

UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL
FACULDADE DE ODONTOLOGIA
PROGRAMA DE PÓS-GRADUAÇÃO – NÍVEL DOUTORADO

Daniela Jorge Corralo

**BACTERIAL COMPOSITION OF MICROBIOME ASSOCIATED TO
SUPRAGINGIVAL BIOFILM IN HEALTH AND CARIES DISEASE**

Porto Alegre

2018

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Tese apresentada ao Programa de Pós-Graduação em Odontologia como parte dos requisitos obrigatórios para a obtenção do título de doutora em Clínica Odontológica com ênfase em Dentística/Cariologia.

Orientadora: Prof^ª Dr^ª Marisa Maltz

Co-orientadora: Prof^ª Dr^ª Clarissa

Cavalcanti Fatturi Parolo

Linha de Pesquisa: Biomateriais e Técnicas
Terapêuticas em Odontologia.

Porto Alegre

2018

CIP - Catalogação na Publicação

Corralo, Daniela Jorge Corralo

Bacterial composition of microbiome associated to supragingival biofilm in health and caries disease / Daniela Jorge Corralo Corralo. -- 2018.

120 f.

Orientadora: Marisa Maltz Maltz.

Coorientadora: Clarissa Cavalcanti Fatturi Parolo Parolo.

Tese (Doutorado) -- Universidade Federal do Rio Grande do Sul, Faculdade de Odontologia, Programa de Pós-Graduação em Odontologia, Porto Alegre, BR-RS, 2018.

1. Dental caries. 2. Non-cavitated lesions. 3. Supragingival dental plaque. 4. RNA-Seq. 5. 16S rRNA. I. Maltz, Marisa Maltz, orient. II. Parolo, Clarissa Cavalcanti Fatturi Parolo, coorient. III. Título.

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Aprovada em 19 de dezembro de 2018.

Banca Examinadora:

Profª Drª Mariza Maltz – UFRGS (orientadora e presidente da banca)

Profª Drª Clarissa Cavalcanti Fatturi Parolo – UFRGS (co-orientadora)

Prof. Dr. Francisco Montagner – UFRGS

Profª Drª Nailê Damé-Teixeira – UnB

Profª Drª Sandra Liana Henz – UFRGS

Esta tese é dedicada a meu companheiro, meu amigo, meu amor, meu “forte”, Maximiliano. E aos meus filhos, Lucas e Laura, meus maiores tesouros. Vocês foram a força e a razão para eu vencer esse desafio.

Agradecimento aos familiares

Aos meus pais Nei e Marlene, pessoas ímpares e maravilhosas. Sempre disponíveis e dedicados. Dispendem esforço imensurável para que todos estejam bem. São nossos grandes incentivadores, sempre torcendo para que alcancemos os nossos objetivos. E, acima de tudo, são exemplos de amor, união e superação! Amo vocês!!!

Aos meus sogros Airbal e Ivanilza (*in memoriam*), que sempre estiveram ao meu lado, muito próximos e sempre preocupados com a concretização desse sonho. Em especial, minha sogra, sempre estimulando para que eu terminasse essa etapa... consegui... mas, você não está mais aqui! Saudades!

A todos os meus familiares que são grandes incentivadores e colaboraram durante todo esse período, compreendendo as minhas ausências constantes... obrigada!!! E, um agradecimento especial às minhas afilhadas Louise, Maria Clara e Maria Carolina. Amo a todos vocês!!!

Aos amigos de coração Marilene e Sérgio Benvegnú e família, pela atenção, carinho e prontidão, dispensando tempo e esforços sem tamanho ao cuidado e bem-estar da nossa família, em especial, para a querida Laura. Nossa eterna gratidão!!

Agradecimentos

À prof^a Dr^a Marisa Maltz, minha orientadora, minha inspiração, exemplo de dedicação, competência e gentileza. Para mim, muito mais que orientadora... considero-a uma grande amiga. Meu agradecimento a você é eterno! Difícil conseguir mensurar e descrever... obrigada... obrigada... obrigada...

À prof^a Dr^a Clarissa Cavalcanti Fatturi Parolo, co-orientadora muito especial!!! Outro exemplo de competência, dedicação, amabilidade... És uma pessoa admirável! Teu apoio incondicional, disponibilidade, delicadeza foi importante e um grande incentivo durante essa caminhada. Muito obrigada!!!

À prof^a Dr^a Nailê Damé Teixeira, pelo compartilhamento de tanto conhecimento! Tua dedicação é e sempre será reconhecida! Você é um exemplo de força, superação e competência. Passamos momentos muito bons juntas que nunca serão esquecidos! Juntas em Leeds... foi demais! Sinto saudades! Te admiro muito e torço pelo teu sucesso!!! E, agradeço e reconheço todo o teu trabalho e esforço nesse estudo que estamos conduzindo com muita dedicação! Muito obrigada!!!

À colega Laís Daniela Ev, pelos incontáveis momentos juntas, compartilhando desafios acadêmicos, muitos cursos, bioinformática, biofilmes, inglês..., momentos de dúvidas e incertezas, mas, principalmente, o compartilhamento de muita amizade e apoio, o que foi de extrema importância nesses anos trabalhando juntas e superando passo-a-passo as dificuldades. Espero termos ainda muito trabalho, juntas. Adoro você! Obrigada pelo carinho e amizade!

Ao acadêmico Ariel Goulart Rup pelo trabalho intenso, muita dedicação, tardes selecionando pacientes e coletando amostras. Também sempre muito disponível e educado e pronto a ajudar! Muito obrigada!

À nossa extremamente dedicada Técnica de Laboratório Luisa Mercado. Também sempre disposta a nos ajudar e orientar. Sempre simpática, dedicada e carinhosa. Um exemplo de bondade e agora, super mamãe coruja da pequena Alice! Te desejo toda a felicidade do mundo!!! Também não tenho palavras para agradecer a você por tudo e pelos vários momentos agradáveis que passamos juntas no LABIM! Obrigada!!!

À aluna, colega e amiga Andréa Catelan Cardoso pela ajuda incondicional durante longos e duros anos em busca de pacientes, atendimentos, coletas de amostras, e, principalmente, as difíceis “rechamadas”. Teu esforço e dedicação foi muito importante! Teu desafio foi grande, mas conseguistes vencer! Parabéns e muito obrigada por tudo!!!

À Prof^a Dr^a Thuy Do, pela receptividade, carinho e orientação durante o período do estágio de doutorado sanduíche no exterior, em Leeds, UK. Sempre educada e preocupada com o nosso bem-estar, preocupada em fazer um trabalho adequado e com bons resultados. Obrigada pelo aprendizado durante o período em que trabalhamos juntas.

Um agradecimento especial a todos os colegas, professores, amigos da UFRGS, da UPF e da Universidade de Leeds que estiveram em algum momento ao meu lado durante todos esses quatro anos. Obrigada pela força, pelo carinho e amizade!

Ao Programa de Pós-Graduação da Faculdade de Odontologia da Universidade Federal do Rio Grande do Sul, em nome da diretora Prof^a. Dr^a. Suzana Werner e do coordenador do Programa de Pós-Graduação em Odontologia, Prof. Dr. Cassiano Kuchenbecker Rösing, pela qualidade curso, do grupo de professores e apoio à formação e aperfeiçoamento acadêmico com muito mérito, incentivando os alunos na participação de eventos e estágios no exterior.

Ao Departamento de Biologia Oral da Faculdade de Odontologia da University of Leeds, por ter aceitado a parceria de trabalho no Laboratório de Microbiologia Oral da instituição, coordenado pela Prof^a Dr^a Deirdre Devine.

À Faculdade de Odontologia da Universidade de Passo Fundo pelo apoio estrutural e a Universidade de Passo Fundo pelo apoio financeiro durante todo o período do meu

aperfeiçoamento profissional, em especial durante o meu desligamento integral para o desenvolvimento do estágio no exterior, na Universidade de Leeds, no Reino Unido.

À Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) pela concessão da bolsa sanduiche durante o período de realização do estágio no exterior.

Um agradecimento especial a todos os colegas, professores, amigos da UFRGS, da UPF e da Universidade de Leeds que estiveram em algum momento ao meu lado durante todos esses quatro anos. Obrigada pela força, pelo carinho e amizade!

This study was financed in part by the Coordenação de Aperfeiçoamento de
Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001

“It’s clear to me that if you wiped all multicellular life-forms off the face of the earth, microbial life might shift a tiny bit ... If microbial life were to disappear, that would be it – instant death for the planet.”

Carl Richard Woese (1928–2012)

Abstract

This research compared the bacterial composition profile and diversity from supragingival biofilm collected in different oral conditions from active- and inactive-caries subjects, and from caries-free subjects. Sixteen individuals (13-76; med=23.5 years-old), selected at the Faculty of Dentistry, Federal University of Rio Grande do Sul, were allocated in three groups: caries-active (CA) (n=7); caries inactive (CI) (n=3); and, caries-free (CF) (n=6). Twenty-one supragingival plaque samples (pools) were obtained from CA subjects from three dental health conditions: ANCL: active non-cavitated lesions (n=7); INCL: inactive non-cavitated lesions (n=7); S: sound dental surfaces (n=7). The supragingival biofilm was collected after 12 hours without toothbrushing, stored in RNA stabilization solution, pelleted and frozen in -80°C. The total RNA extraction was made using Lysozyme and UltraClean® Microbial RNA Isolation kit (MO-BIO). The genomic libraries were prepared using *True Seq® Sample Preparation Guide, Low Sample (LS) Protocol Illumina* (Illumina, Inc., San Diego, CA), and sequenced by Illumina HiSeq 3000, resulting in billions of 2x150 base pairs. The sequences were uploaded into MG-RAST (Metagenomics Analysis Server) for bioinformatics analysis. High-quality sequences (3,542,190) were clustered into genus operational taxonomic units (OTUs; 97% identity; SILVA SSU), representing 915 independent genera belonging to 29 phyla, four considered higher abundant (Actinobacteria, Firmicutes, Bacteroidetes and Fusobacteria). All subjects shared 4493 OTUs (123 genera), indicating the presence of a core plaque microbiome. The α diversity analysis showed less bacterial diversity in sound sites from caries active compared to caries-free (CA-S vs CF-S), and for caries active subjects *versus* caries-free subjects (CA vs CF). The dominant genera included *Actinomyces*, *Corynebacterium*, *Capnocytophaga*, *Leptotrichia*, *Veillonella*, *Prevotella*, *Streptococcus*, *Eubacterium*, and *Neisseria*. *Veillonella* and *Leptotrichia* were positively related with caries, and *Prevotella* with health. *Corynebacterium* and *Capnocytophaga* were closer than *Actinomyces* but together formed an important cluster with high abundance in health and disease. The Metric Multidimensional Scaling Ordination analysis shows that sites from active subjects (CA-ANCL, CA-INCL and CA-S) are closer to each other than CI-INCL subjects or CF-S subjects. We found a high level of diversity in the active fraction of the bacterial community (RNA-based approach) that is related with the high number of organisms detected in supragingival biofilm and not due to dead or inactive species, highlighting that dental caries is a polymicrobial disease, where multispecies microbial consortia are metabolically active in the lesions. Supragingival bacterial communities presents an intrapersonal similarity, but interpersonal diversity and different bacterial composition reveals that the subject's caries activity status matters more than sites.

Key-words: dental caries, non-cavitated caries lesions, supragingival dental plaque, RNA-Seq, 16SrRNA

CORRALO, Daniela Jorge. **Bacterial composition of microbiome associated to supragingival biofilm in health and caries disease.** Porto Alegre, 2018. 105 f. Tese (Doutorado em Odontologia) – Programa de Pós-Graduação em Odontologia, Faculdade de Odontologia, Universidade Federal do Rio Grande do Sul, Porto Alegre, 2018.

