The Influence of Smoking on the Peri-Implant Microbiome

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A.A. Tsigarida^{1,2}, S.M. Dabdoub², H.N. Nagaraja³, and P.S. Kumar²

Abstract

Smokers are at high risk for 2 bacterially driven oral diseases: peri-implant mucositis and peri-implantitis. Therefore, the purpose of this investigation was to use a deep-sequencing approach to identify the effect of smoking on the peri-implant microbiome in states of health and disease. Peri-implant biofilm samples were collected from 80 partially edentulous subjects with peri-implant health, peri-implant mucositis, and peri-implantitis. Bacterial DNA was isolated and 16S ribosomal RNA gene libraries sequenced using 454-pyrosequencing targeting the V1 to V3 and V7 to V9 regions. In total, 790,692 classifiable sequences were compared against the HOMD database for bacterial identification. Community-level comparisons were carried out using UniFrac and nonparametric tests. Microbial signatures of health in smokers exhibited lower diversity compared to nonsmokers, with significant enrichment for disease-associated species. Shifts from health to mucositis were accompanied by loss of several health-associated species, leading to a further decrease in diversity. Peri-implantitis did not differ significantly from mucositis in species richness or evenness. In nonsmokers, by contrast, the shift from health to mucositis resembled primary ecological succession, with acquisition of several species without replacement of pioneer organisms, thereby creating a significant increase in diversity. Again, few differences were detected between peri-implantitis and mucositis. Thus, our data suggest that smoking shapes the peri-implant microbiomes even in states of clinical health, by supporting a pathogen-rich community. In both smokers and nonsmokers, peri-implant mucositis appears to be a pivotal event in disease progression, creating high-at-risk-for-harm communities. However, ecological succession follows distinctly divergent pathways in smokers and nonsmokers, indicating a need for personalized therapeutics for control and prevention of disease in these 2 cohorts.

Keywords: high-throughput nucleotide sequencing, peri-implantitis, 16S ribosomal RNA, tobacco, biofilms, microbiota

Introduction

According to the Centers for Disease Control and Prevention (2012), nearly 44 million people in the United States are current smokers. Considering that heavy smokers are nearly 7 times more prone to tooth loss (Mai et al. 2013), increasing numbers of this cohort are expected to require replacement of missing teeth.

Ever since Chercheve developed the first root-form or endosseous implants in 1966 (Chercheve 1966), they have become increasingly popular options for replacement of missing teeth. Dental implants have a 10-y survival rate of over 95% (Jung et al. 2012), but the past several years have seen an increase in 2 bacterially driven oral diseases: peri-implant mucositis and peri-implantitis (Mombelli et al. 2012). Studies have reported that peri-implant mucositis occurs in 50% to 90% of implants, while 20% of implants with an average function time of 5 to 11 y develop peri-implantitis (Roos-Jansaker et al. 2006; Zitzmann and Berglundh 2008; Mombelli et al. 2012).

Although early evidence was equivocal on the effect of smoking on dental implants, burgeoning evidence within the past 2 y strongly suggests that smoking is a significant risk factor for implant failure following functional loading (Chen et al. 2013; Doan et al. 2014; French et al. 2014; Twito and Sade

2014). Taken together with the higher rates of tooth loss in smokers (Salvi et al. 2014), this suggests that these individuals represent a high-need, high-risk cohort for implant therapy. Since bacteria play an important etiological role in the pathogenesis of implantitis and mucositis, it is important to understand the impact of smoking on the peri-implant microbiome to improve therapeutic outcomes.

We have previously demonstrated that smoking negatively affects the subgingival microbiome in states of both periodontal health and disease, supporting the formation of pathogen-rich communities (Kumar, Matthews, et al. 2011; Mason et al.

¹Present address: Division of Periodontics, Eastman Institute for Oral Health, School of Medicine and Dentistry, University of Rochester, Rochester, NY, USA

²Division of Periodontology, College of Dentistry, The Ohio State University, Columbus, OH, USA

³Division of Biostatistics, College of Public Health, The Ohio State University, Columbus, OH, USA

A supplemental appendix to this article is published electronically only at <http://jdr.sagepub.com/supplemental>.

Corresponding Author:

P.S. Kumar, The Ohio State University, 4111 Postle Hall, 305 W 12th Avenue, Columbus, OH 43210, USA.
Email: kumar.83@osu.edu

2014). Therefore, the purpose of the present investigation was to examine the impact of smoking on the peri-implant microbiome in states of health and disease (mucositis and implantitis), by harnessing the phylogenetic resolution provided by 16S ribosomal RNA (rRNA) sequencing to characterize these communities.

Methods

Subject Recruitment

Approval for this study was obtained from the Institutional Review Board of The Ohio State University (protocol number: 2011H0023). Eighty dentate adults with at least 1 tooth-bounded dental implant in function for at least 4 y were recruited from those seeking care at the College of Dentistry and written consent obtained. Exclusion criteria included diabetes; pregnancy; human immunodeficiency virus (HIV); use of immunosuppressant medications, bisphosphonates, or steroids; antibiotic therapy or oral prophylactic procedures within the past 3 mo; need for antibiotic coverage before dental treatment; and fewer than 20 teeth present in the dentition. Tobacco exposure was assessed by questionnaire, and current smokers with a 10 pack-year history or greater were recruited. A diagnosis of implant health and disease was made according to the criteria delineated by the Consensus Report of the Sixth European Workshop of Periodontology (Lindhe and Meyle 2008). Briefly, peri-implant health (20 smokers and 20 nonsmokers) was diagnosed when the peri-implant crevice demonstrated no bleeding on probing (BOP), redness, and suppuration and the implant demonstrated radiographic evidence of less than 2 mm of marginal bone loss after being at least 1 y in function. Implants with only clinical signs of inflammation (redness, swelling, BOP, suppuration) and absence of radiographic bone loss following loading were classified as peri-implant mucositis (10 smokers and 10 nonsmokers), whereas implants with the presence of both clinical inflammation and radiographic evidence of more than 2 mm bone loss since the prosthesis installation were diagnosed as peri-implantitis cases (10 smokers and 10 nonsmokers). A minimum sample size of 10 in each subgroup was determined based on our previous investigation (Kumar et al. 2012). The study and reporting conform to STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) guidelines.

Examiner Calibration

All subjects were examined by 1 of 2 periodontists calibrated to a Gold Standard examiner. The calibration was carried out as part of an annual exercise within the Graduate Periodontology Clinics at The Ohio State University College of Dentistry. All examiners were calibrated for probe depths (PDs), clinical attachment levels (CALs), BOP, and plaque and gingival indices (PI and GI). The 2 examiners were found to have an agreement coefficient (κ statistic) of 0.94 and 0.96 for both PDs and CALs with the Gold Standard examiner.

Sample Collection and DNA Isolation

The selected sites were isolated using cotton rolls, and marginal plaque was removed. Peri-implant biofilm samples were collected by inserting 10 sterile endodontic paper points (DENTSPLY-Caulk, Milford, DE, USA) into each peri-implant crevice for 10 s. Samples were placed in 1.5-mL microcentrifuge tubes and frozen at -80°C for later analysis. Bacteria were separated from the paper points by adding 200 μL of phosphate-buffered saline to the tubes and vortexing. The points were then removed, and DNA was isolated with a Qiagen DNA MiniAmp kit (Qiagen, Valencia, CA, USA) using the tissue protocol according to the manufacturer's instructions.

Sequencing and Data Analysis

Multiplexed bacterial tag-encoded FLX amplicon pyrosequencing was performed using the Titanium platform (Roche Applied Science, Indianapolis, IN, USA) in a commercial facility (MRDNALab, Shallowater, TX, USA). Briefly, a single-step polymerase chain reaction (PCR) with broad-range universal primers and 22 cycles of amplification was used to amplify the 16S rRNA genes as well as to introduce adaptor sequences and sample-specific barcode oligonucleotide tags into the DNA. Two regions of the 16S rRNA genes were sequenced: V1 to V3 (spanning *Escherichia coli* 16S gene regions 8–27 and 519–536) and V7 to V9 (spanning *E. coli* 16S gene regions 1099–1114 and 1528–1541). The primers used for sequencing have been previously described (Kumar, Brooker, et al. 2011). Adaptor sequences were trimmed from sequences with an average quality score of 25 and sequences binned into individual sample collections based on barcode sequence tags, which were then trimmed. Sequences <200 bp were discarded, and the rest were clustered into species-level operational taxonomic units (s-OTUs) at 97% sequence similarity and assigned a taxonomic identity by alignment to the HOMD database (Chen et al. 2010) using the Blastn algorithm. Analyses were conducted using the QIIME pipeline (Caporaso et al. 2010), as well as our own internally developed analysis pipeline (Dabdoub et al., PhyloToAST: Bioinformatics tools for species-level analysis and visualization of complex microbial communities, manuscript submitted), available at <http://github.com/smdabdoub/phylotoast>. Results were visualized with the Python library matplotlib (principal coordinates analysis [PCoA] plots) and R-project (diversity curves).

Statistical Analysis

Smokers and nonsmokers were grouped into the following 3 categories based on the health status of each site: peri-implant health, peri-implant mucositis, and peri-implantitis. Single and multiple comparisons of distributions were carried out with the statistical facilities provided by JMP (SAS Institute, Cary, NC, USA). Statistical significance of differences between the groups was determined by ADONIS of UniFrac distances (McArdle

and Anderson 2001) or analysis of variance (ANOVA) with the Tukey post hoc test for multiple comparisons.

Results

The Appendix Table shows the clinical and demographic characteristics of the subjects. There were no significant differences between smokers and nonsmokers in clinical characteristics or demographics ($P > 0.05$, Tukey honestly significant difference [HSD]). Within the groups, however, subjects with peri-implant disease (mucositis and implantitis) demonstrated significantly greater BOP and PDs compared with health (significant differences are shown in bold). In addition, peri-implantitis lesions demonstrated significantly greater suppuration, redness, pain, thread exposure, and bone loss compared with health and mucositis in both smokers and nonsmokers.

In total, 790,008 classifiable sequences were obtained from 80 implants, representing 515 species-level operational taxonomic units OTUs (s-OTUs), with 112 ± 32 s-OTUs in each individual. The data are available at the National Center for Biotechnology Information's sequence read archive (SRR192 1025). Figure 1A shows the diversity (Chao) and Chao estimate of shared species in the health-associated peri-implant microbiomes of smokers and nonsmokers. Smokers had a significantly lower diversity and shared greater numbers of species than did nonsmokers ($P < 0.05$, Welch ANOVA). The Table shows the distribution of sequences in healthy implants of smokers and nonsmokers by s-OTUs. In total, 166 of the 486 health-associated s-OTUs were different between smokers and nonsmokers ($P < 0.05$, Welch ANOVA assuming unequal variances); 79 species, notably those belonging to the genera *Lactobacillus*, *Prevotella*, *Treponema*, *Propionibacterium*, and *Pseudomonas*, demonstrated higher abundances in smokers, while 77 species, especially those belonging to *Streptococcus*, *Selenomonas*, and *Porphyromonas*, were elevated in nonsmokers. The core microbiome (species shared by at least 75% of individuals) of peri-implant health in smokers and nonsmokers is shown in Figure 1B. Both smokers and nonsmokers exhibited a core peri-implant microbiome comprising 13% of the 486 species; 34 species were common to both smokers and nonsmokers, 19 species were unique to smokers, and 12 were unique to nonsmokers.

Figure 2A shows the PCoA plot of health, mucositis, and implantitis in nonsmokers. The microbial profiles of nonsmokers exhibited significant clustering by health status ($P = 0.016$, ADONIS). Figure 2B shows the diversity associated with peri-implant health, mucositis, and peri-implantitis in nonsmokers (Chao diversity index). There was no difference in diversity during shifts from health to disease ($P > 0.05$, Tukey HSD). The Table shows the distribution of sequences by species in nonsmokers. The greatest differences in abundances were observed between health and implantitis or health and mucositis ($P < 0.05$, Tukey HSD). Very few differences were observed between mucositis and implantitis. Figure 2C shows the unique species acquired in each state; 19 species were unique to peri-implant health, while 25 unique species were detected in mucositis and 9 in implantitis. Importantly, the core

microbiome associated with peri-implant health remained unchanged during transitions to disease in this group.

Figure 3A shows the PCoA plot of health, mucositis, and implantitis in smokers. The microbial profiles of smokers exhibited significant clustering based on health or disease association ($P < 0.05$, ADONIS). Figure 3B shows the alpha diversity associated with peri-implant health, mucositis, and implantitis in smokers. Both mucositis and implantitis were associated with a significantly lower diversity than health; however, only mucositis was statistically significant ($P < 0.0001$, Tukey HSD). The Table shows the distribution of sequences by species in smokers. The greatest differences in abundances were observed between health and implantitis or health and mucositis ($P < 0.05$, Tukey HSD). Fewer differences were observed between mucositis and implantitis. Figure 3C shows the unique species acquired in each state; 44 species were unique to periodontal health, while 15 species were uniquely found in mucositis and only 6 in implantitis. Furthermore, two-thirds of the core microbiome in smokers demonstrated a change in either abundance or frequency during shifts to disease.

Discussion

The oral cavity hosts a complex microbial ecosystem, with several habitat-specific communities. Several studies have shown that the tooth surface, the subgingival crevice, and the oral mucosa each host distinct microbial communities (Human Microbiome Project 2012; Socransky and Haffajee 2005). With the rising popularity of dental implants, a significant fraction of the population now has a new oral habitat for bacterial colonization. Our previous work has shown that dental implants, although functionally similar to the tooth, provide a distinct ecological niche for microbial colonization (Kumar et al. 2012; Dabdoub et al. 2013). The purpose of the present investigation was to characterize the peri-implant microbiome in health and disease in current and never smokers by combining a case-control study design with a high-throughput, deep-sequencing methodology and computational phylogenetics. The results provided a new insight into the shifts that occur in these ecological niches during transitions from health to disease and suggest that peri-implant mucositis may create an at-risk-for-harm microbial community.

Smoking and Peri-Implant Health

We have previously demonstrated that smoking is associated with pathogen-rich subgingival microbial communities even in states of clinical periodontal health (Kumar, Matthews, et al. 2011; Mason et al. 2014). In the present investigation, we examined the effect of smoking on the peri-implant microbiome using 2 analytical approaches. We initially examined the difference in abundances of species between 20 clinically healthy nonsmokers and 20 smokers. The peri-implant microbiome of smokers exhibited a significantly lower diversity than did nonsmokers (Fig. 1A) and was enriched for species

Figure 1. Microbial characteristics of peri-implant health in smokers and nonsmokers. **(A)** Kernel density plots of shared species and diversity estimates in the health-associated microbiomes of smokers and nonsmokers (***) $P < 0.001$, Tukey honestly significant difference). **(B)** Core peri-implant microbiome in smokers and nonsmokers. The core microbiome was defined as species present in 75% or greater of samples.

Table. Relative Abundances of Species-Level Operational Taxonomic Units in Health, Peri-Implant Mucositis, and Peri-Implantitis in Smokers and Nonsmokers.

