ELSEVIER

Journal of Nutritional Biochemistry 15 (2004) 24–29

THE JOURNAL OF Nutritional Biochemistry

# Decreased serum leptin and muscle oxidative enzyme activity with a dietary loss of intra-abdominal fat in rats

Buhao Zou[a], Masataka Suwa[b], Hiroshi Nakano[c], Yasuki Higaki[d], Tatsumi Ito[e], Shigeru Katsuta[f], Shuzo Kumagai[b,*]

[a]*Graduate School of Human-Environment Studies, Kyushu University, Kasuga, Fukuoka 816-8580, Japan*
[b]*Institute of Health Science, Kyushu University, Kasuga, Fukuoka 816-8580, Japan*
[c]*Department of Human Development, Nakamura Gakuen University, Fukuoka 814-0198, Japan*
[d]*Department of Preventive Medicine, Saga Medical School, Saga 849-8501, Japan*
[e]*Department of Bioscience and Biotechnology, Kyushu University Graduate School, 6-10-1 Hakozaki, Fukuoka 812-8581, Japan*
[f]*Graduate School of Integrated Science and Art, University of East Asia, Shimonoseki, Yamaguchi 751-8503, Japan*

**Abstract**

The purpose of the present study was to investigate the relationship among intra-abdominal adipose storage, adaptation in the serum leptin concentration and skeletal muscle enzyme activity after a 4-week energy restriction (ER). Thirty-one male Wistar rats were divided into 40% energy restricted ($n$=24) or ad libitum-fed control (CL) rats ($n$ = 7). The energy-restricted rats were grouped into the most fat (MF, $n$=7), medium ($n$ 10) and the least fat (LF, $n$=7) by their intra-abdominal fat pads mass (epididymal, mesenteric, and perirenal) after ER. A superficial portion of M. gastrocnemius tissue obtained before and after the diet period were analyzed to determine the activities of hexokinase (HK), β-hydroxyacyl CoA dehydrogenase (β-HAD) and citrate synthase (CS). Blood samples were also collected for a serum leptin assay. At the baseline, no difference was found in either the leptin concentration or the enzyme activities among LF, MF and CL. The serum leptin concentration was positively correlated with the muscle activities of β-HAD and CS, while it negatively correlated with HK/β-HAD. After ER, the activities of HK, β-HAD and CS were all significantly lower in LF than in CL. Among the energy-restricted rats, the intra-abdominal fat pad weight, leptin concentration and the activities of β-HAD, CS, β-HAD/CS all significantly correlated with one another. The changes in leptin and the activity of β-HAD were also positively correlated. These findings indicate that parallel decreases in the serum leptin and skeletal muscle enzyme activities with the energy restriction-induced intra-abdominal adipose reduction, thus may suggest the leptin to have a regulative effect on the muscle enzyme activity during ER. 

*Keywords:* Energy restriction; Intra-abdominal adipose; Leptin; Muscle oxidative enzyme activity

## 1. Introduction

The association between the risk of chronic diseases, including type II diabetes and coronary heart disease, and visceral adipose accumulation [1, 2], rather than subcutaneous adipose accumulation [3–6], has well been recognized. The prevalence of these chronic metabolic diseases has made it urgent to clarify the mechanism of visceral adipose storage and utilization.

Skeletal muscle represents more than 30% of body mass and plays important role in the consumption of carbohydrates and lipids. As a result, the metabolic characteristics of such muscle has been investigated in both cross-sectional and longitudinal studies regarding its relationship with body fat accumulation [7–13].

Leptin, the adipose-derived hormone, has been shown to regulate food intake and energy metabolism [14–18]. High correlations have been shown between plasma leptin and either the body mass index (BMI) [16, 19, 20] or the percentage of body fat [20, 21]. In the rodent skeletal muscle, fatty acid oxidation can be enhanced by leptin [22–25]. Leptin thus appears to play a protective role which helps to inhibit further energy accumulation under energy-sufficient conditions.

We recently reported a greater upregulation in the oxidative enzyme activity in skeletal muscle of rats with

This research was supported by a research grant from the Japanese Ministry of Education, Culture, Sports, Science and Technology (No.13480009) to Dr. S. Kumagai.

* Corresponding author. Tel. and fax: +81-92-583-7853.
*E-mail address:* shuzo@ihs.kyushu-u.ac.jp (S. Kumagai).

