#### Genomics Data 5 (2015) 326-328

Contents lists available at ScienceDirect

# Genomics Data

journal homepage: http://www.journals.elsevier.com/genomics-data/



Data in Brief

# Gene expression profile in the fat tissue of Fsp27 deficient mice

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#### ARTICLE INFO

Article history: Received 30 June 2015 Accepted 3 July 2015 Available online 11 July 2015

Keywords: Obesity Fsp27 Fat tissue Microarray

### 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<sup>-/-</sup>* vs Wild type; *ob/ob/Fsp27<sup>-/-</sup>* 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. © 2015 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license

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Specification	
Organism/cell line/tissue	Mus musculus/gonadal white adipose tissue
Sex	Male
Sequencer or array type	Microarray
Data format	Raw data
Experimental factors	<i>ob/ob</i> mice and <i>ob/ob/Fsp27<sup>-/-</sup></i> mice
Experimental features	Microarray gene expression profiling to identify
	Fsp27 regulated genes
Consent	Data are publicly available
Sample source location	Beijing, China

#### 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/Fsp* $27^{-/-}$  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<sup>-/-</sup>* 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





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http://dx.doi.org/10.1016/j.gdata.2015.07.003

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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<sup>-/-</sup>* 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<sup>-/-</sup>* 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<sup>-/-</sup>* and *ob/ob* mice by microarray analysis and compared their expression profile with that in *Fsp27<sup>-/-</sup>* and WT mice. 8000 genes were changed in the GWAT *ob/ob/Fsp27<sup>-/-</sup>* mice 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<sup>-/-</sup>* mice compared with that in *ob/ob* mice (Table 1). We reanalysed the microarray data of GWAT in *Fsp27<sup>-/-</sup>* 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<sup>-/-</sup>* mice, only 6 pathways were similar to the *ob/ob/Fsp27<sup>-/-</sup>* 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, B&T 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*<sup>-/-</sup> mice as in the *ob/ob/Fsp27*<sup>-/-</sup> mice (Table 2). These data indicate that the reduced inflammatory response was specific in the *ob/ob/Fsp27*<sup>-/-</sup> mice but not in *Fsp27*<sup>-/-</sup> mice when comparing with their partners.

#### Table 1

The most significant up-regulated and down-regulated pathways in the GWAT of *ob/ob/Fsp27<sup>-/-</sup>* 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 upregulated 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.

Up-regulated pathways:					
Pathway	Positive (r)	Measured (n)	Total	%	Z score
Electron transport chain	91	100	116	91.00%	21.41
Oxidative phosphorylation	52	59	65	88.14%	15.75
TCA cycle	27	31	45	87.10%	11.22
Fatty acid beta oxidation	26	34	46	76.47%	10.02
Fatty acid biosynthesis	16	22	26	72.73%	7.56
Mitochondrial LC-Fatty acid beta-oxidation	13	16	21	81.25%	7.39
Amino acid metabolism	37	92	205	40.22%	6.78
Glycolysis and gluconeogenesis	23	48	70	47.92%	6.37
Triacylglyceride synthesis	13	23	26	56.52%	5.55
Adipogenesis	42	132	134	31.82%	5.43
Heme biosynthesis	6	9	21	66.67%	4.32
Glycogen metabolism	14	34	42	41.18%	4.26
Arachidonate epoxygenase epoxide hydrolase	3	3	13	100.00%	4.1
Nuclear receptors	12	38	38	31.58%	2.84
Cholesterol biosynthesis	6	15	30	40.00%	2.69
Tryptophan metabolism	12	43	48	27.91%	2.35
Diurnally regulated genes with circadian orthol	ogs 13	48	48	27.08%	2.32
One carbon metabolism and related pathways	12	45	86	26.67%	2.17
Kennedy pathway	5	14	29	35.71%	2.15
Oxidative stress	7	23	29	30.43%	2.05
Pentose phosphate pathway	3	7	19	42.86%	2.05
Acetylcholine synthesis	3	7	17	42.86%	2.05
Mitochondrial gene expression	6	19	23	31.58%	2.01

