Gouty arthritis (GA) is a type of chronic inflammatory disease caused by the generation and deposition of monosodium urate (MSU) crystals. This can trigger gouty arthritis (GA), which in turn induces inflammation. Activation of the Nod-like receptor pyrin domain containing 3 (NLRP3) inflammasome plays a critical role in the onset and progression of GA. Autophagy may have a dual effect on GA with regard to the NLRP3 inflammasome. Therefore, the present study aimed to gain a deeper comprehension of the interaction between autophagy and NLRP3 inflammasome activation is imperative for developing more efficacious treatments for GA. Methods: Peripheral blood monocytes (PBMCs) were first isolated from GA patients and healthy controls and underwent bulk RNA sequencing analysis. Overexpression and knockdown of dual specificity phosphatase 1 (DUSP1) was performed in THP-1 monocytes to investigate its role in the immune response and mitochondrial damage. The luciferase assay and Western blot analysis were used to study the interaction between autophagy and NLRP3 inflammasome activation. Results: Bulk RNA sequencing analysis showed significant upregulation of DUSP1 expression in PBMCs from GA patients compared to healthy controls. This result was subsequently verified by reverse transcription quantitative polymerase chain reaction (RT-qPCR). DUSP1 expression in human THP-1 monocytes was also shown to increase after MSU treatment. Downregulation of DUSP1 expression increased the secretion of inflammatory cytokines after MSU treatment, whereas the overexpression of DUSP1 decreased the secretion levels. Lipopolysaccharides (LPS) combined with adenosine-triphosphate (ATP) led to mitochondrial damage, which was rescued by overexpressing DUSP1. DUSP1 overexpression further increased the level of autophagy following MSU treatment, whereas downregulation of DUSP1 decreased autophagy. Treatment with the autophagy inhibitor 3-Methyladenine (3-MA) restored inflammatory cytokine secretion levels in the DUSP1 overexpression group. MSU caused pronounced pathological ankle swelling in vivo. However, DUSP1 overexpression significantly mitigated this phenotype, accompanied by significant downregulation of inflammatory cytokine secretion levels in the joint tissues. Conclusions: This study revealed a novel function and mechanism for DUSP1 in promoting autophagy to mitigate the MSU-induced immune response in GA. This finding suggests potential diagnostic biomarkers and anti-inflammatory targets for more effective GA therapy.

Keywords: gouty arthritis; monosodium urate; autophagy; dual specificity phosphatase 1

1. Introduction

Gouty arthritis (GA) is a type of chronic inflammatory disease caused by the generation and deposition of monosodium urate (MSU) crystals in articular and periarticular spaces. This occurs in the context of persistent hyperuricemia and can subsequently activate the innate immune system [1]. The prevalence of GA in adults ranges from about 0.68% to 3.9% worldwide [2]. Current therapeutic approaches for GA consist primarily of reducing hyperuricemia and inflammation. However, these treatments are far from optimal due to various factors, including adverse reactions [1,3–5]. Many studies have shown that activation of the Nod-like receptor family, pyrin domain containing 3 (NLRP3) inflammasome plays a crucial role in the initiation and progression of GA [6–10]. Elucidating the functions and mechanisms of the NLRP3 inflammasome in the pathogenesis of GA may therefore have important implications for the development of therapeutic drugs against GA.

Various pathogen-associated molecular patterns (PAMPs), or damage-associated molecular patterns (DAMPs), have been identified as priming signals that effectively promote the transcriptional activation of NLRP3, pro-IL-1β, and pro-IL-18 genes via the Toll-like receptor 4 (TLR4)/nuclear factor kappa-B (NF-κB) signaling pathway [7,11]. Activation signals such as adenosine-triphosphate (ATP), pore-forming toxins, mitochondrial damage and particulate matter then trigger NLRP3 oligomerization and the recruitment of ASC adaptor protein and pro-caspase-1 to assemble the NLRP3 inflammasome [12]. Subsequently, the activated NLRP3 inflammasome triggers hydrolysis of dormant caspase-1 to the activated form, thereby inducing pyroptosis. This is followed by the conversion of interleukin-1β (IL-1β) and IL-18 precursors to mature forms, which then recruit and modulate the activity of innate immune cells [13]. The targeting of NLRP3 inflammasome-induced IL-1β and IL-18 by recombinant receptor antagonist, neutralizing antibody, and soluble decoy receptor has shown impressive
results in alleviating GA symptoms [14,15]. However, the upstream and downstream mechanisms involving the NLRP3 inflammasome in GA pathophysiology remain unclear.