0955-2863/04/$ – see front matter 
doi:10.1016/j.jnutbio.2003.09.004

greater high-fat diet-induced intra-abdominal adipose accumulation [26]. From the results of that study, we considered that the adipose storage, as manifested by intra-abdominal fat pads, might therefore induce the increase in serum leptin, thus also increasing the oxidative potential. In other words, the oxidative capacity of skeletal muscle might change in parallel with the changes in both the intra-abdominal adipose accumulation and serum leptin levels. However, little is still known about the relationship between leptin and the skeletal muscle metabolism under energy-insufficient conditions. In the current study, we focused on the relationship among the remnants of intra-abdominal fat deposition, changes in the serum leptin concentration, and the skeletal muscle enzyme activity after a 4-week ER. If the regulation of the enzyme activity in skeletal muscle is regulated by the serum leptin, then the decrease in leptin concentration owing to the consumption of adipose storage by ER should be able to induce a comparable decrease in the skeletal muscle enzyme activity.

## 2. Methods and materials

### 2.1. Animals

Male Wistar rats ($n=31$) at 15 weeks of age weighing 440.5 ± 2.7g were used in this study. All rats were housed individually under controlled conditions (12:12-hr light-dark cycle and a 20°C room temperature) and given a regular rat chow diet (Oriental Yeast Co. Tokyo Japan, consisting of 12.9% fat, 26.6% protein, 60.5% carbohydrate, and 3.6 kcal/g) and water ad libitum. All experimental procedures were conducted strictly in accordance with the Guiding Principles for Research Involving Animals and Human Beings.

### 2.2. Experimental protocol

At the beginning of the study, all rats were weighed and anesthetized with pentobarbital sodium (50 mg/kg ip). Blood samples were taken from the tail. The lateral side of the right leg was shaved and then sterilized with 70% ethanol. The skin was opened (~1 cm) with a blade, and muscle samples (~100 mg) were obtained from the superficial portion of M. gastrocnemius. All samples were immediately frozen in liquid nitrogen and stored −80°C until assayed. The skin was closed with stainless steel autoclips and then the rats were injected with penicillin (2.5 mg/kg im). After a 2-week recovery period, 24 randomly selected rats underwent a 40% reduction of their baseline average calorie intake (18g/day) for 4 weeks. The remaining 7 rats continued to feed ad libitum as the control group. The body weights were recorded once a week. After the 4-week ER period, and an over-night fast (12 hr), all rats were weighed and anesthetized with pentobarbital sodium (50 mg/kg ip). The superficial potion of the M. gastrocnemius in the left leg was dissected. The intra-abdominal fat pads (epididymal, mesenteric, and perirenal) were excised and weighed after blood samples were taken.

### 2.3. Enzyme Assay

An enzyme assay was carried out in samples extracted from the superficial portion of the M. gastrocnemius. The activity of hexokinase (HK, key enzyme of glucose utilization), β-hydroxyacyl CoA dehydrogenase (β-HAD, key enzyme of β-oxidation of fatty acids) and citrate synthase (CS, key enzyme of tricarboxylic acid cycle) were spectrophotometrically determined at 30°C according to previously established techniques [27–29]. The coefficients of variation for the enzyme assay were 1.8% for HK, 1.2% for β-HAD and 1.7% for CS by same sample repeated measurements.

### 2.4. Serum measurements

Serum leptin, glucose, free triiodothyronine (FT3) and free fatty acid (FFA) concentration were measured before and after ER. The leptin concentrations were assayed using a sensitive commercially available radioimmunoassay kit (Rat Leptin RIA, Linco Research Inc., St. Charles, MO, USA) according to the manufacturer's instructions [30]. The assay lower limit of detection is 0.5ng/mL. The serum glucose concentration was assayed using a glucose analyzer (YSI 2300STAT, OH). The FT3 concentrations were assayed using an automated chemiluminescent immunoassay system (Advia Centaur, Bayer Medical Ltd., Tokyo, Japan). FFA concentrations were assayed using an enzymatic determination device (Bio Majesty JCA-BM1650, Japan Electron Optics Laboratory Co., Ltd., Tokyo, Japan).

