Introduction

Obesity is caused by a multiple factors, including genetic, metabolic, behavioral and cultural factors. More specifically, a high fat intake and low energy expenditure are the main causes of obesity, as well as metabolic disorders such as insulin resistance, type 2 diabetes, and cardiovascular diseases [1,2]. A variety of programs and treatments including drug therapeutics, surgical intervention and dietary control for obesity management or prevention have been developed; however, these are often associated with safety issues. Therefore, the development of a safe and effective dietary supplement to assist with body weight management is essential.

Lactobacilli and bifidobacteria are representative probiotic microorganisms that benefit human health through modulation of the immune system [3], prevention of cancer [4], enhancement of intestinal functions [5] and a hypocholesterolemic effect [6]. Recently, some studies have expanded the functionality of probiotics to obesity management. Some probiotics have been demonstrated to have an anti-obesity property by regulating lipid metabolism [7,8], producing conjugated linoleic acid [9,10], reducing the adipocyte size and increasing the number of small adipocytes in white adipose tissue [11], and regulating leptin [12].

We have observed the effects of L. gasseri BNR17, a probiotic strain isolated from human breast milk, on the high-sucrose diet-fed SD rat and transgenic db/db mouse [13,14]. In those studies, L. gasseri BNR17 suppressed the body weight and fat weight gain, fasting and postprandial blood glucose, and improved oral glucose tolerance. The purpose of the current study was to extend these observations and elucidate the mechanism involved in the anti-obesity activity of L. gasseri BNR17. We investigated the impact of L. gasseri BNR17 on body weight gain, fat accumulation, and mRNA expression of obesity-related genes in diet-induced obese mice.

Materials and Methods

Animals and Experiment

Male C57BL/6J mice (6-week-old, n=8 per group) were obtained from Central Lab Animal Inc. (Seoul, South Korea). All animals were housed in standard plastic cages (two mice per cage), and maintained under a 12-h light-dark cycle at constant temperature and humidity (23±1°C and 55±5%, respectively) with free access to food and water. This study was carried out in accordance with the recommendations in the guide for the care and use of the Animal, Plant and Fisheries Quarantine and Inspection Agency (Republic of Korea). The protocol was approved by the Committee on the Ethics of Animal Experiments of the Bioneer Corporation (AEC-20081229-0004). Following acclimatization for 1 week, the mice were fed a normal diet (ND) (2918G, containing 6.0% fat and 18.5% protein by weight; Koatech Animal Inc., Pyeongtaek, South Korea), or a high-sucrose diet (HSD) (AIN-76A, 5.0% fat, 50.0% sucrose, 15.0% cornstarch and 20.0% protein by weight; Central Lab Animal Inc.), or high-sucrose diet and BNR17 10^9 CFU (HSD+BNR17)
or 10^10 CFU (HSD+BNR17/10) for 10 weeks. *L. gasseri* BNR17 was prepared fresh daily and orally administered twice per day. Body weight and food intake were measured once a week. At the end of the 10-week treatment period, mice were killed by cervical dislocation after blood gathering. Liver, spleen, kidney, and adipose tissues (mesenteric, subcutaneous, epididymal, perirenal) were dissected precisely and weighed. An *in vivo* CT analysis (Inveon™, Siemens Medical Solutions USA Inc.) was carried out prior the killing of animals under 1.5–2% isoflurane in O₂ anesthesia.

**Real-time PCR Analysis**

RNA was extracted from ~0.1 g of tissues using the RNeasy Mini kit (Qiagen) for liver and RNeasy Lipid Tissue Mini kit (Qiagen) for white adipose tissue, according to the manufacturer’s protocols. cDNA was synthesized using the Accupower® Rockscript™ Cycle RT Premix kit from Bioneer (Daejeon, South Korea). qPCR was performed using an Exicycler (Bioneer) with Accupower® 2× Greenstar qPCR Master Mix (Bioneer). Primer sequences for the targeted mouse genes are listed in Table 1.

**Biochemical Analyses**

Endocrine peptides (ghrelin, GIP, GLP-1, glucagon, insulin, leptin) were determined using a Bio-Plex suspension array system (Luminex, Austin, USA). Metabolic parameters including glucose, total cholesterol, HDL-cholesterol, and LDL-cholesterol levels in serum were analyzed using a Clinical Analyzer 7020 (HITACHI, Tokyo, Japan).

