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IL-10 affects mechanism of intervertebral disc degenerative lesions treated with curcumin by regulating the MAPK signaling pathway

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Abstract: **Background**: The pathogenesis of intervertebral disc degenerative disease (IDDD) remains unclear. While the anti-inflammatory role of IL-10 and the therapeutic potential of curcumin are well recognized, their specific interplay in IDDD remains poorly understood. **Objectives**: This study aimed to investigate whether curcumin alleviates IDDD by upregulating IL-10 to suppress MAPK pathway overactivation, thereby exerting anti-inflammatory, anti-apoptotic and pro-anabolic effects on nucleus pulposus cells. **Methods**: Nucleus pulposus cells were isolated from patients with IDDD and divided into the following groups: control, varying concentrations of curcumin (10-80) µmol/L, varying concentrations of IL-10 (30-60) mM and a combination group of curcumin and IL-10. Cell proliferation and gene/protein expression were assessed using MTT assay, qPCR, Western blot and ELISA. **Results**: IL-10 promoted myeloid cell proliferation, upregulated Bax and GAG expression, enhanced collagen II synthesis and ERK1/2 phosphorylation, while downregulating Bcl-2 expression and reducing TNF-α and IL-6 secretion (P<0.05). These effects exhibited a dose-dependent enhancement, with high-dose IL-10 showing significantly greater efficacy compared to the low-dose group (P<0.05). **Conclusion**: IL-10 mitigates disc degeneration by modulating MAPK signaling, reducing inflammation and apoptosis and promoting matrix synthesis in nucleus pulposus cells.

Keywords: Collagen II; Degenerative disc disease; Inflammation; IL-10; MAPK; Nucleus pulposus

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INTRODUCTION

Intervertebral discs are fibrocartilaginous structures situated between adjacent vertebrae, primarily composed of water, collagen and proteoglycans. They are essential for spinal stability and mobility (Mohd Isa *et al*., 2022; Xin *et al*., 2022). With global aging and increasingly sedentary lifestyles, the clinical incidence of intervertebral disc degenerative disease (IDDD) has risen (Yurube *et al*., 2023; Wang *et al*., 2023). Degenerative disc disease and its associated disorders often manifest as lower back pain and reduced mobility (Taylor *et al*., 2024). IDDD can occur across age groups, with prevalence increasing with age (Novais *et al*., 2021). Symptoms such as pain, numbness and segmental spinal dysfunction significantly impair quality of life, necessitating effective treatment strategies (Ohyama *et al*., 2023). Under the combined effect of various physical and chemical factors, the pathological process of IDDD can cause molecular biological, mechanical and structural changes in the extracellular matrix of the intervertebral disc (Madhu *et al*., 2021). The overall structure of the disc is incomplete due to changes in the components of the extracellular matrix, such as collagen fiber II and a decrease or loss of GAG, which is an early marker for disc degeneration, which ultimately causes loss of water and decreased loading capacity of disc (Bhattacharya and Dubey, 2025; Dong *et al*., 2022). The causative factors for IDDD include genetic factors, aging of the organism, decreased immunity in the nucleus pulposus region, apoptosis or death of nucleus pulposus cells and many other factors (Wang *et al*., 2023; Li *et al*., 2022).

To date, the pathogenesis of disc degeneration is unclear. Inflammatory factors can participate in extracellular matrix metabolism and cell proliferation and, therefore, are currently considered to be key factors in the development of IDDD, causing disc matrix degradation and inducing nucleus pulposus cell injury (Zhang et al., 2024; Gong *et al*., 2023). IL-10 regulates cell growth and differentiation with immunosuppressive roles (Yang *et al*., 2025; Zhang *et al*., 2025) and is involved in several diseases (Li *et al*., 2022; York *et al*., 2024). However, the effect of IL-10 on IDDD inflammation and related mechanisms has not been elucidated.

Curcumin is a diketone compound and can effectively inhibit platelet aggregation and reduce plasma viscosity to a certain extent, in addition to its anti-tumor, lipid-lowering and anti-inflammatory effects. Curcumin has been reported in the treatment of intervertebral disc diseases. It has been found that curcumin could slow down the degeneration of intervertebral discs by upregulating LC3 and

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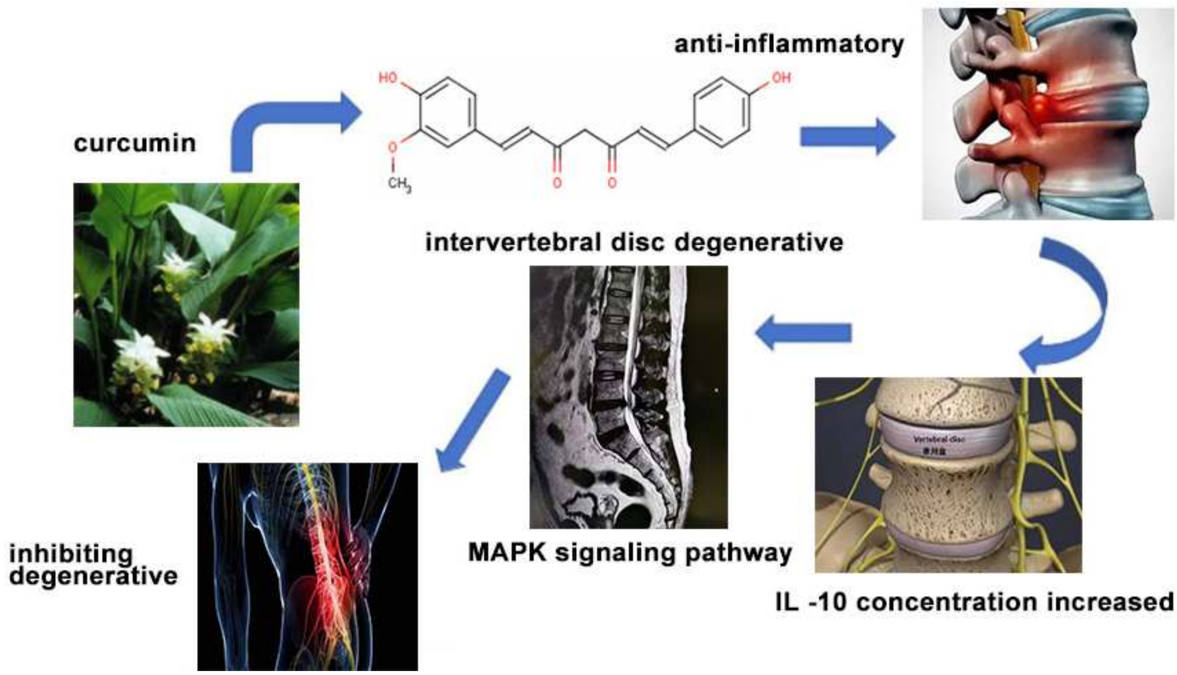

Fig. 1: Schematic diagram of mechanism for curcumin in treatment of intervertebral disc degeneration.

Table 1: Primer sequences.

Genetics	Upstream primers 5-3	Downstream primers 5-3
GAPDH	ACCAGGTATCTTGGTTG	TAACCATGTCAGCGTGGT
collagen II	GCCAGGCATCTACTCACAGT	TCTTAGGGAGCTTAGCCATT
Bcl-2	CGATCCTCTTGACGCACAGGC	TTAGCTCAGTCTAAGCCATACC
Bax	AGGCATCTTGACGCGCCAGG	TTAGCCTAGGGATCTAAAGC
Aggrecan	CTACCGCTGCGATCCTGAG	TCAGAGGTCTCGCATCGGT
MMP-3	CAGGCATCCAGGGATTAATGG	GCCTTGGCTGAGTGGTAGAG
MMP-13	TGGTCCAGGAGATGAAGACC	GGTCCTTGGAGTGGTCAGAC

downregulating P62 in autophagy cells and at the same time, increasing the level of aggrecan and collagen II and decreasing the MMP-3 and MMP-13 expressions in nucleus pulposus cells (Xiao *et al*., 2020). In addition, it has also been found through animal experiments that curcumin inhibited NF-KB-p65 activity in degenerated intervertebral discs, reduced the expression level of TNF-alpha and collagen fiber damage and effectively inhibited the degree of degeneration of lumbar intervertebral discs (Zamboni *et al*., 2022). However, it is not clear whether its therapeutic effect on degenerative disc disease is affected by IL-10 and further studies are thus needed (Zamboni *et al*., 2022). A schematic overview is presented in Fig. 1.

