Inflammation is associated with a decrease of lipogenic factors in omental fat in women

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Running head: lipogenic factors decrease in omental fat

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Abstract

Obesity is characterized by systemic low-grade inflammation where adipose tissue, especially the omental depot, is thought to play a key role. We have previously shown that inflammation impairs 3T3-L1 preadipocyte cell line differentiation. To explore whether this interaction takes also place in vivo, the expression of several genes related to inflammation and adipocyte differentiation was assessed in human samples. Paired adipose tissue biopsies (from omental and subcutaneous depots) were obtained from 24 women: 6 lean normoglycaemic and 18 obese volunteers with different glycaemic states (normoglycaemic, glucose intolerant or type 2 diabetic). The expression levels of CD14, IL-18, leptin, adiponectin, SREBP1, PPARγ, PBEF1 (visfatin), GPD1, LPL, FABP4 and HIF1α were determined by quantitative real time PCR. CD14 and IL-18 were overexpressed in omental adipose tissue as compared to the subcutaneous depot irrespective of the subjects obesity or diabetes status. A significant decrease of LPL, GPD1 and leptin expression was observed in omental tissue and an inverse correlation between expression of CD14 and IL-18 and that of PPARγ, LPL and FABP4 was observed. The underexpression of omental lipogenic markers was more accentuated in the presence of glucose intolerance. Furthermore, adiponectin and SREBP1 expression were also significantly decreased in omental tissue of type 2 diabetic patients. PBEF1 and HIF1α expressions remained comparable in all samples. Therefore, in humans, inflammation is increased in the omental depot as evidenced by CD14 and IL-18 expression. In this localisation, the inflammatory state is associated with a decreased expression of lipogenic markers, which is more pronounced in diabetic subjects.

Keywords: obesity, CD14, IL-18, subcutaneous and visceral adipose tissue, diabetes
Abbreviations:

FABP4, fatty acid binding protein 4, adipocyte

GPD1, glycerol-3-phosphate dehydrogenase 1 (soluble)

LPL, lipoprotein lipase

PPARγ, peroxisome proliferator-activated receptor gamma

ADIPOQ, adiponectin

PBEF1, pre-B-cell colony enhancing factor 1 = visfatin

SREBP1, sterol regulatory element binding transcription factor 1

HIF1α, hypoxia-inducible factor 1, alpha subunit

T2DM, type 2 diabetes mellitus

TLR, toll-like receptor
Introduction

An increase in circulating levels of several inflammatory markers has been shown in obesity (22) coexisting with macrophage infiltration of white adipose tissue (39). These macrophages together with adipocytes, maintain an inflammatory environment through the secretion of pro-inflammatory products. Furthermore, adipocytes are now recognized as innate immune components and endocrine cells, in addition to their central role in lipid storage (29, 34). Several adipose tissue secreted pro-inflammatory products, such as TNFα or IL-6, have been shown to induce insulin resistance and are thought to link obesity and type 2 diabetes (31).

We recently demonstrated in the 3T3-L1 preadipocyte cell line, that an inflammatory environment is able to maintain the preadipocyte status (25). In this context, preadipocytes that are phenotypically related to macrophages (6) with high pro-inflammatory features, are impaired in their differentiation and a decrease in the expression of lipogenic enzymes is observed. These results suggest that in adipose tissue, the inflammatory environment induces chemokine secretion and leucocyte recruitment, which disturbs adipogenesis and perpetuates pro-inflammatory adipokine secretion. Thus, a vicious circle of chronic inflammation is established that leads to insulin resistance and the metabolic syndrome.

Epidemiological studies have clearly shown a relationship between intra-abdominal fat amount and metabolic abnormalities (4, 10, 26). Whether visceral fat is the major effector of the metabolic syndrome is still discussed (15).

