Mesothelial Stem Cells and Stromal Vascular Fraction

Use in Functional Disorders, Wound Healing, Fat Transfer, and Other Conditions

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KEYWORDS

• Stromal vascular fraction • Adipose-derived stem cells • Nitric oxide • Cellular therapy

KEY POINTS

- Autologous stromal vascular fraction can be released enzymatically from lipoaspirate harvested under a local anesthetic; this is currently not a procedure approved by the US Food and Drug Administration.
- Stromal vascular fraction contains a heterogeneous population of cells, including adipose-derived stem cells, hematopoietic stem cells, endothelial progenitor cells, macrophages, red blood cells, platelets, growth factors, and T-regulatory cells.
- With proper homing and activation events, stromal vascular fraction possesses several key properties, including regenerative, antiinflammatory, immunomodulatory, and pain mitigation.
- Multiple conditions have been treated with stromal vascular fraction, including osteoarthritis, musculoskeletal disease, neurodegenerative disorders, and autoimmune conditions.
- With ongoing research, safety data should continue to be recorded, as well as symptom improvement data, which will continue to validate this form of regenerative therapy.

INTRODUCTION

The ability to regenerate or heal damaged tissue was once considered science fiction, but now autologous fat-derived mesenchymal stem cells is opening new frontiers for patients, particularly those with degenerative, inflammatory, and autoimmune conditions. With the soaring costs of health care, the development of autologous cellular therapies using cells isolated from the human body with cost-effective, safe, sterile, and reliable surgical procedures and tissue transfer techniques could help to dramatically decrease the costs of health care by enabling the science in our bodies to recuperate itself.[1] Additionally, having a supply of one's own cells on demand may also change how accidents, myocardial infarcts, strokes, concussions, paralysis, or sudden

Disclosures: None.

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Facial Plast Surg Clin N Am ■ (2018) ■–■
https://doi.org/10.1016/j.fsc.2018.06.009

illness are treated. The ability to use mesenchymal stems cells in the treatment of carcinoma also exists. Stem cells possess the ability to home in on cancerous tissue. The stem cells can partner with the small pox virus and chemotherapy drugs to selectively attack cancer primaries and metastases, leaving healthy tissue unaffected. Further applications include treatment of acne, alopecia, psoriasis, eczema, sinusitis, healing wounds and wound beds, burns, hypertrophic scars, and keloids. This article provides an overview of mesothelial stem cells and stromal vascular fractionation; however, owing to the cutting-edge nature of these methods, they are not currently approved by the US Food and Drug Administration for use in the United States.[2]

THE SCIENCE OF MESENCHYMAL STEM CELLS

Mesenchymal stem cells possess self-renewal and multilineage differentiation potentials, which makes them an attractive source of stem cells for tissue engineering. Because these mesenchymal cells can be grown and multiplied, they effectively provide one with a long-term supply of a person's own stem cells for treating multiple conditions. Comparative analyses of various sources of mesenchymal stem cells, such as from bone marrow, adipose tissue, umbilical cord, and placental blood, have been done and many evidence-based articles suggest that MSCs have a potentially therapeutic use in the treatment of degenerative, inflammatory, and autoimmune conditions, and in scar mitigation.[3–10] In addition to treating diseases, Song and colleagues[11] demonstrated that injected MSCs activated the Wnt signaling cascade to alleviate pain. Adipose-derived stem cells have also demonstrated the ability to differentiate into many other cells and tissues, other than mesenchymal lines. In veterinary medicine, adipose-derived stem cells have been used to effect chondrogenesis and for other orthopedic conditions. Currently, the most common joints treated with success, include the knees, hips, shoulders, backs, ankles, elbows, fingers, feet, thumbs, and wrists.

THE SCIENCE OF STROMAL VASCULAR FRACTIONATION

Stromal vascular fraction (SVF) can be isolated from subcutaneous fat, and is known to contain adult mesenchymal stem cells, endothelial precursor cells, preadipocytes, antiinflammatory macrophages, T-regulatory cells, and cytokine growth factors.[12,13] Early veterinary experience with SVF explored its safety and efficacy, whereas various other studies highlighted SVF's immunomodulatory capabilities.[14,15] Recently, Guo and Nguyen and their colleagues reviewed the concepts, safety, and efficacy of SVF to date.[16,17] Subsequent research has yielded innovative methods of cryogenically freezing SVF so as to provide multiple deployments, both economically and conveniently (Cells on Ice; American Cryostem Corporation, Eatontown, NJ). Despite all that has been published, there are few articles in the literature that specifically looked at therapeutic outcomes. Drs Mark Berman and Elliot Lander initiated The Cell Surgical Network to address this knowledge deficit and fostered a multidisciplinary approach to exploring the potential efficacy of SVF in treating multiple diseases (Cell Surgical Network Data Base, Unpublished Data).[18] Their database includes safety study results on 2000 patients, with a 0.05% complication rate, as well as results from more than 400 physicians working in more than 100 clinics around the world who have treated more than 4000 patients.[19] **Box 1** lists the current institutional review board–approved areas of research within the Cell Surgical Network.

The major cellular components of SVF along with their most defining cell surface markers are listed in **Table 1**. When examined under flow cytometry, no 2 patients' SVF is identical in composition. As shown, the main properties of SVF are antiinflammatory, regenerative, and immunomodulatory. The stem cells deploy to a site that is secreting signaling molecules associated with degenerated, damaged, or inflamed tissue via a process referred to as *homing*. The second essential event in a stem cell operation is *activation*, wherein the stem cells must be effectively turned on by other signaling molecules that are associated with degeneration, damage, or inflammation to effect healing. The antiinflammatory property of SVF explains the pain relief that arthritis and other inflammatory condition patients typically describe, often within 48 to 72 hours of deployment. The second SVF property is its *regenerative potential*, which typically takes several months to occur. With this process, cells are capable of promoting healing by directly replacing damaged cells or secreting cytokine growth factors that affect cellular repair. Last is SVF's ability to be *immunomodulatory.* This capability allows SVF to effectively reset the immune system to correct the malfunction. The main properties of SVF after homing and activation criteria are met include antiinflammatory, regenerative, immunomodulatory, scar mitigation, and pain reduction. Several common problems and disease states affecting the patient undergoing