Data in Brief

Gene expression profile in the fat tissue of Fsp27 deficient mice

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ABSTRACT

Fsp27 is a lipid droplet-associated protein almost exclusively expressed in adipocytes where it facilitates unilocular lipid droplet formation. In mice, Fsp27 deficiency is associated with increased basal lipolysis, browning of white fat and a healthy metabolic profile, whereas energetically challenged Fsp27 deficient mice (ob/ob/Fsp27−/−) show dramatically reduced fat mass, hepatic steatosis and insulin resistance which represents a typical lipodystrophy phenotype. Here, we investigate the effect of Fsp27 depletion on the gene expression of gonadal white adipose tissue (GWAT) under normal or energetically challenged condition (Fsp27−/− vs Wild type; ob/ob/Fsp27−/− vs ob/ob). We systematically analyzed the change in signaling pathway in Fsp27 deficient mice. The raw data have been deposited into Gene Expression Omnibus (GEO): GSE59807 and GSE22693.

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1. Direct link to deposited data

The deposited data can be found at: http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE59807 and http://www.ncbi.nlm.nih.gov/sites/GDSbrowser?acc=GDS3768.

2. Experimental design, materials and methods

2.1. Mouse handling, RNA isolation and data analysis

ob/ob and ob/ob/Fsp27−/− mice were maintained in the animal facility of the Center of Biomedical Analysis at Tsinghua University (Beijing, China). Four months old mice were used. Total RNA was isolated from GWAT with TRIzol (Invitrogen). Equal amounts of total RNA from 3 mice were combined to form RNA pools. In total, we analyzed 3 RNA pools from 9 ob/ob mice and 3 RNA pools from 9 ob/ob/Fsp27−/− mice. First-strand cDNA synthesis was performed using the Superscript First-Strand Synthesis System (Invitrogen). Six Affymetrix gene chips (GeneChip Mouse Gene 1.0 ST Array, Affymetrix, USA) were used for hybridization and data collection. Microarray data related to WT and Fsp27−/− mice were from Li et al. (GSE22693) [1]. Quality control and statistical analysis of all the Mouse Gene 1.0 ST microarray data were conducted using R/Bioconductor. Methods including scatterplots, distribution histograms, boxplots, and unsupervised Principle Component Analysis (PCA) were employed to visualize the data before and after preprocessing procedures. All arrays were consistent and comparable for further analysis, and we performed background adjustment, quantile normalization and summaries of transcript-level intensity for all arrays using the Robust Multi-array Average (RMA) algorithm followed by two rounds of probeset filtering. After removing control probesets, 28,858 probesets from the original 35,556 were retained.

Next, the detection above background (DABG) p-values for probesets
were calculated using the xps package, and only the significant ones (p < 0.05) were considered as “present”. We only retained probesets flagged as present in at least one sample for each type of tissue, and used the package LIMMA to identify probesets which were differentially expressed between the ob/ob/Fsp27−/− and ob/ob mice. The Benjamini and Hochberg method was used to estimate the false discovery rate (FDR) and correct for multiple hypotheses testing. Annotation was taken, and genes that changed by log fold of at least 0.5 between ob/ob/Fsp27−/− and ob/ob mice and with a FDR < 0.05 were considered significant. The up- and down-regulated genes were further mapped to biological pathways using PathVisio with Wiki Pathways content, and the results were sorted by Z-score, which is the standard statistical test under the hypergeometric distribution.

3. Results and discussion

3.1. Multilocular LDs in the adipocytes of ob/ob/Fsp27−/− mice

ob/ob/Fsp27−/− mice show reduced fat mass and TAG storage compared with ob/ob mice [2]. The gonadal white adipose tissue (GWAT) was dramatically reduced compared with ob/ob mice. In mature adipocytes, only one large LD per adipocyte was detected in ob/ob adipocytes, whereas Fsp27 deficiency in ob/ob mice caused multilocular lipid droplets, about more than 200 LDs per mature adipocyte.