Our purpose was to analyze in paired human adipose tissue samples from the subcutaneous and omental depots the expression of two inflammation markers (CD14 and IL-18) and to characterize in the same samples the expression of several markers of adipogenesis and lipogenesis. The differences in CD14 and IL-18 in omental and subcutaneous adipose tissue served to assess depot-specific differences in the inflammatory state. We hypothesized that, as
we had previously shown in cell culture (25), inflammation might interact with lipogenesis also in human tissues. Correlation between genes and enzymes involved in lipogenesis and inflammation was therefore studied. Since hypoxia has been shown in an adipocyte culture model to rise inflammation-related adipokines such as IL6 and MIF, and to decrease adiponectin (38), inclusion of hypoxia as an underlying factor involved in elicitation of inflammation was further taken into consideration. HIF is a heterodimer consisting of the O2-regulated subunit, HIF-1α, and the constitutively expressed aryl hydrocarbon receptor nuclear translocator, HIF-1β. Under hypoxic conditions, HIF-1α is stable, accumulates, and migrates to the nucleus where it binds to HIF-1β to form a complex that stimulates the expression of genes involved in angiogenesis, anaerobic metabolism, vascular permeability, and inflammation.(17). For this reason, HIF1α is considered as a marker of hypoxia level, and its expression was analyzed to test its implication in inflammation in our samples. Our study was designed to analyze these hypotheses in relation to the common setting of obesity but under the different metabolic spectrum encompassing from normoglycemia and insulin resistance up to glucose intolerance and type 2 diabetes mellitus (T2DM).
Subjects, materials and methods

Subjects. Twenty-four female Caucasian volunteers attending either the Department of Endocrinology and Surgery of the Clínica Universitaria de Navarra or the “Département de Chirurgie Générale et Endocrinienne, CHRU de Lille” were enrolled in the study. The subjects were classified as normal-weight (n = 6) or obese (n = 18) according to WHO criteria (BMI<25 kg/m² or BMI≥30 kg/m² respectively). Obese patients were further subclassified into 3 groups according to the recently established diagnostic thresholds (based on an oral glucose tolerant test, OGTT) for diabetes and lesser degrees of impaired glucose regulation [(normoglycemia: fasting plasma glucose concentration (FPG) <100 mg/dl and 2-h PG <140 mg/dl after OGTT; IGT: FPG >100 mg/dl and <125 mg/dl or 2-h PG between 140-199 mg/dl after OGTT; T2DM: FPG ≥126 mg/dl or 2-h PG ≥200 mg/dl after OGTT)]. The lean group included 6 patients undergoing laparoscopic abdominal surgery due to benign diseases, such as cholecystectomy, while the 18 obese patients strictly met the criteria for bariatric surgery. In both lean and obese groups surgery was performed by the minimally invasive laparoscopic approach. Informed consent was obtained from all subjects and the experimental design was approved from an ethical and scientific standpoint by the Hospitals’ Ethical Committee responsible for each research project. All patients underwent a pre-operative evaluation including medical history and physical examination.

Blood assays. Plasma samples were obtained by venipuncture after an overnight fast. Plasma glucose was analyzed by an automated analyzer (Roche/Hitachi Modular P800), with quantification based on the enzymatic colorimetric reactions described by Trinder (36). Total cholesterol and triglyceride concentrations were determined by enzymatic spectrophotometric methods (Boehringer Mannheim, Mannheim, Germany). Insulin concentrations were
determined by means of an enzyme-amplified chemiluminescence assay (IMMULITE®, Diagnostic Products Corp., Los Angeles, CA). Leptin was measured by the double-antibody RIA method (Linco Research, Inc., St. Charles, MO). The relevant clinical and metabolic characteristics of the 24 subjects are shown in Table 1. No statistically significant differences for age between all groups or for BMI among the obese sub-groups were observed. Furthermore, no significant differences in clinical values were observed according to the patient’s origin among obese groups.