MATERIALS AND METHODS

General information

Six patients diagnosed with IDDD who underwent surgical treatment between June 2015 and June 2016 were included (three males and three females, aged 35–49 years, mean age 36.2±3.2 years). *Inclusion criteria* (Ji *et al*., 2020) involved all patients diagnosed with IDDD by magnetic resonance imaging (MRI) of the lumbar spine; degeneration grade 3 was selected according to the Christian MRI grading criteria; patients were selected to be younger than 45 years old; and patients underwent surgery to remove the nucleus pulposus or resect the intervertebral disc. *Exclusion criteria* (Ji *et al*., 2020) included concomitant other lumbar disc pathologies, complicated with infectious diseases, malignant tumors, severe diabetes mellitus, severe hepatic and renal diseases, pulmonary fibrosis and osteometabolic diseases. Six patients with idiopathic scoliosis during the same period were selected, including three males and three females (age: 28-45 years, mean: 36.1±3.3 years), excluding IDDD or other lumbar disc diseases. Nucleus pulposus tissue specimens from the lumbar intervertebral discs were obtained from all individuals with informed consent.

Reagents

IL-10 was purchased from Sigma, USA; PVDF was from Pall Life Sciences. Antibodies against pERK1/2, ERK1/2 and HRP-labeled IgG were purchased from Cell Signaling, U.S.A. Curcumin (Sigma Aldrich (Shanghai) Trading Co., Ltd; CAS: 458-37-7).

Acquisition, culture and grouping of primary nucleus pulposus cells

Nucleus pulposus tissues were collected during surgery and the annulus fibrosus was carefully removed. A sterile ultra-clean bench was utilized to process each specimen. Specimens were rinsed in Petri dishes with D-Hank's solution until blood stains were completely removed from the nucleus pulposus tissue. The medullary tissue was cut into lmm3-sized pieces and the tissue was digested with collagenase at a concentration of 0.1% type II collagenase for 45 min with shaking and digestion followed by centrifugation of supernatant at 1,500 rpm for 5 min and addition of 4 mL of fresh DMEM medium for 24-48 h. The LECs were then cultured in a culture dish with D-Hank solution until blood stains were completely removed. LECs cells were inoculated at 1×10^5 cells/cm^2 in 6-well plates with 10% FBS, 90% high sugar DMEM/F12 medium (containing 100 U/mL penicillin, 100 μg/mL streptomycin) and incubated at 37ºC, 5% CO_2 incubator. The fluid was changed every 3 d and cell passaging was performed when the cells were spread to 80%-90% from the bottom of the bottle. The cell passaging included removing the old culture medium, washing the cells using D-Hanks solution, digesting the cells and conducting cell passaging culture in the ratio of 1:2. 2-5 generations were selected for experiments. Nucleus pulposus cells were randomly divided into the following groups: a control group (without intervention), curcumin groups at different concentrations (10, 20, 40, 80 μmol/L), IL-10 groups at different concentrations (30, 60 mM) and a combined treatment group with curcumin (10 μmol/L) and IL-10 (60 mM). Cells in each group were treated for 48 h in a 37ºC, 5% CO_2 incubator before subsequent experiments.

Cell proliferation analysis

Cells in 96-well plates were divided into control group and IL-10 group with different dosages (30 and 60 mM). After 48h, 20 μL of MTT was added for 4 h and then 150 μL of DMSO was added 10 min to measure absorbance (A) value.

ELISA to detect changes of TNF-α, IL-6 and GAG expression in the supernatants from cells in each group

All specimens were used to detect TNF-α, IL-6 and GAG levels in supernatants from cells in each group by ELISA kit. The experimental procedures were performed according to the instructions from the ELISA kit.

Real- time PCR

mRNA was isolated for cDNA synthesis followed by CPR with primers in table 1. Gene level was analyzed semi-quantitatively according to 2-ΔCt method.

Western blot

Whole protein was extracted and quantified by the Bradford method, followed by separation on SDS-PAGE for Western blot using primary antibodies with different ratios of dilutions of pERK1/2 (1:1000) and ERK1/2 (1:1000), as well as β-actin (1:5000), respectively. X-films were scanned and strip densitometry was performed. The experiments were repeated four times (n=4), respectively, and statistically analyzed.

Statistical analysis

Data analysis was performed using SPSS 21.0 software, with results expressed as mean ± standard deviation. Due to the small sample size, the Kruskal-Wallis test was used for comparisons among multiple groups. P<0.05 indicated a difference.

RESULTS

Curcumin significantly reduces degenerative disc lesions while increasing IL-10 levels

The results of the Thiazolyl Blue (MTT) assay showed that a curcumin concentration of 10 μmol/L significantly enhanced nucleus pulposus cell proliferation compared to the control (P=0.005). Therefore, this concentration was selected for subsequent experiments (Fig. 2). Hematoxylin staining further indicated that curcumin promoted osteogenic differentiation, as shown in Fig. 3. RT-PCR assay revealed that curcumin treatment significantly upregulated Collagen II and aggre-can mRNA and downregulated MMP-3 and MMP-13 mRNA (P=0.000, 0.000, 0.000, 0.008), as shown in Fig. 4A. Western blot assay revealed that curcumin treatment significantly and markedly upregulated collagen II and aggrecan protein expression and downregulated MMP-3 and MMP-13 protein expression (P=0.003, 0.000, 0.000, 0.000), as shown in Fig. 4B. Further ELLSA assay revealed that IL-10 levels were elevated in curcumin group compared with control group (P=0.011), as shown in Fig. 5.

IL-10 has an ameliorative effect on degenerative disc lesions and MAPK signaling pathway is also involved in this process

IL-10 promoted proliferation of IDDD nucleus pulposus cells after acting on IDDD nucleus pulposus cells (P=0.008) and effect of promoting proliferation was more significant with increased dosage (Fig. 6). IL-10 significantly inhibited the expression of Bcl-2 (P＝0.003), promoted the expression of Bax (P＝0.008) and enhanced the expression of collagen II (P＝0.005) in IDDD nucleus pulposus cells. Moreover, with increased dosage, the effect on Bcl-2 and Bax in medullary cells of IDDD was more pronounced (Fig. 7). Immunofluorescence results showed that the promotion of collagen II expression was also more pronounced with increased dose in the presence of IL-10 (Figs. 8 and 9). The above results indicated that IL-10 exerted an inhibitory effect on IDDD by inhibiting the apoptosis of IDDD myeloid cells and then promoting the proliferation of IDDD myeloid cells.

