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APPLIED MICROBIAL AND CELL PHYSIOLOGY

The beneficial effects of ultraviolet light supplementation on bone density are associated with the intestinal flora in rats

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Abstract

The general public spends one-third of its time under artificial lighting, which lacks bands beneficial to human health, and long-term exposure will have a negative impact on bone health. Here, we report the effects of long-term, low-dose ultraviolet (UV) supplementation to white light-emitting diode (LED) light exposure on intestinal microorganisms and bone metabolism, as well as the correlations between the two. Normal and ovariectomized rats were irradiated with LED white light with or without supplementation with UV. The effects of UV supplementation on the intestinal flora and the relationship between the intestinal flora and bone were investigated by measuring the intestinal flora, bone metabolism markers, and bone histomorphology. UV supplementation affected the bone density and bone mass by changing the relative content of *Firmicutes*, *Saccharibacteria*, and *Proteobacteria*; however, the intestinal flora were not the only factors affecting bone. Ultraviolet supplementation changed the composition and function of the gut flora in the bone loss model. By increasing the synthesis of short-chain fatty acids and affecting immunomodulatory, intestinal flora directly or indirectly regulate the activity of osteoclasts and thus mediate UV-mediated improvements in bone metabolism. Our work shows that UV supplementation affects bone density by influencing the intestinal flora, introducing a novel strategy to develop healthier artificial light sources and prevent bone loss.

Key points

- *We measured the bone metabolism markers and bone histomorphometry of rats.*
- *The diversity, composition, and function of intestinal flora were analyzed.*
- *The relationship between gut microbiota and host bone physiology was analyzed.*

Keywords UV supplementation · Intestinal flora · Bone metabolism markers · Bone histomorphology

Introduction

In modern society, individuals spend most of their time working and living under artificial lighting environments; this is especially true for professional groups, such as astronauts and divers, who spend extended time periods working in environments without sunlight. Compared with sunlight, artificial lighting sources are often lacking infrared, ultraviolet, and other bands beneficial to human health (Jou et al. 2019). Working and living in an artificial lighting environment for a long duration has a negative impact on bone health in humans. It has been reported that submariners and night workers are more likely to suffer from bone mineral density decline and osteoporosis (Bukowska-Damska et al. 2019; Luria et al. 2010), while appropriate ultraviolet (UV) exposure can alleviate bone health issues (Cranney et al. 2007; Falkenbach et al. 1993).

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UV irradiation accelerates the absorption of intestinal calcium, maintains bone mass, prevents osteoporosis, and reduces the incidence of bone fractures by promoting vitamin D synthesis (Mead 2008; Nikolikj-Dimitrova 2013). In addition, UV regulates bone metabolism through other distal effects on tissues. Recent studies have shown that alterations in the intestinal flora are also associated with the maintenance of bone mass and bone quality (Hernandez et al. 2016). Other studies have shown that manipulation of the microbiome or its metabolites may afford the ability to optimize bone growth and health (Yan et al. 2016). It has also been observed that gut microbiota regulate bone mass in mice by altering immune status in the bone and affecting osteoclast-mediated bone resorption (Sjögren et al. 2012). The studies mentioned above demonstrate that both UV and gut microbiota play important roles in bone health. However, it is unclear whether UV exposure modulates gut microbiota–associated bone metabolism.

Here, we examined the effects of long-term, low-dose UV supplementation to light-emitting diode (LED) white light on intestinal microorganisms and bone metabolism in normal and ovariectomized rats. We found that UV improved bone metabolism by affecting the intestinal microbial community. The results of our study not only provide the foundation for creating strategies and developing artificial lighting for a healthy artificial light environment but also reveal that intestinal flora play an important role in the UV prevention of bone loss.

Methods

Animals

Forty 180 ± 20 g specific-pathogen-free (SPF) 8-week-old female Sprague-Dawley (SD) rats (provided by Beijing Weitong Lihua Animal Experiment Technology Co., Ltd., Beijing, China) were used in this study. They were held in four plastic squirrel cages, with ten rats per group. SPF feed and drinking water were available ad libitum. The animals were maintained in controlled conditions (12-h light-dark cycle, temperature 20–25°C, air humidity 55–65%).

Experimental design

The SD rats were allowed to acclimate to the animal room for 1 week prior to the start of the experiment (supplementary Fig. S1). In order to observe the effects of UV supplementation on bone loss inhibition and osteoporosis prevention, ovariectomy was performed on 20 rats to establish a rat model of bone loss. The 40 rats were divided into four treatment groups: (1) normal (Normal UV-), (2) normal supplemented with ultraviolet (Normal UV+), (3) ovariectomized (Ovx UV-), and (4) ovariectomized supplemented with ultraviolet (Ovx UV+) as shown in supplementary Fig. S1a. The Normal UV- and Ovx UV- groups were reared under a white LED lighting environment. The Normal UV+ and Ovx UV+ groups were reared under white LED light supplemented with UV. Each group of rats was given light exposure from 10:00 to 22:00. The light intensity and UV light intensity of the active area of the rats were detected weekly by optical fiber spectrometry. The illumination intensity on each rat in the activity area of the cage was about 1000 lx, and the ultraviolet intensity was about 13 W/cm^2 (supplementary Fig. S1b). The experiment lasted 12 weeks, and the rats were sacrificed at the end of the experiment.

Micro-CT analyses

Femurs were fixed in 10% phosphate-buffered-formalin and stored at −80°C (n=6/group). The mCT analyses were performed on the distal femur using a Skyscan 1076 scanner (Kontich, Belgium), X-ray tube potential = 18 kVp; X-ray intensity = 145 μA; and integration time = 200 ms. Calibrated three-dimensional images were reconstructed by NRecon (version 1.7.3.1) software. Femur trabecular bone morphology was analyzed using the CT Analyzer (version 1.17.7.2) software.