*Adipose tissue sampling and RNA extraction.* Adipose tissue biopsies were obtained from both the subcutaneous and omental fat depots of lean and obese volunteers. Subcutaneous adipose tissue was collected at the site of surgical incision for trocar placement (superficial subcutaneous abdominal depot), while omental adipose tissue was collected from the greater omentum (epiploon). Fat samples were immediately frozen in liquid nitrogen and stored at −85 °C. Total RNA was extracted from each human fat sample by homogenization with an ULTRA-TURRAX® T 25 basic equipment (IKA® Werke GmbH, Staufen, Germany) using the Qiazol reagent (QIAGEN Inc., Valencia, CA) and further purified with RNeasy Lipid Tissue Kit (QIAGEN). The integrity of the RNA extracted was determined after migration on an agarose gel. The RNA concentration was determined by absorbance at 260 nm ($A_{260}$), and the purity was estimated by determining the $A_{260}/A_{280}$ ratio with a Nanodrop spectrophotometer (Nanodrop Technologies, Wilmington, DE).

*Relative quantitative real-time PCR.* The relative quantification of mRNA was performed with a quantitative RT-PCR assay. One microgram of total RNA was transcribed into cDNA using the cDNA Archive Kit (Applied Biosystems, Foster City, CA, USA). Each cDNA sample was analyzed for gene expression by quantitative real-time PCR (qPCR) using the
fluorescent TaqMan 5′-nuclease assay on an Applied Biosystems 7900HT sequence detection system. The TaqMan RT-PCR was performed using 2× TaqMan Master Mix and 20× premade TaqMan gene expression assays (Applied Biosystems). Both isoforms of PPARγ (g1 and g2) and SREBP1 (1a and 1c) were detected in our assay. Analysis was performed with the ABI 7900HT SDS 2.2 Software. Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was used as reference gene. GAPDH expression in our samples exhibited a coefficient of variation of 0.022 in subcutaneous fat and of 0.014 in the omental depot. Furthermore, no significant differences in GAPDH mRNA levels between samples of the different phenotypical groups were observed by the Kruskal–Wallis test (p=0.276). 18S rRNA was also tested as a reference gene but it exhibited a larger coefficient of variation (0.074) in these samples. The data are given as the ratio of the levels of the target gene mRNA to that of GAPDH mRNA after defining constant threshold and baseline values for a given gene for all the plates in the ABI RQ Manager Software.

**Statistical analysis.** Given the relatively small sample size in each phenotypic group the relative quantitative real-time PCR data are presented as medians ± SD. The statistical analysis was performed with the SPSS software package (14.0.2, Chicago, IL). According to sample size the test on ranks was performed and two-tailed exact p-values are given. The mRNA levels between lean and obese patients were analysed by U Mann-Whitney’s test. Comparisons of mRNA levels between subcutaneous and omental adipose tissues were performed using the paired Wilcoxon test. Correlations between continuous variables were determined using the non-parametric Spearman’s rank correlation. The threshold of significance was set at p < 0.05.
Results

Depot-specific inflammation and gene expression

The inflammatory state of the two fat depots was first tested by CD14 and IL-18 expression analysis. An increase in omental tissue as compared to subcutaneous tissue was observed for CD14 (two fold) and for IL-18 (eight fold) (Table 2). These differences were statistically significant (p=3.6 10^{-7}) in a global analysis of all patients. Individual analysis of each group always showed higher expression levels in omental adipose tissue, which was statistically significant for three of the four groups studied (Table 3) with the omental fat depot exhibiting a more inflammatory phenotype than the subcutaneous one, irrespective of the subjects’ obesity and diabetes state.

Then we tested if the expression of the inflammation markers CD14 and IL-18 correlated with a decrease in lipogenic enzymes expression. Analysis of known markers of adipocyte differentiation (leptin, ADIPOQ, SREBP1, PPARγ, PBEF1) and lipogenesis (GPD1, LPL, FABP4) was performed. Leptin, LPL, GPD1, ADIPOQ and SREBP1 were underexpressed in omental adipose tissue while PPARγ, PBEF1 and FABP4 expression did not display significant differences according to depot location (Table 2).