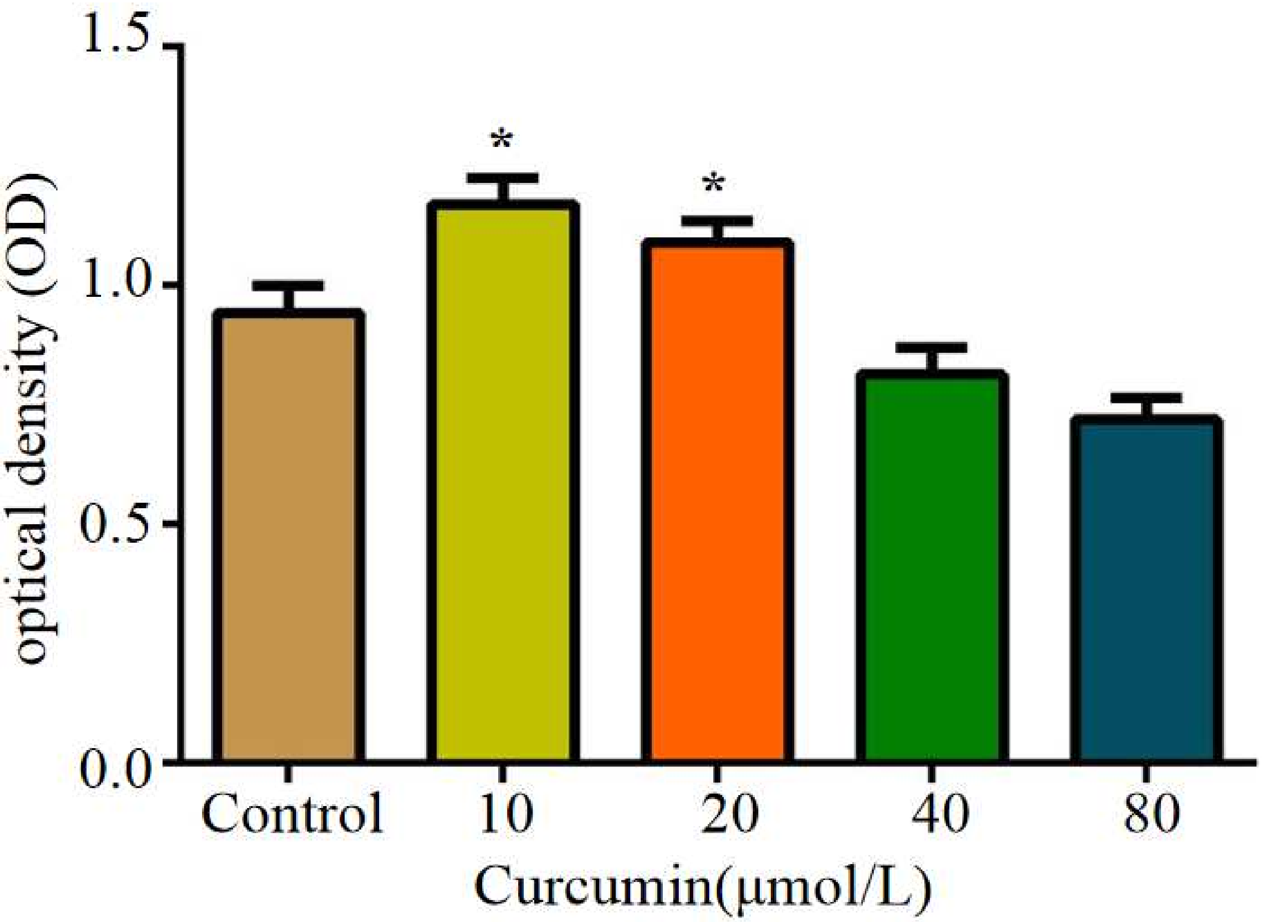

Fig. 2: Effect of curcumin on myeloid cell activity by MTT assay. The bar graph shows the absorbance (OD) values representing cell proliferation in control group and curcumin groups at concentrations of 10, 20, 40, and 80 μmol/L. Compared with control group, * P<0.05. Abbreviations: MTT, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; μmol/L, micromoles per liter. Symbol: $P < 0.05$ indicates statistical significance.

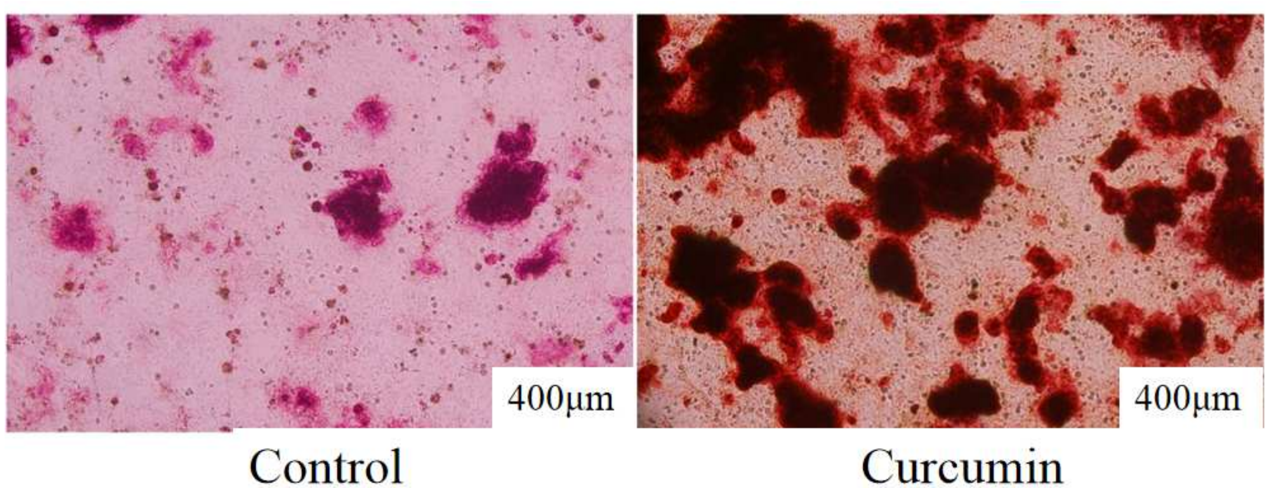

Fig. 3: Effect of curcumin on osteogenic differentiation assessed by hematoxylin staining. The staining intensity and distribution of osteogenic markers were assessed in nucleus pulposus cells treated with curcumin (10 μmol/L) compared to the control group.

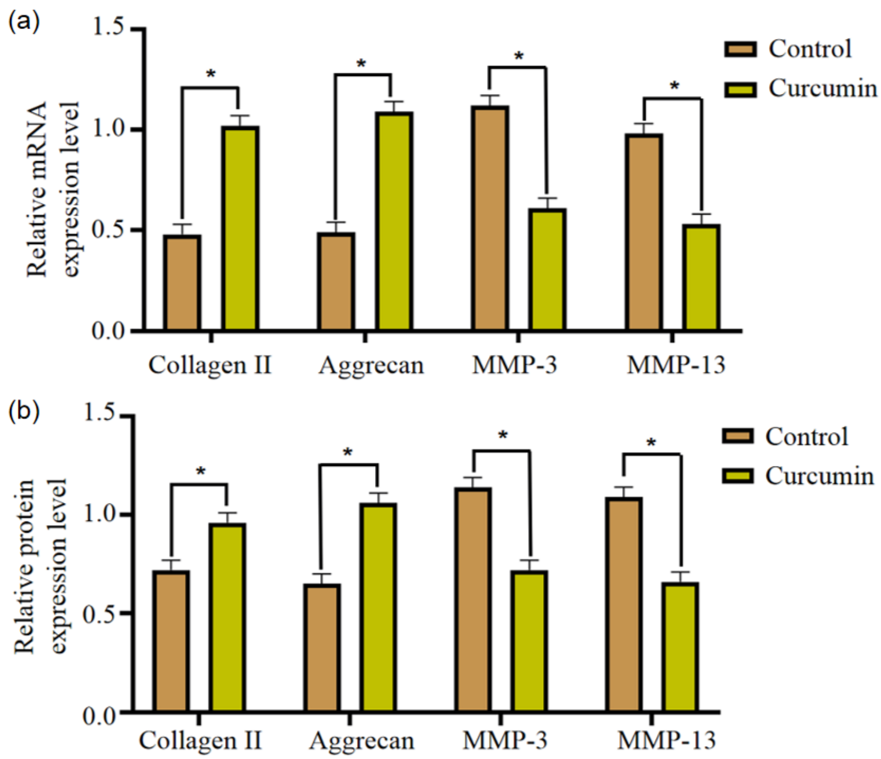

Fig. 4: RT-PCR and Western blot analyses were used to detect the expression of collagen II, aggrecan, MMP-3 and MMP-13. (a) RT-PCR detection of collagen II, aggrecan, MMP-3 and MMP-13 mRNA expression levels; (b) Western blot detection of collagen II, aggrecan, MMP-3 and MMP-13 protein expression levels. β-actin was used as a loading control. Compared with control group, * P<0.05. Abbreviations: RT-PCR, real-time polymerase chain reaction; MMP-3, matrix metalloproteinase-3; MMP-13, matrix metalloproteinase-13.

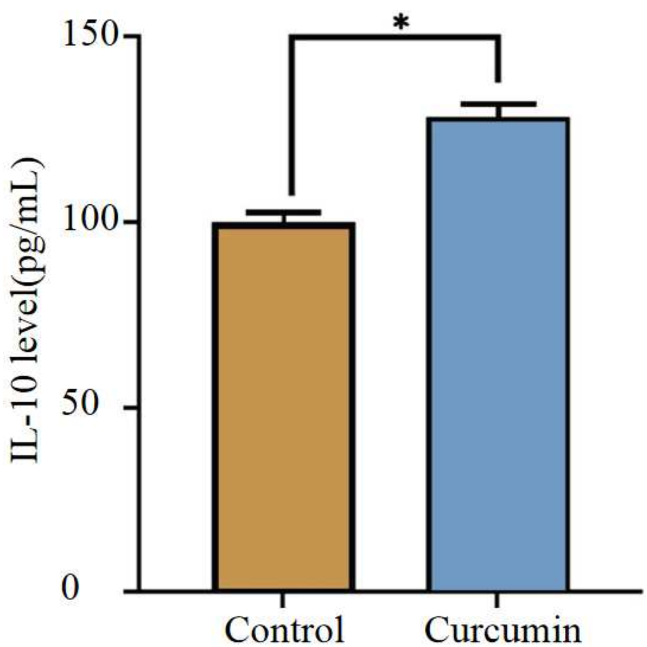

Fig. 5: Comparison of IL-10 levels between the two groups. The bar graph shows IL-10 levels measured by ELISA in the control group and curcumin group. Compared with control group, * P<0.05. Abbreviations: IL-10, interleukin-10; ELISA, enzyme-linked immunosorbent assay.

