

MiR-151a-3p Alleviates Gouty Arthritis by Targeting DKK-1 and Activating the Wnt/ β - Catenin Pathway

Xuefeng Peng

First Affiliated Hospital of Fujian Medical University

Yanling Mao

Quanzhou First Hospital Affiliated to Fujian Medical University

Jingwen Fang

Quanzhou First Hospital Affiliated to Fujian Medical University

Zhaozhao Zhu

Quanzhou First Hospital Affiliated to Fujian Medical University

Beverly Sy Hong

Quanzhou First Hospital Affiliated to Fujian Medical University

Yafen Zhuo

Quanzhou First Hospital Affiliated to Fujian Medical University

Xiaomiao Wu

Quanzhou First Hospital Affiliated to Fujian Medical University

Tingjin Zheng

Quanzhou First Hospital Affiliated to Fujian Medical University

Yihui Lin

Quanzhou First Hospital Affiliated to Fujian Medical University

Zhichun Sun

Quanzhou First Hospital Affiliated to Fujian Medical University

Fang He

Quanzhou First Hospital Affiliated to Fujian Medical University

Yi Zhang

Quanzhou First Hospital Affiliated to Fujian Medical University

Peiwen Wu

wpeiwen@fjmu.edu.cn

First Affiliated Hospital of Fujian Medical University

Article

Keywords: gouty arthritis, miR-151a-3p, DKK-1, Wnt/ β -catenin pathway

Posted Date: August 19th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10292789/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.
[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Objective

To investigate the expression, function and molecular mechanism of miR-151a-3p in gouty arthritis (GA) and provide a new therapeutic target for GA.

Methods

Clinical samples (30 normal controls and 34 GA patients) were collected and the expression of miR-151a-3p and DKK-1 were detected. A GA in vitro cell model was established (THP-1 cells were treated with PMA, LPS and MSU crystals), and miR-151a-3p mimic, DKK-1 overexpression vectors and controls were transfected respectively. Cell proliferation, inflammatory factors, Wnt pathway proteins, and targeting relationships were analyzed by qRT-PCR, Western blot, ELISA, CCK-8, flow cytometry, and dual-luciferase reporter assay. Additionally, an acute GA rat model was established, and the miR-151a-3p agonist was injected into the articular cavity to evaluate changes in ankle joint swelling, histopathology, serum inflammatory factors, and Wnt pathway proteins.

Results

Compared with the control group, the expression of miR-151a-3p was down-regulated and the expression of DKK-1 was up-regulated in GA patients and cell models. Overexpression of miR-151a-3p inhibits MSU-induced cell proliferation, reduces the proportion of S-phase cells, and reduces TNF- α and IL-1 β secretion. Mechanistically, miR-151a-3p directly targets the 3'UTR of DKK-1, suppresses its expression, and then activates the Wnt/ β -catenin pathway (β -catenin, LRP5/6 increase, GSK3 β , APC, and Axin decrease). Overexpression of DKK-1 reverses these effects. In animal models, miR-151a-3p agonist significantly reduced ankle swelling, synovial hyperplasia and inflammatory infiltration in rats, reduced serum TNF- α , IL-1 β and DKK-1 levels, upregulated the expression of β -catenin and LRP5/6 in ankle joint tissue, and down-regulated the expression of GSK3 β , APC, and AXIN2.

Conclusion

As an anti-inflammatory factor in GA, miR-151a-3p inhibits inflammatory responses and abnormal cell proliferation by targeting DKK-1 and activating the Wnt/ β -catenin pathway. In vivo and in vitro experiments jointly revealed the important role of the miR-151a-3p/DKK-1/Wnt axis in the pathogenesis of GA, providing new basis for molecular targeted therapy of GA.

Introduction

Gouty arthritis (GA) is a local or systemic inflammatory disease [1]. Its etiology is the deposition of monosodium urate (MSU) crystals in joints and surrounding tissues [2]. In recent years, the prevalence of GA has reached 11%-13%, and the incidence rate among individuals over 80 years old was reported to be 0.4%[3]. Acute gouty arthritis is characterized by severe pain in the affected joint, usually lasting 3–14 days [4, 5]. Monocytes/macrophages (inflammatory cells) can regulate the inflammatory response in gouty arthritis caused by urate [6]. It has been reported that monocytes and macrophages in the synovial fluid of patients with acute gouty arthritis release more pro-inflammatory cytokines [7]. In addition, in an in vitro model of gouty arthritis, urate treatment has been shown to activate caspase-1 and promote the production of pro-inflammatory factors in monocytes/macrophages [8]. Currently, first-line therapies used for routine treatment of GA include corticosteroids, colchicine, and non-steroidal anti-inflammatory drugs. However, these drugs have significant adverse effects and limited efficacy, which limits their further clinical use[9]. Therefore, it is crucial to find more effective therapies to treat GA.

Microribonucleic acid (miRNA) is a small non-coding RNA composed of 22 to 24 nucleotides [10]. It recognizes specific sequences in the 3'untranslated region (3'UTR) of target genes via base pairing. Therefore, it is capable of inhibiting the translation of messenger RNA (mRNA) of target genes at the post-transcriptional level and/or promoting its degradation [11]. Studies have shown that abnormal miRNA expression is strongly associated with hyperuricemia, cardiovascular disease, kidney disease, inflammation, and the pathogenesis, progression, and prognosis of tumors[12–15]. miR-22-3p and miR-22-3-3p inhibit gouty inflammation triggered by MSU stimulation by negatively regulating the NLR family pyrin domain-containing protein 3 (NLRP3) [16]. miR-155 reduces the expression of inositol polyphosphate 5-phosphatase D (SHIP-1) and promotes the production of pro-inflammatory cytokines triggered by MSU [17]. miR-151a-3p has been reported to be closely associated with the progress of multiple diseases. In osteoarthritis, inhibiting the expression of miR-151a-3p can enhance the activity of lipopolysaccharide induced osteoarthritis cells and reduce apoptosis [18]. In polycystic ovary syndrome, there is a significant correlation between the expression of miR-151a-3p and the expression of target TNIK, and miR-151a-3p promotes disease development by activating the PI3K/AKT signaling pathway [19]. Despite these findings in other pathologies, the specific function of miR-151a-3p in GA remains entirely unexplored.

In this study, we employed MSU to construct an in vitro cell model and an in vivo rat model of GA, and systematically investigated the biological role and possible molecular mechanisms of miR-151a-3p in GA. We hypothesized that miR-151a-3p may regulate the inflammatory response in GA by targeting downstream gene DKK-1 and modulating the Wnt/ β -catenin signaling pathway. Through in vitro functional experiments, dual-luciferase reporter assays, and validation in an in vivo animal model, this study aims to reveal the key role of the miR-151a-3p/DKK-1/Wnt axis in the pathogenesis of GA, and to explore potential molecular targets for GA therapy, thereby providing a new theoretical and experimental basis for targeted GA therapy.

Materials and methods

Cell culture

THP-1 cells (CL-0233) were purchased from Procell Biotech and were cultured in specific medium (CM-0233, Procell) in a 37°C, 5% CO2 incubator(BPN-80CW, Shanghai Yiheng Scientific Instrument Co., Ltd.); 293T cells (CL-0005) were purchased from Procell Biotech Company and cultured in DMEM complete medium (containing 10% FBS, 1% penicillin-streptomycin) (KGM12800S, KeyGenBiotec) in a 5% CO2 incubator (BPN-80CW, Shanghai Yiheng Scientific Instrument Co., Ltd.) at 37°C.

Establishment of a cell model of gouty arthritis

A cellular model of GA was established as described in Reference[20]. Specifically, PMA was added to undifferentiated THP-1 cells and incubated for 24 hours. Once the THP-1 cells had adhered to the culture dish, 100 ng/mL LPS was added for a 3-hour incubation. The cells were then stimulated with 100 µg/mL MSU crystal suspension for 24 hours. Following a wash with PBS, the cells were harvested for subsequent experiments.

Vector construction

A miR-151a-3p mimic was designed and synthesized based on the human sequence obtained from the miRDB database (<https://mirdb.org/mirdb/index.html>): CUAGACUGAAGCUCCUUGAGG, a mimic was designed and synthesized. The sequence of the mimic is shown in Table 1. The CDS sequence of the DKK-1 gene (transcript accession number: NM_012242.4) was retrieved from the NCBI database. The CDS sequence of the target gene was chemically synthesized and cloned into the pcDNA3.1(+) vector via homologous recombination to generate the DKK-1-pcDNA3.1(+) recombinant plasmid.

Table 1
Sequence of miR-151a-3p mimic

Name	Sequence
hsa-miR-151a-3p mimic	CUAGACUGAAGCUCCUUGAGG CCUCAAGGAGCUUCAGUCUAG
mimic NC	UCACAACCUCCUAGAAAGAGUAGA UCUACUCUUUCUAGGAGGUUGUGA

Cell transfection

When the cell density reaches 70%, prepare for transfection; replace the cell culture medium with 1 mL of serum-free medium; in two sterile Eppendorf tubes, add 125 µL of Opti-MEM to each. To the first tube, add 5 µL of Lipofectamine 3000 (L3000015, Invitrogen). To the second Eppendorf tube, add either 0.1 OD of Mimic or a mixture of 5 µL of Lipofectamine 3000 and 2.5 µg of plasmid. Mix the contents of each tube well and incubate at room temperature for 5 minutes; combine the contents of the two Eppendorf

tubes, mix well, and incubate at room temperature for 15 minutes; dispense the mixture into the corresponding wells of a six-well plate, and return the plate to the incubator for culture; Four hours post-transfection, add 1 mL of complete medium containing 20% serum to the six-well plate; proceed with subsequent experiments after 48 hours.

