Mesenchymal Stem Cells: Aesthetic Applications

Adult stem cells may have significant aesthetic surgery applications. Their replicative capacity and plasticity may be useful in engineering autologous grafts for soft tissue and facial skeletal augmentation. Another possibility is that increasing the concentration of mesenchymal stem cells in the facial soft tissue at regular intervals during adulthood will maintain volume and elasticity. (Aesthetic Surg J 2003;23:504-506.)

Identification of multipotential mesenchymal stem cells (MSCs) derived from adult human tissues has led to exciting prospects for cell-based tissue engineering and regeneration. Ongoing research in regenerative medicine may enable us to use living cells and their signaling mediators to repair and rejuvenate tissue. In aesthetic surgery, these therapeutic strategies may be used in the future not only to treat physical signs of aging but also to prevent them.

Several strategies are under investigation. Stem cells can be processed and implanted directly or modified ex vivo before implantation. They can also be combined with biomaterials that provide structural support and growth factors. In addition, endogenous stem cells may be activated by the administration of signaling factors.

Characteristics of Adult MSCs

A stem cell is a cell from the embryo, fetus, or adult that can undergo extensive proliferation before senescence and can be differentiated to specialized cells of body tissues and organs. These cells remain in their undifferentiated state through suppression by some intrinsic or extrinsic factor until stimulated. As stem cells self-renew in vivo, their progeny include both new stem cells and committed progenitors with a more restricted differentiation potential. These progenitors, in turn, give rise to differentiated cell types.

The quintessential pluripotent cell is the embryonic stem cell (ESC), which has the ability to differentiate into all bodily tissues. This cell type has been isolated and cultured from 2 sources: (1) the inner cell mass of human embryos at the blastocyst stage, and (2) fetal tissue from terminated pregnancies. During embryonic development, the pluripotency of the ESC is narrowed to tissue-specific determined stem cells. The determined stem cells differentiate into committed progenitor cells that retain a limited capacity to replicate. Despite the pluripotency of ESCs, legal and moral controversies concerning their therapeutic and clinical application have prompted examination of adult MSCs.

Most cells in adult organs are composed of differentiated cells with specific phenotypic and genotypic characteristics. In the past decade, undifferentiated stem cells with varying capacity to develop into different mature tissues have been identified in mesenchymal tissues of adult humans. These quiescent adult stem or progenitor cells have been isolated from many anatomic sites, including brain, pancreas, liver, skin, fat, muscle, blood, bone marrow, lung, and tooth pulp. Adult stem cells may be activated for tissue regeneration during the natural processes of cell turnover and wound healing. As direct precursor cells for mature tissue, adult MSCs differentiate to several lineages, including chondrocytes, adipocytes, lymphocytes, fibroblasts, marrow stroma, osteocytes, myoblasts, cardiomyoblasts, and astrocytes. MSCs not only have the capacity to make specialized cells for the immediate repair or replacement of tissue, but also retain a high regenerative potential to guarantee correct function and cell turnover over time, possibly for a lifetime.

Adult MSCs were thought to develop into a narrow range of cell types that reflected the tissue composition from which they were isolated. However, in recent laboratory experimentation, adult stem cells have exhibited unexpected flexibility, differentiating into many tissue types. The term transdifferentiation is being used to describe this capacity. The plasticity of adult stem cells is thought to be similar to that of ESCs, creating new hope for their use in cell-based therapies. In addition, MSCs demonstrate a high capacity for replication, with about...
38 ± 4 population doublings before senescence. This replication would allow a small population of harvested cells to be expanded in culture before use.