Down-regulated pathways:					
Pathway	Positive (r)	Measured	(n) Total	%	Z score
B cell receptor signaling pathway	61	155	157	39.35%	7.63
Chemokine signaling pathway	63	180	198	35.00%	6.65
IL-5 signaling pathway	30	69	70	43.48%	5.97
IL-3 signaling pathway	37	99	101	37.37%	5.53
Kit receptor signaling pathway	28	67	67	41.79%	5.51
T cell receptor signaling pathway	45	132	134	34.09%	5.38
Focal adhesion	57	184	192	30.98%	5.24
Toll-like receptor signaling pathway	34	94	98	36.17%	5.07
DNA replication	18	41	47	43.90%	4.66
Cell cycle	30	86	90	34.88%	4.52
EGFR1 signaling pathway	49	174	177	28.16%	4.08
G1 to S cell cycle control	22	61	64	36.07%	4.05
IL-4 signaling pathway	21	61	63	34.43%	3.7
Apoptosis	26	83	84	31.33%	3.57
Toll like receptor signaling	13	33	33	39.39%	3.48
Complement and coagulation cascades	20	60	64	33.33%	3.44
G13 signaling pathway	14	38	38	36.84%	3.31
Regulation of actin cytoskeleton	40	150	157	26.67%	3.28
IL-7 signaling pathway	15	44	45	34.09%	3.08
Type II interferon signaling (IFNG)	12	33	36	36.36%	3.01
MAPK signaling pathway	40	157	162	25.48%	2.95
Inflammatory response pathway	11	30	32	36.67%	2.92
Complement activation, classical pathway	7	16	18	43.75%	2.89
Prostaglandin synthesis and regulation	11	31	40	35.48%	2.79
Hypertrophy model	8	20	21	40.00%	2.78
Apoptosis modulation by HSP70	7	17	18	41.18%	2.69
TGF-beta receptor signaling pathway	37	150	152	24.67%	2.61
Endochondral ossification	18	62	67	29.03%	2.59
Matrix metalloproteinases	10	29	30	34.48%	2.55
Small ligand GPCRs	7	18	19	38.89%	2.51
Nucleotide metabolism	7	19	36	36.84%	2.34
Senescence and autophagy	25	98	100	25.51%	2.33
Glucuronidation	5	12	33	41.67%	2.3
IL-2 signaling pathway	20	76	76	26.32%	2.23
Integrin-mediated cell adhesion	24	97	102	24.74%	2.11
IL-1 signaling pathway	11	37	38	29.73%	2.11
Homologous recombination	5	13	13	38.46%	2.09
Androgen receptor signaling pathway	26	109	114	23.85%	1.99
Signaling of hepatocyte growth factor receptor	10	34	34	29.41%	1.97

#### Table 2

The most significant up-regulated and down-regulated pathways in the GWAT of  $Fsp27^{-/-}$  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. Z score means the standard statistical test under the hypergeometric distribution. Green indicates same pathway changed both in this table and in Table 1.

#### Un-regulated nathways:

op regulated pathways.					
Pathway	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	85.19%	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	40.85%	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	35.71%	4.15
Synthesis and degradation of ketone bodies	2	4	8	50.00%	2.47
Eicosanoid synthesis	4	14	36	28.57%	2.08
Nuclear receptors in lipid metabolism and toxic	ity 4	15	40	26.67%	1.92
Cholesterol biosynthesis	4	15	30	26.67%	1.92

#### Down-regulated pathways:

Pathway	Positive (r)	Measured (n)	Total	%	Z score
Cytoplasmic ribosomal proteins	45	76	82	59.21%	9.56
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%	4.03
Glucuronidation	7	11	33	63.64%	3.98
Endochondral ossification	16	41	67	39.02%	3.57
Senescence and autophagy	25	76	100	32.89%	3.48
Aflatoxin B1 metabolism	3	4	11	75.00%	2.99
Myometrial relaxation and contraction pathway	s 29	102	161	28.43%	2.85
Dopminergic 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	39.13%	2.68
Hypertrophy model	6	13	21	46.15%	2.67
Regulation of actin cytoskeleton	25	93	157	26.88%	2.32
SHH, FGF8, Stat3	1	1	6	100.00%	2.15
Glucocorticoid & mineralcorticoid metabolism	1	1	31	100.00%	2.15
Irinotecan pathway	4	9	13	44.44%	2.09
Ptf1a related regulatory pathway	3	6	14	50.00%	2.06
TGF beta signaling pathway	11	36	52	30.56%	2.01
Alpha6-beta4 integrin signaling pathway	14	49	67	28.57%	1.98

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.

### Acknowledgments

This work was supported by grants from the China Postdoctoral Science Foundation (2012M520249 and 2013T60103 to L.Z.).

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