Dual-energy x-ray analysis

The rats were deeply anesthetized with a 1% pentobarbital sodium solution by intraperitoneal injection (n=6/group). The rats were scanned with a bone densitometer (Hologic Discovery A, San Diego, USA). The whole-body bone mass content (BMC) and bone mineral density (BMD) of each mouse were measured. Before measurements, a tissue calibration scan was performed with a Hologic phantom (HOLOGIC Discovery A Bone, San Diego, USA). All measurements were performed by the same operator, followed by the software analysis for small animals carried by Hologic Discovery A (San Diego, USA); the determined BMC and BMD were recorded.

Serum biochemical assays

Blood samples (n=6/group) were drawn from rat tail veins. Each blood sample was dispensed into a centrifuge tube and centrifuged at 845g for 20 min using a cryogenic centrifuge. Then, the separated plasma supernatant was collected and stored at −20°C until the time of measurement. Repeated freezing and thawing were avoided. This method was based on that described in a previous study (Abulmeaty 2017). 1,25-Dihydroxyvitamin D_3 (1,25-$(OH)_2$-D_3), tartrate-resistant acid phosphatase (TRACP), and bone alkaline phosphatase (BALP) serum levels were measured using ELISA kits

(Beijing Ruigebo Technology Development Co., Ltd., Beijing, China) according to the manufacturer's instructions.

16S rRNA gene sequencing

Fresh stool samples were collected from the rats and immediately stored at −20°C (n=6/group). Genomic DNA was extracted from stool using the Qiagen QIAamp DNA stool Mini Kit (Hilden, Germany) according to the manufacturer's instructions. The V3-V4 16S rRNA region (338F-806R, 338F: 5′-ACTCCTACGGGAGGCAGCA-3′; 806R: 5′-GGACTACHVGGGTWTCTAAT-3′) was amplified by thermal cycling consisting of an initial denaturation at 98°C for 2 min, followed by 30 cycles of denaturation at 98°C for 30 s, annealing at 50°C for 30 s, and elongation at 72°C for 1 min, and finally, holding at 72°C for 5 min. High-throughput pyrosequencing of the PCR products was performed on an Illumina MiSeq/HiSeq2500 platform (Biomarker Technologies Co, Ltd., Beijing, China).

Sequence data analysis

Reads were chimera-checked and clustered into 97% operational taxonomic units (OTUs) using the vsearch (Rognes et al. 2016) implementation of the UPARSE pipeline (Edgar 2013). A representative sequence (the most abundant) of each OTU was selected for searching against the SILVA 16S rRNA gene database (www.drive5.com/sintax/silva_16s_v123.fa.gz) using the syntax function (Edgar 2016) in vsearch version 2.8.1 with a confidence cut-off (P) value of 0.6. We then excluded the OTUs with < 10 reads from all the samples as their sequences could contain PCR or sequencing errors. The diversity indices of bacterial communities were assessed with the "vegan" package (Oksanen et al. 2007). Alpha and richness diversity indices were evaluated with the Chao1 and Shannon index. Community distance between samples was calculated using the Canberra distance, implemented in the vegan package. Distance-based redundancy analysis (DB-RDA) was performed with the capscale function in vegan. A statistically significant ($p < 0.05$) Spearman's correlation coefficient with an absolute value greater than 0.6 was used as the basis for the selection of the core genera of the bacterial community in each group. All core genera in each group were visualized in a network, where genera and the correlation coefficients were set as nodes and edges, respectively, using the Gephi software (Bastian et al. 2009). The network features in each group were analyzed, including average node connectivity, average path length, diameter, and cumulative degree distribution. An open-source R package, Tax4Fun, was used to analyze the enrichment of functional genes of the microbiome of each group (Aßhauer et al. 2015). The output from QIIME (Caporaso et al. 2010) with a SILVA database extension (SILVA 123) was used for this analysis. Tax4Fun can survey the functional genes of bacterial communities based on the 16S rRNA sequencing data.

Statistical analysis

All statistical analyses were implemented in R version 3.6.1 (Team 2013). Observed OTU, Shannon, and Chao1 diversity measures were used to estimate alpha diversity, and the significance of differences in alpha diversity under different light treatments for normal rats or ovariectomized rats was evaluated by Student's t-test. For beta diversity and partitioning of variance, Canberra distance matrices for bacteria communities were subjected to permutational analysis of variance (PERMANOVA) using the "adonis" test from the vegan package. The two-sided Student's t-test analysis was performed to test the significance of the effect of UV supplementation on bone metabolism. Spearman's correlation analysis between bone metabolism and bacterial taxa was performed in R. $p < 0.05$ was considered statistically significant.

Results

BMC, BMD, and the concentration of serum bone metabolism markers

In order to confirm the effects of UV supplementation on bone mineral content (BMC) and bone mineral density (BMD) in rats, we analyzed the BMC, BMD, and trabecular bone in the four treatment groups (Fig. 1, n=6/group). Although there was no significant difference in femur BMC (Fig. 1a, $p > 0.05$), UV supplementation significantly increased the BMC of normal and ovariectomized rats ($p < 0.05$, Fig. 1b). The BMD of normal and ovariectomized rats was significantly increased after the UV supplementation ($p < 0.01$).

Through micro-CT scanning to obtain the cross-sectional image of the distal femur, we observed an increase in trabecular bone density after UV supplementation (supplementary Fig. S2e). Micro-CT analysis revealed that UV supplementation also increased trabecular separation (Tb.Sp; $p = 0.08$, supplementary Fig. S2d) in the distal femur of normal rats. Interestingly, Tb.Sp (supplementary Fig. S2d) and Tb.Th (trabecular thickness; $p = 0.07$, supplementary Fig. S2c) were decreased, but Tb.N (trabecular number; $p = 0.09$, supplementary Fig. S2b) was increased in the ovariectomized rats after the UV supplementation. The BV/TV (the trabecular bone volume fraction, supplementary Fig. S2a) of normal and ovariectomized rats was no significant change after the UV supplementation. These results show that long-term, low-energy UV supplementation has a positive effect on local BMD and BMC in both control and ovariectomized rats and can promote bone formation, especially in ovariectomized rats.