Resumo

Esta pesquisa comparou o perfil e diversidade da composição bacteriana do biofilme supragengival coletado em diferentes condições bucais de sujeitos carie ativos, carie inativos e livres de caries. Dezesesseis indivíduos (13-76; med=23.5 anos), selecionados na Faculdade de Odontologia da Universidade Federal do Rio Grande do Sul, foram alocados em três grupos: cárie ativos (CA) (n=7); cárie inativos (CI) (n=3); e, sem experiência de cárie (CF) (n=6). Vinte e uma amostras de placa supragengival (“pool”) foi obtida dos sujeitos CA a partir de três condições de saúde dental: LNCA: lesão não cavitada ativa (n=7); LNCI: lesão não cavitada inativa (n=7); S: superfície saudável. O biofilme supragengival foi coletado depois de 12 horas sem escovação dental, armazenado em solução estabilizadora de RNA, concentrado e congelado a -80°C. O RNA total foi extraído utilizando Lisozima e o kit UltraClean® Microbial RNA Isolation (MO-BIO). As bibliotecas genômicas foram preparadas com o protocolo *True Seq® Sample Preparation Guide, Low Sample (LS) Protocol Illumina* (Illumina, Inc., San Diego, CA) e sequenciadas no sequenciador Illumina HiSeq 3000, resultando em bilhões de 2x150 pares de base. As sequências foram enviadas para o servidor MG-RAST (Metagenomics Analysis Server) para as análises de bioinformática. Sequência de alta qualidade (3,542,190) foram agrupadas em unidades taxonômicas operacionais (OTUs; 97% identidade; SILVA SSU), representando 915 gêneros independentes pertencentes a 29 filos, quatro considerados com elevada abundância (Actinobacteria, Firmicutes, Bacteroidetes and Fusobacteria). Todos os sujeitos compartilharam 4493 OTUs (123 gêneros), indicando a presença de um microbioma central da placa dental. A análise de alfa diversidade revelou uma menor diversidade microbiana para os sítios saudáveis dos sujeitos carie ativos *versus* os dos sem carie (CA-S *vs* CF-S), e para os sujeitos carie ativos *versus* os sujeitos sem carie (CA *vs* CF). Os gêneros dominantes incluíram *Actinomyces*, *Corynebacterium*, *Capnocytophaga*, *Leptotrichia*, *Veillonella*, *Prevotella*, *Streptococcus*, *Eubacterium* e *Neisseria*. *Veillonella* e *Leptotrichia* foram correlacionados positivamente com caries, e *Prevotella* com saúde. *Corynebacterium* e *Capnocytophaga* estavam mais próximos do que *Actinomyces*, mas aguparam-se juntos formando um importante “cluster” com elevada abundância tanto em saúde como em doença. A análise da Ordenação por Escalonamento Métrico Multidimensional mostra que os sítios nos sujeitos carie-ativos (CA-LNCA, CA-LNCI e CA-S) estão mais próximos uns dos outros do que os sujeitos CI-LNCI ou dos sujeitos CF. Nós observamos um alto nível de diversidade da fração ativa da comunidade bacteriana (abordagem baseada em RNA) que está relacionada com o elevado número de organismos detectados no biofilme supragengival e não devido a espécies mortas ou inativas, destacando que a cárie dentária é uma doença polimicrobiana, onde consórcios microbianos multiespécie são metabolicamente ativos nas lesões. As comunidades bacterianas supragengivais apresentam uma semelhança intrapessoal, mas a diversidade interpessoal e a composição bacteriana diferente revelam que o status de atividade de cárie do indivíduo é mais importante do que os sítios.

Palavras-chave: carie dental, lesões de caries não cavitadas, placa dental supragengival, RNA-Seq, 16S rRNA

CORRALO, Daniela Jorge. **Composição bacteriana do microbioma associado ao biofilme supragingival em saúde e em doença cárie.** Porto Alegre, 2018. 105 f. Tese (Doutorado em Odontologia) – Programa de Pós-Graduação em Odontologia, Faculdade de Odontologia, Universidade Federal do Rio Grande do Sul, Porto Alegre, 2018.

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1 INTRODUCTION

The human body features a dynamic relationship with billions of microorganisms, termed *Human Microbiome*, inhabiting distinct niches and involved with different processes and perturbations on the environment that can lead to deleterious consequences for the host, sometimes resulting in a pathology (a process denominated *dysbiosis*) (Turnbaugh et al., 2007; Dewhirst et al., 2010; Human Microbiome Project Consortium; 2012; Marsh; Zaura, 2017; Marsh, 2018; Rosier et al., 2018; Solbiati; Frias-Lopez, 2018; Tanner et al., 2018).

The oral cavity presents extensive and diverse niches for microbial colonization, supporting distinct combination of consortia of oral microorganisms, responding and reflecting to ecological determinants at each site, like nutrients, degree of anaerobiosis, and pH (Marsh, 1994; 2018; Aas et al., 2005; Do et al., 2013). On the solid and non-shedding tooth surfaces, the microbiota forms multispecies biofilms with composition and metabolic activity determined by the host and environmental factors (Bowden, 2000; Filoche et al., 2010; Peterson et al., 2011; Do et al., 2013; Arweiler; Netuschil, 2016; Mark Welch et al., 2016; Marsh, 2018). Therefore, microbial biofilms organize themselves in complexes functional structures with highly interactive microbial communities, achieving a relatively stable consortia at a site (homeostasis) (Do et al., 2013; Mark Welch et al., 2016; Marsh; Zaura, 2017; Marsh, 2018). The ability to maintain homeostasis in a microbial community increases with its species diversity (Alexander, 1971). In oral health conditions, the microbiome that naturally colonizes the teeth coexists in harmonious relationship with the host and can counterbalance acid production from carbohydrates ingestion (Marsh, 1994; Do et al., 2013; Rosier et al., 2014; 2018; Tanner et al., 2018).

Biofilms on teeth (dental plaque) accumulate at stagnant or retentive sites (Marsh, 1994). The increase in fermentable carbohydrate ingestion can induce to a break down in the microbial community homeostasis and bring a shift in the composition and metabolism of the microbiota ecosystem (Marsh, 1991; 1994). If this increase in the frequency of fermentable dietary carbohydrate intake is maintained for long periods, it induces to a longer time at low pH in dental plaque environment, resulting in the loss of mineral of dental enamel (demineralization) (Loesche, 1986; Marsh, 1994; Paes Lemes et al., 2006) that will be clinically observed as a white spot lesion, with opaque and roughness surface aspect, termed acive non-cavitated lesion (ANCL) (Kidd; Fejerskov, 2004), which can progress if low pH condition is not changed, resulting in a breakdown of enamel structure (Kidd; Fejerskov, 2004). The

stability of microbial community can return if changes occur in the ecosystem in the dental plaque, inducing to an increase in pH to neutral conditions and leading to a remineralization of initial caries lesion, which will turn shiny and smooth, termed inactive non-cavitated lesion (INCL) (Kidd; Fejerskov, 2004). Both conditions (ANCL and INCL), as well as non-affected sites, can be found in the same subjects, since oral cavity presents several niches for the establishment of distinct microbial communities (Marsh, 1994; 2018; Bowden, 2000; Aas et al., 2005; Filoche et al., 2010; Simón-Soro et al., 2014; Do et al., 2013; Arweiler; Netuschil, 2016).

The microbial characteristic of dental caries has been studied for a long time, and, although the etiopathogenesis of caries was described by Miller more than a hundred years ago, this condition remains the most prevalent noncontagious biofilm-mediated disease in humans (Vieira et al., 2012). During this long time, the studies have sought to understand the role of microorganisms in the caries disease process (Orland et al., 1954; 1955; Fitzgerald; Keyes, 1960; Gibbons et al., 1964; Krasse, 1966; Krasse et al., 1967; Loesche et al., 1975; Van Houte et al., 1981; 1994; Loesche, 1986). However, interactions between organisms are of essential importance to understand ecosystem dynamics and the evolutionary ecology of individual organism; *i.e.* the oral microbial communities are more than the sum of the individual species (Konopka; 2009; Diaz et al., 2014; Mark Welch et al., 2016; Marsh, 2018).

Currently, culture independent molecular biology methods, and more recently, next-generation DNA sequencing technologies (NGS), are improving the understanding of diversity, composition and functional aspects of microbial communities sampled from naturally habitats, including organisms that were previously intractable to laboratory-controlled culturing (Simón-Soro et al., 2013; Benitez-Páez et al., 2014; Simón-Soro et al., 2014; Johansson et al., 2016; Keegan et al., 2016; Xiao et al., 2016; Eriksson et al., 2017; He et al., 2018). In oral habitats, these methods have enhanced and rectified the knowledge of the microbial diversity and composition (Aas et al., 2005; 2008; Gross et al., 2010; Zaura et al., 2009; Human Microbiome Project Consortium, 2012; Siqueira et al., 2012; Xiao et al., 2016; Eriksson et al., 2017; He et al., 2018). Studies have demonstrated substantial differences in the composition of the microbiota in biofilms overlying caries lesions, showing a disruption of community stability, with an enrichment of acidogenic and acid-tolerant species (Aas et al., 2008; Gross et al., 2010; Benitez-Páez et al., 2014; Simón-Soro et al., 2014; Johansson et al., 2016; Xiao et al., 2016; Eriksson et al., 2017). Marsh (2018) reports that there is a definite specificity in terms of biochemical function in the etiology of caries, despite a lack of apparent specificity in terms of bacterial name; but the organisms are highly relevant to understand the structure, function, and dynamics of the members in a microbial consortium (Mark Welch, 2016).

Considering that dental caries have a polymicrobial etiology within a complex dental biofilm ecosystem (Simón-Soro et al., 2014; Mark Welch, 2016; Xiao et al., 2016; He et al., 2017), and the composition of microbiota is not the same on different surfaces due to the prevailing physical and biological conditions at distinct sites (Aas et al., 2008; Simón-Soro et al., 2014; Do et al., 2013), so it is essential to understand the microbial communities that lead to sickness or health could help to find the key to caries disease monitoring. In this sense, we proposed to characterize the microbial composition profile and diversity of the active microbiome associated to biofilm in caries-free, caries inactive, and in three different dental health conditions from caries active subjects.

2 BACKGROUND

2.1 DENTAL CARIES: concept and etiology

The development of the microbiology since the first microbes were revealed by Antony Von Leeuwenhoek in the XVII century (Porter, 1976) brought a new scientific era for the understanding of infectious human diseases. Although the relationship between caries and microorganisms had been previously observed by Leber and Rottenstein (1874), Miller was the first to propose the theory of the chemo-parasitic relationship of the caries disease (Miller, 1890). Even working beside Robert Koch in Germany, he disregarded caries as a specific disease, considering that all microorganisms in the mouth and saliva producing acids by carbohydrates metabolism could be responsible for the degradation of tooth (Suddick; Harris, 1990). The Koch's postulates were proposed in the latter half of the 19th-century to establish causal relationships between a specific agent related with a specific disease, and they continue to receive significant attention (Ross; Woodward, 2016). However, Ross and Woodward (2016) discussed that the Koch's criteria are best understood when applied to specific laboratory techniques, and experimental results, on which he relies to argued causality of the disease processes, once they do not take into consideration other biological aspects involved in host-microbial relationship. In spite of these considerations, the principles proposed by Koch have remained a cornerstone in microbiology (Simón-Sóro; Mira, 2015).

The dental caries as an infectious disease was recognized by scientists and proved by several studies developed over the past century. Driven by Koch's premises, the main focus was to find a specific microorganism that could shown the causality of the disease. The first microbiological studies described streptococci and *Lactobacillus* implicated in acid production and mineral loses resulting in caries lesions (Howe, 1917; Clarke, 1924; Maclean, 1927; Krasse, 1954; Fitzgerald et al., 1966). Some studies observed that streptococci organisms could develop lesions when inoculated in hamsters, germ-free and/or gnotobiotic rats (Fitzgerald et al., 1960; Fitzgerald; Keyes, 1960). The same streptococci isolated from humans proved to be able to provoke dental disease in hamsters (Krasse, 1966; Krasse; Carlsson, 1970). Later, Edwardsson (1968) observed that the streptococci, called *Streptococcus mutans* by Clarke (1924), was the same that they were studying. At that time, *S. mutans* became the main microorganism related with caries disease (Krasse, 1968; Loesche; Syed, 1973; Loesche et al., 1975; Loesche, 1986), and it have been studied for the last fifty years, despite other microbial species were also isolated

from carious lesions and have been related to the process of the disease (Duchin; Van Houte, 1978, Mantzourani et al., 2009; Beighton et al., 2010).

The scientific research aimed at this microorganism was relevant and contributed for the understanding of the disease etiology, diagnostic, preventive, and therapeutic strategies. Probably due to this specific theory of causality of infectious diseases, and the acidogenic and aciduric species of *S. mutans* that were isolated in the 1920s from carious lesions (Clarke, 1924), it was considered to be the etiological agent of dental caries (Simón-Sóro; Mira, 2015). However, despite more than 100 years of accumulated knowledge on the pathogenesis of this disease, caries is still a major oral health problem in most industrialized countries, affecting 60-90% of schoolchildren and the vast majority of adults (Vieira et al., 2012). Attempts to define the specific etiological agents of dental caries have proven to be elusive, supporting the notion that caries etiology is perhaps complex and multi-faceted (Peterson et al., 2011).