	Nonsmokers (n = 40)			Smokers (n = 40)		
	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)
<i>Abiotrophia defectiva</i>	0.43 ± 0.86	0.07 ± 0.06	0.1 ± 0.18	0.2 ± 0.67	0.06 ± 0.07	0.04 ± 0.05
<i>Acinetobacter baumannii</i>	0.04 ± 0.12	0.01 ± 0.05	0.28 ± 0.9	0.01 ± 0.05	0 ± 0 ^B	0 ± 0 ^B
<i>Acinetobacter</i> HOT.408	0.02 ± 0.04	0.01 ± 0.01	0.3 ± 0.93	0.11 ± 0.05	0 ± 0 ^B	0 ± 0 ^B
<i>Actinobaculum</i> HOT.183 ^A	0.01 ± 0.02	0.05 ± 0.12	0.01 ± 0.04	0.64 ± 0.03	0.03 ± 0.06	0.04 ± 0.11
<i>Actinomyces cardiffensis</i>	0 ± 0	0 ± 0	0.01 ± 0.02	0 ± 0	0 ± 0	0.01 ± 0.03
<i>Actinomyces dentalis</i>	0.01 ± 0.01	0.01 ± 0.02	0 ± 0.01	0.01 ± 0.03	0.02 ± 0.04	0.01 ± 0.02
<i>Actinomyces georgiae</i> ^A	0.01 ± 0.02	0.04 ± 0.01 ^{B,C}	0 ± 0.01	0.12 ± 0.03	0.03 ± 0.06	0.04 ± 0.06
<i>Actinomyces gerencseriae</i>	0.03 ± 0.05	0.05 ± 0.12	0.02 ± 0.02	0.07 ± 0.18	0.01 ± 0.02	0.02 ± 0.03
<i>Actinomyces graevenitzi</i> ^A	0.03 ± 0.01	0 ± 0	0 ± 0.01	0 ± 0	0 ± 0	0 ± 0
<i>Actinomyces</i> HOT.169	0.05 ± 0.08	0.01 ± 0.02	0.05 ± 0.13	0.1 ± 0.24	0 ± 0	0.03 ± 0.08
<i>Actinomyces</i> HOT.170	0.04 ± 0.09	0.01 ± 0.02	0.06 ± 0.15	0.02 ± 0.04	0.01 ± 0.01	0.01 ± 0.02
<i>Actinomyces</i> HOT.171	0.09 ± 0.15	0.06 ± 0.05	0.15 ± 0.37	0.06 ± 0.14	0.03 ± 0.03	0.04 ± 0.05
<i>Actinomyces</i> HOT.172	0.08 ± 0.11	0.07 ± 0.09	0.05 ± 0.1	0.07 ± 0.01	0.01 ± 0.07 ^B	0.01 ± 0.02 ^B
<i>Actinomyces</i> HOT.175	0.01 ± 0.03	0.01 ± 0.04	0.04 ± 0.1	0.02 ± 0.04	0.11 ± 0.35	0 ± 0
<i>Actinomyces</i> HOT.177	0.01 ± 0.02	0 ± 0.01	0.02 ± 0.04	0.02 ± 0.05	0 ± 0	0 ± 0
<i>Actinomyces</i> HOT.178 ^A	0 ± 0	0.02 ± 0.01 ^{B,C}	0 ± 0	0.02 ± 0.01 ^C	0.03 ± 0.08 ^C	0 ± 0
<i>Actinomyces</i> HOT.180	0.09 ± 0.12	0.08 ± 0.14	0.05 ± 0.05	0.07 ± 0.13	0.05 ± 0.04	0.02 ± 0.02
<i>Actinomyces</i> HOT.181 ^A	0.32 ± 0.01	0 ± 0 ^B	0 ± 0 ^B	0.02 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Actinomyces</i> HOT.414 ^A	0.03 ± 0.01	0 ± 0	0 ± 0.01	0 ± 0 ^C	0 ± 0 ^C	0.03 ± 0.01
<i>Actinomyces</i> HOT.448	0.09 ± 0.25	0.01 ± 0.01	0.01 ± 0.02	0.07 ± 0.19	0.01 ± 0.01	0 ± 0.01
<i>Actinomyces</i> HOT.449 ^A	0.04 ± 0.01	0.01 ± 0.02	0 ± 0.01	0.01 ± 0.01	0 ± 0.01	0 ± 0.01
<i>Actinomyces</i> HOT.525	0.01 ± 0.02	0.02 ± 0.02	0 ± 0.01	0.03 ± 0.06	0 ± 0.01	0.02 ± 0.04
<i>Actinomyces</i> HOT.848	0 ± 0.01	0.02 ± 0.06	0.01 ± 0.04	0 ± 0.01	0 ± 0	0 ± 0
<i>Actinomyces</i> HOT.877 ^A	0 ± 0.01	0.02 ± 0.0 ^C	0 ± 0	0.01 ± 0.03	0.04 ± 0.11	0 ± 0.01
<i>Actinomyces</i> HOT.896	0 ± 0.01	0 ± 0	0 ± 0	0 ± 0.01	0 ± 0	0.01 ± 0.01
<i>Actinomyces</i> HOT.897	0 ± 0	0.01 ± 0.02	0 ± 0	0 ± 0.01	0.01 ± 0.04	0 ± 0.01
<i>Actinomyces israelii</i> ^A	0.02 ± 0.01	0.02 ± 0.02	0.02 ± 0.04	0.05 ± 0.01	0.09 ± 0.21	0.05 ± 0.07
<i>Actinomyces johnsonii</i>	0.02 ± 0.07	0.02 ± 0.03	0.05 ± 0.13	0.02 ± 0.09	0.06 ± 0.14	0.01 ± 0.02
<i>Actinomyces massiliensis</i> ^A	0 ± 0	0.01 ± 0.01	0.01 ± 0.02	0.05 ± 0.02	0 ± 0	0 ± 0.02
<i>Actinomyces meyeri</i>	0.05 ± 0.1	0.06 ± 0.07	0.09 ± 0.17	0.06 ± 0.1	0.03 ± 0.04	0.02 ± 0.04
<i>Actinomyces naeslundii</i>	0.05 ± 0.07	0.15 ± 0.28	0.05 ± 0.1	0.05 ± 0.07	0.06 ± 0.11	0.02 ± 0.02
<i>Actinomyces odontolyticus</i>	0.03 ± 0.05	0.01 ± 0.01	0.02 ± 0.04	0.02 ± 0.07	0 ± 0.01	0 ± 0
<i>Actinomyces oricola</i> ^A	0.03 ± 0.01	0 ± 0.01	0 ± 0.01	0 ± 0	0 ± 0.01	0 ± 0
<i>Actinomyces oris</i>	0.03 ± 0.03	0.04 ± 0.04	0.17 ± 0.42	0.02 ± 0.04	0.06 ± 0.02 ^C	0 ± 0.01
<i>Actinomyces radidentis</i>	0 ± 0	0.01 ± 0.04	0 ± 0.01	0.02 ± 0.08	0 ± 0.01	0 ± 0
<i>Actinomyces timonensis</i>	0 ± 0	0.03 ± 0.01 ^{B,C}	0 ± 0	0 ± 0	0 ± 0	0 ± 0
<i>Aggregatibacter actinomycetemcomitans</i>	0 ± 0	0 ± 0	0 ± 0.01	0 ± 0	0 ± 0	0.06 ± 0.19
<i>Aggregatibacter aphrophilus</i>	0.08 ± 0.26	0.02 ± 0.06	0.45 ± 1.35	0.24 ± 0.61	0.14 ± 0.25	0.48 ± 1.37
<i>Aggregatibacter</i> HOT.458	0.02 ± 0.05	0.02 ± 0.03	0.04 ± 0.11	0.01 ± 0.05	0.07 ± 0.14	0.12 ± 0.31
<i>Aggregatibacter</i> HOT.512	0 ± 0 ^C	0 ± 0 ^C	0.2 ± 0.01	0 ± 0	0 ± 0	0 ± 0
<i>Aggregatibacter</i> HOT.513 ^A	0 ± 0.01	0 ± 0.01	0 ± 0	0.04 ± 0.01	0 ± 0.01	0 ± 0.01
<i>Aggregatibacter</i> HOT.898	0.03 ± 0.1	0 ± 0	0 ± 0.01	0.01 ± 0.02	0 ± 0.01	0.02 ± 0.04
<i>Aggregatibacter paraphrophilus</i> ^A	0.01 ± 0.02	0 ± 0	0.02 ± 0.06	0.08 ± 0.02	0 ± 0.01	0.06 ± 0.1
<i>Aggregatibacter segnis</i> ^A	0 ± 0.01	0 ± 0	0.02 ± 0.06	0.05 ± 0.03	0.01 ± 0.01	0.01 ± 0.02
<i>Alloprevotella</i> HOT.308	0.01 ± 0.02	0 ± 0	0 ± 0	0.03 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Alloprevotella</i> HOT.473	0.01 ± 0.03	0.05 ± 0.17	0.01 ± 0.02	0.04 ± 0.14	0 ± 0	0 ± 0.01
<i>Alloprevotella</i> HOT.474	0.01 ± 0.02	0 ± 0.01	0 ± 0	0.03 ± 0.05	0 ± 0 ^B	0 ± 0 ^B
<i>Alloprevotella</i> HOT.912 ^A	0 ± 0	0 ± 0	0 ± 0	0.02 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Alloprevotella</i> HOT.913 ^A	0 ± 0	0.02 ± 0.01 ^{B,C}	0 ± 0	0.03 ± 0.01	0 ± 0.01	0 ± 0.01
<i>Alloprevotella</i> HOT.914	0 ± 0	0.01 ± 0.01	0 ± 0	0 ± 0	0 ± 0	0 ± 0
<i>Alloprevotella rava</i>	0.01 ± 0.02	0.01 ± 0.04	0 ± 0	0.01 ± 0.01	0.02 ± 0.04	0.03 ± 0.04
<i>Alloprevotella tanneriae</i>	0.1 ± 0.21	0.14 ± 0.35	0.1 ± 0.18	0.17 ± 0.33	0.45 ± 0.93	0.33 ± 0.6
<i>Anaeroglobus geminatus</i> ^A	0.47 ± 0.07	0.38 ± 0.67	0.42 ± 0.67	0.17 ± 0.12	1.27 ± 1.4 ^B	0.7 ± 0.84
<i>Atopobium</i> HOT.199	0.08 ± 0.27	0.02 ± 0.03	0.11 ± 0.3	0.03 ± 0.08	0.02 ± 0.03	0.07 ± 0.14
<i>Atopobium</i> HOT.416 ^A	0 ± 0	0 ± 0	0 ± 0	0.03 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Atopobium parvulum</i> ^A	0.27 ± 0.05	0.17 ± 0.37	0.04 ± 0.05	0.07 ± 0.01	0.28 ± 0.14	0.11 ± 0.03
<i>Atopobium rimae</i>	0.4 ± 0.77	0.35 ± 0.44	0.12 ± 0.13	0.46 ± 1.54	0.71 ± 0.85	1.24 ± 1.85
Bacteroidaceae [G-1] HOT.272	0.04 ± 0.1	0.2 ± 0.64	0.07 ± 0.14	0.02 ± 0.07	0.03 ± 0.05	0.08 ± 0.16
Bacteroidales [G-2] HOT.274	1.32 ± 3.61	0.17 ± 0.25	0.79 ± 1.83	0.58 ± 1.17	0.06 ± 0.1	0.45 ± 1.23
Bacteroidetes [G-3] HOT.365 ^A	0 ± 0.01	0.01 ± 0.02	0.02 ± 0.07	0.03 ± 0.01 ^C	0.02 ± 0.01 ^C	0 ± 0
<i>Bergeyella</i> HOT.322	0.07 ± 0.09	0.01 ± 0.03	0.01 ± 0.02	0.06 ± 0.01	0.01 ± 0.03 ^B	0.01 ± 0.01 ^B
<i>Bergeyella</i> HOT.900 ^A	0 ± 0 ^C	0 ± 0.01	0.01 ± 0.03	0.03 ± 0.01	0 ± 0.01	0 ± 0
<i>Bifidobacterium dentium</i> ^A	0 ± 0.01	0.01 ± 0.02	0.02 ± 0.04	0.05 ± 0.02	0.02 ± 0.04	0.01 ± 0.02
<i>Bifidobacterium longum</i>	0 ± 0	0.01 ± 0.03	0.01 ± 0.01	0.01 ± 0.02	0.02 ± 0.01 ^C	0 ± 0
<i>Brevundimonas diminuta</i> ^A	0.01 ± 0.02	0.01 ± 0.01	0 ± 0	0.07 ± 0.01	0 ± 0.01 ^B	0 ± 0 ^B

(continued)

Table. (continued)