Autophagy is a programmed digestion process that is involved in cell development, metabolism, immune regulation and aging. It does this via the sequestration of damaged proteins and organelles, as well as the destruction of intracellular pathogens, within a double-membrane vesicle-autophagosome, and then fusing with lysosomes to cause degradation [16–19]. Autophagy has been demonstrated to play a dual role in some inflammatory diseases associated with the NLRP3 inflammasome, including GA [18,20–23]. Autophagy can reduce NLRP3 inflammasome activation and the inflammatory response by removing activators such as damaged mitochondria that produce reactive oxygen species (ROS), as well as inflammasome components and cytokines [24–28]. Activation of the NLRP3 inflammasome regulates autophagy through several different pathways to promote the occurrence and development of GA [18,21,29–31]. Therefore, a better understanding of the inter-regulatory mechanisms between autophagy and activation of the NLRP3 inflammasome is required to develop more efficient treatments for GA.

Dual specificity phosphatase 1/mitogen-activated protein kinase phosphatase-1 (DUSP1/MKP-1) is a dual-specific phosphatase involved in the regulation of MAPK family isoforms. It plays an important anti-inflammatory role in acute and chronic diseases such as asthma, diabetes and cancers [32–35]. A recent study showed that upregulation of DUSP1 can attenuate renal tubular mitochondrial dysfunction by promoting autophagy and restoring parkin-mediated mitophagy in diabetic nephropathy [36]. Fan et al. [37] demonstrated that RGD1564534 protected neurons in cerebral ischemia/reperfusion injury by competitively binding with miR-101a-3p to upregulate DUSP1, thereby promoting mitochondrial autophagy and blocking NLRP3 inflammasome activity. However, the expression and function of DUSP1 in GA is still unknown.

In the present study, peripheral blood monocytes (PBMCs) were isolated from GA patients and healthy controls and used for bulk RNA sequencing analysis. DUSP1 expression of DUSP1 (lv-DUSP1) and for the control (lv-NC) and tested negative for mycoplasma. Lentiviruses for over-expression of DUSP1 (lv-DUSP1) and for the control (lv-NC) were designed and purchased from Biosmedi Technology Co., Ltd. (Shanghai, China). THP-1 cells were transfected with the above viruses in parallel with MSU treatment. After 24 h, the supernatant and cells were collected for subsequent experiments.

2. Materials and Methods

2.1 Collection of Clinical Samples

Gout patients and healthy controls from the First Affiliated Hospital of Jiamusi University were enrolled in the study after signing an informed consent form. This study was approved by the Ethics Committee of Jiamusi University. Peripheral blood samples were collected from GA patients and healthy controls and the PBMCs were isolated and harvested for subsequent experiments according to the protocol described in the kit (11350D, ThermoFisher, Carlsbad, CA, USA).

2.2 Cell Culture, Treatments and Flow Cytometry (FACS) Analysis

The human THP-1 cell line, which were purchased from the Cell Bank of Type Culture Collection of the Chinese Academy of Sciences, Shanghai Institute of Cell Biology (Shanghai, China) was grown in RPMI-1640 media containing 10% FBS, 0.05 mM β-mercaptoethanol, and 1% penicillin/streptomycin at 37 °C in humidified air with 5% CO2. All cell lines were validated by STR profiling and tested negative for mycoplasma. Lentiviruses for over-expression of DUSP1 (lv-DUSP1) and for the control (lv-NC) were designed and purchased from Biosmedi Technology Co., Ltd. (Shanghai, China). THP-1 cells were transfected with the above viruses in parallel with MSU treatment. After 24 h, the supernatant and cells were collected for subsequent experiments.