A relevant discussion concerning the dental and medical research over the last 100 years is that it was focused on the planktonic phase of bacteria (Arweiler; Netuschil, 2016). However, it is known that oral microorganisms are organized as biofilms. On any non-shedding surfaces of the oral cavity dental plaque starts to form, which meets all criteria for a microbial biofilm and is subject to the bacterial succession. When the sensitive ecosystem is unbalanced - either by overload or weak immune system - it becomes a challenge for local or systemic health (Arweiler; Netuschil, 2016).

The first reference to bacterial biofilms and its significance was performed in 1936, by Zobell and Mathews. And its recognition as an ubiquitous structure was cited in 1978, by Costerton et al., several decades later (Costerton et al., 1978; 1995). The biofilms constitute a distinct growth phase of bacteria and it is different from the planktonic growth phase, studied for more than a hundred decades, since Louis Pasteur's discoveries (Costerton et al., 1995). Bacteria within biofilms present a higher level of organization, being benefited from similar stable juxtaposition and similar physiological cooperativity, with a coordinated functional community that is much more efficient than mixed populations of floating planktonic organisms (Costerton et al., 1978; 1995).

In 1993, in the annual meeting of American Society for Microbiology, the biofilm mode of growth was extensively discussed by scientists. The major implication from modern microbiology was to answer the question "What are the essential differences between a planktonic cell growing in the conventional batch culture and a cell of the same species growing in a natural multispecies biofilm?" This question was risen from observations that microbiologists were extrapolated between laboratory cultures and real ecosystems for hundreds of years and, these extrapolations appear to have become increasingly strained and

inaccurate (Costerton et al., 1994). Although it is estimated that a high microbial biomass lives in the planktonic mode (Bjarnsholt et al., 2012; 2013), the National Institutes of Health (NIH) revealed that among all microbial and chronic infections, 65% and 80%, respectively, are associated with biofilm formation (Lewis, 2001; 2005; Donné; Dewilde, 2015; Jamal et al., 2018). It is suggested that, in biofilms, the virulence of their residents is favored because the dislocation to a less favorable environment is avoided; members develop mechanisms to optimize binding to specific cell and tissue sites, and the species-species aggregation is promoted by specific cell surface receptors (Jakubovics et al., 2014). These aspects contribute against nonresident species invading its ecological niche (Kreth; Herzberg, 2015), and antimicrobial treatment is not completely effective, requiring at 10- to 1000-fold greater concentrations of a conventional antibiotic to combat infecting microbes in biofilms (Kaplan, 2011).

Therefore, the conventional microbiology approaches allowed to obtain valuable insights with the relative few bacteria from dental plaque that could be cultured at that time, but inevitably the true microbial complexity of the biofilm structure could not be fully established (Diaz et al., 2006; Langfeldt et al., 2014; Heller et al., 2016). Contrary to Koch's postulates, dental caries is not considered etiologically the outcome of a single-agent, but it is associated to an unbalance of microbial species that synergistically cause enamel demineralization by their acidogenic activity (Marsh, 2006; Benítez-Páez et al., 2014). In summary, dental caries is currently recognized as a biofilm-mediated disease, resulting from the disturbance of the homeostasis in a dynamically changing microbial ecosystem (Nyvad et al., 2013; Marsh et al., 2015; Henne et al., 2016), as a result from a substrate-driven disruption of the bacterial ecosystem, conceptualized by Marsh (1991) and termed the "ecological plaque hypothesis." Caries results when the fermentation of readily available carbohydrates to lactate by acid-producing species first lowers pH and then leads to suppression of acid-sensitive species and overgrowth of acid-tolerant species. The net result is a reduction in bacterial community diversity as caries progresses, and a shrinking number of species can survive the harsh conditions (Li et al., 2004; Gross et al., 2010).

The complexity of oral cavity, with sheeding and non-sheeding structures, enables the development of different microbial communities in the mouth. The variety of microhabitats, in particular, the non-shedding surface of enamel, allows the accumulation of several microbial communities (biofilms) that provides a protected habitat that supports a wide range of bacterial genera and species interacting among them and with the structural, physical and biological components of their habitats (Bowden, 2000). The interactions among the bacteria in dental plaque together with the variations in nutrient, buffer, fluoride, concentrations

of various ions and pH in the biofilm will determine the formation of a caries lesion (Bowden, 2000). However, the dental disease process is hard to understand from the microbial ecology aspect, because many of the events that induce to a caries development are common and associated with health enamel (Bowden, 2000). Caries in an individual is characterized by a series of interactions and succession within the dental plaque. According Bowden (2000), as the microbial populations respond to environmental changes and succession probably the same occurs in the lesion, leading to progression or stagnation of caries development. Considering a chronic characteristic of caries disease, active lesions, inactive lesions, and sound dental surfaces can be found in the same individual justifying the analysis of the three dental conditions in caries-active subjects. In the same way, understanding the biofilm microbiome from subjects with controlled disease (caries inactive) and health (caries-free) can help to gain a better understanding of the microbial ecology aspect of biofilm microbiome related with dental health or disease.

2.2 MOLECULAR STUDIES IN SUPRAGINGIVAL BIOFILM

The currently microbial studies have developed an increasing interest in understanding the human microbiome and its role in health and disease (Solbiati; Frias-Lopez, 2018). Molecular approaches to study the human microbiome revealed that the oral ecosystem is inhabited by hundreds of bacterial species (Aas et al., 2005; 2008; Zaura et al., 2009; Bik et al., 2010; Dewhirst et al., 2010; Wade, 2013), most of which are considered commensals, and those species regarded as pathogens are frequently found in healthy individuals, although at lower levels than in diseased subjects (Turbaugh; Stintzi, 2011). In polymicrobial diseases, pathogens detected at low levels in health suggests that they cannot be considered to have an infectious nature and that the microbial causative agents are better described as pathobionts (Chow; Mazmanian, 2010; Chow et al., 2010). These organisms are therefore resident bacteria with the potential to cause disease, and under unbalanced conditions the immune system does not have an active response against them (Simón-Sóro; Mira, 2015).

The characterization of changes in the composition of the microbial communities under different conditions are an important aim from microbiome studies and allow the observation that an unbalance in the composition of the microbiome (referred as *microbial dysbiosis*) is directly linked to developing certain conditions (Dewhirst et al., 2010; Marsh; Zaura, 2017; Marsh, 2018; Solbiati; Frias-Lopez, 2018; Tanner et al., 2018). Based on these

previous efforts, a conceptual framework has been established suggesting that dental biofilm contains both health-associated and disease-associated microbiota. However, Peterson et al. (2011) consider dental decay a more complex structure, once many species in specific combinations will dictate the signatures associated with dental health and disease or the transition between the two states; but it may be more complex such as those groups of related bacterial species that may be thought of as inter-changeable components in defining caries signatures. This possibility appears reasonable since the genomes of related bacterial species share a larger number of genes/functions than do more distantly related species (Peterson et al., 2011).

Although dental plaque microbiota has high interpersonal variability, interesting efforts have been made towards the possibility of predicting caries development. Studies searching for caries-associated microbial patterns have been conducted using preferentially DNA-based methodologies. Non-targeted methods are warranted to characterize a disease-associated bacterial community, i.e., methods not limited by present knowledge or expectations.

2.2.1 DNA-based studies from supragingival microbiome in health and caries

Aas et al. (2008) aimed to identify all species associated with health and disease, especially early on in the infection, that would provide alternative targets for biological intervention. They collected plaque samples from the 39 healthy subjects, and from 51 carious subjects, from two to 21 years-old. They presented the results from primary and secondary dentitions separately. In carious subjects, plaque was collected from surfaces of intact enamel, surfaces of white-spot lesions, cavitated dentin lesions, and deep-dentin lesions, separately. The DNA analysis was carried out by Sanger sequencing and additionally by reverse-capture checkerboard assay. The authors performed a parallel analysis assessing those bacterial species associated with the progression of dental caries in permanent teeth using pooled samples representing the disease states from five subjects with severe caries (three with *S. mutans* recovered from samples, and two without *S. mutans* detected), and two healthy controls. The authors concluded that, in addition to *S. mutans*, species of *Veillonella*, *Lactobacillus*, *Bifidobacterium*, *Propionibacterium*, low-pH non-*S. mutans* streptococci, *Actinomyces*, and *Atopobium*, also may play an important role in caries production. *Actinomyces* spp. and non-*S. mutans* streptococci may be involved in the initiation of the disease. Bacterial profiles change with the progression of the disease and differ from the primary to the secondary dentition. The

present findings support the ecological plaque hypothesis in caries disease, in that changes in ecologic factors require different bacterial qualities and stimulate alterations in the bacterial composition.

Gross et al. (2010) compared bacterial community profiles associated with severe dental caries (n=21) and health (n=18) in the young permanent dentition by using an open-ended molecular approach, 16S rRNA gene cloning, and Sanger sequencing. For the healthy subjects' dental plaque was sampled from the healthy enamel. For the subjects with dental caries, plaque was collected separately from the surfaces of each of three types of sites: intact enamel, white spot lesions, and cavitated lesions. In addition, carious dentin was harvested from one tooth. Considering the four genera that had positive estimates with disease (levels increased as caries severity increased), only *Lactobacillus* and *Propionibacterium* were significant. Levels of *Scardovia* genus and *S. mutans* were not significantly related to caries severity in this study. Additional candidates in disease included strains of *S. mitis*, *Selenomonas*, and *Neisseria*. Some species could be associated with health conditions, once levels of species decreased as caries progressed, and for nine species these changes were statistically significant, including *Streptococcus mitis*-*S. pneumoniae*-*S. infantis* (combined because they cannot be distinguished by 16S sequence analysis), *Corynebacterium matruchotii*, *Streptococcus gordonii*, *Streptococcus cristatus*, *Capnocytophaga gingivalis*, *Eubacterium* IR009, *Campylobacter rectus*, and *Lachnospiraceae* sp. C1. Overall, bacterial diversity decreased significantly as caries progressed from healthy to cavitated and deep dentinal lesions, providing additional support for the ecologic disruption model of caries pathobiology, confirming a decline in diversity between healthy sites and all stages of caries and an increase in the fraction of the microbiota accounted for by cariogenic species. The authors commented an example from advanced caries samples obtained from two subjects that consisted entirely of lactobacilli, indicating a complete loss of pH-modulating species and in agreement with the classic catastrophic ecological disruption (Marsh, 2003).

Belda-Ferre et al. (2012) collected plaque material from all tooth surfaces from healthy and carious individuals for DNA pyrosequencing. In volunteers with active caries, the dental plaque samples were taken without touching cavities. In those cases, material from individual cavities was also extracted and kept separately. The volunteers were asked not to brush their teeth 24 h before the sampling. Supragingival dental plaque samples were taken from six individuals that were divided in three groups according to caries experience and that represented different degrees of oral health: two individuals had never developed caries in their lives (healthy controls), another two individuals had been regularly treated for caries in the past and had a low number of active caries at the moment of sampling (one and four cavities,

respectively); and the last two individuals had a high number of active caries (eight and 15) and poor oral hygiene. In addition, samples from individual cavities were collected, from two of them enough DNA for pyrosequencing was obtained: one at an intermediate stage and the other one at an advanced stage of caries development (dentin lesion). The DNA extracted and prepared was sequenced by GS-FLX sequencer (Roche, Basel, Switzerland) with Titanium chemistry. Samples were uploaded to the MGRAST server and the functional assignment based on SEED subsystems was retrieved for the three hierarchical levels. For taxonomic assignment, 16S rRNA sequences were extracted from the reads of each metagenome by similarity search using BLASTn against the RDP database. The results showed a tendency for Bacilli and GammaProteobacteria to be more common in healthy individuals, whereas typically anaerobic taxa like Clostridiales and Bacteroidetes are more frequent in diseased samples. Reads assigned to beta-Proteobacteria (mainly Neisseriales) and TM7 were at very low proportions in diseased samples. Some genera, like *Rothia* or *Aggregatibacter* appeared to be specifically associated to healthy samples. The metagenomic recruitments for PCR complementary analysis also showed *Aggregatibacter* and *Streptococcus sanguis* were among the prevalent species in individuals without caries. On the other hand, *Streptococcus gordonii* and *Leptotrichia buccalis* were abundant in individuals with caries. Strains of *Veillonella parvula* were the most abundant in all individuals with caries. The authors affirm that, despite the limited number of samples analyzed in this study, important differences between healthy and diseased sites and individuals could be observed at the taxonomic and functional level, suggesting that the dental plaque of individuals that have never suffered from caries can be a genetic reservoir of new anticaries compounds and probiotics.

