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Differential expressions of biomarkers in gingival crevicular fluid of Han and Uygur populations with peri-implantitis

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Abstract

This study aims to investigate and compare the biomarkers in the gingival crevicular fluid between the Han and Uygur subjects with healthy implants and peri-implantitis.

Totally 80 subjects were divided into the H-case (Han patients with peri-implantitis), U-case (Uygur patients with peri-implantitis), H-control (Han subjects with healthy implants), and U-control (Uygur subjects with healthy implants) groups. Cytokine levels in the gingival crevicular fluid were detected, and the dominant bacteria species were analyzed.

The matrix metalloproteinase (MMP)-13 level in the gingival crevicular fluid in the U-control group was significantly higher than the H-control group, whereas the C-reactive protein level in the H-control group was significantly higher than in the U-control group. No significant difference was observed in the dominant subgingival bacteria species between the H- and U-control groups. The levels of interleukin (IL)-1β and MMP-8 were significantly higher in the H-case group than the U-case group, whereas the IL-17A level in the U-case group was significantly higher. The shared dominant subgingival bacteria species of the case groups mainly included *Prevotella*, *clostridium*, *Porphyromonas*, *treponema*, *Streptococcus*, *neisseria*, and *hemophilus*. Moreover, *Acinetobacter*, *Micrococcus*, and *Moraxella* were found to be the specific dominant subgingival bacteria species for the U-case group. In addition, compared with the H-case group, the IL-1β levels were negatively correlated with *Acinetobacter*, *Micrococcus*, and *Moraxella* in the U-case group.

Han and Uygur populations with healthy implants and peri-implantitis have differentially expressed cytokines in the gingival crevicular fluid. Moreover, dominant subgingival bacteria species differ between the Han and Uygur populations with peri-implantitis.

Abbreviations: BOP = bleeding of probing, CRP = C-reactive protein, IL = interleukin, MMPs = matrix metalloproteinases, PPD = periodontal pocket depth.

Keywords: biomarkers, gingival crevicular fluid, Han and Uygur populations, healthy implants, peri-implantitis

1. Introduction

Peri-implantitis is a kind of chronic progressive inflammation, which occurs in the soft and/or hard tissues surrounding the functional osseointegrated implants. Peri-implantitis might induce the loss of alveolar bone and lead to the formation of peri-implant pocket.[1] After the complete absorption of the osseointegration region, the implants would become loose, which would possibly result in the implantation failure. At present, routine periodontal examination and X-ray detection can only served for the disease severity determination, rather than predict or reflect the whole pathogenic process. However, monitoring and detection of the biomarkers in the gingival crevicular fluid of the patients with peri-implantitis would contribute to the prediction of the disease activity.[2,3] Biomarkers in the gingival crevicular fluid, saliva, and serum could also help to evaluate the normal biological processes and disease pathogenesis, as well as the responses to drug treatment.

There are several kinds of biomarkers, which are associated with peri-implantitis. Detection of proteomics biomarkers could intuitively and accurately determine the survival of oral microbes and their responses to the environment changes, including the osteocalcin, alkaline phosphatase, matrix metalloproteinases (MMPs), and C-reactive protein (CRP).[4–8] Moreover, genetic biomarkers have been shown to be associated with the pathogenesis of peri-implantitis, including the interleukin (IL), prostaglandin E2, CD14, lipopolyssacharide receptors, and osteoprotegerin.[9–16] Furthermore, there are numerous microbial biomarkers. More than 600 species of bacteria have been detected and identified in the subgingival plaques, although a relative minority of them has been related to the induction of peri-implantitis. Currently, it has been widely accepted that the pathogenic process for peri-implantitis is similar to that for the periodontal disease, especially in terms of the involved pathogenic bacteria. Based on the clustering characteristics and the relationship with the periodontal status, these subgingival bacteria could be divided into 6 main microbial complexes,

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designated as red, orange, yellow, green, purple, and blue, respectively. However, as claimed by the report from the European Society of Periodontology, current studies of peri-implantitis-associated microbes have mainly focused on the periodontal pathogens, and the activities and effects of potential pathogenic microbes relatively unimportant for the periodontal diseases might be ignored or underestimated. It has been shown that, compared with the healthy implants, many strains of bacteria are significantly increased in the peri-implantitis cases.[17] Importantly, detection of marker packages, that is, the combination of multiple indicators, is characterized by high accuracy, which can be used as effective detection and prediction tool for peri-implantitis.

