

Identification of metabolically distinct adipocyte progenitor cells in human adipose tissues

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There remains intense interest in understanding how adipocytes develop and in unraveling the mechanisms that control metabolic and endocrine functions, especially in the face of overnutrition. Adipocyte progenitor cells (APCs) provide the reservoir of regenerative cells to produce new adipocytes, although their identity in humans remains elusive. Using fluorescent activated cell sorting we identified three APCs subtypes in human white adipose tissues based on their expression of specific CD markers. Gene expression profiling by RNAseq and metabolic and proteomic analyses was used to assess the differences between these APCs and the adipocytes derived from APCs. The APC subtypes are molecularly distinct but possess similar capacities for proliferation and adipogenesis. Adipocytes derived from APCs with high CD34 expression exhibit high rates of lipid flux compared with APCs with low or no CD34 expression, while adipocytes produced from CD34- APCs display beige-like adipocyte properties and a unique endocrine profile. APCs were more abundant in gluteofemoral compared with abdominal subcutaneous and omental adipose tissues, and the distribution of APC subtypes varies between depots and in patients with type 2 diabetes. These findings provide a mechanistic explanation for the heterogeneity of human white adipose tissue and a potential basis for dysregulated adipocyte function in type 2 diabetes.