	Nonsmokers (n = 40)			Smokers (n = 40)		
	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)
<i>Bulleidia extructa</i>	0.02 ± 0.08	0.02 ± 0.05	0.02 ± 0.06	0.02 ± 0.04	0.02 ± 0.03	0.02 ± 0.05
<i>Campylobacter concisus</i>	0.04 ± 0.08	0.05 ± 0.11	0.02 ± 0.04	0.03 ± 0.05	0.03 ± 0.04	0.07 ± 0.18
<i>Campylobacter curvus</i>	0.02 ± 0.04	0.02 ± 0.03	0.12 ± 0.3	0.01 ± 0.02	0.03 ± 0.05	0.04 ± 0.09
<i>Campylobacter gracilis</i>	0.7 ± 1.19	0.27 ± 0.21	0.27 ± 0.23	0.45 ± 0.46	0.41 ± 0.35	0.91 ± 0.84
<i>Campylobacter</i> HOT.044 ^A	0.05 ± 0.01	0.01 ± 0.03	0 ± 0	0.02 ± 0.04	0.01 ± 0.01	0.01 ± 0.01
<i>Campylobacter rectus</i>	0.07 ± 0.12	0.13 ± 0.25	0.23 ± 0.32	0.05 ± 0.13	0.06 ± 0.07	0.08 ± 0.12
<i>Campylobacter showae</i>	0.07 ± 0.12	0.03 ± 0.04	0.12 ± 0.16	0.1 ± 0.19	0.04 ± 0.06	0.16 ± 0.47
<i>Campylobacter sputorum</i>	0 ± 0.01	0 ± 0	0.01 ± 0.01	0 ± 0	0 ± 0	0.01 ± 0.03
<i>Capnocytophaga gingivalis</i>	0.25 ± 0.52	0.07 ± 0.05	0.21 ± 0.45	0.26 ± 0.44	0.11 ± 0.25	0.79 ± 2.39
<i>Capnocytophaga granulosa</i>	0.05 ± 0.08	0.06 ± 0.07	0.27 ± 0.64	0.04 ± 0.08	0.08 ± 0.2	0.03 ± 0.05
<i>Capnocytophaga</i> HOT.323 ^A	0 ± 0	0.03 ± 0.01 ^{B,C}	0 ± 0	0.03 ± 0.01 ^C	0.02 ± 0.01 ^C	0 ± 0
<i>Capnocytophaga</i> HOT.324 ^A	0.01 ± 0.01	0.01 ± 0.02	0 ± 0.01	0.04 ± 0.01	0.02 ± 0.04	0 ± 0.01
<i>Capnocytophaga</i> HOT.326	0.06 ± 0.16	0.01 ± 0.01	0 ± 0	0.02 ± 0.03	0 ± 0.01	0.01 ± 0.02
<i>Capnocytophaga</i> HOT.332	0 ± 0	0 ± 0.01	0 ± 0.01	0.01 ± 0.01 ^C	0.02 ± 0.01 ^C	0 ± 0
<i>Capnocytophaga</i> HOT.334 ^A	0 ± 0 ^C	0 ± 0 ^C	0.04 ± 0.01	0.03 ± 0.01	0 ± 0 ^B	0.01 ± 0.02
<i>Capnocytophaga</i> HOT.335 ^A	0.01 ± 0.02	0.01 ± 0.02	0 ± 0	0.06 ± 0.01	0 ± 0.01 ^B	0 ± 0.01 ^B
<i>Capnocytophaga</i> HOT.336	0.02 ± 0.05	0 ± 0.01	0 ± 0.01	0.01 ± 0.03	0.01 ± 0.02	0 ± 0.01
<i>Capnocytophaga</i> HOT.338	0.01 ± 0.03	0.02 ± 0.05	0 ± 0.01	0.01 ± 0.02	0.01 ± 0.01	0.02 ± 0.04
<i>Capnocytophaga</i> HOT.380 ^A	0.03 ± 0.01	0 ± 0.01	0 ± 0	0 ± 0	0.01 ± 0.01	0 ± 0
<i>Capnocytophaga</i> HOT.412 ^A	0 ± 0.01	0 ± 0.01	0 ± 0.01	0.03 ± 0.01	0.01 ± 0.02	0.01 ± 0.03
<i>Capnocytophaga</i> HOT.863	0.04 ± 0.08	0.06 ± 0.1	0.3 ± 0.74	0.04 ± 0.12	0.06 ± 0.12	0 ± 0.01
<i>Capnocytophaga</i> HOT.864 ^A	0 ± 0.01	0.01 ± 0.03	0 ± 0	0.05 ± 0.01	0.01 ± 0.02	0.04 ± 0.11
<i>Capnocytophaga</i> HOT.878 ^A	0 ± 0.01	0 ± 0	0 ± 0	0.04 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Capnocytophaga</i> HOT.901	0.04 ± 0.14	0.01 ± 0.02	0.05 ± 0.12	0.02 ± 0.03	0 ± 0.01	0 ± 0
<i>Capnocytophaga</i> HOT.902	0 ± 0.01	0 ± 0.01	0.02 ± 0.03	0.01 ± 0.02	0 ± 0.01	0 ± 0
<i>Capnocytophaga</i> HOT.903 ^A	0.03 ± 0.01	0 ± 0.01	0.01 ± 0.02	0.06 ± 0.01 ^C	0.02 ± 0.04 ^C	0 ± 0
<i>Capnocytophaga leadbetteri</i>	0.08 ± 0.15	0.08 ± 0.15	0.09 ± 0.2	0.11 ± 0.29	0.03 ± 0.1	0.21 ± 0.55
<i>Capnocytophaga ochracea</i> ^A	0 ± 0.01	0 ± 0	0 ± 0	0.03 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Capnocytophaga sputigena</i>	0.14 ± 0.28	0.12 ± 0.16	0.16 ± 0.32	0.06 ± 0.12	0 ± 0.01	0.01 ± 0.02
<i>Cardiobacterium hominis</i>	0.01 ± 0.02	0.02 ± 0.02	0.05 ± 0.08	0.01 ± 0.02	0.01 ± 0.04	0.01 ± 0.01
<i>Cardiobacterium valvulorum</i>	0 ± 0.01	0 ± 0.01	0.01 ± 0.02	0.02 ± 0.01 ^C	0.01 ± 0.01	0 ± 0
<i>Catonella</i> HOT.164	0 ± 0	0.01 ± 0.02 ^B	0.02 ± 0.01 ^B	0 ± 0	0.01 ± 0.01	0 ± 0
<i>Catonella</i> HOT.451	0 ± 0.01	0 ± 0.01	0.06 ± 0.19	0 ± 0.01	0.04 ± 0.06	0.1 ± 0.08 ^B
<i>Catonella morbi</i>	0.17 ± 0.27	0.32 ± 0.52	0.11 ± 0.09	0.15 ± 0.2	0.12 ± 0.14	0.14 ± 0.14
<i>Centipeda periodontii</i>	0.01 ± 0.04	0.02 ± 0.04	0.03 ± 0.08	0.01 ± 0.01	0.01 ± 0.02	0.02 ± 0.04
<i>Chloroflexi</i> [G-I] HOT.439	0 ± 0.01	0 ± 0.01	0.06 ± 0.15	0.01 ± 0.04	0.01 ± 0.01	0.04 ± 0.12
<i>Clostridiales</i> [F-2][G-I] HOT.075 ^A	0.01 ± 0.02	0.15 ± 0.06	0 ± 0.01	0.15 ± 0.05	0.03 ± 0.08	0.05 ± 0.12
<i>Clostridiales</i> [F-2][G-I] HOT.085 ^A	0.03 ± 0.01	0.02 ± 0.04	0 ± 0.01	0.01 ± 0.01	0 ± 0	0.05 ± 0.16
<i>Comamonas testosteroni</i>	0.01 ± 0.02	0.01 ± 0.02	0.01 ± 0.02	0.18 ± 0.77	0 ± 0.01	0 ± 0.01
<i>Corynebacterium diphtheriae</i>	0 ± 0	0.02 ± 0.01 ^{B,C}	0 ± 0	0 ± 0	0 ± 0	0 ± 0
<i>Corynebacterium durum</i>	0.03 ± 0.05	0.01 ± 0.02	0.01 ± 0.04	0.05 ± 0.13	0 ± 0	0 ± 0.01
<i>Corynebacterium matruchotii</i>	0.45 ± 0.85	0.26 ± 0.31	0.69 ± 1.67	0.28 ± 0.51	0.32 ± 0.79	0.03 ± 0.04
<i>Corynebacterium mucifaciens</i>	0 ± 0 ^C	0 ± 0 ^C	0.03 ± 0.01	0 ± 0	0 ± 0	0 ± 0
<i>Desulfobulbus</i> HOT.041	0.21 ± 0.86	0.72 ± 2.25	1.59 ± 3.41	0.08 ± 0.24	0.91 ± 1.87	0.14 ± 0.3
<i>Desulfomicrobium orale</i>	0 ± 0	0.02 ± 0.01 ^B	0.13 ± 0.03 ^B	0 ± 0	0 ± 0	0 ± 0
<i>Desulfovibrio fairfieldensis</i> ^A	0.15 ± 0.05	0 ± 0 ^B	0 ± 0 ^B	0.04 ± 0.02 ^C	0.02 ± 0.01 ^C	0 ± 0
<i>Desulfovibrio</i> HOT.040	0 ± 0	0.03 ± 0.01 ^{B,C}	0 ± 0	0 ± 0	0 ± 0	0 ± 0
<i>Dialister</i> HOT.119	0.01 ± 0.03	0.08 ± 0.26	0.01 ± 0.02	0.01 ± 0.04	0.09 ± 0.19	0.05 ± 0.12
<i>Dialister</i> HOT.502	0.13 ± 0.32	0.24 ± 0.22	0.45 ± 0.03 ^B	0.07 ± 0.13	0.44 ± 0.15 ^B	0.54 ± 0.12 ^B
<i>Dialister invisus</i> ^A	1.54 ± 1.93	0.97 ± 0.82	1.88 ± 0.2	0.88 ± 1.14	1.71 ± 0.62	2.97 ± 0.51 ^B
<i>Dialister micraerophilus</i> ^A	0 ± 0	0.03 ± 0.01 ^B	0.02 ± 0.01 ^B	0.04 ± 0.01 ^C	0.02 ± 0.03 ^C	0 ± 0
<i>Dialister pneumosintes</i>	0.27 ± 0.63	0.6 ± 0.9	1 ± 1.21	0.14 ± 0.33	0.33 ± 0.42	0.75 ± 0.28 ^B
<i>Eikenella corrodens</i>	0.24 ± 0.31	0.19 ± 0.18	0.3 ± 0.48	0.22 ± 0.54	0.29 ± 0.68	0.6 ± 1.64
<i>Eikenella</i> HOT.011 ^A	0.03 ± 0.01	0.01 ± 0.01	0.01 ± 0.02	0 ± 0.01	0 ± 0	0 ± 0.01
<i>Enterobacter cancerogenus</i>	0.01 ± 0.01	0 ± 0	0 ± 0	0.02 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Enterobacter hormaechei</i>	0.12 ± 0.26	0.03 ± 0.06	0.02 ± 0.05	0.15 ± 0.42	0.01 ± 0.02	0.01 ± 0.01
<i>Enterobacter sakazaki</i> ^A	0.04 ± 0.01	0 ± 0.01	0.01 ± 0.04	0 ± 0 ^C	0 ± 0 ^C	0.03 ± 0.02
<i>Enterococcus durans</i>	0.01 ± 0.02	0.01 ± 0.02	0 ± 0.01	0.01 ± 0.02	0.01 ± 0.03	0 ± 0
<i>Enterococcus faecalis</i>	0 ± 0.02	0.04 ± 0.01 ^{B,C}	0 ± 0	0.01 ± 0.02	0.01 ± 0.03	0 ± 0.01
<i>Enterococcus italicus</i>	0 ± 0.01	0 ± 0.01	0 ± 0	0.01 ± 0.01	0 ± 0.01	0 ± 0
<i>Enterococcus saccharolyticus</i>	0.01 ± 0.01	0.02 ± 0.04	0.01 ± 0.02	0.01 ± 0.01	0.01 ± 0.02	0 ± 0
<i>Erysipelotrichaceae</i> [G-I] HOT.904	0.03 ± 0.12	0 ± 0	0.2 ± 0.4	0.01 ± 0.02	0.01 ± 0.02	0.03 ± 0.08
<i>Erysipelotrichaceae</i> [G-I] HOT.905	0.01 ± 0.02	0.03 ± 0.1	0.04 ± 0.08	0.02 ± 0.04	0.03 ± 0.05	0.08 ± 0.16
<i>Escherichia coli</i>	0.13 ± 0.25	0.08 ± 0.15	0.08 ± 0.24	0.31 ± 0.84	0.03 ± 0.07	0.01 ± 0.02
<i>Eubacterium</i> [XII][G-I] infirmum ^A	0.11 ± 0.04	0.17 ± 0.4	0.04 ± 0.05	0.05 ± 0.08	0.11 ± 0.24	0.19 ± 0.24
<i>Eubacterium</i> [XII][G-I] sulci	0.07 ± 0.15	0.1 ± 0.13	0.04 ± 0.09	0.03 ± 0.07	0.11 ± 0.24	0.1 ± 0.14

(continued)

Table. (continued)

