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Research article

miR-379-3p inhibits fat grafting survival and angiogenesis by targeting SOCS1-mediated adipose inflammation☆

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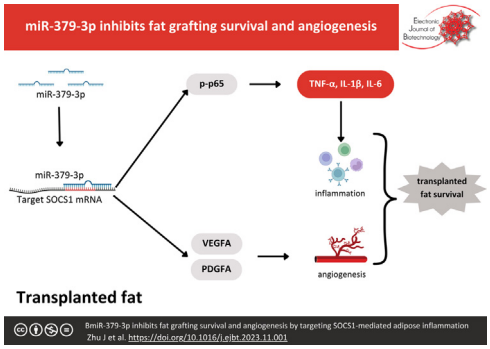
GRAPHICAL ABSTRACT



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ABSTRACT

Background: This research probed the relevant mechanism of miR-379-3p by regulating suppressor of cytokine signaling1 (SOCS1) in the processes of inflammation, oxidative stress, and angiogenesis in fat grafting. An increasing body of research indicates the involvement of miRNA/mRNA pathways in the process of fat transplantation, yet the underlying molecular mechanisms remain to be fully elucidated.
Results: miR-379-3p knockdown improved the survival rate of adipocytes, promoted adipose tissue angiogenesis, and reduced inflammation and oxidative stress levels. miR-379-3p targeted SOCS1. SOCS1 upregulation improved adipose tissue survival and angiogenesis and reduced inflammation. miR-379-3p affected adipose tissue survival, angiogenesis, and inflammation by targeting SOCS1 expression.
Conclusions: miR-379-3p inhibits fat grafting survival and angiogenesis by targeting SOCS1 to mediate adipose inflammation, suffering a novel way to improve fat grafting technique development.
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1. Introduction

Fat grafting is a commonly used procedure in which adipose tissue is transferred from one part of the body to another by processing and direct injection [1]. The transplanted graft is living tissue and contains stem cells that have tissue-regenerating properties.

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The main concern with this technique is long-term graft survival and retention. Over the past decades, each step of fat grafting process is continuously optimized to maximize graft survival [2]. Adipose tissue grafts are easy to obtain and have low morbidity, so they can be used as biological scaffolds. And the vasculature of adipose tissue includes a major niche where pluripotent progenitor cells generate new adipocytes that are necessary for tissue repair [3]. Fat grafts can be properly centrifuged and can reliably produce purified fat and adipose-derived stem cells with concentrated growth factors, all of which contribute to improved graft survival [4]. The survival of the fat graft depends on its contact with the recipient site for imbibition and neovascularization, so the fat graft needs to be evenly distributed [5].

A complex and intricate relationship exists between inflammation and angiogenesis in adipose tissue transplantation [6]. Inflammation typically emerges in the initial stages following the transplantation procedure, precipitated by the surgical trauma and ischemic conditions encountered during the process, eliciting a natural immune response. This inflammatory reaction, when moderate, can be instrumental in promoting angiogenesis within the transplanted adipose tissue [7]. Angiogenesis, the formation of new blood vessels, not only facilitates the integration and survival of the transplanted fat but also tempers the inflammatory response, establishing a delicate balance pivotal for successful transplantation outcomes [8]. However, the balance can be jeopardized. Excessive or prolonged inflammation can be deleterious, inflicting damage to both the transplanted adipose tissue and nascent blood vessels, consequently diminishing the success rate of the transplantation [9]. Thus, mitigating the intensity of inflammation emerges as a strategy to bolster angiogenesis. Angiogenesis relies on pro-angiogenic and anti-angiogenic molecules to regulate endothelial cell activities. Well-regulated angiogenesis is a key in many physiological conditions such as reproduction [10]. Notably, studies have mentioned and validated the significance of angiogenesis to improve fat graft survival [11,12,13].

miRNAs are small non-coding RNAs that regulate gene expression by recognizing homologous sequences and interfering with transcription, translation, or epigenetic processes [14]. The target of miRNA in endothelial cells and angiogenesis signals is relatively clear, and miRNAs not only regulate transcripts in situ but also influence distal angiogenesis as paracrine mediators [15]. miR-379-3p has been concerned to regulate adipose deposition [16]. However, not much is known as to its mediation in grafting survival and angiogenesis. This research, based on the bioinformatics analysis, focused on suppressor of cytokine signaling1 (SOCS1) as an interesting target of miR-379-3p. SOCS1, a protein that functions as a negative regulator of cytokine signaling, is a potent and multifaceted regulator of cytokines and inflammation [17,18].

Therefore, this research probed the relevant mechanism of miR-379-3p by regulating SOCS1 in the processes of inflammation, oxidative stress, and angiogenesis, thereby investigating novel targets to improve grafting survival.