**Measurement of Adipocyte Size**

Adipocyte sizes in the mesenteric, subcutaneous, epididymal and perirenal adipose tissues were measured in paraffin-embedded tissue. Briefly, adipocyte tissues were fixed in 10% neutral formalin solution, embedded in paraffin, cut into 4-μm sections, and stained with hematoxylin and eosin. Cell sizes were measured using a DIXI3000 (Leica, Wetzlar, Germany).

**Statistical Analysis**

The data were expressed as mean values with their standard errors. Analyses were performed using pairwise *t*-tests and Wilcoxon rank sum tests. Differences were considered to be statistically significant at values of *P*<0.05.

**Results**

*L. gasseri* BNR17 Inhibits High-sucrose Diet-induced Body Weight Gain and Fat Weight Accumulation

High-sucrose diet feeding induced significant body weight gain throughout the study period compared to the ND group (Figure 1A and Table 2). The administration of BNR17 induced less body weight gain than the HSD group, although not in a dose-dependent manner. Food intake differed significantly between the ND and HSD groups (Figure 1B and Table 2); whereas no significant differences were observed in daily food intake between the HSD and HSD+BNR17 groups. Moreover, energy intake were similar for all groups. This suggests that BNR17 contributed to the reduced body weight gain. Total cholesterol and LDL-cholesterol in the HSD group and HSD+BNR17 groups increased compared to the ND group; however, no significant reduction was caused by BNR17 administration (Table 2). In addition, glucose levels did not change with BNR17 administration. High-sucrose diet also induced increased adipose tissue weight as compared with normal diet feeding (Table 2). BNR17 administration significantly suppressed the increase of fat mass in all white adipose tissues, including mesenteric, subcutaneous, epididymal and perirenal adipose tissue (Table 2). Further, CT imaging showed a significant reduction in body fat profile with BNR17 treatment (Figures 1C and D). Moreover, HE staining of white adipose tissues revealed that supplementation with BNR17 was associated with a significant reduction in average adipocyte size in mesenteric, subcutaneous, epididymal and perirenal adipose tissues, as compared with the HSD group (Figures 1E and F).

| Target gene | Forward Primer (5’-3’) | Reverse Primer (5’-3’) | Ref. |
|------------|------------------------|------------------------|-----|
| PPARα      | GTACGGTGTGATGAGAGCATCTT | GCCGTCAGCAGATGACCAT    | [15] |
| PPARδ      | GCCATTCTCCAGGTCGTCGTC  | CAGGACAAGGCTCATCTC    |     |
| CPT1       | GTGACTCTGGTGGGAGGAATAC | GAGCACTTCAGTGGCTAG     |     |
| ACO        | GTGACGGTCTCAGCTGCTGAC  | TACTGCTGGTCTGAAATCCA   |     |
| UCP3       | CCAGACATTGGTGCCTCTC    | CTCGTCAGCAGCAGG       |     |
| GLUT4      | GGGAGAAGAAAGGGCTATGCTG | TGGAGAACGGTCCAAGAATG   |     |
| SREBP-1c   | AGGGGAGCAATGGTACCAT    | AAGGTGCAAGTGTCACCTT   |     |
| ACC        | ATGGGGCAGATGTCTCTC    | TGGGGAGCTTCATCAT       |     |
| LPL        | CCACAGCCAGCAAGCTCTTC  | AGGGCCGCAAGTTTTG      |     |
| FAS        | TGTCAGGAGGCAGGCCGAC   | GCCGGTGACGCTCGTTGTA    |     |
| Adiponectin| GAGTGGCAAGCTCTTCTGTG  | GCTCTTCCACTGTCGCA     |     |
| TNF-α      | AAAGCTTGAGCAGCAGCTGA  | GAGCCACCTAGTTGGGTCTT   |     |
| ANGPTL4    | AAAAGGTCTGCCCCAGAGT  | TCTTCTTAACCCGAGA      |     |
| β-Actin    | GAGGGGAAGGCTAGTCTGTG  | GGCACTGACTGATCTC      |     |

PPARα, peroxisome proliferator-activated receptor α; PPARδ, peroxisome proliferator-activated receptor δ; CPT, carnitine palmitoyl-transferase; ACO, acyl CoA oxidase; UCP3, uncoupling proteins3; GLUT4, glucose transporter 4; SREBP-1c, ster ol regulatory element-binding protein-1c; ACC, acetyl-CoA carboxylase; FAS, fatty acid synthetase; PPARγ, peroxisome proliferator-activated receptor γ; LPL, liprotein lipase; TNF-α, tumor necrosis factor-α.

