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Dissecting adipose tissue at single-cell resolution during metabolic disease development

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Visceral adipose tissue (VAT), with its significant heterogeneity, plays a crucial role in the development of metabolic diseases like obesity and type 2 diabetes. Recent advancements in single-cell RNA technology made it possible to understand the complexity of VAT on pathophysiological changes. However, recent studies have focused on Western populations, primarily Caucasians. In this study, we present a detailed analysis of VAT within the context of metabolic diseases in East Asian, Korean population.

Our comprehensive study categorized individuals into three groups: those with a normal body weight (BMI<23 kg/m^2, n=3), no metabolic disease, individuals with morbid obesity (BMI>30 kg/m^2, n=5), and individuals with obesity and diabetes (BMI>30 kg/m^2, n=5). We used single nuclei analysis to scrutinize a total of 67,391 cells (26,876 from normal-weight subjects, 16,243 from those with morbid obesity, and 24,466 from individuals with obesity and diabetes). Our analysis unveiled notable changes in specific cell types associated with disease progression.

The upregulation of a specific pro-inflammatory macrophage population in obese diabetic patients was observed. Adipose stem cells (ASC) showed distinct cell fate decisions in individuals with obesity and it was further discriminated by the presence of diabetes. Trajectory analysis indicated a divergence in ASC development, with a particular cluster exhibiting fibrotic and pro-inflammatory traits significantly upregulated in both obese and obese diabetic patients.

Furthermore, we observed a specific cluster of adipocytes that was enriched in individuals with obesity and diabetes. This cluster shared fibrotic and pro-inflammatory characteristics observed in ASCs and displayed a suppressed response to insulin signals.

Our investigation of cell-to-cell communication revealed specific clusters, including ASCs, adipocytes, and immune cells, as key participants in intercellular communication. As our next step, we are working to identify the key factors responsible for the development and progression of metabolic diseases in this East Asian population.