patients and ox-LDL-induced HUASMCs. A. qRT-PCR analysis of BASP1 expression in the serum of AS patients and healthy controls. B. qRT-PCR analysis of BASP1 expression in HUASMCs treated with ox-LDL (25, 50 or 100 μg/mL). C. Predicted binding sites between BASP1 and miR-185. D. qRT-PCR analysis of miR-185-5p expression in the serum of AS patients and healthy controls. E. qRT-PCR analysis of miR-185-5p expression in HUASMCs treated with ox-LDL (25, 50 or 100 μg/mL). F. qRT-PCR analysis of miR-185-5p expression in HUASMCs transfected with si-BASP1 or OE-BASP1. G. Dual-luciferase reporter assay confirming the direct binding between BASP1 and miR-185-5p. **P<0.01, ***P<0.001. Notes: ox-LDL, oxidized low-density lipoprotein; AS, atherosclerosis; HUASMCs, Human umbilical artery smooth muscle cells.

BASP1 inhibition enhanced cell proliferation and suppressed apoptosis in ox-LDL-induced HUASMCs

To investigate the role of BASP1 in AS, we inhibited BASP1 expression by stably introducing siRNA in HUASMCs. Western blot analysis confirmed that exposure to ox-LDL induced BASP1 expression in HUASMCs, whereas siRNA-mediated knockdown effectively suppressed BASP1 expression (**Figure 2A**). The CCK-8 assay showed that BASP1 knockdown remarkably restored the ox-LDL-induced reduction in cell viability (**Figure 2B**). Additionally, the EDU assay further demonstrated that ox-LDL suppressed cell proliferation, as evidenced by a decreased rate of EDU-positive cells. However, BASP1 silencing notably reversed this inhibitory effect and restored the proliferative capacity of HUASMCs (**Figure 2C**, **2D**). Flow cytometry analysis revealed that ox-LDL stimulation notably promoted HUASMC apoptosis, which was markedly attenuated by BASP1 silencing (**Figure 2E**).

BASP1 inhibition mitigated ox-LDL-induced inflammation and adhesion molecule expression

To investigate the inflammatory response triggered by ox-LDL, we examined the role of BASP1 in regulating inflammation. ELISA results revealed a significant increase in the concentrations of pro-inflammatory cytokines - TNF-α, IL-1β, and IL-6 - in ox-LDL-exposed HUASMCs. Notably, BASP1 knockdown reversed this cytokine surge (**Figure 3A-C**). In parallel, Western blotting showed upregulation of adhesion molecules such as VCAM-1 and ICAM-1 in ox-LDL-treated HUASMCs. However, BASP1 knockdown effectively suppressed this molecular response (**Figure 3D-F**).