Xinjiang, China, is well known as the living region for the minorities, where Han and Uygur populations represent the main residents. There are significant differences in the ethnic origin, living habits, and religious believes between the Han and Uygur populations. Moreover, significant differences have been found in the clinical disease incidence and biomarker expression levels between these 2 populations. In this study, the biomarkers in the gingival crevicular fluid associated with the healthy implants and peri-implantitis for the Han and Uygur subjects were investigated and compared.

2. Materials and methods

2.1. Study subjects and grouping

Totally 105 samples of gingival crevicular fluid of patients with healthy implants and peri-implantitis were included in this study, who were admitted to the Fifth Affiliated Hospital of Xinjiang Medical University, the Second Affiliated Hospital of Xinjiang Medical University, the Urumqi Stomatological Hospital, and three other minority clinics (including the Aizezi Oral Clinic). All the study subjects receive dental implantation, from 2013 to 2016, with at least 1 implant for over half a year. According to the Guidelines for Periodontal Disease in the United States, peri-implantitis was defined as bleeding of probing (BOP) and/or periodontal pocket depth (PPD), accompanied by bone tissue loss below the first thread of the implant.[18] Exclusion criteria were as follows: patients with systematic diseases; patients who accepted periodontal therapy, or received immunosuppressive agents and antibiotics, within 6 m; patients who received long-term contraceptives; and pregnant women, or smokers. Previous written and informed consents were obtained from every patient and the study was approved by the local ethics review board.

These subjects were divided into the following 4 groups: the H-case group contained 20 cases of Han subjects with peri-implantitis; the U-case group contained 20 cases of Uygur subjects with peri-implantitis; the H-control group contained 20 cases of Han subjects with healthy implants; and the U-control group contained 20 cases of Uygur subjects with healthy implants.

2.2. Sample collection

After gargling, the sampling site within the patient's mouth was gently wiped with the sterile cotton. Sterile absorbent paper tip (the sharp tip was cut off) was softly inserted into the gingival sulcus around the implant. There were totally 6 sampling points for each case, including the proximal, middle, and distal points on the buccal and tongue (palate) sides, respectively. After 30 seconds, the paper tip with the gingival crevicular fluid was taken out (with no blood or pus), and immediately placed in the frozen tube and stored at −80°C.

2.3. Cytokine detection

Cytokines in the gingival crevicular fluid were detected with the ProcartaPlex TM Multiplex Immunoassay. Briefly, 50 μL of microsphere mix solution was put into each well in the 96-well detection kit. After 30 minutes, the solution was discarded. Following washing, 30-μL Universal Assay Buffer + 20-μL standard or sample were added. The kit was sealed and incubated with vibration at room temperature for 2 hours. After unsealing, the 96-well kit was placed on the magnetic separation plate for 3 minutes, and the solution within each well was discarded. Following washing, 25-μL biotin-labeled detection antibody was added into each well for 30 minutes. The 96-well kit was again placed on the magnetic separator for 3 minutes, and the solution was discarded. After washing, 50-μl Streptavidin-PE was added into each well, followed by incubation with vibration at room temperature for 30 minutes. The 96-well kit was again placed on the magnetic separator for 3 minutes, and the solution was discarded. After washing, 100-μL Reading Buffer was added into each well, followed by vibration at room temperature for 5 minutes and then detection.

2.4. Bacterial diversity monitoring

Genomic DNA was extracted with the DNA extraction kit. Bacterial diversity identification was performed based on the 16S V3-V4 region (primers 343F and 798R). For the purification, PCR products were analyzed by electrophoresis, and mixed according to the sample products, which were then sequenced. The 16S rRNA gene clone library was constructed.

2.5. Statistical analysis

Cytokine detection results were analyzed using the ProcartaPlex Analyst 1.0 analysis software. The spearman statistical method was used for statistical analysis. Subgingival bacterial diversity were determined with the UPARSE software, and classified into multiple operational taxonomic units (OTUs) based on the sequence similarity (no $<97\%$). Representative OUT sequences were picked out with the QIIME software package, which were compared against the databases and annotated. The 16S rRNA gene clone library was compared against the Greengenes or Silva (Version 123) databases. Species comparison and annotation were performed using the RDP classifier software, and the annotation results with the confidence interval >0.7 were preserved.