2. Materials and methods

2.1. Establishment of fat grafting model

This study was approved by the Animal Ethics Committee of Plastic Surgery Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College. Thirty adult male Sprague-Dawley rats (210 ± 20 g) with specific pathogen-free grade, purchased from Hunan SJA Co., LTD., were kept in standard laboratory conditions and had food and water supply. The fat grafting model was established in rats after one week of adaptive feeding. In brief, under the condition of sodium pentobarbital anesthesia (30 mg/kg), a 2.5 cm incision was made at the inguinal fold to obtain about 50 mg of inguinal fat, followed by a 1 cm incision on the back of the shoulder blade to place the fat pad. Finally, the incisions were sutured and treated with antibiotics. To evaluate the effects of miR-379-3p and SOCS1 on fat grafting, miR-379-3p antagomir (100 nmol/kg for 3 d), antagomir NC, sh-SOCS1 lentiviral vector (5×10^8 PFU), sh-NC lentiviral vector, SOCS1-overexpressing lentiviral vector (oe-SOCS1, 5×10^8 PFU/rat), and negative control (oe-NC) were injected into rats by caudal vein. Antagomir was purchased from RiboBio (Guangzhou, China), and lentivirus vectors were from Clontech. After 28 d of grafting, the rats were euthanized and the transplanted adipose tissue was collected and fixed with 4% paraformaldehyde or preserved at −80°C.

2.2. Hematoxylin and eosin (HE) staining

Paraformaldehyde-fixed adipose tissue was paraffin-embedded and cut into 4-micron sections using a microtome (Leica SM2000R, Germany). It was then stained with hematoxylin-eosin and analyzed by optical microscope (Nikon E200) at × 400.

2.3. Enzyme-linked immunosorbent assay (ELISA)

As requested by the manufacturer, tumor necrosis factor (TNF)-α, interleukin (IL)-1β, and IL-6 in adipose tissue were assessed by ELISA kits (Multisciences (Lianke) Biotech, Co., Ltd., China).

2.4. Oxidative stress level detection

Malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione peroxidase (GSH-Px) in adipose tissue were detected using commercial kits (Nanjing Jiancheng Bioengineering Institute, China).

2.5. Reverse transcription quantitative real-time polymerase chain reaction (RT-qPCR)

Total RNA was collected using TRIzol (Invitrogen), and then, complementary DNA was prepared from the collected RNA by reverse transcription using PrimeScript RT Kits (Invitrogen). This work utilized the Mx3000P real-time PCR system (Thermo Fisher) for RT-qPCR using SYBR Green SuperMix (Roche, Basel, Switzerland). Genes were then analyzed using $2^{-\Delta\Delta Ct}$ and their expression was normalized to glyceraldehyde-3-phosphate dehydrogenase (GAPDH) and U6, respectively. All primers are listed in Table 1.

2.6. Western blot

After extracting total proteins using radio-immunoprecipitation assay (RIPA) buffer (Beyotime, China), concentration quantification was performed using a bicinchoninic acid kit. Thirty micrograms of protein were subjected to 10% sodium dodecyl sulfate–polyacrylamide gel electrophoresis and electroblotted onto a polyvinylidene fluoride membrane by wet transfer method. After sealing the membrane with 5% skim milk powder for 1h, the primary antibody was incubated overnight, and the secondary antibody labeled by horseradish peroxidase was re-detected for 1 h. The membrane was covered on a clean glass plate, followed by visualization using an enhanced chemiluminescence detection kit (BB-3501, Amersham, Little Chalfont, UK) and quantification using Bio-Rad image analysis system with Quantity One v4.6.2 software. Primary antibody information: GAPDH (2118, Cell Signaling Technology), p-p65 (3031, Cell Signaling Technology), vascular endothelial growth factor A (VEGFA; ab46154, Abcam), Platelet-derived growth factor subunit A (PDGFA, sc-9974, Santa Cruz Biotechnology).

Table 1
Primers used in PCR.

Genes	Primers (5′–3′)
microRNA-379-3p	Forward: 5′-GCGCTATGTAACATGGTCCA-3′ Reverse: 5′-TGGTGTCGTGGAGTCG-3′
SOCS1	Forward: 5′-CCGACAATGCAGTCTCCACA -3′ Reverse: 5′-AGGCCATCTTCACGCTAAGG-3′
PPARγ	Forward: 5′-TTCGCTGATGCACTGCCTAT-3′ Reverse: 5′-GTCAGCTCTTGTGAACGGGA-3′
C/EBPα	Forward: 5′-GGCCAAGAAGTCGGTGGATA-3′ Reverse: 5′-CGTTGCGCTGTTTGGCTTTA-3′
FABP4	Forward: 5′-AGAAGTGGGAGTTGGCTTCG-3′ Reverse: 5′-ACTCTCTGACCGGATGACGA-3′
GAPDH	Forward: 5′-CACCCACTCCTCCACCTTTG-3′ Reverse: 5′-CCACCACCCTGTTGCTGTAG −3′
U6	Forward: 5′-CTCGCTTCGGCAGCACA-3′ Reverse: 5′-AACGCTTCACGAATTTGCGT-3′

Note: SOCS1: Suppressor of cytokine signaling1; PPARγ: Peroxisome proliferator-activated receptor gamma; C/EBPα: CCAAT/enhancer binding protein alpha; FABP4: Fatty acid binding protein 4; GAPDH: glyceraldehyde-3-phosphate dehydrogenase.

