Porphyromonas gingivalis-derived lipopolysaccharide inhibits brown adipocyte differentiation via lncRNA-BATE10

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Abstract. Epidemiological studies have suggested an association between obesity and periodontal disease. Brown adipose tissue (BAT) has an anti-obesity effect. However, the effects of periodontitis on obesity and BAT remain unclear. Therefore, the present study aimed to determine the effects of lipopolysaccharide derived from *Porphyromonas gingivalis* (*P. gingivalis* LPS) on brown adipocytes. For this purpose, the present study examined the effects of the intravenous administration of *Porphyromonas gingivalis* (*P. gingivalis*) in mice, the treatment of brown adipocytes with *P. gingivalis* LPS during differentiation, and the administration of small interfering RNA targeting interferon on brown preadipocytes by assessing the expression of genes involved in differentiation, using a long non-coding (lnc)RNA, and pro-inflammatory factors using reverse transcription-quantitative PCR. In addition, the accumulation of lipid droplets was examined using Oil Red O staining. *P. gingivalis* LPS reduced the expression of uncoupling protein 1 (UCP1) and lncRNA-BATE10 in brown adipocytes during differentiation. Consistent with this finding, *P. gingivalis* reduced UCP1 and lncRNA-BATE10 expression in the BAT of mice. lncRNA-BATE10 may thus be involved in the regulation of UCP1 expression that occurs during the differentiation of brown adipocytes treated with *P. gingivalis LPS*. Thus, *P. gingivalis* LPS may inhibit BAT differentiation by reducing lncRNA-BATE10 expression.

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Abbreviations: BAT, brown adipose tissue; *P. gingivalis*, *Porphyromonas gingivalis*; *P. gingivalis* LPS, lipopolysaccharide derived from *Porphyromonas gingivalis*; lncRNA, long non-coding RNA; UCP1, uncoupling protein 1; BMI, body mass index; DM, diabetes mellitus; NC, negative control; siRNA, small interfering RNA

Key words: Porphyromonas gingivalis LPS, brown adipose tissue, lncRNA, inflammation

Introduction

Periodontal disease has become a global public health concern, with a high prevalence (1). Periodontal disease is defined as the chronic inflammation of the periodontal supporting tissue, caused by chronic infection with bacteria, including *Porphyromonas gingivalis* (*P. gingivalis*) (2). Lipopolysaccharide (LPS) derived from *Porphyromonas gingivalis* (*P. gingivalis* LPS) is responsible for a substantial proportion of its systemic effects. When a host is invaded by a periodontal pathogen, the LPS released is recognized by the immune system, leading to a robust inflammatory response, and this can cause alveolar bone resorption (3). In addition, the inflammation may extend from the gingiva into the periodontal membrane, alveolar bone and cementum, leading to periodontitis. Chronic periodontal inflammation is also associated with the entry of host and bacterially-derived factors into the circulation (4). In addition, periodontal bacteria may colonize the gut via the oral route (5,6). Thus, periodontal bacteria can cause or affect systemic disease.

Epidemiological research has demonstrated an association between obesity and periodontal disease (7). In addition, a number of previous studies have demonstrated a link between periodontal inflammation and obesity (4,8-10). Obesity is associated with a higher incidence of tooth loss over a period of 5 years, and the periodontal conditions of individuals with obesity are significantly worse following periodontal treatment than those of individuals without obesity (11). Furthermore, the periodontal inflamed surface area index is positively associated with body mass index (BMI) (4).

Periodontal disease may affect glucose metabolism via low-grade inflammation (12). Accordingly, diabetes mellitus (DM) has been identified as a risk factor for the progression of periodontal disease (13,14). Furthermore, obesity predisposes towards type 2 DM (4). Host pro-inflammatory factors released by immune cells activated by bacterial products may reach the adipose tissue via the circulation in patients with periodontal inflammation. Therefore, local inflammation may have widespread effects on the body through effects on adipose tissue (4,15). However, the effects of periodontitis on obesity remain unclear.

Brown adipocytes are thermogenic, helping to maintain body temperature by increasing basal metabolism in cold environments. Thermogenesis in brown adipocytes is induced by the uncoupling of mitochondrial oxidative from phosphorylation by uncoupling protein 1 (UCP1) (4), and this has been shown to protect against obesity and obesity-related disease (16). Periodontopathic bacteria affect the development of obesity, glucose intolerance and hepatic steatosis, and also alter lipid metabolism and the thermogenesis of brown adipose tissue (BAT) (17,18). In addition, *P. gingivalis* administration has been shown to modify gene expression in the BAT of pregnant mice (17).