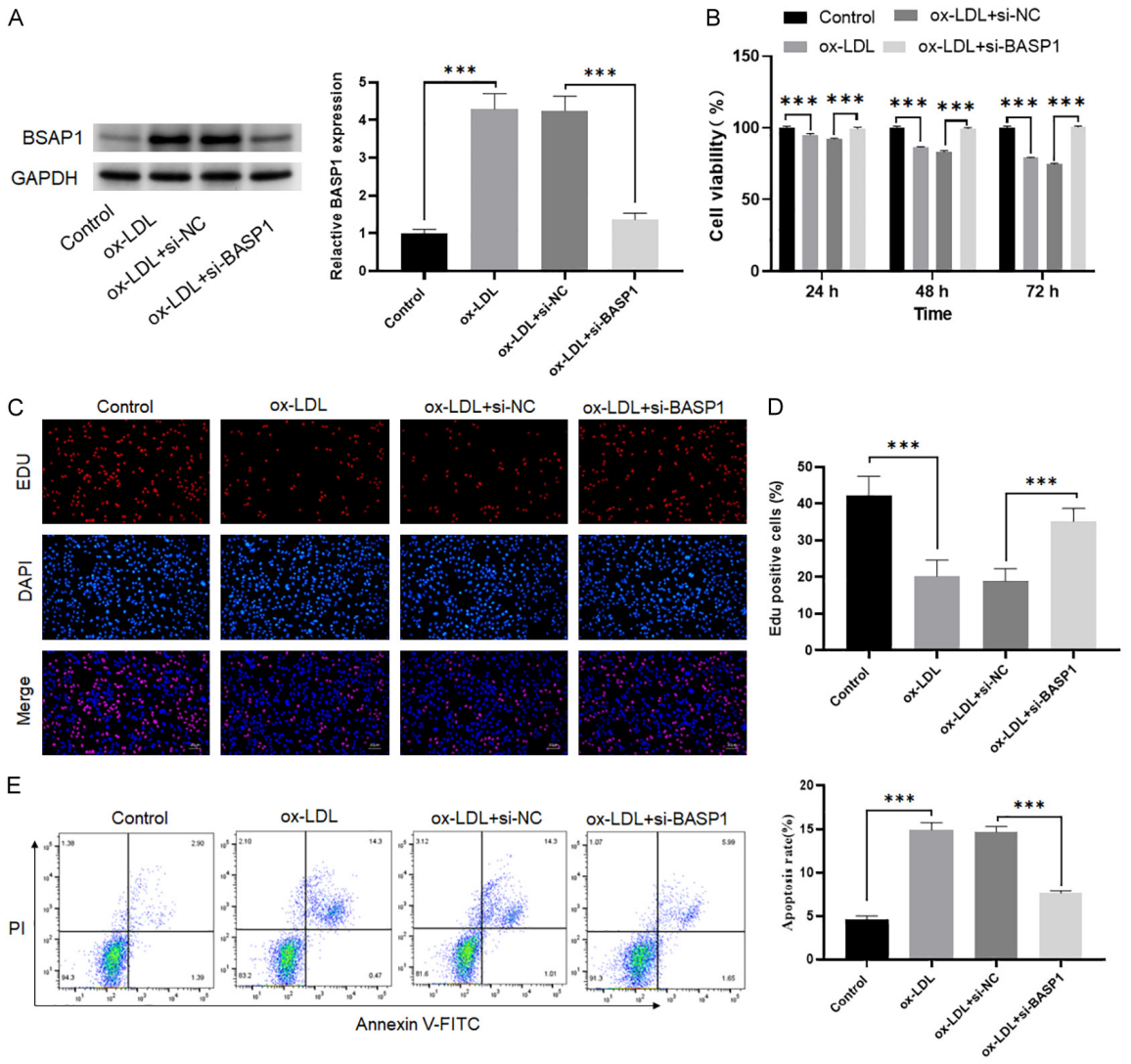

Figure 2. BASP1 knockdown promoted proliferation and alleviated apoptosis in ox-LDL-induced HUASMCs. A. Western blot assays of BASP1 expression in HUASMCs. B. CCK-8 assays showing the effect of BASP1 knockdown on HUASMC proliferation. C and D. EdU assay evaluating the effect of BASP1 knockdown on the percentage of EdU-positive cells. Scale Bar = 20 μm; Magnification: 500×. E. Flow cytometry analysis showing the effect of BASP1 knockdown on HUASMC apoptosis. ***P<0.001. Notes: ox-LDL, oxidized low-density lipoprotein; HUASMCs, Human umbilical artery smooth muscle cells.

miR-185-5p overexpression enhanced cell proliferation and suppressed apoptosis in ox-LDL-induced HUASMCs

To explore the potential role of miR-185-5p in AS pathogenesis, we established a stable miR-185-5p-overexpressing HUASMC mode by transfecting the cells with synthetic mimics. qPCR analysis showed that ox-LDL stimulation reduced miR-185-5p expression, while transfection with miR-185-5p mimics effectively increased its expression (**Figure 4A**). Functional assays were performed to evaluate the impact of this change on cell viability and proliferation. The CCK-8 assay showed that miR-185-5p overexpression completely reversed that the ox-LDL-induced decrease in cell viability, effectively restoring cell function (**Figure 4B**). Consistent with the CCK-8 results, the EDU assay demonstrated that miR-185-5p overexpression rescued the ox-LDL-induced suppression of cell proliferation, significantly increasing the number of EDU-positive cells (**Figure 4C**, **4D**). Furthermore, the ox-LDL-induced increase in apoptosis was remarkably suppressed by transfection with miR-185-5p mimics (**Figure 4E**).

