Adipose-Derived Stem Cells: True or False? A Different Point of View

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In the past decade, isolation of multipotent cells from adipose tissue, termed adipose-derived stem cells (ASCs) or mesenchymal stromal cells (MSCs), has triggered an increasing interest for application in tissue engineering.[1] This type of stem cells has shown the ability to differentiate toward different mesenchymal cell lineages, such as osteogenic, chondrogenic, and adipogenic[2,3] as well as other cell types, including myocytes, and nerve cells.[4,5] Unlike MSCs harvested from bone marrow, ASCs are abundant and easy to harvest, with no morbidity to the donor site, and because of their osteogenic properties, they have been used in craniofacial surgery animal models for calvarial defect reconstruction.

When referring to these cells, however, the term *stem cell* has broadly applied to a specific cell population, harvested through liposuction of healthy donors and displaying specific properties, such as adherence to plastic, fibroblastlike morphology, and the ability to differentiate toward selected mesenchymal cell lineages. As described, however, such cells share few characteristics with stem cells from other tissues.

The work of our department during the last decade has shown that stem cells from different organs grow under different culturing conditions (in suspension), in serum-free conditions, and display a phenotype characterized by round cells that do not adhere to plastic supports and aggregate in clusters termed *spheroids* (multiclonal) and *spheres* (monoclonal).[6,7]

Recently, our group is studying a cell fraction extracted from the adipose tissue that resembles stem cells present in other tissues, reopening the debate on the proper nomenclature of ASCs. Upon isolation of these cells, we noted that they clearly displayed a different phenotype from that of the traditional ASCs commonly used in tissue engineering. This stem cell fraction could, indeed, represent an upstream stage of the traditional ASCs before they enter an early differentiation pathway and adhere to plastic solid supports. Certainly, the manipulation of lipoaspirate and culture conditions in which the stem cells grow plays a pivotal role in the maintenance of the undifferentiated stage of the cells in suspension.

We hope, with our future studies, to put an end to the scientific diatribe on whether true stem cells are present in the adipose tissue. Our preliminary data suggest that the fibroblastlike adherent stromal cells, considered as stem cells until now, may be downstream precursors of the true stem cells present in the adipose tissue. Indirectly, the presence of such downstream precursors and the presence of upstream spherelike cells represent indirect proof of the existence of true stem cells in the adipose tissue.

Should these cells prove to be upstream progenitors of the traditional ASCs, their ability to grow in suspension as spheres (and not as a monolayer) could provide new directions for tridimensional tissue engineering, whereas their growth in serum-free cultures could overcome the important limitations of autologous, allogenic, and xenograft serum necessary for the growth of the adherent ASCs. This could represent an initial step toward clinical translation and routine application of such cells. Furthermore, their use in serum-free conditions may find an indication in the immunomodulation of vascularized composite allografts, providing advantages over the currently used infusion of MSCs harvested from bone marrow.

The characterization and assessment of the biologic behavior, the differentiation properties (multipotency versus pluripotency), and the immunomodulatory properties of this cell niche, in comparison with other stem cell types, are currently under investigation in our laboratory.

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REFERENCES

1. Gimble JM, Katz AJ, Bunnell BA. Adipose-derived stem cells for regenerative medicine. *Circ Res* 2007;100:1249–1260
2. Huang JI, Zuk PA, Jones NF, et al. Chondrogenic potential of multipotential cells from human adipose tissue. *Plast Reconstr Surg* 2004;113:585–594
3. Zuk PA, Zhu M, Mizuno H, et al. Multilineage cells from human adipose tissue: implications for cell-based therapies. *Tissue Eng* 2001;7:211–228
4. Ning H, Lin G, Lue TF, et al. Neuron-like differentiation of adipose tissue-derived stromal cells and vascular smooth muscle cells. *Differentiation* 2006;74:510–518
5. Choi YS, Dusting GJ, Stubbs S, et al. Differentiation of human adipose-derived stem cells into beating cardiomyocytes. *J Cell Mol Med* 2010;14:878–889
6. Todaro M, Alea MP, Di Stefano AB, et al. Colon cancer stem cells dictate tumor growth and resist cell death by production of interleukin-4. *Cell Stem Cell* 2007;1:389–402
7. Todaro M, Iovino F, Eterno V, et al. Tumorigenic and metastatic activity of human thyroid cancer stem cells. *Cancer Res* 2010;70