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Supplemental Information

Mechanisms and Metabolic Implications of Regional Differences among Fat Depots

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Nomenclature of Fat Cell Progenitors

A variety of names have been attached to cells capable of differentiating into fat cells in culture following isolation from fat tissue stromal vascular digests. Whether these cells represent truly distinct progenitor subtypes is unclear from available evidence, as recently reviewed in (Cawthorn et al., 2012). Some of the terms used include “fat cell progenitors”, “adipose-derived stem cells (ADSCs)”, “processed lipoaspirate cells”, “adipose-derived adult stromal cells”, “adipose-derived adult stem cells”, “adipose tissue derived cells”, “preadipocytes”, “undifferentiated preadipocytes”, “committed preadipocytes”, and “differentiating preadipocytes”. These terms are often applied by different laboratories without consistency in the methods used to derive the cells and without cross-referencing in bibliographic databases.

Two of the more common terms are “ADSCs” and “preadipocytes”. Some consider “ADSCs” to be a multipotent cell type that can become a lineage-specific “committed preadipocyte”. How distinct “ADSCs” are from mesenchymal stem cells on the one hand or preadipocytes on the other has been questioned (Cawthorn et al., 2012),

an issue that needs much more study to settle. After exhaustively considering the growing literature about surface markers reported to distinguish "ADSCs" from "committed" preadipocytes, only endoglin (also known as SH2 or CD105) and PDGFR-α (CD140a) were felt to be expressed more highly in possibly more multipotent "ADSCs" than "committed" preadipocytes (Cawthorn et al., 2012). We examined endoglin and PDGFR-α expression in genome-wide expression analysis data of primary human undifferentiated and differentiating preadipocytes from a study of ours ((Tchkonia et al., 2007); data deposited at http://www.ncbi.nlm.nih.gov/geo/; accession # GSE1657). Interestingly, both genes were downregulated after inducing adipogenesis in primary preadipocytes, as were other genes reported to be higher in "ADSCs" (ALCAM [CD166], FGF2, FGF7, MMP2). Thus, some "ADSC" markers might be genes that are downregulated during adipogenesis, rather than indicators of distinct progenitor subtypes. What has been felt by some to be lineage commitment might represent early stages of adipogenesis with concomitant loss of multipotency. This needs to be resolved through further study. While we acknowledge that there are likely to be several preadipocyte subtypes, we elected to call the group of stromal vascular cells capable of differentiating into fat cells "preadipocytes" pending further study.

We did not find regional differences in "ADSC" markers within primary preadipocyte populations prepared by differential plating to remove non-plastic adhering cells as well as to remove trypsin-resistant macrophages and endothelial cells. Data from our genome-wide expression analyses of primary abdominal subcutaneous, mesenteric, and omental human preadipocytes ((Tchkonia et al., 2007); GEO accession # GSE1657) did not indicate consistent differences among depots in endoglin, PDGFR-α, or other

markers that may distinguish multipotent progenitors from more committed or differentiating preadipocytes (including ALCAM [CD166], FGF2, FGF7, MMP2, MMP3, PPARγ, LPL, ZFP423, and CD34; publications about these markers are summarized in (Cawthorn et al., 2012)). Furthermore, these markers were present, but did not differ between depots in clones made by stably transducing single subcutaneous and omental human fat tissue stromal-vascular cells with human telomere reverse transcriptase (hTERT) that were then serially subcultured for 40 population doublings (Tchkonia et al., 2007). These hTERT clones were shown to be capable of differentiating into fat cells as evidenced from capacity for lipid accumulation and to develop gene expression profiles characteristic of fat cells (Tchkonia et al., 2006 and 2007).

Supplemental References

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