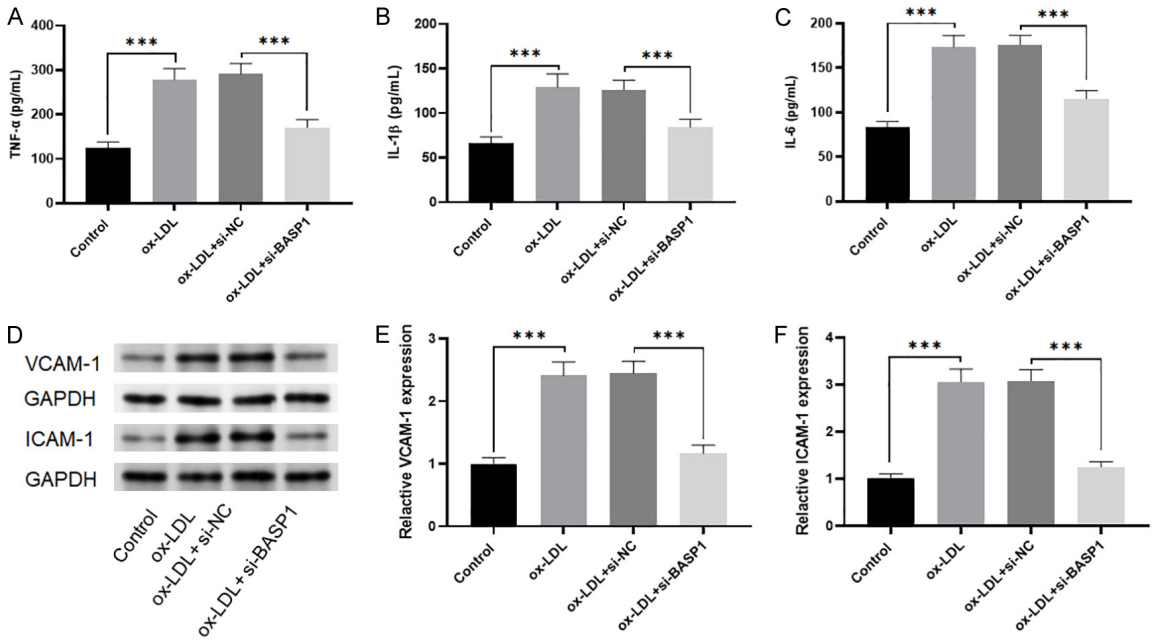

Figure 3. BASP1 knockdown alleviated inflammation and adhesion molecule expression in ox-LDL-induced HUASMCs. A-C. EILSA analysis showing the effect of BASP1 knockdown on TNF-α, IL-1β and IL-6 production in HUASMCs. D-F. Western blotting analysis showing the effect of BASP1 knockdown on VCAM-1 and ICAM-1 expression in HUASMCs. ***P<0.001. Notes: ox-LDL, oxidized low-density lipoprotein; HUASMCs, Human umbilical artery smooth muscle cells.

miR-185-5p overexpression mitigated ox-LDL-induced inflammation and adhesion molecule expression

We next examined the effects of miR-185-5p overexpression on inflammation and adhesion molecule expression in ox-LDL-induced HUASMCs. ELISA quantification revealed significantly elevated concentrations of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) in ox-LDL-exposed HUASMCs, which were effectively counteracted by miR-185-5p mimic transfection (**Figure 5A-C**). In parallel, WB showed upregulation of adhesion molecules (VCAM-1 and ICAM-1) in ox-LDL-treated cells, while miR-185-5p overexpression significantly attenuated this molecular response (**Figure 5D-F**).

BASP1 abrogated miR-185-5p overexpression-mediated HUASMC proliferation, apoptosis, inflammation, and adhesion molecule expression

To verify whether BASP1 is a functional target of miR-185-5p, we performed a rescue assay. Transfection with miR-185-5p mimic successfully suppressed BASP1 expression, and this suppression was reversed by co-transfection of OE-BASP1 (**Figure 6A**). CCK-8 assay demonstrated that miR-185-5p mimic enhanced cell proliferation, whereas co-transfection with OE-BASP1 significantly attenuated this pro-proliferative effect (**Figure 6B**). BASP1 overexpression also remarkably attenuated the anti-apoptosis effects of miR-185-5p mimic in ox-LDL-induced HUASMCs (**Figure 6C**). Western blotting further demonstrated that miR-185-5p mimics upregulated the anti-apoptotic protein Bcl-2 and downregulated the pro-apoptotic proteins Bax and caspase-3. Importantly, these effects were largely reversed by co-expression of OE-BASP1 (**Figure 6D**, **6E**). Furthermore, BASP1 overexpression reversed the suppression of TNF-α, IL-1β, and IL-6 production induced by miR-185-5p mimics in ox-LDL-treated HUASMCs (**Figure 6F-H**). Consistent with the inflammatory results, the miR-185-5p mimic-induced downregulation of adhesion molecules (VCAM-1 and ICAM-1) was effectively counteracted by OE-BASP1 overexpression (**Figure 6I**).