2.7. Immunohistochemistry (IHC)

After paraformaldehyde fixation, the adipose tissue section thickness was 4 μm after embedding. Slides were then soaked in 100%, 95%, 85%, and 75% alcohol, rinsed with double distilled water, plugged with serum from phosphate buffer saline with 0.05% Tween-20 (PBST) buffers, and incubated overnight with primary antibody CD31 (ab28364, Abcam). After rinsing with PBST buffer, the secondary antibody (Dako Glostrup, Denmark) coupled with horseradish peroxidase was again and finally encapsulated. The results were observed under a microscope, and the microvascular density was quantified.

2.8. Cell culture

Human umbilical vein endothelial cells (HUVECs) (ATCC, MD, USA) were stored in Dulbecco's modified Eagle medium (DMEM) supplemented with 10% fetal bovine serum and 1% penicillin–streptomycin antibiotics. The culture medium was changed every 2 to 3 d and maintained at 37°C in a humid atmosphere of 95% air and 5% CO_2.

2.9. Cell transfection

miR-379-3p mimic/inhibitor, mimic/inhibitor NC, pcDNA 3.1, pcDNA 3.1-SOCS1, si-NC, and si-SOCS1 were purchased from RiboBio. Lipofectamine 3000 (Invitrogen) was transiently transfected into HUVECs as requested by the manufacturer. The transfection efficiency was evaluated 48 h after transfection.

2.10. Tube formation test

HUVECs were suspended in DMEM supplemented with 2% fetal bovine serum and seeded on Matrigel-coated 96-well plates at 1.5×10^4 cells/well. Culture dishes were incubated at 37°C 5% CO_2 for 6 h. HUVECs were then stained with Calcein-AM solution (Yeason, Shanghai, China) and photographed under a fluorescence microscope (Carl Zeiss, Germany). The number of tubes was calculated using the ImageJ software.

2.11. Dual luciferase reporter experiment

Genepharma constructed PGL4 luciferase reporter vectors (Promega) containing SOCS1 wild-type sequences (with miR-379-3p binding site) and mutant-type sequences (with mutated binding site), respectively. The vectors (SOCS1-WT and SOCS1-MUT) and miR-379-3p mimic or mimic NC were co-transfected into HEK293 cell line using Lipofectamine 3000 (Invitrogen). Luciferase activity in co-transfected cells was examined 48 h after transfection using a dual luciferase assay system (Promega).

2.12. RNA immunoprecipitation (RIP) experiment

HEK293 cells were washed twice with PBS and lyzed with a RIPA lysis buffer containing a protease inhibitor mixture. The lysates were then incubated with magnetic beads conjugated with human anti-AgO2 antibody and normal rabbit immunoglobulin G controls. The beads were washed twice with 700 mM NaCl, and the RNA in the immunoprecipitate was isolated by TRIzol reagent (ThermoFisher Scientific, 15,596,018) and analyzed by RT-qPCR.

2.13. Data analysis

All experiments were performed independently at least 3 times. Statistical analysis was performed using GraphPad Prism 9.0 software. Data were expressed as mean ± standard deviation (SD) and conditioned to comparative study using independent sample t-test or one-way analysis of variance dependent on the number of groups involved. The difference of $p < 0.05$ was statistically significant.

3. Results

3.1. Silencing miR-379-3p improves fat grafting survival and angiogenesis and reduces inflammation

miR-379-3p antagomir was utilized to knock down miR-379-3p, aiming at exploring its effect on fat grafting survival (Fig. 1A). HE staining results observed that after knocking down miR-379-3p, there were more small fat cells, reduced vacuolation and higher integrity (Fig. 1B). ELISA results showed that knocking down miR-379-3p reduced the levels of inflammatory cytokines TNF-α, IL-1β, and IL-6 in adipose tissue (Fig. 1C). Subsequently, activation of the nuclear factor-kappaB (NF-κB) pathway was evaluated by Western blot. Knocking down miR-379-3p reduced the phosphorylation level of NF-κB (Fig. 1D). In addition, knocking down miR-379-3p also reduced MDA and activated SOD and GSH-PX activities (Fig. 1E). Then, adipose tissue angiogenesis was assessed. IHC staining showed that knocking down miR-379-3p significantly increased the positive rate of CD31 in adipose tissue (Fig. 1F) and Western blot measured that knocking down miR-379-3p increased the protein expression of angiogenesis-related proteins VEGFA and PDGFA (Fig. 1G). Subsequently, the effect of miR-379-3p on adipogenic genes was evaluated. Knockdown of miR-379-3p promoted peroxisome proliferator-activated receptor γ (PPARγ), CCAAT/enhancer binding protein alpha (C/EBPα), and fatty acid binding protein 4 (FABP4) mRNA expression (Fig. 1H). *In vitro* studies discovered that knocking down miR-379-3p can promote the formation of nodules of HUVECs (Fig. 1I). These data suggest that knocking down miR-379-3p can improve adipocyte survival, promote adipocyte angiogenesis, and reduce inflammation and oxidative stress levels.

