METABOLISM

Characterizing bone marrow adipocytes


Credit: Klaus Vedfelt/Getty

Bone marrow adipose tissue (BMAT) comprises 10% of total fat mass in healthy humans, and evidence suggests that BMAT mass increases with age, in osteoporosis and in obesity. Interestingly, bone marrow adipocytes do not decrease in size under conditions of caloric restriction. A study published in *Cell Reports* now shows that the lipid metabolism profile of bone marrow adipocytes is distinct from that of subcutaneous adipocytes.

To examine the characteristics of human bone marrow adipocytes, BMAT and subcutaneous adipose tissue (SCAT) were obtained from patients undergoing hip replacement surgery. Samples from the different depots were paired from each patient. Adipocytes in BMAT had similar morphological properties to white adipocytes in SCAT; both cell types contain a large, lipid filled droplet.

Notably, proteomic analysis of bone marrow and subcutaneous adipocytes showed differences in the expression of proteins related to lipid metabolism pathways. Specifically, bone marrow adipocytes were enriched in pathways for cholesterol metabolism, arachidonic metabolism and sphingolipid signalling and show decreases in lipolytic enzymes. The lipid profiles of both cell types were also examined, showing enrichment of diverse lipid species, for example cholesterol and monoacylglycerols.

Functional characterization assays were performed on bone marrow adipocytes, comparing them to subcutaneous adipocytes from the same patient. Interestingly, bone marrow adipocytes show a defect in lipolysis, which is associated with a substantial downregulation in monoacylglycerol lipase, a key enzyme involved in lipolysis. This finding was not recapitulated in primary bone marrow-derived mesenchymal stromal cells (BM-MSCs) differentiated to become adipocytes in vitro. Owing to this discrepancy, the study authors suggest that future experiments with BM-MSCs be interpreted with caution.

In summary, bone marrow adipocytes show distinct lipid metabolism to subcutaneous adipocytes, with decreased lipolysis and enriched cholesterol metabolism. As such, bone marrow adipocytes preserve their triglyceride stores and might be speculated not to release free fatty acids. The precise physiological functions of this cell type, however, remain to be elucidated.

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ORIGINAL ARTICLE Attané, C. et al. Human bone marrow is comprised of adipocytes with specific lipid metabolism. *Cell Rep.* **30**, 949–958 (2020)

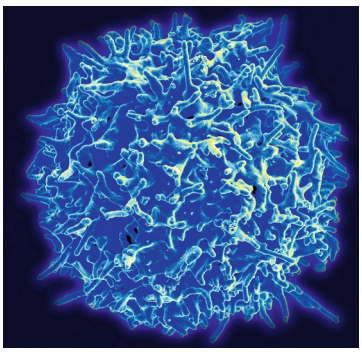
ADIPOSE TISSUE

Ketogenic diet affects immune cells in mice

The ketogenic diet, which is high in fat and very low in carbohydrates, limits glucose availability and causes a switch to fatty acid metabolism. This diet is associated with weight loss and improved metabolic health in people with obesity, and it reduces inflammation in mice. However, how the ketogenic diet affects adipose tissue has been unclear; a new study suggests complex effects.

The researchers fed mice a normal chow diet (calories were 58% carbohydrates, 24% protein and 18% fat) or a ketogenic diet (calories were 0.1% carbohydrates, 10.4% protein and 89.5% fat) for 1 week and used single-cell RNA sequencing to analyse the adipose tissue-resident immune cells. They showed that the number of γδ T cells increased following a ketogenic diet. Further analyses revealed that the γδ T cells were metabolically protective. "Ketogenic diet feeding for 1 week in mice is a key mechanism that reduces inflammation and improves metabolic outcomes," explains author Vishwa Deep Dixit.

After 1 week on a ketogenic diet, the mice experienced modest increases in whole-body fat mass. However, after longer term ad libitum consumption of the ketogenic diet (2–3 months), mice gained considerably more weight than chow-fed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REPRODUCTIVE ENDOCRINOLOGY

Changes to microbiota in girls with PCOS

Girls with polycystic ovary syndrome (PCOS) and obesity have a less diverse (that is, unhealthier) overall gastrointestinal microbiota than girls with obesity who do not have PCOS, a new study has shown. The findings are notable because the differences in microbiota composition were found early in the course of PCOS, suggesting that changes to the microbiota could be an early manifestation of PCOS.

"Our lab was initially focused on insulin resistance, and we were surprised to find that 50% of adolescents with PCOS and obesity had hepatic steatosis," explains corresponding author Melanie Cree-Green. "We know that there are microbiota changes in populations with hepatic steatosis, and while there are some limited data on changes to the microbiota in adults with PCOS, there were no data in youth cohorts."

To diagnose PCOS, the team used the gold standard NIH criteria and liquid chromatography–mass spectrometry, which is used to measure serum levels of testosterone. The investigators also assessed measures of the metabolic syndrome, including blood pressure and serum lipid status, in addition to measuring hepatic fat status by MRI. As a measure of gastrointestinal microbiota, Cree-Green and colleagues used PCR to amplify the 16S rRNA genes in stool samples supplied by participants.

"We found that girls with PCOS and obesity had an increase in gastrointestinal organisms that were related to PCOS status, as well as elevated serum levels of testosterone (the defining feature of PCOS)," explains Cree-Green. Whether increases in serum levels of testosterone influence the microbiota or whether changes in the microbiota influence testosterone