2.3 Measurements of Mitochondrial Function

THP-1 cells were incubated with 1 µg/mL Lipopolysaccharide (LPS) + 20 µM adenosine triphosphate (ATP) or vehicle for 4 h following DUSP1 over-expression. To measure mitochondrial ROS, inner transmembrane potential, and mitochondrial mass, the cells were stained with 5 µM MitoSOX and 25 nM MitoTracker Deep Red + 25 nM MitoTracker Green for 15 min. The signals were then detected by flow cytometry (FACS). The degree of mitochondrial membrane polarization in THP-1 cells was measured by staining with 2 µM JC-1, followed by signal detection with confocal microscopy.

2.4 Establishment of a Mouse Model of Acute GA

Male C57BL/6 mice (6-weeks old) were purchased from SPF (Beijing, China) Biotechnology Co., Ltd. The mice were maintained in accordance with institutional policies, and the study was approved by the Ethics Committee of the First Affiliated Hospital, Jiamusi University (2022-500-177). The mice were anesthetized with 50 mg/kg sodium pentobarbital via intraperitoneal injection (i.p.) and then injected at the hind ankle joint with phosphate-buffered saline (PBS) (20 µL) or MSU (1 mg MSU dissolved in 20 µL PBS) after 1 week of lv-NC or MSU + lv-DUSP1 (1.2 × 10⁹ TU/mL, n = 10). The thickness of the foot was measured at 0, 6, 12 and 24 h after treatment. At the final time
DUSP1 expression is upregulated in peripheral blood monocytes (PBMCs) from gouty arthritis (GA) patients, and in monosodium urate (MSU)-treated THP-1 monocytes. (A) Volcano plot of differential mRNA expression in PBMCs from GA patients and healthy controls. (B) Reverse transcription quantitative polymerase chain reaction (RT-qPCR) analysis of dual specificity phosphatase 1 (DUSP1) mRNA expression in PBMCs from GA patients and healthy controls (n = 10). (C) RT-qPCR analysis of DUSP1 mRNA expression in MSU-treated THP-1 and in THP-1 controls (n = 3). (D) Representative Western blot analysis of DUSP1 protein expression in MSU-treated THP-1 and in THP-1 controls (n = 3). **p < 0.01. no-DEGS, no differentially expressed genes.

2.5 Microtubule-associated Protein 1A/1B-light Chain 3 (LC3)-Adenovirus Infection and Analysis of Immunofluorescence (IF) Staining

THP-1 cells were infected with the tandem GFP-LC3 reporter adenovirus (Beyotime, Shanghai, China, C3006) according to the manufacturer’s instructions. To investigate the function of DUSP1 in regulating autophagy, vectors for DUSP1 overexpression, DUSP1 knockdown (short hairpin RNA, shRNA), or controls were added to the cell culture medium for 24 h. The THP-1 cells were then harvested and the cell nuclei stained with Hoechst 33342 (Beyotime, C1029) for 10 min to detect signals by confocal microscopy.
Fig. 2. DUSP1 inhibits the inflammatory response in MSU-treated THP-1 monocytes. (A) Representative Western blot analysis of the DUSP1 protein level in THP-1 monocytes following infection with shRNA (downregulation), or with adeno-associated virus (overexpression) (n = 3). (B) Enzyme-linked immunosorbent assay (ELISA) analysis of inflammatory cytokine levels in THP-1 with DUSP1 overexpression (upper panel) or knockdown (lower panel) in the MSU treatment or control groups (n = 3). *p < 0.05, **p < 0.01, ***p < 0.001. shNC, non-target negative control; shDUSP1, shRNA for DUSP1.