IL-10 promoted proteoglycan expression and inhibited TNF-α and IL-6 in the supernatant from IDDD myeloid cells after its action in IDDD myeloid cells (P=0.000, 0.000). The promotion of GAG expression and inhibition of TNF-α and IL-6 expressions were more significant with increased dosage (Figs. 10 and 11). IL-10 significantly inhibited ERK1/2 phosphorylation after acting on IDD myeloid cells (*P*=0.001) and the inhibitory effect on MAPK signaling pathway was more pronounced with increased dosage (Fig. 12). ERK1/2 phosphorylation was significantly inhibited in the presence of IL-10.

Curcumin promotes inhibition of MAPK signaling pathway by IL-10, thus improving degenerative disc lesions

The inhibitory effect of curcumin+IL-10 on ERK1/2/MAPK signaling pathway was significantly stronger than that of curcumin group and IL-10 group (*P*=0.001), (Fig. 13). Curcumin + IL-10 promoted the proliferation of medullary cells after acting on IDDD medullary cells compared with curcumin group and IL-10 group (*P*=0.022) (Fig. 14). At the same time, curcumin + IL-10 inhibited TNF-α and IL-6 levels (*P*=0.007、0.035, Fig. 15). This shows that, curcumin can promote IL-10 to inhibit the MAPK signaling pathway, thus improving the degenerative disc lesions.

DISCUSSION

Nucleus pulposus cells contain proteoglycan-based GAG and type II collagen, which are essential for maintaining disc structure and biomechanical function. GAG retains water, ensuring disc elasticity and load-bearing capacity (Madhu *et al*., 2023; Zhao *et al*., 2025). As one of the main constituents of extracellular matrix, GAG maintains the mitigation of external shocks, as well as elasticity, which is a unique function of cartilage tissue (Kazemi *et al*., 2025). During IDDD pathology, the loss of GAG leads to water loss, which in turn causes changes in the function and structure of medullary cells, leading to IDDD (Xiang *et al*., 2025). Under normal physiological conditions, the synthesis and degradation of GAG are in dynamic balance, which in turn maintains the normal function of the intervertebral disc. However, under the action of external factors, the expression of degradative enzymes can be increased, causing excessive degradation of matrix, disrupting the dynamic balance of GAG and inducing intervertebral disc degeneration (Zhao *et al*., 2024). During IDDD process, IL-1 and IL-6 secretion are increased, leading to inflammation, inducing damage to the nucleus pulposus cells and consequently the loss of collagen fibers (Li *et al*., 2020).

In summary, IDDD is a complex pathological process involving inflammatory responses, extracellular matrix metabolic imbalance and cell apoptosis. This study is the first to explore *in-vitro,* the synergistic effects and underlying mechanisms of curcumin and IL-10 in regulating the MAPK signaling pathway and alleviating IDDD. The findings provide experimental evidence for understanding the pathophysiology of IDDD and developing novel therapeutic strategies. One of the key findings of this study is the protective effect of IL-10 on nucleus pulposus cells. The results indicate that IL-10 dose-dependently promotes the proliferation of nucleus pulposus cells, upregulates the synthesis of Collagen II and GAG, while suppressing the expression of the pro-apoptotic protein Bax and reducing the secretion of pro-inflammatory factors TNF-α and IL-6. These findings align with the classical role of IL-10 as a key anti-inflammatory cytokine.

Previous studies have confirmed that IL-10 can inhibit the release of inflammatory mediators and promote matrix synthesis in degenerative diseases such as osteoarthritis and cartilage degeneration (Zhang *et al*., 2025; Dalton *et al*., 2025). This study extends its effect to the field of IDD, demonstrating that IL-10 not only alleviates inflammation but also directly promotes the anabolic metabolism of nucleus pulposus cells, thereby counteracting matrix degradation during the degenerative process. This study revealed that the protective effect of IL-10 is partially mediated through the inhibition of the ERK1/2/MAPK signaling pathway. Experimental results showed that after IL-10 treatment, the levels of phosphorylated ERK1/2 significantly decreased in a dose-dependent manner. The MAPK/ERK pathway is a core signaling cascade mediating cellular stress, inflammation and apoptosis and its persistent activation in IDDD leads to upregulated expression of matrix metalloproteinases (MMPs) and subsequent matrix degradation (Li *et al*., 2020; Li *et al*., 2021). The findings of this study suggest that IL-10 may inhibit the overactivation of this pathway, thereby downregulating the expression of degradative enzymes such as MMP-3 and MMP-13 and consequently maintaining extracellular matrix homeostasis. This discovery provides a novel mechanistic explanation for the cytoprotective role of IL-10 in IDDD at the signaling level.

Research has found that curcumin can upregulate autophagy, inhibit apoptosis and reduce the phenotype loss of endplate chondrocytes induced by high-intensity tensile stress, thereby alleviating mechanical imbalance-induced intervertebral disc degeneration (Xiao *et al*., 2020). It can also alleviate inflammation and back pain (Altaf *et al*., 2025). This study discovered that curcumin can elevate the levels of IL-10 in nucleus pulposus cells and the combination of curcumin and IL-10 exhibits synergistic effects. As a natural polyphenol, curcumin has been confirmed by multiple studies for its anti-inflammatory and antioxidant properties, which contribute to alleviating IDDD (Wu *et al*., 2025; Wan *et al*., 2025).

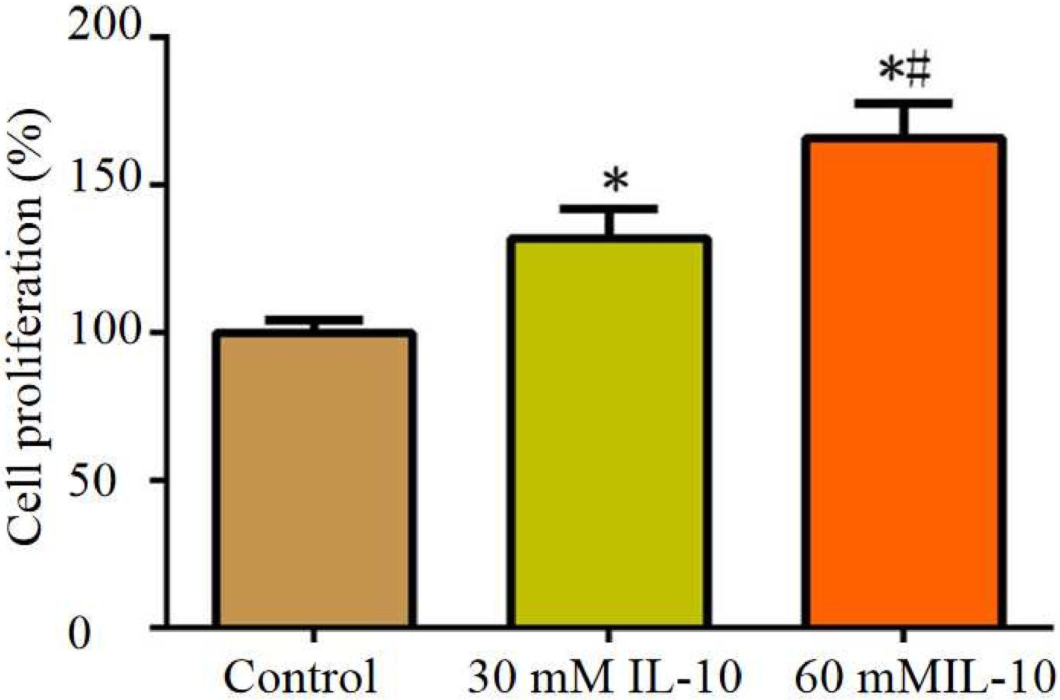

Fig. 6: Effect of IL-10 on the proliferation of myeloid cells. The bar graph shows cell proliferation in control group, IL-10 30 mM group, and IL-10 60 mM group. Compared with control group, * P<0.05; compared with 30 mM IL-10 group, # P<0.05. Abbreviations: IL-10, interleukin-10; mM, millimolar.