Long non-coding RNAs (lncRNAs) are RNA transcripts of >200 nucleotides in length that do not encode proteins and exhibit poor sequence conservation (19,20). lncRNAs play roles in a number of physiological and pathological processes, including development and differentiation. They regulate gene expression by functioning as microRNA sponges and by affecting transcription, splicing, and translation (20). Recent research has also demonstrated that lncRNAs are involved in brown adipogenesis, the browning of white adipose tissue, and brown adipose thermogenesis (21). These lncRNAs include lncRNA-BATE1, lncRNA-BATE10, AK079912, Blnc1, H19, Lnc-Uc.417 and Lnc-dPrdm16 (21).

To date, research into the effects of periodontitis on obesity has mainly focused on *P. gingivalis*-induced endotoxemia; however, it remains unclear whether there are direct effects of *P. gingivalis* LPS on brown adipocytes, and whether these are mediated by lncRNAs. Therefore, the present study aimed to determine the effects of *P. gingivalis* LPS on BAT.

Materials and methods

Mice. C57BL/6J mice (n=10, male, 6-8 weeks old, weighing 20-22 g) were purchased from Shanghai Laboratory Animal Center, housed under standard environmental conditions at a temperature of 22±2˚C and 55-60% humidity, with free access to food and water and a 12-h light/dark cycle and were allocated into two groups as follows: The first was administered a sonicated *P. gingivalis* suspension in PBS buffer (*P. gingivalis* group, n=5) via the tail vein, and the second was administered PBS alone (control group, n=5). According to a previous study (18), after 18 h, the mice were euthanized, and samples of BAT were collected for use in reverse transcription-quantitative PCR (RT-qPCR). The mice were monitored before and 18 h after the *P. gingivalis injection*. All mice were euthanized using 30% vol/min CO_2 inhalation. Death was verified by confirming the following: The cessation of respiratory and cardiovascular movements by observation at room air for at least 10 min. The experimental protocols were approved by the Institutional Animal Care and Use Committee of Zhejiang University (Approval no. ZJU20170237,2017-02-24).

Culture of P. gingivalis. *Porphyromonas gingivalis* [donated by Dr Peihui Ding (22)] was cultured on trypticase soy agar (Qiangdao Hope Bio-Technology Co., Ltd.), containing 10% defibrinated horse blood, hemin and menadione (Qiangdao Hope Bio-Technology Co., Ltd.), under anaerobic conditions at 37˚C. The bacteria were collected in PBS buffer (pH 7.4) (Shandong Victoryx Biotechnology Co., Ltd.; http://www.vxbiotech.com/en/) and 10^9 CFU/ml of the bacterial suspension was sonicated at 20 kHz for 5 min on ice using a Vibra cell sonicator (Sonics & Materials, Inc.).

Brown adipocyte culture in vitro. Preadipocytes obtained from the BAT of mice according to a previously described method (23) [donated by Professor Zhuoxian Meng (24)] were cultured in high-glucose Dulbecco's modified Eagle medium (DMEM; Gibco; Thermo Fisher Scientific, Inc.) containing 10% fetal bovine serum (Gibco; Thermo Fisher Scientific, Inc.). To induce the adipogenic differentiation of the preadipocytes, they were cultured in induction medium containing 20 nM insulin (cat. no. I5500, MilliporeSigma), 1 μM dexamethasone (cat. no. D1756, MilliporeSigma), 0.5 mM 3-isobutyl-1-methylxanthine (cat. no. I-5879, MilliporeSigma), 1 nM triiodothyronine (T3) (cat. no. T2877, MilliporeSigma), 125 μM indomethacin (cat. no. I-7378, MilliporeSigma) and 10% fetal bovine serum (FBS, Gibco, Thermo Fisher Scientific, Inc.) for 2 days and then in differentiation medium containing 20 nM insulin, T3, and 10% FBS for an additional 2 days. Subsequently, the differentiation medium was replaced every 2 days until day 7. *P. gingivalis* LPS (cat. no. tlrl-pglps, InvivoGen) or LPS from *Escherichia coli* (*E. coli* LPS) (cat. no. L4391, MilliporeSigma) was added to the induction and differentiation media.