2.6 Reverse Transcription Quantitative Polymerase Chain Reaction (RT-qPCR)

Total RNA from samples was extracted with Trizol reagent (Thermo Fisher Scientific, 15596026, Waltham, MA, USA) and phenol-chloroform precipitation. After undergoing removal of genomic DNA and reverse transcription, qRT-PCR was performed using the ABI PRISM 7900 system (Applied Biosystems, Carlsbad, CA, USA) with the SYBR Green Real time PCR Master Mix plus (TOYOBO, Osaka, Japan). GAPDH was used for internal normalization. The primers used for RT-qPCR were: human GAPDH (Forward: 5′-CTGGGCTACACTGAGCACC-3′, Reverse: 5′-AAGTGGTCGTTGAGGGCAATG-3′); human DUSP1 (Forward: 5′-ACCACCACCGTGTTCAACTTC-3′, Reverse: 5′-TGGGAGAGGTCGTAATGGGG-3′).

2.7 mRNA Sequencing Analysis

The RNA quality and purity of samples were assessed and only those showing RNA Integrity Number ≥ 8.0 and A260/230 ≥ 1.5 were used for bulk RNA sequencing. The samples were sequenced by BGISEQ-500 from the BGI Group (Shenzhen, China), and raw sequencing reads were aligned to the mouse genome (mm10). Differential expression analyses were performed with R and Bioconductor packages of edger. The threshold required for genes to be considered significantly altered was a significance level of p < 0.05 and a fold-change of > 1.5.

2.8 Western Blot Analysis

Following the different treatments, total protein was extracted from THP-1 cells using Radioimmunoprecipitation (RIPA) lysis buffer (Beyotime) on ice. Protein concentrations were determined using a bicinchoninic acid (BCA) kit (Beyotime). A total of 20 µg protein was separated by electrophoresis and then transferred to polyvinylidene fluoride (PVDF) membranes. The membranes were blocked with 5% skimmed milk and incubated overnight at 4 °C with primary antibodies (Abconal, Wuhan, China) against DUSP1 (1:1000 dilution), IL-6 (1:1000), TNF-α (1:1000), IL-1β (1:1000), P62 (1:1000), LC3 (1:1000), and GAPDH (1:5000). After 3 rinses with PBST, secondary antibodies (goat anti-mouse, or goat anti-rabbit) purchased from Jackson ImmunoResearch Labs (West Lebanon, NH, USA) were incubated with the membranes. Finally, the protein bands were visualized using an enhanced chemiluminescence (ECL) kit (Perkin Elmer, Foster City, CA, USA) and quantified by densitometry.

2.9 Analysis by Enzyme-Linked Immunosorbtent Assay (ELISA)

Following different treatments for 24 h, the culture media from THP-1 cells was collected and the level of inflammatory cytokines was assessed using ELISA kits as recommended by the manufacturer (Sangon Biotech, Shanghai, China).
Fig. 3. DUSP1 decreases mitochondrial damage in Lipopolysaccharide (LPS) + adenosine triphosphate (ATP)-treated THP-1 monocytes. (A) Flow cytometry (FACS) analysis of mitoSOX positive cells in THP-1 with DUSP1 overexpression and in THP-1 controls after LPS + ATP treatment (n = 3). (B) FACS analysis of damaged mitochondria in THP-1 with DUSP1 overexpression and in THP-1 controls after LPS + ATP treatment (n = 3). (C) Analysis of the JC-1 ratio in THP-1 with DUSP1 overexpression and in THP-1 controls after LPS + ATP treatment (n = 3). *p < 0.05, **p < 0.01, ***p < 0.001.

### 2.10 Statistical Analysis

Statistical analysis was performed using GraphPad Prism software version 9.0 (GraphPad Software, San Diego, CA, USA). Measurement data was presented as the mean ± SD. Potential differences between two groups were analyzed using Student’s t-test, while one-way ANOVA was used to compare three or more groups. A p value of <0.05 was considered statistically significant.