	Nonsmokers (n = 40)			Smokers (n = 40)		
	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)
<i>Eubacterium</i> [XI][G-3] <i>brachy</i> ^A	0.75 ± 0.2	1.68 ± 1.24	1.41 ± 1.77	0.34 ± 0.53	0.63 ± 0.05 ^B	2.18 ± 0.61 ^B
<i>Eubacterium</i> [XI][G-5] <i>saphenum</i>	0.12 ± 0.46	0.08 ± 0.19	0.12 ± 0.27	0.04 ± 0.08	0.1 ± 0.19	0.05 ± 0.15
<i>Eubacterium</i> [XI][G-6] <i>minutum</i>	0 ± 0.01	0 ± 0	0.01 ± 0.01	0.01 ± 0.04	0 ± 0	0.03 ± 0.09
<i>Eubacterium</i> [XI][G-6] <i>nodatum</i>	0.01 ± 0.04	0.02 ± 0.04	0.11 ± 0.01 ^B	0.01 ± 0.02	0.03 ± 0.06	0.03 ± 0.07
<i>Eubacterium</i> [XI][G-7] <i>yurii</i> ^A	0.03 ± 0.09	0.03 ± 0.06	0.1 ± 0.27	0.19 ± 0.03	0 ± 0.01 ^B	0.01 ± 0.03 ^B
<i>Eubacterium</i> [XIVa][G-1] <i>saburreum</i> ^A	0.05 ± 0.07	0.11 ± 0.2	0.02 ± 0.04	0.1 ± 0.01	0.05 ± 0.06 ^B	0.03 ± 0.03 ^B
<i>Filifactor alois</i>	0.77 ± 1.61 ^C	0.52 ± 0.98 ^C	3.21 ± 0.94	1.59 ± 3.89	0.52 ± 0.97	0.34 ± 0.65
<i>Fretibacterium fastidiosum</i>	0 ± 0.02	0.2 ± 0.34	0.92 ± 0.48 ^B	0.28 ± 0.83	0.17 ± 0.25	0.62 ± 0.86
<i>Fretibacterium</i> HOT.358 ^A	0.16 ± 0.01	0 ± 0	0.01 ± 0.03	0 ± 0	0.02 ± 0.01 ^{B,C}	0 ± 0
<i>Fretibacterium</i> HOT.359	0.06 ± 0.2	0.27 ± 0.66	0.83 ± 1.7	0.17 ± 0.57	0.2 ± 0.38	0.09 ± 0.28
<i>Fretibacterium</i> HOT.360	0.08 ± 0.2 ^C	0.1 ± 0.18 ^C	0.57 ± 0.08	0.21 ± 0.75	0.16 ± 0.18	0.52 ± 0.85
<i>Fretibacterium</i> HOT.361	0 ± 0 ^C	0 ± 0 ^C	0.27 ± 0.04	0 ± 0	0.02 ± 0.01 ^{B,C}	0 ± 0
<i>Fretibacterium</i> HOT.362	0.01 ± 0.03	0 ± 0.01	0.01 ± 0.02	0 ± 0.01	0.01 ± 0.02	0 ± 0
<i>Fretibacterium</i> HOT.452	0.01 ± 0.02	0.03 ± 0.08	0.04 ± 0.06	0 ± 0.01	0.03 ± 0.09	0.02 ± 0.04
<i>Fretibacterium</i> HOT.453	0.15 ± 0.6	0.09 ± 0.23	0.25 ± 0.27	0.16 ± 0.42	0.03 ± 0.05	0.08 ± 0.13
<i>Fusobacterium gonidiaformans</i> ^A	1.73 ± 1.3	0 ± 0 ^B	0 ± 0 ^B	0 ± 0	0.01 ± 0.01	0 ± 0
<i>Fusobacterium</i> HOT.203	0.26 ± 0.33	0.29 ± 0.29	1.4 ± 2.58	0.98 ± 2.6	1.5 ± 2.43	4.37 ± 8.39
<i>Fusobacterium</i> HOT.205	0 ± 0	4.29 ± 4.72	2.03 ± 2.76	1.45 ± 2.42	3.56 ± 3.06	4.35 ± 2.31 ^B
<i>Fusobacterium</i> HOT.370	0.01 ± 0.01	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0.23 ± 0.74
<i>Fusobacterium naviforme</i> ^A	2.13 ± 3.81	3.27 ± 3.65	4.81 ± 7.09	5.56 ± 1.63	1.42 ± 2.05	3.03 ± 3.69
<i>Fusobacterium nucleatum</i>	10.44 ± 12.29	6.83 ± 6.37	11.29 ± 9.12	9.45 ± 10.28	5.69 ± 5.43	12.21 ± 9.09
<i>Fusobacterium periodonticum</i>	0.16 ± 0.55	0.02 ± 0.03	0.06 ± 0.11	0.05 ± 0.09	0 ± 0	0.02 ± 0.04
<i>Gemella bergeri</i> ^A	0.34 ± 0.04	0 ± 0 ^B	0 ± 0 ^B	0.01 ± 0.06	0.01 ± 0.02	0.01 ± 0.02
<i>Gemella haemolysans</i> ^A	0.98 ± 0.07	0.79 ± 1.1	0.24 ± 0.3	0.51 ± 0.08	1.18 ± 2.13	0.16 ± 0.18
<i>Gemella morbillorum</i>	0.63 ± 0.91	0.38 ± 0.27	0.56 ± 0.8	0.55 ± 0.49	0.42 ± 0.55	0.32 ± 0.32
<i>Gemella sanguinis</i> ^A	0.07 ± 0.13	0.04 ± 0.06	0.03 ± 0.05	0.12 ± 0.01	0.03 ± 0.03 ^B	0.02 ± 0.02 ^B
<i>Granulicatella adiacens</i>	0.76 ± 0.56	0.68 ± 0.75	0.58 ± 0.77	0.71 ± 0.79	0.33 ± 0.27	0.23 ± 0.3
<i>Granulicatella elegans</i>	0.08 ± 0.13	0.02 ± 0.02	0.07 ± 0.09	0.05 ± 0.08	0.02 ± 0.03	0.02 ± 0.05
<i>Haemophilus aegyptius</i> ^A	0 ± 0	0 ± 0	0 ± 0	0.09 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Haemophilus haemolyticus</i>	0.05 ± 0.16	0 ± 0.01	0 ± 0.01	0.06 ± 0.22	0.01 ± 0.02	0 ± 0.01
<i>Haemophilus</i> HOT.035	0.01 ± 0.05	0.01 ± 0.05	0 ± 0	0.01 ± 0.03	0.04 ± 0.13	0 ± 0.01
<i>Haemophilus</i> HOT.036	0.01 ± 0.05	0 ± 0.01	0.02 ± 0.04	0.03 ± 0.12	0 ± 0.01	0 ± 0.01
<i>Haemophilus</i> HOT.908	0 ± 0.01	0.01 ± 0.02	0 ± 0.01	0 ± 0	0 ± 0.01	0 ± 0
<i>Haemophilus influenzae</i>	0 ± 0	0.02 ± 0.04	0 ± 0	0.01 ± 0.02	0.02 ± 0.05	0 ± 0
<i>Haemophilus parainfluenzae</i> ^A	0.12 ± 0.16	0.15 ± 0.31	0.09 ± 0.13	0.35 ± 0.05	0.1 ± 0.16	0.02 ± 0.04
<i>Johnsonella</i> HOT.166 ^A	0.03 ± 0.01	0.01 ± 0.02	0.01 ± 0.03	0 ± 0	0 ± 0	0 ± 0
<i>Johnsonella ignava</i>	0.01 ± 0.03	0.04 ± 0.1	0.06 ± 0.17	0.06 ± 0.27	0 ± 0	0.01 ± 0.03
<i>Kingella denitrificans</i>	0.12 ± 0.26	0.06 ± 0.06	0.13 ± 0.23	0.11 ± 0.36	0.05 ± 0.1	0.01 ± 0.03
<i>Kingella</i> HOT.012	0.01 ± 0.01	0.01 ± 0.02	0.01 ± 0.02	0.01 ± 0.02	0 ± 0	0 ± 0.01
<i>Kingella</i> HOT.459	0 ± 0.01	0.05 ± 0.14	0.02 ± 0.05	0.05 ± 0.19	0 ± 0.01	0 ± 0
<i>Kingella kingae</i>	0.04 ± 0.15	0.04 ± 0.04	0.04 ± 0.05	0.03 ± 0.06	0.02 ± 0.05	0.01 ± 0.03
<i>Kingella oralis</i>	0.25 ± 0.44	0.11 ± 0.23	0.15 ± 0.33	0.28 ± 0.59	0.15 ± 0.31	0.1 ± 0.24
<i>Lachnoanaerobaculum</i> HOT.083	0 ± 0.01	0.01 ± 0.01	0 ± 0	0.04 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Lachnoanaerobaculum</i> HOT.089	0.01 ± 0.03	0.03 ± 0.09	0 ± 0	0 ± 0	0 ± 0	0.01 ± 0.03
<i>Lachnoanaerobaculum</i> HOT.496 ^A	0 ± 0 ^C	0 ± 0 ^C	0.02 ± 0.01	0.05 ± 0.02	0 ± 0 ^B	0 ± 0 ^B
<i>Lachnoanaerobaculum orale</i>	0.06 ± 0.2	0.03 ± 0.03	0.01 ± 0.01	0.02 ± 0.03 ^C	0.01 ± 0.04 ^C	0 ± 0
<i>Lachnoanaerobaculum saburreum</i> ^A	0.01 ± 0.01	0 ± 0.01	0 ± 0	0 ± 0	0.03 ± 0.01	0 ± 0
<i>Lachnoanaerobaculum umeaense</i>	0.05 ± 0.05	0.07 ± 0.07	0.04 ± 0.05	0 ± 0	0.02 ± 0.04	0.01 ± 0.02
<i>Lachnospiraceae</i> [G-2] HOT.088 ^A	0 ± 0	0.02 ± 0.08 ^{B,C}	0 ± 0	0.08 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Lachnospiraceae</i> [G-2] HOT.096 ^A	0.03 ± 0.01	0.18 ± 0.56	0 ± 0	0 ± 0	0 ± 0	0.01 ± 0.02
<i>Lachnospiraceae</i> [G-3] HOT.100	0.03 ± 0.05	0.09 ± 0.14	0.09 ± 0.13	0 ± 0	0.03 ± 0.07	0.01 ± 0.01
<i>Lachnospiraceae</i> [G-5] HOT.080 ^A	0 ± 0	0.15 ± 0.37 ^{B,C}	0 ± 0	0.04 ± 0.01 ^C	0.01 ± 0.01	0 ± 0
<i>Lachnospiraceae</i> [G-7] HOT.086	0.03 ± 0.05	0.02 ± 0.02	0.03 ± 0.04	0.02 ± 0.03	0.02 ± 0.03	0.04 ± 0.04
<i>Lachnospiraceae</i> [G-7] HOT.163	0 ± 0	0.01 ± 0.04	0 ± 0	0 ± 0	0.02 ± 0.05	0.01 ± 0.01
<i>Lachnospiraceae</i> [G-8] HOT.500	0.06 ± 0.16	0.07 ± 0.15	0.1 ± 0.19	0 ± 0.01	0.03 ± 0.06	0.07 ± 0.15
<i>Lactobacillus acidophilus</i> ^A	0 ± 0	0 ± 0	0 ± 0	0.05 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Lactobacillus coleohominis</i> ^A	0 ± 0	0 ± 0	0 ± 0	0.03 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Lactobacillus crispatus</i> ^A	0 ± 0	0 ± 0	0.01 ± 0.02	0.34 ± 0.05 ^C	0.02 ± 0.05 ^C	0 ± 0
<i>Lactobacillus fermentum</i>	0 ± 0.01	0.01 ± 0.01	0 ± 0	0.04 ± 0.01 ^C	0.03 ± 0.02 ^C	0 ± 0
<i>Lactobacillus gasseri</i>	0.01 ± 0.04	0.01 ± 0.04	0 ± 0	0 ± 0	0.13 ± 0.2	0 ± 0
<i>Lactobacillus</i> HOT.052 ^A	0 ± 0	0 ± 0	0 ± 0	0.06 ± 0.03	0.01 ± 0.01	0 ± 0
<i>Lactobacillus</i> HOT.461 ^A	0 ± 0	0 ± 0	0 ± 0	0.05 ± 0.01	0 ± 0.01 ^B	0 ± 0 ^B
<i>Lactobacillus jensenii</i> ^A	0 ± 0	0 ± 0	0 ± 0	0.43 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Lactobacillus johnsonii</i>	0.02 ± 0.01	0 ± 0 ^B	0 ± 0 ^B	0.01 ± 0.02	0 ± 0.01	0 ± 0
<i>Lactobacillus oris</i> ^A	0 ± 0	0.01 ± 0.01	0 ± 0	0.02 ± 0.11	0 ± 0.01	0 ± 0

(continued)

Table. (continued)

	Nonsmokers (n = 40)			Smokers (n = 40)		
	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)
<i>Lactobacillus panis</i> ^A	0 ± 0 ^C	0 ± 0 ^C	0.03 ± 0.01	0.03 ± 0.01 ^C	0.01 ± 0.03	0 ± 0
<i>Lactobacillus paracasei</i>	0.01 ± 0.02	0 ± 0.01	0 ± 0.01	0.01 ± 0.03 ^C	0.05 ± 0.03 ^C	0 ± 0
<i>Lactobacillus reuteri</i> ^A	0 ± 0	0.02 ± 0.01 ^{B,C}	0 ± 0	0.01 ± 0.03	0.01 ± 0.02	0 ± 0
<i>Lactobacillus rhamnosus</i>	0 ± 0.01	0.01 ± 0.01	0 ± 0	0 ± 0.02	0.09 ± 0.22	0 ± 0
<i>Lactobacillus salivarius</i> ^A	0 ± 0.01	0.01 ± 0.01	0 ± 0	0.08 ± 0.02 ^C	0.11 ± 0.23	0 ± 0
<i>Lactobacillus vaginalis</i> ^A	0.01 ± 0.03	0.01 ± 0.01	0 ± 0	0.61 ± 0.14	0.08 ± 0.16	0 ± 0
<i>Lautropia mirabilis</i>	1.86 ± 5.25	0.14 ± 0.19	0.74 ± 1.47	0.71 ± 1.86	0.02 ± 0.05	0.46 ± 1.38
<i>Leptothrix</i> HOT.024	0 ± 0.01	0 ± 0	0 ± 0	0.02 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Leptothrix</i> HOT.025	0.01 ± 0.03	0.02 ± 0.05	0 ± 0	0.04 ± 0.15	0.01 ± 0.02	0 ± 0
<i>Leptotrichia buccalis</i>	0.06 ± 0.2	0.05 ± 0.1	0.02 ± 0.04	0.07 ± 0.26	0.07 ± 0.14	0.03 ± 0.06
<i>Leptotrichia goodfellowii</i>	0.02 ± 0.05	0.02 ± 0.05	0.04 ± 0.09	0.02 ± 0.08	0.05 ± 0.16	0.01 ± 0.01
<i>Leptotrichia hofstadii</i>	0.01 ± 0.03	0.14 ± 0.32	0.23 ± 0.59	0.06 ± 0.22	0.12 ± 0.24	0.03 ± 0.06
<i>Leptotrichia hongkongensis</i>	0.09 ± 0.15	0.36 ± 0.87	0.08 ± 0.23	0.11 ± 0.25	0.24 ± 0.43	0.41 ± 0.82
<i>Leptotrichia</i> HOT.212	0.11 ± 0.26	0.18 ± 0.49	0.13 ± 0.22	0.15 ± 0.3	0.01 ± 0.04	0.03 ± 0.09
<i>Leptotrichia</i> HOT.215	0.07 ± 0.17	0.01 ± 0.02	0.03 ± 0.05	0.03 ± 0.06	0 ± 0 ^B	0 ± 0 ^B
<i>Leptotrichia</i> HOT.217 ^A	0 ± 0	0.01 ± 0.01	0 ± 0	0.03 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Leptotrichia</i> HOT.219 ^A	0.01 ± 0.02	0.01 ± 0.03	0 ± 0	0.15 ± 0.02	0 ± 0 ^B	0.01 ± 0.02 ^B
<i>Leptotrichia</i> HOT.221	0.05 ± 0.24	0.01 ± 0.02	0 ± 0	0.02 ± 0.07	0.01 ± 0.03	0 ± 0.01
<i>Leptotrichia</i> HOT.223 ^A	0 ± 0.01	0.01 ± 0.03	0.01 ± 0.03	0.04 ± 0.01	0.04 ± 0.08	0.05 ± 0.16
<i>Leptotrichia</i> HOT.225 ^A	0.01 ± 0.02	0.01 ± 0.01	0.02 ± 0.05	0.05 ± 0.01	0 ± 0.02	0 ± 0.01
<i>Leptotrichia</i> HOT.392	0.04 ± 0.14	0.01 ± 0.02	0.06 ± 0.14	0.01 ± 0.03	0 ± 0.01	0.03 ± 0.1
<i>Leptotrichia</i> HOT.417	0.12 ± 0.28	0.05 ± 0.1	0.04 ± 0.12	0.14 ± 0.38	0.08 ± 0.24	0.11 ± 0.34
<i>Leptotrichia</i> HOT.462	0.03 ± 0.08 ^C	0.02 ± 0.01 ^C	0 ± 0	0.06 ± 0.24	0 ± 0.01	0 ± 0.01
<i>Leptotrichia</i> HOT.463 ^A	0 ± 0	0 ± 0	0 ± 0	0.03 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Leptotrichia</i> HOT.498	0 ± 0.01 ^C	0.24 ± 0.77 ^C	0 ± 0	0.01 ± 0.03	0.08 ± 0.27	0.17 ± 0.54
<i>Leptotrichia</i> HOT.879 ^A	0 ± 0	0.03 ± 0.01 ^B	0.04 ± 0.01 ^B	0.03 ± 0.01	0.15 ± 0.26	0.08 ± 0.23
<i>Leptotrichia</i> HOT.909	0 ± 0	0.02 ± 0.01 ^B	0.34 ± 0.02 ^B	0 ± 0	0 ± 0	0 ± 0
<i>Leptotrichia shahii</i> ^A	0 ± 0	0 ± 0	0.05 ± 0.15	0.34 ± 0.05	0 ± 0	0.01 ± 0.02
<i>Leptotrichia wadei</i>	0.08 ± 0.15	0.45 ± 1.13	0.02 ± 0.03	0.19 ± 0.66	0.19 ± 0.27	0.04 ± 0.07
<i>Leptotrichiaceae</i> [G-I] HOT.210	0.11 ± 0.17	0.16 ± 0.3	0.42 ± 0.85	0.11 ± 0.19	0.35 ± 0.87	0.15 ± 0.25
<i>Leptotrichiaceae</i> [G-I] HOT.220	0.01 ± 0.02	0.01 ± 0.02	0.05 ± 0.12	0.01 ± 0.01	0.01 ± 0.03	0.01 ± 0.03
<i>Lysinibacillus fusiformis</i>	0.01 ± 0.03	0.01 ± 0.01	0.02 ± 0.03	0.01 ± 0.02	0 ± 0.01	0 ± 0
<i>Megasphaera</i> HOT.123	0.05 ± 0.14	0.3 ± 0.97	0.04 ± 0.09	0.11 ± 0.26	0.69 ± 1.14	0.23 ± 0.64
<i>Megasphaera</i> HOT.841	0 ± 0	0 ± 0.01	0.01 ± 0.02	0 ± 0	0.03 ± 0.06	0.01 ± 0.02
<i>Megasphaera micronuciformis</i> ^A	0.21 ± 0.04	0.16 ± 0.22	0.15 ± 0.3	0.06 ± 0.14	0.89 ± 0.26 ^{B,C}	0.16 ± 0.27
<i>Mogibacterium diversum</i> ^A	0.02 ± 0.01	0.01 ± 0.01	0.01 ± 0.01	0 ± 0.01	0.02 ± 0.03	0.01 ± 0.01
<i>Mogibacterium neglectum</i>	0.01 ± 0.02	0.05 ± 0.01 ^{B,C}	0.01 ± 0.02	0.01 ± 0.01	0.03 ± 0.06	0.01 ± 0.02
<i>Mogibacterium pumilum</i>	0 ± 0	0.01 ± 0.01	0 ± 0.01	0 ± 0 ^C	0 ± 0 ^C	0.03 ± 0.01
<i>Mogibacterium timidum</i>	0.04 ± 0.08 ^C	0.06 ± 0.01 ^C	0.18 ± 0.06	0.05 ± 0.11	0.06 ± 0.08	0.09 ± 0.14
<i>Mogibacterium vescum</i> ^A	0 ± 0	0.02 ± 0.01 ^{B,C}	0 ± 0	0.05 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Moraxella catarrhalis</i> ^A	0 ± 0.01	0 ± 0	0.03 ± 0.08	0.03 ± 0.01	0 ± 0	0 ± 0
<i>Moraxella osloensis</i>	0.02 ± 0.05	0 ± 0.01	0.04 ± 0.12	0.03 ± 0.01 ^C	0 ± 0.02	0 ± 0
<i>Moryella</i> HOT.097	0.01 ± 0.04	0.04 ± 0.09	0.01 ± 0.01	0.01 ± 0.02	0 ± 0.01	0 ± 0.01
<i>Moryella</i> HOT.373 ^A	0.05 ± 0.01	0 ± 0	0 ± 0	0 ± 0	0 ± 0.01	0.01 ± 0.01
<i>Moryella</i> HOT.419	0.05 ± 0.07	0.08 ± 0.11	0.04 ± 0.07	0.06 ± 0.2	0.02 ± 0.03 ^B	0.01 ± 0.02 ^B
<i>Moryella</i> HOT.910	0 ± 0.01 ^C	0.01 ± 0.02 ^C	0 ± 0	0.01 ± 0.03	0.03 ± 0.01 ^C	0 ± 0
<i>Mycoplasma faucium</i> ^A	0 ± 0.01	0.01 ± 0.02	0 ± 0	0.06 ± 0.02	0 ± 0.01 ^B	0.01 ± 0.03 ^B
<i>Mycoplasma salivarium</i>	0.02 ± 0.07	0.01 ± 0.01	0.01 ± 0.02	0.02 ± 0.04	0.01 ± 0.01	0.01 ± 0.02
<i>Neisseria bacilliformis</i>	0.18 ± 0.54	0.05 ± 0.13	0.01 ± 0.02	0.13 ± 0.37	0.4 ± 1.26	0.68 ± 2.13
<i>Neisseria elongata</i>	0.47 ± 1.12	0.17 ± 0.24	0.02 ± 0.03	0.37 ± 1.1	0.01 ± 0.02	0.25 ± 0.63
<i>Neisseria flava</i>	1.01 ± 3.1	0.36 ± 0.68	0.36 ± 0.94	0.37 ± 0.84	0.01 ± 0.02	0.14 ± 0.44
<i>Neisseria flavescens</i>	0.14 ± 0.02	0.03 ± 0.06 ^B	0.11 ± 0.21	0.25 ± 0.77	0.05 ± 0.14	0.01 ± 0.01
<i>Neisseria gonorrhoeae</i>	0.58 ± 1.6	1.54 ± 2.13	1.12 ± 3.19	1.22 ± 3.06	0.05 ± 0.13	0.65 ± 1.06
<i>Neisseria</i> HOT.015	0.01 ± 0.02	0.01 ± 0.02	0 ± 0.01	0.01 ± 0.01	0 ± 0.01	0.01 ± 0.02
<i>Neisseria</i> HOT.016	2.32 ± 8.14	0.24 ± 0.54	0.09 ± 0.16	0.98 ± 3.73	0.07 ± 0.16	0.32 ± 0.53
<i>Neisseria</i> HOT.018 ^A	0.13 ± 0.03	0 ± 0 ^B	0 ± 0 ^B	0 ± 0	0 ± 0	0 ± 0.01
<i>Neisseria</i> HOT.020	0.04 ± 0.12	0 ± 0.01	0.01 ± 0.01	0.01 ± 0.03	0.01 ± 0.04	0 ± 0.01
<i>Neisseria</i> HOT.499	3.28 ± 5.55	2.78 ± 1.71	2.69 ± 2.64	5.63 ± 10.18	0.99 ± 1.86	0.98 ± 1.22
<i>Neisseria</i> HOT.523	0 ± 0 ^C	0 ± 0 ^C	0.32 ± 0.31	0 ± 0	0 ± 0	0 ± 0
<i>Neisseria lactamica</i> ^A	0.04 ± 0.01	0 ± 0 ^B	0 ± 0 ^B	0 ± 0	0 ± 0	0 ± 0
<i>Neisseria meningitidis</i>	0.03 ± 0.05	0.01 ± 0.01	0.14 ± 0.34	0.03 ± 0.06	0.04 ± 0.11	0 ± 0
<i>Neisseria mucosa</i>	0.47 ± 1.27	0.31 ± 0.63	0.05 ± 0.11	0.53 ± 1.65	0.25 ± 0.67	0.21 ± 0.49
<i>Neisseria oralis</i>	0.49 ± 1.35	0.75 ± 1.67	0.33 ± 0.87	0.33 ± 0.85	0.47 ± 1.3	0.24 ± 0.53
<i>Neisseria pharyngis</i>	0.06 ± 0.15	0.02 ± 0.05	0 ± 0.01	0.03 ± 0.08	0 ± 0	0.01 ± 0.02
<i>Neisseria polysacchara</i> ^A	0.01 ± 0.01	0.01 ± 0.01	0.05 ± 0.13	0.04 ± 0.01	0.01 ± 0.01 ^B	0.01 ± 0.01 ^B
<i>Neisseria sicca</i>	1.02 ± 2.37	1.49 ± 2.92	0.6 ± 0.95	1.27 ± 2.5	0.49 ± 1.2	0.14 ± 0.2
<i>Neisseria subflava</i>	0.05 ± 0.11	0.05 ± 0.11	0.11 ± 0.28	0.08 ± 0.21	0.14 ± 0.38	0.01 ± 0.03