CCK-8 assay

Following transfection and model induction, cells were digested, counted, and seeded into 96-well plates in groups, with 1×10^4 cells per well. The plates were incubated in an incubator for 24 hours. Cell proliferation in each group was assessed using the CCK-8 assay. The culture medium in the 96-well plates was replaced with fresh medium (100 μ L per well), followed by the addition of 10 μ L of CCK-8 reagent (KGA317, Kaiji Biotechnology), and the plates were incubated for 2 hours. The absorbance of each well was measured at a wavelength of 450 nm using a microplate reader (SuPer Max 3100, Shanghai Shanzhuo Biotechnology Co., Ltd.).

Flow cytometry for cell cycle detection

Collect 1×10^6 cells, centrifuge the cell suspension at 1,500 rpm for 3 minutes, and discard the supernatant. Resuspend the pellet in 1 mL of PBS, centrifuge at 1,500 rpm for 3 minutes, and discard the supernatant. In accordance with the manufacturer's protocol for the Cell Cycle Assay Kit (CCS102, MULTI SCIENCES), add 1 mL of DNA Staining Solution and 10 μ L of Permeabilization Solution to each sample. Vortex for 5–10 seconds to mix, then incubate at room temperature in the dark for 30 minutes. Analyze the cell cycle using a flow cytometer (NovoCyte 2060R, Aisen Bio).

Enzyme-Linked Immunosorbent Assay

The levels of TNF- α and IL-1 β in cell supernatants and rat serum from each group were measured using the Human Tumor Necrosis Factor- α (TNF- α) Assay Kit (E-EL-H0109, Eliret) and the Human Interleukin-1 β (IL-1 β) Assay Kit (E-EL-H0149, Eliret). Cell supernatants were collected and centrifuged at $1,000 \times g$ for 15 min, after which the assays were performed according to the manufacturer's instructions. The optical density (OD) of each well was measured at 450 nm using a microplate reader (model WD-2012B; Beijing Liuyi).

Quantitative Real-Time Polymerase Chain Reaction (qPCR)

Total RNA was extracted from cells using Trizol reagent (CW0580S, CWBIO), and miRNA was isolated using the miRNA extraction kit (CW0627S, CWBIO). The concentration and purity of the miRNA (OD260/OD280) were determined using a UV-Vis spectrophotometer (NP80, NanoPhotometer). cDNA was synthesized using the stem-loop-based miRNA 1st Strand cDNA Synthesis Kit (MR101-02, Vazyme), and quantitative real-time PCR was performed using a fluorescence PCR instrument (CFX Connect™

Real-Time, Bio-Rad Life Sciences (Shanghai) Co., Ltd.). The reaction protocol is as follows: initial denaturation at 95°C for 10 min; denaturation at 95°C for 10 s; annealing at 58°C for 30 s; extension at 72°C for 30 s; 40 cycles. U6 was used as an internal control, and the relative miRNA expression was calculated using the $2^{-\Delta\Delta Ct}$ method. The primer sequences are shown in Table 2 below:

Table 2
Primer sequence

Primer	Forward(5'-3')	Reverse(5'-3')
U6	CTCGCTTCGGCAGCACA	AACGCTTCACGAATTTGCGT
miR-151a-3p	CGCGCTAGACTGAAGCTCC	AGTGCAGGGTCCGAGGTATT

Western Blot

Cells were harvested via centrifugation, after which the culture medium was carefully aspirated. Total protein was extracted using RIPA lysis buffer (C1053, Beijing Pulilai Gene Technology Co., Ltd.) supplemented with protease and phosphatase inhibitors. The lysates were centrifuged at 12,000 × g for 10 min at 4°C using an Eppendorf Centrifuge 5424R, and the resulting supernatants were collected. Protein concentration was determined using the BCA Protein Assay Kit (E-BC-K318-M, Elabscience). Equal amounts of protein were denatured in SDS-PAGE loading buffer and subjected to electrophoresis on a 10% polyacrylamide gel for 1.5 h. Electrophoretically separated proteins were transferred onto a PVDF membrane (Millipore) via wet transfer at a constant current of 300 mA for 1 h. The membrane was blocked with 5% (w/v) non-fat dry milk in TBST for 1 h at room temperature, followed by overnight incubation at 4°C with primary antibody diluted in blocking buffer. After three 10-min washes with TBST, the membrane was incubated with HRP-conjugated secondary antibody for 2 h at room temperature. Immunoreactive bands were visualized with an ultrasensitive chemiluminescent substrate (RJ239676, Thermo Fisher Scientific) and imaged detected using a high-resolution chemiluminescence detection system (Tanon-5200, Shanghai Tianneng Technology Co., Ltd.). The antibodies used and their corresponding dilution factors are listed in Table 3.

Table 3
Antibody information

Antibody name (Catalog number, Manufacturer)	dilution ratio
Mouse Anti- β -Actin(HC201, TransGen Biotech)	1:2000
Rabbit Anti DKK-1(14754-1-AP, Servicebio)	1:1000
Rabbit Anti GSK3 β (GB11099, Servicebio)	1:1000
Rabbit Anti Axin(GB11729, Servicebio)	1:1000
Rabbit Anti β -Catenin(GB11015, Servicebio)	1:1000
Rabbit Anti APC(ab40778, Abcam)	1:1000
Rabbit Anti LRP5(AF4645, Affinity)	1:1000
Rabbit Anti LRP6(DF2995, Affinity)	1:1000
HRP conjugated Goat Anti-Mouse IgG (H + L) (GB23301, Servicebio)	1:2000
HRP conjugated Goat Anti-Rabbit IgG(H + L) (GB23303, Servicebio)	1:2000

Dual-luciferase assay

The binding site between the 3'UTR of DKK1 and miR-151a-3p was predicted using the miRanda online tool. The 3'UTR sequence of chemically synthesized DKK1 mRNA was cloned into the F-Luc 3'UTR region of the pmirGLO vector to construct wild-type and mutant DKK1 dual-luciferase vectors, and miR-151a-3p mimics and mimic NCs were synthesized. Cells were plated according to experimental groups and transfected with the DKK1 wild-type and mutant dual-luciferase vectors, along with the miR-151a-3p mimic or mimic NC. Cells were Collected 48 hours after transfection, 200 μ L of lysis buffer was added to each well to lyse the cells, and the samples were incubated at 4°C for 20 minutes. For the assay, 70 μ L of cell lysate from each group was transferred into a white 96-well plate. Subsequently, 100 μ L of luciferase assay reagent was added to each well, and firefly luciferase activity was measured using a microplate reader (WD-2012B, Beijing Liuyi). Finally, 100 μ L of sea kidney luciferase assay reagent (prepared with a substrate-to-buffer ratio of 1:100) was added to each well, and sea kidney luciferase activity was measured using the same microplate reader.

Establishment of Acute Gouty Arthritis Rat Model and Group-Based Intervention

Twenty-four male SPF-grade SD rats, aged 6–8 weeks, were maintained under conditions of a room temperature of 20–26°C, relative humidity of 40–70%, and a 12-hour light-dark cycle. The housing area was well-ventilated, and the rats were provided with a standard pellet diet with free access to water.

Modeling began after all rats had undergone a 1-week acclimatization period. The experimental rats were randomly divided into the following four groups (6 rats per group): control group, acute gouty arthritis (GA) group, GA + naivety group (GA + NC), and GA + miR-151a-3p agonist group (GA + miR-151a-3p). Except for the control group, acute gouty arthritis was induced in the other three groups: Rats were anesthetized, placed in a supine position in an anesthetic machine, and maintained under anesthesia. The circumference of the right hind limb's tarsometatarsal joint (ankle joint) was measured three times using a tape measure, and the average value was recorded as the pre-induction ankle circumference. After measurement, the right hind limb ankle joint was disinfected with povidone-iodine. The tibia and foot were flexed to approximately 45°, and a needle attached to a syringe was inserted into the ankle joint cavity from the lateral side of the right hind ankle at a 45° angle to the tibia. When a sensation of entering an air pocket was felt, the syringe needle was considered to be within the joint cavity; the solution was then injected, administering 0.2 mL of MSU suspension (25 mg/mL) per rat. The syringe was removed, and pressure was applied with a cotton swab for several seconds to prevent leakage of the solution. After injection, the ankle circumference was measured three times using a tape measure, and the average was taken as the post-modeling ankle circumference. Four weeks after modeling, the ankle circumference was measured three times again, and the average value was calculated.

Animal Intervention: Rats in the GA + miR-151a-3p group received intra-articular injections of a miR-151a-3p agonist three times weekly on alternate days, starting one week prior to model induction, followed by model induction. Rats in the GA + NC and GA groups received intra-articular injections of an empty vector or saline, respectively, at the same time points. Four weeks after model induction, the animals were euthanized, and serum and ankle joint tissues were collected.

At the end of the experiments (4 weeks post-intervention), all rats were deeply anesthetized by intraperitoneal injection of sodium pentobarbital (150 mg/kg). Following the loss of pedal withdrawal reflex, the animals were euthanized via exsanguination and cervical dislocation to ensure death. Serum and ankle joint tissues were then promptly collected for subsequent analyses.

Measurement of the rat ankle joint circumference

The diameter of the right ankle joint was measured in rats using a vernier caliper before modeling, 3 hours post-modeling, and 4 weeks post-intervention, and the values were recorded. Ankle swelling was calculated using the following formula: Ankle swelling = (ankle diameter at each time point post-modeling) – (ankle diameter pre-modeling).