As would be expected from PPARγ’s key role in adipogenesis regulation, a significant positive correlation between its expression and that of LPL, ADIPOQ, GPD1, FABP4 and SREBP1 in both fat depots was observed (data not shown). In omental adipose tissue LPL, FABP4 and PPARγ were inversely correlated with CD14 and IL-18 expression (Figure 1). This inverse correlation with CD14 was not dependent on the obese state and remained significant in lean subjects for LPL (p=0.005) and PPARγ (p=0.042). Only PPARγ remained inversely correlated to IL-18 (p=0.019) in lean subjects.
Associations between gene expression and BMI were studied by Spearman’s analysis. Only leptin and adiponectin showed a correlation with BMI while no significant correlations were observed between BMI and any of the other genes studied (data not shown).

**Depot-specific effect of glycemic state on gene expression in obesity**

The expression of adipogenic enzymes in omental fat in the context of obesity was then analyzed in each group of glycemic control. When Wilcoxon paired analysis was performed in each phenotypic group of obese subjects, a depot-specific leptin, LPL, GPD1, ADIPOQ and SREBP1 gene underexpression was more pronounced in diabetic subjects especially following the development of chronic hyperglycaemia from glucose intolerance (Table 3).

To explore the differences between the lean and obese normoglycemic groups, as well as between each of the obese groups, for all genes studied in both fat depots, further analyses were performed (Figure 2). Some of the genes studied displayed a great inter-individual variation but for LPL, GPD1, SREBP1, PPARγ and FABP4, a trend towards a decreased expression in relation to obesity and diabetic state was observed. CD14 and IL-18 overexpression in omental adipose tissue was observed irrespective of obesity and glycemic state. However, CD14 gene expression in the subcutaneous fat significantly increased in T2DM obese subjects (Figure 2). Although leptin expression was increased 3- to 4-fold in obese subjects irrespectively of the fat depot studied (Figure 2), this pattern was not modified further by the glycemic state. HIF1α expression showed no depot-specific differences (Table 3). In addition, neither obesity nor the glycemic state exerted a differential effect on HIF1α expression (Figure 2).
Discussion

CD14 is a membrane glycoprotein which serves as a receptor for the lipopolysaccharide-binding protein lipopolysaccharide complex reportedly shown to be upregulated by lipopolysaccharide and other bacterial cell wall constituents (20) and that can be considered as an inflammation marker. IL-18 is a member of the proinflammatory IL1 family and has been shown to be an important regulator of innate immunity (11). These two markers have also been implicated in metabolic pathologies. CD14 expression has already been studied in diabetes and shown to be enhanced in circulating monocytes (7, 9, 23). IL-18 was found to be secreted by human adipocytes (32) and to be up-regulated by TNFα (40). The present study provides evidence that CD14 and IL-18 are enhanced in omental compared to subcutaneous adipose tissue irrespective of BMI or glycemic state. Macrophage infiltration into adipose tissue has been demonstrated (39). Mast cells were also described in adipose depots (5, 21). While these two cell types express CD14 and IL-18, they can also be detected in adipocytes of human origin (18, 40). Whether CD14 and IL-18 overexpression in omental fat is only due to adipose tissue immune cell infiltration or can be also attributed to adipocyte expression remains to be analyzed in further detail and was not explored in the present study. CD14 and IL-18 omental overexpression was noticeable in lean subjects. Higher macrophage infiltration in omental fat was documented even in lean subjects (12). This suggests that subcutaneous fat is less prone to inflammation than omental fat, where the portal irrigation could be a source of inflammatory compounds coming from the gastrointestinal system such as free fatty acids (14) or bacterial components of the microflora (1), independently of the presence of obesity.