3.2. Targeting miR-379-3p regulates SOCS1 expression

Subsequently, the bioinformatics website starbase predicted the potential binding sites of miR-379-3p and SOCS1 (Fig. 2A). Subsequently, this study examined whether miR-379-3p affects SOCS1 expression. Knocking down miR-379-3p increased SOCS1 protein expression in adipose tissue (Fig. 2B). Subsequently, the targeting relationship between miR-379-3p and SOCS1 was detected by dual luciferase reporting assay. WT-SOCS1 and miR-379-3p mimic

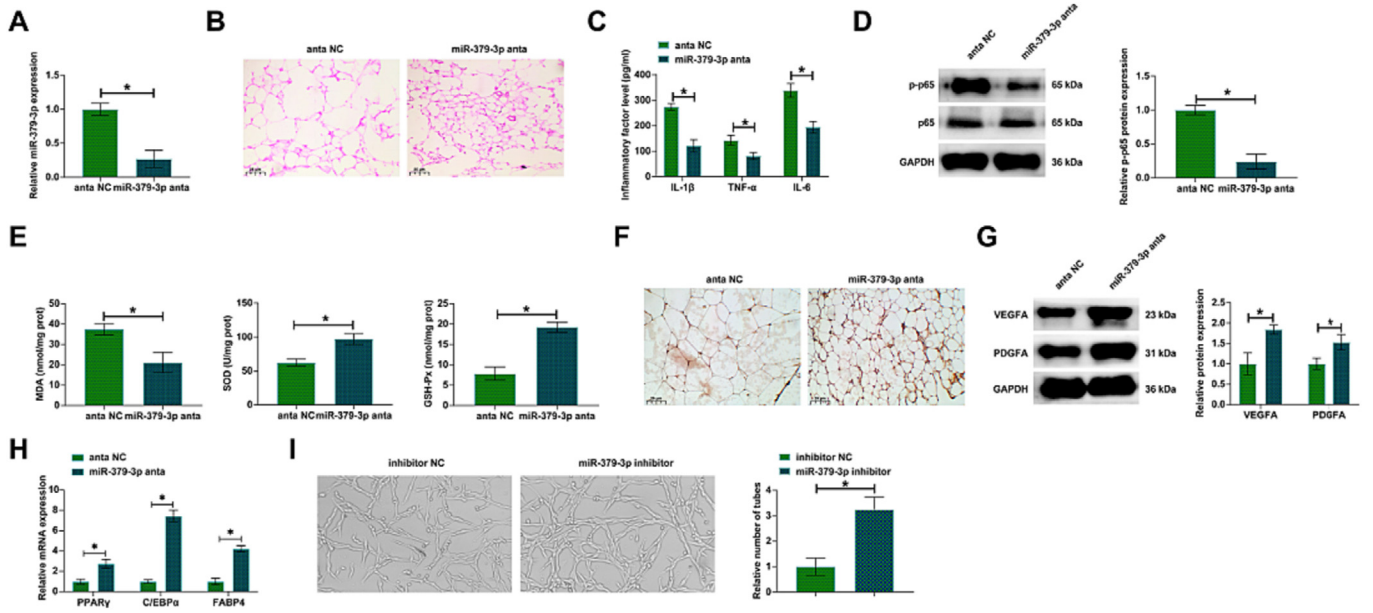

Fig. 1. miR-379-3p silencing improves fat grafting survival and angiogenesis and reduces inflammation. miR-379-3p antagomir was injected into rats receiving fat grafting. (A) RT-qPCR evaluation of miR-379-3p in adipose tissue. (B) HE staining evaluation of the pathological damage of adipose tissue. (C) ELISA analysis of TNF-α, IL-1β, and IL-6 in adipose tissue. (D) Western blot analysis of p-p65 phosphorylation. (E) Commercial kits measured MDA, SOD, and GSH-PX. (F) IHC staining measurement of the positive rate of CD31 in adipose tissue. (G) Western blot analysis of VEGFA and PDGFA in adipose tissue. (H) RT-qPCR evaluation of adipogenic genes PPARγ, C/EBPα, and FABP4 in adipose tissue. (I) Tube formation assay to evaluate the angiogenesis capacity of HUVECs; Data were expressed as mean ± SD (A-H, n = 5; I, N = 3). * $P < 0.05$.