Hematoxylin and Eosin (HE) staining

Four weeks after the intervention, rat ankle joint tissues were harvested and fixed in 4% paraformaldehyde for 24 hours. Subsequently, tissues were decalcified in an EDTA-based solution with a solution-to-tissue volume ratio of 15–20:1. The decalcification solution was refreshed every 2–3 days throughout the procedure until the tissue became pliable. After decalcification, the tissues were dehydrated through a graded ethanol series, paraffin-embedded, and sectioned. Following dewaxing and rehydration of the sections, they were stained with hematoxylin and eosin. The sections were then

dehydrated and mounted. Images of the rat ankle synovial tissue were acquired using a light microscope and subsequently analyzed.

Immunohistochemistry

Paraffin sections were routinely deparaffinized in water, rinsed with distilled water for 1 minute, and placed in PBS. Antigen retrieval was performed, followed by blocking of endogenous peroxidase activity and rinsing with PBS. Sections were incubated with the primary antibody, followed by incubation with the secondary antibody, developed with DAB, counterstained with hematoxylin, differentiated, rinsed to remove excess stain, dehydrated, cleared, mounted with neutral resin, and examined under a microscope.

Statistical Analysis

GraphPad Prism 9.0 was used for graphing and statistical analysis. All experiments were performed in triplicate, and quantitative results are expressed as mean $\pm$ standard deviation ($X \pm S$). One-way analysis of variance (ANOVA) was used to compare means among multiple groups, and the Student-Newman-Keuls (SNK) method was used for pairwise comparisons. Statistical significance was defined as a P-value < 0.05 .

Results

miR-151a-3p and DKK-1 exhibit opposite expression patterns in gouty arthritis

Serum samples from 30 normal controls and 34 patients with gouty arthritis were collected. All participants were matched for gender and age. The expression level of miR-151a-3p in blood was measured by qPCR, and the concentration of DKK-1 in serum was determined by ELISA. The results indicated that, compared with healthy controls, miR-151a-3p expression in the blood of patients with GA was significantly reduced (Fig. 1A), whereas DKK-1 levels in the serum of patients with GA were significantly increased (Fig. 1B). THP-1 cells were induced by PMA and then treated with LPS and MSU crystals to establish a gouty arthritis cell model. The expression level of miR-151a-3p in cells was detected by qPCR, and the protein expression level of DKK-1 in cells was detected by WB. Results demonstrated that, relative to the control group, miR-151a-3p expression in the GA group cells was significantly downregulated (Fig. 1C), while DKK-1 protein expression was significantly upregulated (Figs. 1D-E). miR-151a-3p and DKK-1 exhibit opposite expression patterns in GA.

miR-151a-3p inhibits cell proliferation and inflammatory responses in GA cellular models

After transfecting miR-151a-3p mimic and NC into cells, the level of miR-151a-3p in cells was detected by qPCR. The results showed that compared with the Control group and mimic NC, the level of miR-151a-

3p in cells in the miR-151a-3p mimic group was significantly increased (Fig. 2A), indicating that transfection was effective. After transfection with miR-151a-3p mimic, the cells were further treated with LPS and MSU crystals. Cell proliferation in each group was assessed using the CCK-8 assay (Fig. 2B), while cell cycle distribution was analyzed via flow cytometry (Figs. 2C-D). Compared with the Control group, both the GA and GA + mimic NC groups exhibited significantly enhanced cell proliferation and a marked increase in the proportion of S-phase cells. S phase (DNA synthesis phase) is a very critical stage in the cell cycle. At this stage, DNA within cells replicates. The proportion of S-phase cells increased significantly, indicating that cells are more actively preparing for division, which leads to an increase in proliferation; compared with the GA + mimic NC group, the proliferation activity of cells in the GA + miR-151a-3p mimic group was significantly reduced, and the proportion of S-phase cells was significantly reduced. These findings demonstrate that miR-151a-3p inhibits cell proliferation in the GA model. TNF- α and IL-1 β levels in the cell culture supernatants of each group were quantified by ELISA (Figs. 2E-F). The results showed that compared with the Control group, the expression levels of TNF- α and IL-1 β in the cell supernatant of GA group and GA + mimic NC group were significantly increased; compared with the GA + mimic NC group, the expression levels of TNF- α and IL-1 β in the cell supernatant of GA + miR-151a-3p mimic group were significantly decreased. The results showed that miR-151a-3p inhibited the expression of inflammatory factors in GA model cells.

Effect of miR-151a-3p on the expression of DKK-1 and WNT pathway-related proteins in the GA cell model

We further assessed the protein expression levels of DKK-1 and key WNT pathway components (β -catenin, GSK3 β , LRP5/6, APC, and Axin) in cells from each group via Western blot analysis. Results indicated that, relative to the Control group, both the GA and GA + mimic NC groups displayed significantly decreased expression of β -catenin and LRP5/6, whereas expression of GSK3 β , APC, Axin, and DKK-1 was significantly upregulated (Fig. 3). Compared to the GA + mimic NC group, the GA + miR-151a-3p mimic group showed significantly elevated levels of β -catenin and LRP5/6, accompanied by a significant downregulation of GSK3 β , APC, Axin, and DKK-1.

miR-151a-3p can specifically regulate DKK-1 expression

The wild-type and mutant dual luciferase vectors of DKK-1 were constructed; miR-151a-3p mimic and mimic NC were synthesized and transfected into 293T cells in respective experimental groups. Dual luciferase experiments were performed to verify whether miR-151a-3p and DKK-1 interacted. The results showed that compared with the DKK-1WT + mimic NC group, the fluorescence intensity of the DKK-1-WT + miR-151a-3p mimic group was significantly reduced; compared with the DKK-1-MUT + mimic NC group, the fluorescence intensity of the DKK-1-MUT + miR-151a-3p mimic group was not significantly different, indicating that there was an interaction between miR-151a-3p and DKK-1 (Fig. 4). Combined with the previous results, it is shown that miR-151a-3p can target the inhibition of DKK-1 expression.

Overexpression of DKK-1 reverses the decline in cell viability and the inhibition of the inflammatory response in cells in the GA model induced by miR-151a-3p mimic

After establishing the GA cell model, we investigated whether the effect of miR-151a-3p on this model could be reversed by DKK-1 by co-transfecting cells with miR-151a-3p mimic and a DKK-1 overexpression vector. First, a DKK-1 overexpression vector (OE-DKK-1) was constructed and transfected into cells. Western blot results (Figs. 5A-B) showed that after transfection of OE-DKK-1, the level of DKK-1 protein in cells increased significantly, confirming the effectiveness of the vector. The proliferation activity of cells in each group was assessed by the CCK-8 assay, and the cell cycle distribution was analyzed by flow cytometry. The results showed (Figs. 5C-E) that compared with the GA + OE-NC + mimic NC group, the cell viability of the GA + OE-NC + miR-151a-3p mimic group was significantly reduced, and the proportion of S-phase cells was significantly reduced; while compared with the GA + OE-NC + miR-151a-3p mimic group, the cell viability of the GA + OE-DKK1 + miR-151a-3p mimic group was significantly restored; although the proportion of S-phase cells also showed an increasing trend, this difference did not reach statistical significance ($P > 0.05$). The above results suggest that overexpression of DKK-1 can reverse the decline in GA cell viability caused by miR-151a-3p mimic to a certain extent. In addition, the concentrations of IL-1 β and TNF- α in cell supernatants of each group were detected by ELISA. The results showed (Figs. 5F-G) that compared with the GA + OE-NC + mimic NC group, the levels of IL-1 β and TNF- α in the GA + OE-NC + miR-151a-3p mimic group were significantly reduced; while the concentrations of these inflammatory factors in the GA + OE-DKK-1 + miR-151a-3p mimic group were significantly increased. These data further confirmed that overexpression of DKK-1 can reverse the inhibition of inflammatory response in GA cells caused by miR-151a-3p mimic.

DKK-1 Overexpression reverses the regulation of the WNT pathway mediated by miR-151a-3p

Further, the expression levels of DKK-1 protein and WNT pathway-related proteins β -Catenin, GSK3 β , LRP5/6, APC, and Axin in cells were analyzed by Western blotting. As shown in Fig. 6, compared with the GA + OE-NC + mimic NC group, the protein expression levels of β -Catenin and LRP5/6 in the GA + OE-NC + miR-151a-3p mimic group were significantly increased, while the protein levels of GSK3 β , APC, Axin, and DKK1 were significantly decreased. Compared with the GA + OE-NC + miR-151a-3p mimic group, the protein expression levels of β -Catenin and LRP5/6 in the GA + OE-DKK-1 + miR-151a-3p mimic group were significantly decreased, while the protein levels of GSK3 β , APC, Axin, and DKK1 were significantly increased. These results indicate that the regulatory effect of miR-151a-3p on the WNT pathway was reversed by the overexpression of DKK-1.

miR-151a-3p attenuates pathological damage in a rat model of acute gouty arthritis

The ankle circumferences of rats in each group were measured before modeling, after modeling, and before tissue collection; the results are shown in Fig. 7A. Before modeling, the ankle circumferences of the four groups were comparable, with no significant differences between groups. After modeling, ankle circumferences in all three model groups were significantly increased compared with the control group. After 4 weeks of intervention, compared with the GA group, the ankle circumference of rats in the GA + miR-151a-3p group was significantly reduced.

HE staining results (Fig. 7B) showed that the ankle joints of rats in the control group were structurally intact, with no obvious pathological changes. In the GA and GA + NC groups, synovial hyperplasia, inflammatory infiltration, tissue edema, and structural disorganization were observed, indicating significant pathological damage. Compared with the two model groups, the GA + miR-151a-3p group showed markedly reduced synovial hyperplasia, inflammatory infiltration, and edema, with joint structures tending toward integrity, suggesting that miR-151a-3p can effectively alleviate pathological damage in rat gouty arthritis.

