Mesenchymal Autologous Stem Cells

Asdrubal Falavigna[1] *and Jaderson Costa da Costa*[2]

Key words
- Cell transplantation
- Clinical translations
- Mesenchymal stem cells
- Neuronal differentiation
- Spinal cord injury

Abbreviations and Acronyms
BDNF: Brain: derived neurotrophic factor
BM: Bone marrow
CNS: Central nervous system
CS: Chondroitin sulfate
ESC: Embryonic stem cells
iPS: Induced pluripotent cells
IV: Intravenous
LP: Lumbar puncture
MHC: Major histocompatibility complex
MSC: Mesenchymal stem cells
PG: Proteoglycans
SC: Stem cell
SCI: Spinal cord injury
VEGF: Vascular endothelial growth factor

From the [1]*Department of Neurosurgery, Medical School of the University of Caxias do Sul, Caxias do Sul; and* [2]*Neurology Service and Instituto do Cérebro, Pontifical Catholic University of Rio Grande do Sul, Brazil*

To whom correspondence should be addressed: Asdrubal Falavigna M.D., Ph.D. [E-mail: asdrubalmd@gmail.com]

Citation: World Neurosurg. (2015) 83, 2:236-250.
http://dx.doi.org/10.1016/j.wneu.2013.02.026

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

The use of cell-based therapies for spinal cord injuries has recently gained prominence as a potential therapy or component of a combination strategy. Experimental and clinical studies have been performed using mesenchymal stem cell therapy to treat spinal cord injuries with encouraging results. However, there have been reports on the adverse effects of these stem cell–based therapies, especially in the context of tumor modulation. This article surveys the literature relevant to the potential of mesenchymal autologous stem cells for spinal cord injuries and their clinical implications.

INTRODUCTION

There is no single effective treatment that can improve the severe and permanent neurological outcome for patients with traumatic spinal cord injury (SCI). The main problem is the complexity of the SCI physiopathology, which includes: 1) the physical and chemical barrier formed by glial cell activation, migration, and hypertrophy, the cavity that develops after injury, and the presence of inhibitory neuronal molecules at the injury site; 2) an absence of Schwann cells to guide any regenerating axons; 3) axons damaged and glial apoptosis caused by an inflammatory local environment; 4) the absence of neurotrophic factors to enhance axonal growth; and 5) inhibition of axonal growth by postinjury myelin-associated proteins such as the Nogo family, glycoproteins, oligodendrocyte myelin glycoprotein, semaphorin 4D, and epherin B3 (121, 176, 192, 193).

Several strategies to regenerate and repair the central nervous system (CNS) have been used at the molecular and cellular level, such as manipulating gene expression, removing inhibitory factors of glial cells, making antibodies against destructive myelin-associated proteins, and therapy with neurotrophins, other growth factors, and stem cell (SC) therapy.

The use of SC is a novel therapeutic strategy for functional recovery of the patients with SCI, but like any other treatment, there are always two expected effects: the good and the bad. The advantages of the current SC therapy are enhancing survival and neuronal differentiation, repairing areas with damaged myelin by grafting cells, myelinating formation, neuroprotection, reducing the inflammatory response, providing a tissue bridge for nerve fiber growth, and promoting regeneration (3, 20, 22, 40, 46, 47, 52, 53, 71, 84, 87, 103, 143, 144, 166, 168, 214, 230, 237). However, the disadvantages are the differentiating into anaplastic cell types after transplantation, exacerbating the inflammatory response by expanding the lesion volume, and the potential contribution to the glial scar, inappropriate sprouting with enhanced pain perception, and allodynia (48, 93, 102, 105, 107, 112, 114, 120, 139, 162, 175, 198, 201, 209, 221, 224, 226).

Mesenchymal stem cells (MSC) are a group of heterogeneous nonhematopoietic, multipotent progenitor cells that have the ability to influence immune effector cell development, maturation, and function as well as alloreactive T-cell responses through the production of bioactive cytokines and proteins (23). In addition, MSC have been extensively studied due to their ability to self-renew and differentiate into many different cell types, particularly cells of mesodermal origin such as osteoblasts, chondrocytes, and adipocytes in culture (17, 72, 167). Even more interestingly, these cells can differentiate into cells of nonmesodermal origin, such as hepatocytes (89, 203), neural cells (103), and epithelial cells (131). For these reasons they have been used for cell replacement, repair and regeneration, immunomodulation, and disease modeling (196).