Simón-Soro et al. (2013) analyzed samples from plaque material obtained from volunteers with active caries and without caries. In cavities, material was also extracted and kept separately. Caries samples were classified as enamel caries (including white-spot lesions), dentin caries and deep dentin caries. All samples were from active caries and all dentin caries samples were open and deep dentin caries. DNA was extracted, prepared and sequenced using the GS FLX sequencer (Roche, Basel, Switzerland) with Titanium chemistry. Taxonomic assignment of the 16S rRNA reads indicated that the bacterial composition varied depending on the tissue affected. The bacterial composition of enamel caries was significantly different from those of dental plaque and dentin caries, occurring a dramatic reduction in the number of species from a healthy to a diseased site. In dentin caries, *Streptococcus* and *Prevotella* increased in proportion whereas *Neisseria*, *Capnocytophaga* and *Fusobacterium* significantly decreased in relative numbers. Interestingly, *Lactobacillus* species, which have been associated with dental caries because of their acidogenic potential, only appeared in deep dentin caries.

The presence of a distinctive, tissue-dependent microbiota suggests that the etiological factors of caries can be different at different stages of caries progression, as it is confirmed by the data on gene function representation.

Xiao et al. (2016) conducted a bacterial analysis to identify bacterial shifts related with dental health and caries, and to investigate the presence of a core plaque microbiome. They examined supragingival biofilm from 131 patients grouped in no-caries (n=29), low-caries (n=32), moderate-caries (n=37), and high-caries (n=62) by 454 pyrosequencing technology. They found six most abundant phyla which were Bacteroidetes (35.1% of the total sequences), Actinobacteria (28.6%), Proteobacteria (14.6%), Firmicutes (11.3%), Fusobacteria (5.8%), and TM7 (3.6%), together accounting for 99% of the total sequences. The six rarest phyla were Spirochaetes, SR1, Synergistetes, GN02, Tenericutes, and Chloroflexi. The most prevalent genera were *Capnocytophaga* (18.1%), *Prevotella* (12.8%), *Actinomyces* (12.3%), *Corynebacterium* (9.8%), *Neisseria* (7.0%), *Streptococcus* (6.3%), *Rothia* (3.7%), *Leptotrichia* (3.7%), *TM7_[G-1]* (3.1%), *Porphyromonas* (2.8%), *Lautropia* (2.8%), *Fusobacterium* (2.1%), *Selenomonas* (2.1%), *Veillonella* (1.7%), *Actinobaculum* (1.7%), *Campylobacter* (1.2%), and *Propionibacterium* (1.0%), together comprising 92.3% of the total sequences. *Lautropia*, *Cardiobacterium*, *Lachnoanaerobaculum*, *Lachnospiraceae_G_3*, *Corynebacterium*, and *Aggregatibacter* were observed in the non-caries group and higher abundances of *Neisseria* and *Campylobacter* observed in the low-caries group. Nevertheless, the *Streptococcus* and *Ottowia* genera exhibited similar abundances in each group. They observed similar community structures between healthy and caries groups by analysis of PCoA and PCA. UPGMA hierarchical clustering analysis also revealed that the samples did not form well-separated clusters corresponding to the four groups, indicating similarity in the bacterial community structures. Considering the composition, some differences were observed. Tenericutes was significantly enriched in group with moderate-caries, and *Desulfomicrobiaceae*, *Mycoplasmataceae*, *Clostridiales_F_1* and *Veillonellaceae* presented enriched, as well. *Corynebacteriaceae*, *Pasteurellaceae*, and *Cardiobacteriaceae* was enriched in non-caries group. The existence of an identifiable common core microbiome was observed. 7522 OTUs were shared among the four groups, occupying 72.6% of all OTUs (10,365 OTUs) and 97.5% of all OTU abundance. Among the 99 core genera, the 6 most abundant genera were *Capnocytophaga* (17.8% of total abundances), *Prevotella* (13.5%), *Actinomyces* (13.0%), *Corynebacterium* (8.9%), *Streptococcus* (6.6%), and *Neisseria* (6.4%). The results indicated the occurrence of similar community structures of supragingival plaques among groups. However, they could not identify a list of caries-related and health-related bacteria, whose specific functions need further testing and verification.

Eriksson et al. (2017) characterized and compared saliva (n=64) and tooth biofilm (n=49) microbiota via deep sequencing using the Illumina MiSeq and the PacBio SMRT platforms, compared to Human Oral Microbiome Database (HOMD) for taxa resolution in an adolescent population with long-term caries prevention and low disease activity. Firmicutes dominated in saliva (48% abundance, % of all sequences) followed by Actinobacteria (20%), whereas the abundances of Firmicutes and Actinobacteria were more similar (32% and 24%, respectively) in tooth biofilms. Bacteroidetes, Fusobacteria, and Proteobacteria, which were also represented in all adolescents and both sample types, together constituted 32% and 41% in saliva and tooth biofilm, respectively. Eleven genera, in tooth biofilm, each represented 2% or more of all sequences. Of these, seven genera were detected in both sample types (*Actinomyces*, *Fusobacterium*, *Leptotrichia*, *Prevotella*, *Rothia*, *Streptococcus*, and *Veillonella*). Although these genera were represented in all adolescents, the individual abundance was highly varied. At the genus level, *Streptococcus* dominated (32% abundance) in saliva, followed by *Prevotella* (17%), *Rothia* (14%), and 8 additional genera (5-2%). In tooth biofilm, *Streptococcus*, *Actinomyces*, *Leptotrichia*, and *Prevotella* prevalence rates were more similar (18%, 12%, 11%, and 10%, respectively) as well as seven additional genera (6-2%). In tooth biofilm, 11% of all sequences were recognized by the *Streptococcus* Genus probe 4. Other prevalent species/phylotypes/Genus probes (>2% abundance) in tooth biofilm included *Corynebacterium matruchotii* (4%), *Actinobaculum* sp. HOT183, *Actinomyces gerencseriae*, *Actinomyces* sp. HOT448, *Campylobacter gracilis*, species recognized by *Fusobacterium* Genus probe 4, *Leptotrichia wadei*, *Prevotella melaninogenica*, *Prevotella nigrescens*, *Veillonella dispar*, and species recognized by *Veillonella* Genus probe 2 (all between 2 and 3%). In this study, species richness in saliva and tooth biofilm samples did not differ between subjects with or without caries. The species in the Synergistetes phylum, Synergistia class, Clostridiales [F-1] and Synergistaceae families, and *Dialister*, *Scardovia*, *Clostridiales* [F-1][G-1], *Fretibacterium*, *Shuttleworthia*, *Peptostreptococcaceae* [11][G-6] and [11][G-9], and *Veillonellaceae* [G-1] genera were enriched in subjects with caries, whereas taxa in the Fusobacteria phylum, Fusobacteria class, Actinomycetaceae and Ruminococcaceae families, and *Actinomyces*, *Ruminococcaceae* [G-1], and [G-2] genera were enriched in caries-free subjects. Strongest associations (with the presence of caries) were found for *Scardovia wiggsiae*, *Streptococcus mutans*, *Selenomonas* Genus probe 1, *Bifidobacterium longum*, and *Leptotrichia* sp. HOT498, whereas *Mycoplasma orale* and *Porphyromonas* sp. HOT278 were most strongly associated with being caries free. In addition, the mean percent of all sequences (abundance) of *S. mutans* was significantly higher in caries-affected than in caries-free adolescents and tended to be higher for *Bifidobacterium longum*, *Fusobacterium nucleatum* subsp. *nucleatum*, and

Selenomonas Genus probe 1, whereas the opposite was found for *Mycoplasma orale* and *Porphyromonas* sp. HOT278. The study could separate saliva microbiota from caries-affected from caries-free subjects, whereas microbiota from tooth biofilm did not separate these groups. The authors discussed that there are several plausible explanations for this finding, including that tooth biofilm samples only represent sampled surfaces, whereas saliva is the pool from which tooth colonizers are recruited and reflects most surfaces in the mouth. They conclude that saliva can reflect tooth biofilm microbiota and variations among single tooth surfaces.

Dental plaque from subjects with caries (n=25) and matched healthy controls (n=12) were selected and had their plaque collected for DNA sequencing (MiSeq Illumina) and analyzed for taxonomic and functional aspects (He et al., 2018). At the phylum level, both caries and healthy individuals were dominated by Proteobacteria, Firmicutes, Actinobacteria, Bacteroidetes, Fusobacteria, and Spirochaetes. Among these phyla, the relative abundance levels of Bacteroidetes and Spirochaetes were significantly higher in the caries patients than in the healthy individuals. At the genus level, only four genera with different abundances were found between caries and healthy individuals. *Selenomonas*, *Treponema* (detected exclusive in caries), and *Atopobium* showed higher relative abundance in the caries group (caries-associated genera), whereas the genus *Bergeriella* had a higher relative abundance in healthy subjects. *Prevotella* was more related with carious than healthy conditions. The taxonomic and functional differences between carious and healthy controls, suggested that the teeth of caries subjects may be “primed for caries due to fundamental differences in the ecology of supragingival dental plaque microflora. Comparative analysis of bacterial networks in this study indicated that caries patients had simpler networks within the supragingival microbiome and the species in cariogenic dental plaque were more sparsely connected with each other, as evidenced by fewer nodes and links, as well as a lower average connectivity and modularity, less average inter-module connectivity, and was even diminished among some modules compared to health subjects. An important observation is a reduction in negative relationships in the caries network, indicating decreased antagonism among the dental plaque residents.

2.2.2 RNA-based studies from supragingival microbiome in health and caries

Over recent decades, non-targeted multiplex DNA sequencing of the 16S rRNA gene and taxonomic determination from gene databases have commonly been used. A drawback of these DNA-based studies is that the PCR step may amplify DNA from inactive or even dead

microorganisms, making it necessary to determine the functional bacteria that effectively contribute to the disease (Nyvad et al., 2013). A way to achieve this is to perform the 16S gene amplification starting from RNA material, given that the amount of rRNA material in bacterial cells is known to be related to their degree of metabolic activity (Nyvad et al., 2013). Studies RNA-based have shown different recovered bacterial communities from the same environment when compared to DNA-based methods (Benitez-Paez et al., 2014; Simón-Sóro et al., 2014). Therefore, the RNA-based studies give us a better view of the metabolic active bacteria related to dental caries.

Benitez-Páez et al. (2014) conducted a metatranscriptome analysis of *in vivo* human oral biofilm samples through two approaches: a short read-length, high coverage Illumina® approach to study oral biofilm formation through time, and a long read-length, lower coverage pyrosequencing strategy to study changes in community composition before and after a meal. For the first approach, a total of 16 samples of supragingival plaque from four healthy individuals were collected at four different time points (6, 12, 24 and 48 hours after a professional ultrasound cleaning) to disclose the microbiota and gene expression dynamics during oral biofilm formation (the RNA was extracted and processing until cDNA, and finally sequenced in parallel single-end sequencing using HiSeq2000 system/Illumina®). For the second experiment, the metatranscriptome of dental plaque from five individuals was studied 30 minutes before and after a controlled meal, in order to characterize the potential shifts in the active bacterial community when dietary nutrients are available for growth. The subjects were asked not to brush their teeth for 16 hours. Three of them had active caries at the moment of sampling and the other two had no history of dental caries. The RNA was extracted, and the long cDNA fragments were sequenced using 454 GS-FLX technology with titanium chemistry (Roche). For the high-coverage biofilm samples, microbial diversity was established by taxonomic assignment using reads matching 16S rRNA sequences and compared to RDP-based database. In the case of samples before/after a meal, microbial diversity was established using the 16S and 23S rRNA gene. The authors preliminarily developed a comparison through the analysis of metagenome versus metatranscriptome from a 24-hour dental plaque sample from the same individual (without caries). The results show a very different pattern of bacterial genera in the metagenome and the metatranscriptome. Actinomyces, Corynebacterium and Neisseria were the three most abundant genera in the RNA-based community, whereas Veillonella, Streptococcus and Leptotrichia were the most commonly found in the total DNA-based metagenome. In addition, a long tail of low-proportion genera is observed in the metagenome but absent in the metatranscriptome, suggesting they could correspond to transient or inactive bacteria. The authors' comments based on this observation are the importance of