Serum levels of the inflammatory cytokines TNF- α and IL-1 β in rats were measured using ELISA; the results are shown in Fig. 7C. Compared with the control group, TNF- α and IL-1 β levels were significantly elevated in the GA and GA + NC groups; compared with the GA group, TNF- α and IL-1 β levels were significantly reduced in the GA + miR-151a-3p group.

Effect of miR-151a-3p on DKK-1 and WNT pathway signaling protein expression in a rat model of acute gouty arthritis

DKK-1 levels in rat serum were measured using ELISA; the results are shown in Fig. 7D. Compared with the control group, DKK-1 levels were significantly elevated in the GA and GA + NC groups ($P < 0.05$). Furthermore, compared with the GA group, DKK-1 levels were significantly reduced in the GA + miR-151a-3p group ($P < 0.05$).

Immunohistochemical analysis (Fig. 7E) revealed that, compared with the control group, the GA group exhibited significantly reduced expression of β -catenin, LRP5, and LRP6 proteins, while showing a significant increase in the expression of GSK3 β , APC, and AXIN2 proteins. Conversely, compared with the GA group, the GA + miR-151a-3p group exhibited significantly increased expression of β -catenin, LRP5, and LRP6 proteins in rat ankle joint tissues, accompanied by a significant decrease in the expression of GSK3 β , APC, and AXIN2 proteins.

Discussion

GA is a common joint disease characterized by repeated episodes of joint inflammation due to stimulation from MSU [21]. MSU crystals are the crystalline form of uric acid deposited in joints and other tissues, triggering the release of pro-inflammatory factors, which in turn leads to sterile inflammation [22]. In this study, we used MSU to treat THP-1 cells to establish an in vitro GA model, and

further established an acute GA rat model to explore the role of miR-151a-3p in regulating the inflammatory response stimulated by MSU.

Several studies have shown that multiple miRNAs are involved in the pathogenesis of GA, including miR-17-5p, miR-30c-5p, miR-142-3p, miR-18a-5p, and miR-223-3p [12]. Studies have shown that HOTTIP levels are significantly increased and miR-101-3p levels are significantly decreased in plasma of GA patients. Decreased HOTTIP levels significantly inhibited MSU-induced release of the pro-inflammatory factors interleukin (IL)-1 β , IL-8, and transforming growth factor- α from macrophages, but this inhibition was reversed by silencing miR-101-3p [23]. Other studies have shown that the expression of HOTAIR in synovial fluid monocytes (SFMCs) in GA patients and MSU stimulated THP-1 cells is up-regulated, while the expression of miR-20b is down-regulated. Knockout of long non-coding RNA HOTAIR inhibits the secretion of inflammatory cytokines by upregulating miR-20b, thereby reducing ankle swelling in GA [24]. In leukocytes from GA patients, the levels of miR-488 and miR-920 were significantly reduced, while MSU crystals could inhibit the expression of miR-488 and miR-920. The upregulation of miR-488 and miR-920 can inhibit the expression of IL-1 β protein in THP-1 cells induced by MSU and inhibit the inflammatory response [25]. In this study, we observed a decrease in the expression level of miR-151a-3p in GA patients and MSU-treated THP-1 cells, indicating that miR-151a-3p may act as an anti-inflammatory gene during GA. Further studies found that after MSU stimulated THP-1 cells, cell proliferation increased and levels of inflammatory factors TNF- α and IL-1 β increased. Upregulation of miR-151a-3p inhibited the proliferation of MSU-treated THP-1 cells and inhibited the levels of TNF- α and IL-1 β . In animal models, intraarticular injection of the miR-151a-3p agonist also significantly reduced serum TNF- α and IL-1 β levels in rats, and reduced ankle joint swelling and synovial pathological damage. This further suggests that miR-151a-3p plays the role of an anti-inflammatory gene in the GA process.

A large number of studies have shown that the Wnt/ β -catenin signaling pathway can participate in the reconstruction of tissue homeostasis by regulating inflammatory responses [26]. For example, Zhang et al. found that in a tularemia model, activation of Wnt/ β -catenin signaling in macrophages effectively suppresses the inflammatory response [27]. In addition, alarm S100A8/A9 can induce activation of the classical Wnt signaling pathway in macrophages, which in turn down-regulates the expression levels of matrix metalloproteinase 3 (MMP-3) and interleukin-6 (IL-6). In GA, Wnt5a and its receptor FZD5 in macrophages are regulated by NF- κ B and TLR2/4 [28], which recognize MSU crystals and further activate the NOD-like receptor family pyrin domain containing protein 3 (NLRP3) inflammasome containing NACHT, leucine-rich repeats (LRR), and pyrin domain (PYD) [29]. This study found that in the GA cell model stimulated by MSU, the levels of β -catenin and LRP5/6 proteins decreased, accompanied by the upregulation of negative regulatory proteins such as GSK3 β , APC, and Axin, suggesting that the Wnt pathway is inhibited under GA inflammation. It is worth noting that overexpression of miR-151a-3p can reverse the above protein expression changes, that is, promote the expression of β -catenin and LRP5/6, and inhibit the expression of GSK3 β , APC, Axin and DKK-1, indicating that overexpression of miR-151a-3p activates the Wnt pathway. To further verify the applicability of this mechanism in vivo, we established an acute GA rat model. The results showed that intraarticular injection of miR-151a-3p agonist could also significantly upregulate the expression of β -catenin and LRP5/6 in ankle joint tissue,

and down-regulate the expression of GSK3 β , APC, and AXIN2, which was highly consistent with the results of in vitro cell experiments. These in vivo and in vitro data jointly support the view that miR-151a-3p plays an anti-inflammatory role by activating the Wnt/ β -catenin pathway.

Studies have shown that the Wnt signaling pathway is strictly controlled by a series of negative regulators, of which DKK1 is one [30]. DKK1 inhibits the classical Wnt signaling pathway by binding to LRP5/6 co-receptors and blocking Wnt binding, resulting in degradation of β -catenin [31, 32]. In this study, we observed significant upregulation of DKK-1 expression levels in the GA state in both clinical samples and cell models, which is exactly the opposite of the expression pattern of miR-151a-3p, suggesting a potential regulatory relationship between the two. Subsequent dual luciferase reporter gene experiments confirmed that DKK-1 is the direct target gene of miR-151a-3p. Functional experiments further revealed that the upregulation of DKK-1 plays a pivotal role in mediating the pathological process of GA: in MSU-induced cell models, the overexpression of DKK-1 not only reversed the inhibitory effect of miR-151a-3p on cell proliferation, but also reactivated the inflammatory response, manifested by the recovery of the secretion of pro-inflammatory factors TNF- α and IL-1 β . From a mechanistic perspective, as a classic Wnt pathway inhibitor, changes in DKK-1 expression directly affect the homeostasis of key proteins in the pathway. Our results show that DKK-1 promotes the expression of GSK3 β , APC, Axin and other proteins by inhibiting the Wnt/ β -catenin pathway, thereby exacerbating the inflammatory response and abnormal cell proliferation. Therefore, in GA, inflammatory stimuli lead to increased expression of DKK-1, which in turn inhibits Wnt pathway activity, which has potential anti-inflammatory effects, and ultimately amplifies inflammatory damage.

It is worth emphasizing that this study verified the therapeutic potential of miR-151a-3p at the animal level for the first time. Through local injection of the miR-151a-3p agonist, we not only observed a significant relief of ankle joint swelling, but also confirmed the reduction of synovial pathological damage and the regulation of Wnt pathway-associated proteins through HE staining and immunohistochemistry. These in vivo results corroborate the in vitro findings, significantly strengthening the reliability of the conclusions. In addition, the anti-inflammatory function of miR-151a-3p in GA is similar to its inhibitory effect on cell proliferation in prostate cancer [33], while in polycystic ovary syndrome, it promotes disease progression through the PI3K/AKT pathway, indicating that the function of miR-151a-3p is significantly disease-dependent, and its final effect depends on the expression profile of downstream target genes.

Of course, this study also has certain limitations. First, animal experiments only observed the short-term intervention effect of acute GA models, but did not evaluate the safety and potential side effects of long-term treatment. Secondly, the upstream regulatory mechanism of miR-151a-3p remains unclear, and the underlying mechanisms for its down-regulation in GA require further exploration. In addition, although we have confirmed that miR-151a-3p functions by targeting DKK-1, whether it relies entirely on this pathway in animal models still needs to be verified by rescue experiments such as co-injection of DKK-1 overexpressing vectors. Finally, no previous studies have reported a direct association between miR-151a-3p and gouty arthritis. This study reveals the expression pattern and functional mechanism of miR-

151a-3p in GA for the first time. However, more independent cohorts and translational studies are needed to validate these findings.

Conclusion

In summary, miR-151a-3p activates the Wnt/ β -catenin signaling pathway by targeting DKK-1, thereby inhibiting the inflammatory response triggered by MSU. Our results highlight the potential role of the miR-151a-3p/DKK-1 axis in anti-inflammatory therapeutic strategies for GA.

Declarations

Acknowledgments

We would like to express our sincere gratitude to Dr. Zhao Bin and Dr. Wang Jing from the Central Laboratory of Quanzhou First Hospital affiliated to Fujian Medical University, for their invaluable technical and material support throughout this study. We also extend our appreciation to Mr. Chen Dengyun from the Department of Laboratory Medicine at the same institution for his assistance in the clinical specimen testing. Furthermore, we acknowledge the Central Laboratory and the Department of Laboratory Medicine of Quanzhou First Hospital for providing the experimental platform and additional technical support.