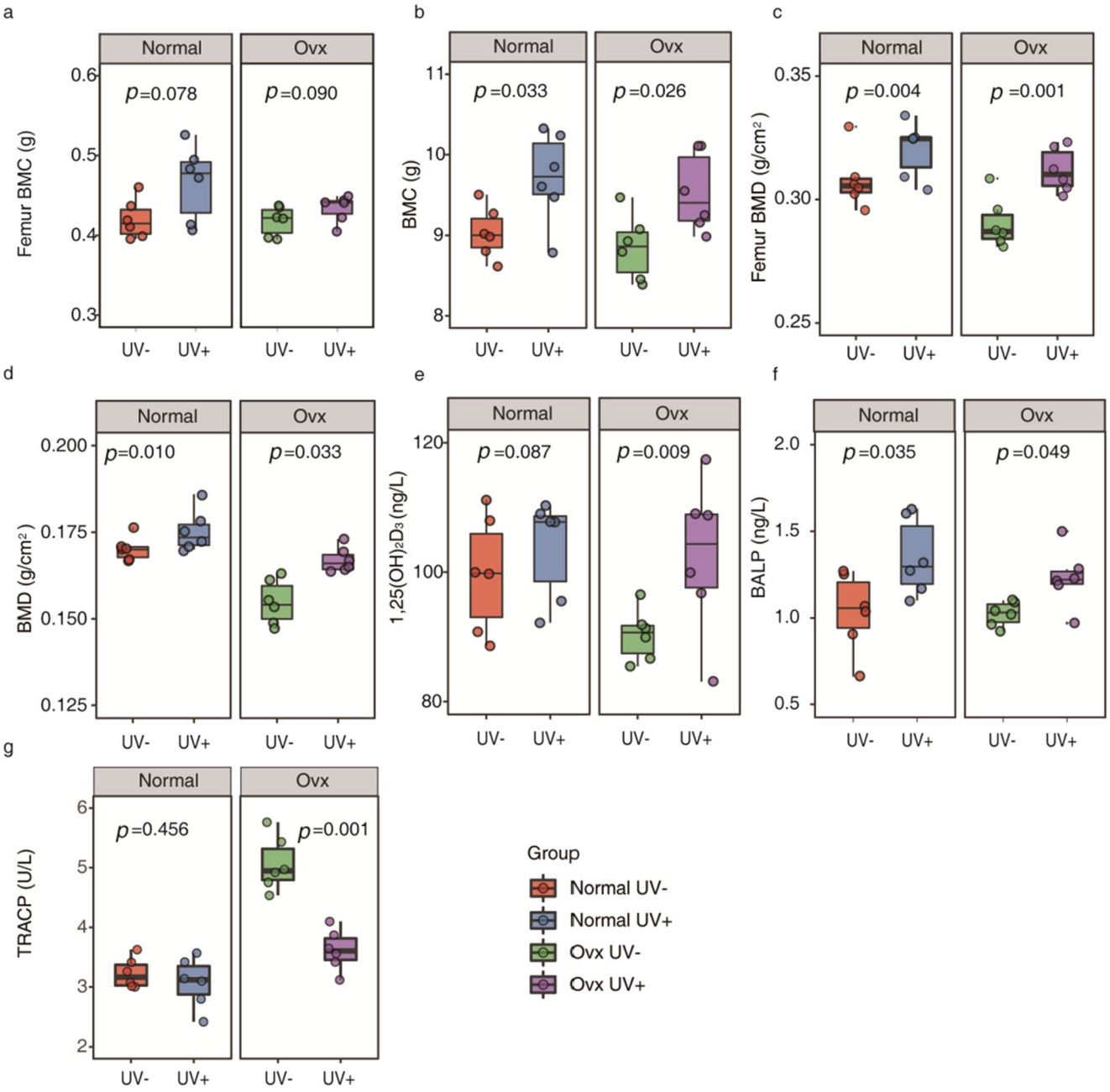

Fig. 1 Bone mass of the femur (**a**) and whole body (**b**) of rats. Bone mineral density of the femur (**c**) and whole body (**d**) of rats. Trabecular bone parameters were analyzed by mCT in the distal region of femurs from 12-week-old rats. **e** 1,25-Dihydroxyvitamin D3 (1,25-$(OH)_2$-D_3); **f** Bone alkaline phosphatase (BALP); **g** Tartrate-resistant acid phosphatase (TRACP). $p < 0.05$ indicate significant differences between conditioning treatments (two-sided Student's *t*-tests)

The results of serum bone metabolism marker assays are presented in Fig. 1. Concentrations of 1,25-$(OH)_2$-D_3 and BALP were significantly increased in both normal and ovariectomized rats after the UV supplementation ($p < 0.05$, Fig. 1e, f), suggesting that UV supplementation contributes to the increase in the concentration of bone formation markers in rats. The concentration of TRACP was decreased in normal ($p = 0.458$) and ovariectomized ($p = 0.001$) rats with bone loss (Fig. 1g), indicating that the UV supplementation decreased the bone absorption rate in rats.

