AB0196

MESENCHYMAL STEM CELLS TUNE THE DIFFERENTIATION OF MYELOID-DERIVED SUPPRESSOR CELLS IN SJÖGREN'S SYNDROME THROUGH INHIBITING IL-12

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Background: The preliminary animal and human studies, including ours, showed that mesenchymal stem cell (MSC) transplantation could reestablish salivary function and reduce lymphocytic infiltration in salivary glands in Sjögren's syndrome (SS). However, the mechanisms of the encouraging results of MSCs on the SS remain to be elucidated. Myeloid-derived suppressor cells (MDSCs) represent an important class of immunoregulatory cells. MDSCs have multiple phenotypes which inhibit T cell responses by multiple mechanisms, and the environment dictates the development of suppressive properties and activation. Previous studies have demonstrated that MDSCs played important roles in systemic lupus erythematosus and rheumatic arthritis. However, the involvement of MDSCs in the immunopathology of SS is largely unknown.

Objectives: This study aims to investigate effects of MDSCs in SS progression and the potential association of MDSCs with the therapeutic effects of MSCs in the patients with SS and mice with SS-like symptoms.

Methods: The frequencies of MDSCs in the blood and bone marrow were detected by flow cytometry analysis in SS mice (NOD mice) and patients with SS. The NOD mice were adoptively transferred with MDSCs or treated with anti-Gr1 antibody to eliminate MDSCs. The salivary flow rate was measured and inflammatory infiltration in salivary glands was assessed. MSCs were infused into NOD mice to investigate the effects of MSCs on SS-like syndrome and changes of MDSCs. The percentages of MDSCs in SS patients before and after MSC transplantation were determined.

Results: The percentage of MDSCs increased significantly with the development of SS-like syndrome in NOD mice. The SS-like syndrome exacerbated after transfer of MDSCs, whereas deletion of MDSCs alleviated SS-like syndrome in NOD mice. MSC transplantation enhanced salivary flow rates and decreased lymphocyte infiltration in salivary glands in NOD mice. The percentages of MDSCs were down-regulated after MSC transplantation. MSC reduced IL-12 production in dendritic cells in vitro and in vivo. The IL-12 promoted generation of MDSCs in vitro. The numbers of MDSCs were positively correlated with disease activities of SS patients. The percentages of MDSCs were reduced after MSC transplantation in patients with SS.

Conclusion: 1. MDSC expansion positively correlated with inflammation during the progression of SS. 2. MSC transplantation had beneficial effects in SS mice. 3. IL-12 production by dendritic cells was reduced by MSCs. 4. The MDSCs expansion was induced by inflammatory IL-12 and reversed by MSC transplantation in SS. Thus, we have revealed a previously unrecognized function of MSC-mediated reduction of MDSCs in suppressing SS-like syndrome through inhibition of IL-12 production by DCs, which provided novel therapeutic strategies to treat patients with SS.

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AB0197

VITAMIN D PROTECTS PODOCYTES FROM AUTOANTIBODIES INDUCED INJURY IN LUPUS NEPHRITIS BY REDUCING ABERRANT AUTOPHAGY

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Background: Recent data suggest that vitamin D insufficiency may play a role in the progression of SLE and the nephropathy such as chronic kidney disease[1]. We previously show that severe vitamin D deficiency increases the risk for moderate to severe disease activity[2]. Moreover, vitamin D has been demonstrated a protective effect on podocyte injury via diverse mechanisms in proteinuric glomerular disease[3-7]. However, there is a paucity of data to demonstrate the mechanisms through which the autophagy functions on the protective role vitamin D plays on podocyte in the pathogenesis of lupus nephritis.

Objectives: The aim of this study was to investigate whether vitamin D play a protective role in podocyte injury induced by autoantibodies purified from lupus nephritis (LN) patients serum via autophagic way.

Methods: Autophagic activities of LN patients renal tissues were evaluated under transmission electronic microscope. IgG from patients with LN were purified to induce human podocyte injury and the role of vitamin D in injury was observed. Podocytes were observed under TEM and autophagic activity was evaluated by western blot analysis and qRT-PCR, mRFP-GFP-LC3B adenovirus were infected into HPC in vitro.