Transfection with small interfering RNA (siRNA). 50 nM LncRNA-BATE10-siRNA or scramble siRNA [negative control (NC)] were provided by Biomics Biotechnologies Co., Ltd. and mixed with transfection reagent (INVI DNA RNA, 20 μM/μl; Invigentech) and added to the preadipocytes; the mix of siRNA and the transfection reagent were kept at room temperature for 15 min before transfection (50 nM siRNA) into the cells, and then after 48 h, the cells were induced to differentiate. The siRNA duplex sequences were as follows: lncRNA-BATE10, 5'-GAGUACUGAUCAUCAUUAAdTdT-3' (sense) and 5'-UUAAUGAUGAUCAGUACUCdTdT-3' (antisense); and NC, 5'-UUCUCCGAACGUGUCACGUdTdT-3' (sense) and 5'-ACGUGACACGUUCGGAGAAdTdT-3' (antisense).

RT-qPCR. RNA was extracted using TRIzol reagent (cat. no. 15596026; Invitrogen; Thermo Fisher Scientific, Inc.) from BAT following the manufacturer's instructions. cDNA was synthesized using the WCGENE mRNA cDNA kit (cat. no. WC-SJH0001; WCGENE Biotech), at 37˚C for 15 min and 85˚C for 5 sec. qPCR (WcGene mRNA qPCR mix; cat. no. WC-SJH0002, WCGENE Biotech) was performed using the Bio-Rad CFX96 Touch Real-Time PCR Detection System

(Bio-Rad Laboratories, Inc.) and StepOnePlus™ Real-Time PCR Detection System (Thermo Fisher Scientific, Inc.), using the following primers synthesized by Sangon Biotech (Shanghai) Co., Ltd.: Mouse UCP1 forward, 5'-GGCATTCAG AGGCAAATCAGCT-3' and reverse, 5'-CAATGAACACTG CCACACCTC-3'; mouse Actb forward, 5'-CGTTGACAT CCGTAAAGACC-3' and reverse, 5'-AACAGTCCGCCTAGA AGCAC-3'; lncRNA-BATE10 forward, 5'-AAGCAGCAG AGCCAGAACTC-3' and reverse, 5'-CCATGCAGACCTCCT TGGTT-3'. The following PCR conditions were used: 1 cycle at 95˚C for 30 sec, then 40 cycles at 95˚C for 5 sec and 60˚C for 34 sec.

For the analysis of the mRNA expression data, relative quantification was used (25). Relative quantification relates the PCR signal of the target transcript in a treatment group to that of another sample such as an untreated control. The analysis used the $2^{-\Delta\Delta Cq}$ method. ΔC_q=the target C_T-the average of the reference (β-actin) C_q $\Delta\Delta C_q$=treated ΔC_q-untreated (or other reference group) ΔC_q. Relative expressive was calculated as the $2^{-\Delta\Delta Cq}$ values of the treat groups/mean of the $2^{-\Delta\Delta Cq}$ value of the reference group (as '1.0').

Statistical analysis. Data are presented as the mean ± standard error of the mean. Difference between groups were compared using ANOVA and Tukey's multiple comparisons test (for more than two groups) or the Student's t-test (for two groups) using Prism software (GraphPad Software, Inc.). P-values ≤0.05 were considered to indicate statistically significant differences.

Results

P. gingivalis LPS reduces UCP1 expression and oil droplet formation in preadipocytes during their differentiation. The present study first examined the effects of *P. gingivalis* LPS on differentiating brown adipocytes. The expression of *UCP1* decreased with the increasing concentration of *P. gingivalis* LPS (Fig. 1A). In addition, the accumulation of lipid droplets decreased as the concentration of *P. gingivalis* LPS increased (Fig. 1B). These results suggested that *P. gingivalis* LPS exerted a negative effect on the differentiation of preadipocytes into brown adipocytes. *E. coli* LPS exerted a similar effect on *UCP1* expression during brown preadipocyte differentiation (Fig. 1D). In addition, the present study examined the effects of an intravenous injection of 10^8 CFU *P. gingivalis* suspension in 100 μl saline or 100 μl PBS on the BAT *UCP1* expression of mice, and it was found that the bacterial administration reduced *UCP1* expression (Fig. 1C).