Changes in microbial diversity after UV supplementation

Bacterial diversity within each sample was analyzed based on the Chao1 and the Shannon diversity index (Fig. 2, $n = 6$/group). For diversity and evenness estimates, we found a

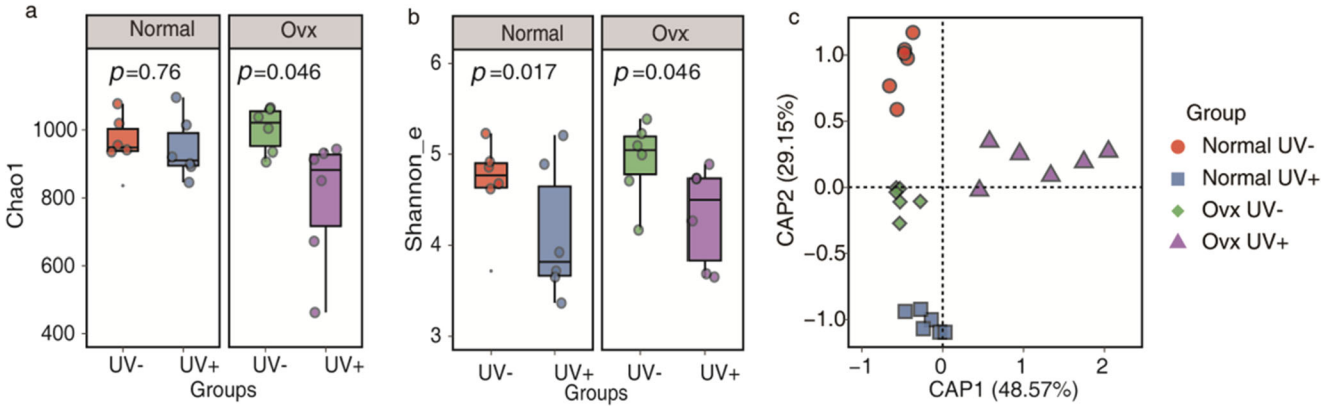

Fig. 2 **a** Chao1, **b** Shannon diversity, and **c** bacterial communities were constrained by four different surface types using distance-based redundancy analysis (DB-RDA). Significant differences among the types, based on Canberra taxonomic distances (p = 0.001 from permutational multivariate analysis of variation), were observed. $p < 0.05$ indicate significant differences between conditioning treatments (two-sided Student's t-tests)

marked rise in the UV+ samples compared to that in the UV- samples in both ovariectomized and normal rats ($p < 0.05$; Fig. 2a, b). The four groups of rats harbored significantly different communities based on permutational multivariate analysis of variance on Canberra distances ($p < 0.05$; Fig. 2c). Thus, UV supplementation had a markedly significant effect on the diversity of gut bacterial communities.

Correlation and network analysis

To dissect whether microbial communities were modulated by interactions between bacteria, we performed Spearman correlation analysis and observed both positive and negative microbial interactions. Although correlation analysis does not elucidate cause and effect, it reveals highly connected OTUs, regardless of their relative abundance. The network nodes were mostly *Firmicutes*, *Bacteroidetes*, and *Proteobacteria* (Fig. 3). Construction of correlation-based networks in each group resulted in four networks, consisting of 75, 81, 79, and 81 nodes connected by 213, 256, 225, and 592 edges, respectively (supplementary Table S1). Each network had a much higher number of strongly positive correlations than negative correlations. Furthermore, we found that the network of the Ovx UV+ group had a greater degree and was more modular but exhibited a lower average path length than the Ovx UV- network. However, network features in normal rats only exhibited a small change between UV+ and UV- treatments.

Taxonomic composition of the bacterial communities in rats

The bacterial community compositions in the normal (UV- and UV+) and ovariectomized (UV- and UV+) samples (n = 6/group) are shown in Fig. 4. In all samples, *Firmicutes*, *Saccharibacteria*, and *Bacteroidetes* were the three dominant phyla (Fig. 4a). The relative abundance of *Firmicutes* and *Saccharomycetes* showed an increase and a decrease, respectively, after the UV supplementation in both normal and ovariectomized rats, although these differences did not reach statistical significance (supplementary Fig. S3). The ratio of *Firmicutes* to *Bacteroidetes* showed a tendency to increase (supplementary Fig. S3e, $p > 0.05$). It is worth noting that *Proteobacteria* exhibited a significant decrease only in the ovariectomized rat group after UV supplementation (p = 0.025, supplementary Fig. S3d).

At the family level, *Ruminococcaceae*, *Lachnospiraceae*, and *Bacteroidales s24-7 group* are the three most significant bacterial families (Fig. 4b). After the UV supplementation, the relative abundance of most *Clostridiaceae_1*, *Desulfovibrionaceae* significantly decreased in ovariectomized rats ($p < 0.05$, supplementary Table S2), but normal rats did not exhibit significant changes (supplementary Table S3). At the genus level, three genera showed significant increases, and ten genera showed significant decreases in relative abundance in Ovx rats after the UV supplementation (Fig. 4c). However, only one genus (*Prevotella*) in the normal rats significantly decreased ($p < 0.05$, Fig. 4d). The effect of UV supplementation on the ovariectomized rats was generally greater than that in normal rats.

Gut bacteria function prediction

To understand the effect of UV supplementation on the function of the flora, the 16s sequencing data were used to predict gene function. After the UV supplementation, the intestinal flora function of normal rats did not change significantly (supplementary Fig. S4), while the intestinal flora function of ovariectomized rats did exhibit a significant change (Fig. 5, supplementary Table S4). Genes related to hematopoietic cell lineage, antigen processing and presentation, fatty acid biosynthesis, biosynthesis of