doi:10.1371/journal.pone.0054617.t001
**Figure 1.** *L. gasseri* BNR17 supplementation decreases high-sucrose diet-induced body weight gain and fat mass accumulation. (A) Change in body weight, (B) change in food intake, (C) representative CT scanning images of abdominal (left) and whole body (right) fat accumulation (in black) at 10 weeks (D) correspond to the volume of subcutaneous and abdominal fat, (E) representative adipose tissue-staining images in mice of four groups, (F) adipocyte mean area (μm²). Data represent the means ± SD. Pairwise t-test: *P*<0.05, **P*<0.01, ***P*<0.001 versus the ND group; *#P*<0.05, ##*P*<0.01, ###*P*<0.001 versus the HSD group.

doi:10.1371/journal.pone.0054617.g001

*L. gasseri* BNR17 Affects the mRNA Expression of Obesity and Diabetes-related Genes in Liver and White Adipose Tissue

The effect of BNR17 on the expression of obesity-related genes was investigated using real-time RT-PCR. The mRNA expressions of ACO, CPT1, PPARγ, PPARδ and ANGPTL4 were significantly higher in the BNR17 groups compared to the HSD group (Figure 2). Furthermore, mRNA expressions of ACC and SREBP-1c showed tendencies to be lower in BNR17 groups. The mRNA expressions of adiponectin, UCP3, LPL, PPARα and TNF-α in white adipose tissue were measured. There were no significant differences between the HSD and BNR17-fed groups (Figure 3). However, the mRNA expression of GLUT4 was higher in the BNR17 groups compared with the HSD group.

**Table 2.** Body weight, fat weight and organs weight of mice fed the experimental diets for 10 weeks.

|                  | ND          | HSD         | HSD+BNR17(9) | HSD+BNR17(10) |
|------------------|-------------|-------------|--------------|---------------|
| Initial body weight (g) | 22.41±1.06  | 22.88±1.20  | 22.44±1.19   | 22.90±0.77    |
| Final body weight (g)   | 27.63±1.77  | 30.59±1.46**| 27.98±1.93** | 28.35±0.93*   |
| Food intake (g/mouse/day) | 3.15±0.20   | 2.57±0.15***| 2.58±0.14*** | 2.47±0.16***  |
| Energy intake (kcal/mouse/day) | 9.75±0.63   | 9.74±0.56   | 9.78±0.53    | 9.36±0.60     |
| Mesenteric fat pad (g)   | 0.27±0.10   | 0.44±0.10** | 0.29±0.06**  | 0.37±0.05     |
| Subcutaneous fat pad (g) | 0.64±0.10   | 1.15±0.22***| 0.73±0.15*** | 0.95±0.13**   |
| Epididymal fat pad (g)   | 0.78±0.17   | 1.11±0.23** | 0.80±0.20**  | 0.87±0.14     |
| Perirenal fat pad (g)    | 0.43±0.12   | 0.65±0.14** | 0.47±0.14**  | 0.55±0.10     |
| Liver weight (g)        | 1.16±0.13   | 1.18±0.09   | 1.01±0.09**  | 1.06±0.15     |
| Spleen weight (g)       | 0.16±0.03   | 0.18±0.02   | 0.15±0.02**  | 0.16±0.02     |
| Kidney weight (g)       | 0.30±0.02   | 0.29±0.01   | 0.28±0.02    | 0.29±0.02     |
| Cholesterol             | 140.57±12.88| 192.00±24.60**| 177.63±19.30**| 188.18±18.88**|
| HDL-cholesterol         | 69.22±4.91  | 75.00±4.60  | 79.28±7.91*  | 79.32±8.16    |
| LDL-cholesterol         | 6.19±0.95   | 18.2±3.40** | 16.47±3.44** | 18.34±3.20**  |
| Glucose                 | 209.63±30.29| 204.00±32.70| 200.06±62.73*| 214.21±56.52  |

C57BL/6J mice were fed a normal diet (ND), a high-sucrose diet (HSD) or a HSD containing *L. gasseri* BNR17 (10⁹ or 10¹⁰ CFU) for 10 weeks. After measurement of body weight and feed intake, the white adipose tissue, liver, spleen and kidney were removed and weighed. Data represent the means ± SD of eight mice per group. Pairwise t-test:

*P*<0.05,
**P*<0.01,
***P*<0.001 versus the ND group;

*P*<0.05,
##*P*<0.01,
###*P*<0.001 versus the HSD group.

doi:10.1371/journal.pone.0054617.t002

Discussion

Although there was no difference in food and energy intake between the HSD group and BNR17 groups (Figure 1B and Table 2), the increase in body weight was suppressed in the BNR17 groups (Figure 1A and Table 2). There was a significant reduction in subcutaneous and abdominal fat mass in BNR17-fed groups compared to the HSD group (Figure 1C and D). Subcutaneous fat and abdominal fat are the major types of white adipose tissue. Abdominal obesity is associated with increased risk of insulin resistance and cardiovascular diseases, whereas increased subcutaneous fat correlates with a favorable plasma lipid profile [16,17]. Indeed, the mean adipocyte sizes of all white adipose tissues were remarkably reduced in BNR17-fed mice (Figures 1E and F). Subcutaneous adipocytes are the main source of leptin and adiponectin [16]. Leptin is an adipocyte hormone that controls body weight by regulating food intake and energy expenditure [18,19]. Leptin concentrations are correlated with the percentage of body fat; higher serum levels have been found in obese individuals compared with non-obese individuals [20]. BNR17 suppressed the elevation of plasma leptin (Figure 3), suggesting...
that the reductions in fat mass and body weight are associated with a reduction in leptin. Similar effects have been observed in other studies [9,20,21]. For the liver, the weight reduction were observed in BNR17 groups (Table 2), however HE staining and O-red staining of liver tissue did not show any changes between groups (Data not shown).

In this study, glucose was not change between groups. In the paper that investigated the role of fatty acid composition in the development of metabolic disorders in sucrose-induced obese

**Figure 2.** *L. gasseri* BNR17 affects mRNA expression in the liver. C57BL/6J mice were given ND, HSD, or HSD containing BNR17 (10^9 or 10^10 CFU) for 10 weeks. The liver was then removed and mRNA expression was measured by real-time RT-PCR using β-actin as a housekeeping gene. Data represent the means ± SD. Pairwise t-test: *P*<0.05, **P**<0.01, versus the ND group; #P<0.05, ##P<0.01 versus the HSD group. doi:10.1371/journal.pone.0054617.g002

**Figure 3.** *L. gasseri* BNR17 affects mRNA expression in white adipose tissue. C57BL/6J mice were given ND, HSD, or HSD containing BNR17 (10^9 or 10^10 CFU) for 10 weeks. The white adipose tissue was then removed and mRNA expression was measured by real-time RT-PCR using β-actin as a housekeeping gene. Data represent the means ± SD. Pairwise t-test: *P*<0.05, **P**<0.01 versus the ND group; #P<0.05 versus the HSD group. doi:10.1371/journal.pone.0054617.g003
rates, the different time courses of the increases in plasma glucose, insulin, and triglycerides during the course of developing obesity suggest that some time- or tissue-dependent process is necessary to induce these metabolic abnormalities [22].

Some studies have reported that the feeding of a low-protein, high-carbohydrate diet (6% protein and 74% carbohydrate) induced an increase in lipid content in the whole carcass, epididymal adipose tissue and retroperitoneal adipose tissue [23–25]. Long-term (16 weeks) feeding of a high-sucrose (65%) diet to C57BL/6 mice induced obesity, hepatic steatosis, and insulin resistance [26]. In Asian populations, including Koreans, Chinese and Japanese, the traditional diet is characterized as being high in carbohydrate rather than fat, thus the increasing prevalence of obesity is associated with a high carbohydrate intake. Among Korean adults, a high carbohydrate intake is inversely associated with HDL-cholesterol [27]. In the current study, significant increases in body weight and fat mass in HSD groups were induced for 10 weeks as compared to the normal diet (Figure 1 and Table 2), and increases in lipid profile (total cholesterol, LDL- and HDL-cholesterol) were induced by high-sucrose diet feeding.