### 3. Results

#### 3.1 DUSP1 is Upregulated in Gout Patients and in THP-1 Monocytes after MSU Treatment

Monocytes and macrophages have been shown to play a vital role in MSU-driven, pro-inflammatory cytokine production, thereby initiating an acute inflammatory response [30,38,39]. PBMCs were isolated from GA patients and healthy controls and analyzed by bulk RNA sequencing to screen for differential gene expression between the two groups. Altered genes reaching a significance level of p < 0.05 and a fold-change of >1.5 are shown in a volcano plot (Fig. 1A). Amongst these, DUSP1 has been reported to play an important role in inflammatory and autophagy process in different diseases [32–35] and was therefore selected for further study. Using RT-qPCR, DUSP1 expression was found to be significantly upregulated in PBMCs from GA patients (Fig. 1B). Furthermore, DUSP1 gene and protein expression were significantly upregulated in human THP-1 monocytes following MSU treatment (Fig. 1C,D). These results suggest that DUSP1 may play an important role in the pathogenesis of GA.

#### 3.2 DUSP1 Inhibits Inflammation and Mitochondrial Damage in THP-1 after MSU Treatment

The NLRP3 inflammasome requires initiation and activation signals before it can trigger IL-1β and IL-18 precursors to mature, thereby driving the acute inflammatory response [11,40,41]. To investigate the role of DUSP1 in the pathogenesis of GA, lentivirus constructs were used to induce the overexpression and knockdown of DUSP1. Fol-
Fig. 4. DUSP1 promotes autophagy in THP-1 monocytes following MSU treatment. (A) Representative immunofluorescence (IF) staining and analysis of autophagy in THP-1 cells with DUSP1 overexpression and in THP-1 controls after MSU treatment (n = 3). Scale bar, 200 µm. (B) Representative Western blot results for autophagy-related proteins in THP-1 cells with DUSP1 overexpression and in THP-1 controls after MSU treatment (n = 3). (C) Representative IF staining and analysis of autophagy in THP-1 cells with DUSP1 knockdown and in THP-1 controls after MSU treatment (n = 3). Scale bar, 200 µm. (D) Representative Western blot analysis of autophagy-related proteins in THP-1 cells with DUSP1 knockdown and in THP-1 controls after MSU treatment (n = 3). *p < 0.05, **p < 0.01. LC3, Microtubule-associated protein 1A/1B-light chain 3; DAPI, 4′,6-diamidino-2-phenylindole.

Following 24 h of infection, Western blot analysis showed successful upregulation or downregulation of DUSP1 in THP-1 monocytes (Fig. 2A), thus confirming the effectiveness of the lentiviral constructs. The levels of inflammatory cytokines were then assessed by ELISA analysis. As reported previously [30,42–44], MSU treatment significantly upregulated the level of secreted inflammatory cytokines such as IL-1β, tumor necrosis factor-α (TNF-α), and IL-6. Surprisingly, cells with downregulated DUSP1 expression showed even higher cytokine levels (Fig. 2B, upper panel). In contrast, DUSP1 overexpression lowered the cytokine levels (Fig. 2B, lower panel).

Mitochondrial damage is an essential trigger for inflammasome formation and is increased following MSU treatment [9,31,45]. To evaluate the level of cellular oxidative stress/ROS, LPS combined with ATP was added to the medium of THP-1 monocytes. The number of positive cells for mitochondrial superoxide increased, but overexpression of DUSP1 caused this ratio to decrease (Fig. 3A). In addition, the overexpression of DUSP1 rescued LPS + ATP caused membrane potential of mitochondria downregulation (Fig. 3B,C). Therefore, DUSP1 appears to be an inhibitor of NLRP3 inflammasome activation after MSU treatment in vitro.