P. gingivalis LPS reduces lncRNA-BATE10 expression in differentiating brown adipocytes and *differentiated BAT in mice*. In a previous study, it was shown that lncRNA-BATE10 may be involved in brown adipocyte thermogenesis (26). Therefore, the present study measured the expression of lncRNA-BATE10 in differentiating brown adipocytes treated with *P. gingivalis* LPS and BAT from mice administered *P. gingivalis*. As the concentration of *P. gingivalis* LPS increased, lncRNA-BATE10 expression decreased during brown adipocyte differentiation (Fig. 2A). *E. coli* LPS exerted a similar effect on lncRNA-BATE10 expression during brown preadipocyte differentiation (Fig. 2B). Consistent with *P. gingivalis* LPS, lncRNA-BATE10 expression was lower in the BAT of mice administered *P. gingivalis* (Fig. 2C).

lncRNA-BATE10 is involved in the differentiation of brown adipocytes. To better understand the role of lncRNA-BATE10 in brown adipocyte differentiation, the effects of siRNA targeting this lncRNA on *UCP1* expression were assessed. lncRNA-BATE10 siRNA (Fig. 3A) was added to brown preadipocytes, differentiation was induced and *UCP1* expression was then measured. It was found that *UCP1* expression was decreased following the knockdown of lncRNA-BATE10 expression (Fig. 3B). Thus, lncRNA-BATE10 may be involved in brown adipocyte differentiation. In addition, after lncRNA-BATE10 was knocked down using siRNA, the effects of *P. gingivalis* LPS on *UCP1* expression during the differentiation of brown adipocytes were less pronounced (Fig. 3C). A comparison of the ratios of *UCP1* expression in differentiating brown adipocytes transfected with negative control siRNA ± *P. gingivalis* LPS treatment with that of the expression in cells transfected with lncRNA-BATE10 siRNA ± *P. gingivalis* LPS also revealed that the inhibition of brown adipocyte differentiation by *P. gingivalis* LPS was suppressed by lncRNA-BATE10 knockdown (Fig. 3D). Thus, lncRNA-BATE10 may be involved in the effects of *P. gingivalis* LPS on brown adipocyte differentiation.

Discussion

The present study examined the effects of *P. gingivalis* and *P. gingivalis* LPS on brown adipocytes and mouse BAT. It was found that *P. gingivalis* decreased *UCP1* expression and lncRNA-BATE10 expression in BAT, and that *P. gingivalis* LPS decreased the expression of *UCP1* and lncRNA-BATE10 in differentiating brown adipocytes. In addition, the present study provided evidence that lncRNA-BATE10 may be involved in the effects of *P. gingivalis* LPS on brown adipocyte differentiation.

Periodontitis is a local form of inflammation that may have a systemic effect on obesity. Immune cells are activated in the adipose tissue of individuals with obesity. In addition, certain bacterial products, such as LPS, danger associated molecular patterns, bacterial flagellar protein, etc., activate immune cells (4,27,28), which may be transported to the adipose tissue via the circulation. Thus, local inflammation may have whole-body effects through effects on obese adipose tissue. Thus, obesity may be associated with periodontal disease and the presence of periodontal disease may also exacerbate the inflammation that characterizes obesity (4,15).

In mice with diet-induced obesity, *P. gingivalis* has been shown to exacerbate weight gain and the expansion of adipose tissue (29). Endotoxemia associated with *P. gingivalis* also affects BAT function. The administration of *P. gingivalis* has been shown to increase the expression of inflammation-related genes and to reduce that of *UCP1* and *Cidea,* as well as that of the genes related to lipolysis, Lipe and Pnpla2, in BAT (18). Notably, the expression of *Pparg* and *Adipoq* has been found to be lower in BAT, but not in white adipose tissue from *P. gingivalis*-treated mice (18).

