News Release

Title

Novel cell-to-cell communications between macrophages and fibroblasts regulate obesity- induced adipose tissue fibrosis

Key Points

- Adipose tissue fibrosis is a complex and dynamic process that involves many cell types, such as macrophages and fibroblasts.
- Crown-like structures, which drive inflammation and fibrosis in adipose tissue during the development of obesity, are excellent targets for single-cell and spatial transcriptomics.
- We identified novel cell-to-cell communications between macrophages and fibroblasts in adipose tissue of diet-induced obese mice, particularly during the fibrotic phase in advanced obesity.
- We elucidated the role of the Mincle-Oncostatin M axis in obesity-induced adipose tissue fibrosis.

Summary

Recent evidence has shown that adipose tissue eventually develops fibrosis through complex cellular crosstalk. Although advances in single-cell transcriptomics have provided new insights into cell diversity during this process, little is known about the interactions among the distinct cell types. In this study, we employed single-cell analytical approaches to investigate cell-to-cell communications between macrophages and fibroblasts in the adipose tissue of diet-induced obese mice. Spatial transcriptomics was used to understand local cellular interactions within crown-like structures (CLSs), a characteristic histological feature of adipose tissue in obesity driving inflammation and fibrosis. Macrophages and fibroblasts were divided into several subclusters that appeared to interact more intensely and complexly with the degree of obesity. Besides previously reported Lipid-associated macrophages (LAMs), we identified a small subcluster expressing Macrophage-inducible C-type lectin (Mincle), specifically localizing to CLSs. Mincle signaling increased the expression of Oncostatin M (Osm), which suppressed collagen gene expression in adipose tissue fibroblasts. Consistent with these findings, Osm deficiency in immune cells enhanced obesity-induced adipose tissue fibrosis *in vivo*. Moreover, Osm expression was positively correlated with Mincle expression in human adipose tissue during obesity. Our results suggest that Osm secreted by Mincle-expressing macrophages is involved in dynamic adipose tissue remodeling in proximity to CLSs.

Publication

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