Abstract

Adipose tissue is an endocrine organ, and its homeostatic mechanisms in normal weight, overweight and obese subjects must be elucidated. We sought to determine the basal adipose tissue biology of visceral (VIF) and subcutaneous (SQF) fat depots in 8 month old Sinclair minipigs, an animal that has been shown to be physiologically similar to humans.

Metabolic analysis showed a decrease in LDL, white blood cells (WBC), and lymphocyte percentages as the minipigs aged from 6 to 8 months ($p < 0.0001$ and $= 0.0046$ and 0.0165 respectively). There were no significant changes in triglycerides, HDL, VLDL, and neutrophil percentages. There was a trend in insulin increase ($P=0.0722$).

Microarray analysis was performed to determine transcriptome differences between VIF and SQF. When VIF was compared to SQF, expression of a total of 788 transcript ID's differed: were 240 up-regulated and 548 down-regulated. Examples included hydroxysteroid 11-beta dehydrogenase 2, fatty acid synthase, IL-18, and platelet factor 4 which were all up-regulated in VIF vs. SQF. The down-regulated transcripts included estrogen receptor 1, insulin-like growth factor binding protein 5, and platelet derived growth factor D.

When SQF was compared to VIF, a total of 598 transcript IDs were up or down-regulated by more than a 2 fold difference ($P<0.05$). From this subset of the transcriptome, we found 471 IDs were up-regulated in SQ fat, and 127 were down- regulated. Interestingly, the up-regulated genes included prostaglandin F2 receptor negative regulator, estrogen receptor 1, thrombospondin 1, lipoprotein related receptor protein 2, and platelet derived growth factor D. Down-regulated genes in SQF compared to VIF included IL-18, platelet factor 4, cyclooxygenase, and fatty acid synthase. We found no significant difference in gene expression between SQF and VIF TNF alpha, TLR 4, and adiponectin in our study.

Immunofluorensce (IF) assay revealed that SQF expressed more CD 163 positive (alternatively activated) macrophages than VIF, and little to no CD 68 (classically activated) positive macrophages. Additionally, VIF expressed more CD 68 positive macrophages compared to SQF.

The data from this study is consistent with the human and rodent literature which states that VIF is more metabolically active and pro-inflammatory compared to SQF.