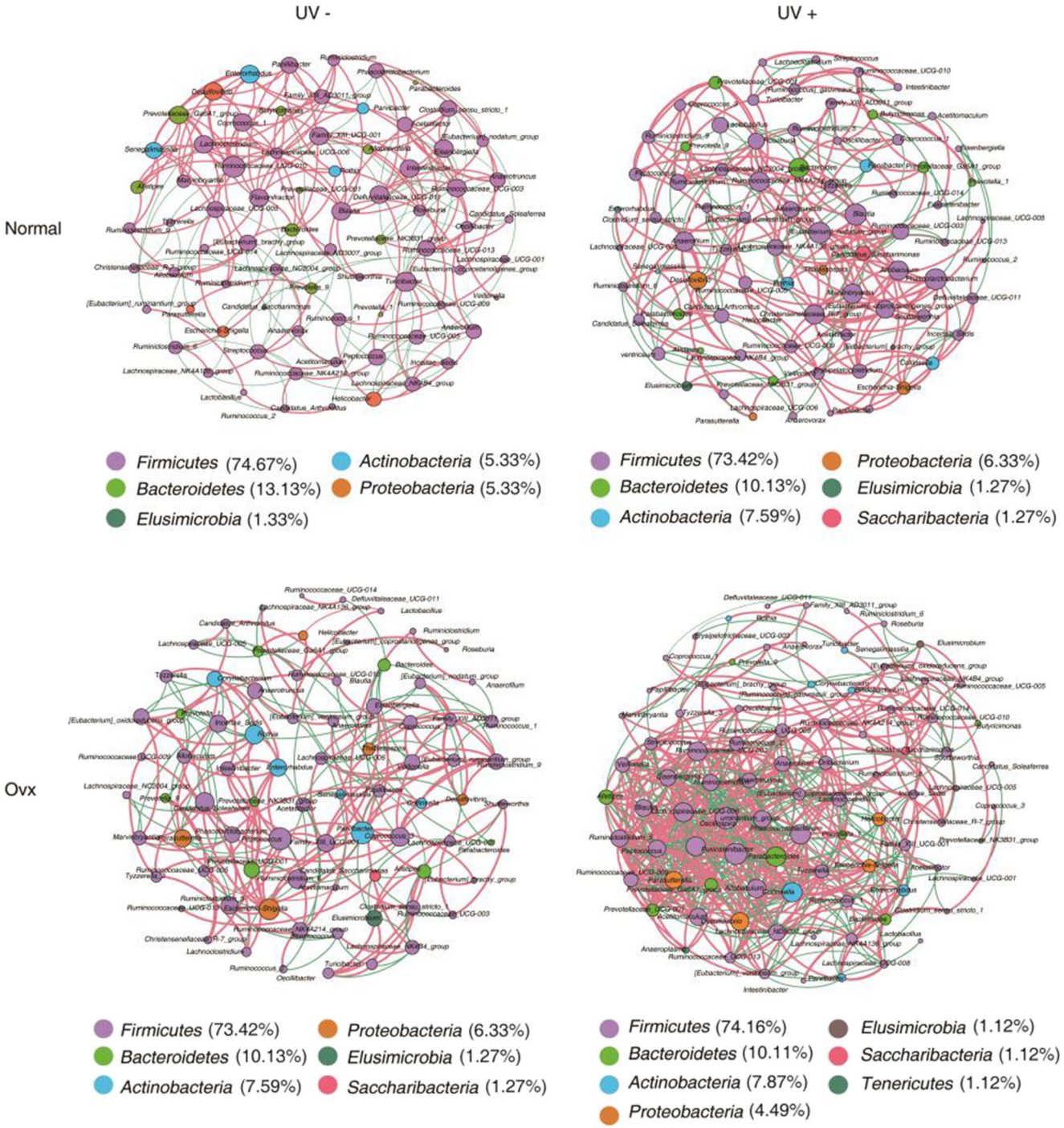

Fig. 3 Microbiome network. Nodes represent genera; node size represents connectivity; colors represent different phylum levels. Edges: red represents positive correlation, green represents negative correlation (Spearman, $|r| > 0.6$, $p < 0.05$)

unsaturated fatty acids, DNA replication homologous recombination, mismatch repair, nucleotide excision repair, lipopolysaccharide biosynthesis, and glycosaminoglycan biosynthesis—chondroitin sulfate/dermatan sulfate were significantly increased after UV irradiation. Among the gene functions noted above, the abundance of genes related to immune diseases, the immune system, lipid metabolism, glycan biosynthesis, and metabolism and replication and repair were significantly higher in the Ovx UV+ samples than in the Ovx UV- samples. However, tyrosine metabolism, pyruvate metabolism, methane metabolism, the bacterial secretion system, and bacterial chemotaxis were significantly decreased (Fig. 5). Based on the prediction of bacterial gene function, it is apparent that