3. Results

3.1. Baseline characteristics of study subjects

Basic information of these subjects was shown in Table 1. Totally 80 subjects were included in this study, 43 males (53.8%) and 37 females (46.3%), with the average age of 44.1 years. In details, the average ages for the Han and Uygur subjects were 45.9 and 42.4 years, respectively, with no significant difference between these 2 populations. Moreover, there was no significant difference in the male/female rate between these 2 populations. Male subjects accounted for 50% (20) and 58% (23) in the Han and Uygur populations, respectively. Significant differences were observed in the PPD between the H-control (2.83 mm) and

Table 1

Basic information of study subjects.

	Han		Uygur	
	H-control	H-case	U-control	U-case
Age, y	45.9		42.4	
	44.4	47.3	39.6	45.2
Sex	43 Males (53.8%) and 37 females (46.3%)			
	20 Males (50%)		23 Males (58%)	
PPD, mm	2.83	5.55	2.71	5.08
BOP (+)	2 (10%)	17 (85)	1 (5%)	20 (100%)

BOP = bleeding of probing, PPD = periodontal pocket depth

H-case (5.55 mm) groups ($P < .01$), as well as between the U-control (2.71 mm) and U-case (5.08 mm) groups ($P < .01$), rather than between the H-control and U-control groups, or between the H-case and U-case groups. Moreover, significant differences were observed in the BOP incidence between the H-control (10%) and H-case (85%) groups, as well as between the U-control (5%) and U-case (100%) groups, rather than between the H-control and U-control groups, or between the H-case and U-case groups (Table 1). These results suggest that no significant differences are observed in the age and sex ratio between the Han and Uygur populations, and no significant differences are observed in the clinical indicators for the healthy implants and peri-implantitis between these 2 populations.

3.2. Evaluation and comparison of cytokine levels in gingival crevicular fluid between Han and Uygur populations

The cytokine contents in the gingival crevicular fluid were investigated and compared between the Han and Uygur populations, with healthy implants and peri-implantitis, respectively. For the subjects with healthy implants, our results showed that the MMP-13 level in the U-control group (169 pg/ml) was significantly higher than the H-control group (166 pg/ml) group, whereas the CRP level in the H-control group (189 pg/mL) was significantly higher than the U-control group (175.1 pg/mL). However, no significant differences were observed in the IL-1β (161.1 vs. 83.03 pg/mL), soluble receptor activator of nuclear factor-kappa B ligand (36.69 vs. 35.47 pg/mL), MMP-8 (19707 vs. 18029 pg/mL), or IL-17A (23.59 vs. 24.93 pg/mL), between the H-control and U-control groups, respectively (Table 2). These results suggest that higher levels of MMP-13 are observed in the gingival crevicular fluid for the Uygur subjects with healthy implants, whereas higher levels of CRP are observed for the Han subjects with healthy implants.

On the contrary, for the subjects with peri-implantitis, our results showed that higher levels of IL-1β (274.9 pg/ml) and MMP-8 (34035 pg/mL) were observed in the H-case group compared with the U-case group (145.6 pg/mL IL-1β, and 22035 pg/mL MMP-8) (both $P < .01$), whereas the IL-17A level in the U-case group (21.44 pg/mL) was significantly higher than the H-case group (19.81 pg/mL) (Table 3). These results suggest that higher levels of IL-1β and MMP-8 are observed in the gingival crevicular fluid for the Han subjects with peri-implantitis, whereas higher levels of IL-17A are observed for the Uygur subjects with peri-implantitis.

3.3. Analysis of dominant subgingival bacteria of Han and Uygur populations

The dominant subgingival bacteria were next investigated and compared between the Han and Uygur populations, with healthy implants and peri-implantitis, respectively. For the subjects with healthy implants, as shown in Figure 1, the dominant subgingival bacteria (>1%) in the H-control group mainly included *neisseria* (11.807%), *Prevotella* (8.015%), *Streptococcus* (6.596%), *Clostridium* (5.609%), *Hemophilus* (4.155%), *Treponema* (3.514%), *Porphyromonas* (3.187%), *Vibrio* (2.831%), *Leptothrix* (2.250%), and *Actinobacillus actinomycetem comitans* (1.837%). The dominant subgingival bacteria species (>1%) in the U-control group mainly included *Neisseria* (8.208%), *Hemophilus* (7.943%), *Streptococcus* (7.475%), *Vibrio* (6.732%), *Prevotella* (4.399%), *Clostridium* (3.600%), *Porphyromonas* (3.453%), *Actinobacillus actinomycetem comitans* (2.576%), *Leptothrix* (2.070%), and *Treponema* (1.981%). These results suggest that no significant difference is observed in

Table 2

Analysis of Han and Uygur subjects with healthy implants.

