CONTACT DYNAMICS BETWEEN MESENCHYMAL STEM CELLS AND T CELLS IN LUPUS-PRONE MRL/lpr MOUSE MODEL

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Background Systemic lupus erythematosus (SLE) is a multi-organ autoimmune disease characterized by autoantibody production and mesenchymal stem cells (MSCs) have emerged as a promising new therapy for the treatment of SLE. MSCs are adult stem cells isolated from various human tissues including bone marrow, adipose tissue, umbilical cord blood, and skeletal muscle; MSCs can differentiate into various cell types and can potentially replace damaged cells in vivo. MSCs suppress T cell proliferation and cytokine production, reduce B cell proliferation and antibody secretion, decrease the generation and function of dendritic cells, and reduce the activity of natural killer cells. MSCs also enhance the activity of regulatory T (Treg) cells. MSCs are thought to inhibit T cell functions by two different mechanisms: by producing soluble mediators and by direct cell-cell contacts. The soluble immunosuppressive factors produced by MSCs include IL-10, nitric oxide (NO), tumor growth factor (TGF)-, prostaglandin E2 (PGE2), and indoleamine 2,3-dioxygenase (IDO), all of which can inhibit the functions of major immune cells. Yet, much remains to be learned about the contact-dependent T cell inhibition by MSCs.

Methods We examined the in vitro efficacy of MSCs in lupus-prone MRL/lpr mouse model and examined how MSCs inhibit MRL/lpr T cells by using time-lapse imaging at the single level.

Results In this study, we show that transfer of human MSCs increased MRL/lpr mouse survival, decreased T cell infiltration in the kidneys, and reduced T cell cytokine expression. In vitro, allogeneic mouse MSCs inhibited MRL/lpr T cell proliferation and cytokine production. Time-lapse imaging revealed that MSCs recruited MRL/lpr T cells establishing long-lasting cellular contacts by enhancing T cell VCAM-1 expression in a CCL2-dependent manner. In contrast, CCL2 deficient MSCs did not induce T cell migration and VCAM-1 expression, resulting in insufficient cell-cell contact. Consequently, CCL2 deficient MSCs did not inhibit IFN- production by T cells and upon transfer no longer prolonged survival of MRL/lpr mice.

Conclusions Taken together, our imaging study demonstrates that CCL2 enables the prolonged MSC-T cell interactions needed for sufficient suppression of autoreactive T cells and helps to understand how MSCs ameliorate symptoms in lupus-prone MRL/lpr mice.

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53 HEALTH-RELATED QUALITY OF LIFE IN TUNISIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOUS

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Background Systemic lupus erythematosus (SLE) is a chronic inflammatory disease which can affect different aspects of the patients life, leading to an impairment of health-related quality of life (HRQOL).

The aim of our study was to investigate the role of demographic, clinical, immunological and psychological aspects in influencing the HRQOL of Tunisian patients with SLE and to compare the efficiency of both generic and specific questionnaires of QOL.