3.2. Altered GWAT pathways in Fsp27 deficient mice

To evaluate the effect of reduced lipid storage and smaller LDs on gene expression, we checked the gene expression profile in the GWAT of ob/ob/Fsp27−/− and ob/ob mice by microarray analysis and compared their expression profile with that in Fsp27−/− and WT mice. 8000 genes were changed in the GWAT of ob/ob/Fsp27−/− compared with ob/ob mice. We analyzed the gene expression network using Wiki pathway and observed that 23 of total 162 Wiki pathways were significantly increased, whereas 39 pathways were significantly decreased in the GWAT of ob/ob/Fsp27−/− mice compared with that in ob/ob mice (Table 1). We reanalyzed the microarray data of GWAT in Fsp27−/− and WT mice [1] (Table 2). 14 of the total 162 pathways were significantly increased in the GWAT of mice when comparing with WT mice. Among the 14 increased pathways, 11 pathways were the same like of the ob/ob/Fsp27−/− mice. However, among the 22 decreased pathways in Fsp27−/− mice, only 6 pathways were similar to the ob/ob/Fsp27−/− mice.

3.3. Up-regulated pathways

Most of the 11 pathways (changed in both Fsp27−/− and ob/ob/Fsp27−/− mice compared with their partners) are involved in electron transport chain, oxidative phosphorylation, fatty acid oxidation and TCA cycle indicating that Fsp27 deficiency leads to a more metabolic active fat tissue [3–4]. We also observed that pathways involved in fatty acid biosynthesis, triacylglyceride synthesis, adipogenesis and cholesterol biosynthesis were also upregulated in ob/ob/Fsp27−/− mice.

3.4. Down-regulated pathways

Importantly, we observed that gene expression levels in IL-1/2/3/4/5/7 signaling pathway, B7T cell receptor signaling pathway, chemokine signaling pathway and inflammatory response pathway were all markedly decreased (Table 1) indicating decreased inflammatory response in leptin and Fsp27 double deficient mice. At the same time, we did not observe a large range of reduced inflammatory response in the Fsp27−/− mice as in the ob/ob/Fsp27−/− mice (Table 2). These data indicate that the reduced inflammatory response was specific in the ob/ob/Fsp27−/− mice but not in Fsp27−/− mice when comparing with their partners.

Table 1

The most significant up-regulated and down-regulated pathways in the GWAT of ob/ob/Fsp27−/− mice were identified using Wiki pathway analysis. The total represents the total number of genes in one gene pathway. The measured represents the number of genes with altered expression pattern (using the criteria described above), and the positive represents the number of up-regulated or down-regulated genes. Z score means the standard statistical test under the hypergeometric distribution. Green indicates same pathway changed both in this Supplementary Tables 1 and 2. Yellow indicates specific changed pathways when compared with Table 2. LFC means log ratio of fold change.

| Pathway | Positive (r) | Measured (n) | Total % | Z score |
|---------|-------------|-------------|---------|---------|
| Up-regulated pathways: | | | | |
| Electron transport chain | 91 | 100 | 116 | 91.03% | 21.41 |
| Oxidative phosphorylation | 52 | 59 | 65 | 88.14% | 15.75 |
| TCA cycle | 27 | 31 | 45 | 72.31% | 7.56 |
| Fatty acid beta oxidation | 26 | 34 | 46 | 76.67% | 10.02 |
| Fatty acid biosynthesis | 16 | 22 | 26 | 72.31% | 7.56 |
| Mitochondrial complex I/Fatty acid oxidation | 13 | 16 | 21 | 85.71% | 7.39 |
| Lipid metabolism | 37 | 52 | 205 | 40.22% | 6.78 |
| Glycolysis and gluconeogenesis | 23 | 48 | 70 | 92.86% | 6.37 |
| Triacylglycerol synthesis | 13 | 23 | 26 | 57.69% | 5.55 |
| Adipogenesis | 42 | 132 | 134 | 31.82% | 5.43 |
| Homeostasis | 6 | 9 | 21 | 66.67% | 4.32 |
| Oxygen metabolism | 14 | 34 | 42 | 41.18% | 4.06 |
| Aromatic polyamine synthesis | 3 | 3 | 13 | 100.00% | 4.1 |
| Nuclear receptors | 12 | 36 | 38 | 63.16% | 3.84 |
| Cholesterol biosynthesis | 6 | 15 | 20 | 75.00% | 2.69 |
| Cryptophagy | 12 | 43 | 48 | 27.11% | 2.35 |
| Down-regulated pathways: | | | | |
| Dihydrofolate | 13 | 45 | 88 | 33.33% | 2.17 |
| Homocysteine | 3 | 7 | 17 | 42.86% | 2.05 |
| Acetylation of lysine | 3 | 7 | 17 | 42.86% | 2.05 |
| Mitochondrial gene expression | 6 | 19 | 21 | 44.89% | 2.25 |
Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.gdata.2015.07.003.