Author contributions

YZ and XFP designed the study. YLM, JWF, ZZZ and BSH performed the experiments. YFZ, XMW and YHL collected the data, TJZ, ZCS and FH analyzed and interpreted the data. PWW and XFP prepared the manuscript. All the authors read and approved the final manuscript.

Funding

This study was supported by the Fujian Provincial Natural Science Foundation (No. 2023J011791), Quanzhou Science and Technology Plan Project (2025QZNG024), Chronic Disease Management Research Project of National Health Commission Capacity Building and Continuing Education Center (GWJJMB202510024058), China Medical and Health Development Foundation supported Project (chmdf 2025-jycx02-3).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

The authors declare that they have no competing interests.

Ethics approval and consent to participate

The study was performed with the approval of the Ethics Committee of Quanzhou First Hospital Affiliated to Fujian Medical University (approval number: [2023] K076). Informed written consent was obtained from each participant prior to the study, ensuring their confidentiality and anonymity throughout the research process. All animal husbandry and experiments were strictly performed in accordance with the regulations for the management and use of laboratory animals.

References

1. Yao TK, Lee RP, Wu WT, Chen IH, Yu TC, Yeh KT. Advances in Gouty Arthritis Management: Integration of Established Therapies, Emerging Treatments, and Lifestyle Interventions. *Int J Mol Sci.* 2024; 25.
2. Fu W, Ge M, Li J. Phospholipase A2 regulates autophagy in gouty arthritis: proteomic and metabolomic studies. *J Transl Med.* 2023; 21: 261.
3. Singh JA, Gaffo A. Gout epidemiology and comorbidities. *Semin Arthritis Rheum.* 2020; 50: S11-s6.
4. Keller SF, Mandell BF. Management and Cure of Gouty Arthritis. *Med Clin North Am.* 2021; 105: 297-310.
5. Hsu DZ, Chen SJ, Chu PY, Liu MY. Therapeutic effects of sesame oil on monosodium urate crystal-induced acute inflammatory response in rats. *Springerplus.* 2013; 2: 659.
6. Lu Y, Fang L, Xu X, Wu Y, Li J. MicroRNA-142-3p facilitates inflammatory response by targeting ZEB2 and activating NF- κ B signaling in gouty arthritis. *Cell Cycle.* 2022; 21: 805-19.
7. Jeong JH, Hong S, Kwon OC, Ghang B, Hwang I, Kim YG, et al. CD14(+) Cells with the Phenotype of Infiltrated Monocytes Consist of Distinct Populations Characterized by Anti-inflammatory as well as Pro-inflammatory Activity in Gouty Arthritis. *Front Immunol.* 2017; 8: 1260.
8. Wang L, Zhu L, Duan C, Li L, Chen G. Total saponin of *Dioscorea collettii* attenuates MSU crystal-induced inflammation via inhibiting the activation of the NALP3 inflammasome and caspase-1 in THP-1 macrophages. *Mol Med Rep.* 2020; 21: 2466-74.
9. Liu F, Bai Y, Wan Y, He J, Li Q, Xie Y, et al. Mechanism of flavonoids in the treatment of gouty arthritis (Review). *Mol Med Rep.* 2024; 30.
10. Saliminejad K, Khorram Khorshid HR, Soleymani Fard S, Ghaffari SH. An overview of microRNAs: Biology, functions, therapeutics, and analysis methods. *J Cell Physiol.* 2019; 234: 5451-65.
11. Rupaimoole R, Slack FJ. MicroRNA therapeutics: towards a new era for the management of cancer and other diseases. *Nat Rev Drug Discov.* 2017; 16: 203-22.
12. Bohatá J, Horváthová V, Pavlíková M, Stibůrková B. Circulating microRNA alternations in primary hyperuricemia and gout. *Arthritis Res Ther.* 2021; 23: 186.
13. Siasos G, Bletsas E, Stampouloglou PK, Oikonomou E, Tsigkou V, Paschou SA, et al. MicroRNAs in cardiovascular disease. *Hellenic J Cardiol.* 2020; 61: 165-73.

14. Mahtal N, Lenoir O, Tinel C, Anglicheau D, Tharaux PL. MicroRNAs in kidney injury and disease. *Nat Rev Nephrol.* 2022; 18: 643-62.
15. Ferragut Cardoso AP, Banerjee M, Nail AN, Lykoudi A, States JC. miRNA dysregulation is an emerging modulator of genomic instability. *Semin Cancer Biol.* 2021; 76: 120-31.
16. Wang X, Chi J, Dong B, Xu L, Zhou Y, Huang Y, et al. MiR-223-3p and miR-22-3p inhibit monosodium urate-induced gouty inflammation by targeting NLRP3. *Int J Rheum Dis.* 2021; 24: 599-607.
17. Jin HM, Kim TJ, Choi JH, Kim MJ, Cho YN, Nam KI, et al. MicroRNA-155 as a proinflammatory regulator via SHIP-1 down-regulation in acute gouty arthritis. *Arthritis Res Ther.* 2014; 16: R88.
18. Liu X, Zhou M, Yang D, Gong L, Chen X, Zeng Z, et al. Analysis of miR-151a-3p as a biomarker of osteoarthritis and its clinical value. *J Orthop Surg Res.* 2025; 20: 832.
19. Lin J, Lin H, Li W, Huang J, Chen L, Wang R. miR-151a-3p regulates the TNIK/PI3K/Akt axis and influences the progression of polycystic ovary syndrome. *J Matern Fetal Neonatal Med.* 2024; 37: 2372695.
20. Yan Y, Yu L, Chen B, Cao C, Zhao H, Wang Q, et al. Mastoparan M Suppressed NLRP3 Inflammasome Activation by Inhibiting MAPK/NF- κ B and Oxidative Stress in Gouty Arthritis. *J Inflamm Res.* 2023; 16: 6179-93.
21. Xu H, Zhang B, Chen Y, Zeng F, Wang W, Chen Z, et al. Type II collagen facilitates gouty arthritis by regulating MSU crystallisation and inflammatory cell recruitment. *Ann Rheum Dis.* 2023; 82: 416-27.
22. Ni X, Wang Q, Ning Y, Liu J, Su Q, Lv S, et al. Anemoside B4 targets NEK7 to inhibit NLRP3 inflammasome activation and alleviate MSU-induced acute gouty arthritis by modulating the NF- κ B signaling pathway. *Phytomedicine.* 2025; 138: 156407.
23. Shao P, Liu H, Xue Y, Xiang T, Sun Z. LncRNA HOTTIP promotes inflammatory response in acute gouty arthritis via miR-101-3p/BRD4 axis. *Int J Rheum Dis.* 2023; 26: 305-15.
24. Liu YF, Xing GL, Chen Z, Tu SH. Long non-coding RNA HOTAIR knockdown alleviates gouty arthritis through miR-20b upregulation and NLRP3 downregulation. *Cell Cycle.* 2021; 20: 332-44.
25. Zhou W, Wang Y, Wu R, He Y, Su Q, Shi G. MicroRNA-488 and -920 regulate the production of proinflammatory cytokines in acute gouty arthritis. *Arthritis Res Ther.* 2017; 19: 203.
26. Zhao Y, Wang C, Hong X, Miao J, Liao Y, Hou FF, et al. Wnt/ β -catenin signaling mediates both heart and kidney injury in type 2 cardiorenal syndrome. *Kidney Int.* 2019; 95: 815-29.
27. Zhang P, Katz J, Michalek SM. Glycogen synthase kinase-3 β (GSK3 β) inhibition suppresses the inflammatory response to Francisella infection and protects against tularemia in mice. *Mol Immunol.* 2009; 46: 677-87.
28. Blumenthal A, Ehlers S, Lauber J, Buer J, Lange C, Goldmann T, et al. The Wingless homolog WNT5A and its receptor Frizzled-5 regulate inflammatory responses of human mononuclear cells induced by microbial stimulation. *Blood.* 2006; 108: 965-73.
29. Cronstein BN, Terkeltaub R. The inflammatory process of gout and its treatment. *Arthritis Res Ther.* 2006; 8 Suppl 1: S3.

30. Liang L, Tu Y, Lu J, Wang P, Guo Z, Wang Q, et al. Dkk1 exacerbates doxorubicin-induced cardiotoxicity by inhibiting the Wnt/ β -catenin signaling pathway. *J Cell Sci.* 2019; 132.

31. Qing W, Hao X, Xuan S, Zhihui R, Jinzhi G. Wnt1 oversees microglial activation by the Wnt/LRP5/6 receptor signaling pathway during lipopolysaccharide-mediated toxicity. *Mol Biol Rep.* 2025; 52: 273.

32. Wo D, Peng J, Ren DN, Qiu L, Chen J, Zhu Y, et al. Opposing Roles of Wnt Inhibitors IGFBP-4 and Dkk1 in Cardiac Ischemia by Differential Targeting of LRP5/6 and β -catenin. *Circulation.* 2016; 134: 1991-2007.

33. Zhang Y, Hao T, Zhang H, Wei P, Li X. [Over-expression of miR-151a-3p inhibits proliferation and migration of PC-3 prostate cancer cells]. *Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi.* 2018; 34: 247-52.