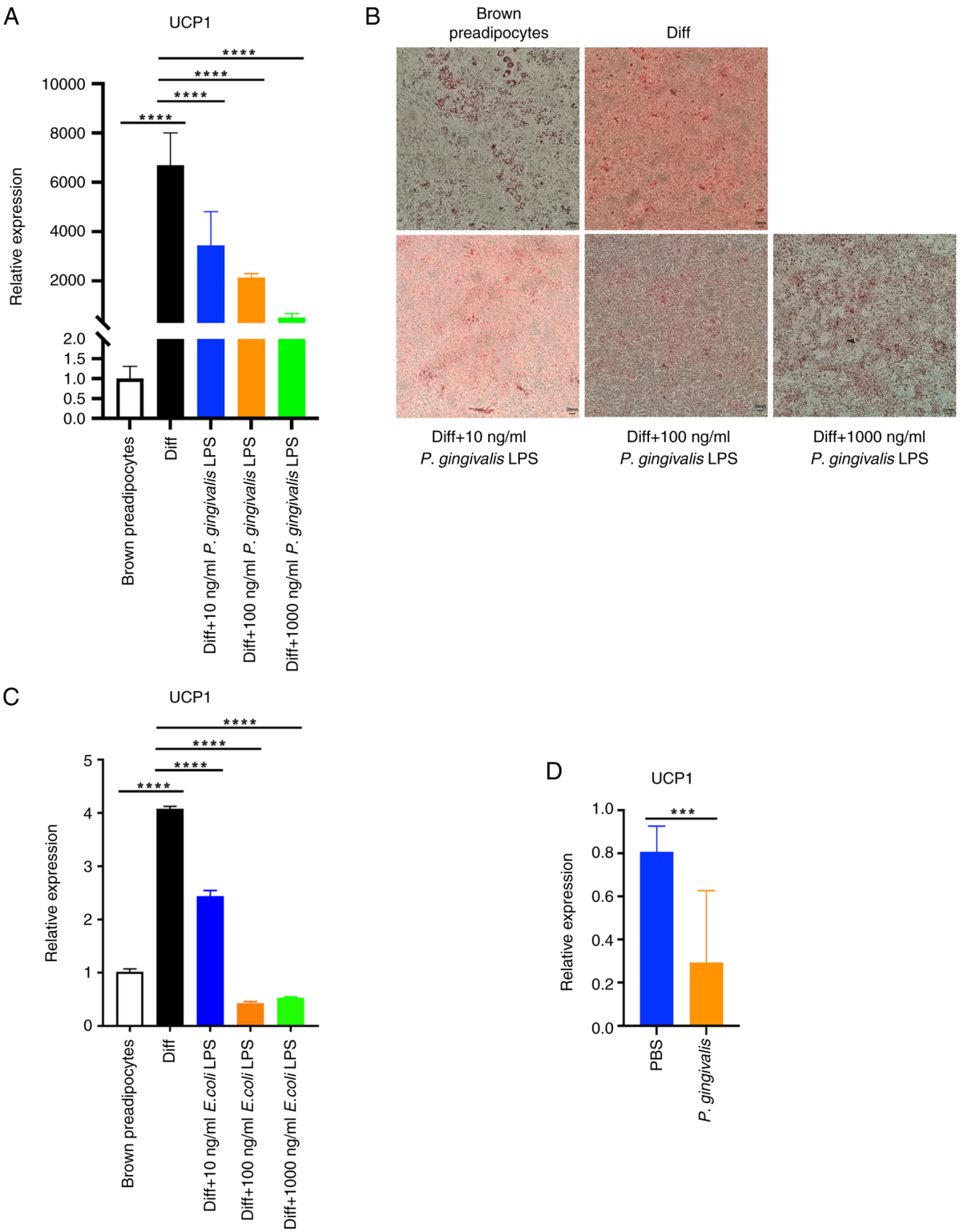

Figure 1. *P. gingivalis* LPS reduces *UCP1* expression and lipid droplet formation in differentiating brown adipocytes. Preadipocytes were induced to differentiate into brown adipocytes, during which *P. gingivalis* LPS was added to the medium. (A) *UCP1* mRNA expression in brown adipocytes (Diff) and preadipocytes. The brown preadipocyte group was used as the reference group and relative expression was calculated as the $2^{-\Delta\Delta Cq}$ values of the other groups/mean of $2^{-\Delta\Delta Cq}$ value of the brown preadipocyte group (as '1.0'). *UCP1*: P<0.0001 for ANOVA. Diff. vs. brown preadipocytes, P<0.0001; Diff vs. Diff + 10 ng/ml *P. gingivalis* LPS, P<0.0001; Diff vs. Diff + 100 ng/ml *P. gingivalis* LPS, P<0.0001; Diff vs. Diff + 1,000 ng/ml *P. gingivalis* LPS, P<0.0001. (B) Oil Red O-stained brown adipocytes (Diff) or preadipocytes. (C) Preadipocytes were induced to differentiate into brown adipocytes, during which *E. coli* LPS was present in the medium. *UCP1* mRNA expression was measured in brown adipocytes (Diff) and preadipocytes. The brown preadipocyte group was used as the reference group and relative expression was calculated as the $2^{-\Delta\Delta Cq}$ values of the other groups/mean of $2^{-\Delta\Delta Cq}$ value of the brown preadipocyte group (as '1.0'). *UCP1*: P<0.0001 for ANOVA. Diff vs. brown preadipocytes, P<0.0001; Diff vs. Diff + 10 ng/ml *E. coli* LPS, P<0.0001; Diff vs. Diff + 100 ng/ml *E. coli* LPS, P<0.0001; Diff vs. Diff + 1,000 ng/ml *E. coli* LPS, P<0.0001. (D) *UCP1* mRNA expression in the brown adipose tissue of mice injected with *P. gingivalis* 100 μl (10^8 CFU) or PBS 18 h previously. The PBS group was used as the reference group and relative expression was calculated as the $2^{-\Delta\Delta Cq}$ values of the other groups/mean of $2^{-\Delta\Delta Cq}$ value of the PBS group (as '1.0'). *UCP1*: PBS vs. *P. gingivalis*, P=0.0005). ***P<0.001 and ****P<0.0001. *P. gingivalis*, *Porphyromonas gingivalis*; *P. gingivalis* LPS, lipopolysaccharide derived from *Porphyromonas gingivalis*; LPS, lipopolysaccharide; UCP1, uncoupling protein 1; *E. coli* LPS, LPS derived from *Escherichia coli*.