Discussion

The study elucidated a critical regulatory axis involving BASP1 and miR-185-5p in modulating HUASMC dysfunction during AS progres-

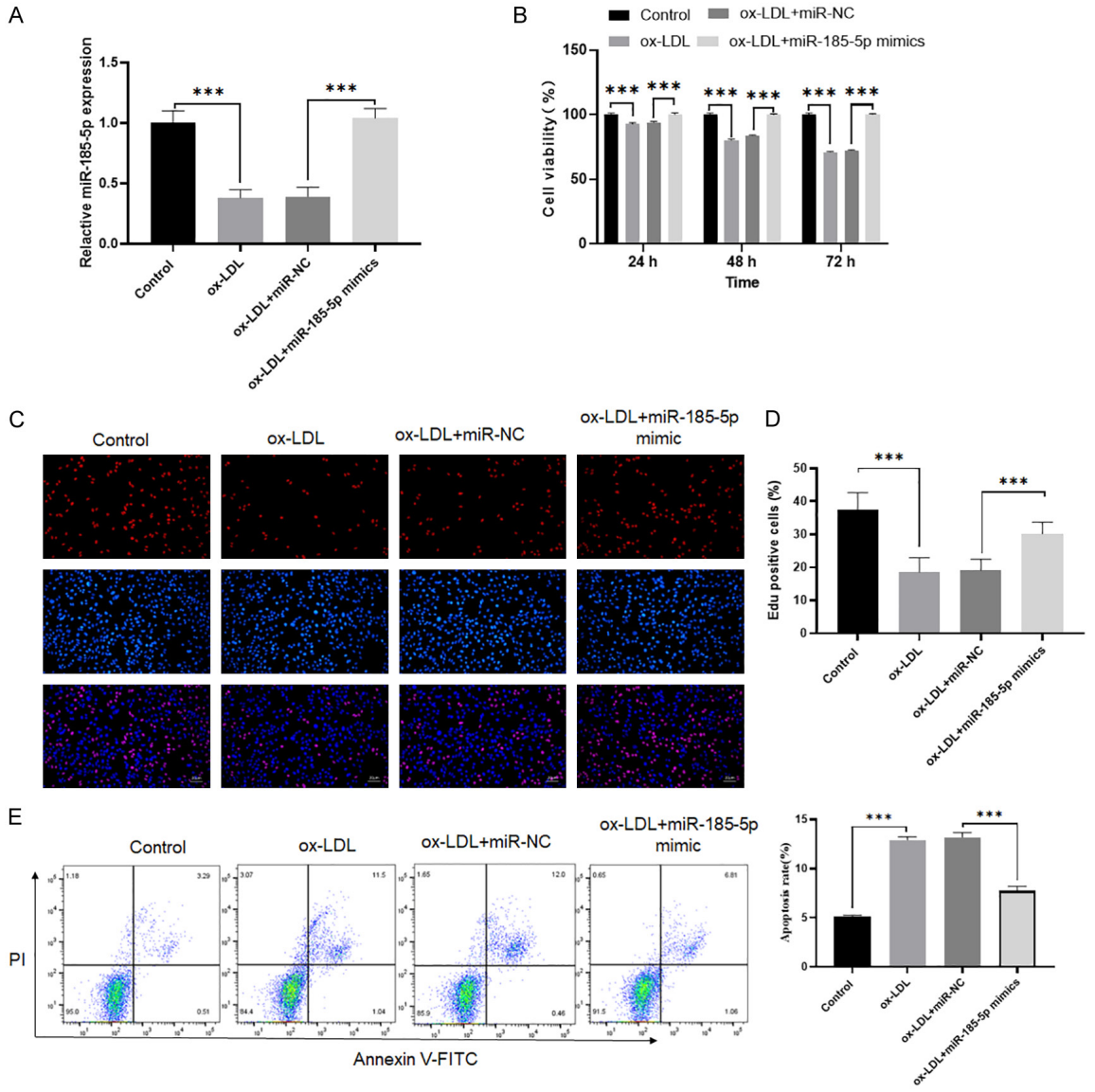

Figure 4. miR-185 overexpression promoted proliferation and alleviated apoptosis in ox-LDL-induced HUASMCs. A. qRT-PCR assays of miR-185-5p expression in HUASMCs. B. CCK-8 assays showing the effect of miR-185-5p overexpression on HUASMC proliferation. C and D. EdU assay evaluating the effect of miR-185-5p overexpression on the proportion of EdU-positive cells. Scale Bar = 20 μm; Magnification: 500×. E. Flow cytometry analysis showing the effect of miR-185-5p overexpression on HUASMC apoptosis. ***P<0.001. Notes: ox-LDL, oxidized low-density lipoprotein; HUASMCs, Human umbilical artery smooth muscle cells.

sion. Through a combination of in vitro experiments, we found that BASP1 was significantly upregulated in the serum of AS patients and dose-dependently increased in ox-LDL-treated HUASMCs. Conversely, miR-185-5p expression was notably downregulated in both AS patient serum and ox-LDL-treated HUASMCs. Mechanistically, we found that BASP1 was a direct target of miR-185-5p. This interaction exacerbated the pathological effects of ox-LDL, including increased apoptosis, inflammation, and adhesion molecule expression in HUASMCs.