Because obesity results from low energy expenditure and increased fatty acid synthesis, we measured the mRNA expression levels of related genes in liver and white adipose tissues. In the liver, the administration of BNR17 significantly increased mRNA expression of ACO, CPT1, ANGPTL4, PPARα and PPARδ, as compared to the HSD group (Figure 2). ACO and CPT1 are considered to be rate-limiting enzymes in mitochondrial fatty acid oxidation [28] and ANGPTL4 is a circulating lipoprotein lipase (LPL) inhibitor that controls triglyceride deposition into adipocytes [29]. These genes are target genes of PPARs, which have essential roles in energy homeostasis and adipogenesis [30], and their expression is increased by the activation and elevation of PPARα and PPARδ, resulting in anti-obesity effects. Excess adipose tissue mass is caused mainly by the differentiation of precursor cells into new adipocytes (adipogenesis). Several transcription factors including CCAAT/enhancer binding protein-α (C/EBPα), PPARγ, SREBP-1c are involved in this process [31]. PPARγ regulates the expression of adipocyte genes such as adipocyte-fatty acid binding protein (A-FABP) [32], and SREBP-1c controls the expression of lipogenic genes such as FAS and ACC [33,34]. We observed tendencies for reduced SREBP-1c and ACC in the BNR17-fed groups compared to the HSD group; however, we did not detect a reduction in mRNA expression of FAS, the rate-limiting enzyme of fatty acid synthesis in the liver (Figure 2). Moreover, PPARγ and LPL, which are related to fat intake, did not differ among the HSD group and BNR17-fed groups (Figure 3). Therefore, it seems that the anti-obesity effect of BNR17 is responsible for the increased expression of fatty acid metabolism-related genes rather than reduced fatty acid synthesis and fat intake in the liver.

In this study, BNR17 did not show dose-dependent suppression of body weight and fat mass gain as there was no significant difference in biomarkers between the BNR17(9) and BNR17(10) groups. This suggests that BNR17 exhibits anti-obesity activity at doses >10^9 CFU. This is not consistent with a previous study of the dose-dependent anti-diabetic activity of BNR17 in db/db mice [14]. Although we did not clarify the reason in this study, recently, it has been reported that immunomodulation of dendritic cells by probiotics showed very different profiles according to the bacterial
inoculum, so the probiotic effect may differ depending on the frequency and size of doses ingested [35]. This means that the determination of the optimal effective dose of probiotics may be required for the future development of commercial products.

Interestingly, we observed changes in several diabetes-related biomarkers in this study. GLUT4 is one of the main glucose transporters expressed in skeletal muscle and adipose tissue. An increase in GLUT4 expression in skeletal muscle is known to ameliorate insulin resistance associated with obesity or diabetes [36], while it has been reported that adipose GLUT4 gene expression changes were more related to insulin resistance and type 2 diabetes rather than obesity [37]. In our study, BNR17 significantly increased GLUT4 mRNA expression in white adipose tissue (Figure 3). Furthermore, the insulin level increased in the HSD group, which was decreased significantly by BNR17 supplementation (Figure 4). In the case of pre-diabetes, increases in blood glucose stimulate the secretion of insulin and subsequently induce hyperinsulinemia with a normal blood glucose range. Hyperinsulinemia is frequently accompanied by obesity, and a biomarker of insulin resistance [38]. It is expected that the regulation of GLUT4 and insulin can likely be attributed to the anti-diabetes activity of BNR17.

Recently, many studies have reported the preventive activity of probiotic lactic acid bacteria on obesity and metabolic syndrome. *L. plantarum* KY1032 cell extract reduced fat mass by modulating adipogenesis in maturing preadipocytes [31]. *L. paracasei* decreased fat storage by increasing the level of ANGPTL4 [29], VSL no. 3, a mixture of bifidobacteria, lactobacilli and *Streptococcus thermophilus*, improved diet-induced obesity, hepatic steatosis and insulin resistance by increasing hepatic natural killer T-cells and reducing inflammatory signaling in mice [39]. On the other hand, it was reported recently that gut microbes play an important role in body weight regulation. Endogenous *Bifidobacterium* spp. were significantly and positively correlated with improved glucose tolerance, glucose-induced insulin secretion and normalized inflammatory tone (decreased endotoxia, plasma and adipose tissue proinflammatory cytokines) in high-fat-diet and prebiotic-treated mice [40]. Whether supplementation with exogenous probiotic strains has the same mechanism of action is unclear [41]. However, *Lactobacillus* and *Bifidobacteria* are main members of the gut microbiota, and therefore it is worthwhile to investigate the effect of probiotics on the relationship between the gut microbiota and obesity or obesity-related diseases. In summary, the probiotic *L. gasseri* BNR17 lowered body weight and adiposity by increasing the expression of fatty-acid oxidation genes and reducing the levels of leptin and insulin in high-sucrose diet-induced obese mice. This suggests that *L. gasseri* BNR17 may facilitate alleviating metabolic syndrome.