The present study shows in human samples that genes related to lipid metabolism are decreased in omental fat tissue. Furthermore, CD14 and IL-18 expression are significantly inversely correlated to PPARγ, LPL and FABP4 expression in this depot. We had
previously shown using the 3T3-L1 cell line, that upon continuous exposure to LPS, which is a TLR4 agonist and favours a pro-inflammatory environment, adipocyte differentiation was impaired (25). In this in vitro model, CD14 mRNA was drastically enhanced by the presence of LPS in the media while FABP4, GPD1, LPL, PPARγ and adiponectin mRNA levels were decreased. Furthermore, pre-adipocytes or adipocytes in less differentiated stage were also shown to keep higher pro-inflammatory features, such as cytokine secretion. In the present study, we confirm in human samples a potential suppression of lipogenic pathways by inflammation.

The design of our study allows analysis of the interference of diabetic status in this regulation. CD14 was raised in the subcutaneous fat in T2DM patients when compared to that of normoglycemic individual. Moreover, in the diabetic group differential expression between subcutaneous and omental adipose tissue is significant for seven out of the ten markers studied. All these data suggest a higher level of inflammation in the diabetic group that enhances the disequilibrium. A direct effect of chronic hyperglycemia on systemic inflammation has been demonstrated by epidemiological studies (8).

Our results show that leptin is regulated differently compared with other adipogenesis markers with a strong sensitivity to BMI variation, on the one hand, and small impact of the glycemic state on leptin mRNA expression, on the other. These observations are in accordance with previous results demonstrating by multiple regression analysis that insulinemia was a determinant of leptin concentration, but explaining only 2% of its variance while 42% was attributable to adiposity (28).

It has been proposed that hypoxia may occur in obesity in relation to adipose tissue mass enlargement (35). Hypoxia has been shown to increase inflammation-related adipokines such as IL6 and MIF, and to decrease adiponectin, in an adipocyte culture model (38) being, therefore, thus representing a good candidate for inflammation induction. Evidence
for hypoxia in white adipose tissue of mouse models of obesity has been reported (13, 27). In our human samples, no significant differential expression of HIF1α, which should be increased under hypoxic conditions, was observed. It was suggested that hypoxia may primarily occur in clusters of adipocytes distant from the vasculature (35). Further studies with broader sampling that may include a representative collection of all the local hypoxic events within the fat depots, are needed to demonstrate the hypoxia hypothesis in humans. Protein levels and activity were not evaluated due to the limited amount of adipose tissue biopsies available and should be analyzed in further studies. Nonetheless, several different lipogenesis genes were examined and the very consistent correlation patterns observed support the validity and relevance of our findings. Further studies in men are also clearly required to derive potential sex-specific differences related to our initial hypothesis.

Perspectives and Significance

We demonstrate here, by the analysis of several relevant genes that were analyzed simultaneously in the same paired human samples, that a global decrease of lipogenic markers is associated with inflammation enhancement. Two main characteristics are underlined: a global inflammation state in omental adipose tissue and an exacerbation of this feature with insulin resistance acquisition. Portal irrigation in vicinity of omental fat depots is a source of exogenous components coming from intestinal flora or from nutrients can explain the difference between omental and subcutaneous adipose tissue. Such components (free fatty acids or bacterial walls) are highly inflammatory and are able to stimulate the TLR4 pathway. TLR4 has been recently implied in obesity as a link between inflammation and insulin resistance development (30, 33, 37). Upon inflammatory stimulation, adipose tissue cells synthesize pro-inflammatory products and via chemokine synthesis induce potential recruitment of leucocytes. Whether the first reacting cells are preadipocytes, adipocytes or pre-existing tissue macrophages remains
unknown. Preadipocytes are coming from a myeloid lineage, in which impairment of differentiation via TLR4 activation has been shown (19). In the 3T3-L1 cell line, we also demonstrated that TLR4 stimulation maintains a pro-inflammatory preadipocyte phenotype (25). In studied human samples, increased inflammation is accompanied by a decrease in lipogenesis. A physiological interpretation might be that more cells are switched to an inflammatory type rather than to a storage phenotype maintaining chronic inflammation and leading to the development of metabolic complications. Disrupting the vicious circle of inflammation represents a therapeutic target for obesity and diabetes control which has been successfully tackled in mouse models impaired for TLR4 functionality, that were protected from insulin resistance development (24, 37). Recently, the demonstration of the impact of the nature of microflora on weight gain prediction opens an exciting research field. Bifidobacteria reportedly improve glucose tolerance and inflammation (3, 16). Monitoring of intestinal flora might be achieved via oral administration of probiotics with anti-inflammatory properties, and thus exert an impact on the inflammatory state of omental fat (2).