### 2.5. Statistical analysis

Among the energy-restricted rats, based on the weight of the intra-abdominal fat pads, the data were divided into 3 groups: the 2 tertiles on both sides with the same number as in the control group for the least fat (LF, $n=7$) and the most fat (MF, $n=7$), the 10 between LF and MF for medium. All data were presented as the means ± SE. To investigate the relationship among intra-abdominal adipose, leptin, and muscle enzyme activities, one-way ANOVA with post-hoc comparisons made using the Tukey-Kramer test was assessed only among the LF, MF and control (CL) groups, the 3 groups with a significant difference in intra-abdominal fat pads (the medium group was not significantly different from MF or LF when it was added to ANOVA). Differences in the body weight, weight loss, intra-abdominal fat pads, intra-abdominal fat pads/final body weight, enzyme activity, serum leptin concentration, change in the enzyme activity and leptin concentration among these 3 groups were assessed in this way. Significant differences in the variables were determined with a 5% significant criterion. Data from the medium group were only used for analyses in all energy-restricted rats, such as pre-post comparisons (using the

Table 1
Effects of ER on the food intake and body composition

| | Food intake (g) | Body weight (g) | | | | | Weight change (g) | Intra-abdominal fat pads (g) |
|---|---|---|---|---|---|---|---|---|
| | | Week 0 | Week 1 | Week 2 | Week 3 | Week 4 | | |
| CL(n=7) | 770.0 ± 17.2 | 481.3 ± 10.1 | 498.6 ± 11.3 | 509.4 ± 12.0 | 526.9 ± 11.6 | 539.4 ± 13.4 | 36.9 ± 4.4 | 18.6 ± 1.9 |
| MF(n=7) | 504.0 ± 0.0* | 480.3 ± 8.2 | 443.9 ± 6.3* | 437.7 ± 5.2* | 435.7 ± 6.0* | 437.4 ± 6.0* | −42.9 ± 8.3* | 10.9 ± 0.2*# |
| LF(n=7) | 504.0 ± 0.0* | 486.1 ± 9.2 | 451.9 ± 6.7* | 445.7 ± 5.9* | 440.7 ± 5.0* | 438.0 ± 5.9* | −48.1 ± 8.0* | 6.3 ± 0.3* |

Values are the means ± SE.
*Significantly different from CL, $p < 0.05$.
#Significantly different from LF, $p<0.05$.

paired *t*-test) and correlation analyses. The correlations at baseline were analyzed using the data from all rats before ER. The correlations after ER or concerning changes in variables were analyzed in either energy-restricted or CL rats, respectively. Correlations were considered significant only when the *P*-value was less than 0.05. All statistical analyses were performed using StatView 5.0 software (SAS Institute, Cary, NC).

## 3. Results

### 3.1. Food intake and body composition

The total food intake, body weight, weight change and intra-abdominal fat pad weight are presented in Table 1. During the 4-week ER period, the food intake in CL was totally 770 ± 17g. Although energy-restricted groups were restricted to 60% (18g/day) of their baseline intake at the beginning of the ER period, their total intake (504g) consequently reached about 65% that of the CL. Significantly much food was consumed by CL than by the energy-restricted groups of rats.

CL had a higher body weight than LF or MF after the first week of ER ($P < 0.05$). This significant difference persisted for the remainder of the dietary restriction period. No significant difference was observed between LF and MF at either time point. The changes in body weight were not different between LF and MF whereas those of CL were higher than those of LF and MF ($P < 0.05$).

The epididymal, mesenteric, and perirenal fat pads were measured and the total intra-abdominal fat pad weight was determined in this study. The energy-restricted rats were divided into LF, medium or MF groups based on this criterion. The ranges of the intra-abdominal fat pad weight were 13.75 to 27.70g for CL, 9.91 to 11.59g for MF, 8.15 to 9.77g for medium, and 4.87 to 7.26g for LF. The rank order (CL > MF > LF) of the intra-abdominal fat pads or intra-abdominal fat pads/final body weight showed significant differences between all 3 groups ($P < 0.05$).

### 3.2. Muscular enzyme activity

The enzyme activities in the superficial portion of the M. gastrocnemius tissue obtained before and after the diet period are shown in Fig. 1. Before ER, no significant differences were seen between LF, MF and CL. After ER, the activities of HK, β-HAD, and CS were all significantly lower in LF than in CL ($P < 0.05$). When the medium group, which was not analyzed by ANOVA, was evaluated together with MF and LF, enzyme activities of HK, β-HAD, and CS in energy-restricted rats were found to significantly decrease, and the enzyme activities showed the following rank order: CL > MF > medium > LF after ER.