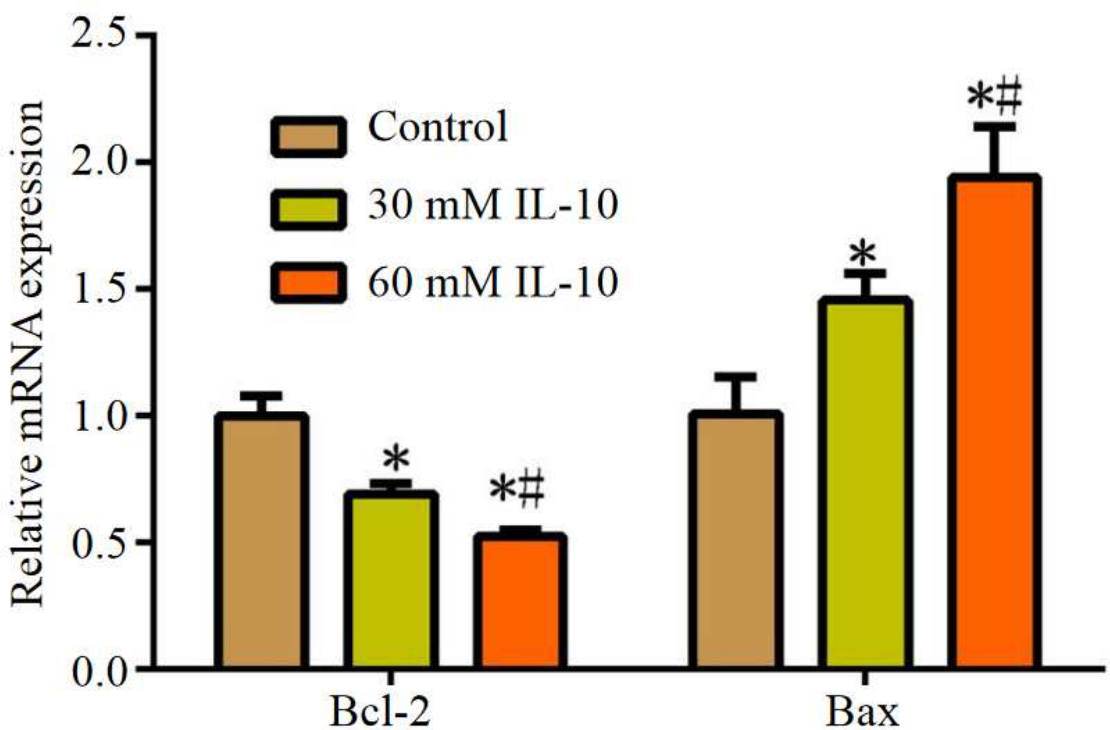

Fig. 7: Effect of IL-10 on Bcl-2 and Bax expression in IDDD medullary cells. The bar graphs show relative expression levels of Bcl-2 and Bax in control group, IL-10 30 mM group, and IL-10 60 mM group. Compared with control group, * P<0.05; compared with 30 mM IL-10 group, # P<0.05. Abbreviations: IL-10, interleukin-10; Bcl-2, B-cell lymphoma 2; Bax, Bcl-2-associated X protein; mM, millimolar.

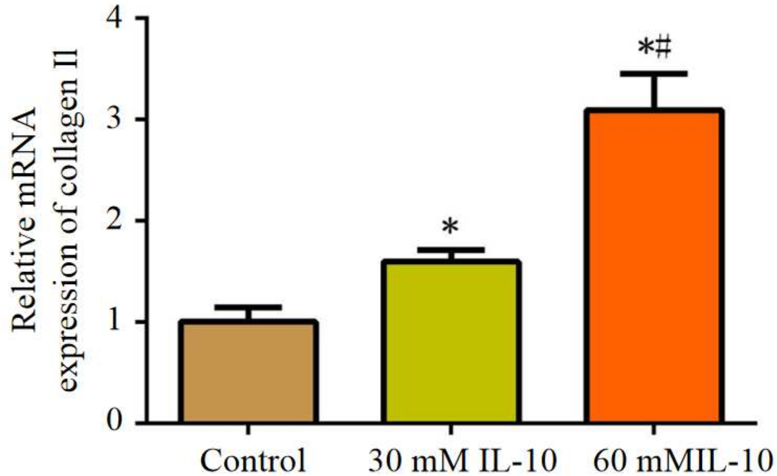

Fig. 8: Effect of IL-10 on collagen II expression in myeloid cells. The bar graph shows collagen II expression levels in control group, IL-10 30 mM group, and IL-10 60 mM group. Compared with control group, * $P<0.05$; compared with 30 mM IL-10 group, # $P<0.05$. Abbreviations: IL-10, interleukin-10; mM, millimolar.

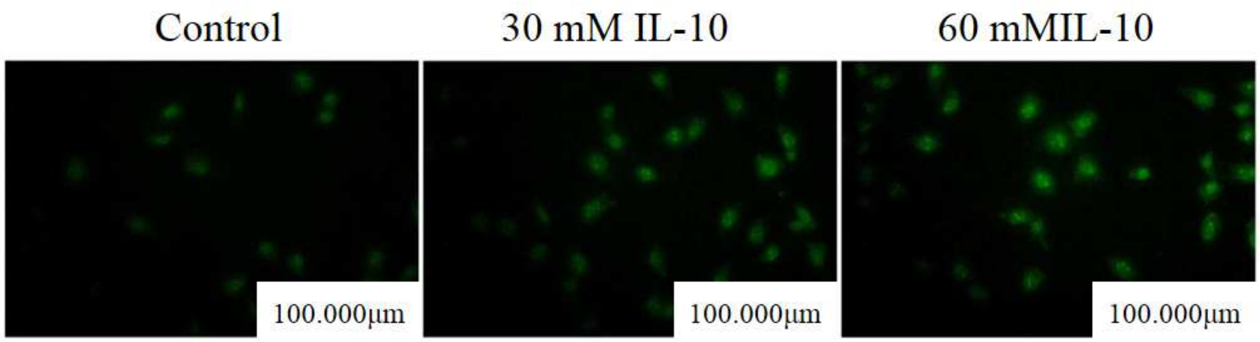

Fig. 9: Immunofluorescence showing effect of IL-10 on collagen II expression in myeloid cells. Representative immunofluorescence images of collagen II (green) in nucleus pulposus cells treated with different concentrations of IL-10 (30 mM and 60 mM) compared to the control group. Scale bar = 100 μm (indicative). Increased fluorescence intensity of collagen II was observed with higher IL-10 doses. Abbreviations: IL-10, interleukin-10; mM, millimolar.

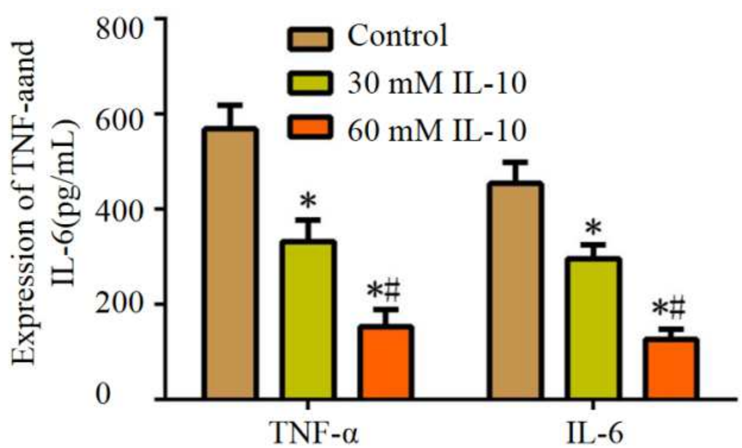

Fig. 10: Effect of IL-10 on expression of inflammatory factors in myeloid cells. The bar graphs show TNF-α and IL-6 expression levels (as measured by ELISA) in control group, IL-10 30 mM group, and IL-10 60 mM group. Compared with control group, * $P<0.05$; compared with 30 mM IL-10 group, # $P<0.05$. Abbreviations: IL-10, interleukin-10; TNF-α, tumor necrosis factor-alpha; IL-6, interleukin-6; mM, millimolar.

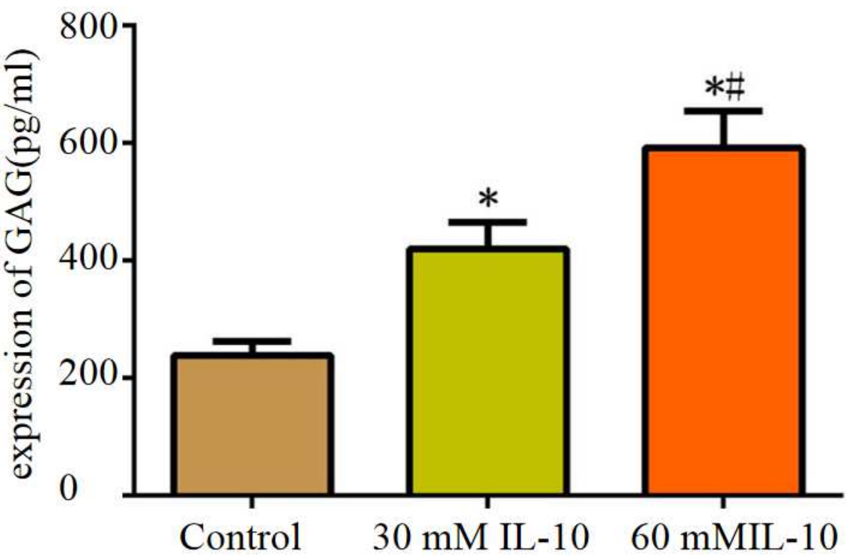

Fig. 11: Effect of IL-10 on GAG expression in myeloid cells. The bar graph shows GAG expression levels in control group, IL-10 30 mM group, and IL-10 60 mM group. Compared with control group, * P<0.05; compared with 30 mM IL-10 group, # P<0.05. Abbreviations: IL-10, interleukin-10; GAG, glycosaminoglycan; mM, millimolar.