Competing interests
The authors have declared that no competing interest exists.

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| Up-regulated pathways: | Positive (r) | Measured (n) | Total | % | Z score |
|------------------------|--------------|--------------|-------|---|---------|
| Electron transport chain | 64 | 81 | 116 | 79.01% | 19.7 |
| Oxidative phosphorylation | 37 | 48 | 65 | 77.08% | 14.65 |
| TCA cycle | 23 | 27 | 45 | 85.18% | 12.29 |
| Fatty acid beta oxidation | 22 | 30 | 46 | 73.33% | 10.88 |
| Mitochondrial LC-fatty acid beta-oxidation | 12 | 15 | 21 | 80.00% | 8.5 |
| Amino acid metabolism | 29 | 71 | 205 | 40.83% | 8.06 |
| Glycolysis and gluconeogenesis | 19 | 36 | 70 | 52.78% | 7.99 |
| Fatty acid biosynthesis | 12 | 20 | 26 | 60.00% | 6.97 |
| Arachidonate epoxygenase epoxide hydrolase | 3 | 3 | 13 | 100.00% | 4.89 |
| Tryptophan metabolism | 10 | 28 | 48 | 57.14% | 4.15 |
| Synthesis and degradation of ketone bodies | 2 | 4 | 8 | 50.00% | 4.7 |
| Eicosanoid synthesis | 4 | 14 | 36 | 28.57% | 4.08 |
| Nuclear receptors in lipid metabolism and toxicity | 4 | 15 | 40 | 26.67% | 4.99 |
| Cholesterol biosynthesis | 4 | 15 | 30 | 26.67% | 4.99 |

| Down-regulated pathways: | Positive (r) | Measured (n) | Total | % | Z score |
|--------------------------|--------------|--------------|-------|---|---------|
| Cytoplasmic ribosomal proteins | 45 | 76 | 182 | 59.21% | 9.16 |
| Complement activation, classical pathway | 10 | 10 | 18 | 100.00% | 6.8 |
| Complement and coagulation cascades | 16 | 28 | 64 | 57.14% | 5.46 |
| Focal adhesion | 45 | 128 | 192 | 35.16% | 5.25 |
| Estrogen metabolism | 7 | 10 | 29 | 70.00% | 4.32 |
| Inflammatory response pathway | 9 | 16 | 32 | 56.25% | 4.01 |
| Glucuronidation | 7 | 11 | 33 | 63.64% | 3.98 |
| Endochondral ossification | 16 | 41 | 67 | 39.02% | 3.57 |
| Sarcopenia and autophagy | 25 | 76 | 100 | 32.89% | 3.48 |
| Aflatoxin B1 metabolism | 3 | 4 | 11 | 50.00% | 2.99 |
| Myometrial relaxation and contraction pathways | 29 | 102 | 161 | 28.43% | 2.85 |
| Dopaminergic neurogenesis | 4 | 7 | 32 | 57.14% | 2.72 |
| Striated muscle contraction | 7 | 16 | 45 | 43.75% | 2.72 |
| Prostaglandin synthesis and regulation | 9 | 23 | 40 | 39.11% | 2.68 |
| Hypertrophy model | 6 | 18 | 24 | 75.00% | 2.56 |
| Regulation of actin cytoskeleton | 25 | 93 | 157 | 64.88% | 2.32 |
| SHH, FGF8, Stat3 | 1 | 1 | 2 | 50.00% | 2.15 |
| Glucocorticoid & mineralocorticoid metabolism | 1 | 1 | 2 | 50.00% | 2.15 |
| Intracranial pathway | 4 | 9 | 13 | 46.15% | 2.09 |
| PTHrP related regulatory pathway | 3 | 6 | 14 | 50.00% | 2.06 |
| TGF beta signaling pathway | 11 | 36 | 52 | 30.58% | 2.01 |
| Alphakin-betakin signaling pathway | 14 | 49 | 67 | 28.57% | 1.98 |