### 3.3. Fasting serum values

The fasting serum leptin, glucose, FT3, FFA concentrations are shown in Table 2. Before ER, there was no significant difference among LF, MF and CL. The serum leptin concentration decreased in all of the energy-restricted groups while it increased in CL during the experimental period. After ER, the serum leptin concentration was significantly lower in LF than in CL. The rank order of the leptin level among all groups after ER was CL > MF > medium > LF. No significant differences were found in the glucose, FT3 or FFA concentrations before or after ER between LF, MF and CL. The changes in the glucose, FT3 or FFA concentrations were not significant between LF, MF or CL.

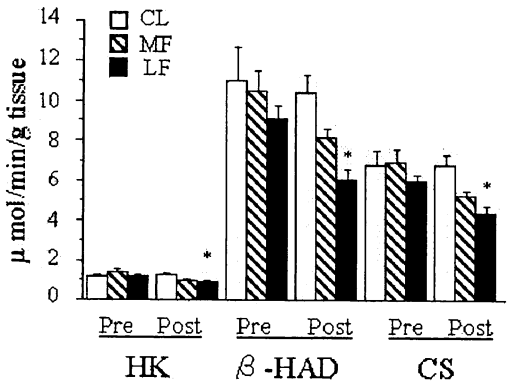


Fig. 1. Enzyme activities of HK, β-HAD and CS. *Significantly different from the activity in CL after ER.

Table 2
Fasting serum values in the CL, MF and LF rats

| | Glucose (mg/dl) | | Leptin (ng/ml) | | FT3 (pg/ml) | | FFA (mEq/l) | |
|---|---|---|---|---|---|---|---|---|
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post |
| CL(n=7) | 112.3 ± 2.6 | 113.0 ± 3.6 | 3.0 ± 0.5 | 4.4 ± 0.6 | 3.3 ± 0.1 | 3.0 ± 0.2 | 0.7 ± 0.1 | 0.6 ± 0.1 |
| MF(n=6) | 116.9 ± 5.9 | 118.5 ± 4.3 | 3.7 ± 0.7 | 3.3 ± 0.5 | 3.4 ± 0.2 | 3.0 ± 0.1 | 0.5 ± 0.1 | 0.4 ± 0.0 |
| LF(n=5, 7) | 109.1 ± 2.8 | 116.0 ± 2.4 | 1.7 ± 0.1 | 1.3 ± 0.1* | 3.0 ± 0.1 | 2.7 ± 0.1 | 0.6 ± 0.0 | 0.5 ± 0.0 |

Values are the means ± SE.
*Significantly different from CL.

### 3.4. Correlation analysis

Before ER, the serum leptin concentration correlated positively with the activities of β-HAD (r = 0.570, $P < 0.01$, Fig. 2A) and CS (r = 0.630, $P < 0.01$), but negatively with HK/β-HAD (r = -0.396, $P < 0.05$), which is an indicator of the fat oxidation capacity. No significant correlation was found regarding the HK activity (r = 0.189, $P = 0.34$) or β-HAD/CS (r = 0.234, $P = 0.23$) ($n$=28).

After ER, correlations were made in energy-restricted or CL rats, respectively. Significant positive correlations with intra-abdominal fat mass were observed regarding the activities of β-HAD (r = 0.550, $P < 0.01$) and CS (r = 0.409, $P < 0.05$), and β-HAD/CS (r = 0.465, $P < 0.05$) in energy-restricted rats ($n$=24) but not in CL ($n$=7). In energy-restricted rats ($n$=21), the serum leptin concentration correlated positively with the intra-abdominal fat pads (r = 0.718, $P < 0.01$), the activities of HK (r = 0.546, $P < 0.01$), β-HAD (r = 0.700, $P < 0.01$, Fig. 2B) and CS (r = 0.513, $P < 0.05$), as well as β-HAD/CS (r = 0.586, $P < 0.01$). The changes in the serum leptin concentration and the activity of β-HAD also correlated significantly (r = 0.432, $P < 0.05$, Fig. 2C). In the CL rats ($n$=7), the leptin concentration correlated positively with the intra-abdominal fat (r = 0.836, $P < 0.05$).