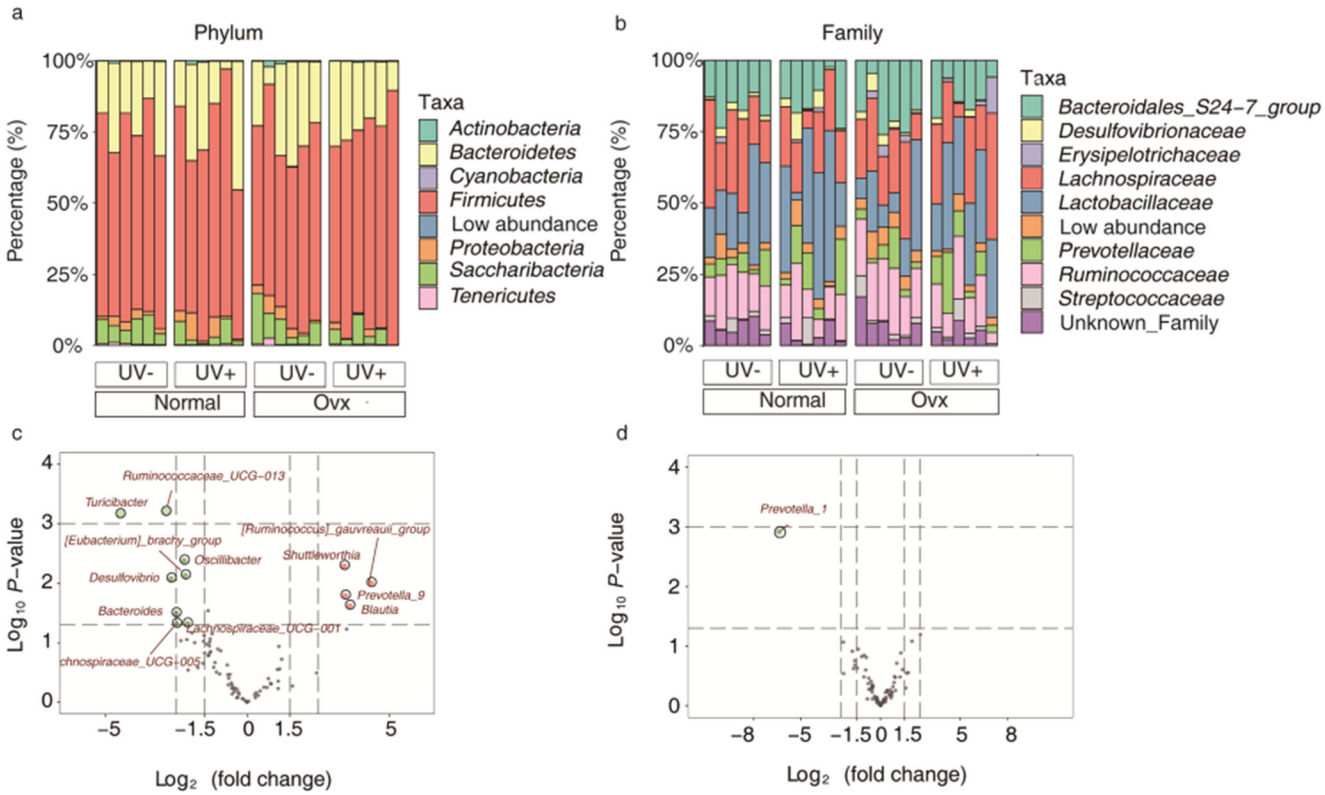

Fig. 4 Taxonomic composition of the bacterial communities at the phylum and family levels. **a** Relative abundances of the 7 most abundant phyla. **b** Relative abundances of the 8 most abundance families. **c** Significantly different genera in ovariectomized rats with and without UV supplementation ($p < 0.05$). **d** Significantly different genera in normal rats with and without UV supplementation ($p < 0.05$)

supplementation with UV light exerts an important influence on the bacterial gene function in ovariectomized rats.

Correlation analysis of microbial communities and indicators of bone

To explore the relationship between gut microbiota and host bone physiology, we conducted a Spearman correlation analysis. The 18 bacterial families, based on their relative abundance, exhibited some differences between the different treatment groups (Fig. 6). The BMC, Femur BMC, BMD, Femur BMD, and Tb.Th correlated negatively with *Ruminococcaceae*, *Bacteroidales*_S24.7_group, *Christensenellaceae*, *Streptococcaceae*, *Defluviitaleaceae*, and positively with *Lactobacillaceae*. The TRACP and Tb.N show opposite trends in relation to the above-mentioned bacterial families. These results suggest that gut bacteria may increase BMC and BMD by inhibiting bone resorption.

Discussion

Working and living under artificial lighting for long durations does not permit sufficient sunlight exposure, resulting in an adverse effect on bone. White LED light often lacks the ultraviolet band, which is known to be important to human bone health (Jou et al. 2019), previous studies have shown that long-term exposure to low-dose ultraviolet irradiation promotes bone metabolism (Guo et al. 2018). Meanwhile, there has been accumulating evidence that the gut microbiome is a key regulator of bone health (Hsu and Pacifici 2018; Yan et al. 2016, 2018). With the long-term goal of creating a "healthy light" for maintaining bone health and to elucidate the potential role of gut flora in the UV regulation of bone metabolism, in this study, we examined the effects of UV supplementation to white LED light on the intestinal flora and bone metabolism in rats, including ovariectomized rats as a bone loss model.

The UV supplementation not only enhanced the BMD in normal rats but also effectively prevented the bone loss induced by the decrease in estrogen in the ovariectomized groups (Fig. 1). This result is consistent with the findings of previous studies (Ho-Pham et al. 2013; Micić et al. 2013). We also found that UV supplementation can significantly increase the concentration of $1,25(OH)_2D_3$ and BALP in serum, indicating that UV promotes bone formation, which is also supported by a previous study (Morita et al. 2016). Interestingly, UV supplementation significantly increased the concentration of plasma TRACP, a major marker of bone resorption, in ovariectomized rats ($p = 0.001$), while there was no significant difference in normal rats ($p = 0.458$). These results indicate