	H-control				W-control				
Biomarker	Mean (SD)	Q1	Q2	Q3	Mean (SD)	Q1	Q2	Q3	*P*
IL-1β, pg/mL	161.1	57.54	111.9	274.4	83.03	52.45	80.94	138.4	0.4407
sRANKL, pg/mL	36.69	17.12	51.45	75.49	35.47	34.65	41.9	72.81	0.4407
MMP-8, pg/mL	19707	5460	21064	28594	18029	10798	16404	29528	0.4196
MMP-13, pg/mL	166	174.1	286.8	464.1	169	150.6	207.2	252.7	0.0382*
CRP, pg/mL	189	37.5	101.5	394.3	175.1	23.76	48.44	109	0.0493*
IL-17A, pg/mL	23.59	27.64	41.33	58.34	24.93	27.64	32.59	50.39	0.2649

Q1, 25th percentile; Q2, median; and Q3, 75th percentile. CRP = C-reactive protein, IL = interleukin, MMP = matrix metalloproteinase, SD = standard deviation.
* $P < .05$.

Table 3

Analysis of Han and Uygur subjects with peri-implantitis.

	H-case				W-case				
Biomarker	**Mean (SD)**	**Q1**	**Q2**	**Q3**	**Mean (SD)**	**Q1**	**Q2**	**Q3**	***P***
IL-1β, pg/mL	274.92	145.64	252.13	473.25	145.56	36.86	109.72	169.26	0.0008*
sRANKL, pg/mL	41.86	28.53	48.45	89.88	34.87	43.54	67.60	97.01	0.2076
MMP-8, pg/mL	34034.53	22715.94	47481.91	73046.88	22034.57	7421.06	21401	39302.72	0.0051**
MMP-13, pg/mL	226.37	175.34	258.05	482.70	162.34	298.07	343.42	396.46	0.1366
CRP, pg/mL	386.98	53.36	157.99	488.64	1121.07	69.96	268.68	684.89	0.3104
IL-17A, (pg/mL	19.81	34.09	41.33	57.79	21.44	39.2	57.76	75.35	0.0898

Q1, 25th percentile; Q2, median; and Q3, 75th percentile. CRP = C-reactive protein, IL = interleukin, MMP = matrix metalloproteinase, SD = standard deviation.

* $P < .002$.

** $P < .05$.

the dominant subgingival bacteria species between the Han and Uygur subjects with healthy implants.

On the contrary, for the subjects with peri-implantitis, as shown in Figure 2, the dominant subgingival bacteria (> 1%) in the H-case group mainly included *Prevotella* (10.625%), *Clostridium* (8.467%), *Porphyromonas* (6.763%), *treponema* (5.345%), *Streptococcus* (4.824%), *Neisseria* (3.594%), *Hemophilus* (3.284%), *Rothia* (3.007%), *Leptothrix* (2.033%), and *Campylobacter* (1.790%). The dominant subgingival bacteria (>1%) in the U-case group mainly included *Streptococcus* (8.007%), *Clostridium* (6.207%), *Acinetobacter* (5.911%), *Neisseria* (5.458%), *Porphyromonas* (5.345%), *Prevotella* (4.210%), *Treponema* (3.534%), *Micrococcus* (3.023%), *Moraxella* (2.100%), and *Hemophilus* (1.841%). These results suggest that significant differences are observed in the following dominant subgingival bacteria species between the Han and Uygur subjects with peri-implantitis: *Rothia*, *Leptothrix*, *Campylobacter*, *Acinetobacter*, *Micrococcus*, and *Moraxella*.

