western blot analysis. Apoptosis was analyzing by annexin V (AV) and propidium iodide (PI) apoptosis detection kit by flow cytometry.

Results: As expected tofacitinib inhibited the expression of the phosphorylated form of STAT3 ($p < 0.01$). Rapamycin caused an increase in autophagy, while the levels of autophagy marker LC3-II were reduced after treatment with tofacitinib in vitro ($p < 0.001$ and $p = 0.02$, respectively, Figure 1B). In addition, the analysis of autophagic vacuoles by specific fluorescence dye confirmed the reduction of autophagy in RA-FLS treated with tofacitinib. The percentage of annexin V-positive apoptotic cells was not influenced by the treatment with tofacitinib.

Conclusion: The results of this study elucidated a new mechanism of action of tofacitinib related to autophagy modulation and led to a better understanding of the role of autophagy in RA. This study was supported by an unconditioned Research grant from Pfizer Inc.

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A. Image of fibroblast-like synoviocytes obtained from synovial tissue of RA patients during total knee replacement and used for in vitro experiments. B. Western blot analysis of autophagy marker LC3-II after in vitro treatment with tofacitinib.

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AB0146

IDENTIFICATION A MARKED INFLAMMATION MEDIATED CARDIAC DYSFUNCTION DURING THE DEVELOPMENT OF ARTHRITIS IN COLLAGEN INDUCED ARTHRITIS MICE

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Background: Systemic inflammation is strong linked to the increased risk of cardiovascular diseases (CVD) in rheumatoid arthritis (RA)¹. Increased cardiovascular risk in RA patients can not be fully explained by the traditional risk factors, such as hypertension, obesity, diabetes, age and smoking^{2,3}. Much more work is needed to elucidate the mechanism of chronic inflammation bridging RA and cardiovascular disease.

Objectives: To investigate the cardiac changes during the development of arthritis in collagen induced arthritis (CIA) mice and to explore the potential role of inflammation on cardiac dysfunction in RA.

Methods: Arthritis severity was evaluated using clinical indices, micro-computed tomography and histopathology. Cardiac function was determined by transthoracic echocardiography at week 5, 7, 9 and 11 after immunization in mice. At week 7 (day 50), mice joints and hearts were removed for pathological study, and cardiomyocytes and cardiac fibroblasts were isolated using Langendorff perfusion method *Ex vivo* to measure expression of inflammatory and cardiac-related genes by real time PCR. The expression of key molecule in cardiac dysfunction (β -MHC) was also tested in H9c2 cardiomyocytes treated with sera derived from CIA mice or RA patients.

Results: At day 50 after immunization, cardiac function in CIA mice was prominently reduced as evidenced by decreased ejection fraction (EF) and fractional shortening (FS), increased left ventricular end-systolic volume (LVESV) and internal systolic diameter (LVIDs). Accordingly, enhanced inflammatory cells infiltration and fibrosis were identified in ventricular tissues pathologically, and increased inflammatory genes expression including TNF- α , IL-6, IL-17 and MMP3 detected in isolated ventricular cardiomyocytes and cardiac fibroblasts from CIA mice. Furthermore, H9c2 cells treated with sera from CIA mice or RA patients exhibited high levels of β -MHC.

Conclusion: Joint inflammation is associated with an obvious cardiac dysfunction and enhanced inflammation infiltration and inflammatory cytokines production in cardiomyocytes and cardiac fibroblasts during CIA development. Our data provide the direct evidence that inflammation contributes to development of cardiac diseases in RA patients.

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AB0147

RESEARCH PROGRESS OF MESENCHYMAL STEM CELL-DERIVED MICROVESICLES BY DELIVERING MICRORNA IN RHEUMATIC DISEASES

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Background: Recently, studies have shown that Mesenchymal Stem Cell-derived Microvesicles (MSC-MVs) can play a role in immune regulation and tissue repair by transporting miRNAs, and their effects are not weaker than that of their mother stem cells. Rheumatoid arthritis is an autoimmune disease characterized by chronic synovitis and progressive cartilage and bone destruction. Current treatments include non-steroidal anti-inflammatory drugs, glucocorticoids, DMARDs, and biological agents, but 30% of patients with rheumatism are ineffective, so there is an urgent need to find a new treatment.

Objectives: To review the research progress of MSC-MVs by delivering micro-RNA (miRNA) in rheumatic diseases.

Methods: Literatures were searched by using MSC-MVs, autoimmune diseases and miRNA as keywords.

Results: In the field of rheumatology, Chen C showed that after MSCT transplantation, mir-151-5p was transferred through exosomes to damaged bone marrow MSC of systemic sclerosis (SSc) mice, and the activation of IL4R/mTOR pathway was down-regulated to improve the osteoporosis of SSc mice^[1]. Exosomes of human synovial mesenchymal stem cells overexpressing miR-140-5p promoted cartilage regeneration and prevented OA in rat models^[2]. In the field of autoimmune diseases, Chen L et al. demonstrated that BMSC-derived exosomes containing miR-223 play a important role in liver protection by down-regulating NLRP3 (nod-like receptor family protein) and caspase-1 (caspase-1) in the experimental model of autoimmune hepatitis^[3]. Human BMSC-derived exosomes transfected with siFas and anti-mir-375 plasmids down-regulated Fas and miR-375 in human NOD scid gamma (NSG) mice, thereby protecting islet function and inhibiting immune rejection in islet transplantation^[4].

Conclusion: MiRNA targeting therapy with MSC-MVs as vector or the construction of MSC-MVs with overexpression of protective miRNA will provide new, accurate and promising treatment strategies for multiple rheumatic diseases.

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