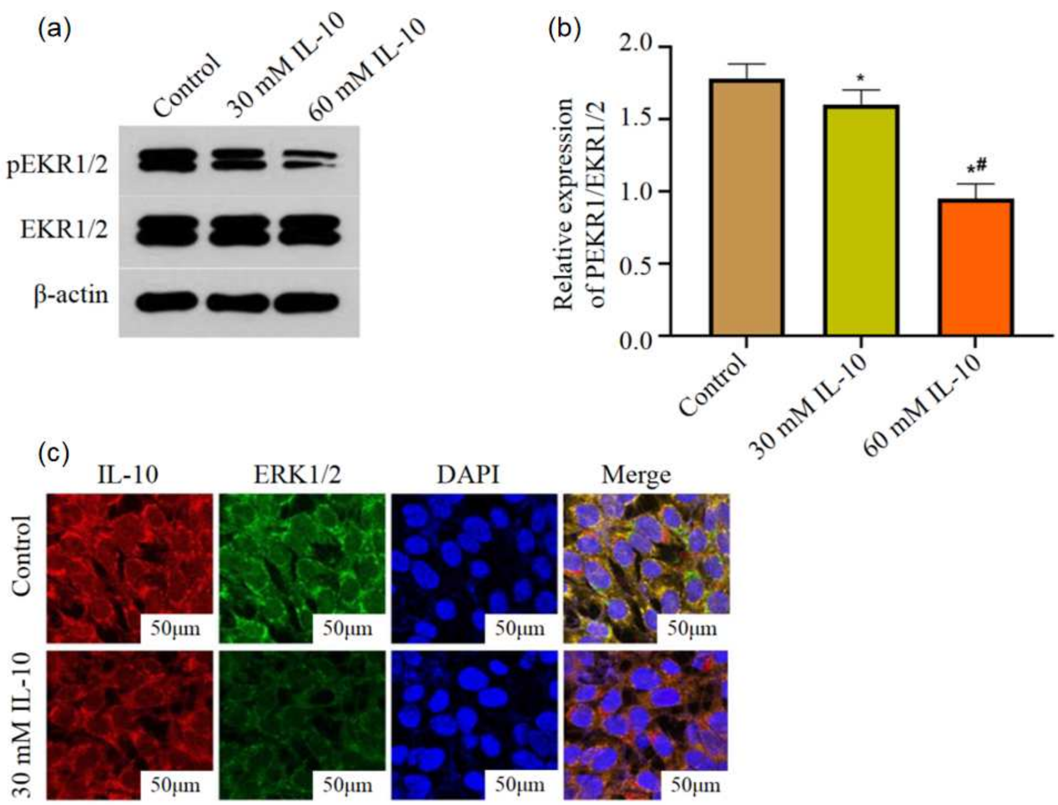

Fig. 12: Effect of IL-10 on ERK1/2/MAPK signaling pathway in myeloid cells. (a) Western blot analysis of effect of IL-10 on ERK1/2/MAPK signaling pathway in myeloid cells. Representative blots show p-ERK1/2, ERK1/2, and β-actin (loading control) in control, IL-10 30 mM, and IL-10 60 mM groups; (b) Quantitative analysis of p-ERK1/2/total ERK1/2 ratio from Western blot results; (c) Immunofluorescence showing analysis of the effect of IL-10 on ERK1/2/MAPK signaling pathway in myeloid cells. Representative images depict ERK1/2 localization (green) and DAPI-stained nuclei (blue). Scale bar = 50 μm (indicative). Compared with control group, * P<0.05; compared with 30 mM IL-10 group, # P<0.05. Abbreviations: IL-10, interleukin-10; ERK1/2, extracellular signal-regulated kinase 1/2; MAPK, mitogen-activated protein kinase; p-ERK1/2, phosphorylated ERK1/2; mM, millimolar; DAPI, 4' ,6-diamidino-2-phenylindole.

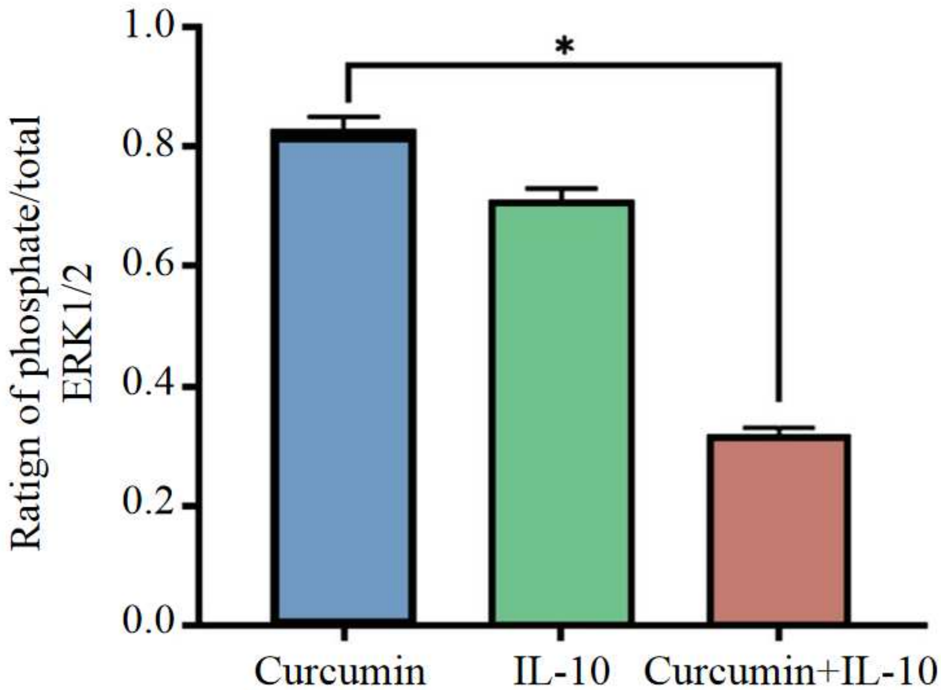

Fig. 13: Effect of each group on ERK1/2/MAPK signaling pathway in myeloid cells. The bar graph shows p-ERK1/2/total ERK1/2 ratio in control group, curcumin group, IL-10 group, and curcumin+IL-10 combination group. Abbreviations: ERK1/2, extracellular signal-regulated kinase 1/2; IL-10, interleukin-10.

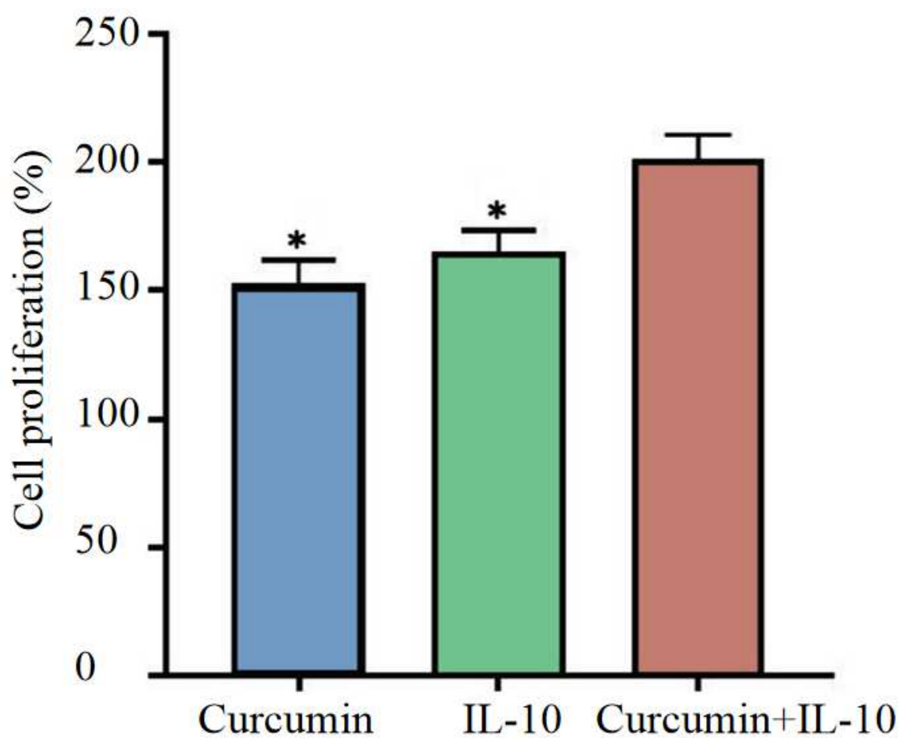

Fig. 14: Effect of each group on myeloid cell proliferation. The bar graph shows cell proliferation in control group, curcumin group, IL-10 group, and curcumin+IL-10 combination group. Compared with curcumin+IL-10 group, * $P<0.05$. Abbreviations: IL-10, interleukin-10.