Figures

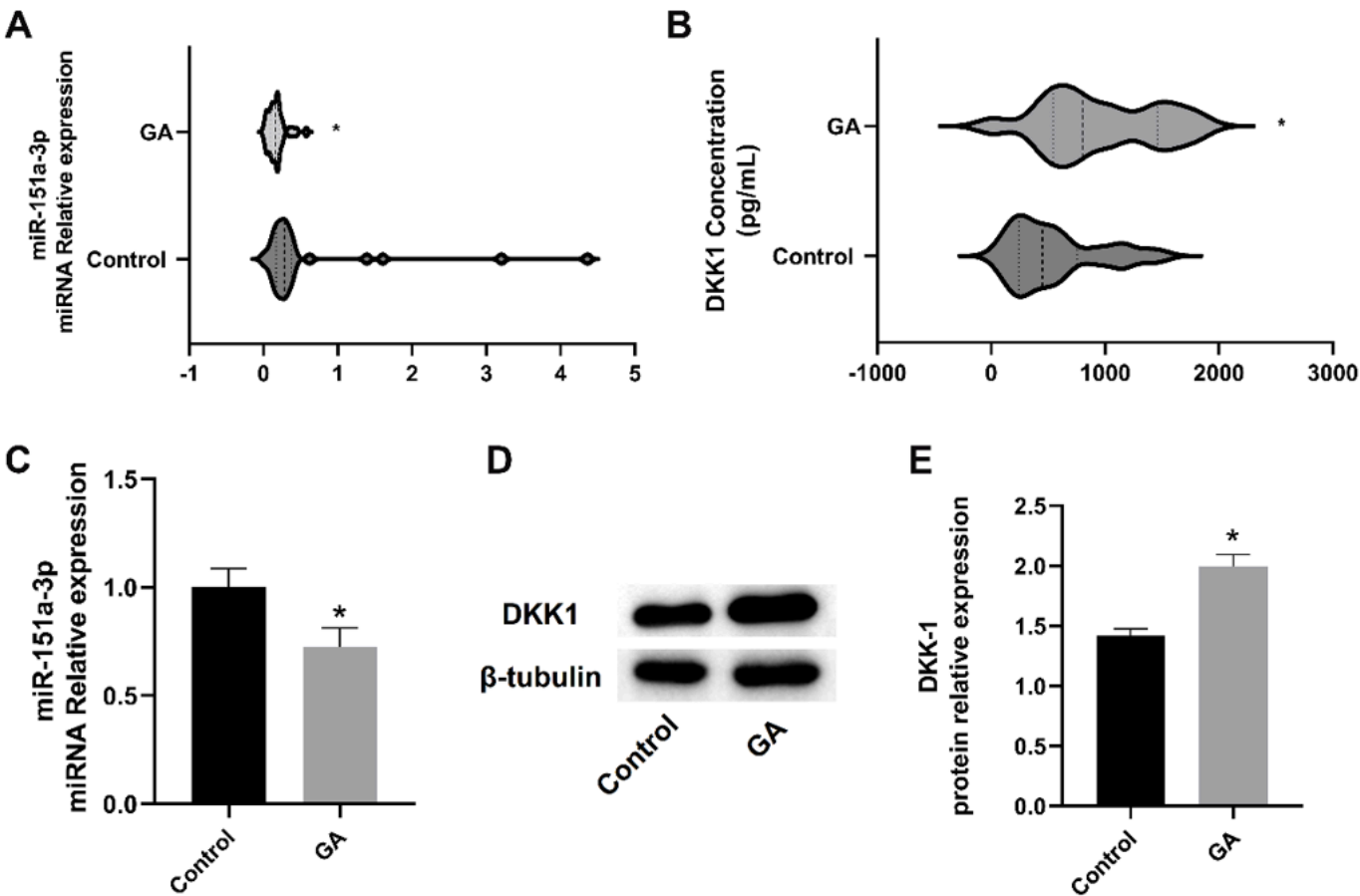


Figure 1

miR-151a-3p and DKK1 exhibit opposing expression patterns in gouty arthritis. (A) qPCR was used to detect the expression level of miR-151a-3p in clinical blood samples; (B) ELISA was used to detect the

content of DKK-1 in clinical serum samples; (C) qPCR was used to detect the expression level of miR-151a-3p in cells; (D-E) DKK-1 protein expression in cells was analyzed by Western blotting. (*P < 0.05 vs. Control group)

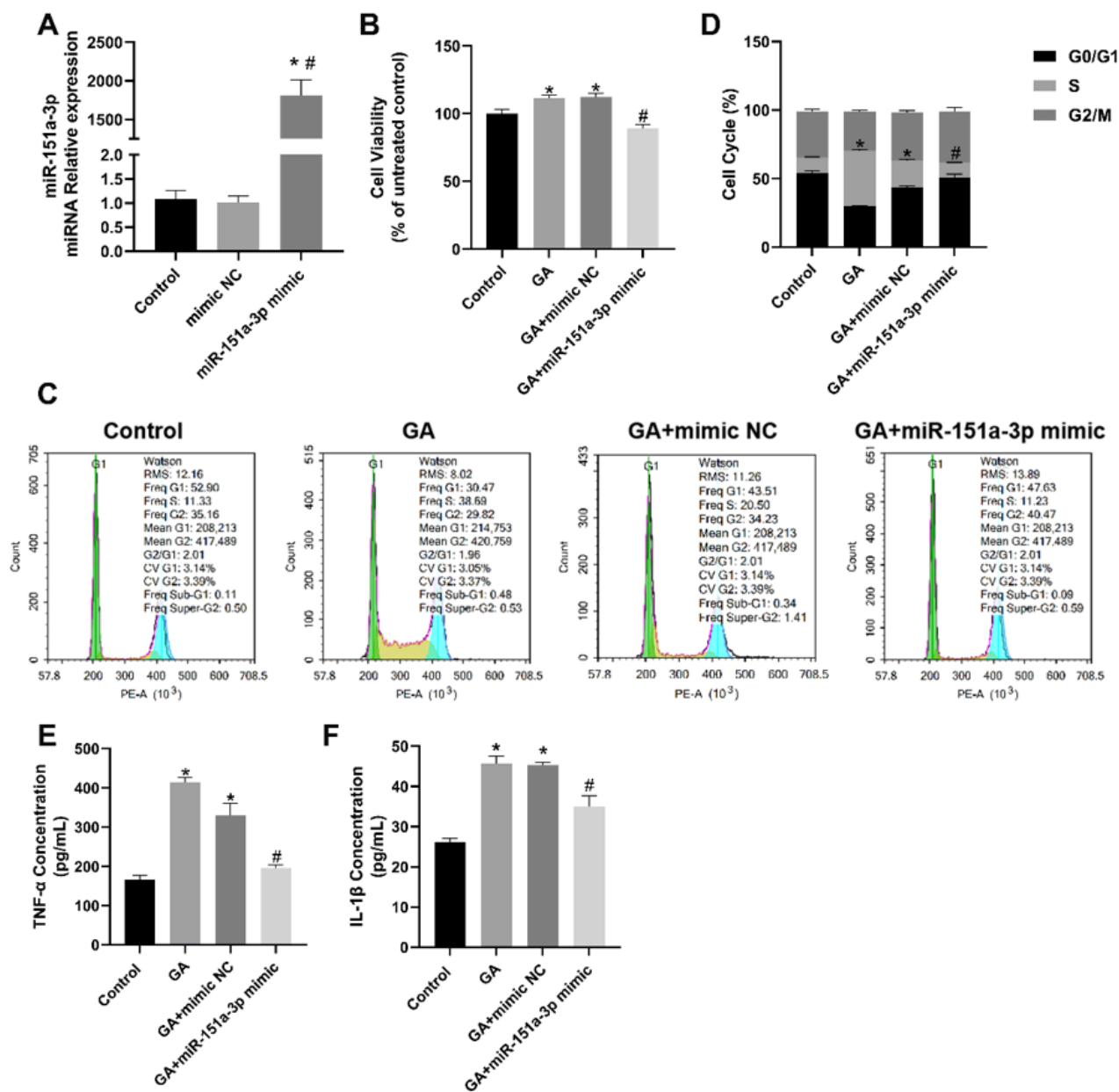


Figure 2

miR-151a-3p inhibits proliferation and the inflammatory response in a GA cell model. (A) Transfection verification of miR-151a-3p mimic, *P < 0.05 vs Control, #P < 0.05 vs mimic NC; (B) CCK-8 assay for cell proliferation; (C-D) Flow cytometry for cell cycle; (D-E) ELISA for the expression levels of TNF-α and IL-1β in the supernatant of each group of cells. (*P < 0.05 vs. Control group; #P<0.05 vs. GA group)

