# Mesothelial Stem Cells and Stromal Vascular Fraction for Skin Rejuvenation

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**KEYWORDS**

• Mesenchymal stem cells • Adipose-derived stem cells • Growth factors
• Stromal vascular fraction (SVF) • Regenerative medicine

**KEY POINTS**

- The process of extracting, concentrating, and administering stem cells has been shown in clinical trials to exhibit beneficial effects in many degenerative conditions.
- Cellular therapies have shown great promise for skin rejuvenation, hair restoration, and many other clinical applications in other areas of medicine.
- Growing evidence now suggests that the 2 aging processes have converging biochemical and molecular pathways that lead to photoaging of skin.
- The common mechanisms of the 2 aging processes may provide several unique opportunities to develop antiaging therapies.
- Although it is unclear how large proteins, such as growth factors, are able to penetrate the skin and become pharmacologically effective, early objective clinical studies and subjective observations indicate that these cosmeceutical products may potentially reduce signs of facial aging.

Disclosure: The authors have nothing to disclose.

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Facial Plast Surg Clin N Am 26 (2018) 513–532
https://doi.org/10.1016/j.fsc.2018.06.011

## INTRODUCTION

The use of stem cells in regenerative medicine and specifically in facial rejuvenation is thought provoking and controversial. Stem cells have a natural ability to repair damaged tissue. They are inherent in most tissues of the body and function in a restorative capacity in many tissues, such as the skin, where stem cells facilitate a rejuvenation of epidermal basal cell layers every day and in the intestinal tract, where mucosal lining tissues are replaced approximately every 4 days. In the case of degenerative diseases, these cells are not activated quickly enough to fully repair damaged tissue. The process of extracting, concentrating, and administering these stem cells has been shown in clinical trials to exhibit beneficial effects in many degenerative conditions. In addition, cellular therapies have shown great promise for skin rejuvenation, hair restoration, and many other clinical applications in other areas of medicine.

Surgeons have previously believed that damaged or diseased human tissue could be replaced only by donor transplants or, in select cases, alloplastic implants. Today there is increased emphasis on tissue engineering and regenerative medicine. Tissue engineering provides a more advanced approach in which organs or tissues can be repaired, replaced, or regenerated for a more focused treatment approach. Tissue engineering combines the principles of bioengineering, cell transplantation, biomaterial engineering, and surgery.

## CATEGORIES OF STEM CELLS

Stem cells possess 2 important characteristics: they can renew themselves and they can give rise to specialized cell types. Essentially, there are 2 different classifications of stem cells: embryonic and adult. Embryonic stem cells (ESCs) are isolated from the inner cell mass of blastocysts. Adult stem cells have been identified in many organs and tissues and reside in a specific area of each tissue called a "stem cell niche." There are 3 different types of adult stem cells: pluripotent, multipotent, and unipotent. Pluripotent stem cells, such as embryonic or induced pluripotent stem cells (iPSCs), have the capacity to generate into tissue from any of the 3 germ layers. The risk for potential teratoma formation has impacted their clinical use. Multipotent stem cells, such as mesenchymal stromal cells, lack this negative effect and have the capacity to differentiate into a more limited number of closely related cells. Unipotent stem cells, although retaining the ability to self-renew, can produce only 1 cell type. This group plays a critical role in normal tissue homeostasis. The stem cells we are talking about for clinical therapies are essentially the multipotent type of stem cells that are derived from mesoderm.[1–3]

In the field of regenerative medicine, there is a need for a reliable source of stem cells in addition to biomaterial scaffolds and cytokine growth factors. Candidates include ESCs, iPSCs, and postnatal adult stem cells. ESCs and iPSCs have significant therapeutic potential, because of their auto reproducibility and their pluripotentiality. However, ethical considerations, cell regulations, and genetic manipulation limit their practical use. Postnatal adult stem cells are immunocompatible and are not fraught with ethical issues regarding their use. Postnatal adult stem cells can be obtained from bone marrow stroma, adipose tissue, dentition, skin, and a multitude of other tissues. They are termed mesenchymal stem cells (MSCs) and have adipogenic, osteogenic, chondrogenic, myogenic, and neurogenic potential.[2–5]

### *Induced Pluripotent Stem Cells*

Ethical concerns associated with the use of ESCs spurred research efforts that would convert adult stem cells into pluripotent cells. In 2006, Shinya Yamanaka (Kyoto, Japan) altered the genes in specialized adult male cells to cause dedifferentiation and return to an embryonic–like stem cell state. The mouse somatic cells were reprogrammed to activate a combination of transcription factors. The cells were termed "induced pluripotent stem cells" (iPSCs). Yamanaka was awarded the Noble Prize "for the discovery that mature cells could be reprogrammed to become pluripotent." In 2007, both Yamanaka and James Thomas (University of Wisconsin) independently developed techniques to reprogram human cells into iPSCs.[6]

Typically, viruses are used to genomically alter the cell to produce iPSCs. There were concerns that this manipulation could trigger the expression of oncogenes (cancer-causing genes). However, in 2008, techniques were discovered that removed oncogenes after induction of pluripotency. This opened the door for the potential use of iPSCs in human disease.[7] Considerable research into antiaging has focused on using iPSCs to reprogram cell senescence. However, it has been noted that altering of iPSCs at a cellular level also allows for the stimulation of collagen synthesis. This potential for iPSCs to generate collagen has significant implications in the field of aesthetic surgery (**Box 1**).

In the past, there was no standard nomenclature and no standard, accepted method for identifying stem cells. For this reason, in 2006, the