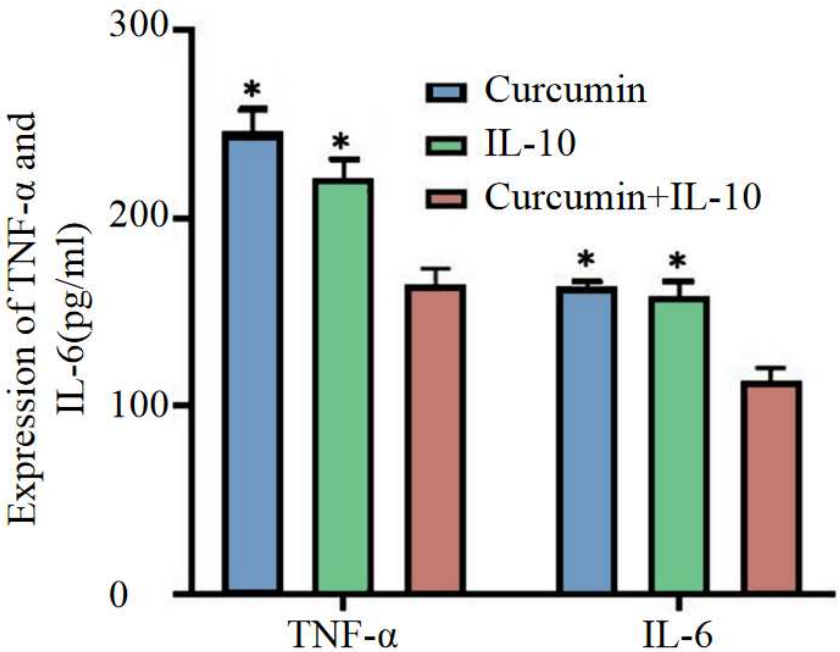

Fig. 15: TNF-α and IL-6 level expression in each group. The bar graphs show TNF-α and IL-6 expression levels in control group, curcumin group, IL-10 group, and curcumin+IL-10 combination group. Compared with curcumin+IL-10 group, * $P<0.05$. Abbreviations: TNF-α, tumor necrosis factor-alpha; IL-6, interleukin-6; IL-10, interleukin-10.

This study further elucidates that part of its beneficial effects may be achieved by upregulating the expression of endogenous IL-10. More importantly, ERK1/2, as a key kinase in the MAPK signaling pathway, is widely present in various mammalian tissues and plays a crucial role in cell proliferation, cycle regulation, growth and survival, while also serving as a critical downstream effector in immune receptor-triggered inflammatory responses (Ozmen *et al*., 2023; Paiva *et al*., 2021). This study suggests that inhibiting ERK1/2 activation can suppress the secretion of inflammatory factors, promote nucleus pulposus cell proliferation, reduce intervertebral disc edema and delay the progression of IDDD. Furthermore, the combination group showed significantly superior effects compared to the single-treatment groups in inhibiting ERK1/2 phosphorylation, promoting cell proliferation and suppressing inflammatory factors. This indicates that curcumin and IL-10 may converge on the inhibition of the MAPK pathway through regulating different targets such as NF-κB and autophagy (Akhter *et al*., 2023; Li *et al*., 2022), thereby producing a better synergistic effect and more effectively blocking key pathogenic pathways in IDDD.

CONCLUSION

In summary, curcumin alleviates intervertebral disc degeneration by elevating IL-10 levels, synergistically inhibiting the MAPK signaling pathway, reducing inflammatory responses and promoting nucleus pulposus cell proliferation and extracellular matrix synthesis. This provides a potential novel strategy for the clinical treatment of degenerative disc disease. Future studies could further validate its efficacy in animal models or clinical trials.

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Authors' contribution

Jingyi Sun: Experimental design, data collection and analysis, manuscript writing; Bipeng Lei: Research supervision, manuscript revision and review; Weijiang Li: Material provision, technical support. All authors have read and approved the final manuscript.

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Data availability statement

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

Ethical approval

This study was approved by the ethics committee of Anqing First People's Hospital Affiliated to Anhui Medical University (Approval No. XYFYLL-2015-012).

Conflicts of interest

The authors declare that the study was conducted in the absence of any commercial or financial interests that could be construed as potential conflicts of interest.

REFERENCES

Akhter N, Wilson A, Arefanian H, Thomas R, Kochumon S, Al-Rashed F, Abu-Farha M, Al-Madhoun A, Al-Mulla F Ahmad R and Sindhu S (2023). Endoplasmic reticulum stress promotes the expression of TNF-α in THP-1 cells by mechanisms involving ROS/CHOP/HIF-1α and MAPK/NF-κB pathways. *Int J Mol Sci*., **24**(20): 15186.

Altaf H, Adil M, Anajirih N, Saeed MA and Hussain N (2025). Decoding human leukocyte antigen Beta-27; its active alleles in ankylosing spondylitis and computational insights of potential inhibitors: HLA-B27 in AS; its variants and inhibitors. *Hum Immunol*., **86**(3): 111303.

Bhattacharya S and Dubey DK (2025). Role of intra-lamellar collagen and hyaluronan nanostructures in annulus fibrosus on lumbar spine biomechanics: insights from molecular mechanics-finite element-based multiscale analyses. *Med Biol Eng Comput*., **63**(1): 139–157.

Dalton J, Narayanan R, Oris RJ, Ezeonu T, Bradley E, Canseco JA, Vaccaro AR, Koerner JD, Markova D and Kepler CK (2025). Can treatment with human mesenchymal stem cells rescue the degenerative disc phenotype? An *in-vitro* pilot study of induced cytokine expression. *Spine J*., **25**(8): 1830–1840.

Dong X, Hu F, Yi J, Zhang Y, Liu C, Geng P, Duan H, Wu CT, Zhang X and Wang H (2022). DPSCs protect architectural integrity and alleviate intervertebral disc degeneration by regulating nucleus pulposus immune status. *Stem Cells Int*., **2022**: 7590337.

Gong Y, Qiu J, Jiang T, Li Z, Zhang W, Zheng X, He Z, Chen W, Wang Z, Feng X, Wang M and Hong Z (2023). Maltol ameliorates intervertebral disc degeneration through inhibiting PI3K/AKT/NF-κB pathway and regulating NLRP3 inflammasome-mediated pyroptosis. *Inflammopharmacology*., **31**(1): 369–384.

Ji Y, Hong W, Liu M, Liang Y, Deng Y and Ma L (2020). Intervertebral disc degeneration associated with vertebral marrow fat, assessed using quantitative magnetic resonance imaging. *Skeletal Radiol*., **49**(11): 1753–1763.

Kazemi M, Yu C, Mehrotra DR, Ersland EE, Zbyn S, Korna F, Staffa SJ, Engiles JB, Li X, Schaer TP, Grinstaff MW, Bergholt MS, Snyder BD and Albro MB (2025). Raman spectroscopic probe provides optical biomarkers of cartilage composition predictive of tissue function. *Osteoarthritis Cartilage*., **33**(4): 461–472.

Li C, Sui C, Wang W, Yan J, Deng N, Du X, Cheng F, Ma X, Wang X and Wang Q (2021). Baicalin attenuates oxygen-glucose deprivation/reoxygenation-induced injury by modulating the BDNF-TrkB/PI3K/Akt and MAPK/Erk1/2 signaling axes in neuron-astrocyte cocultures. *Front Pharmacol*., **12**: 599543.