BASP1 expression levels have been associated with various disease states, including ischemic stroke, essential hypertension, and multiple sclerosis. For example, BASP1 expression correlates with endothelial dysfunction and angiogenesis in cardiovascular diseases [9-11]. BSAP1, regulated by miR-7a-5p, promotes

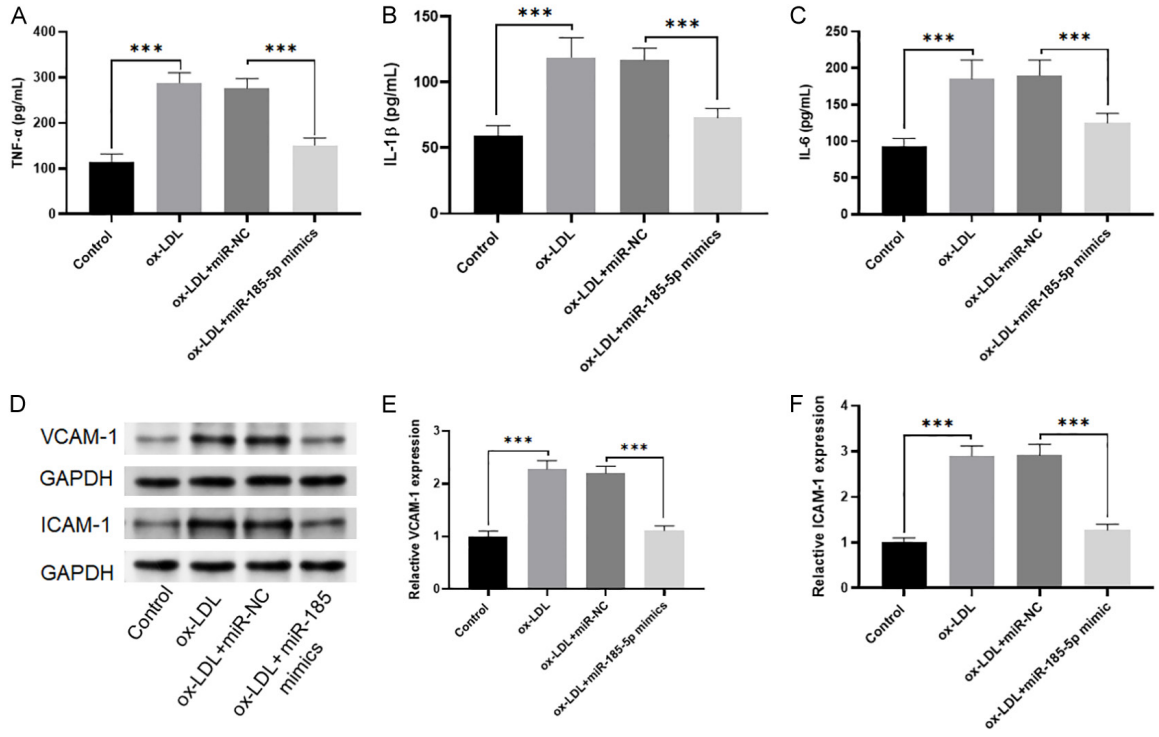

Figure 5. miR-185 overexpression alleviated inflammation and adhesion molecule expression in ox-LDL-induced HUASMCs. A-C. EILSA analysis showing the effects of miR-185-5p overexpression on TNF-α, IL-1β and IL-6 production in HUASMCs. D-F. Western blotting analysis showing the effects of miR-185-5p overexpression on VCAM-1 and ICAM-1 expression in HUASMCs. ***P<0.001. Notes: ox-LDL, oxidized low-density lipoprotein; HUASMCs, Human umbilical artery smooth muscle cells.

apoptosis in myocardial ischemia/reperfusion injury [12]. These findings suggest that BASP1 may play an important role in cardiovascular diseases, not limited to AS. From a mechanistic perspective, BASP1 silencing enhanced proliferation and reduced apoptosis in VSMCs [13, 14], providing a novel explanation for its role in AS. In our study, BASP1 inhibition significantly restored the proliferative capacity and apoptosis ratio of ox-LDL-treated HUASMCs. This suggests that BASP1 may play dual pro-apoptotic and anti-proliferative roles in AS pathology. In addition, BASP1 silencing significantly reduced the expression of pro-inflammatory cytokines (TNF-α, IL-1β, and IL-6) and the expression of adhesion molecules (VCAM-1 and ICAM-1), which are known to contribute to the inflammatory process and promote atherogenesis [15, 16].