(continued)

Table. (continued)

	Nonsmokers (n = 40)			Smokers (n = 40)		
	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)
<i>Neisseria weaveri</i>	0.15 ± 0.26	0.11 ± 0.11	0.21 ± 0.36	0.34 ± 0.08	0.02 ± 0.03	0.05 ± 0.09
<i>Olsenella</i> HOT.807	0.01 ± 0.02	0.01 ± 0.01	0 ± 0	0.07 ± 0.03	0.02 ± 0.02	0.03 ± 0.03
<i>Olsenella profusa</i>	0 ± 0	0 ± 0	0 ± 0	0.04 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Olsenella</i> sp	0 ± 0	0 ± 0	0 ± 0	0.07 ± 0.03	0 ± 0 ^B	0 ± 0 ^B
<i>Olsenella uli</i>	0.01 ± 0.05	0.02 ± 0.04	0.02 ± 0.02	0.01 ± 0.02	0 ± 0	0.03 ± 0.06
<i>Oribacterium</i> HOT.078	0.35 ± 0.62	0.41 ± 0.41	0.22 ± 0.25	0.29 ± 0.95	0.23 ± 0.2	0.83 ± 1.62
<i>Oribacterium</i> HOT.102	0 ± 0.01	0 ± 0	0.02 ± 0.07	0.02 ± 0.08	0.03 ± 0.09	0.05 ± 0.15
<i>Oribacterium</i> HOT.108 ^A	0.04 ± 0.02	0.03 ± 0.06	0.03 ± 0.05	0 ± 0.01	0 ± 0.01	0.02 ± 0.04
<i>Oribacterium</i> HOT.372	0.07 ± 0.1	0.05 ± 0.07	0.06 ± 0.07	0.07 ± 0.18	0.06 ± 0.05	0.18 ± 0.23
<i>Oribacterium sinus</i> ^A	0.05 ± 0.02	0.01 ± 0.01	0.01 ± 0.01	0 ± 0.01	0 ± 0	0.01 ± 0.03
<i>Ottowia</i> HOT.894	0.08 ± 0.22	0.07 ± 0.14	0.05 ± 0.11	0.07 ± 0.23	0 ± 0	0.01 ± 0.04
<i>Parvimonas</i> HOT.110	0.06 ± 0.07	0.38 ± 0.17 ^B	0.47 ± 0.23 ^B	0.07 ± 0.14	0.26 ± 0.39	0.6 ± 0.32 ^B
<i>Parvimonas</i> HOT.393 ^A	0.07 ± 0.02	0.01 ± 0.01	0.02 ± 0.02	0 ± 0.01	0.01 ± 0.01	0.01 ± 0.03
<i>Parvimonas micra</i>	2.11 ± 3.01 ^C	3.69 ± 1.78 ^C	11.26 ± 2.06	1.93 ± 2.5	2.08 ± 1.87 ^B	6.54 ± 4.19 ^B
<i>Parvimonas</i> sp	1.08 ± 2.51	1.15 ± 1.38	0.88 ± 1.32	1.13 ± 1.71	1.65 ± 3.55	0.9 ± 1.64
<i>Peptococcus</i> HOT.167	0.05 ± 0.09	0.15 ± 0.17	0.04 ± 0.09	0.05 ± 0.11	0.05 ± 0.09	0.16 ± 0.27
<i>Peptococcus</i> HOT.168 ^A	0.03 ± 0.01	0.01 ± 0.03	0.01 ± 0.01	0 ± 0	0.01 ± 0.02	0.02 ± 0.04
<i>Peptoniphilus</i> HOT.836	0 ± 0.01	0.01 ± 0.04	0.01 ± 0.02	0 ± 0.01	0.01 ± 0.03	0.1 ± 0.31
<i>Peptoniphilus lacrimalis</i>	0 ± 0	0 ± 0	0 ± 0	0 ± 0 ^C	0 ± 0 ^C	0.21 ± 0.01
<i>Peptostreptococcaceae</i> [XI][G-2] HOT.091	0.01 ± 0.04	0.02 ± 0.03	0.07 ± 0.02 ^B	0.03 ± 0.12	0.02 ± 0.04	0.06 ± 0.05
<i>Peptostreptococcaceae</i> [XI][G-4] HOT.103 ^A	0 ± 0	0.06 ± 0.11	0.1 ± 0.13	0.04 ± 0.01	0.11 ± 0.09 ^B	0.12 ± 0.02 ^B
<i>Peptostreptococcaceae</i> [XI][G-4] HOT.369	0.06 ± 0.15	0.13 ± 0.2	0.21 ± 0.29	0.06 ± 0.13	0.18 ± 0.3	0.2 ± 0.33
<i>Peptostreptococcaceae</i> [XI][G-7] HOT.081	0.01 ± 0.02	0 ± 0	0.04 ± 0.12	0.01 ± 0.02	0.01 ± 0.03	0 ± 0
<i>Peptostreptococcaceae</i> [XI][G-7] HOT.106	0.14 ± 0.61	0.04 ± 0.06	0.34 ± 1.06	0.04 ± 0.14	0 ± 0.01	0.01 ± 0.03
<i>Peptostreptococcaceae</i> [XIII][G-1] HOT.113	0.01 ± 0.05	0.01 ± 0.04	0 ± 0	0.01 ± 0.06	0 ± 0	0.09 ± 0.27
<i>Peptostreptococcus anaerobius</i> ^A	0.03 ± 0.01	0 ± 0	0 ± 0.01	0 ± 0.01	0 ± 0	0 ± 0
<i>Peptostreptococcus stomatis</i>	0.56 ± 1.7	0.37 ± 0.56	0.91 ± 1.51	0.49 ± 1.01	1.11 ± 2.08	0.72 ± 1.44
<i>Porphyromonas asaccharolytica</i> ^A	0.03 ± 0.01	0 ± 0 ^B	0 ± 0 ^B	0 ± 0	0 ± 0	0 ± 0
<i>Porphyromonas catoniae</i>	0.08 ± 0.25	0.03 ± 0.06	0.04 ± 0.05	0.05 ± 0.14	0.01 ± 0.03	0.01 ± 0.01
<i>Porphyromonas endodontalis</i>	0.46 ± 0.9	2.33 ± 4.28	1.39 ± 2.01	0.66 ± 1.73	0.56 ± 0.95	4.06 ± 7.69
<i>Porphyromonas gingivalis</i> ^A	0.21 ± 0.09	0.19 ± 0.33	1.2 ± 2.05	0.04 ± 0.1	0.05 ± 0.11	0.38 ± 0.91
<i>Porphyromonas</i> HOT.275	0.15 ± 0.66	0.01 ± 0.03	0.01 ± 0.02	0.02 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Porphyromonas</i> HOT.277 ^A	0 ± 0	0 ± 0	0 ± 0	0.03 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Porphyromonas</i> HOT.278	0 ± 0.01	0 ± 0.01	0 ± 0.01	0.02 ± 0.01 ^C	0.01 ± 0.01 ^C	0 ± 0
<i>Porphyromonas</i> HOT.279	0.04 ± 0.09	0.06 ± 0.16	0.09 ± 0.22	0.04 ± 0.09	0 ± 0.01	0.01 ± 0.02
<i>Porphyromonas</i> HOT.284	0 ± 0.01	0.01 ± 0.02	0.02 ± 0.05	0.01 ± 0.02	0 ± 0	0 ± 0.01
<i>Porphyromonas</i> HOT.285 ^A	0.04 ± 0.01	0 ± 0.01	0 ± 0	0 ± 0	0.02 ± 0.01 ^B	0 ± 0.01
<i>Porphyromonas</i> HOT.395 ^A	0 ± 0.01	0.03 ± 0.05	0.03 ± 0.05	0.04 ± 0.01	0.03 ± 0.09	0.09 ± 0.26
<i>Porphyromonas uenonis</i> ^A	0.03 ± 0.01	0 ± 0.01	0 ± 0	0 ± 0	0 ± 0	0 ± 0
<i>Prevotella baroniae</i> ^A	0.04 ± 0.01	0.02 ± 0.04	0.02 ± 0.02	0 ± 0.01	0.01 ± 0.01	0.2 ± 0.1 ^B
<i>Prevotella bivia</i> ^A	0.42 ± 0.09	0 ± 0 ^B	0 ± 0 ^B	0 ± 0	0 ± 0	0 ± 0.01
<i>Prevotella buccae</i> ^A	0.05 ± 0.02	0 ± 0	0.01 ± 0.01	0.01 ± 0.01	0.08 ± 0.22	0.04 ± 0.06
<i>Prevotella buccalis</i> ^A	0.03 ± 0.01	0 ± 0	0 ± 0.01	0.01 ± 0.02	0 ± 0	0 ± 0
<i>Prevotella dentalis</i>	0.02 ± 0.03	0.01 ± 0.03	0.12 ± 0.02 ^B	0.01 ± 0.02	0.02 ± 0.03	0.05 ± 0.13
<i>Prevotella denticola</i>	1.11 ± 4.06	0.07 ± 0.1	0.06 ± 0.12	0.36 ± 1.23	0.91 ± 1.39	0.58 ± 1.4
<i>Prevotella enoea</i> ^A	0.04 ± 0.01	0 ± 0 ^B	0 ± 0 ^B	0.01 ± 0.01	0 ± 0.01	0 ± 0
<i>Prevotella fusca</i> ^A	0 ± 0	0 ± 0	0 ± 0	0.04 ± 0.02	0 ± 0	0.01 ± 0.02
<i>Prevotella histicola</i>	0.02 ± 0.04	0.1 ± 0.22	0.15 ± 0.48	0.03 ± 0.08	0 ± 0.01	0.02 ± 0.04
<i>Prevotella</i> HOT.292	0.14 ± 0.27	0.02 ± 0.03	0.01 ± 0.03	0.05 ± 0.09	0.14 ± 0.24	0.2 ± 0.28
<i>Prevotella</i> HOT.293	0.02 ± 0.06 ^C	0 ± 0.01 ^C	0 ± 0	0.01 ± 0.03	0 ± 0	0 ± 0
<i>Prevotella</i> HOT.296	0.02 ± 0.06	0 ± 0.01	0.12 ± 0.24	0.06 ± 0.28	0.26 ± 0.45	0.14 ± 0.28
<i>Prevotella</i> HOT.299	0.01 ± 0.05 ^C	0 ± 0.01 ^C	0 ± 0	0.01 ± 0.03	0 ± 0.01	0 ± 0
<i>Prevotella</i> HOT.300	0.03 ± 0.07	0 ± 0	0 ± 0	0.01 ± 0.01	0.03 ± 0.05	0.04 ± 0.08
<i>Prevotella</i> HOT.301	0.02 ± 0.05	0 ± 0	0.01 ± 0.03	0.01 ± 0.03	0.02 ± 0.04	0.02 ± 0.07
<i>Prevotella</i> HOT.304	0 ± 0	0.4 ± 0.33 ^{B,C}	0 ± 0	0 ± 0	0.01 ± 0.02	0.01 ± 0.01
<i>Prevotella</i> HOT.305	0.01 ± 0.02 ^C	0.01 ± 0.01 ^C	0 ± 0	0.01 ± 0.03	0 ± 0.01	0.01 ± 0.02
<i>Prevotella</i> HOT.306	0.02 ± 0.07 ^C	0.17 ± 0.14 ^C	0 ± 0	0.02 ± 0.03	0 ± 0	0.01 ± 0.02
<i>Prevotella</i> HOT.309	0.02 ± 0.03	0 ± 0 ^B	0 ± 0 ^B	0.01 ± 0.02 ^C	0.04 ± 0.06 ^C	0 ± 0
<i>Prevotella</i> HOT.310	0.01 ± 0.01	0 ± 0 ^B	0 ± 0 ^B	0 ± 0	0 ± 0	0 ± 0
<i>Prevotella</i> HOT.313	0.01 ± 0.03	0.01 ± 0.04	0.07 ± 0.23	0.01 ± 0.02	0.01 ± 0.02	0.01 ± 0.02
<i>Prevotella</i> HOT.314	0 ± 0.01	0 ± 0.01	0 ± 0	0 ± 0	0.02 ± 0.05	0 ± 0.02
<i>Prevotella</i> HOT.315	0.01 ± 0.01	0 ± 0.02	0 ± 0	0 ± 0	0 ± 0	0.05 ± 0.13
<i>Prevotella</i> HOT.317	0.08 ± 0.15	0.09 ± 0.1	0.04 ± 0.11	0.33 ± 0.78	0.13 ± 0.33	0.07 ± 0.19
<i>Prevotella</i> HOT.376	0.07 ± 0.18	0.03 ± 0.07	0.01 ± 0.02	0.01 ± 0.02	0.03 ± 0.07	0.05 ± 0.07
<i>Prevotella</i> HOT.396	0.02 ± 0.06	0.01 ± 0.02	0.01 ± 0.02	0 ± 0	0.01 ± 0.02	0.01 ± 0.02
<i>Prevotella</i> HOT.443	0.01 ± 0.06	0 ± 0	0 ± 0	0 ± 0.01	0 ± 0	0.03 ± 0.08
<i>Prevotella</i> HOT.472	0.51 ± 2.1	0.03 ± 0.08	0.06 ± 0.1	0.29 ± 0.55	0.01 ± 0.01	0.09 ± 0.27
<i>Prevotella</i> HOT.475	0 ± 0	0.07 ± 0.04 ^{B,C}	0 ± 0	0 ± 0.01	0 ± 0	0 ± 0