obtaining both kinds of data to understand the composition and dynamics of human-associated microbial populations. The results observed in the analysis before and after meal found different bacterial composition for each individual. In some cases, over 80% of active bacteria corresponded to only three genera (*Actinomyces*, *Corynebacterium* and *Rothia*) whereas other individuals did not show any dominant genera in their active microbial community. Some individuals were very resilient to changes after the meal, whereas others had more apparent changes in the proportions of some bacteria, but no specific pattern was common to all individuals. Thus, the changes in active bacteria after a meal were not universal and depended on the original microbial population associated to each human host. The striking homeostasis found in one of the individuals who had never suffered from dental caries, and where virtually no changes were found in the active microbiota before and after a meal, could indicate that the microbiota of some individuals is not affected by food ingestion, potentially reducing the risk of acidic pH and promoting dental health. *Actinomyces* was the only genus found at a proportion over 10% in all samples and was found to be significantly more abundant in healthy individuals. On the other hand, late colonizer being strictly anaerobes like *Porphyromonas*, *Fusobacterium*, *Capnocytophaga*, *Tannerella* and *Leptotrichia* were found significantly more abundant in oral biofilm from caries-bearing individuals. From healthy biofilm, the genera *Streptococcus* were predominant (found at relative abundances between 12 to 19% in different samples) and *Actinomyces* (in a range of 3-12%), both being well known partners for coaggregation. Interestingly, *Actinomyces* showed higher frequencies in early biofilm samples, in agreement with its known role as early colonizer. Other frequent genera were the Actinobacteria *Rothia*, *Angustibacter*, and *Kineococcus*; the Proteobacteria *Neisseria*, *Kingella* and *Alysiella*; the Firmicutes *Gemella*, *Paenibacillus* and *Veillonella*, and finally *Capnocytophaga* and *Fusobacterium*. When it was tried to discern a specific pattern of microbial organisms, associated with different times of biofilm formation, it was observed that samples predominantly clustered according to the donor from whom they were extracted. Consequently, the authors could detect no clear association between bacterial composition and biofilm development stage. These results would, globally, fit within the concept that individual-specific microbial communities are a consequence of host-bacterial co-evolution to maintain host health. Consequently, the host-specific microbiota could be considered as a genetic fingerprint, almost unique for every person, and even preserved throughout the years in a very stable fashion. Actinobacteria members appeared to show the same growth pattern during biofilm formation as well as Fusobacteria and Bacteroidetes. In contrast, genera assigned to Proteobacteria and Firmicutes showed lower correlation values because some species within these groups had different patterns of occurrence. Globally, several genera seem to have a

negative correlation with Actinobacteria, particularly *Veillonella* (Firmicutes), *Volucribacter* (Proteobacteria), *Haemophilus* (Proteobacteria), and *Aggregatibacter* (Proteobacteria), the latter showing strong negative correlations against 11 out of 15 different genera of Actinobacteria detected. In contrast, a multiple positive correlation is exemplified by the distribution of *Fusobacterium*, *Bacteroides*, *Porphyromonas* and *Leptotrichia* in full agreement with the coaggregation partners established for *Fusobacterium* and the classical view of species succession during oral biofilm formation, and the establishment of late colonizers. Indeed, *Fusobacteria* species seem to have the same distribution pattern as *Bacteroidetes* given the multiple significant positive correlations observed among their genera.

Simón-Sóro et al. (2014) conducted a metatranscriptomic study to characterize the active bacterial composition of caries. All dentin caries lesions sampled (n=6) were active lesions, and all enamel caries collected (n=15) were non-cavitated (white spot lesions). Supragingival dental plaque samples, in caries-bearing individuals, were taken 24 hours after tooth-brushing. Unstimulated saliva samples were collected, as well. RNA was extracted from samples by a combination of physical and chemical lysis. In three cases, there was enough carious material to obtain both DNA and RNA. In those three individuals, DNA was also extracted from dental plaque and drooling saliva, both used for comparison. The cDNA and the DNA were sequenced by GS-FLX pyrosequencer (Roche, Basel, Switzerland) with Titanium-plus chemistry. Reads were clustered at 97% sequence identity. Enamel caries lesions were the least diverse, with a median of 177.7 bacterial species, whereas the estimates for open and hidden dentin cavities were 250.7 and 201.2, respectively. Bacterial diversity levels varied not only between individuals but also between caries samples from the same individual. The data suggest that white spot lesions appear to be a very restrictive niche. The authors affirm that the existence of such a high level of diversity even in the active fraction of the bacterial community confirms that the high number of organisms detected in caries lesions is not due to dead or inactive species and that dental caries is a polymicrobial disease, where multispecies microbial consortia are metabolically active in the lesions. *Streptococci*, *Rothia*, *Leptotrichia*, and *Veillonella*, were at higher levels in enamel carious lesions. There is also a high number of minority species that were exclusively found in enamel lesions. *S. mitis* was more abundant in enamel lesions. In relation to *S. mutans*, a dramatically low proportion was found in all samples, ranging from 0.73% in enamel lesions to 0.48% in open dentin and 0.02% in hidden dentin lesions. The low proportion detected confirms that this species is a minority and questions its importance as the main etiological agent of tooth decay. Also, bacterial counts of lactobacilli frequently used to predict caries risk in diagnostic tests may not be informative given that they are virtually absent in enamel lesions, and this would imply that they are probably not involved

in caries initiation. A relevant finding of this study was the comparison between DNA-based bacterial composition of a lesion to the RNA-based composition of the same individual lesion. The two methodologies demonstrated a clear difference in composition of the microbiome. The former, metagenomic approach, shows the total bacterial community, whereas the metatranscriptomic approach describes the active players in that community and the authors proposed the latter procedure is, therefore, a closer approximation to the disease etiology.

Table 1 summarized data comparing the supragingival microbiome of permanent dentition in health and caries subjects. Considering all revised literature regarding this subject there is agreement in some points: (1) Caries is well known as a multi-bacterial disease; (2) Bacterial diversity levels varied not only between individuals, but also between caries samples from the same individual; (3) Species diversity decreases with caries progression; (4) Biofilm from non-cavitated enamel lesions represent a very stringent niche. However, some other points still have no consensus: (1) The real existence of a core microbiome related to health and disease; (2) Caries free subject presents a very stable and protective community, not so sensitive to environmental changes. All the studies compare extreme sites related to caries (caries free versus active patient). However, no consideration has been made for the arrestment process and its microbial correlation. The real existence of a core microbiome related to health and disease should also consider the treated patients (former active patients). Do caries-free patients present a protective microbial composition? Will the caries inactive site be microbiologically similar to a caries-free site after arrestment or it will always resemble the caries active site? Is it possible to use microbial markers to evaluate the risk of caries development? Trying to answer some of these questions, this thesis was designed.

Table 1. DNA- and RNA-based studies comparing the supragingival microbiome of permanent dentition in healthy and carious subjects.

Author(s)	Sequencing method	Samples		Caries-active microbiome	Health microbiome	Consideration	
		Supragingival biofilm (n; locals)					
		Caries-active	Caries-free				
Aas et al., 2008	Sanger (DNA; 16S rRNA)	36 permanents (of 51); from: a. intact enamel (IE) b. white-spot lesions (WSL) c. cavitated dentin d. dentin lesions (DL) *pool minimum 3 teeth		25 permanents (of 39) *pool 4 sites (anterior and posterior)	<i>Atopobium</i> spp.** ^{DL} <i>Actinobaculum</i> spp. <i>Capnocytophaga</i> spp. <i>Corynebacterium</i> spp. ^{WSL} <i>Eubacterium</i> spp. <i>Leptotrichia</i> spp. ^{WSL} <i>Prevotella</i> spp. <i>Bifidobacterium dentium</i> ^{DL} <i>S. intermedius</i> <i>S. parasanguis</i> ^{WSL} <i>Lactobacillus</i> spp.** ^{DL} <i>S. mutans</i> ^{DL} <i>S. salivarius</i> ^{WSL} <i>Abiotrophia</i> spp. <i>Granulicatella</i> spp. <i>Actinomyces</i> spp. <i>Eubacterium</i> spp. <i>Fusobacterium</i> spp. <i>Leptotrichia</i> spp. <i>Prevotella</i> spp. <i>Selenomonas</i> spp.** ^{WSL} <i>S. sanguinis</i> <i>Veillonella</i> spp. <i>Propionibacterium FMA5</i> ^{DL}	<i>Bacteroides</i> ** ^{*IE} <i>S. intermedius</i> ** ^{*IE} <i>Kingella oralis</i> ** ^{*IE} <i>Gemella morbilorum</i> <i>S. cristatus</i> ** ^{*IE} <i>Abiotrophia</i> spp. <i>Granulicatella</i> spp. <i>Actinomyces</i> spp. <i>Corynebacterium</i> spp. <i>Eubacterium saburreum</i> ** ^{*IE} <i>Fusobacterium</i> spp. <i>Leptotrichia</i> spp. (DT031) <i>Prevotella</i> spp. <i>Selenomonas</i> spp. <i>S. sanguinis</i> <i>Veillonella</i> spp. <i>Streptococcus</i> sp. CH016 <i>Streptococcus</i> sp. H6 <i>Eubacterium</i> EI074 <i>Campylobacter showae</i> <i>Capnocytophaga sputigena</i>	<i>Actinomyces</i> spp. and non- <i>S. mutans</i> streptococci higher levels in CA-WSL (carie active – white spot lesion) Low presence of <i>S. mutans</i> in health subjects 10% of caries disease subjects without <i>S. mutans</i> Species in addition to <i>S. mutans</i> also may play an important role in caries production: <i>Veillonella</i> <i>Lactobacillus</i> <i>Bifidobacterium</i> <i>Actinomyces</i> <i>Atopobium</i> low-pH non- <i>S. mutans</i> streptococci Bacterial profiles of the intact enamel of healthy subjects differed significantly from the bacterial profiles of intact enamel from diseased subjects Support the ecological plaque hypothesis in caries disease (Marsh, 1994)
	Reverse-capture checkboard assay (DNA; 16S rRNA)	With <i>S. mutans</i>: 3	Without <i>S. mutans</i>: 2	2; without <i>S. mutans</i>	With <i>S. mutans</i>: <i>Atopobium</i> spp.** <i>Actinobaculum</i> spp. <i>Capnocytophaga</i> spp. <i>Corynebacterium</i> spp. <i>Eubacterium</i> spp. <i>Leptotrichia</i> spp. <i>Prevotella</i> spp. <i>Lactobacillus</i> spp.** Without <i>S. mutans</i>: <i>Bifidobacterium dentium</i> ** <i>S. intermedius</i> <i>S. parasanguis</i> <i>Lactobacillus</i> spp.** Low-non- <i>S. mutans</i> (<i>S. mitis</i> , <i>S. sanguinis</i> , <i>S. gordonii</i> , <i>S. salivarius</i> , clones EK048 e BW009)	Negatively associated: <i>Streptococcus</i> <i>Corynebacterium</i> <i>Selenomonas</i> <i>Veillonella</i> <i>Lachnospiraceae</i> <i>Neisseria</i> <i>Abiotrophia</i> <i>Neisseria-Kingella</i> <i>Lautropia</i> <i>Actinomyces</i>	<i>Streptococcus mitis</i> - <i>S. pneumoniae</i> - <i>S. infantis</i> <i>Corynebacterium matruchotii</i> <i>S. gordonii</i> , <i>S. cristatus</i> , <i>Capnocytophaga gingivalis</i> <i>Eubacterium</i> <i>Campylobacter rectus</i> <i>Lachnospiraceae</i> sp.
Gross et al., 2010	Sanger (DNA; 16S rRNA)	21; from: a. intact enamel b. white-spot lesions (WSL) c. cavitated dentin d. dentin lesions (n=1) *pool several lesions		18 *pool all surfaces	Positively associated: <i>Propionibacterium</i> ** <i>Scardovia</i> <i>S. mutans</i> <i>Lactobacillus</i> ** **statistical difference (increased)	Decreased species diversity as caries progressed (less diverse in intact enamel and all caries stages from caries-active subjects vs health) Intact enamel high diversity compared to WSL and dentin lesions Support for the ecologic disruption model of caries pathobiology <i>S. mutans</i> high over WSL and cavitated lesions; elevated level in many healthy subjects	