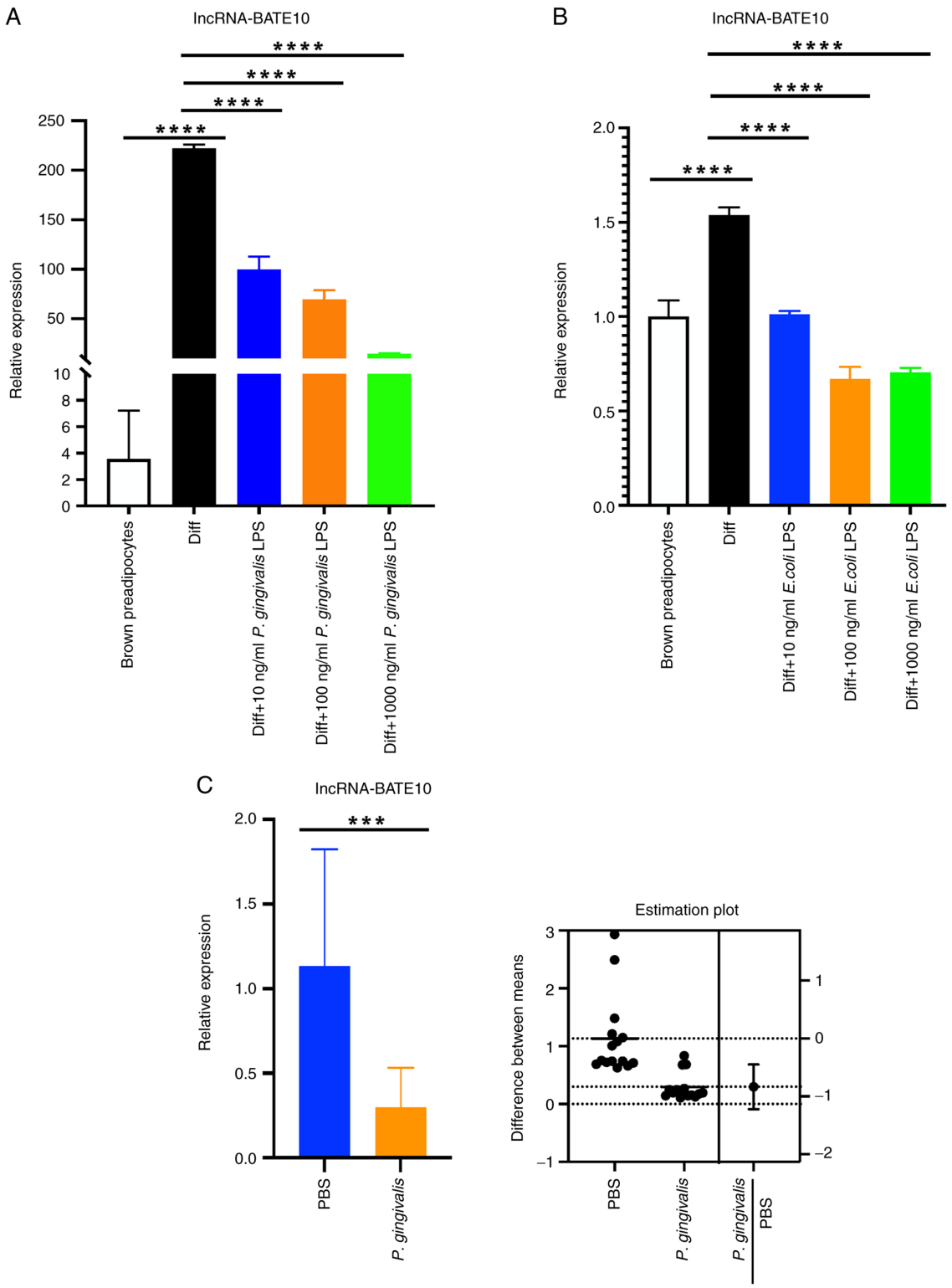

Figure 2. *P. gingivalis* LPS reduces lncRNA-BATE10 expression in differentiating brown adipocytes and *P. gingivalis* reduces lncRNA-BATE10 expression in the BAT of mice. (A) Preadipocytes were induced to differentiate into brown adipocytes, during which *P. gingivalis* LPS was added to the medium. lncRNA-BATE10 expression was examined in brown adipocytes (Diff) and preadipocytes. The brown preadipocyte group was used as the reference group and relative expressive was calculated as the $2^{-\Delta\Delta Cq}$ values of the other groups/mean of $2^{-\Delta\Delta Cq}$ value of the brown preadipocyte group (as '1.0'). P<0.0001 for ANOVA. Diff vs. preadipocytes, P<0.0001; Diff vs. Diff + 10 ng/ml *P. gingivalis* LPS, P<0.0001; Diff vs. Diff + 100 ng/ml *P. gingivalis* LPS, P<0.0001; Diff vs. Diff + 1,000 ng/ml *P. gingivalis* LPS, P<0.0001. (B) Preadipocytes were induced to differentiate into brown adipocytes, during which *E. coli* LPS was present in the medium, then lncRNA-BATE10 expression in brown adipocytes (Diff) and preadipocytes was measured. The brown preadipocyte group was used as