3.4. Correlation analysis between cytokines and dominant subgingival bacteria of Han and Uygur populations

According to the cytokine measurement and dominant subgingival bacteria detection results, correlation analysis was performed (correlation coefficient greater than 0.3 was considered to be correlated). As shown in Table 4, for the subjects with

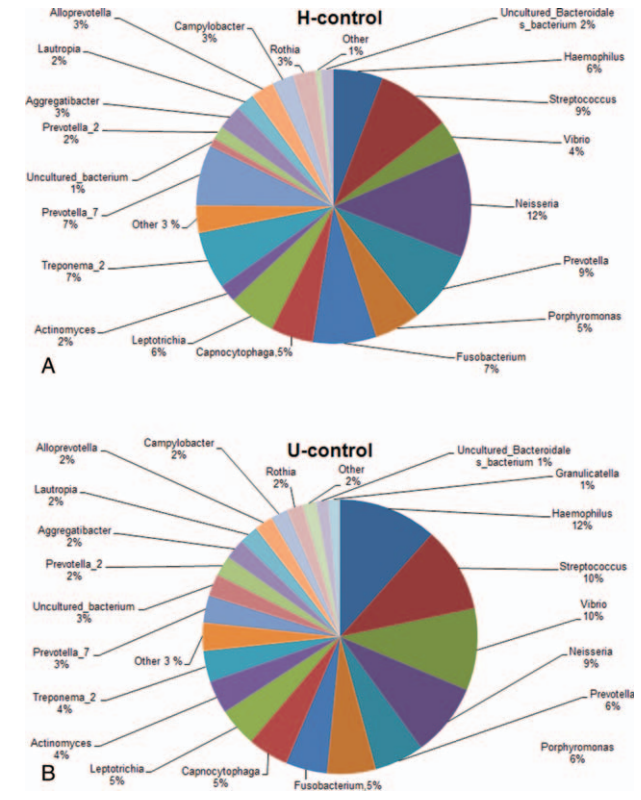

Figure 1. Relative bacterial abundance in the gingival crevicular fluid of the Han and Uygur subjects with healthy implants. (A) Han subjects with healthy implants (H-control group). (B) Uygur subjects with healthy implants (U-control group).

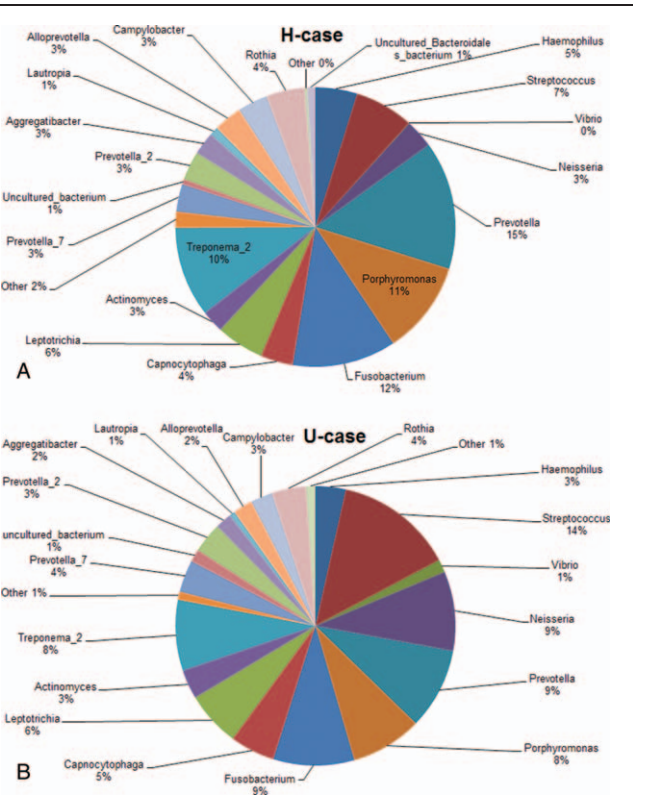

Figure 2. Relative bacterial abundance in the gingival crevicular fluid of the Han and Uygur subjects with peri-implantitis. (A) Han subjects with healthy implants (H-case group). (B) Uygur subjects with healthy implants (U-case group).

Table 4

Correlation analysis.