## 4. Discussion

In the current study, we compared MF, LF and CL, the three groups of rats with a significant difference in the intra-abdominal adipose pads. Other differences among these rats in skeletal muscle or blood variables were expected to clarify their roles in the adaptation to energy restriction, especially regarding the change in intra-abdominal adipose fat.

Energy-restricted rats took in a total amount of 1814.4 kcal from chow. This was 957.6 kcal less than what the CL rats took and corresponded to approximately 106.4 g adipose tissue. In fact, the LF rats lost 48.1 g, while the MF rats lost 42.9 g of body weight. Regarding the caloric intake of the CL rats as the standard, the smaller loss of body weight (nearly 40%) than would normally be expected is due to the fact that the energy-restricted rats exhibited a resistance to weight loss. Significant correlations were found between intra-abdominal fat, leptin and muscle enzyme activities in energy-restricted rats.

Before ER, there was no difference in the leptin concentration or muscular enzyme activity among LF, MF and CL. However, after ER, LF showed a lower serum leptin concentration and lower muscle enzyme activities than CL. Regarding the CL rats, LF had a relatively greater adaptation in both serum leptin concentration and enzyme activity in skeletal muscle than MF under an energy-insufficient

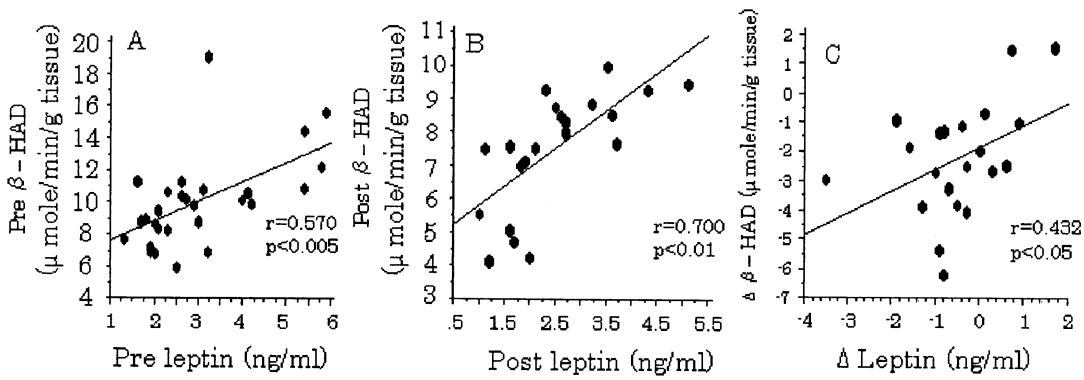


Fig. 2. Correlation between the serum leptin concentration and the activity of β-HAD in all rats ($n$ = 28) before ER (A). Correlation between the serum leptin concentration and the activity of β-HAD in energy-restricted rats ($n$ = 24) after ER (B). Correlation between the changes in serum leptin concentration and the activity of β-HAD (C) in energy-restricted rats ($n$ = 21) after ER.

condition. The decreased leptin concentration observed owing to the consumption of adipose storage, manifested by intra-abdominal adipose in this study, was accompanied with a parallel decrease in the skeletal muscle enzyme activities. To our knowledge, this is the first report concerning the relationship between the serum leptin concentration and the skeletal muscle enzyme activity.

Before ER, these rats had a relatively higher serum leptin concentration and also a higher activity of skeletal muscle enzyme activity due to the free access to food. During the ER, the consumption of adipose storage, such as in the intra-abdominal adipose pads, caused a comparable descent of leptin. When the leptin level dropped, the muscle enzyme activity began to decline from the relatively higher level of the baseline. This is supported by the fact that the leptin concentration correlated with the muscle enzyme activities (except pre HK) both at the baseline and in the energy restricted rats after the ER. Taken together, these findings demonstrate an adaptive effect to cope with the metabolic balance with a restricted energy intake to prevent any further energy consumption or weight loss.

In rodent skeletal muscle, leptin has shown regulative effect on fatty acid oxidation [22–25] or expression of peroxisome proliferator-activated receptor $\gamma$-coactivator 1 (PGC-1) [31], the co-activator that promotes mitochondrial biogenesis and cooperates in transcriptional control of nuclear genes encoding mitochondorial fatty acid oxidation enzymes [32–34]. Together with the significant correlation found in the current study between the ER-induced changes in serum leptin concentration and in $\beta$-HAD in energy-restricted rats, although there is no direct evidence for causality, leptin thus play a putative role in regulating the activity of skeletal muscle enzymes, especially oxidative enzymes.