the reference group and relative expressive was calculated as the $2^{-\Delta\Delta Cq}$ values of the other groups/mean of $2^{-\Delta\Delta Cq}$ value of the brown preadipocyte group (as '1.0'). P<0.0001 for ANOVA. Diff vs. preadipocytes, P<0.0001.; Diff vs. Diff + 10 ng/ml *E. coli* LPS, P<0.0001; Diff vs. Diff + 100 ng/ml *E. coli* LPS, P<0.0001; Diff vs. Diff + 1,000 ng/ml *E. coli* LPS, P<0.0001. (C, left panel) lncRNA-BATE10 expression in the BAT of mice intravenously administered *P. gingivalis* 100 μl (10^8 CFU) or PBS 18 h earlier. The PBS group was used as the reference group and relative expressive was calculated as the $2^{-\Delta\Delta Cq}$ values of the other groups/mean of $2^{-\Delta\Delta Cq}$ value of the PBS group (as '1.0'). PBS vs. *P. gingivalis*, P=0.0001. (C, right panel) Estimation plot displaying the raw data and the confidence interval for the difference between the means. ***P<0.001 and ****P<0.0001. *P. gingivalis*, *Porphyromonas gingivalis*; *P. gingivalis* LPS, lipopolysaccharide derived from *Porphyromonas gingivalis*; LPS, lipopolysaccharide; *E. coli* LPS, LPS derived from *Escherichia coli*.