Additionally, we confirmed direct binding between BASP1 and miR-185-5p, which aligns with emerging evidence suggesting that BASP1 acts as a target protein responsive to miRNA modulation in cardiovascular diseases [17]. For example, miR-185-5p has been shown to alleviate inflammation and VSMC apoptosis by interacting with PIK3R2 in vascular remodeling [18]. Upregulation of miR-185-5p inhibits VSMC apoptosis and inflammatory cytokine production by targeting ADCY7 in abdominal aortic aneurysm formation [19]. MiR-185-5p plays an important regulatory role in AS development. Several studies have shown that miR-185 modulates cholesterol metabolism, lipid uptake, inflammation, and cell proliferation by targeting key genes, such as SREBP2, STIM1, and IRS-1, thus affecting the pathological process of AS [20]. For example, miR-185 reduces cholesterol synthesis and endogenous LDL production by inhibiting SREBP2 expression, which in turn reduces atherosclerotic plaque formation [21]. In addition, downregulation of miR-185 promotes VSMC proliferation, migration, and an inflammatory response, accelerating AS progression [8]. These results suggest that miR-185 may be protective by inhibiting inflammatory responses and cell proliferation, thereby delaying the development of atherosclerosis. Our data revealed that miR-185-5p overex-

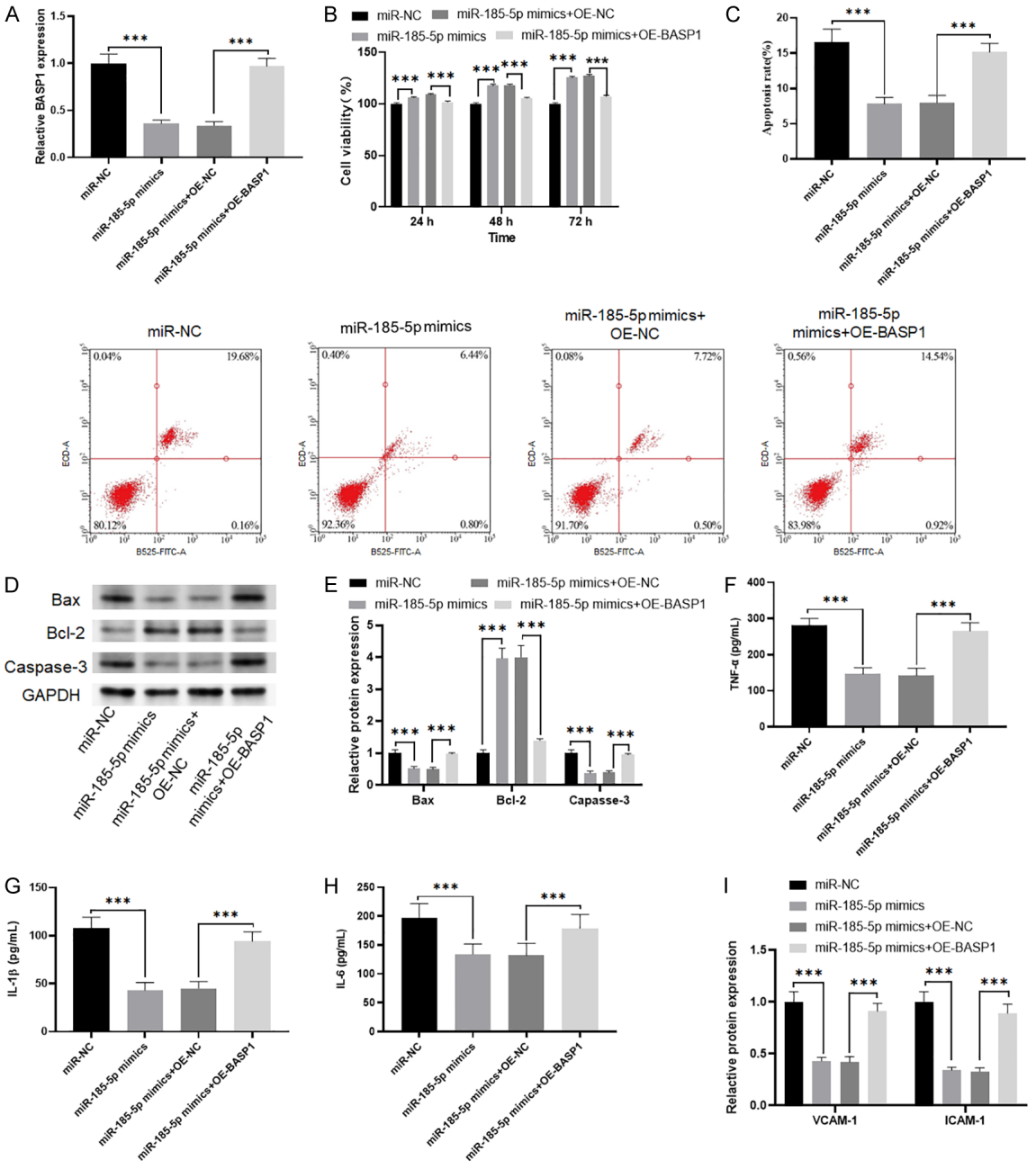

Figure 6. miR-185-5p alleviated proliferation, apoptosis, inflammation and adhesion molecule expression in ox-LDL-induced HUASMCs by inhibition BASP1. A. qRT-PCR analysis of BASP1 expression in HUASMCs overexpressing miR-185-5p. B. CCK-8 assays showing the effect of BASP1 overexpression on the proliferation of miR-185-5p-overexpressing HUASMCs. C. Flow cytometry analysis showing the effect of BASP1 overexpression on the apoptosis rate of miR-185-5p-overexpressing HUASMCs. D, E. Western blotting analysis showing the effects of BASP1 overexpression on the expression of Bcl-2, Bax, and caspase-3 in miR-185-5p-overexpressing HUASMCs. F-H. EILSA analysis showing the effects of BASP1 overexpression on TNF-α, IL-1β and IL-6 production in miR-185-5p-overexpressing HUASMCs. I. qRT-PCR analysis showing the effects of BASP1 overexpression on VCAM-1 and ICAM-1 expression in miR-185-5p-overexpressing HUASMCs. ***P<0.001. Notes: ox-LDL, oxidized low-density lipoprotein; HUASMCs, Human umbilical artery smooth muscle cells.