Currently there is no unifying definition of MSCs or list of specific markers that define cell types characterized as MSCs. Instead they are currently defined by their ability to differentiate along specific mesenchymal lineages when induced. MSC potential is routinely determined with the colony-forming–unit fibroblast assay, and MSCs are identified by their expression of Thy-1 (CD90) vascular cell adhesion molecule-1 (CD106), and hyaluronate receptor (CD44). Although antibodies to several cell surface antigens can be used to recognize MSCs, specific molecular probes do not exist to unequivocally identify these cells in situ. Consequently, it is difficult to quantify their actual numbers or identify their precise locations. Moreover, it is speculated that MSCs are a heterogeneous population containing cells with varying capacities for lineage-specific differentiation.

Stem Cell Procurement

Bone marrow aspirate is considered the most enriched source of MSCs. Given the wide distribution of MSC sources, the bone marrow stroma may be the source of a common pool of multipotent cells that access various tissues by way of the circulation, subsequently adopting characteristics that meet the requirements of maintenance and repair of a specific tissue type. This hypothesis is supported by the finding that liver cells with a donor genotype can be found in the bone marrow of transplant recipients.

To be practical, MSC harvest would have to carry a very low morbidity. Although bone marrow aspiration is not a high-risk procedure, pain at the donor site can be considerable. The ideal source of MSCs for aesthetic use would be tissue that is easily accessible and readily expendable. Zuk and associates have shown that adipose tissue, especially lipoplasty aspirate, is a source of MSCs with the potential for differentiation of adipose-derived stem cells into myogenic, osteogenic, chondrocytic, and adipocytic cells. Moreover, liposarpirate can be easily processed to yield large numbers of stem cells.

Aesthetic Applications

There are several possible strategies for using adult stem cells for aesthetic applications. Although large-scale clinical trials using stem cells for aesthetic indications have not yet begun, current research is under way in many laboratories, laying the foundation for this work in the near future.

One approach is to harness the replicative capacity and plasticity of adult stem cells to engineer autologous grafts for soft tissue and facial skeletal augmentation. Skin substitutes engineered from human cells are already in clinical use (eg, Apligraf [Organogenesis, Canton, MA]) and have generated great enthusiasm for the use of in vitro–engineered cells to generate cartilage, muscle, soft tissue, and bone. For example, adult stem cells could be harvested from lipoplasty aspirate and induced to differentiate (in vitro) to osteocytes. These new cells could then be seeded onto a biodegradable scaffold containing osteogenic growth factors and implanted back into the patient as a malar onlay graft. Once in place, the implant assumes the structure of autologous bone. A similar approach can be used for soft tissue augmentation.

A second strategy is to simply deliver undifferentiated adult stem cells in high concentrations to a specific anatomic site. A “critical mass” of transplanted stem cells may serve to initiate a cascade of angiogenesis and repair in local tissues. A growing body of literature indicates that the number of MSCs decreases with age and/or systemic disease and that their relative presence can control the outcome of reparative events of skeletal tissues. Simply increasing the concentration of MSCs in the facial soft tissue at regular intervals during the aging process has the potential to maintain volume and elasticity of the treated structures. Furthermore, adult stem cells can serve as gene-delivery systems; harvested stem cells can be transfected with genes, coding for a range of vital growth factors before implantation. The transfected cells would actively secrete these agents into the surrounding microenvironment.

A third approach involves activating and manipulating endogenous adult stem cells in situ. Administering growth factors, cytokines, and other signaling agents would activate local MSCs and induce migration of distant MSCs, such as bone marrow, to a specific region. Encapsulating these agents in biodegradable polymers would create a sustained-delivery system capable of releasing different signals during key steps in the process of cell differentiation. This strategy could be used for the prevention and treatment of the stigmata of facial aging.
Clearly the in vivo management of MSCs will require a more detailed understanding of the molecular steps of each differentiation pathway and the regulatory mechanisms that inhibit such differentiation in quiescent cells.16

Conclusion

Manipulation of adult stem cells may play an important role in future aesthetic surgery. Ongoing research to define the cellular and molecular fingerprints of MSCs and to elucidate their role in normal and abnormal tissue functions will lay the groundwork for clinical trials involving the treatment and prevention of aesthetic deformities.

References


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