In summary, the present study demonstrated a lower leptin concentration and enzyme activity of the skeletal muscle in rats who had less remaining of intra-abdominal fat after a 4-week ER in comparison to CL rats. These findings indicate that skeletal muscle enzyme activity, especially oxidative enzymes, adapted to ER in a parallel way to that of intra-abdominal adipose consumption. Together with similar findings from another study based on a high-fat diet [26], leptin is therefore considered to play a regulative role in this process. It is possible that the change of adipose storage induces an adaptation in the serum leptin concentration and then the change in leptin causes the mitochondrial enzyme activity in skeletal muscle to adapt in a parallel way. This adaptation occurs in the early stage of diet change and has a significantly positive protective effect on the body.

## Acknowledgments

This research was supported by a research grant from the Japanese Ministry of Education, Culture, Sports, Science and Technology (No.13480009) to Dr. S. Kumagai.

## References

[1] Despres JP, Lemieux I, Tchernof A, Couillard C, Pascot A, Lemieux S. Fat distribution and metabolism. Diabetes Metab 2001;27:209–14.
[2] Frayn KN. Visceral fat and insulin resistance—causative or correlative? Br J Nutr 2000;83:S71–S77.
[3] Enzi G, Busetto L, Jimenez G, d'Alessio M, Biasion P. Metabolic abnormalities in visceral obesity. Front Diabetes 1992;11:119–23.
[4] Fujioka S, Matsuzawa Y, Tokunaga K, Kawamoto T, Kobatake T, Keno Y, Kotani K, Yoshida S, Tarui S. Improvement of glucose and lipid metabolism associated with selective reduction of intra-abdominal visceral fat in premenopausal women with visceral fat obesity. Int J Obes Relat Metab Disord 1991;15:853–9.
[5] Lefebvre AM, Laville M, Vega N, Riou JP, van Gaal L, Auwerx J, Vidal H. Depot-specific differences in adipose tissue gene expression in lean and obese subjects. Diabetes 1998;47:98–103.
[6] Weinsier RL, Hunter GR, Grower BA, Schutz Y, Darnell BE, Zuckerman PA. Body fat distribution in white and black women: different patterns of intraabdominal and subcutaneous abdominal adipose tissue utilization with weight loss. Am J Clin Nutr 2001;74:631–6.
[7] Aspnes LE, Lee CM, Weindruch R, Chung SS, Roecker EB, Aiken JM. Caloric restriction reduces fiber loss and mitochondrial abnormalities in aged rat muscle. FASEB J 1997;11:573–81.
[8] Hansen PA, Han DH, Marshall BA, Nolte LA, Chen MM, Mueckler M, Holloszy JO. A high fat diet impairs stimulation of glucose transport in muscle. J Biol Chem 1998;273:26157–63.
[9] Helge JW, Fraser AM, Kriketos AD, Jenkins AB, Calvert GD, Ayre KJ, Storlien LH. Interrelationships between muscle fibre type, substrate oxidation and body fat. Int J Obes Relat Metab Disord 1999; 23:986–91.
[10] Imbeault P, Tremblay A, Simoneau JA, Joanisse DR. Rise in plasma pollutant in response to weight loss is associated with a reduction in human skeletal muscle oxidative capacity. Am J Physiol Endocrinol Metab 2002;282:E574–E579.
[11] Simoneau JA, Bouchard C. Skeletal muscle metabolism and body fat content in men and women. Obes Res 1995;3:23–9.
[12] Simoneau JA, Veerkamp JH, Turcotte LP, Kelley DE. Markers of capacity to utilize fatty acids in human skeletal muscle: relation to insulin resistance and obesity and effects of weight loss. FASEB J 1997;13:2051–60.
[13] Wade A, Marbut MM, Round JM. Muscle fibre type and aetiology of obesity. Lancet 1990;335:806–8.
[14] Campfield L, Smith F, Guisez Y, Devos R, Burn P. Recombinant mouse OB protein: evidence for a peripheral signal linking adiposity and central neural networks. Science 1995;269:546–9.
[15] Halaas J, Gajiwala K, Maffei M, Cohen S, Chait B, Rabinowitz D, Lallone R, Burley S. Weight-reducing effects of the plasma protein encoded by the obese gene. Science 1995;269:543–6.
[16] Maffei M, Halaas J, Ravussin E, Pratley RE, Lee GH, Zhang Y, Fei H, Kim S, Lallone R, Ranganathan S, Kerm PS, Friedman JM. Leptin levels in human and rodent: measurement of plasma leptin and ob RNA in obese and weight-reduced subjects. Nature Med 1995;1: 1155–61.
[17] Pellymounter MA, Cullen MJ, Baker MB, Hecht R, Winters D, Boone T, Collins F. Effects of the obese gene product on body weight regulation in ob/ob mice. Science 1995;269:540–3.
[18] Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman J. Positional cloning of the mouse obese gene and its human homologue. Nature 1994;372:425–32.
[19] Lonnqvist F, Wennlund A, Arner P. Relationship between circulating leptin and peripheral fat distribution in obese subjects. Int J Obes Relat Metab Disord 1997;21:255–60.
[20] Ostlund RE, Yang JW, Klein S, Gingerich R. Relation between plasma leptin concentration and body fat, gender, diet, age, and metabolic covariates. J Clin Endocrinol Metab 1996;81:3909–13.

