Annals of Stem Cell Research & Therapy

Editorial
Published: 02 Dec, 2019

Mesenchymal Stem Cell-Based Therapies - A Safe and Curative Alternative for Rheumatoid Arthritis Patients

*Rangnath Mishra and Anand Srivastava**

Department of Stem Cell Therapy and Research, Global Institute of Stem Cell Therapy and Research, USA

Editorial

A number of diseases start in individuals with advancing age. Inherent inflammation, because of several factors like accumulation of free oxygen radicals, is considered as root cause of initiating and promoting many age-related diseases. Rheumatoid Arthritis (RA), which could affect people from mild to extremely debilitating level, is one of several age-related diseases known to be rooted in inflammation is affecting individuals all around the globe. About 1.5 million people in the United States have RA and occur almost three times more in women than in men. RA most commonly begins between ages 30 and 60 years [1]. Rheumatoid arthritis is a degenerative chronic inflammatory disorder that can affect different organs affects different joints more often. In some people, the condition can damage a wide variety of body systems, including the skin, eyes, lungs, heart and blood vessels. RA is an autoimmune disorder leading to progressive tissue destruction and thereby loss of afflicted organ's function and potentially death if not adequately treated [2,3]. Occurrence of RA is a result of activation of adaptive immune system mediated by B- and T-cells. Also, Fibroblast-like Synoviocytes (FLS) have a major role in the initiation and perpetuation of destructive joint inflammation because of their ability to express Immunomodulation-cytokines and mediators as well as a wide array of adhesion molecule and matrix-modeling enzymes [4]. Mesenchymal stem cells (MSCs) are multipotent and can differentiate into various cell types of all the three-germ lineages, like osteocytes, adipocytes, neural cells, vascular endothelial cells, cardiomyocytes, pancreatic β-cells, and hepatocytes. In addition, they are characterized by their immunosuppressive properties and low immunogenicity. Their secretion of trophic factors enforces the therapeutic and regenerative outcome in a wide range of applications. The field of MSCs research, initially aiming on harnessing their remarkable multi-lineage differentiation capabilities for skeletal regeneration, including bone and cartilage, led to another remarkable ability namely Immunomodulation [5,6]. The immunomodulatory effects of MSCs has led to use of these cells as potential therapeutic tools to correct the breakdown of immune tolerance during RA, particularly for a group of cases which are inadequately treated. The mechanisms, by which MSCs modulate the immune response, are studied at great length [6]. It is important to keep in mind that MSCs

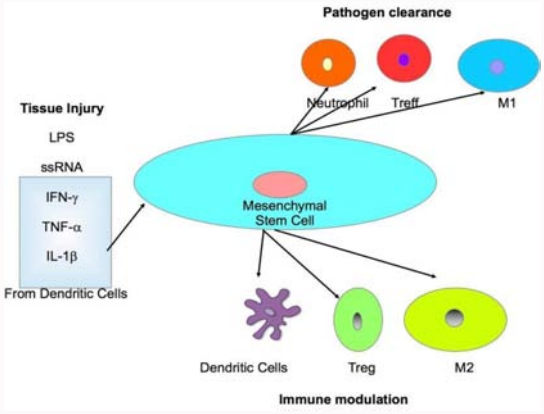

Figure 1: Inflammatory mediators determines the effector mechanisms utilized by MSCs. MSCs activated directed by Lipopolysaccharide (LPS), double-stranded RNA (dsRNA) or indirectly by activated macrophages produced pro-inflammatory cytokines (IFN-γ, TNF-α and IL-1β) during tissue injury. Depending on the stimulus received, MSCs can promote pathogen clearance by secretion of pro-inflammatory cytokines (IL-6 and IL-8), polarization of pro inflammatory M1 macrophages, anti-microbial activity or immune modulation by the secretion of immunosuppressive soluble factors (IDO, PGE-2, TGF-b, NO, TSG-6 and factor H among others), promotion of alternatively activated anti-inflammatory M2 macrophages, tolerogenic DC (Tol DC) or Treg.

