

Mini Review

Mature adipocytes may be a source of stem cells for tissue engineering

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Abstract

Adipose tissue contains a large portion of stem cells. These cells appear morphologically like fibroblasts and are primarily derived from the stromal cell fraction. Mature (lipid-filled) adipocytes possess the ability to become proliferative cells and have been shown to produce progeny cells that possess the same morphological (fibroblast-like) appearance as the stem cells from the stromal fraction. A closer examination of mature adipocyte-derived progeny cells may prove to be an emerging area of growth/metabolic physiology that may modify present thinking about adipose tissue renewal capabilities. Knowledge of these cells may also prove beneficial in cell-based therapies for tissue repair, regeneration, or engineering.

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Attention has been focused on cells that might be useful in tissue engineering [3]. With the observation that fractions of bone marrow-derived cells possess ability to trans-differentiate into other types of cells (reviewed in [12]), a new era of (potential) cell-based therapies have been initiated. Unfortunately, as the number of stem-like cells that may be isolated from bone marrow is quite low (reviewed in [11]), numerous other tissues have been evaluated as a potential source of stem-like cells. One of these, adipose tissue, has been singled-out as a potential tissue to obtain stem cells [13]. Several different cell types reside in adipose tissue, and numerous cell populations display multipotency (reviewed in [14]). Morphologically similar to fibroblasts [11,15], these cells are of potential benefit in the clinical setting. While little is known about potential adipose depot differences in ability to isolate stem cells, or whether developmental aging influences the cell yield, the stromal cell

compartment of adipose tissue has been shown to provide a rich source of multipotent stem cells (500 times that as bone marrow) [11].

Little information is available regarding another cell fraction of adipose tissue, the mature adipocyte cell fraction, and whether this population of cells might produce stem-like cells. Mature adipocytes are not a component of the stromal fraction. Mature fat cells are removed from the fibroblast-like stromal fraction with buoyant centrifuge washes and other manipulations [6]. However, mature adipocyte cultures have been shown by numerous laboratories to contain proliferative-competent cells in vitro [1,2,16–19,21,4–8,20]. Cell estimates, obtained in preliminary experiments with purified cultures, suggested that few of the overall (isolated) population of mature adipocytes possess the ability to revert to a proliferative-competent cell [6], and in light of adipose tissue possessing other types of stem cells, there is no known physiological rationale for the proliferation of lipid-filled (mature) cells. However, many of the purified/cultured fraction of mature adipocytes do proliferate, in vitro, and we may be capable of

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exploiting the proliferative potential of purified progeny cultures for tissue engineering purposes.

Questions

Is the mature adipocyte fraction of adipose tissue a viable source of stem cells for tissue engineering? Several questions will need to be addressed prior to developing clinical strategies these cells. First, do these cells possess the ability to transdifferentiate into other cell types, like cells derived from the stromal fraction? Preliminary studies from our laboratory suggest that mature adipocyte-derived progeny cells possess the ability to re-accumulate some cytosolic lipid [9], but (apparent) differentiation was not complete in all of the cells contained within test cultures. As we were narrowly focusing on the ability of proliferative cells to re-establish the adipocyte phenotype, we were not (at the time) asking whether the maternal cell may have been a multipotent/pleuripotent stem-like cell. Moreover, we have not (yet) evaluated the potency of progeny cells to that of cells from the stromal fraction. Future research efforts will need to focus on the potency of the proliferative-competent progeny cells, as well as the differentiation potential of daughter cells, perhaps as compared to other cell fractions. A second question that needs to be addressed deals with the matter of adipose depots: do mature adipocytes within different adipose depots possess different abilities to produce proliferative-competent progeny cells? Our research was conducted with cells from the subcutaneous adipose depot in beef animals [6–8]. Cells contained within this adipose depot may experience some regulatory differences, than cells within other depots [10]. Thus, evaluating the ability of mature adipocytes to form proliferative-competent progeny cells from other adipose depots seems to be a requirement. One final question might be: does the age of the animal alter the ability of mature adipocytes to proliferate (hence, change the populations of stem cells that result)? Our previous research was conducted with yearling beef animals. Younger animals may prove to possess more mature adipocytes, with the ability to proliferate, than older ones.

Drawback or an advantage?

Even if progeny cells originating from the proliferation of mature adipocytes possess ability to proliferate, and subsequently transdifferentiate, there is time commitment involved in obtaining sufficient cells for clinical application(s). Weeks are involved prior to cultures gaining sufficient cells for any application. Ceiling cultures of the buoyant (mature cells) are established, purified from any contaminant fibroblast-like cell and monitored for proliferation potential. Once progeny (daughter) cells are clearly identified, expansion cultures are then established in order to provide the necessary cells for further use. Consequently, while (perhaps) not being immediately as useful for surgical regenerative medicine [13], unless cultures were already established, characterized, screened for the specific

application and available at the surgical site, progeny cells from the proliferation of the mature adipocytes may be of value in applications whereby time is not a critical component of the treatment.

Summary

The stromal cell fraction of adipose tissue is being critically evaluated as a source for stem cells, while the mature (adipocyte) cell fraction is presently being ignored. A relatively good proportion of mature adipocytes possess ability to proliferate *in vitro*. This simple fact may prove to provide a novel mechanism via which we can learn about the stem-cell nature of the progeny cells, determine if the proliferative-competent progeny cells are capable of becoming other cell types, and capitalize on the properties of the progeny cells for tissue engineering purposes.

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