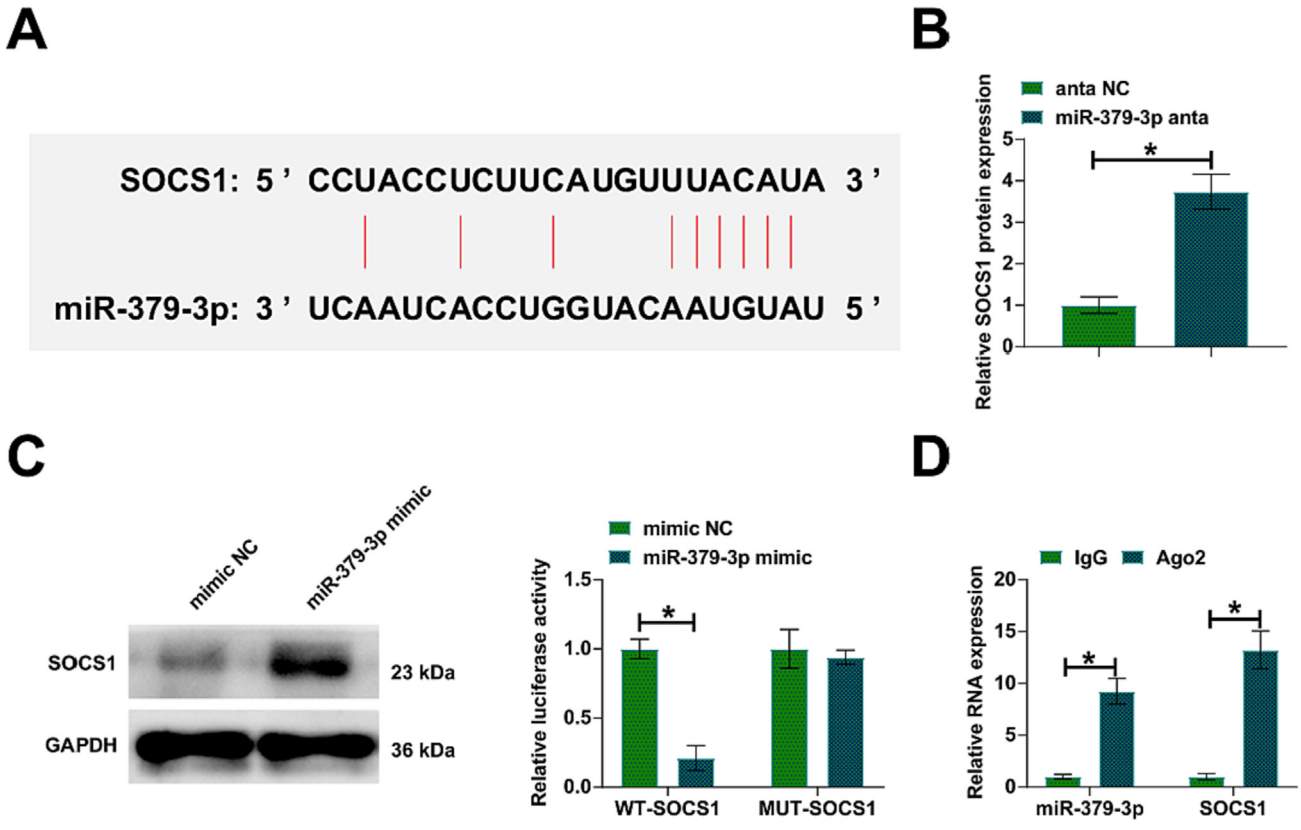

Fig. 2. SOCS1 expression is regulated by miR-379-3p. (A) Bioinformatics website starbase predicted the potential binding sites of miR-379-3p and SOCS1. (B) Western blot analysis of SOCS1 protein expression in adipose tissue. (C) Dual luciferase reporting assay results. (D) RIP experiment detected the targeting relationship between miR-379-3p and SOCS1; Data were expressed as mean ± SD (N = 3). * $P < 0.05$.