Gene	Species	Genus	Cor	*P*
H.CRP	*g_kocuria*	*Kocuria*	0.539351668	.000329105
H.CRP	*g_acinetobacter*	*Acinetobacter*	0.470962443	.002160804
H.CRP	*g_micrococcus*	*Micrococcus*	0.3736316	.01755633
H.CRP	*g_brevundimonas*	*Brevundimonas*	0.363339303	.021195964
H.CRP	*g_bacillus*	*Bacillus*	0.362174075	.021645138
H.CRP	*g_chryseobacterium*	*Chryseobacterium*	0.348939818	.027328796
H.CRP	*g_vibrio*	*Vibrio*	0.333474728	.035482314
H.IL.17A	*g_vibrio*	*Vibrio*	0.321454314	.043111981
H.MMP.8	*g_H-case exiguobacterium*	*Exiguobacterium*	−0.31221612	.049838013
H.CRP	*g_selenomonas_3*	*Selenomonas*	−0.315336328	.047477826
H.IL.1beta	*g_vibrio*	*Vibrio*	−0.323420686	.041780024
H.MMP.8	*g_gemella*	*Gamella*	−0.3315197	.036641855
H.IL.1beta	*g_bacillus*	*Bacillus*	−0.336539057	.033725423
H.MMP.8	*g_stomatobaculum*	*Oral Bacillus*	−0.343263726	.030119385
H.MMP.13	*g_peptostreptococcus*	*Peptostreptococcus*	−0.344873638	.029305017
H.IL.1beta	*g_moraxella*	*Moraxella*	−0.384563051	.014281322
H.MMP.8	*g_chryseobacterium*	*Chryseobacterium*	−0.426898893	.006011117
H.IL.1beta	*g_kocuria*	*Kocuria*	−0.429192309	.005717793
H.IL.1beta	*g_acinetobacter*	*Acinetobacter*	−0.437172272	.004791533
H.IL.1beta	*g_stomatobaculum*	*Oral Bacillus*	−0.448883334	.00366866
H.IL.1beta	*g_brevundimonas*	*brevundimonas*	−0.480179901	.001714259
H.IL.1beta	*g_gemella*	*Gamella*	−0.495121951	.001161645
H.IL.1beta	*g_exiguobacterium*	*Exiguobacterium*	−0.55116853	.000227954
H.IL.1beta	*g_micrococcus*	*Micrococcus*	−0.589047865	.0000637
H.IL.1beta	*g_chryseobacterium*	*Chryseobacterium*	−0.603036376	.0000382

Cor = correlation coefficient. Cor >0, positive correlation; and Cor <0, negative correlation.

healthy implants, the MMP-13 level was negatively correlated with the *Peptostreptococcus*, while the CRP level was positively correlated with the *Kocuria*, *Acinetobacter*, *Micrococcus*, *Brevundimonas*, *Bacillus*, *Chryseobacterium*, and *Vibrio*, respectively. However, for the subjects with peri-implantitis, the MMP-8 level was negatively correlated with the *Exiguobacterium*, *Gamella*, *Oral Bacillus*, and *Chryseobacterium*, respectively, and the IL-1β level was negatively correlated with the *Vibrio*, *Bacillus*, *Moraxella*, *Kocuria*, *Acinetobacter*, *Oral Bacillus*, *brevundimonas*, *Gamella*, *Exiguobacterium*, *Micrococcus*, and *Chryseobacterium*. However, the IL-17A level was positively correlated with the *Vibrio*. Taken together, these results suggest that, compared with the Han subjects with peri-implantitis, the IL-1β level is negatively correlated with the *Moraxella*, *Acinetobacter*, and *Micrococcus*, respectively, for the Uygur subjects with peri-implantitis.

4. Discussion

In the process of human evolution, owing to genetic drift in populations of different races and regions, the genetic structure has been gradually changing, leading to differential gene frequency distribution and different susceptibility genes.[19] Currently, majority of the studies concerning the peri-implantitis have been focusing on the Caucasian race. Xinjiang, China, is one of the most typical regions of multi-ethnic settlement, among which the Han and Uygur populations account for a considerable proportion. Zhao et al[20] have shown that the Uygur people is the descendants of Turks, with both the descent from white people and the genetic characteristics from the Oriental Mongolian, whereas the Han population belongs to the Mongolian race. In the present study, our results showed that there were some differences in the gene expression associated with peri-implantitis between the 2 populations with different race origins.