(continued)

Table. (continued)

	Nonsmokers (n = 40)			Smokers (n = 40)		
	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)
<i>Prevotella</i> HOT.515	0 ± 0 ^C	0 ± 0 ^C	0.02 ± 0.01	0 ± 0	0 ± 0	0 ± 0
<i>Prevotella</i> HOT.526	0 ± 0	0 ± 0.01	0.01 ± 0.03	0.02 ± 0.02	0.01 ± 0.02	0 ± 0
<i>Prevotella</i> HOT.820	0 ± 0 ^C	0 ± 0 ^C	0.03 ± 0.05	0.03 ± 0.02	0.01 ± 0.02	0 ± 0
<i>Prevotella intermedia</i>	0.03 ± 0.12	0.01 ± 0.02	0.06 ± 0.2	0.39 ± 1.72	0.02 ± 0.05	0.42 ± 1.29
<i>Prevotella loeschii</i>	0.01 ± 0.03	0 ± 0.01	0.05 ± 0.1	0.1 ± 0.29	0.02 ± 0.03	0 ± 0.01
<i>Prevotella maculosa</i>	0.05 ± 0.11	0.02 ± 0.05	0 ± 0.01	0.03 ± 0.06	0.08 ± 0.11	0.1 ± 0.24
<i>Prevotella marshallii</i>	0 ± 0.01	0.03 ± 0.07	0 ± 0.01	0.01 ± 0.03	0.01 ± 0.02	0.01 ± 0.02
<i>Prevotella melaninogenica</i>	0.53 ± 0.16	0.25 ± 0.5 ^B	0.05 ± 0.08 ^B	0.23 ± 0.41	0.41 ± 0.76	0.26 ± 0.56
<i>Prevotella micans</i>	0.01 ± 0.02	0.08 ± 0.26	0 ± 0	0 ± 0.01	0.01 ± 0.01	0.01 ± 0.03
<i>Prevotella multiformis</i>	0 ± 0.01	0 ± 0	0.01 ± 0.02	0.03 ± 0.02	0 ± 0 ^B	0 ± 0 ^B
<i>Prevotella multisaccharivorax</i> ^A	0 ± 0	0.01 ± 0.01	0 ± 0	0.04 ± 0.02	0 ± 0 ^B	0 ± 0 ^B
<i>Prevotella nigrescens</i>	0.33 ± 1.14	0.06 ± 0.11	0.07 ± 0.13	0.22 ± 0.46	0.09 ± 0.15	0.2 ± 0.34
<i>Prevotella oralis</i> ^A	0.15 ± 0.04	0.12 ± 0.38	0.02 ± 0.02	0.03 ± 0.06	0.1 ± 0.16	0.22 ± 0.06 ^B
<i>Prevotella oris</i>	2.37 ± 3.57	1.29 ± 1.53	0.59 ± 1.25	1.77 ± 2.07	0.95 ± 0.82	3.54 ± 6.05
<i>Prevotella oulorum</i>	0.09 ± 0.15	0.03 ± 0.05	0.01 ± 0.02	0.11 ± 0.19	0.1 ± 0.14	0.07 ± 0.16
<i>Prevotella pallens</i>	0.11 ± 0.3	0.01 ± 0.02	0.02 ± 0.07	0.06 ± 0.22	0.01 ± 0.02	0.04 ± 0.07
<i>Prevotella pleuritidis</i>	0.01 ± 0.02	0.02 ± 0.05	0.02 ± 0.03	0.02 ± 0.06	0.17 ± 0.31	0.06 ± 0.12
<i>Prevotella saccharolytica</i> ^A	0.01 ± 0.02	0.02 ± 0.04	0.01 ± 0.03	0.13 ± 0.05	0.01 ± 0.01 ^B	0.01 ± 0.02 ^B
<i>Prevotella salivae</i>	0.09 ± 0.22	0.36 ± 1.09	0.02 ± 0.04	0.05 ± 0.13	0.04 ± 0.07	0.07 ± 0.16
<i>Prevotella scopos</i>	0.01 ± 0.02 ^C	0 ± 0.01	0 ± 0	0 ± 0	0 ± 0.01	0.01 ± 0.01
<i>Prevotella shahii</i>	0 ± 0	0.01 ± 0.02	0 ± 0	0 ± 0	0.01 ± 0.01	0.01 ± 0.02
<i>Prevotella veroralis</i>	0 ± 0.01	0.03 ± 0.01 ^{B,C}	0 ± 0	0.03 ± 0.01 ^C	0.01 ± 0.02 ^C	0 ± 0
<i>Propionibacterium acidifaciens</i> ^A	0.01 ± 0.01	0.01 ± 0.03	0 ± 0	0.03 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Propionibacterium acnes</i> ^A	0.01 ± 0.02	0.01 ± 0.02	0 ± 0.01	0.13 ± 0.06	0.06 ± 0.01	0.12 ± 0.01
<i>Propionibacterium avidum</i> ^A	0 ± 0	0.02 ± 0.01 ^B	0 ± 0.01	0.06 ± 0.02 ^C	0.02 ± 0.01 ^C	0 ± 0
<i>Propionibacterium</i> HOT.192 ^A	0 ± 0	0 ± 0	0 ± 0	0.03 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Propionibacterium</i> HOT.193 ^A	0.01 ± 0.02 ^C	0.02 ± 0.06 ^C	0 ± 0	0.06 ± 0.02	0 ± 0 ^B	0 ± 0 ^B
<i>Propionibacterium</i> HOT.194 ^A	0 ± 0	0.02 ± 0.01 ^B	0.01 ± 0.01	0.04 ± 0.01	0 ± 0.01	0 ± 0 ^B
<i>Propionibacterium propionicum</i> ^A	0.01 ± 0.02	0.04 ± 0.05	0.02 ± 0.04	0.07 ± 0.04	0.01 ± 0.02 ^B	0.03 ± 0.06
<i>Pseudomonas aeruginosa</i> ^A	0 ± 0	0.12 ± 0.32	0.13 ± 0.39	0.05 ± 0.02	0.02 ± 0.05	0 ± 0.01
<i>Pseudomonas fluorescens</i> ^A	0.01 ± 0.02	0.01 ± 0.01	0 ± 0.01	0.27 ± 0.08	0 ± 0.01	0 ± 0
<i>Pseudomonas</i> HOT.032 ^A	0 ± 0.01	0 ± 0	0 ± 0	0.03 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Pseudomonas pseudoalcaligenes</i>	0.02 ± 0.01	0 ± 0 ^B	0 ± 0 ^B	0.01 ± 0.01	0 ± 0	0 ± 0
<i>Pseudomonas stutzeri</i>	0.01 ± 0.02	0 ± 0	0.01 ± 0.02	0 ± 0.01	0 ± 0.01	0 ± 0
<i>Pseudoramibacter alactolyticus</i> ^A	0 ± 0.01	0.01 ± 0.01	0.01 ± 0.01	0.09 ± 0.01	0.01 ± 0.02	0.03 ± 0.08
<i>Ralstonia</i> HOT.027	0.01 ± 0.01	0.01 ± 0.03	0 ± 0	0.01 ± 0.03	0 ± 0	0 ± 0
<i>Ralstonia</i> HOT.406 ^A	0.08 ± 0.03	0.07 ± 0.19	0.02 ± 0.06	0 ± 0	0.01 ± 0.01	0.01 ± 0.01
<i>Ralstonia pickettii</i>	0.05 ± 0.13	0.04 ± 0.13	0.01 ± 0.03	0.11 ± 0.4	0 ± 0	0.01 ± 0.03
<i>Rhizobium loti</i>	0.01 ± 0.01	0.01 ± 0.02	0 ± 0.01	0.06 ± 0.24	0 ± 0 ^B	0 ± 0 ^B
<i>Rothia aeria</i>	0.17 ± 0.29	0.08 ± 0.07	0.06 ± 0.12	0.11 ± 0.01	0.02 ± 0.04 ^B	0.01 ± 0.03 ^B
<i>Rothia dentocariosa</i>	0.22 ± 0.49	0.23 ± 0.39	0.12 ± 0.22	0.2 ± 0.39	0.14 ± 0.2	0.02 ± 0.03
<i>Rothia mucilaginosa</i>	0.11 ± 0.18	0.19 ± 0.29	0.04 ± 0.08	0.14 ± 0.08	0.05 ± 0.1	0.02 ± 0.04 ^B
<i>Scardovia inopinata</i> ^A	0 ± 0	0.01 ± 0.01	0 ± 0	0.04 ± 0.02 ^C	0.01 ± 0.02 ^C	0 ± 0
<i>Scardovia wiggsiae</i> ^A	0 ± 0.01	0.03 ± 0.06	0.01 ± 0.05	0.04 ± 0.02	0.36 ± 1.04 ^B	0 ± 0
<i>Selenomonas artemidis</i>	0.08 ± 0.19	0.03 ± 0.05	0.12 ± 0.17	0.11 ± 0.24	0.07 ± 0.18	0.49 ± 1.18
<i>Selenomonas diana</i> ^A	0.2 ± 0.41	0.1 ± 0.1	0.06 ± 0.06	0.07 ± 0.09	0.07 ± 0.15	0.22 ± 0.45
<i>Selenomonas flueggei</i>	0.06 ± 0.15	0.14 ± 0.22	0.02 ± 0.04	0.05 ± 0.08	0.04 ± 0.06	0.13 ± 0.31
<i>Selenomonas</i> HOT.126 ^A	0.04 ± 0.01	0.07 ± 0.1	0.04 ± 0.09	0.01 ± 0.02	0.01 ± 0.01	0.04 ± 0.08
<i>Selenomonas</i> HOT.133	0 ± 0	0 ± 0.01	0.04 ± 0.12	0 ± 0.01	0.01 ± 0.01	0.16 ± 0.48
<i>Selenomonas</i> HOT.134 ^A	0.48 ± 0.09	0.3 ± 0.87	0.49 ± 0.59	0.06 ± 0.23	0.16 ± 0.16	0.53 ± 0.82 ^B
<i>Selenomonas</i> HOT.136	0.04 ± 0.12	0.06 ± 0.14	0.01 ± 0.03	0.01 ± 0.03	0.04 ± 0.06	0.11 ± 0.28
<i>Selenomonas</i> HOT.137	0.04 ± 0.07	0.01 ± 0.01	0.11 ± 0.21	0.05 ± 0.13	0.09 ± 0.18	0.05 ± 0.1
<i>Selenomonas</i> HOT.138	0.03 ± 0.06	0.01 ± 0.02	0.01 ± 0.01	0 ± 0.01	0.04 ± 0.12	0.01 ± 0.01
<i>Selenomonas</i> HOT.140 ^A	0.08 ± 0.01	0.01 ± 0.02	0.02 ± 0.03	0.03 ± 0.09	0.06 ± 0.16	0.06 ± 0.15
<i>Selenomonas</i> HOT.143	0.01 ± 0.02	0.01 ± 0.02	0.01 ± 0.01	0.01 ± 0.01	0 ± 0.01	0.02 ± 0.03
<i>Selenomonas</i> HOT.146	0.03 ± 0.05	0.09 ± 0.23	0.05 ± 0.1	0.01 ± 0.03	0.02 ± 0.02	0.09 ± 0.13 ^B
<i>Selenomonas</i> HOT.149 ^A	0.18 ± 0.05	0.15 ± 0.24	0.09 ± 0.17	0.03 ± 0.05	0.09 ± 0.18	0.34 ± 0.77
<i>Selenomonas</i> HOT.388 ^A	0.03 ± 0.01	0.01 ± 0.03	0.01 ± 0.03	0 ± 0 ^C	0 ± 0 ^C	0.02 ± 0.01
<i>Selenomonas</i> HOT.442 ^A	0.04 ± 0.01	0.03 ± 0.04	0.04 ± 0.08	0.01 ± 0.01	0.07 ± 0.2	0.02 ± 0.03
<i>Selenomonas</i> HOT.478 ^A	0.04 ± 0.01	0.01 ± 0.02	0 ± 0.01	0 ± 0	0 ± 0.01	0 ± 0.01
<i>Selenomonas</i> HOT.479 ^A	0.15 ± 0.04	0.09 ± 0.1	0.04 ± 0.03	0.02 ± 0.02	0.01 ± 0.02	0.06 ± 0.11
<i>Selenomonas</i> HOT.481 ^A	0.18 ± 0.03	0.12 ± 0.24	0.24 ± 0.46	0.02 ± 0.04	0.04 ± 0.06	0.1 ± 0.17
<i>Selenomonas</i> HOT.501 ^A	0.03 ± 0.01	0 ± 0.01	0 ± 0.01	0 ± 0	0 ± 0.02	0.02 ± 0.01 ^B
<i>Selenomonas</i> HOT.892	0.03 ± 0.07	0.13 ± 0.31	0.24 ± 0.71	0.02 ± 0.03	0.02 ± 0.02	0.03 ± 0.05
<i>Selenomonas infelix</i> ^A	0.18 ± 0.09	0.13 ± 0.16	0.21 ± 0.3	0.08 ± 0.01	0.14 ± 0.01 ^B	0.11 ± 0.15