[21] Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, Nyce MR, Ohannesian JP, Marco CC, McKee LJ, Bauer TL, Caro JF. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. N Engl J Med 1996;334:292–5.
[22] Muoio DM, Dohm GL, Fiedorek FT, Tapscott EB, Coleman RA, Dohn GL. Leptin directly alters lipid partitioning in skeletal muscle. Diabetes 1997;46:1360–3.
[23] Steinberg GR, Bonen A, Dyck DJ. Fatty acid oxidation and triacylglycerol hydrolysis are enhanced after chronic leptin treatment in rats. Am J Physiol Endocrinol Metab 2002;282:E593–E600.
[24] Steinberg GR, Dyck DJ. Development of leptin resistance in rat soleus muscle in response to high-fat diets. Am J Physiol Endocrinol Metab 2000;279:E1374–E1382.
[25] Minokoshi Y, Kim YB, Peroni OD, Fryer LG, Muller C, Carling D, Kahn BB. Leptin stimulates fatty-acid oxidation by activating AMP-activated protein kinase. Nature 2002;415:339–43.
[26] Zou, B, Suwa, M, Nakano, H, Higaki, Y, Ito, T, Katsuta, S, Kumagai, S. Adaptation of skeletal muscle characteristics to a high-fat diet in rats with different intra-abdominal-obesity susceptibilities. J Nutr Sci Vitaminol. In press.
[27] Kobayashi A, Jiang LL, Hashimoto T. Two mitochondrial 3-hydroxyacyl-CoA dehydrogenases in bovine liver. J Biochem 1996;119:775–82.
[28] Srere PA. Citrate synthase. Methods Enzymol 1969;13:3–6.
[29] Uyeda K, Racker E. Regulatory mechanisms in carbohydrate metabolism VII. Hexokinase and phosphofructokinase. J Biol Chem 1965;240:4682–8.
[30] Landt M, Gingerich RL, Havel PJ, Mueller WM, Schoner B, Hale JE, Heiman ML. Radioimmunoassay of rat leptin: sexual dimorphism reversed from humans. Clin Chem 1998;44:565–70.
[31] Kakuma T, Wang ZW, Pan W, Unger RH, Zhou YT. Role of leptin in peroxisome proliferator-activated receptor gamma coactivator-1 expression. Endocrinology 2000;141:4576–82.
[32] Wu Z, Puigserver P, Andersson U, Zhang C, Adelmant G, Mootha V, Troy A, Cinti S, Lowell B, Scarpulla RC, Spiegelman BM. Mechanisms Controlling Mitochondrial Biogenesis and Respiration through the Thermogenic Coactivator PGC-1. Cell 1999;98:115–24.
[33] Lin J, Wu H, Tarr PT, Zhang CY, Wu Z, Boss O, Michael LF, Puigserver P, Isotani E, Olson EN, Lowell BB, Bassel-Duby R, Spiegelman BM. Transcriptional co-activator PGC-1 alpha drives the formation of slow-twitch muscle fibres. Nature 2002;418:797–801.
[34] Vega RB, Huss JM, Kelly DP. The coactivator PGC-1 cooperates with peroxisome proliferator-activated receptor alpha in transcriptional control of nuclear genes encoding mitochondrial fatty acid oxidation enzymes. Mol Cell Biol 2000;20:1868–76.