snRNA-seq reveals a subpopulation of adipocytes that regulates thermogenesis

Introduction

The adipose tissue organ is generally perceived to function as a buffer for lipids in times of excess calorie intake[1]. Work in recent years however has demonstrated that adipose tissue also functions as an endocrine organ, which regulates systemic metabolism through cross talk with other organs[2]. Furthermore, it is nowadays accepted that adipose tissue is a very heterogeneous organ, comprised of different cells with varying functionalities[3].

Besides the stromal vascular cells, which make up most of the tissue heterogeneity, the main parenchymal cell type of adipose tissue are mature adipocytes, characterized by high lipid content and a unique morphology. This particular fraction is comprised of white adipocytes, which can store excess lipids in a unilocular lipid droplet as well as brown, brite or beige adipocytes, which function as thermogenic cells.

Methods

To deconvolute the heterogeneity of mature adipocytes, we used single nucleus analysis of adipocytes from different anatomical locations in mice and humans under different physiological conditions. This approach enabled us to identify diverse subpopulations of adipocytes with different functionalities, which contribute to regulation of adipose tissue metabolism.

Results

We have identified several novel adipocyte subpopulations and used different model systems to study their functionality. On adipocyte subtype was demonstrated to be an important regulator of adipose tissue thermogenic capacity through paracrine signaling mechanisms via short chain fatty acids[4]. Regulation of the abundance of this cell subtype led to changes in energy expenditure as well as lipid and glucose homeostasis. Furthermore, we could show that this adipocyte subtype is highly abundant in human adipose tissue, which could explain the resistance to induce uncoupled thermogenesis in humans

Conclusion

This unexpected finding demonstrates that tissue heterogeneity precludes the identification of specific cell subpopulations with distinct functions using a bulk approach and illustrates the importance of single cell and nucleus approaches to deconvolute tissue heterogeneity and plasticity.

References

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