Paradoxical role of adipocytes and adipose tissue macrophages (ATMs) in the regulation of lipid homeostasis in obesity

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Obesity is the major cause of the development of insulin resistance and Type 2 Diabetes. Recently, the notion that obesity-induced inflammation mediates the development of insulin resistance in animal models and humans has been gaining strong support. Furthermore, numerous studies have also shown that immune cells in local tissues, in particular in visceral adipose tissue, play a major role in the regulation of obesity-induced inflammation. It has been shown that obesity disrupts the immune balance by suppressing anti-inflammatory cells (*e.g.,* regulatory T cells [Tregs]) while simultaneously activating pro-inflammatory cells (*e.g.,* adipose tissue macrophages [ATMs]). Hence most of the current studies have focused on the regulation of immune cells in the development of obesity-induced inflammation. However, we found that adipose tissue immune cells also play different roles in obesity beside regulation of classical inflammation. We found that ATMs become adipose tissue foam cells (ATFCs) that play an important role in controlling systemic lipid homeostasis, thereby mediating the development of insulin resistance in obesity, in particular in morbid obesity. Interestingly, we also found that adipocytes also regulate systemic lipid homeostasis. However, their roles are more limited in early obesity and their functions appear to be opposite to the roles played by ATMs. Hence, our studies may provide important preclinical evidence for the notion that lipid metabolism regulated by ATMs could be a therapeutic target for the treatment of insulin resistance and Type 2 Diabetes.