**indicate higher abundance, with statistical significance

Author(s)	Sequencing method	Samples		Caries-active microbiome	Health microbiome	Consideration		
		Supragingival biofilm (n; locals)						
		Caries-active	Caries-free					
Belda-Ferre et al., 2012	454 GS-FLX, Roche (DNA; 16S rRNA)	24, but used for analysis 2 by group:		<i>S. gordonii</i> <i>Leptotrichia</i>	<i>S. gordonii</i> <i>Veillonella parvula</i> <i>Leptotrichia buccalis</i> <i>Clostridiales</i> <i>Bacteroidetes</i>	Different diversity between CA vs CF subjects		
Low caries (LC) activity: 2	High caries (HC) activity: 2	2						
Simon-Soro et al., 2013	454 GS-FLX, Roche (DNA; 16S rRNA)	22; from: a. intact enamel (health) b. enamel caries white-spot lesions (WSL)* c. dentin caries (D)* d. deep dentin caries (DD)* *3 representative samples from each condition		<i>Streptococcus</i> <i>S. gordonii</i> <i>S. mitis</i> <i>S. mutans</i> ^{WSL} (low proportion in all samples) <i>Prevotella</i> <i>Rothia</i>	<i>Leptotrichia</i> <i>Veillonella</i> <i>Neisseria</i> <i>Capnocytophaga</i> <i>Fusobacterium</i> <i>Lactobacillus</i> (deep dentin)	Observe lowest level of diversity in enamel lesions (indicates it is the most stringent niche in human teeth, suggesting that the acidic environment probably acts as the main selective force reducing the number of species able to thrive in enamel caries) compared to health in the same individual Dental plaque from sound teeth presented more similar functional profile with WSL in caries subjects		
Johansson et al., 2015	454 GS-FLX, Roche (DNA; 16S rRNA)	High caries prevalence (Romanian): 14	Low caries prevalence (Swedish): 12	12 (Swedish)	High caries prevalence: <i>C. matruchotti</i> <i>Dialister pneumosintes</i> <i>Gemella haemolysans</i> <i>Leptotrichia shahii</i> <i>Peptostreptococcaceae</i> <i>Porphyromonas catoniae</i> <i>Prevotella nigrecens</i> <i>S. mitis</i> <i>Streptococcus</i> sp.** <i>Abiotrophia</i> ** <i>Peptostreptococcus</i> ** <i>Pseudoramibacter</i> ** <i>Neisseria</i> * <i>S. sobrinus</i> ** <i>S. mutans</i> ** <i>Fusobacterium</i> <i>Granulicatella</i> <i>Lactobacillus</i> <i>Parvimonas</i> <i>Shuttleworthia</i> <i>S. cristatus</i> <i>Alloprevotella tannareae</i>	Low caries prevalence: <i>Dialister pneumosintes</i> <i>Gemella haemolysans</i> <i>Leptotrichia shahii</i> <i>Peptostreptococcaceae</i> <i>Porphyromonas catoniae</i> <i>Prevotella</i> <i>S. mitis</i> <i>Streptococcus</i> sp. <i>Campylobacter</i> ** <i>Selenomonas</i> ** <i>Actinomyces</i> <i>Eubacterium</i> <i>Streptococcus</i> <i>Gemella</i> <i>Kingella</i> <i>Mitsuokella</i> <i>Treponema</i> <i>Parvimonas</i> <i>Bergeyella</i>	<i>Actinomyces</i> sp. <i>Capnocytophaga</i> sp. <i>F. nucleatum</i> subsp. <i>animalis</i> <i>Prevotella maculosa</i> <i>P. nigrescens</i>	Species richness and diversity was higher in Romanian adolescents Role of mutans streptococci as a primary caries pathogen is less pronounced in populations exposed to preventive programs, whereas both <i>S. mutans</i> and <i>S. sobrinus</i> are prevalent in populations without routine caries treatment and prevention strategies Core microbiome: -24 species (<i>Streptococcus cristatus</i> , <i>S. mitis</i> , <i>S. mitis</i> Bv2, <i>S. sanguinis</i> , <i>Actinomyces</i> , <i>Prevotella</i> , <i>Fusobacterium</i> , <i>Alloprevotella</i> , <i>Campylobacter</i> , <i>Capnocytophaga</i> , <i>Corynebacterium</i> , <i>Eikenella</i> , <i>Granulicatella</i> , <i>Lachnoanaerobaculum</i> , <i>Veillonella</i>)
		*pool all teeth		**indicate higher abundance, with statistical significance				

Author(s)	Sequencing method	Samples		Caries-active microbiome	Health microbiome	Consideration	
		Supragingival biofilm (n; locals)					
		Caries-active	Caries-free				
Xiao et al., 2016	454 GS-FLX, Roche (DNA; 16S rRNA)	131; divided in: NC (No-caries; DMFT=0, n=29) LC (Low-caries; DMFT≤4, n=32) MC (Moderate-caries; 4<DMFT<8, n=37) HC (High-caries; DMFT≥8, n=62)	29	<i>Campylobacter</i> ** <i>TM7</i> <i>Neisseria</i> <i>Atopobium</i> ** <i>Bacteroidetes</i> ** <i>Dialister</i> ** <i>Veillonella</i> ** <i>Rothia</i> ** <i>Selenomonas</i> * <i>Streptococcus</i> <i>Actinomyces</i> ** <i>Prevotella</i> ** <i>Fusobacterium</i> <i>Lautropia</i> <i>Porphyromonas</i> <i>Leptotrichia</i> <i>Corynebacterium</i> <i>Capnocytophaga</i> <i>Aggregatibacter</i> <i>Lacnoanaerobaculum</i> <i>Lachnospiraceae</i>	<i>Cariobacterium</i> <i>Eubacterium</i> <i>GN02</i> <i>Clostridiales</i> <i>Tannerella</i> <i>Flavobacteriales</i> <i>Clostridium</i> <i>Catonella</i> <i>Peptostreptococcus</i> <i>Fretibacterium</i> <i>Eikenella</i> <i>SRI</i> <i>Fusobacterium</i> ** <i>Lautropia</i> <i>Porphyromonas</i> <i>Leptotrichia</i> <i>Corynebacterium</i> ** <i>Capnocytophaga</i> <i>Aggregatibacter</i> **	<i>Lacnoanaerobaculum</i> ** <i>Lachnospiraceae</i> ** <i>Cariobacterium</i> ** <i>Eubacterium</i> ** <i>GN02</i> ** <i>Clostridiales</i> ** <i>Tannerella</i> ** <i>Campylobacter</i> ** <i>TM7</i> <i>Neisseria</i> <i>Atopobium</i> <i>Bacteroidetes</i> <i>Dialister</i> <i>Veillonella</i> <i>Rothia</i> <i>Selenomonas</i> <i>Streptococcus</i> <i>Actinomyces</i> <i>Prevotella</i>	<p>Similar community structures</p> <p>Higher bacterial diversity in NC group: more health and stable ecosystem</p> <p>Bacterial components were not markedly affected by the disease status or pathological factors</p> <p><i>Veillonella</i>, <i>Rothia</i> and <i>Actinomyces</i> higher abundance in HC group</p> <p>Core microbiome: -72.6% all OTUs shared -81.1% genera shared (n=99): <i>Capnocytophaga</i> 17.8% <i>Prevotella</i> 13.5% <i>Actinomyces</i> 13.0% <i>Corynebacterium</i> 8.9% <i>Streptococcus</i> 6.6% <i>Neisseria</i> 6.4%</p> <p><i>S. mutans</i> low abundant in all groups</p> <p><i>S. sobrinus</i> absent in NC group</p> <p>Support ecological catastrophe (Marsh, 2003)</p>
				**indicate higher abundance, with statistical significance			
He et al., 2017	MiSeq, Illumina (DNA; 16S rRNA)	25	12	<i>Bacteroidetes</i> ** <i>Spirochaetes</i> ** <i>Leptotrichia</i> <i>Selenomonas</i> <i>Treponema</i>	<i>Atopobium</i> <i>Prevotella</i> <i>Bergeriella</i> <i>Prevotella</i> <i>Leptotrichia</i>	<p>Similar community structures</p> <p>Similar alpha diversity</p> <p>Dissimilar microbial communities (network)</p> <p>Caries: -higher evenness -simpler networks -species sparsely connected -lower negative relationships (decreased antagonism among the dental plaque residents)</p> <p>Healthy: -lower degree of variation -more complexes network -species highly diverse and strongly connected</p> <p>Support the ecological plaque hypothesis in caries disease (Marsh, 1994)</p> <p>“Data suggested that the “shift” could be observed at the community topology level without significant microbial composition changes.”</p>	
				**indicate higher abundance, with statistical significance			

Author(s)	Sequencing method	Samples		Caries-active microbiome	Health microbiome	Consideration	
		Supragingival biofilm (n; locals)					
		Caries-active	Caries-free				
Eriksson et al., 2018	MiSeq Illumina (DNA; 16S rRNA)	With <i>S. mutans</i>: 43 (61%)	Without <i>S. mutans</i>: 28 (39%)	82 (43/52% without <i>S. mutans</i>)	<p>With <i>S. mutans</i>:</p> <p><i>Actinomyces</i> <i>Scardovia wiggisiae</i> <i>Stomatobaculum longum</i> <i>Veillonella atypica</i></p> <p>Without <i>S. mutans</i>:</p> <p><i>Actinomyces</i> <i>Selenomonas</i> <i>Tannerella</i> <i>TM7</i> <i>Treponema</i> <i>Dialister</i> <i>Neisseria</i> <i>Butyrivibrio</i> <i>Leptotrichia</i> <i>Fusobacterium</i> <i>Peptostreptococcaceae</i> <i>Shuttleworthia</i> <i>Lautropia</i> <i>Cardiobacterium</i> <i>Peptococcus</i> <i>Rothia</i> <i>Propionibacterium</i> <i>Corynebacterium</i></p>	<p>findings are consistent with this ecologic concept (Marsh, 1994)</p> <p><i>S. mutans</i>:</p> <ul style="list-style-type: none"> -significant higher prevalence in caries adolescents -associated with the presence of a few additional influential species, including the acidogenic and aciduric/acidophilic <i>Scardovia wiggisiae</i> 	
Eriksson et al., 2017	MiSeq, Illumina and PacBio SMRT (DNA; 16S rRNA)	26 (low-caries prevalence)	37	<p><i>Scardovia wisgiae</i> <i>S. mutans</i> <i>Selenomonas</i> <i>Bifidobacterium</i> <i>Leptotrichia</i> <i>Clostridiales</i> <i>Fretibacterium</i> <i>Capnocytophaga</i> <i>Veillonellaceae</i> <i>Treponema</i> <i>Shuttleworthia</i> <i>Sinergitstes</i> <i>Prevotella</i> <i>Fusobacterium</i> <i>Streptococcus</i> <i>Actinomyces</i> <i>Actinobaculum</i></p>	<p><i>Porphyromonas</i> <i>Johnsonella</i> <i>Eubacterium</i> <i>Catonella</i> <i>Rothia</i> <i>Prevotella</i> <i>Atopobium</i> <i>Parvimonas</i> <i>Mogibacterium</i> <i>Dialister</i> <i>Corynebacterium matruchotii</i> <i>Fusobacterium</i> <i>Campylobacter</i> <i>Actinobaculum</i></p>	<p><i>Mycoplasma</i> <i>Veillonella</i> <i>Porphyromonas</i> <i>Granulicatella</i> <i>Parvimonas</i> <i>Peptostreptococcus</i> <i>Selenomonas</i> <i>Fusobacteria</i> <i>Actinomyces</i> <i>Actinomycetaceae</i></p>	<p>Species richness did not differ from CA and CF subjects</p> <p>Genera more prevalent in tooth biofilm:</p> <ul style="list-style-type: none"> <i>Streptococcus</i> (8%) <i>Actinomyces</i> (12%) <i>Leptotrichia</i> (11%) <i>Prevotella</i> (10%) <p>Core microbiome:</p> <p>23 genera:</p> <ul style="list-style-type: none"> -<i>Campylobacter gracilis</i>, -<i>Corynebacterium matruchotii</i> -<i>Streptococcus mitis</i> -<i>V. dispar</i> -<i>V. parvula</i>
Benitez-Paez et al., 2014	HiSeq 2000 (RNA; 16S rRNA) GS-FLX, Roche (DNA; 16S rRNA)	3; before and after meal	4; from 6, 12, 24, 48h plaque accumulation 2; before and after meal	<p><i>Leptotrichia</i>** <i>Tannerella</i>** <i>Porphyromonas</i>** <i>Actinomyces</i></p>	<p><i>Fusobacterium</i>** <i>TM7</i> <i>Capnocytophaga</i>** <i>Corynebacterium</i> <i>Rothia</i></p>	<p><i>Actinomyces</i>^{RNA} <i>Rothia</i> <i>Corynebacterium</i>^{RNA} <i>Neisseria</i>^{RNA} <i>Veillonella</i>^{DNA} <i>Leptotrichia</i>^{DNA} <i>Streptococcus</i>^{DNA}</p>	<p>Homeostasis found in one of the individuals CF: virtually no changes were found in the active microbiota before and after a meal</p>

Author(s)	Sequencing method	Samples		Caries-active microbiome	Health microbiome	Consideration
		Supragingival biofilm (n; locals)				
		Caries-active	Caries-free			
Simon-Soro et al., 2014	GS-FLX, Roche (RNA; 16S rRNA)	13; from: White spot lesions; n=15 Open dentin caries; n=6 Hidden dentin lesions; n=6	-	<i>Streptococci</i> <i>Rothia</i> <i>Leptotrichia</i> <i>Veillonella</i> <i>Lactobacillus</i> <i>Shleglella</i> <i>Pseudoaramibacter</i> <i>Atopobium</i> <i>S. mitis</i>	-	White spot lesions is a very restrictive niche, with less diversity S. mutans: low proportion in all samples Bacterial diversity levels varied not only between individuals but also between caries samples from the same individual The varying polymicrobial nature of cavities shown in the current manuscript and the currently accepted ecology-based hypothesis of caries disease underline that the functional output of the microbial community is probably more important than its species-composition in order to understand and combat the disease.