Author Contributions

Conceived and designed the experiments: JHK SIY. Performed the experiments: JHK SIY MHP JHP SYJ. Analyzed the data: JHK HOP. Wrote the paper: JHK.

### References

1. Wood SC, Sleevey RJ, Porte JD, Schwartz MW (1998) Signal that regulate food intake and energy homeostasis. Science 280: 1378–1383.

2. Wickelgren I (1998) Obesity: How big a problem? Science 280: 1364–1367.

3. Gill H, Prasad J (2008) Probiotics, immunomodulation, and health benefits. Adv Exp Med Biol 606: 423–434.

4. Kumar M, Kumar A, Nasu P, Mok D, Ochiw A, et al. (2010) Cancer-preventing attributes of probiotics: An update. Int J Food Sci Nutr 61: 473–496.

5. Menniq M, Bruewer ME (2009) Effect of probiotics on intestinal barrier function. Ann N Y Acad Sci 1165: 183–189.

6. Shin HS, Park SY, Lee DK, Kim SA, An HM, et al. (2010) Hypocholesterolemic effect of *Lactobacillus gasseri* PL60, isolated from healthy adult Koreans in high cholesteral fed rats. Arch Pharm Res 33: 1425–1431.

7. Xi N, Cui Y, Yin YN, Zhao X, Yang JW, et al. (2011) Effects of two *Lactobacillus* strains on lipid metabolism in adult microflora in rats fed a high-cholesterol diet. BMC Complement Altern Med 11: 53.

8. Ali AA, Velasquez MT, Hansen GT, Mohamed AI, Bhatta NS (2005) Modulation of carbohydrate metabolism and peptide hormones by soybean isolflavones and probiotics in obesity and diabetes. J Nutr Biochem 16: 693–699.

9. Lee HY, Park JH, Seo YH, Park DW, Kim DJ, et al. (2006) Human originated bacteria, *Lactobacillus rhamnosus* PL60, produce conjugated linoleic acid and show anti-obesity effects in diet-induced obese mice. Biochim Biophys Acta 1761: 736–744.

10. Lee K, Park K, Lee KY, Park JH, Lee Y, et al. (2007)Anti-obesity effect of trans-10, cis-12-conjugated linoleic acid-producing *Lactobacillus plantarum* PL62 on diet-induced obese mice. J Appl Microbiol 103: 1140–1146.

11. Takamura N, Okubo T, Sonoyama K (2010) *Lactobacillus plantarum* strain No.14 reduces adipocyte size in mice fed high-fat diet. Exp Biol Med 235: 849–856.

12. Sousa R, Halper J, Zhang J, Lewis SJ, Li Wi, et al. (2008) Effect of *Lactobacillus acidophilus* on fatty acid composition in the development of metabolic disorders in sucrose-induced obese rats. Exp Biol Med (Maywood) 233: 406–493.

13. Kang JH, Yun SI, Park HO (2010) Effects of *Lactobacillus gasseri* BNR17 on body weight and adipose tissue mass in diet-induced overweight rats. J Microbiol 48: 712–714.

14. Yun SI, Park HO, Kang JH (2009) Effect of *Lactobacillus gasseri* BNR17 on blood glucose levels and body weight in a mouse model of type 2 diabetes. J Appl Microbiol 107: 1669–1679.

15. Barasheli N, Tsaki T, Okawa T, Ito K, Ochiai W, et al. (2011) Anti-obesity and anti-diabetic effects of acacia polyphenol in obese diabetic KK-Ay mice fed high-fat diet. Evid Based Complement Alternat Med 2011: 952031.

16. Jequier E (2002) Leptin signaling, adiposity, and energy balance. Ann N Y Acad Sci 967: 379–388.

17. Frederur RC, Hamann A, Anderson S, Lollmann B, Lowell BB, et al. (1995) Leptin levels reflect body lipid content in mice: evidence for diet-induced resistance to leptin action. Nat Med 1: 1311–1314.

18. Buzelle SL, Dos Santos MP, Biviera AM, Lopes CF, Garofalo MAR, et al. (2010) A low-protein, high-carbohydrate diet increases the adipose lipid content without increasing the glycerol-3-phosphate or fatty acid content in growing rats. Nutrition 25: 1106–1109.