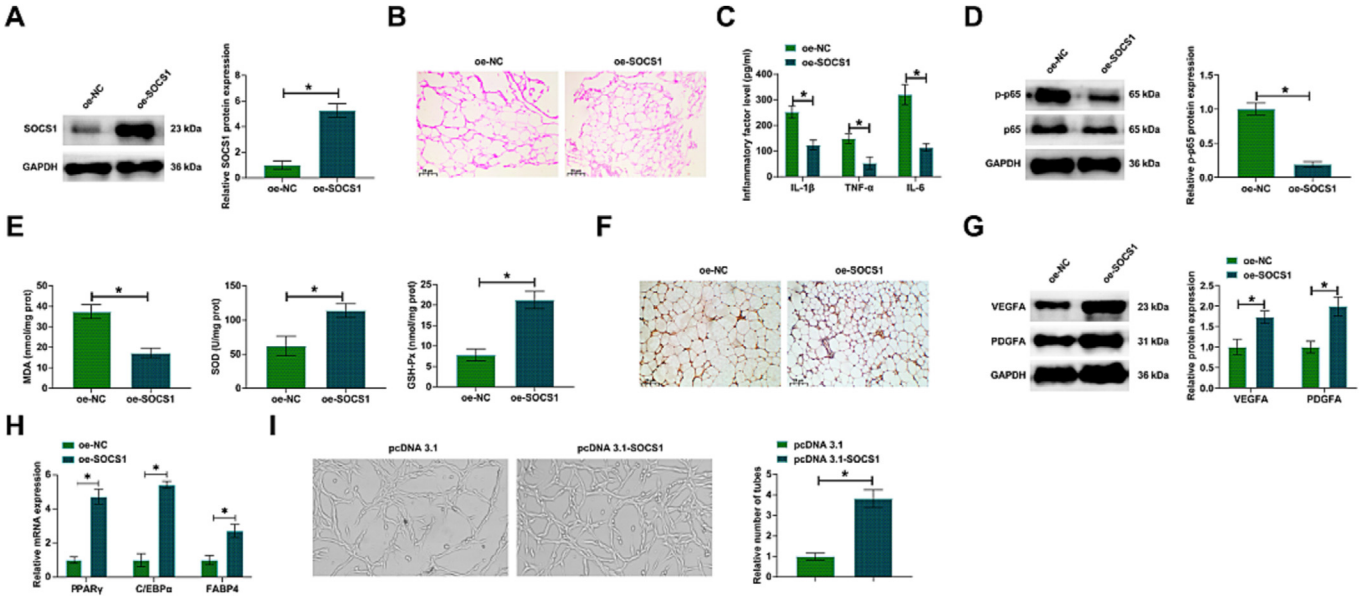

Fig. 3. Upregulating SOCS1 improves adipose tissue survival and angiogenesis and reduces inflammation. oe-SOCS1 lentivirus vectors were injected into rats receiving fat grafting. (A) Western blot analysis of SOCS1 protein expression in adipose tissue. (B) HE staining evaluation of the pathological damage of adipose tissue. (C) ELISA analysis of TNF-α, IL-1β, and IL-6 in adipose tissue. (D) Western blot analysis of p-p65 phosphorylation. (E) Commercial kits measured MDA, SOD, and GSH-PX. (F): IHC staining measurement of the positive rate of CD31 in adipose tissue. (G) Western blot analysis of VEGFA and PDGFA in adipose tissue. (H) RT-qPCR evaluation of adipogenic genes PPARγ, C/EBPα, and FABP4 in adipose tissue. (I) Tube formation assay to evaluate the angiogenesis capacity of HUVECs; Data were expressed as mean ± SD (A-H, n = 5; I, N = 3). * $P < 0.05$.

could reduce luciferase activity, but MUT-SOCS1 and miR-379-3p mimic did not affect luciferase activity (Fig. 2C). RIP experiments confirmed that SOCS1 and miR-379-3p were highly enriched in Ago2 magnetic beads (Fig. 2D). These data indicate that miR-379-3p regulates SOCS1 expression.

3.3. Upregulating SOCS1 improves adipose tissue survival and angiogenesis and reduces inflammation

Subsequently, oe-SOCS1 lentivirus vector was injected into rats. Injection of oe-SOCS1 successfully upregulated SOCS1 protein expression (Fig. 3A). HE staining showed that upregulatingSOCS1 could increase the generation of small and medium adipose cells in adipose tissue, reduce the phenomenon of adipose vacuolation and improve the integrity (Fig. 3B). Upregulating SOCS1 reduced inflammatory cytokines TNF-α, IL-1β, and IL-6 and decreased the phosphorylation of NF-κB (Fig. 3C, D). Upregulating SOCS1 also decreased MDA and activated SOD and GSH-PX in adipose tissue (Fig. 3E). Subsequently, the effect of SOCS1 overexpression on adipose tissue angiogenesis was evaluated. As determined, upregulating SOCS1 increased the positive rate of CD31 in adipose tissue (Fig. 3F) and promoted VEGFA and PDGFA protein expression