3 OBJECTIVES

3.1 General objective

The aim of this study was to describe and compare the metabolically active bacterial composition profile and diversity from supragingival biofilm collected in different oral conditions from active- and inactive-caries subjects, and from caries-free subjects.

3.2 Specific objectives

The specific aims of this study were to describe and compare the metabolically active bacterial composition profile and diversity from supragingival biofilm, considering:

1. three different sites from caries active subjects (active non-cavitated lesions *versus* inactive non-cavitated lesions *versus* sound dental surface);
2. sites presenting inactive non-cavitated lesions from caries-active subjects *versus* the same condition from caries-inactive subjects;
3. sound dental sites from caries-active subjects *versus* the same condition from caries-free subjects;
4. overall supragingival biofilm from caries-active subjects *versus* overall supragingival biofilm from caries-free subjects.

4 MATERIALS AND METHODS

This research was developed at the Biochemistry and Microbiology Oral Laboratory (LABIM), of the Faculty of Dentistry, from Federal University of Rio Grande do Sul, Porto Alegre, Brazil; and, at laboratory of Division of Oral Biology, School of Dentistry, Faculty of Medicine and Health, University of Leeds, United Kingdom.

4.1 Ethical aspects

The study protocol was approved by the Ethics Committee of Federal University of Rio Grande do Sul, Brazil (CAAE 56583316.8.0000.5347) (Annex 1). All the subjects provided informed consent or assent, if they were under eighteen years old, prior to their participation, according to the principles outlined in the Resolution number 466/2012, from National Commission of Ethic in Research, Department of National Health, Brazil (CONEP, 2012) on experimentation involving human subjects. All patients received dental treatment at the Dental Clinic of the Federal University of Rio Grande do Sul.

4.2 Subjects

Subjects with permanent dentition, between 12 to 72 years-old (19.3 ± 29.6) selected for dental treatment at Faculty of Dentistry, Federal University of Rio Grande do Sul (UFRGS) were examined for caries disease diagnosis. Subjects presenting active, and subjects presenting inactive caries activity were selected for this study, as well as subjects without visual caries activity or inactivity during all life until the exam time (caries-free). The subjects recruited for the study were screened about oral and systemic health histories by answering a questionnaire about their socio-demographics, oral health related behavior and practices, as well as patient-reported outcomes. All subjects should not use antimicrobial agents (intravenous, muscle or oral route) at least two months before the samples being collect.

The subjects that fit the inclusion criteria in the study were allocated in three groups: in caries active group (CA) (n=10) were included caries-active subjects with DMF-T and DMF-S indexes equal or major than one, presenting active non-cavitated caries lesions (ANCL); the caries inactive group (CI) (n=6) was formed by caries-inactive subjects, presenting DMF-T and DMF-S indexes equal or major than one, but presenting only inactive non-cavitated caries lesions (INCL). The subjects included in caries-free (CF) (n=6) were subjects presenting DMF-T and DMF-S indexes equal zero (figure 1).

4.3 Sampling

For the bacterial composition profile and diversity, a total of 42 samples of supragingival plaque from 22 subjects were collected. The subjects were categorized according to caries activity status being Caries Active (CA) (n=10), Caries Inactive (CI) (n=6) and Caries-free (CF) (n=6). The collection sites varied according to patient status. From CA subjects, ten active non-cavitated lesions sites, ten inactive non-cavitated lesions sites, and ten sound sites were collected (figure 1).

4.4 Sample collection and storage

Clinical examinations took place on different days, with one-week interval, at the Dental Clinical at the UFRGS. All clinical examinations were performed once at baseline using the visual-tactile method. Prior, gingival index (GI) and, visible dental plaque index (VPI) were measured. Then, dental biofilm was removed, using a prophylaxis hand piece with rubber cup and dental prophylactic paste, by a dentistry student prior dental exam to verify the patient caries activity condition and to select the enamel surfaces included in the sample collection. The visual-tactile dental exam was performed using a dental equipment, with artificial light, isolation with cotton rolls and, air-drying the enamel surface before caries activity diagnostic. Active non-cavitated caries lesions (ANCL) were those with a whitish/yellowish opaque surface with loss of luster, exhibiting a chalky or neon-white appearance. The surface felt rough when the tip of a sharp probe was moved gently across it (Kidd; Fejerskov, 2004). Inactive non-cavitated caries lesions (INCL) were shiny and felt smooth on gentle probing, and the color

varied from whitish to brownish or black (Kidd; Fejerskov, 2004). The patients did not receive recommendations about diet or dental hygiene in the first examination. They returned after one week to collect the dental biofilm sample. They should let dental biofilm being accumulated for 12 hours, and do not eat and do not drink anything at least one hour before the clinical examination. They were recommended to avoid using topical antimicrobial agents, at least one week before the return to Dental Clinic. The dental biofilm was collected using a sterilized Gracey curette (one for each collection) from three different conditions in caries-active group: CA-ANCL= pool of supragingival biofilm from active non-cavitated lesions; CA-INCL= pool of supragingival biofilm from inactive non-cavitated lesions; and, CA-S= pool of supragingival biofilm from sound dental surfaces; from one dental condition in caries-inactive group : CI-INCL= pool of supragingival biofilm from inactive non-cavitated lesions; and from caries-free group: CF-S: pool of supragingival biofilm from all sound surfaces.

The samples collected were immediately stored in a 2 mL microtubes content 1 mL of RNA stabilization solution (RNAprotect, Qiagen, Valencia, CA) at room temperature, for a maximum 24 hours. The microtubes were centrifuged for 30 seconds, at 10.000 rpm. The supernatant was discarded, and the dental biofilm pellet was frozen at -80 Celsius degrees, until being sent to Leeds, United Kingdom. Before sending the samples to Oral Biology Department, School of Dentistry, University of Leeds, the microtubes were removed from freeze and resuspended in 1 mL of RNA stabilization solution.

4.5 Samples processing

4.5.1 RNA Extraction and Quantification

The total RNA extraction was done using the protocol UltraClean® Microbial RNA Isolation kit (MO-BIO). The samples were thawed and treated with Lysozyme for 10 minutes, at 37 Celsius degrees, before processing. After finishing the UltraClean protocol, the DNase I in column was used for DNA residual removal. It was obtained 100 uL of RNA after process.

The measurement of the total RNA in each biofilm sample was done using the protocol Quant-iT™ RiboGreen® RNA Reagent and Kit (Invitrogen, Ltd.). A 2.5 uL aliquote of total RNA extracted was used for this protocol. A Spectrofluorometer with excitation ~480 nm, and emission ~520 nm, enabled the fluorescence analysis and RNA quantification.

4.5.2 Library preparation and RNA-sequencing

The True Seq® Sample Preparation Guide, Low Sample (LS) Protocol Illumina (Illumina, Inc., San Diego, CA) was used for preparation of genomic libraries, following the steps: RNA fragmentation (preparation for complementary strand ligation); cDNA repair (complementary DNA); adenylation of 3'-end; adaptors ligation (enabling the pools identification after sequencing in the same lane); fragment purification; DNA enrichment (by polymerization chain reaction – PCR).

The genomic library quality validation was made in Agilent Technologies 2200 TapeStation. The genomic libraries with a peak of approximately 269 base pairs were considered with good quality for sequencing (Padmanaban, 2014).

For normalization of genomic libraries and posterior preparation of pools to sequencing, the dsDNA (double strand DNA) was quantified with Quant-iT™ PicoGreen® dsDNA Kit (Turner BioSystems, Inc., CA) protocol.

Two pools with 11 samples were prepared for sequencing in the Illumina HiSeq 3000, available at the Genomics facility at Leeds St James' Teaching Hospital, using two lanes of sequencer equipment, generating billions of short paired-end sequences of 150 base pairs (2x150bp).

4.5.3 Data analysis

The sequences generated by Illumina HiSeq 3000 were cleaned to removal less than 150 bp and expected error higher than 0.5. The resulting fasta format files were sent to web-based, open source system Metagenomics RAST Server (MG-RAST) (Meyer et al., 2008) for analyzing shotgun metagenomes against a comprehensive nonredundant database. For this study, a phylogenetic reconstruction was computed from set of hits against SILVA SSU database, considering 97% of similarity to genus taxonomic level.

To compare dental biofilm microbial composition profile and bacterial diversity among groups, the following tests were used:

- a. Friedman test at 95% of significance, post-hoc Nemenyi: three conditions for caries active subjects (paired analysis) (CA-ANCL vs CA-INCL vs CA-S)

- b. Kruskal-Wallis at 95% of significance, post-hoc Bonferroni and Nemenyi: comparisons among all dental conditions (CA-ANCL vs CA-INCL vs CA-S vs CI-INCL vs CF-S)
- c. Mann-Whitney U test (Wilcoxon-run sum test) at 95% of significance: comparisons between similar dental health conditions from different groups (CA-INCL vs CI-INCL; CA-S vs CF-S)
- d. Mann-Whitney U test (Wilcoxon-run sum test) test at 95% of significance: comparison between subjects' caries active versus caries-free (CA vs CF).

The estimator of richness Chao-1, ACE (Abundance-based Coverage Estimator), and Fisher-alpha was used for alpha diversity analysis, as well as the alpha diversity indexes Shannon-Wiener, Simpson, Simpson Inverse, and Pielou-Shannon.

For beta-diversity analysis was done the hierarchical clustering obtained by UPGMA (Unweighted Pair Group Method with Arithmetic Mean) clustering method, the K-means clustering method for comparison between sites and subjects, and metric Multidimensional Distance Scaling (mMDS) for compare all groups.

The gplots package (RStudio, version 3.5.0) was used to generate a Venn diagram to show the shared and unique OTUs among groups, based on the occurrence of OTUs in subjects' groups regardless their abundance. Shared genera present in all subjects (100% core threshold) were defined as the core microbiome (Xiao et al., 2016).

All analysis was conducted on RStudio (version 3.5.0) using packages for ecologic data analysis (Vegan, BiodiversityR, Phyloseq).

5 RESULTS

The supragingival biofilm samples analyzed for genus taxonomic level, by each subjects' groups and sites, after total RNA extraction, library preparation, and quality filtering of sequences are shown in figure 1. From each subject, a pool of supragingival biofilm, from sites presenting similar dental condition, were obtained.