Li G, Duan L, Yang F, Yang L, Deng Y, Yu Y, Xu Y and Zhang Y (2022). Curcumin suppress inflammatory response in traumatic brain injury via p38/MAPK signaling pathway. *Phytother Res*., **36**(3): 1326–1337.

Li H, Tian L, Li J, Li Y, Du L Huo Z and Xu B (2022). The roles of circRNAs in intervertebral disc degeneration: Inflammation, extracellular matrix metabolism and apoptosis. *Anal Cell Pathol (Amst)*, **2022**: 9550499.

Li P, Hu F, Cao X, Luo L and Tu Q (2020). Melatonin receptor protects cardiomyocyte against oxidative stress-induced apoptosis through the MAPK-ERK signaling pathway. *J Recept Signal Transduct Res*., **40**(2): 117–125.

Li S, Huang C, Xiao J, Wu Y, Zhang Z, Zhou Y, Tian N, Wu Y, Wang X and Zhang X (2022). The potential role of cytokines in diabetic intervertebral disc degeneration. *Aging Dis*., **13**(5): 1323–1335.

Li Z, Wystrach L, Bernstein A, Grad S, Alini M, Richards RG, Kubosch D, Südkamp N, Izadpanah K, Kubosch EJ and Lang G (2020). The tissue-renin-angiotensin-system of the human intervertebral disc. *Eur Cell Mater*., **40**: 115–132.

Madhu V, Guntur AR and Risbud MV (2021). Role of autophagy in intervertebral disc and cartilage function: Implications in health and disease. *Matrix Biol*., **100**: 207–220.

Madhu V, Hernandez-Meadows M, Boneski PK, Qiu Y, Guntur AR, Kurland IJ, Barve RA and Risbud M V. (2023). The mitophagy receptor BNIP3 is critical for the regulation of metabolic homeostasis and mitochondrial function in the nucleus pulposus cells of the intervertebral disc. *Autophagy*., **19**(6): 1821–1843.

Mohd Isa IL, Teoh SL, Mohd Nor NH and Mokhtar S A (2022). Discogenic low back pain: Anatomy, pathophysiology and treatments of intervertebral disc degeneration. *Int J Mol Sci*., **24**(1): 208.

Novais EJ, Tran VA, Johnston SN, Darris KR, Roupas AJ, Sessions GA, Shapiro IM, Diekman B O and Risbud MV (2021). Long-term treatment with senolytic drugs dasatinib and quercetin ameliorates age-dependent intervertebral disc degeneration in mice. *Nat Commun*., **12**(1): 5213.

Ohyama S, Aoki Y, Inoue M, Nakajima T, Sato Y, Sato M, Yoh S, Takahashi H, Nakajima A, Kotani T, Eguchi Y, Orita S, Inage K, Shiga Y, Nakagawa K and Ohtori S (2023). Effect of preoperative severity and location of lumbar intervertebral disc vacuum phenomenon on surgical outcomes after single-level transforaminal lumbar interbody fusion. *World Neurosurg*., **173**: e727–e737.

Ozmen A, Nwabuobi C, Tang Z, Guo X, Larsen K, Guller S, Blas J, Moore M, Kayisli UA, Lockwood C J and Guzeloglu-Kayisli O (2023). Leptin-mediated induction of IL-6 expression in Hofbauer cells contributes to preeclampsia pathogenesis. *Int J Mol Sci*., **25**(1): 135.

Paiva Ferreira LKD, Paiva Ferreira LAM, Bezerra Barros GC, Mozzini Monteiro T, de Araújo Silva L A, Pereira RA, Figueiredo PTR, Alves AF, Rodrigues L C and Piuvezam MR (2021). MHTP, a synthetic alkaloid, attenuates combined allergic rhinitis and asthma syndrome through downregulation of the p38/ERK1/2 MAPK signaling pathway in mice. *Int Immunopharmacol*., **96**: 107590.

Taylor W and Erwin WM (2024). Intervertebral disc degeneration and regeneration: New molecular mechanisms and therapeutics: Obstacles and potential breakthrough technologies. *Cells*., **13**(24): 2103.

Wan C, Liu S, Zhao L, Chang C, Li H, Li R and Chen B (2025). Curcumin protects rat endplate chondrocytes against IL-1β-induced apoptosis via Bcl-2/Bax regulation. *J Mol Histol*., **56**(2): 111.

Wang Y, Hu S, Zhang W, Zhang B and Yang Z (2023). Emerging role and therapeutic implications of p53 in intervertebral disc degeneration. *Cell Death Discov*., **9**(1): 433.

Wang Y, Cheng H, Wang T, Zhang K, Zhang Y and Kang X (2023). Oxidative stress in intervertebral disc degeneration: Molecular mechanisms, pathogenesis and treatment. *Cell Prolif*., **56**(9): e13448.

Wu Z, Chen J, Luo W and Kuang T (2025). Natural products for intervertebral disc degeneration: mechanistic insights and therapeutic potentials. *Front Pharmacol*., **16**: 1605764.

Xiang M, Peng Q, Dai F, Wu Y, Liu L and Liu H (2025). Machine learning-enabled identification of nucleus pulposus senescence-associated genes as potential biomarkers for intervertebral disc degeneration. *Eur J Med Res*., **30**(1): 887.

Zhao D, Dou YX, Zeng LF, Han YH, Lin FZ, Xu N J, Liu J and Zeng YP (2024). The effects of extracellular matrix-degrading enzymes polymorphisms on intervertebral disc degeneration. *JOR Spine*., **7**(4): e70012.

Xiao L, Ding B, Gao J, Yang B, Wang J and Xu H (2020). Curcumin prevents tension-induced endplate cartilage degeneration by enhancing autophagy. *Life Sci*., **258**: 118213.

Xin J, Wang Y, Zheng Z, Wang S, Na S and Zhang S (2022). Treatment of intervertebral disc degeneration. *Orthop Surg*., **14**(7): 1271–1280.

Yang S, Shi J, Qiao Y, Teng Y, Zhong X, Wu T, Liu C, Ge J, Yang H and Zou J (2025). Harnessing anti-inflammatory and regenerative potential: GelMA hydrogel loaded with IL-10 and kartogenin for intervertebral disc degeneration therapy. *ACS Biomater Sci Eng*., **11**(3): 1486–1497.

York AG, Skadow MH, Oh J, Qu R, Zhou QD, Hsieh WY, Mowel WK, Brewer JR, Kaffe E, Williams K J, Kluger Y, Smale ST, Crawford JM, Bensinger SJ and Flavell RA (2024). IL-10 constrains sphingolipid metabolism to limit inflammation. *Nature*., **627**(8004): 628–635.

Yurube T, Takeoka Y, Kanda Y, Kuroda R and Kakutani K (2023). Intervertebral disc cell fate during aging and degeneration: Apoptosis, senescence and autophagy. *N Am Spine Soc J*., **14**: 100210.

Zhang W, Li G, Zhou X, Liang H, Tong B, Wu D, Yang K, Song Y, Wang B, Liao Z, Ma L, Ke W, Zhang X, Lei J, Lei C, Feng X, Wang K, Zhao K and Yang C (2024). Disassembly of the TRIM56-ATR complex promotes cytoDNA/cGAS/STING axis-dependent intervertebral disc inflammatory degeneration. *J Clin Invest*., **134**(6): e165140.

Zhang SP, Tong M, Mo J, Dong ZY and Huang YF (2025). M2 macrophages activate the IL-10/JAK2/STAT3 pathway to induce pathological microangiogenesis in the nucleus pulposus exacerbating intervertebral disc degeneration. *J Orthop Surg Res*., **20**(1): 532.

Zamboni F, Ren G, Culebras M, O'Driscoll J, O'Dwyer J, Ryan EJ and Collins MN (2022). Curcumin encapsulated polylactic acid nanoparticles embedded in alginate/gelatin bioinks for in situ immunoregulation: Characterization and biological assessment. *Int J Biol Macromol*., **221**: 1218–1227.

Zhao DW, Zhang J, Chen C, Sun W, Liu Y, Han M, Zhang Y, Fu Z, Shi C, Zhao X, Yang Z, Tang C, Zhao K, Zhu D, Zhang Y, Cheng L and Jiang X (2025). Rejuvenation modulation of nucleus pulposus progenitor cells reverses senescence-associated intervertebral disc degeneration. *Adv Mater*., **37**(7): e2409979.

Zhang K, Wang Z, He J, Lu L, Wang W, Yang A, Xie H, Huang L, Huang Y, Zhang K, Jiang M and Wei R (2025). Mechanisms of synovial macrophage polarization in osteoarthritis pathogenesis and their therapeutic implications. *Front Immunol*., **16**: 1637731.