(continued)

Table. (continued)

	Nonsmokers (n = 40)			Smokers (n = 40)		
	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)
<i>Selenomonas noxia</i> ^A	0.19 ± 0.04	0.19 ± 0.23	0.55 ± 1.15	0.07 ± 0.09	0.26 ± 0.52	0.44 ± 0.62
<i>Selenomonas sputigena</i> ^A	1.27 ± 0.29	0.78 ± 1.22	0.56 ± 0.75	0.35 ± 0.64	0.39 ± 0.36	2.13 ± 0.47 ^B
<i>Shuttleworthia satelles</i>	0.09 ± 0.19	0.11 ± 0.19	0.1 ± 0.22	0.04 ± 0.12	0.29 ± 0.47	0.36 ± 1.01
<i>Simonsiella muelleri</i>	0.14 ± 0.53	0.06 ± 0.07	0.06 ± 0.08	0.03 ± 0.07	0.1 ± 0.27	0.02 ± 0.04
<i>Solobacterium moore</i> ^A	0.35 ± 0.07	0.19 ± 0.21	0.14 ± 0.22	0.28 ± 0.04	0.15 ± 0.27	0.39 ± 0.4
<i>Sphingomonas</i> HOT.003	0.01 ± 0.03 ^C	0.01 ± 0.02 ^C	0 ± 0	0.01 ± 0.04 ^C	0.01 ± 0.02 ^C	0 ± 0
<i>Sphingomonas</i> HOT.004	0.06 ± 0.21	0.07 ± 0.16	0.01 ± 0.03	0.08 ± 0.29	0.02 ± 0.04	0 ± 0
<i>Sphingomonas</i> HOT.006	0.01 ± 0.02	0.01 ± 0.02	0 ± 0.01	0.04 ± 0.15	0 ± 0.01	0 ± 0
<i>Sphingomonas</i> HOT.007	0 ± 0	0.01 ± 0.01	0 ± 0.01	0 ± 0	0 ± 0	0 ± 0
SRI [G-I] HOT.345 ^A	0 ± 0	0.04 ± 0.01 ^B	0.01 ± 0.02 ^B	0.04 ± 0.01 ^C	0.01 ± 0.02 ^C	0 ± 0
SRI [G-I] HOT.874	0.02 ± 0.01	0 ± 0 ^B	0 ± 0 ^B	0 ± 0.01	0 ± 0	0.01 ± 0.02
<i>Staphylococcus aureus</i> ^A	0.03 ± 0.02 ^C	0 ± 0.01 ^C	0 ± 0	0 ± 0	0 ± 0	0 ± 0
<i>Staphylococcus caprae</i>	0 ± 0.01	0.02 ± 0.06	0 ± 0	0.01 ± 0.04	0.01 ± 0.02	0 ± 0
<i>Staphylococcus epidermidis</i>	0 ± 0.01	0.04 ± 0.09	0.01 ± 0.01	0.02 ± 0.06	0 ± 0.01	0 ± 0.01
<i>Staphylococcus warneri</i>	0.01 ± 0.02	0.06 ± 0.16	0 ± 0	0.01 ± 0.05	0 ± 0	0 ± 0.01
<i>Streptococcus agalactiae</i>	0 ± 0.01	0.02 ± 0.02	0 ± 0.01	0 ± 0.01	0.05 ± 0.02 ^{B,C}	0 ± 0
<i>Streptococcus anginosus</i> ^A	0.31 ± 0.01	0.19 ± 0.31	0.17 ± 0.17	0.1 ± 0.12	0.24 ± 0.2 ^{B,C}	0.16 ± 0.13
<i>Streptococcus australis</i>	0.14 ± 0.16	0.19 ± 0.28	0.08 ± 0.13	0.17 ± 0.25	0.22 ± 0.33	0.17 ± 0.27
<i>Streptococcus constellatus</i>	0.55 ± 1.54	0.08 ± 0.14	0.07 ± 0.12	0.25 ± 0.63	0.1 ± 0.19	0.27 ± 0.35
<i>Streptococcus cristatus</i>	0.09 ± 0.12	0.49 ± 0.18 ^B	0.17 ± 0.32	0.13 ± 0.23	0.22 ± 0.27	0.16 ± 0.26
<i>Streptococcus downei</i>	0.05 ± 0.08	0.12 ± 0.14	0.08 ± 0.07	0.04 ± 0.06	0.1 ± 0.12	0.04 ± 0.05
<i>Streptococcus gordonii</i>	0.88 ± 1.32	0.62 ± 0.8	0.33 ± 0.74	0.75 ± 1.19	1.25 ± 1.89	0.09 ± 0.09
<i>Streptococcus</i> HOT.055	0.04 ± 0.02	0 ± 0 ^B	0 ± 0 ^B	0.02 ± 0.05	0.01 ± 0.02	0 ± 0
<i>Streptococcus</i> HOT.056	0.02 ± 0.06	0.03 ± 0.04	0 ± 0.01	0.07 ± 0.26	0.02 ± 0.02	0.03 ± 0.05
<i>Streptococcus</i> HOT.057	0.02 ± 0.02	0.05 ± 0.01 ^B	0.03 ± 0.03	0.03 ± 0.06	0.03 ± 0.03	0.05 ± 0.07
<i>Streptococcus</i> HOT.058	0.21 ± 0.51	0.18 ± 0.26	0.07 ± 0.13	0.12 ± 0.23	0.11 ± 0.08	0.04 ± 0.05
<i>Streptococcus</i> HOT.061	0.06 ± 0.12	0.03 ± 0.04	0 ± 0	0.04 ± 0.07	0.07 ± 0.14	0.03 ± 0.07
<i>Streptococcus</i> HOT.064	6.87 ± 11.62	1.48 ± 2.02	1.11 ± 2.24	8.34 ± 16.09	4.71 ± 8.82	1.99 ± 3.15
<i>Streptococcus</i> HOT.065	0.04 ± 0.1	0.04 ± 0.06	0.02 ± 0.03	0.03 ± 0.03	0.06 ± 0.08	0.01 ± 0.01
<i>Streptococcus</i> HOT.066	0.04 ± 0.05	0.24 ± 0.69	0.08 ± 0.11	0.11 ± 0.22	0.04 ± 0.07	0.01 ± 0.02
<i>Streptococcus</i> HOT.067	0.01 ± 0.01	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
<i>Streptococcus</i> HOT.068	0.01 ± 0.03	0.02 ± 0.02	0.01 ± 0.01	0.03 ± 0.07	0.03 ± 0.03	0 ± 0.01
<i>Streptococcus</i> HOT.069	0 ± 0.01	0.06 ± 0.17	0.01 ± 0.01	0.01 ± 0.01	0.04 ± 0.08	0 ± 0.01
<i>Streptococcus</i> HOT.070 ^A	0.4 ± 0.08	0.05 ± 0.08	0 ± 0.01	0.13 ± 0.23	0.31 ± 0.46	0.13 ± 0.26
<i>Streptococcus</i> HOT.071	0.7 ± 0.84	0.6 ± 0.7	0.38 ± 0.48	0.72 ± 0.94	1.14 ± 1.15	0.3 ± 0.32
<i>Streptococcus</i> HOT.074	0.14 ± 0.31	0.18 ± 0.28	0.09 ± 0.13	0.13 ± 0.22	0.15 ± 0.16	0.02 ± 0.02
<i>Streptococcus</i> HOT.423	0.08 ± 0.2	0 ± 0.01	0 ± 0.01	0.1 ± 0.3	0.01 ± 0.01	0.01 ± 0.03
<i>Streptococcus</i> HOT.431	0.07 ± 0.1	0.08 ± 0.13	0.03 ± 0.04	0.13 ± 0.45	0.05 ± 0.07	0.06 ± 0.14
<i>Streptococcus</i> HOT.486	0.03 ± 0.03	0.04 ± 0.07	0.02 ± 0.02	0.03 ± 0.03	0.04 ± 0.03	0.04 ± 0.07
<i>Streptococcus</i> HOT.487	0.03 ± 0.04	0.06 ± 0.07	0.05 ± 0.09	0.05 ± 0.07	0.08 ± 0.09	0.05 ± 0.14
<i>Streptococcus infantis</i> ^A	0.47 ± 0.28	0.11 ± 0.14	0.03 ± 0.07	0.08 ± 0.09	0.11 ± 0.08	0.04 ± 0.04
<i>Streptococcus intermedius</i>	1.55 ± 1.82	3.57 ± 3.33	1.73 ± 1.3	2.06 ± 2.73	1.67 ± 1.51	6.15 ± 10.64
<i>Streptococcus mitis</i> ^A	1.48 ± 1.81	0.95 ± 0.7	0.33 ± 0.5	3.89 ± 0.63	1.26 ± 1.56	0.4 ± 0.48
<i>Streptococcus mutans</i>	0.08 ± 0.15	0.35 ± 0.16 ^C	0.02 ± 0.03	0.11 ± 0.25	1.7 ± 0.73 ^C	0.05 ± 0.07
<i>Streptococcus oligofermentans</i>	3.93 ± 2.33	11.8 ± 3.35 ^C	7.36 ± 5.22	7.44 ± 9.58	10.08 ± 10.39	1.69 ± 2.24
<i>Streptococcus oralis</i>	2.34 ± 2.81	3.09 ± 2.3	1.51 ± 2.87	2.75 ± 4.44	3.09 ± 3.33	0.74 ± 0.78
<i>Streptococcus parasanguinis</i>	0.26 ± 0.48	0.7 ± 1.37	0.16 ± 0.34	0.32 ± 0.57	0.47 ± 0.56	0.08 ± 0.1
<i>Streptococcus peroris</i>	0.16 ± 0.53	0.25 ± 0.71	0.01 ± 0.02	0.04 ± 0.08	0.21 ± 0.37	0.04 ± 0.05
<i>Streptococcus pneumoniae</i>	1.18 ± 2.34	4.14 ± 6.51	1.41 ± 3.12	0.88 ± 1.8	7.03 ± 11.44 ^{B,C}	0.58 ± 1.1
<i>Streptococcus pyogenes</i>	0.07 ± 0.23	0.04 ± 0.05	0.05 ± 0.09	0.02 ± 0.03	0.02 ± 0.03	0.01 ± 0.04
<i>Streptococcus salivarius</i>	0.12 ± 0.12	0.33 ± 0.44	0.1 ± 0.2	0.15 ± 0.26	0.22 ± 0.19	0.12 ± 0.16
<i>Streptococcus sanguinis</i>	1.79 ± 3.34	0.86 ± 0.66	0.78 ± 1.3	1.28 ± 2.91	0.36 ± 0.28	0.95 ± 1.51
<i>Streptococcus sinensis</i>	0.01 ± 0.03	0.08 ± 0.01 ^B	0.05 ± 0.08	0.02 ± 0.03	0.09 ± 0.03 ^{B,C}	0.02 ± 0.02
<i>Streptococcus sobrinus</i> ^A	0.74 ± 1.23	1.06 ± 0.96	1.38 ± 1.37	1.87 ± 0.69	2.51 ± 0.72 ^B	0.3 ± 0.46
<i>Streptococcus vestibularis</i> ^A	0.06 ± 0.14	0.12 ± 0.21	0.06 ± 0.18	0.19 ± 0.05	0.08 ± 0.06 ^B	0.05 ± 0.07 ^B
<i>Tannerella forsythia</i>	0.28 ± 0.81	0.15 ± 0.23	0.67 ± 0.9	0.21 ± 0.55	0.11 ± 0.19	0.24 ± 0.33
<i>Tannerella</i> HOT.286	0.01 ± 0.02	0.01 ± 0.01	0.03 ± 0.1	0.01 ± 0.04	0.01 ± 0.01	0.01 ± 0.02
<i>Tannerella</i> HOT.808	0.01 ± 0.03	0.07 ± 0.15	0.01 ± 0.02	0.01 ± 0.02	0.04 ± 0.09	0.02 ± 0.05
<i>Tannerella</i> HOT.916 ^A	0.01 ± 0.04	0 ± 0 ^B	0 ± 0 ^B	0.12 ± 0.02	0 ± 0 ^B	0 ± 0 ^B
<i>Terrahaemophilus aromaticivorans</i> ^A	3.31 ± 1.15	0.68 ± 1.89	0.08 ± 0.17	1.06 ± 0.34	0.3 ± 0.84	0.4 ± 0.97

(continued)

Table. (continued)