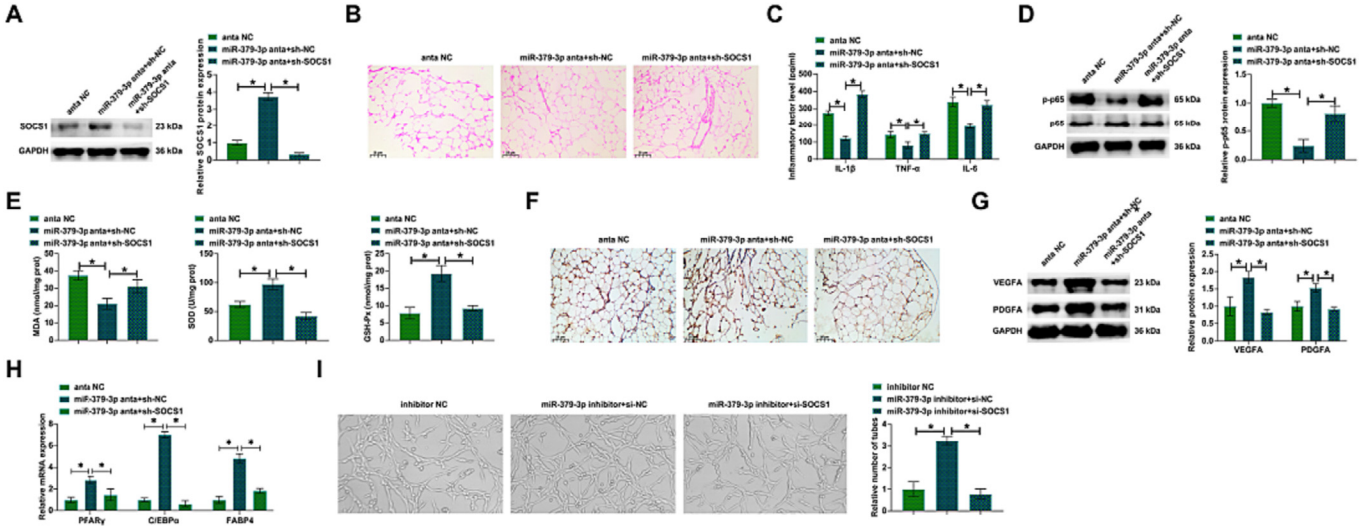

Fig. 4. miR-379-3p affects adipose tissue survival and angiogenesis by regulating SOCS1. miR-379-3p antagomir and sh-SOCS1 lentivirus vectors were injected into rats receiving fat grafting. (A) Western blot analysis of SOCS1 protein expression in adipose tissue. (B) HE staining evaluation of the pathological damage of adipose tissue. (C) ELISA analysis of TNF-α, IL-1β, and IL-6 in adipose tissue. (D) Western blot analysis of p-p65 phosphorylation. (E) Commercial kits measured MDA, SOD, and GSH-PX. (F) IHC staining measurement of the positive rate of CD31 in adipose tissue. (G) Western blot analysis of VEGFA and PDGFA in adipose tissue. (H) RT-qPCR evaluation of adipogenic genes PPARγ, C/EBPα, and FABP4 in adipose tissue. (I) Tube formation assay to evaluate the angiogenesis capacity of HUVECs; Data were expressed as mean ± SD (A-H, n = 5; I, N = 3). * $P < 0.05$.

(Fig. 3G). PCR showed that overexpression of SOCS1 promoted PPARγ, C/EBPα, and FABP4 mRNA expression in adipose tissue (Fig. 3H). Tube formation experiments showed that upregulating SOCS1 increased the number of tube nodules in HUVECs (Fig. 3I). In summary, upregulating SOCS1 has a positive effect on fat grafting survival.

3.4. miR-379-3p affects adipose tissue survival and angiogenesis by regulating SOCS1

This research evaluated the effects of the miR-379-3p/SOCS1 axis on adipose tissue survival and angiogenesis by a functional salvage assay. The promoting effect of miR-379-3p antagomir on SOCS1 was reversed by sh-SOCS1 (Fig. 4A). Pathological tissue staining showed that knocking down miR-379-3p could improve the vacuolation of adipose tissue, increase the number of small fat cells and stabilize the adipose structure, but this effect was reversed by SOCS1 knockdown (Fig. 4B). The action of knocking down miR-379-3p on inflammatory cytokines TNF-α, IL-1β and phosphorylation of IL-6 and NF-κB was mitigated by knocking down SOCS1 (Fig. 4C, D). Also, knocking down miR-379-3p decreased MDA levels and increased SOD and GSH-PX, but knocking down SOCS1 prevented changes in these factors (Fig. 4E). Knocking down miR-379-3p increased the positive rate of CD31 in adipose tissue, which was reversed by SOCS1 knockdown (Fig. 4F). Western blot showed that knocking down miR-379-3p promoted VEGFA and PDGFA protein expression, but SOCS1 knockdown prevented this phenomenon (Fig. 4G). PCR results showed that knockdown of miR-379-3p promoted PPARγ, C/EBPα, and FABP4 mRNA expression in adipose tissue, but this effect was reversed by knockdown of SOCS1 (Fig. 4H). Tube formation experiments showed that the stimulative effect of miR-379-3p knockdown on angiogenesis in HUVECs was saved by SOCS1 knockdown (Fig. 4I). These data suggest that miR-379-3p affects adipose tissue survival, angiogenesis, and inflammation by targeting SOCS1 expression.

4. Discussion

There has been a significant increase in research interest in identifying ways to optimize fat grafting survival. Although there are some differences in harvesting and implantation techniques in the lab, these findings have not yet translated into a universal protocol for fat grafting [19]. In view of molecules, this research paid attention to miR-379-3p and its target SOCS1 in fat grafting and eventually summarized that silencing miR-379-3p improved fat grafting survival and angiogenesis and suppressed inflammatory responses.