19. Aparecida de França S, Dos Santos MP, Garofalo MA, Navegantes C, Kettelhut Ido C, et al. (2009) Low protein diet changes the energetic balance and sympathetic activity in brown adipose tissue of growing rats. Nutrition 25: 1106–1109.

20. Choi HU, Song SJ, Kim BH, Chung JJ, Yoon JH, et al. (2012) High carbohydrate intake was inversely associated with high-density lipoprotein cholesterol among Korean adults. Nutr Res 32: 100–106.

21. Kobayashi Y, Miyazawa M, Kamoi A, Abe K, Kojima T (2010) Ameliorative effects of mulberry (*Morus alba* L) leaves on hyperlipidemia in rats fed a high-fat diet. J Physiol Biochem 66: 1057–1064.

22. Kawamura M, Inokuchi K, Ueda A, et al. (2007) Suppression of inflammatory signaling in mice [39]. On the other hand, it was reported recently that gut microbes play an important role in body weight regulation. Endogenous *Bifidobacterium* spp. were significantly and positively correlated with improved glucose tolerance, glucose-induced insulin secretion and normalized inflammatory tone (decreased endotoxia, plasma and adipose tissue proinflammatory cytokines) in high-fat-diet and prebiotic-treated mice [40]. Whether supplementation with exogenous probiotic strains has the same mechanism of action is unclear [41]. However, *Lactobacillus* and *Bifidobacteria* are main members of the gut microbiota, and therefore it is worthwhile to investigate the effect of probiotics on the relationship between the gut microbiota and obesity or obesity-related diseases. In summary, the probiotic *L. gasseri* BNR17 lowered body weight and adiposity by increasing the expression of fatty-acid oxidation genes and reducing the levels of leptin and insulin in high-sucrose diet-induced obese mice. This suggests that *L. gasseri* BNR17 may facilitate alleviating metabolic syndrome.

Author Contributions

Conceived and designed the experiments: JHK SIY. Performed the experiments: JHK SIY MHP JHP SYJ. Analyzed the data: JHK HOP. Wrote the paper: JHK.
31. Park DY, Ahn YT, Huh CS, Jeon SM, Choi MS (2011) The inhibitory effect of Lactobacillus plantarum KY1032 cell extract on the adipogenesis of 3T3-L1 cells. J Med Food 14: 670–675.
32. Furuhashi M, Hotamisligil GS (2008) Fatty acid-binding proteins: Role in metabolic diseases and potential as drug targets. Nat Rev Drug Discov 7: 489–503.
33. Kim JB, Sarraf P, Wright M, Yao KM, Mueller E, et al. (1998) Nutritional and insulin regulation of fatty acid synthetase and leptin gene expression through ADD1/SREBP1. J Clin Invest 101: 1–9.
34. Guillou H, Martin PG, Pineau T (2008) Transcriptional regulation of hepatic fatty acid metabolism. SubCell Biochem 49: 3–47.
35. Evrard B, Coudeyras S, Dougiliert A, Charbonnel N, Alamé J, et al. (2011) Dose-dependent immunomodulation of human dendritic cells by the probiotic Lactobacillus rhamnosus Lcr35. PLoS one 6: e18735.
36. Zorzano A, Palacin M, Gumà A (2005) Mechanisms regulating GLUT4 glucose transporter expression and glucose transport in skeletal muscle. Acta Physiol Scand 183: 43–58.
37. Koudhi S, Berrhouma R, Rouissi K, Jarboui S, Clerget-Froidevaux MS, et al. (2011) Human subcutaneous adipose tissue Glut4 mRNA expression in obesity and type 2 diabetes. Acta Diabetol (in press).
38. Tabak AG, Herder C, Rathmann W, Brunner EJ, Kivimaki M (2012) Prediabetes: A high-risk state for diabetes development. Lancet 379: 2279–2290.
39. Ma X, Hua J, Li Z (2008) Probiotics improve high fat diet-induced hepatic steatosis and insulin resistance by increasing hepatic NKT cells. J Hepatol 49: 821–830.
40. Cani PD, Neyrinck AM, Fava F, Krauff C, Burcelin RG, et al. (2007) Selective increases of bifidobacteria in gut microbiota improve high-fat-diet-induced diabetes in mice through a mechanism associated with endotoxaemia. Diabetes 56: 2374–2383.
41. Blaut M, Bachofen SC (2010) Probiotics and obesity. Ann Nutr Metab 57 (Suppl. 1), 20–28.