pression ameliorated ox-LDL-induced HUASMC apoptosis and restored proliferative capacity, effects similar to those observed with BASP1 inhibition. Additionally, when BASP1 expression was restored via overexpression plasmid, the functional improvements observed with miR-

185-5p overexpression were reversed, further supporting a direct, causal link between BASP1 and miR-185-5p. While these in vitro models provide valuable mechanistic insights, the next critical step is to validate these findings in animal models and eventually in human atherosclerotic plaques. Furthermore, expanding the clinical cohort would enhance our understanding of how the levels of miR-185-5p and BASP1 correlate with the severity of AS in patients.

Conclusion

The findings from this study highlight BASP1 as a significant pathogenic protein that exacerbates AS by acting as a molecular antagonist to miR-185-5p. This interaction triggers a cascade of downstream cellular events, including the acceleration of VSMC apoptosis, the amplification of local inflammatory responses, and the overexpression of various adhesion molecules. From a therapeutic perspective, targeting the miR-185-5p/BASP1 axis presents a promising and novel approach to potentially slowing or mitigating the pathological vascular remodeling that drives AS progression.

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Disclosure of conflict of interest

None.

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References

[1] Khyzha N, Alizada A, Wilson MD and Fish JE. Epigenetics of atherosclerosis: emerging mechanisms and methods. Trends Mol Med 2017; 23: 332-347.

[2] Shan K, Jiang Q, Wang XQ, Wang YN, Yang H, Yao MD, Liu C, Li XM, Yao J, Liu B, Zhang YY, J Y and Yan B. Role of long non-coding RNA-RNCR3 in atherosclerosis-related vascular dysfunction. Cell Death Dis 2016; 7: e2248.

[3] Xi X, Zheng X, Zhang R and Zeng L. Upregulation of circFOXP1 attenuates inflammation and apoptosis induced by ox-LDL in human umbilical vein endothelial cells by regulating the miR-185-5p/BCL-2 axis. Can J Physiol Pharmacol 2022; [Epub ahead of print].

[4] Dou Y, Chen Y, Zhang X, Xu X, Chen Y, Guo J, Zhang D, Wang R, Li X and Zhang J. Non-proinflammatory and responsive nanoplatforms for targeted treatment of atherosclerosis. Biomaterials 2017; 143: 93-108.