3.3 DUSP1 Promotes Autophagy in THP-1 Monocytes following MSU Treatment

The mechanisms involved in regulating NLRP3 inflammasome activation have only been partially elucidated. The manipulation of autophagy via suppression of the NLRP3 inflammasome may be a therapeutic approach for GA [18,25,46,47]. The autophagy level in THP-1 monocytes was evaluated here by estimating the density of LC3 puncta after MSU treatment. MSU was found to activate autophagy, but more importantly, DUSP1 overexpression further increased the level of autophagy (Fig. 4A). Moreover, Western blot analysis showed that LC3II protein after MSU treatment was increased in the presence of DUSP1 overexpression, whereas P62 protein was decreased (Fig. 4B). In contrast, downregulation of DUSP1 markedly suppressed the level of autophagy, decreased the expression of LCII, and increased the expression of p62 (Fig. 4C,D).

Next, we used a well-established drug for autophagy inhibition, 3-Methyladenine (3-MA), to investigate whether DUSP1-mediated inhibition of MSU-driven inflammation was via the promotion of autophagy. 3-MA was found to efficiently abolish the promotion of autophagy by DUSP1 overexpression (Fig. 5A). Furthermore, the level of inflam-
Fig. 5. DUSP1 inhibits MSU-driven inflammation by promoting autophagy. (A) Representative IF staining and analysis of autophagy in DUSP1-overexpressing THP-1 and in control THP-1 after 3-Methyladenine (3-MA) treatment (n = 3). Scale bar, 200 µm. (B) ELISA analysis of inflammatory cytokine levels in DUSP1-overexpressing THP-1 and in control THP-1 after 3-MA treatment (n = 3). *p < 0.05, **p < 0.01.

Fig. 5. DUSP1 inhibits MSU-driven inflammation by promoting autophagy. (A) Representative IF staining and analysis of autophagy in DUSP1-overexpressing THP-1 and in control THP-1 after 3-Methyladenine (3-MA) treatment (n = 3). Scale bar, 200 µm. (B) ELISA analysis of inflammatory cytokine levels in DUSP1-overexpressing THP-1 and in control THP-1 after 3-MA treatment (n = 3). *p < 0.05, **p < 0.01.

3.4 DUSP1 Suppresses Gouty Arthritis in Vivo by Down-Regulating MSU-Driven Inflammation

To assess whether DUSP1 overexpression alleviates GA, lv-DUSP1 or lv-NC were injected into the ankle joint of C57BL/6 mice, with subsequent injection of MSU (Fig. 6A). MSU induced ankle swelling with distinct pathological morphology, and also significantly increased foot thickness (Fig. 6B). These changes were significantly reduced in the lv-DUSP1 group compared to the lv-NC group. MSU also activated an inflammatory response, as reported previously [42,48,49]. However, lv-DUSP1 treatment significantly downregulated the protein levels for IL-1β, TNF-α and IL-6 in joint tissues (Fig. 6C). These results demonstrate that DUSP1 overexpression suppressed inflammation, thereby reducing the pathological extent of GA in vivo.

4. Discussion

This study identified a novel role for DUSP1 as a suppressor of NLRP3 inflammasome activation via the enhancement of autophagy in MSU-induced GA. DUSP1 expression was significantly elevated in PBMCs from GA patients compared to healthy controls. Overexpression of DUSP1 also reduced the inflammation response and mitochondrial damage in THP-1 monocytes after MSU treatment. Furthermore, DUSP1 knockdown worsened the MSU-induced disease phenotype. DUSP1 appears to upregulate the level of autophagy, thereby suppressing NLRP3 inflammasome activation both in vitro and in vivo. These findings help to clarify the function and mechanism of DUSP1 in suppressing NLRP3 inflammasome activation during GA. Moreover, they suggest that downstream targets of DUSP1 may be useful in the development of new drugs for GA therapy.

