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Concise Review: Mesenchymal Stem Cell Treatment of the Complications of Diabetes Mellitus

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Key Words. Mesenchymal stem cell • Cardiomyopathy • Nephropathy • Neuropathy • Wound • Diabetes mellitus

ABSTRACT

Mesenchymal stem cells (MSCs) are multipotent, self-renewing cells that can be found in almost all postnatal organs and tissues. The main functional characteristics of MSCs are their immunomodulatory ability, capacity for self-renewal, and differentiation into mesodermal tissues. The ability of MSCs to differentiate into several cell types, including muscle, brain, vascular, skin, cartilage, and bone cells, makes them attractive as therapeutic agents for a number of diseases including complications of diabetes mellitus. We review here the potential of MSCs as new therapeutic agents in the treatment of diabetic cardiomyopathy, diabetic nephropathy, diabetic polyneuropathy, diabetic retinopathy, and diabetic wounds. Also, in this review we discuss the current limitations for MSCs therapy in humans. STEM CELLS *2011;29:5–10*

Disclosure of potential conflicts of interest is found at the end of this article.

INTRODUCTION

Mesenchymal stem cells (MSCs), also known as multipotent mesenchymal stromal cells, are self-renewing cells that can be found in almost all postnatal organs and tissues [1]. MSCs are most frequently isolated from bone marrow but can generally be derived from any organ [2]. Depending on their intended purpose, experimental or therapeutic use, MSCs can be isolated from adipose tissue, umbilical cord blood, compact bone, and other tissues [2]. MSCs show variable expression levels of several molecules: CD105 (SH2), CD73 (SH3/4), stromal antigen 1, CD44, CD90, CD166 (vascular cell adhesion molecule), CD54/CD102 (intracellular adhesion molecule), and CD49 (very late antigen) [3, 4]. Conversely MSCs lack the expression of surface markers characteristic for hematopoietic cells (CD14, CD45, and CD11a/lymphocyte function-associated antigen 1 (LFA-1)), erythrocytes (glycophorin A), and platelet and endothelial cell markers (CD31) [5] (Supporting Information Fig. 1).

The main functional characteristics of MSCs are their immunomodulatory ability, capacity for self-renewal, and differentiation into tissues of mesodermal origin [6, 7]. Through production of soluble factors, MSCs can alter the secretion profile of dendritic cells (DCs) resulting in increased production of anti-inflammatory cytokine interleukin (IL)-10 and decreased production of interferon-gamma (IFN-γ) and IL-12 [6–8]. MSCs can inhibit T-cell proliferation by engagement of the inhibitory molecule programmed death 1(PD-1) to its ligands PD-L1 and PD-L2, thereby producing soluble factors that suppress T-cell proliferation (such as TGF-β or IL-10) and through interacting with DCs [7, 8]. MSCs can increase the number of $CD4^+CD25^+FoxP3^+$ T-regulatory cells that suppress the immune response [6–8]. Susceptibility to diabetes induction and development may be related to the activity of T-regulatory cells [9] and expansion of Th17 cells [10]. MSCs are able to render T cells anergic by blocking differentiation of monocytes to DCs or by inhibiting DC maturation [6]. Through production of soluble factors, MSCs can inhibit proliferation and IgG secretion of B cells [8]. Thus, it appears that therapeutic effects and use of MSCs would be primarily based on their release of trophic and immunomodulatory factors [8, 9] (supporting information Fig. 2).

Previous studies have shown that MSCs are able to differentiate into several cell types, including cardiomyocytes, vascular endothelial cells, neurons, hepatocytes, epithelial cells, and adipocytes, making them a potentially important source for the treatment of debilitating human diseases [11]. Such multipotent differentiation characteristics coupled to their capacity for self-renewal and capability for the regulation of immune responses, described MSCs as potentially new therapeutic agents for treatment of the complications of diabetes mellitus (DM) [11].

Author contributions: V.V.: conception and design, manuscript writing; N.A.: manuscript writing and editing; M.L.L.: manuscript writing and editing; M.S.: conception and design, manuscript writing and editing.

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