Acknowledgments

We are indebted to all the subjects who participated in the study. We thank David Meyre for critical reading of this manuscript. We are indebted to Marie-France Six for her help in sample and clinical data collection. All the members of the Multidisciplinary Obesity Diagnosis and Treatment Team of the Clínica Universitaria de Navarra are gratefully acknowledged. CIBER de Fisiopatología de la Obesidad y Nutrición (CIBEROBN) is an initiative of the Instituto de Salud Carlos III, Spain. We also thank ALFEDIAM (French Language Association for the Study of Diabetes and Metabolic Disease) and ANR (Agence Nationale de la Recherche) for their financial support.
References


Legends to tables and figures

**Figure 1** Correlation between CD14 and IL-18 mRNA expression and that of LPL, FABP4 and PPARγ in subcutaneous and omental adipose tissue of lean (n=6; open circle) and obese subjects (n=18; plain circle).

\( \rho \) = correlation coefficient and p value obtained by Spearman correlation analysis according to range in lean (\( \rho_{l} \)) or obese (\( \rho_{ob} \)) subjects (ns = non significant, p>0.05)

**Figure 2.** Adipose tissue mRNA expression according to depot location (SC=subcutaneous; OM= omental) and clinical state of the patients (LN = lean, NG = obese normoglycaemic; IT = obese glucose intolerant; DM = obese diabetic). Data are presented as the ratio of the levels of the target gene mRNA to that of GAPDH mRNA.

Data are plotted in box and whiskers graphs. The box extends from the 25th to the 75th percentile, with a line at the median (the 50th percentile). The whiskers extend above and below the box to show the highest and lowest values.

U Mann-Whitney’s analysis was performed between the lean and obese normoglycemic groups as well as pair-wise comparisons between each of the obese groups (* p<0.05; ** p<0.005).

**Table 1.** General characteristics of the study subjects

Mean value ± SD. Comparisons were made between the various categories of obese patients using the Kruskal–Wallis test; n.d. = not done

**Table 2.** Subcutaneous and omental adipose tissue mRNA expression of all subjects
Data (medians ± SD) are presented as the ratio of the levels of the target gene mRNA to that of *GAPDH* mRNA. Comparisons between subcutaneous and omental expression were analysed by Wilcoxon’s paired test. p value is indicated in bold when significant.

**Table 3:** Ratio between subcutaneous and omental adipose tissue mRNA expression in each group

Ratios of subcutaneous versus omental medians are given for each group. Comparisons between subcutaneous and omental expression were analysed by Wilcoxon’s paired test, in each group. Comparisons between subcutaneous and omental expression were analysed by Wilcoxon’s paired test. p value is indicated in bold when significant.
Table 1. General characteristics of the study subjects