Bulk RNA sequencing data from this study revealed considerable differential gene expression between PBMCs from GA patients compared with healthy controls. Im-
Fig. 6. DUSP1 suppresses GA in vivo by downregulating MSU-induced inflammation. (A) Representative macroscopic views of ankle swelling in different treatment groups. (B) Foot thickness in mice overexpressing DUSP1 and in controls after MSU treatment (n = 6). (C) Western blot analysis and levels of inflammatory cytokines in mice overexpressing DUSP1 and in controls after MSU treatment (n = 3). *p < 0.05, **p < 0.01. Lv-NC, lentivirus negative control; Lv-DUSP1, lentivirus carrying DUSP1.

Importantly, the observed upregulation of DUSP1 expression in PBMCs from GA patients was also observed in THP-1 monocytes following MSU treatment. MSU is commonly used to mimic the human GA phenotype in cells and mice. It does this by activating the NLRP3 inflammasome, thereby promoting the maturation of interleukins and inducing immune cell migration, leading to an immune response [42,48,49]. In the present study, increased levels of secreted inflammatory cytokines (IL-1β, TNF-α and IL-6) were observed in THP-1 monocytes following MSU treatment. Importantly however, the overexpression of DUSP1 negatively regulated this process. These observations are consistent with previous reports that DUSP1 is upregulated via TLR-MAPK and IL-10-STAT3 signaling, thereby suppressing the immune response by modifying inflammatory gene expression or miRNA stability [33–35].

A comprehensive mechanism for NLRP3 inflammasome-mediated GA disease is yet to be fully elucidated, but the dual role of autophagy in this process is intriguing [18,25,46,47]. MSU was shown to induce autophagy by increasing the levels of LC3-II and the presence of LC3 puncta, thereby activating the NLRP3 inflammasome [38,50,51]. This effect could be attenuated in different cell types by the autophagy inhibitor 3-MA. In contrast, the upregulation of autophagy by AMPK activators and SIRT1 agonist was reported to prevent the accumulation of p62 by MSU crystals and to inhibit NLRP3 inflammasome activation [38,46,50]. The present study also found that MSU triggers autophagy after increasing the extent of mitochondrial damage. In addition, DUSP1 overexpression further enhanced the level of autophagy, thereby reducing mitochondrial damage and the MSU-induced immune response in vitro and in vivo. Therefore, the benefit of DUSP1 upregulation in GA is derived primarily by increasing the level of autophagy in monocytes. The origin of high DUSP1 expression observed in PBMCs from GA patients requires further study, since PBMCs are comprised of different cell populations characterized by anti- or pro-inflammatory activities [39]. Whether there are potential factors that antagonize DUSP1 to suppress the immune response in GA also needs to be investigated. Furthermore, in order to better understand the mechanism by which DUSP1 regulates autophagy, the downstream signaling pathway needs to be clarified using proteomic analysis.

5. Conclusions

In conclusion, the results of this study revealed that DUSP1 expression was significantly increased in the PBMCs of GA patients. Moreover, DUSP1 overexpression could mitigate the MSU-induced immune response by enhancing the level of autophagy. This finding suggests that DUSP1 may be an attractive candidate target for human GA therapy.
Abbreviations

DUSP1, dual specificity phosphatase 1; GA, gouty arthritis; MSU, monosodium urate.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

Conceptualization and investigation: JN and HQ; methodology and resources: JN; writing and Original Draft Preparation: JN and HQ; Critical review and Editing: JN and HQ. Both authors contributed to editorial changes in the manuscript. Both authors have read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Informed consent was obtained from all participants included in the study. The study was approved by the Ethics Committee of the First Affiliated Hospital, Jiamusi University (QKW2021015). All procedures related to the care and sacrifice of animals were reviewed and approved by the Ethics Committee of the First Affiliated Hospital of Jiamusi University (2022-500-177) and performed in accordance with international regulations.

Acknowledgment

Not applicable.

Funding

This work was supported by grants from the key program of the Natural Science Foundation, Heilongjiang Province of China (ZD2022H006) and Jiamusi University youth innovative talent training program (JM-SUQP2020015).

Conflict of Interest

The authors declare no conflict of interest.

References