OPEN ACCESS

Correspondence:
Anand Srivastava, Department of Stem Cell Therapy and Research, Global Institute of Stem Cell Therapy and Research, 4660 La Jolla Village Drive, San Diego, CA 92122, USA, Tel: 858-344-2492;
E-mail: anand@giostar.com

Received Date: *23 Oct 2019*
Accepted Date: *29 Nov 2019*
Published Date: *02 Dec 2019*

Citation:
Mishra R, Srivastava A. Mesenchymal Stem Cell-Based Therapies - A Safe and Curative Alternative for Rheumatoid Arthritis Patients. Ann Stem Cell Res Ther. 2019; 3(2): 1034.

become immunosuppressive only after exposure to IL-1β, TNF-α or similar proinflammatory cytokines. In addition to pro-inflammatory cytokines, role of TLR signaling, especially by TLR3 and TLR4, also has been suspected in the promoting MSCs anti-inflammatory activity. Immunomodulation by MSCs involves multistage processes like possible migration to the site of injury after sensing inflammation, activation of MSCs' needed mode of immunomodulation, promotion of pathogen clearance, if required and thereby suppression of inflammation (Figure 1). MSCs may exert their immunosuppressive effects at a distance also [7]. Adipose-derived MSCs are considered to be better suited for application in regenerative therapies because of their main advantage over MSCs from other sources, e.g. from bone marrow, like easy availability as they can be easily and repeatedly harvested using minimally invasive techniques without causing much morbidity [8]. The exact pathology of RA is poorly understood. The suspicion that activated TNF-α- mediated inflammatory pathway is underlying causative factor, a number of biologics like Infliximab and Adalimumab are in clinical use. However, there are a couple of factors of concern with those in general. First of all these drugs inhibit one particular pathway and a biological system can learn to avoid that particular inhibition, and, second, these drugs have quite few undesired side-effects which can be prohibitive for long term use. As mentioned earlier, MSCs are immunomodulatory and become immuno-suppressive when activate by proinflammatory signaling molecules. Also, these cells being immuno-privileged do not provoke immune response in the recipient. As these cells can migrate to the site of inflammation, settle there and differentiate into cell types of the host tissue, can impart to some cure in addition to alleviating the pain in RA patients. There have been some concerns while using MSCs in clinics. As these cells are isolated freshly, protocols practiced in laboratories can affect the yield and purity of the cells and thereby affecting the therapeutic efficacy of the cells. Also, MSCs from every individual are not equally efficacious in alleviating the symptoms. At present, it appears that there is still some way to go to figure out how to keep the MSCs in undifferentiated state for longer time in cell culture conditions so that these could provide desired number of cells with known therapeutic strength consistently. Other few factors still need some investigation to find out.

- If pretreatment of stem cells with certain cytokines or growth factors which may potentiate their therapeutic value.
- Ways to promote their migration to afflicted body regions of an individual. Therefore, the future direction may be to pre-treat MSCs with organ specific signaling factors to make cells more specific for specific diseases.

References

1. What is Rheumatoid Arthritis?
2. McGonagle D, McDermott MF. A proposed classification of the immunological diseases. PLoS Med. 2006;3(8):297.
3. McInnes IB, Schett G. The Pathogenesis of Rheumatoid Arthritis. N Engl J Med. 2011;365(23):2205-19.
4. Bottini N, Firestein GS. Duality of fibroblast-like synoviocytes in RA: passive responders and imprinted aggressors. Nat Rev Rheumatol. 2013;9(1):24-33.
5. Le Blanc K, Tammik C, Rosendahl K, Zetterberg E, Ringdén O. HLA expression and immunologic properties of differentiated and undifferentiated mesenchymal stem cells. Exp Hematol. 2003;31(10):890-6.
6. English K. Mechanisms of mesenchymal stromal cell immunomodulation. Immunol Cell Biol. 2013;91(1):19-26.
7. Roddy GW, Oh JY, Lee RH, Bartosh TJ, Ylostalo J, Coble K, et al. Action at a distance: systemically administered adult stem/progenitor cells (MSCs) reduce inflammatory damage to the cornea without engraftment and primarily by secretion of TNF-α stimulated gene/protein 6. Stem Cells. 2011;29(10):1572-9.
8. Frese L, Dijkman PE, Hoerstrup SP. Adipose tissue-derived stem cells in regenerative medicine. Transfus Med Hemother. 2016;43(4):268-74.