

Polarization of T Lymphocytes Is Regulated by Mesenchymal Stem Cells

Abstract

Mesenchymal stem cells (MSCs) have been shown to suppress proliferation and activation of T lymphocytes *in vivo* and *in vitro* although the molecular mechanism of the immunosuppressive effect is not completely understood. To investigate the immunoregulatory effects of mice bone marrow mesenchymal stem cells on T lymphocyte, MSCs from NZBWF1 and BALB/c mice were isolated and expanded from bone marrow, and identified with cell morphology and the surface phenotypes. CD3+ T lymphocytes isolated by nylon wool columns were co-cultured with PMA with or without the two strains of MSCs. Then T cell apoptosis and intercellular cytokines of T cell were assessed by flow cytometry. Quantification of transcription factors T-box (T-bet) and GATA-binding protein 3 (GATA-3) expressed in T cells was detected by RT-PCR and western blot. Our results showed that there was a decrease of CD3+ T cell apoptosis when NW MSCs or Bc MSCs were added, and an increase of Th2 subset by NW MSCs and Th1 subset by Bc MSCs were observed by co-culturing MSCs with T lymphocytes. It is suggested that, by favoring Th1- cell development and inhibitory Th2-cell development, normal MSCs might interfere with the SLE development, and that marrow-derived NW MSCs had defective immunoregulatory function when compared with MSCs from healthy mouse strains.

Keywords: NZBWF1 mice • BALB/c mice • mesenchymal stem cells (MSCs) • systemic lupus erythematosus (SLE) • T lymphocytes • Th1/Th2..

Introduction

There is a complex immunologic dysregulation in the background of SLE. It is now well established that T cells play a key role in the regulation of immunologic processes. Much evidence supports the central role of T cells in the pathogenesis and development of SLE. Depletion of T cells was shown to prevent the development of SLE in SLE-prone mice. T helper subsets can be distinguished according to their cytokine secretion capacities and contradictory data about the dominance of Th1 or Th2 cytokines in SLE were presented. On the other hand, some reports thought that autoimmune diseases might be stem cell disorders and found that defects of hematopoietic cells in the diseases. Preliminary reports on cotransplantation of MSCs and hematopoietic stem cells (HSCs) indicated a significant reduction in acute and chronic graft-versus-host disease (GVHD) and an enhancement of HSCs engraftment [1]. In addition, *in vitro* culture-expanded autologous MSCs could be infused intravenously without toxicity. It was reported that cotransplantation of MSCs along with HSCs was prior to simple HSCs transplantation in MRL/lpr mice. These mice manifest clinical and immunological abnormalities, including high levels of antinuclear antibodies, hemolytic anemia, proteinuria, and progressive immune complex glomerulonephritis. In our studies, BALB/c mice were used as control. The lupus-prone NZBWF1 animals are henceforth referred as NW, whereas the control BALB/c strain is indicated as Bc.

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Results

MSCs from mouse bone marrow were isolated based on the enhanced adherence to plastic in culture plates. Homogeneous population of fibroblast-like cells with 90 % confluence in NZBWF1 and BALB/c mice were seen at a median of 7 or 10 days after initial plating, respectively. After the first passage, the cells grew exponentially, requiring weekly passages [2]. Morphologically, NW MSCs appeared very similar to normal counterparts. However, in primary and continued culture NW MSCs seemed to be more viable in the same culture conditions. As shown in Figure A2 and B2, isolated colonies of NW MSCs are more typical. We have six NZBWF1 and six BALB/c mice conducted, with each marrow sample yielding similar results.

Discussion

MSCs have shown to be poorly immunogenic and suppress allogeneic or autologous T cell response, which suggested MSCs might be used in therapeutic applications. In this paper, we have examined interactions between mice MSCs and T lymphocytes in order to understand better the mechanisms of MSC-mediated immune modulation. Some researchers have investigated effects of allogeneic bone marrow-derived mesenchymal stem cells on T lymphocytes from BXSb mice [3]. The present study is the first report showing that MSCs from lupus mice interact with T cells from normal mice and are capable of altering the outcome of immune response. The balance of Th1 and Th2 cells among different groups was then detected. We tested the expression of T-bet and GATA-3 and intercellular cytokines in T cells co-cultured with different MSCs. T-bet and GATA-3 are two major T helper-specific transcription factors that regulate the expression of Th1 or Th2 cytokine genes and play a crucial role in T-helper cell differentiation [4]. The results

imply that lupus MSCs might be defective, but whether these defects are pathogenic to the disease remains to be explored. Normal MSCs made T-subset a shift to Th1, which might lead to an improvement of the illness and may offer one explanation for the clinical outcome observed by other authors. So we hypothesize that MSCs would influence the maturation and differentiation of T cells and hence the Th polarization of an immune response in vivo. Interestingly we also find there are differences in passage-time and proliferation between Bc MSCs and NW MSCs. The latter has higher proliferation and shorter passage-time. This implies NW MSCs may be defective in their function, which is supported by El-Badri who reported that MSCs from lupus murine model had defective structure and function when compared with MSCs from healthy mouse strains [5].

Acknowledgement

None

Conflict of Interest

No conflict of interest

References

1. Wofsy D, Seaman W E. Successful treatment of autoimmunity in NZB/NZW F1 mice with monoclonal antibody to L3T4. *J. Exp Med*, 161, 378-391(1985).
2. Wofsy D. Administration of monoclonal anti-T cell antibodies retards murine lupus in BXSb mice. *J. Immunol*, 136, 4554-4560(1986).
3. Funauchi M, Ikoma S, Enomoto H, Horiuchi A et al. Decreased Th1-like and increased Th-2 like cells in systemic lupus erythematosus. *Scand. J. Rheumatol*, 27, 219-224(1998).
4. Takahashi S, Fossati L, Iwamoto M, Merino R, Motta R, Kobayakawa T et al. Imbalance towards Th1 predominance is associated with acceleration of lupus-like autoimmune syndrome in MRL mice. *J. Clin. Invest*, 97, 1597-1604(1996).
5. Ikehara S. Autoimmune diseases as stem cell disorders: normal stem cell transplant for their treatment. *Int. J. Mol. Med*, 1, 5-16(1998).