Wnt/β-catenin signaling mediates the senescence of bone marrow-mesenchymal stem cells from systemic lupus erythematosus patients through the p53/p21 pathway

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Abstract Recent studies have shown that allogeneic bone marrow (BM)-mesenchymal stem cell transplantation (MSCT) appears to be effective in systemic lupus erythematosus (SLE) patients and lupus-prone mice, contrary to studies in syngeneic BM-MSCT. These studies indicated that the abnormalities of BM-MSCs may be involved in the pathogenesis of SLE. Our studies and other previous studies have revealed that BM-MSCs from SLE patients exhibited early signs of senescence, such as flattened morphology, slow proliferation, increased senescence-associated β-galactosidase (SA-β-gal) activity, and so on. However, the mechanisms by which these cells senesces were still unclear. Previous studies have demonstrated that Wnt/β-catenin signaling plays an important role in stem cell senescence. In the current study, we investigated whether Wnt/β-catenin signaling mediates the senescence of BM-MSCs from SLE patients. We have found that Wnt/β-catenin signaling and the p53/p21 pathway were significantly hyperactivated in senescent SLE BM-MSCs. Treatment with 100 ng/mL Dickkopf-1 (DKK1), a Wnt/β-catenin signaling inhibitor or β-catenin siRNA for 48 h could reverse the senescent features of SLE BM-MSCs. Additionally, the expression levels of p53 and p21 were reduced in treated-SLE BM-MSCs compared with the untreated group. In summary, our study indicated that Wnt/β-catenin signaling may play a critical role in the senescence of SLE BM-MSCs through the p53/p21 pathway.

Keywords Bone marrow-mesenchymal stem cells (BM-MSCs) · Systemic lupus erythematosus (SLE) · Senescence · Wnt/β-Catenin signaling · p53/p21 pathway

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease characterized by multi-organ involvement and a remarkable variability in clinical presentations [1]. Deregulated activation of both B and T cells and the aberrant production of pro-inflammatory cytokines are critically involved in the initiation and progression of tissue pathology and organ damage in SLE [2]. Mesenchymal stem cells (MSCs) are multipotent stem cells with the capacity for self-renewal and the potential to differentiate into a variety of cell types, including osteoblasts, chondrocytes, adipocytes, and myoblasts [3]. It has become evident that MSCs can exert immune regulatory functions, both in vivo and in vitro, on a wide range of