miR-379 is a miRNA transcribed from the MIR379 locus on 14q32.31. It is discussed that miR-379 can increase adipose inflammation, mitochondrial dysfunction, endoplasmic reticulum stress, and impaired lipogenesis and angiogenesis in obesity [20]. Additionally, in a mouse model of diabetic kidney disease, knocking out miR-379 protects against mitochondrial dysfunction, endoplasmic reticulum, and oxidative stress [21]. miR-379-3p and −5p are produced after machining the 3′end and 5′end of the precursor of miR-379, respectively. It has been documented that *in vitro* experiments, suppressing miR-379-5p inhibits the production of inflammatory cytokines including IL-17, TNF-α, and IL-β in uveitis [22]. However, the relevant mechanism associated with miR-379-3p has been rarely delineated. Based on a fat grafting model, the current study discovered that miR-379-3p knockdown promoted the production of adipocytes, reduced cavitation, and improved integrity in the adipose tissue. Meanwhile, depleting miR-379-3p inhibited the production of inflammatory stimuli and the activation of the NF-κB pathway, as well as oxidative stress in the adipose tissue. CD31, as an adhesive stress response protein, is highly expressed at the endothelium-cell junction which not only maintains the integrity of the endothelial cell junction but also accelerates the restoration of the vascular permeability barrier after inflammatory attack [23]. VEGFA is a major factor in angiogenesis, which binds with VEGF receptor (VEGFR)-1 and VEGFR-2 to regulate endothelial functions [24] and PDGFs are inducers of cell angiogenesis [25]. To study angiogenesis in fat grafting, CD31, VEGFA, and PDGFA were evaluated after interfering with miR-379-3p expression. Finally, it was recognized that miR-379-3p downregulation improved angiogenesis as reflected by increased positive rate of CD31 and elevated protein expressions of VEGFA and PDGFA in the adipose tissue, and the ability of HUVECs to form tube nodules. Shortly, silencing miR-379-3p improved fat graft survival and angiogenesis and reduced inflammation.

SOCS1 was studied as a downstream target of miR-379-3p in fat grafting. SOCS1 overexpression had an improving effect on adipose tissue survival, angiogenesis, and anti-inflammation, but SOCS1 downregulation could impair the protective impact of silencing miR-379-3p in fat grafting, confirming that miR-379-3p affects adipose tissue survival and angiogenesis by regulating SOCS1. SOCS is a family of proteins that mediate inflammatory responses in immune cells and metabolic organs such as adipose tissue [26]. Studies have investigated SOCS1 and validated its anti-inflammatory property [27,28,29] and antioxidant actions in pathological conditions [30]. It has been confirmed that SOCS1 is a negative regulator of NF-κB signaling [31]. Specifically, genistein reverses inflammation by downregulating miR-155 and upregulating SOCS1 to inhibit the NF-κB pathway in atherosclerotic HUVECs [32]. Moreover, miR-210-3p downregulation rescues obesity-induced adipose tissue inflammation by upregulating SOCS1 to inactivate the NF-κB pathway [33].

In our recent investigation, attention was particularly given to the impact of the miR-379-3p/SOCS1 axis on adipocytes and vascular endothelial cells. A critical observation was the pivotal role of adipose stem/progenitor cells, highlighted by their inherent capacities for self-renewal and multipotent differentiation. These cells demonstrated their capacity to differentiate into adipocytes, a process instrumental in compensating for the cell loss and injury precipitated by ischemia and nutrient inadequacy following transplantation [34,35]. An extensive body of literature has delineated the instrumental role of miRNAs in steering the adipogenic differentiation of these stem cells, underscoring their regulatory prominence [36,37]. Within this context, we postulated that the miR-379-3p/SOCS1 axis might harbor its beneficial influence on the survival rate of transplanted adipose tissue through its modulation of the adipogenic capabilities of adipose stem cells. This premise engendered a compelling case for subsequent in-depth exploration, poised to unveil nuanced molecular dynamics and foster innovative stratagems to augment adipose transplantation efficacy. The intersection of cellular mechanisms and miRNA-mediated regulatory pathways was pinpointed as a fertile ground for future investigative endeavors, promising to enrich our comprehension and harnessing of the underlying biology to optimize clinical outcomes in adipose tissue transplantation.

Other pathways are related to the function of SOCS1 in maintaining appropriate inflammatory responses, such as janus kinase/signal transduction and transcription activation signaling pathway [38]. Regarding this point, further investigations are required to identify other signaling pathways related to miR-379-3p/SOCS1 axis-mediated adipose tissue inflammation following fat grafting. Overall, this research concludes that miR-379-3p

inhibits fat grafting survival and angiogenesis by targeting SOCS1 to mediate adipose inflammation, suffering a novel way to improve fat grafting technique development.

Ethical approval

This study followed the guidelines of Plastic Surgery Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College based on the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health. The animal experiments were approved by the ethics committee of the Division of Laboratory Animal Science of Plastic Surgery Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College.

Author contributions

- Study conception and design: J Zhu, F Zhao.
- Data collection: X Han, F Li.
- Analysis and interpretation of results: X Han, F Li.
- Draft manuscript preparation: J Zhu, F Zhao.
- Revision of the results and approval of the final version of the manuscript: J Zhu, F Zhao; F Li.

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Conflicts of interest

The authors declare no conflicts of interest.

Data available

Data are available from the corresponding author on request.

Supplementary material

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