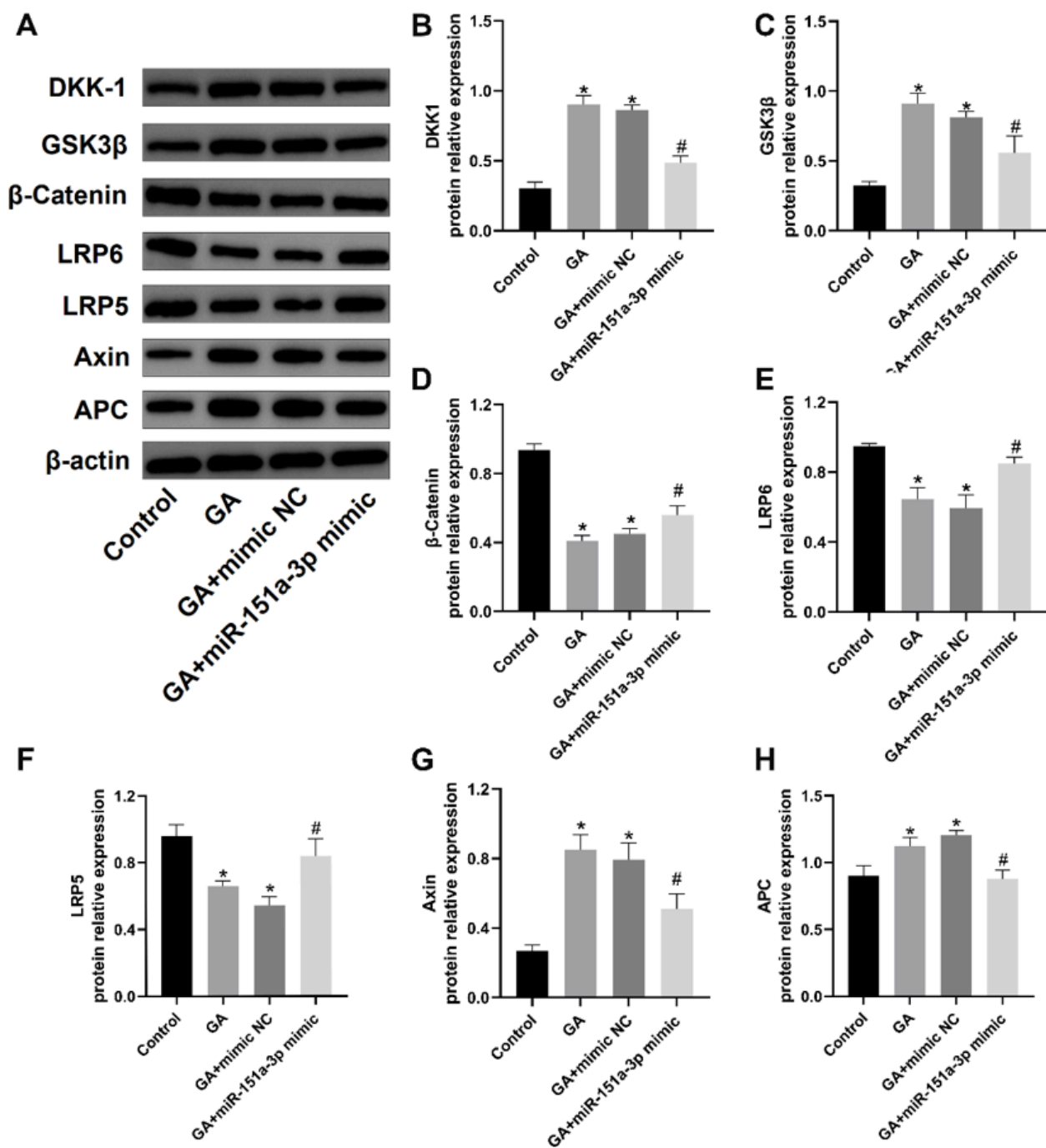
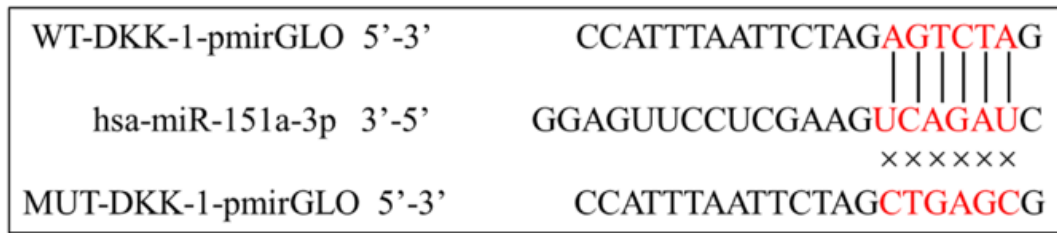
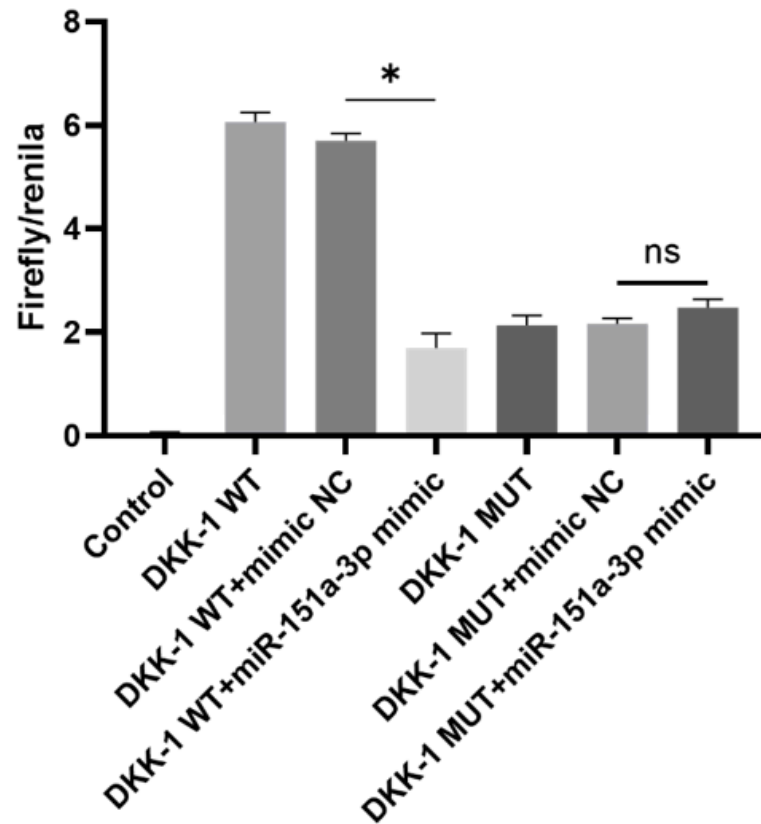


Figure 3

Effects of miR-151a-3p on the expression of DKK-1 and WNT pathway-related proteins in the GA cell model. (A) Representative protein expression band diagrams of each index; (B-H) Bar charts of protein expression levels of DKK-1, GSK3β, β-Catenin, LRP6, LRP5, Axin and APC. (*P < 0.05 vs. Control group; #P<0.05 vs. GA group)

A**B****Figure 4**

Dual-luciferase assay to verify the interaction between miR-151a-3p and DKK-1. (A) Binding sites; (B) Results of the dual-luciferase assay (*P < 0.05 vs. DKK-1WT + mimic NC group)

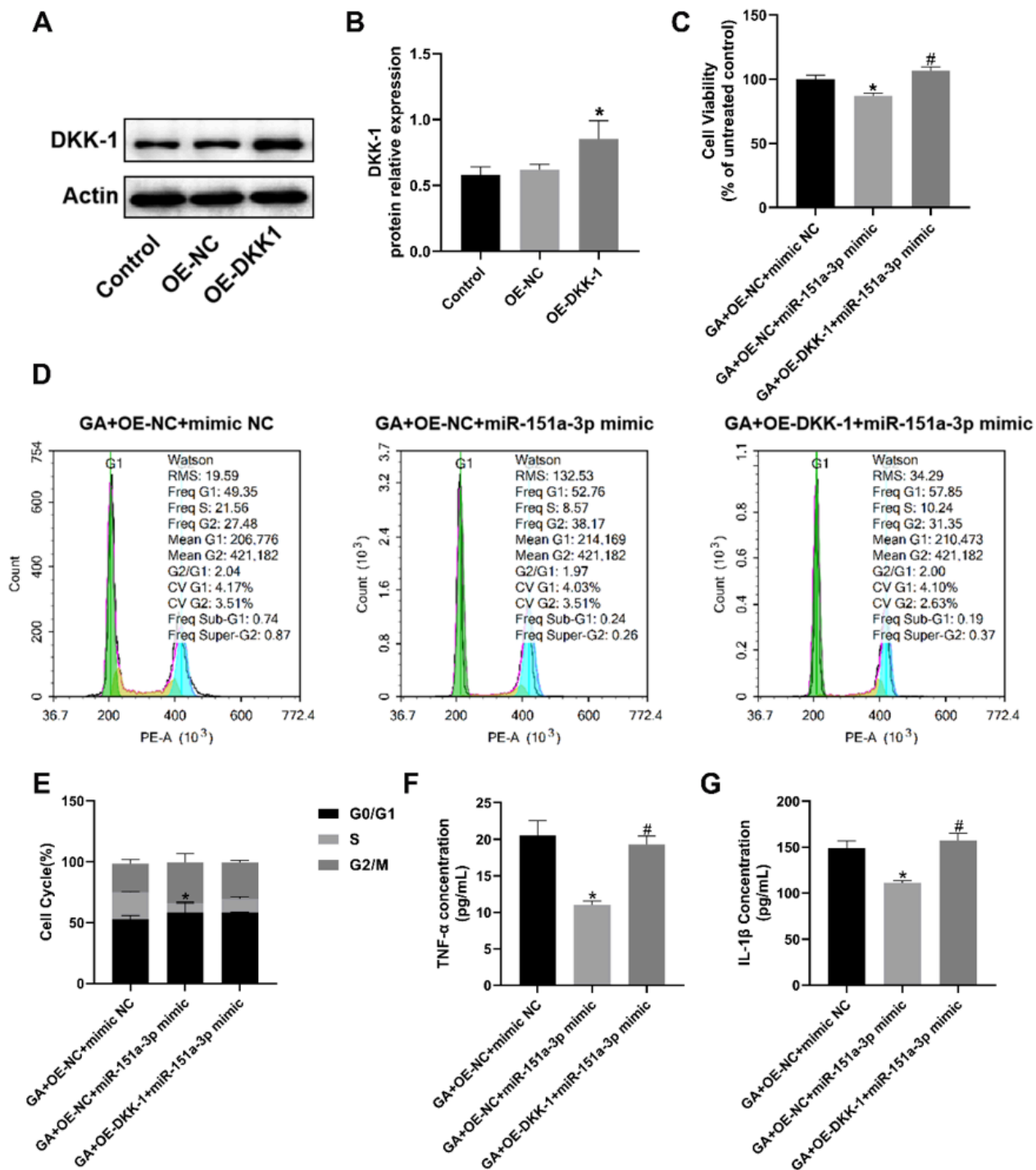


Figure 5

Overexpression of DKK-1 can reverse the decline in cell viability and inhibition of inflammatory response in GA model cells caused by miR-151a-3p mimic. (A-B) Western blot verification of the DKK-1 overexpression vector; (C) CCK-8 result; (D-E) Flow cytometry results of cell cycle detection; (F-G) The results of ELISA for detecting the contents of TNF- α and IL-1 β in the cell supernatant. (* $P < 0.05$ vs. DKK-1WT + mimic NC group; # $P < 0.05$ vs. OE-NC + miR-151a-3p mimic group)