Results: Significantly higher autophagic levels were observed in LN patients ($p < 0.05$) and apparently greater autophagic levels in podocytes were shown ($p < 0.05$). Among different classifications of LN, Class V ($n=5$), III+V ($n=5$) and IV+V ($n=5$) gained higher autophagic levels than Class III ($n=5$) and IV ($n=5$). Induced autophagy, which was evident by increased LC3B-II and Beclin 1 level, caused consumption of p62, more autophagosomes observed under TEM, and more LC3B dots observed under confocal microscope in IgG group, along with decreased Nephlin expression, which suggests podocyte injury. Reduction of autophagy as well as alleviated podocyte injury was observed in the IgG+ VD group.

CONCLUSION:

This study demonstrates that vitamin D plays a protective role in podocytes injury induced by autoantibodies from LN patients and that appears to be a novel therapy target in LN.

REFERENCES:

- [1] Mok CC, Bro ET, Ho LY, Singh RJ, Jannetto PJ: **Serum 25-hydroxyvitamin D3 levels and flares of systemic lupus erythematosus: a longitudinal cohort analysis.** *Clinical rheumatology* 2018.
- [2] Gao CC, Liu SY, Wu ZZ, Li TF, Gao GM, Liu ZS, Zheng ZH: **Severe vitamin D deficiency increases the risk for moderate to severe disease activity in Chinese patients with SLE.** *Lupus* 2016, **25**(11):1224-1229.
- [3] **Vitamin D down-regulates TRPC6 expression in podocyte injury and proteinuric glomerular disease.** *The American journal of pathology* 2013, **182**(4):1196-1204.
- [4] Zhang XL, Guo YF, Song ZX, Zhou M: **Vitamin D prevents podocyte injury via regulation of macrophage M1/M2 phenotype in diabetic nephropathy rats.** *Endocrinology* 2014, **155**(12):4939-4950.
- [5] Guo J, Lu C, Zhang F, Yu H, Zhou M, He M, Wang C, Zhao Z, Liu Z: **VDR Activation Reduces Proteinuria and High-Glucose-Induced Injury of Kidneys and Podocytes by Regulating Wnt Signaling Pathway.** *Cellular physiology and biochemistry : international journal of experimental cellular physiology, biochemistry, and pharmacology* 2017, **43**(1):39-51.
- [6] Chandel N, Ayasolla K, Wen H, Lan X, Haque S, Saleem MA, Malhotra A, Singhal PC: **Vitamin D receptor deficit induces activation of renin angiotensin system via SIRT1 modulation in podocytes.** *Experimental and molecular pathology* 2017, **102**(1):97-105.
- [7] Garsen M, Sonneveld R, Rops AL, Huntink S, van Kuppevelt TH, Rabelink TJ, Hoenderop JG, Berden JH, Nijenhuis T, van der Vlag J: **Vitamin D attenuates proteinuria by inhibition of heparanase expression in the podocyte.** *The Journal of pathology* 2015, **237**(4):472-481.

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AB0198

THE ROLE OF LOW EXPRESSION OF MIR-127-3P IN THE PATHOGENESIS OF LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) is one of the most severe organ lesions in systemic lupus erythematosus (SLE). Overactivation of the type I interferon (IFN-I) signaling pathway is associated with the pathogenesis of LN. Overexpression of the IFN stimulated genes (ISGs) was found in the kidneys of LN patients, and the absence of the IFN receptor reduced nephritis in lupus prone mice. Abnormal expression of microRNA in renal tissue is involved in the pathogenesis of LN.

Objectives: We aimed to investigate the role of renal microRNA related to LN in the over-activation of the IFN signaling pathway of LN kidney.

Methods: The expression of microRNA was determined by Taqman method. Interferon stimulation response element (ISRE)-luciferase reporter gene assay and western blot assay were used to study the function of candidate microRNA in IFN signal transduction pathway. mRNA expression was measured by SYBR green method. Gene expression profile was detected by gene expression microarray. Antagomir and Agomir (chemically modified microRNA mimics and antagomir inhibitors) of candidate microRNAs were used for functional gain and functional loss experiments.