	Nonsmokers (n = 40)			Smokers (n = 40)		
	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)	Health (n = 20)	Mucositis (n = 10)	Implantitis (n = 10)
TM7 [G-I] HOT.346	0.68 ± 2.11	0.23 ± 0.32	0.99 ± 2.25	0.25 ± 0.56	0.68 ± 1.63	0.33 ± 0.57
TM7 [G-I] HOT.347	0.01 ± 0.02	0.03 ± 0.09	0.28 ± 0.9	0.01 ± 0.03	0 ± 0 ^B	0 ± 0 ^B
TM7 [G-I] HOT.348	0.03 ± 0.12	0 ± 0.01	0 ± 0.01	0.01 ± 0.03 ^C	0.05 ± 0.01 ^C	0 ± 0
TM7 [G-I] HOT.349	0.19 ± 0.51	0.24 ± 0.43	0.17 ± 0.31	0.13 ± 0.25	0.06 ± 0.09	1.28 ± 3.79
TM7 [G-I] HOT.352 ^A	0.09 ± 0.07	0.01 ± 0.02	0 ± 0	0 ± 0.01	0 ± 0.01	0 ± 0
TM7 [G-I] HOT.353	0.42 ± 1.56	0.15 ± 0.23	0.04 ± 0.07	0.06 ± 0.11	0.03 ± 0.06	0.1 ± 0.14
TM7 [G-I] HOT.488	0.01 ± 0.03	0 ± 0.01	0 ± 0	0 ± 0.01	0 ± 0	0 ± 0.01
TM7 [G-5] HOT.356	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0.01 ± 0.02	0.03 ± 0.07
TM7 [G-5] HOT.437	0.04 ± 0.14	0.75 ± 2.01	0.03 ± 0.06	0.28 ± 1.02	0.29 ± 0.91	0.86 ± 1.68
<i>Treponema amylovorum</i>	0 ± 0.01	0.02 ± 0.04	0 ± 0.01	0.01 ± 0.02	0 ± 0	0 ± 0
<i>Treponema denticola</i> ^A	0.01 ± 0.02	0.09 ± 0.22	0.21 ± 0.5	0.03 ± 0.07	0.03 ± 0.05	0.1 ± 0.24
<i>Treponema</i> HOT.226 ^A	0 ± 0	0 ± 0	0 ± 0	0.02 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Treponema</i> HOT.230 ^A	0 ± 0	0.02 ± 0.04	0 ± 0	0.04 ± 0.02	0 ± 0 ^B	0 ± 0 ^B
<i>Treponema</i> HOT.231	0.02 ± 0.05	0.05 ± 0.1	0.01 ± 0.02	0.02 ± 0.05	0.04 ± 0.06	0.01 ± 0.02
<i>Treponema</i> HOT.232 ^A	0 ± 0.01	0 ± 0.01	0 ± 0	0.03 ± 0.02	0 ± 0.01	0 ± 0
<i>Treponema</i> HOT.234	0 ± 0	0 ± 0.01	0 ± 0	0 ± 0	0 ± 0	0 ± 0
<i>Treponema</i> HOT.235	0 ± 0	0.01 ± 0.01	0 ± 0	0 ± 0	0 ± 0	0 ± 0
<i>Treponema</i> HOT.236 ^A	0 ± 0.01	0 ± 0	0 ± 0	0.08 ± 0.04	0 ± 0 ^B	0 ± 0 ^B
<i>Treponema</i> HOT.237	0.01 ± 0.03	0.01 ± 0.04	0 ± 0.01	0.02 ± 0.05	0.01 ± 0.02	0.07 ± 0.19
<i>Treponema</i> HOT.242 ^A	0 ± 0	0 ± 0	0 ± 0	0.03 ± 0.02	0 ± 0 ^B	0 ± 0 ^B
<i>Treponema</i> HOT.246	0 ± 0	0.04 ± 0.01 ^B	0.03 ± 0.01 ^B	0.01 ± 0.02	0.02 ± 0.03	0 ± 0
<i>Treponema</i> HOT.247	0.03 ± 0.1	0 ± 0	0 ± 0	0.03 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Treponema</i> HOT.249 ^A	0.01 ± 0.02	0 ± 0.01	0 ± 0.01	0 ± 0	0 ± 0.01	0.02 ± 0.01 ^B
<i>Treponema</i> HOT.253 ^A	0 ± 0	0 ± 0.01	0 ± 0	0.04 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Treponema</i> HOT.257	0.01 ± 0.04	0.11 ± 0.35	0 ± 0.01	0.06 ± 0.28	0 ± 0 ^B	0 ± 0 ^B
<i>Treponema</i> HOT.258	0 ± 0	0.02 ± 0.03	0.01 ± 0.01	0 ± 0	0 ± 0	0 ± 0
<i>Treponema</i> HOT.260	0 ± 0	0.04 ± 0.01 ^B	0.02 ± 0.01 ^B	0 ± 0	0 ± 0	0 ± 0
<i>Treponema</i> HOT.262 ^A	0 ± 0	0 ± 0.01	0 ± 0.01	0.02 ± 0.01 ^B	0.01 ± 0.03	0 ± 0
<i>Treponema</i> HOT.265	0 ± 0	0 ± 0	0 ± 0	0.02 ± 0.03	0.01 ± 0.01	0 ± 0
<i>Treponema</i> HOT.268	0.13 ± 0.49	0.04 ± 0.08	0.08 ± 0.09	0.04 ± 0.09	0.03 ± 0.04	0.03 ± 0.04
<i>Treponema</i> HOT.269 ^A	0.15 ± 0.3	0.07 ± 0.12	0.05 ± 0.06	0.01 ± 0.03	0.07 ± 0.01 ^B	0.02 ± 0.03
<i>Treponema</i> HOT.270	0.01 ± 0.01	0 ± 0.01	0 ± 0	0 ± 0	0 ± 0.01	0 ± 0.01
<i>Treponema</i> HOT.490 ^A	0 ± 0	0 ± 0	0 ± 0	0.05 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Treponema</i> HOT.517	0 ± 0	0.01 ± 0.01	0 ± 0	0 ± 0	0 ± 0	0 ± 0
<i>Treponema leathinolyticum</i> ^A	0.01 ± 0.03	0.01 ± 0.03	0.19 ± 0.05 ^B	0.15 ± 0.01	0.02 ± 0.03 ^B	0.12 ± 0.24 ^B
<i>Treponema maltophilum</i>	0.08 ± 0.2	0.06 ± 0.07	0.25 ± 0.44	0.05 ± 0.13	0.03 ± 0.05	0.05 ± 0.12
<i>Treponema medium</i>	0.02 ± 0.08	0.01 ± 0.02	0.01 ± 0.01	0.01 ± 0.02	0.01 ± 0.01	0 ± 0
<i>Treponema parvum</i>	0 ± 0	0 ± 0.01	0.01 ± 0.03	0 ± 0.01	0 ± 0	0.01 ± 0.02
<i>Treponema pectinovorum</i> ^A	0 ± 0	0 ± 0	0 ± 0	0.05 ± 0.01	0 ± 0 ^B	0 ± 0 ^B
<i>Treponema putidum</i>	0.02 ± 0.05	0.01 ± 0.03	0.05 ± 0.08	0.01 ± 0.02	0.01 ± 0.02	0.01 ± 0.02
<i>Treponema socranskii</i>	0.26 ± 0.4	0.23 ± 0.3	0.37 ± 0.41	0.19 ± 0.28	0.22 ± 0.27	0.24 ± 0.17
<i>Treponema vincentii</i>	0 ± 0	0.01 ± 0.01	0 ± 0	0 ± 0	0 ± 0	0 ± 0
<i>Variorax paradoxus</i>	0.02 ± 0.07	0.03 ± 0.08	0 ± 0.01	0 ± 0	0 ± 0.01	0.01 ± 0.04
<i>Veillonella atypica</i>	0.31 ± 0.47	0.39 ± 0.34	0.21 ± 0.22	0.29 ± 0.43	0.78 ± 1.74	0.12 ± 0.17
<i>Veillonella denticariosi</i>	0.01 ± 0.01	0.03 ± 0.09	0 ± 0.01	0.01 ± 0.01	0.03 ± 0.05	0.02 ± 0.04
<i>Veillonella dispar</i>	0.07 ± 0.09	0.1 ± 0.1	0.08 ± 0.11	0.11 ± 0.14	0.39 ± 0.14 ^{B,C}	0.06 ± 0.02
<i>Veillonella</i> HOT.780 ^A	0 ± 0.01	0.03 ± 0.08	0.09 ± 0.26	0.01 ± 0.01	0.03 ± 0.01	0 ± 0.01
<i>Veillonella</i> HOT.917	0 ± 0.01	0.01 ± 0.02	0 ± 0.01	0 ± 0	0 ± 0.01	0 ± 0
<i>Veillonella parvula</i>	8.03 ± 7.81	7.64 ± 6.71	3.72 ± 5.75	5.46 ± 5.15	13.73 ± 10.34 ^{B,C}	3.38 ± 3.33
<i>Veillonella rogosa</i> ^A	0.12 ± 0.07	0.01 ± 0.03	0.02 ± 0.05	0.02 ± 0.03	0.01 ± 0.04	0.01 ± 0.03
Veillonellaceae [G-I] HOT.129	0.14 ± 0.35	0.07 ± 0.16	0.05 ± 0.08	0.05 ± 0.1	0.15 ± 0.2	0.42 ± 0.52 ^C
Veillonellaceae [G-I] HOT.132	0.03 ± 0.1	0.04 ± 0.12	0.01 ± 0.02	0.03 ± 0.06	0.05 ± 0.1	0.32 ± 0.76
Veillonellaceae [G-I] HOT.135 ^A	0 ± 0.01	0 ± 0	0.01 ± 0.03	0.11 ± 0.04	0.01 ± 0.02	0.01 ± 0.01
Veillonellaceae [G-I] HOT.145	0 ± 0	0.04 ± 0.01 ^B	0.02 ± 0.02 ^B	0 ± 0	0.01 ± 0.01	0 ± 0.01
Veillonellaceae [G-I] HOT.148	0.05 ± 0.19	0.02 ± 0.03	0.04 ± 0.04	0.03 ± 0.09	0.11 ± 0.27	0.04 ± 0.08
Veillonellaceae [G-I] HOT.150	0.19 ± 0.47	0.19 ± 0.21	0.26 ± 0.55	0.1 ± 0.22	0.39 ± 0.42	0.68 ± 0.09 ^B
Veillonellaceae [G-I] HOT.155	0.1 ± 0.28	0.14 ± 0.26	0.08 ± 0.13	0.06 ± 0.11	0.14 ± 0.15	0.41 ± 0.08 ^B
Veillonellaceae [G-I] HOT.483 ^A	0 ± 0	0.06 ± 0.02 ^B	0.17 ± 0.08 ^B	0.05 ± 0.02	0.02 ± 0.06	0.01 ± 0.02
Veillonellaceae [G-I] HOT.918	0 ± 0.01	0.01 ± 0.01	0.01 ± 0.02	0 ± 0.01	0.01 ± 0.02	0.03 ± 0.01 ^B

Species with relative abundances of 0.01% or greater and found in two or more samples were included in the analysis. Species that were a part of the core microbiome of smokers (light gray), nonsmokers (dark gray), or both (black with white font) are highlighted.

^ASpecies that were significantly different between healthy smokers and nonsmokers.

^BSpecies that differed from health.

^CSpecies that differed from implantitis.

Figure 2. Microbial shifts accompanying shifts from peri-implant health to disease in nonsmokers. **(A)** The principal coordinates analysis (PCoA) plot of community membership (unweighted UniFrac distances) of the peri-implant microbiomes in health, mucositis, and implantitis in nonsmokers. Kernel plots of Chao estimates of diversity **(B)** and unique species **(C)** are also shown.

Figure 3. Microbial shifts accompanying shifts from peri-implant health to disease in smokers. **(A)** The principal coordinates analysis (PCoA) plot of UniFrac distances of the peri-implant microbiomes in health, mucositis, and implantitis in smokers. The microbial profiles of health and disease were significantly different ($P < 0.05$, analysis of similarity [ANOSIM]). Chao estimates of diversity **(B)** and unique species **(C)** are also shown.

traditionally regarded as periodontal and/or systemic pathogens, including those belonging to the genera *Capnocytophaga*, *Treponema*, *Propionibacterium*, *Pseudomonas*, *Lactobacillus*, and *Leptotrichia* (Table). These results are very similar to those seen in our investigation of subgingival microbiota (Mason et al. 2014). Especially intriguing is the presence of *Lactobacilli*, *Propionibacteria*, and *Rothia* exclusively in smokers. While *Lactobacilli* were detected in 45% to 60% of samples, *Propionibacterium propionicus* was found in the core microbiome of smokers. *Propionibacteria* have been found in several periprosthetic joint infections (Achermann et al. 2014) and are increasingly being implicated in the etiology of failing shoulder and knee implants, as well as neurosurgical shunts and endodontic infections (Portillo et al. 2013). It is long known that *Lactobacilli* and *Propionibacteria* share a nutritional symbiosis (Liu and Moon 1982). It is possible that this cooperativity contributes to the persistence of *Propionibacteria* in the peri-implant sulcus and predisposes it to future disease. *Rothia aerea* and *Rothia mucilaginosa* have been implicated in prosthetic hip and knee infections, and it has been suggested that oral habitats may play a role in predisposing susceptible individuals to infections elsewhere in the body (Verrall et al. 2010; Mahobia et al. 2013). While these events are biologically plausible, there is currently no evidence to suggest this as a pathogenic mechanism and warrants further investigation.

We then examined the differences in the core peri-implant microbiome between smokers and nonsmokers. The term *core microbiome* was introduced by the Human Microbiome Project (2012) to identify bacterial consortia that were present in most of the study population, implying that these species are best adapted to that particular microenvironment. We defined the core peri-implant microbiome as that which is found in 75% or more of individuals. This is a far more conservative approach than that used by other investigations (Human Microbiome Project 2012; Abusleme et al. 2013) and ensured that the species under investigation were truly representative of the peri-implant microbiome. The core peri-implant microbiome of both smokers and nonsmokers comprised 65 species, which represented a mere 13% of the health-compatible peri-implant microbiome, typifying the great interindividual variability in oral bacterial communities. However, while smokers and nonsmokers shared 34 species, they differed by 31. The data indicate that while there exists a core microbiome composed of species that are most suited to the peri-implant habitat, smoking modifies this environment.

Shifts from Health to Disease in Nonsmokers

PCoA revealed that the health-compatible peri-implant microbiome was distinct from that associated with disease (Fig. 2A). To understand how these communities were different, we first examined changes in microbial diversity associated with shifts in health status. Diversity did not change from health to disease (Fig. 2B). Since diversity is a measure of both species richness (number of species) and evenness (abundance of each species), we compared relative abundances of community members (community structure) as well as the loss and gain of species

(community membership). Shift from health to mucositis was associated with a decrease in the abundance of a few species (Table), loss of certain others, and, most important, gain of several new species (Fig. 2C). Thus, the similar diversities in health and mucositis were attributable to 2 entirely different phenomena; while health was associated with higher abundances of fewer species, mucositis was characterized by a decrease in abundances and loss of a few health-associated species, along with acquisition of several new members. Thus, a key event in the development of mucositis appears to be an increase in community membership. These new species demonstrated heterogeneity in their prevalence among different individuals, and the core microbiome associated with peri-implant health remained unaffected. However, an important observation was that species acquired in mucositis persisted into implantitis; implantitis was similar to mucositis both in species richness and evenness. The results thus suggest that peri-implant mucositis may be a key event in the pathogenesis of peri-implantitis. It is important to investigate this hypothesis with prospective studies.

Shifts from Health to Disease in Smokers

Smokers began with a “reduced” microbiome in states of clinical health, which was enriched for several oral and systemic pathogens (Fig. 1B and Table). This microbiome became further reduced during the shift from health to mucositis, with loss of several species belonging to the core microbiome (Fig. 3B, C and Table). A similar observation has been previously reported in the subgingival microbiome of smokers in periodontal health and disease (Bizzarro et al. 2013; Mason et al. 2014). Thus, in smokers, 2 important events were evident in the transition from health to disease: not only did the process of pathogen enrichment observed in health continue into disease, but also the species that were being replaced were similar between individuals. Very few species were acquired between mucositis and implantitis, suggesting that the pathogen-rich state established in mucositis persists in implantitis.

In summary, the data support previous studies that the peri-implant sulcus provides a unique colonization niche for oral bacteria, as evidenced by the presence of a distinct core microbiome. The data also suggest that peri-implantitis and peri-implant mucositis are microbiologically similar entities. In nonsmokers (but not smokers), the transition from health to mucositis and progression to implantitis resemble primary ecological succession, with acquisition of several species without replacement of pioneer organisms. Thus, peri-implant mucositis appears to be an important transitional event in the progression to peri-implantitis, at least from a microbiological standpoint.

Smoking shapes the peri-implant microbiome even in states of clinical health, depleting commensals from this niche and enriching for pathogens. This effect appears to be a nonrandom event. The transition from health to mucositis and progression to implantitis take an alternate pathway in smokers, with further enrichment of the microbiome and decrease in diversity. Thus, in both groups, peri-implant mucositis is a sentinel event

indicating the environment is primed for future disease, albeit by different mechanisms.

The clinical implications of these findings are manifold, but the primary message appears to be the importance of treating and preventing peri-implant mucositis, in the prevention of peri-implantitis. Another important implication is the risk associated with smoking for implant longevity.

Author Contributions

A.A. Tsigarida, P.S. Kumar, contributed to conception, design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript; S.M. Dabdoub, contributed to data analysis and interpretation, drafted and critically revised the manuscript; H.N. Nagaraja, contributed to design and data analysis, drafted and critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

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