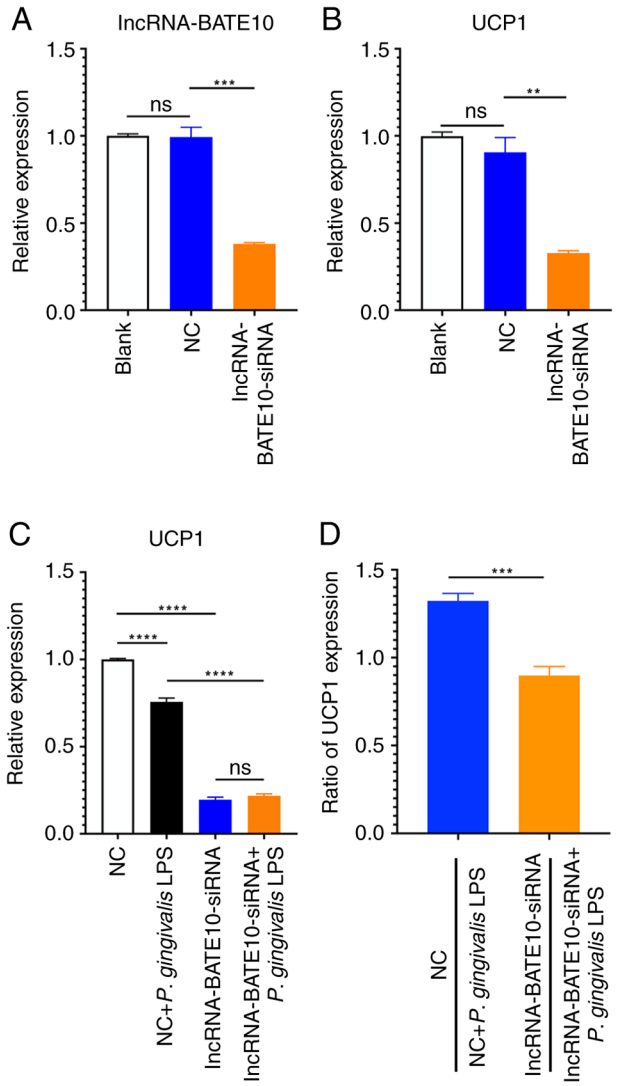

Figure 3. lncRNA-BATE10 is involved in the differentiation of brown adipocytes. lncRNA-BATE10-siRNA or scramble siRNA (NC) 50 nM were added to the culture medium of preadipocytes, and 48 h later, the cells were induced to differentiate. (A) lncRNA-BATE10 and (B) *UCP1* expression during the differentiation of brown adipocytes. lncRNA-BATE10: P<0.0001 for ANOVA. NC vs. blank, P=0.9774; lncRNA-BATE10-siRNA vs. blank, P=0.0008; *UCP1*, P<0.0001 for ANOVA. NC vs. blank, P=0.3112; lncRNA-BATE10-siRNA vs. NC, P=0.0032. (C) Following lncRNA-BATE10 knockdown, the cells were induced to differentiate in the presence or absence of *P. gingivalis* LPS, and *UCP1* expression was measured using reverse transcription-quantitative PCR. The NC group was used as the reference group and relative expressive was calculated as the $2^{-\Delta\Delta Cq}$ values of the other groups/mean of $2^{-\Delta\Delta Cq}$ value of the NC group (as '1.0'). *UCP1*, P<0.0001 for ANOVA. NC vs. NC + *P. gingivalis* LPS, P<0.0001; NC vs. lncRNA-BATE10-siRNA, P<0.0001; NC + *P. gingivalis* LPS vs. lncRNA-BATE10-siRNA + *P. gingivalis* LPS, P<0.0001; lncRNA-BATE10-siRNA vs. lncRNA-BATE10-siRNA + *P. gingivalis* LPS, P=0.3282. (D) Ratio of UCP1 expression between the NC and NC + *P. gingivalis* LPS, lncRNA-BATE10-siRNA or lncRNA-BATE10-siRNA + *P. gingivalis* LPS groups. For the comparison between the ratios of NC to NC + *P. gingivalis* LPS and lncRNA-BATE10-siRNA to lncRNA-BATE10-siRNA + *P. gingivalis* LPS, P=0.0004. **P<0.01, ***P<0.001 and ****P<0.0001. ns, no significant; NC, negative control; *P. gingivalis*, *Porphyromonas gingivalis*; *P. gingivalis* LPS, lipopolysaccharide derived from *Porphyromonas gingivalis*; LPS, lipopolysaccharide; UCP1, uncoupling protein 1.

Periodontal bacteria have been identified in the gut of patients with inflammatory bowel disease. They may be transported to ectopically colonize the gut via the oral route (5,6). Thus, the systemic effects of periodontal inflammation may be mediated through *P. gingivalis*.

lncRNA-BATE10 is BAT-specific and is a member of the lncRNA-BATE family. lncRNA-BATE10 is transcribed from four exons in an intergenic region of mouse chromosome 18 and is ~1.7 kb in length (21). lncRNA-BATE10 expression in white adipose tissue is increased by exposure to cold, β-adrenergic agonists and intense physical exercise (26). Accordingly, lncRNA-BATE10 expression is increased by exposure to cold in BAT and is lower at 30˚C (26). During the differentiation of brown preadipocytes, the knockdown of lncRNA-BATE10 leads to a decrease in the expression levels of BAT-specific genes, including *UCP1* and *Pgc1a* (26,30). These findings demonstrate that lncRNA-BATE10 may play a role in BAT thermogenesis; therefore, it was hypothesized that *P. gingivalis* LPS inhibits the expression of UCP1 during the differentiation of brown adipocytes by reducing lncRNA-BATE10 expression.

In conclusion, *P. gingivalis* may have deleterious effects on BAT that are mediated by LPS. Specifically, *P. gingivalis* reduces UCP1 expression, and lncRNA-BATE10 promotes a pro-inflammatory state. The results of the present study may enhance the current understanding of the association between periodontal disease and obesity.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

WD conceived and designed the study. FZ, LS, NZ, LL and JG performed the experiments. FZ, LS, NZ, LL, JG and WD prepared a draft of the manuscript, and WD and FZ finalized the manuscript. FZ, LS and WD confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The animal experimental protocols were approved by the Institutional Animal Care and Use Committee of Zhejiang University (Approval no. ZJU20170237, 2017-02-24).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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