[5] Yuan L, Wang D and Zhou Z. LINC00452 overexpression reverses oxLDL-induced injury of human umbilical vein endothelial cells (HUVECs) via regulating miR-194-5p/IGF1R axis. Front Cardiovasc Med 2022; 9: 975640.

[6] Tian Z, Li W, Wang J and Li S. WTAP-mediated m6A modification on BASP1 mRNA contributes to ferroptosis in AAA. Gen Thorac Cardiovasc Surg 2025; 73: 665-674.

[7] Krol J, Loedige I and Filipowicz W. The widespread regulation of microRNA biogenesis, function and decay. Nat Rev Genet 2010; 11: 597-610.

[8] Fang M, Li Y, Wu Y, Ning Z, Wang X and Li X. miR-185 silencing promotes the progression of atherosclerosis via targeting stromal interaction molecule 1. Cell Cycle 2019; 18: 682-695.

[9] Sun F, Liu J, Wang Y, Yang H, Song D, Fu H and Feng X. BASP1 promotes high glucose-induced endothelial apoptosis in diabetes via activation of EGFR signaling. J Diabetes Investig 2023; 14: 535-547.

[10] Khajavi M, Zhou Y, Schiffer AJ, Bazinet L, Birsner AE, Zon L and D'Amato RJ. Identification of Basp1 as a novel angiogenesis-regulating gene by multi-model system studies. FASEB J 2021; 35: e21404.

[11] Pan X, Li X, Dong L, Liu T, Zhang M, Zhang L, Zhang X, Huang L, Shi W, Sun H, Fang Z, Sun J, Huang Y, Shao H, Wang Y and Yin M. Tumour vasculature at single-cell resolution. Nature 2024; 632: 429-436.

[12] Zi C, Zhu Y, Ma X and Wei Y. BASP1/HTRA2 axis, targeted by miR-7a-5p, exerted a pro-apoptosis role in myocardial ischemia/reperfusion injury. Toxicol Appl Pharmacol 2025; 502: 117437.

[13] Tian Z, Sun Y, Sun X, Wang J and Jiang T. LINC00473 inhibits vascular smooth muscle cell viability to promote aneurysm formation via miR-212-5p/BASP1 axis. Eur J Pharmacol 2020; 873: 172935.

[14] Santiago FS, Li Y, Zhong L, Raftery MJ, Lins L and Khachigian LM. Truncated YY1 interacts with BASP1 through a 339KLK341 motif in YY1 and suppresses vascular smooth muscle cell growth and intimal hyperplasia after vascular injury. Cardiovasc Res 2021; 117: 2395-2406.

[15] Ling S, Nheu L and Komesaroff PA. Cell adhesion molecules as pharmaceutical target in atherosclerosis. Mini Rev Med Chem 2012; 12: 175-83.
[16] Chistiakov DA, Melnichenko AA, Grechko AV, Myasoedova VA and Orekhov AN. Potential of anti-inflammatory agents for treatment of atherosclerosis. Exp Mol Pathol 2018; 104: 114-124.
[17] You L, Zheng Y, Yang J, Hou Q, Wang L, Zhang Y, Zhao C and Xie R. LncRNA MDRL mitigates atherosclerosis through miR-361/SQSTM1/NLRP3 signaling. Mediators Inflamm 2022; 2022: 5463505.
[18] Yan Y, Wu Q, Li JH, Wei X, Xiao J, Yang L, Xie A, Zhang L, Mei WJ, Yang YJ, Zeng Y, Wen D, Deng LJ and Zheng LF. Chitosan inhibits vascular intimal hyperplasia via LINC01615/MIR-185-5p/PIK3R2 signaling pathway. Gene 2024; 892: 147850.
[19] Wang Y, Zhai S, Xing J, He Y and Li T. LncRNA GAS5 promotes abdominal aortic aneurysm formation through regulating the miR-185-5p/ADCY7 axis. Anticancer Drugs 2022; 33: 225-234.
[20] Rotllan N, Price N, Pati P, Goedeke L and Fernández-Hernando C. microRNAs in lipoprotein metabolism and cardiometabolic disorders. Atherosclerosis 2016; 246: 352-60.
[21] Tan W, Wang G, Liu G, You D, Wei M, Jin X, Zhao W and Zheng M. The elevation of miR-185-5p alleviates high-fat diet-induced atherosclerosis and lipid accumulation in vivo and in vitro via SREBP2 activation. Aging (Albany NY) 2022; 14: 1729-1742.