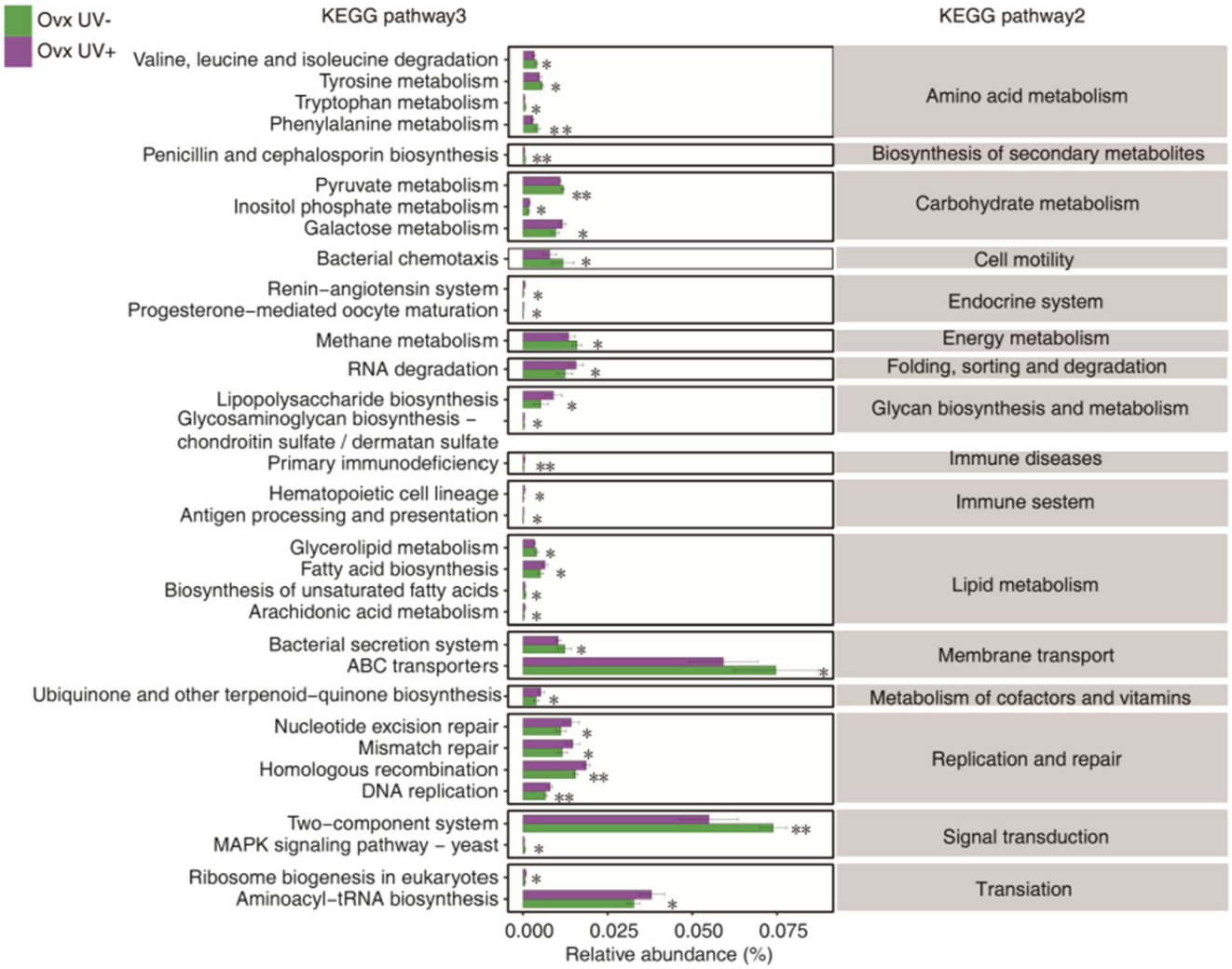

Fig. 5 Relative abundance of the KEGG tertiary pathways in ovariectomized group. The total number of KEGG pathways is displayed on the y-axis. Stars indicate significant differences between conditioning treatments. (Wilcox test, $*p < 0.05$; $**p < 0.01$; $***p < 0.001$)

that UV exposure may affect bone absorption in the ovariectomized and normal rats, possibly via different mechanisms and effects on rats in different states. Additional experiments will be necessary to reveal the specific mechanisms and efficacy UV supplementation light on bone.

UV supplementation significantly decreased the diversity and richness of intestinal flora in ovariectomized rats but had no significant effect on the richness of intestinal flora in normal rats (Fig. 2). In addition, UV supplementation significantly increased the modularity of the gut bacterial network in ovariectomized rats (Fig. 3). However, there was no significant effect on the gut flora network of normal rats after UV supplementation, indicating that the intestinal flora in ovariectomized rats was more sensitive to UV exposure, compared to that of normal rats. These results show that the effects of UV supplementation on the intestinal flora of ovariectomized rats were more significant than those in normal rats.

At the phylum level, the relative abundance of *Firmicutes* increased, while that of *Sacro bacteroides* decreased after UV supplementation in the Ovx group (supplementary Fig. S3). Numerous studies have shown that *Firmicutes* are actively related to bone metabolism and bone mass increase, due to enhanced calcium absorption (Ai et al. 2016; Dhama et al. 2016; Kasselman et al. 2018; Wu et al. 2015). However, some members of *Sacro bacteroides*, such as *Saccharibacteri* (TM7), have exhibited an important relationship with oral pathogens and can affect the body's immune function (Kuehbacher et al. 2008). Furthermore, UV supplementation significantly reduced the relative content of *Proteobacteria* in ovariectomized rats (supplementary Fig. S3d). *Proteobacteria* is positively associated with bone loss by causing inflammation in the intestines (Carvalho et al. 2012). The ratio of *Firmicutes* to *Bacteroidetes* gut microbiota is indicative of a dysregulation of various biological processes, such as maintenance of bone volume. As this ratio increases, intestinal