MMP-13 has been shown to be present in the tissues with periapical disease,[21] which is generally less expressed in normal adult tissues.[18] Recker et al[4] have shown that there is no significant difference in the CRP contents in the gingival crevicular fluid between from the implants and natural teeth. It has been shown that MMP-13 and CRP are present in the normal oral tissues. In this study, our results showed that the contents of MMP-13 and CRP were among the normal ranges in the healthy implants, whereas they were differentially expressed between the Han and Uygur populations. Significant higher level of MMP-13 was observed in the gingival crevicular fluid for the Uygur subjects with healthy implants, whereas CRP was highly expressed in the Han subjects with healthy implants. However, Siamak et al[22] have found that the incidence of peri-implantitis is increased along with the increasing IL-β content in the gingival crevicular fluid. Moreover, Christoph et al[23] have shown that the elevated contents of IL-β and MMP-8 are closely related to the pathogenesis of periodontitis and peri-implantitis. Emilia et al[24] have demonstrated that the increased level of MMP-8 in the gingival crevicular fluid is closely associated with the development of peri-implantitis. Furthermore, Arakawa et al[25] have shown that MMP-8 is the most important collagenase in the gingival crevicular fluid in the active phase of bone destruction. Mahdi et al[26] have shown that, compared with the subjects with healthy implants, the serum IL-17 levels were significantly higher for the patients with peri-implantitis or chronic periodontal diseases. Severino et al[27] have suggested that IL-17 is closely associated with the pathogenesis of peripheral mucositis and peri-implantitis. These findings are in

line with our results. Compare with the Han and Uygur subjects with healthy implants, the contents of IL-β, MMP-8, and L-17 in the gingival crevicular fluid were significantly higher than the patients with peri-implantitis. Moreover, our results showed that, compared with the U-case group, the IL-1β and MMP8 level were significantly higher in the H-case group, whereas the IL-17A level in the U-case group was significantly higher than the H-case group. These results suggest that these three cytokines are differentially expressed between these 2 populations. Furthermore, our results showed no significant difference in the dominant subgingival bacteria between the H-control and U-control groups. However, the H-case and U-case groups shared the following dominant subgingival bacteria: *Prevotella*, *clostridium*, *Porphyromonas*, *treponema*, *Streptococcus*, *neisseria*, and *hemophilus*. These findings were in line with the common pathogenic bacteria for peri-implantitis.[28] In addition to this, the following specific dominant subgingival bacteria were observed for the U-case group: *Acinetobacter*, *Micrococcus*, and *Moraxella*. In these specific dominant subgingival bacteria species, *Acinetobacter* is a kind of Gram-negative bacteria which is usually found in the human tissues such as skid, respiratory tract, digestive tract, and genitourinary tract. It can be a conditional pathogen for those with low immunity and has certain resistance to immunosuppression. *Acinetobacter* has been commonly reported in the respiratory tract infection, but rarely seen in the pathogenesis of peri-implantitis. *Micrococcus* is a kind of Gram-positive *cocci* commonly parasitic in the human skin and throat, which is conditional pathogen usually observed in the open fracture infection in clinic.[29] The Gram-negative *Moraxella* induces infantile ear infection, which is also the main cause of heart disease in children. In recent years, *Moraxella* has been reported as pathogen for child caries. These bacteria species have been rarely seen in the reports of peri-implantitis. Further in-depth studies are still needed to investigate their roles in the pathogenesis of peri-implantitis in the Uygur population.

Correlation analysis between cytokines and dominant subgingival bacteria of Han and Uygur populations showed that, compared with the H-case group, the IL-1β level is negatively correlated with the *Moraxella*, *Acinetobacter*, and *Micrococcus* in the U-case group. These results suggest that along with the increasing IL-1β in the gingival crevicular fluid, the growth of these correlated bacteria species would be inhibited. Further in-depth studies are still needed to clarify the related mechanisms.

In conclusion, our results showed that the Han and Uygur populations with healthy implants and peri-implantitis had differentially expressed cytokines in the gingival crevicular fluid. Moreover, dominant subgingival bacteria differed between the Han and Uygur populations with peri-implantitis. Compared with the Han subjects with peri-implantitis, the IL-1β levels were negatively correlated with *Acinetobacter*, *Micrococcus*, and *Moraxella* in the Uygur subjects with peri-implantitis. These findings might contribute to the understanding of the pathogenesis of peri-implantitis and the disease treatment in the Uygur population in clinic.

Author contributions

Data curation: Lin Wang.
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Investigation: Yue Sun.
Methodology: Xiaowei Gao.
Software: Xiaowei Gao.
Supervision: Yanmin Zhou.
Writing – original draft: Xiaowei Gao.
Writing – review & editing: Yanmin Zhou.

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