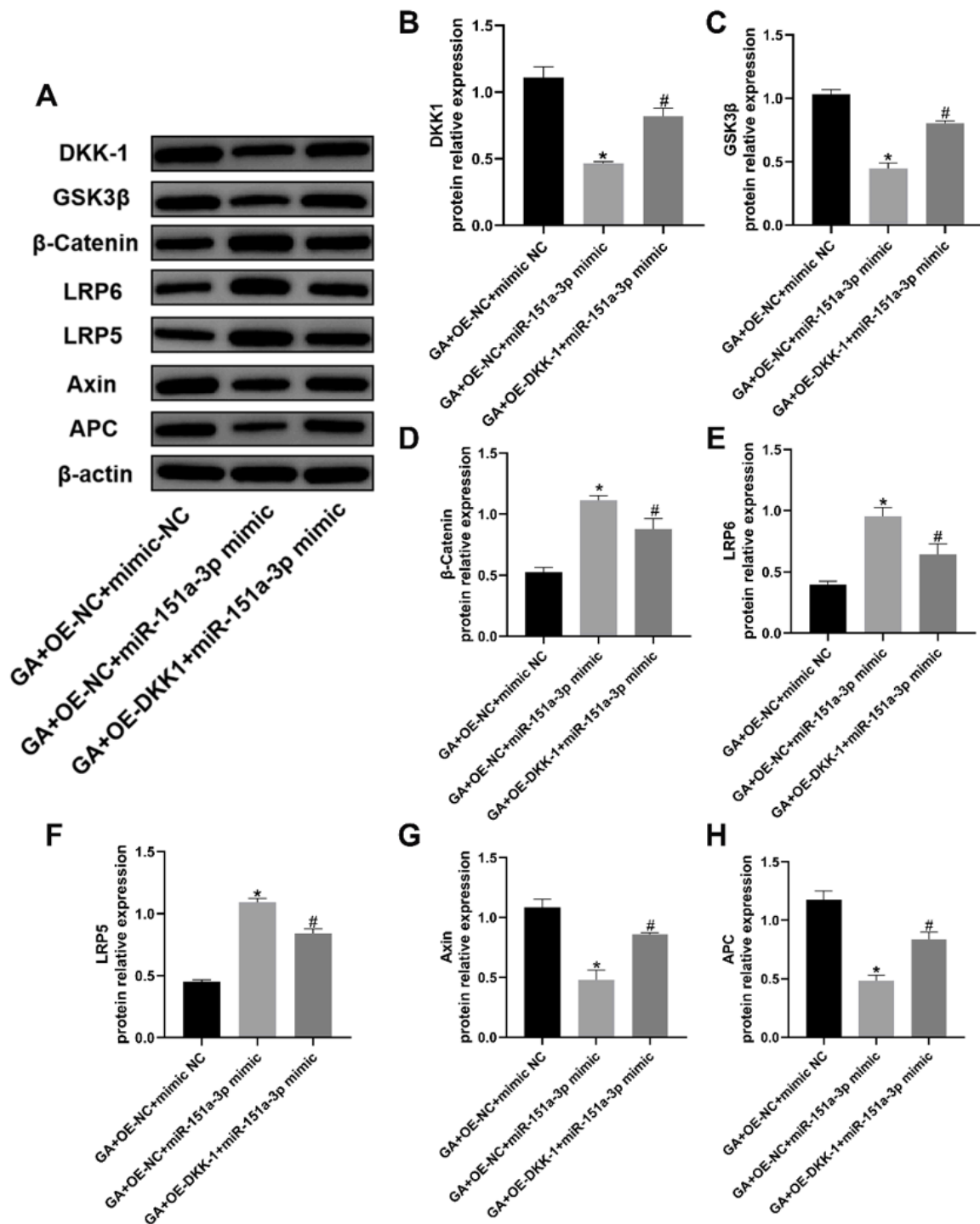


Figure 6

Overexpression of DKK-1 can reverse the regulatory effect of miR-151a-3p on the WNT pathway. (A) Representative protein expression band diagrams of each index (B-H) Bar charts of protein levels of DKK-1, GSK3β, β-Catenin, LRP6, LRP5, Axin and APC. (* $P < 0.05$ vs. GA + OE-NC + mimic NC group; # $P < 0.05$ vs. OE-NC + miR-151a-3p mimic group)

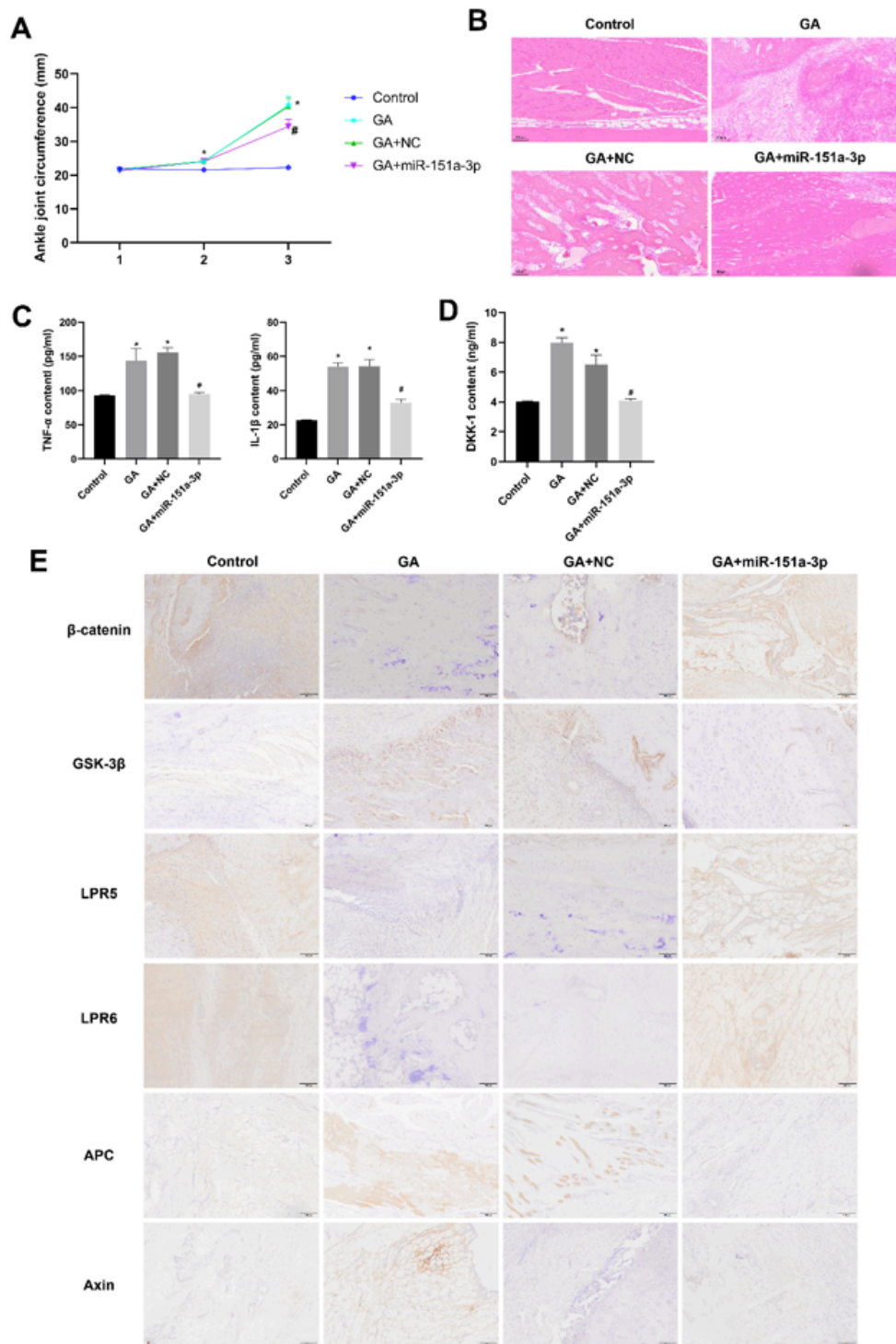


Figure 7

Effects of miR-151a-3p on pathological damage and expression of DKK-1 and WNT pathway-related proteins in rats with acute gouty arthritis. (A) Ankle circumference of rats in each group: 1, before modeling; 2, after modeling; 3, 4 weeks after intervention. (B) HE staining results of ankle joint tissues in each group, scale bar = 100 μ m. (C) ELISA detection of TNF- α and IL-1 β contents in serum of rats in each group. (D) ELISA detection of DKK-1 protein expression in serum of rats in each group. (E)

Immunohistochemical detection of GSK3 β , β -Catenin, LRP6, LRP5, Axin and APC protein expressions in rats. (*P<0.05 vs. Control group; #P < 0.05 vs. GA group)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [WesternBlot.pptx](#)