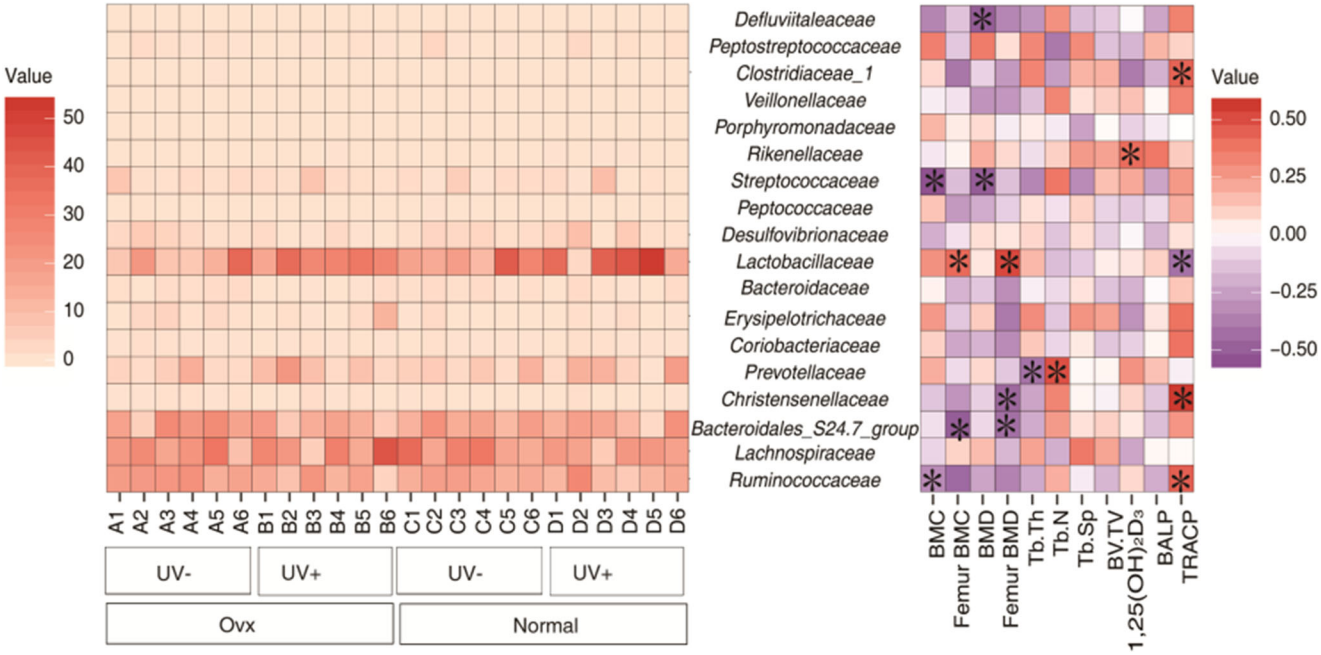

Fig. 6 Heatmap of the bacterial families (left) and Spearman correlation analysis between the bacterial families and indicators of bone (right) in the four samples. Stars indicate significant differences between conditioning treatments. (two-sided Student's *t*-tests, $*p < 0.05$; $**p < 0.01$; $***p < 0.001$)

permeability may be altered, leading to greater susceptibility to disease (David Yatsonsky et al. 2019). At the family level, the relative abundances of *Desulfovibrionaceae* and *Clostridiaceae* can cause intestinal inflammation (Babidge et al. 1998; Wagner et al. 1998); these were both significantly decreased only in the Ovx UV+ group. An animal study suggested that gut microbiota can regulate bone mass in mice by altering immune status in the bone and affecting osteoclast-mediated bone resorption (Sjögren et al. 2012). Thus, based on our results, UV supplementation may impart its effects on bone metabolism through mediating the intestinal flora.

To establish a role of intestinal flora in UV-improved bone metabolism, it is insufficient to only examine changes in the composition of the flora. Therefore, we further analyzed the mechanism of the effect of gut flora on bone metabolism in rats under UV supplementation conditions from a gene function perspective. Previous studies have demonstrated that functional genes of the bacterial community can be related to 16S rRNA marker genes, allowing the functional capacities of the gut microbiome to be surveyed using the 16S rRNA gene sequencing (Aßhauer et al. 2015). The UV irradiation did not significantly alter the microbiome function in normal rats (supplementary Fig. S4)., but strongly altered that of ovariectomized rats (Fig. 5). In particular, the relative content of fatty acid biosynthesis, antigen processing and presentation, glycosaminoglycan biosynthesis—chondroitin sulfate/dermatan sulfate genes in the intestinal flora of ovariectomized rats significantly increased. It has been shown that short-chain fatty acids, as an essential product of the fat synthesis pathway, indirectly regulate osteoclast activity by modulating the immune system, thus affecting the regulation of bone synthesis (Lucas et al. 2018). Bone metabolism is closely related to immune system activity, which can affect osteoclast activity through T cells (Grčević et al. 2000). In addition, chondroitin sulfate can promote chondroitin formation and reduce inflammation (McCarty et al. 2000; Ronca et al. 1998). Therefore, we speculate that the gut flora mediates UV-mediated improvements in bone metabolism in ovariectomized rats by affecting osteoclast activity by directly or indirectly affecting the immune system. The intestinal flora may also promote cartilage formation and reduce inflammation.

To further clarify the relationship between primary bacterial composition and indicators of bone, we performed correlation analysis between bacterial composition and indicators of bone (Fig. 6, supplementary Fig. S5). Most bacterial families are negatively correlated with BMC and BMD, especially the *Bacteroidales_S24.7_group* and *Streptococcaceae*. It has been shown that *Streptococcaceae* is related to osseous inflammation (Davidson et al. 2003). *Lactobacillaceae* was positively correlated with BMC and BMD, which is consistent with prior observations (Li et al. 2019). *Lactobacillaceae* also showed a negative correlation with the bone resorption marker, TRACP. These bacterial families are potential compositional targets involved in the UV improvement of bone metabolism.

In summary, our present study shows that UV supplementation to white LED exposure changes the structure and function of intestinal flora in a rat model of bone loss. By

increasing the synthesis of short-chain fatty acids and affecting immunomodulatory, intestinal flora directly or indirectly regulate the activity of osteoclasts and thus mediates UV-mediated improvements in bone metabolism. However, the composition and function of the intestinal flora in normal rats did not apparently change after UV supplementation. Our findings open new avenues for the protection of bone health in individuals who work under artificial lighting for extended durations and provide a theoretical basis for the prevention and treatment of bone loss by combining ultraviolet radiation supplementation with intestinal probiotics. The detailed molecular mechanisms by which supplementation with UV affects bone metabolism through intestinal flora warrants further exploration.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00253-021-11282-2.

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Availability of data and material The data that support the findings of this study are openly available in the NCBI SRA repository, reference number PRJNA671564.

Author contribution JC and YF conceived and designed research. JC conducted experiments. JC, ZY, and CD analyzed data. YF and HL guided most experiments. JC and YF wrote the manuscript. All authors read and approved the manuscript.

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Declarations

Ethics approval All animal experiments were performed with approval by the Science and Ethics Committee of the School of Beihang University (Approval ID: BM20180003).

Consent to participate Not applicable.

Consent for publication Not applicable.

Conflict of interest The authors declare no competing interests.

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