<table>
<thead>
<tr>
<th></th>
<th>Lean (n=6)</th>
<th>Obese (n=6)</th>
<th>Obese (n=6)</th>
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<td></td>
<td>Normoglycemic</td>
<td>Glucose intolerant</td>
<td>Type 2 diabetic</td>
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<td>Age (yr)</td>
<td>43.7 ± 14.8</td>
<td>46.3 ± 7.4</td>
<td>40.5 ± 11.0</td>
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<td>BMI (kg/m²)</td>
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<td>Fasting glucose (mg/dl)</td>
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<td>Glucose 2h OGTT (mg/dl)</td>
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<td>177.0 ± 14.5</td>
<td>327.8 ± 117.8</td>
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<td>Triglycerides (mmol/l)</td>
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<td>1.2 ± 0.3</td>
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<td>Total cholesterol (mmol/l)</td>
<td>4.5 ± 1.3</td>
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<td>Insulin (mUI/l)</td>
<td>4.2 ± 1.9</td>
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<td>Leptin (µg/l)</td>
<td>n.d.</td>
<td>62.4 ± 34.8</td>
<td>49.2 ± 23.0</td>
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<td>Omental (median ± SD)</td>
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<td>CD14</td>
<td>0.104 ± 0.045</td>
<td>0.212 ± 0.122</td>
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<td>IL-18</td>
<td>2.56 x10^-3 ± 1.41 x10^-3</td>
<td>2.10 x10^-2 ± 1.29 x10^-2</td>
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<td>LEPTIN</td>
<td>2.769 ± 1.260</td>
<td>0.859 ± 0.779</td>
<td>2.38 x10^-7</td>
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<td>LPL</td>
<td>3.296 ± 1.235</td>
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<td>GPD1</td>
<td>2.722 ± 1.117</td>
<td>1.899 ± 1.137</td>
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<td>SREBP1</td>
<td>0.166 ± 0.091</td>
<td>0.124 ± 0.092</td>
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<td>PPARγ</td>
<td>0.552 ± 0.260</td>
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<td>PBEF1</td>
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<td>FABP4</td>
<td>17.39 ± 9.31</td>
<td>17.91 ± 9.75</td>
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<td>HIF1α</td>
<td>0.047 ± 0.018</td>
<td>0.055 ± 0.010</td>
<td>1.01 x10^-1</td>
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**Table 2**: Subcutaneous and omental adipose tissue mRNA expression.
<table>
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<th>Genes</th>
<th>Lean (n=6)</th>
<th>Obese normoglycemic (n=6)</th>
<th>Obese glucose intolerant (n=6)</th>
<th>Obese diabetic (n=6)</th>
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<td>0.411 (3.13 $10^{-2}$)</td>
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<td>0.135 (3.13 $10^{-2}$)</td>
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<td>LEPTIN</td>
<td>3.399 (6.25 $10^{-2}$)</td>
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<td>2.458 (3.13 $10^{-2}$)</td>
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<td>1.838 (3.13 $10^{-2}$)</td>
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<td>GP1D1</td>
<td>0.973 (8.44 $10^{-1}$)</td>
<td>1.198 (5.63 $10^{-1}$)</td>
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<td>ADIPQ</td>
<td>0.714 (5.63 $10^{-1}$)</td>
<td>1.066 (6.88 $10^{-1}$)</td>
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<td>SREBP1</td>
<td>0.864 (8.44 $10^{-1}$)</td>
<td>0.825 (5.63 $10^{-1}$)</td>
<td>1.310 (9.38 $10^{-2}$)</td>
<td>1.688 (3.13 $10^{-2}$)</td>
</tr>
<tr>
<td>PPARγ</td>
<td>1.067 (6.88 $10^{-1}$)</td>
<td>0.865 (6.88 $10^{-1}$)</td>
<td>1.142 (4.38 $10^{-1}$)</td>
<td>1.182 (6.25 $10^{-2}$)</td>
</tr>
<tr>
<td>PBEF1</td>
<td>0.991 (5.63 $10^{-1}$)</td>
<td>1.076 (5.63 $10^{-1}$)</td>
<td>0.838 (1)</td>
<td>0.917 (1)</td>
</tr>
<tr>
<td>FABP4</td>
<td>0.963 (1)</td>
<td>1.005 (8.44 $10^{-1}$)</td>
<td>0.850 (6.25 $10^{-2}$)</td>
<td>1.163 (4.38 $10^{-1}$)</td>
</tr>
<tr>
<td>HIF1α</td>
<td>0.955 (1)</td>
<td>0.812 (1.56 $10^{-1}$)</td>
<td>0.637 (1.56 $10^{-1}$)</td>
<td>0.918 (1)</td>
</tr>
</tbody>
</table>

Table 3: Ratio between subcutaneous and omental adipose tissue mRNA expression in each group
Figure 1
Figure 2