SOURCES

MSC have received considerable interest as possible donor cells for transplantation therapies because they can be easily harvested (**Figure 1**). The principal sources from which MSC were usually isolated were bone marrow (BM) (60), adipose tissue (242), umbilical cord blood (116), embryonic stem cells (ESC), and induced pluripotent cells (iPS). The other reported sources were olfactory tissue (44, 213), dental tissue (81), synovial fluid (88), palatine tonsil (83), parathyroid gland (197), fallopian tube (85), and skeletal muscles (82). It is unclear whether MSC isolated from different tissue sources have similar therapeutic potentials and which isolation protocol is optimal for therapeutic purposes (90). The main issues of the principal sources of MSC isolation are described.

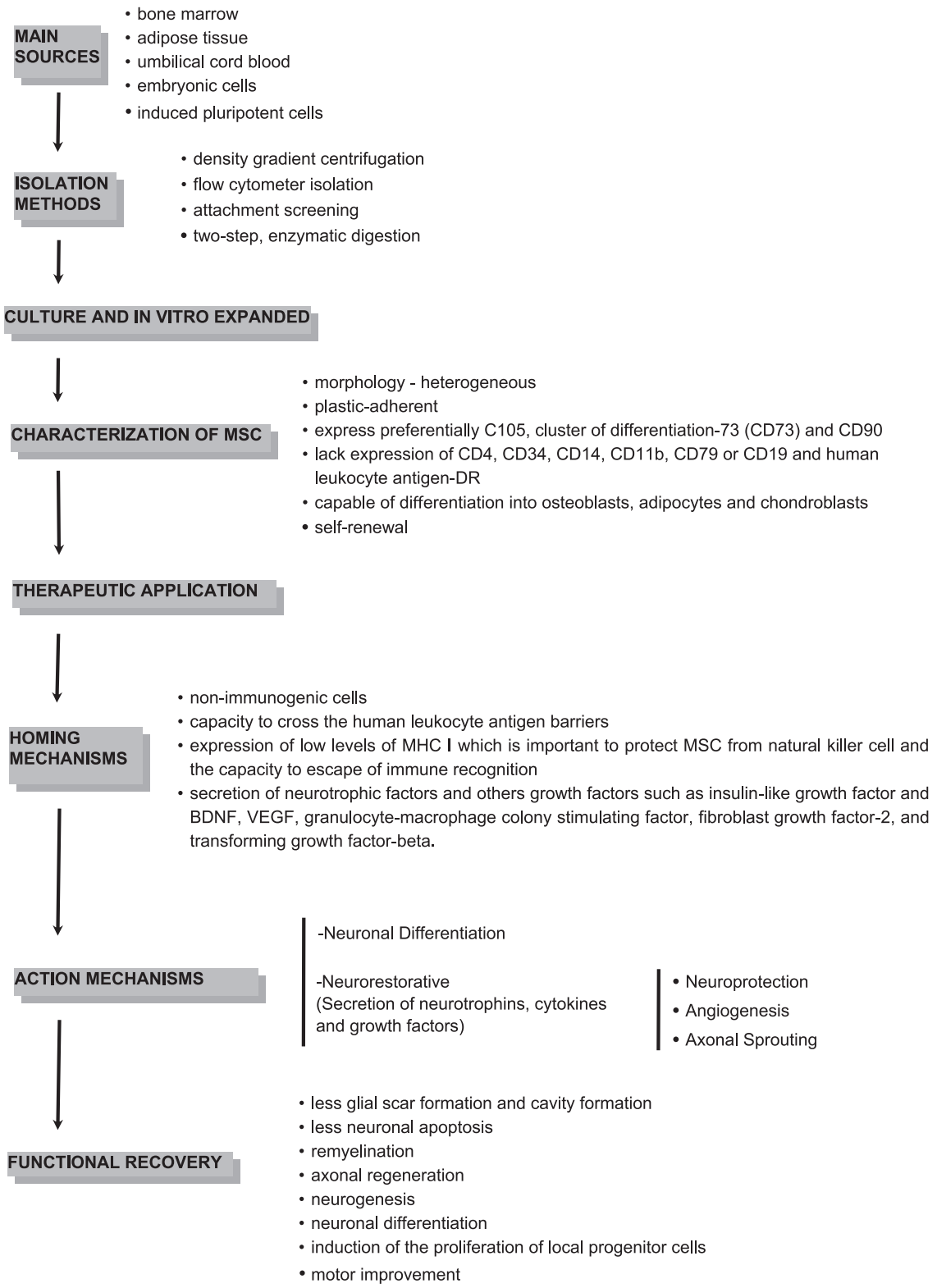

Figure 1. Flowchart showing all steps of the mesenchymal stem cells (MSC) process. It begins by describing the main harvesting sources in MSC, the methods used to isolate these cells, the criteria used to characterize them as mesenchymal cells, the mechanisms used to facilitate homing, the possible action mechanisms for MSC, and the functional improvement reported in the studies after MSC therapy.