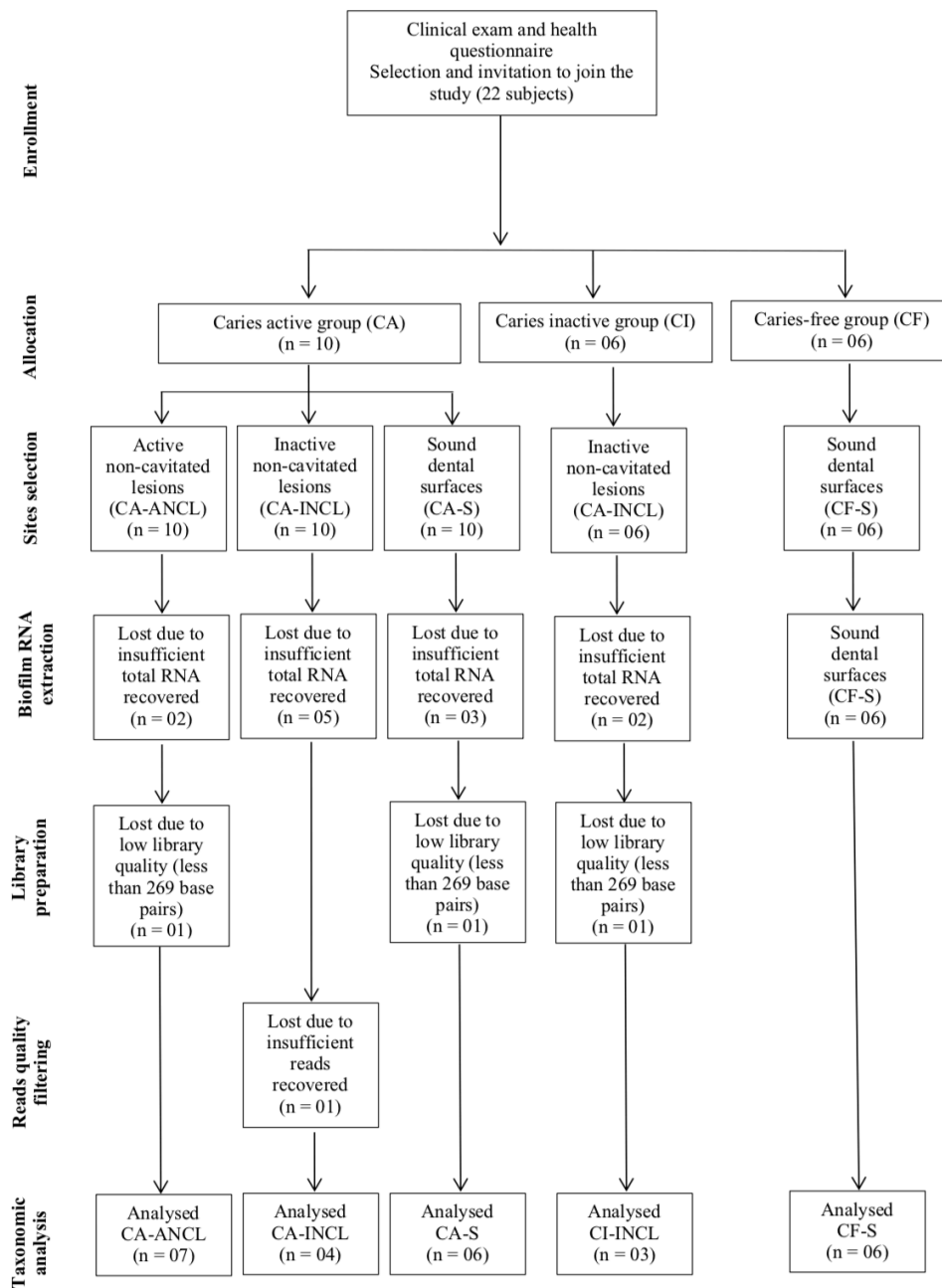


Figure. 1. Flow chart showing the number of subjects that were enrolled and allocated to groups, and the supragingival biofilm sites collected from each group and lost throughout RNA extraction, library preparation and sequences quality filtering, and the final number of biofilm samples analysed in the subjects and groups.

The characteristics of the subjects included in the study are shown in table 2. The DMF-T/S index (Decayed, Missing and Filled Permanent Teeth/Surface), visible plaque, and gingival index were similar in caries active subjects (CA) compared to caries inactive subjects (CI). Caries-free subjects (CF) presented less amount of visible plaque compared to the other groups ($p<0.05$).

Table 2. Comparison of dental clinical parameters between caries active (CA), caries inactive (CI) and caries-free (CF) subjects (Med: median; Q1: first quartile; Q3: third quartile).

Parameters	CA (n=7)			CI (n=3)			CF (n=6)		
	Med	Q1	Q3	Med	Q1	Q3	Med	Q1	Q3
Visible plaque	25.6 ^a	18.7	28.9	21 ^a	13.8	55	5.4 ^b	6	8
Gingival index	9.6 ^a	3.5	14	22.2 ^a	18.1	28.1	4.0 ^a	1	6
DMF-T	16 ^a	15	18	9 ^{ab}	4.5	17.5	0 ^b	0	0
DMF-S	31 ^a	25.5	39	11 ^{ab}	5.5	63.5	0 ^b	0	0

DMF-T = Decayed, Missing and Filled Permanent Teeth

DMF-S = Decayed, Missing and Filled Permanent Surface

Different lowercase letters indicate statistical difference between groups by Kruskal-Wallis test, with Bonferroni correction, at 95% confidence level ($p<0.05$)

5.1 SEQUENCES QUALITY

After quality filtering, high-quality sequences were recovered from all samples, with Good's coverage $>97\%$, except for one subject in caries active group (number 3; table 2), for sites with inactive non-cavitated lesion (CA-INCL), presenting no sufficient recovered reads (rRNA) for taxonomic analysis.

The rarefaction curve for all subjects is observed in figure 2 (*a to c*). Considering the average of sequences count (table 3), a plateau was achieved for all samples, indicating that the dataset was representative of the bacterial communities allowing comparison of alpha and beta diversity measures.

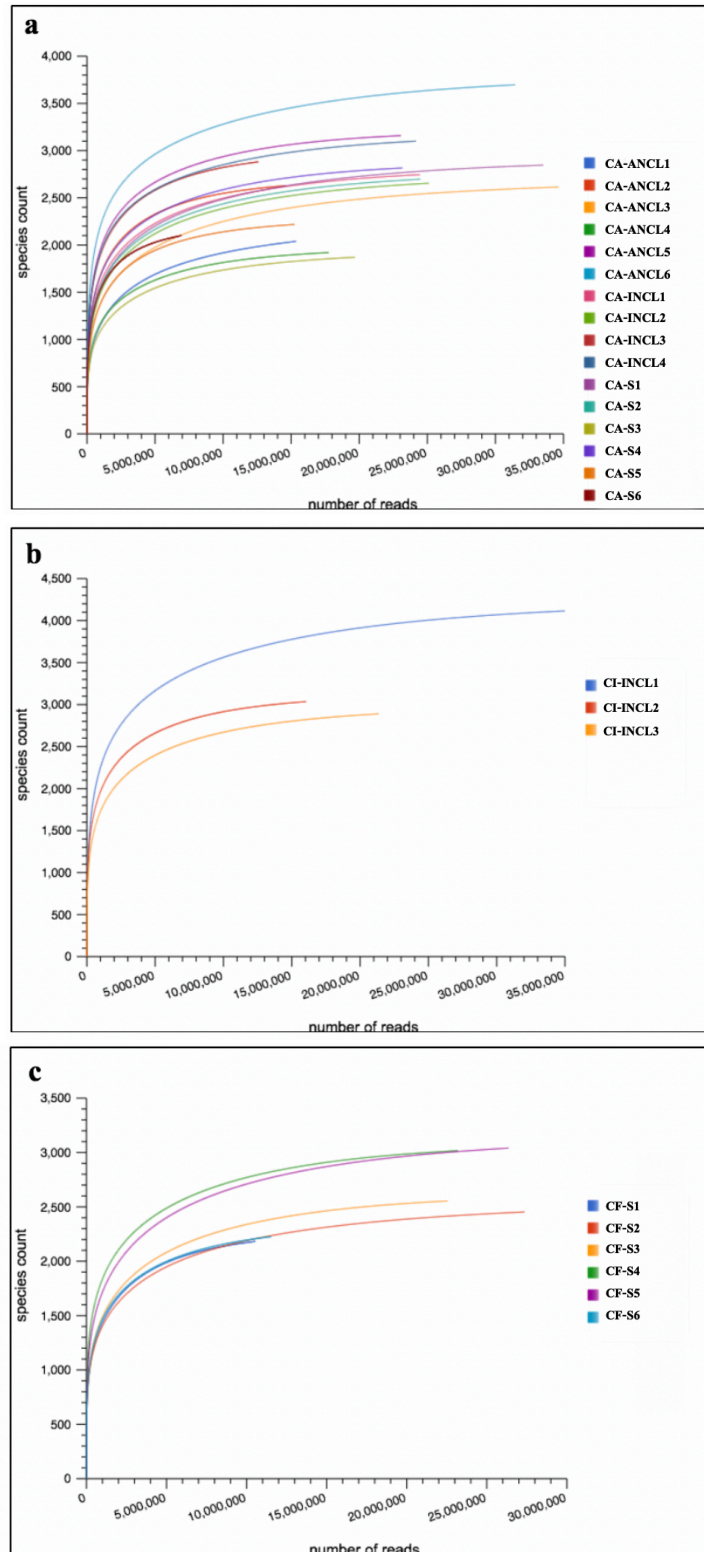


Figure 2. Rarefaction curve of microbial communities from supragingival biofilm. (a) CA: caries active subjects; ANCL: active non-cavitated lesion; INCL: inactive non-cavitated lesion; S: sound (1 to 7: subjects); (b) CI: caries inactive subjects; INCL: inactive non-cavitated lesion (1 to 3: subjects); (c) CF: caries-free patients; S: sound (1 to 6: subjects). Font: MG-RAST.

After data trimming and quality filtering of reads through removing artifacts, an average of 3,542,190 high-quality sequences with 147.7 ± 3.7 base pairs (bp) was recovered,

corresponding to 16.48% of sequences generated by sequencer Illumina HiSeq 3000. The average of data for each group is shown in table 4.

Table 4. Average of data quality control of sequences generated by HiSeq 3000 sequencer, after data trimming and quality filtering by metagenomics analysis server (MG-RAST). CA: caries active subjects: ANCL: active non-cavitated lesion; INCL: inactive non-cavitated lesion; S: sound; CI: caries inactive subjects: INCL: inactive non-cavitated lesion; CF: caries-free subjects: S: sound.

Groups	Sites	Base pair counts	Sequence count	Sequence passed QC pipeline	Sequences with predicted proteins (known function)	Identified protein features	Identified functional categories
CA	ANCL	3,421,366,425	22,809,110	4,003,372	160,929	60,776	38,916
	INCL	3,236,337,600	21,575,584	3,331,748	323,411	90,173	51,277
	S	3,075,707,000	20,504,713	7,041,334	477,783	130,751	77,717
CI	INCL	3,619,432,050	24,129,547	1,716,188	32,510	26,173	15,897
CF	S	3,038,822,400	20,258,816	1,618,307	39,009	27,459	15,592

5.2 MICROBIAL COMPOSITION

There were recovered reads from domain Archaea (mean= 2.76 reads), Bacteria (mean= 8602231.96 reads), Eukaryota (mean= 72118.12 reads), Viruses (mean= 758.28 reads) and unclassified sequences (mean= 65841.56 reads) (figure 3). Bacteria were the most abundant domain.

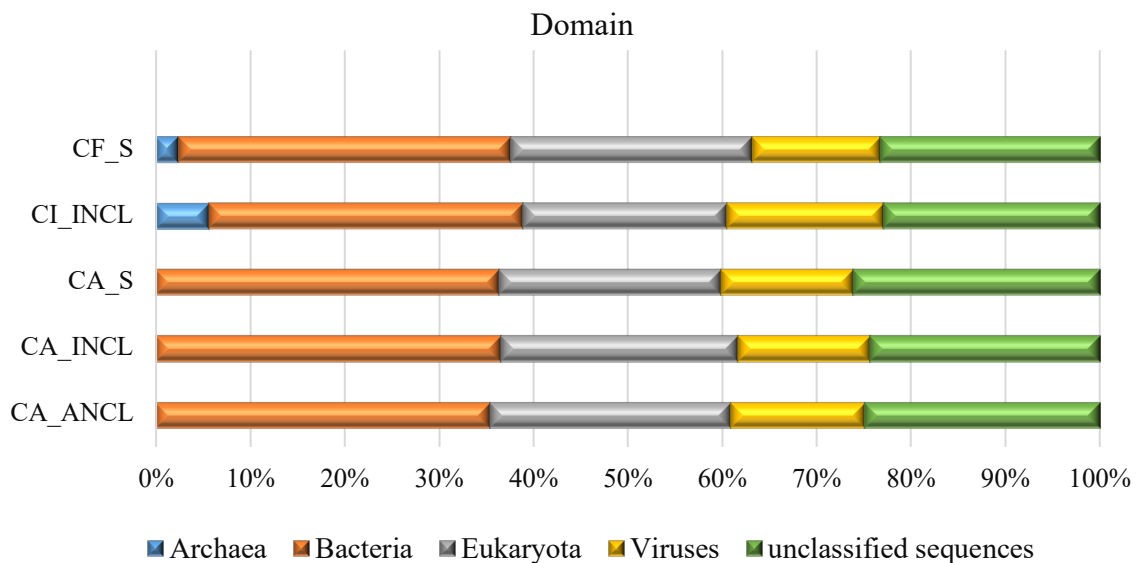


Figure 3. Domain relative abundance recovered from all groups (Caries active subjects: CA-ANCL: active non-cavitated lesion; CA-INCL: inactive non-cavitated lesion; CA-S: sound; Caries inactive subjects: CI-INCL: inactive non-cavitated lesion; Caries-free subjects: CF-S: sound).

The table 5 presents a summary for Operational Taxonomic Units (OTUs) recovered by taxonomic levels from microbiome of total supragingival biofilm (SILVA SSU database, 97% sequence identity).

Table 5. Summary of operational taxonomic units (OTUs) identified in supragingival biofilm sites, considering all taxonomic levels. (CA: caries active subjects: ANCL: active non-cavitated lesion; INCL: inactive non-cavitated lesion; S: sound; CI: caries inactive subjects: INCL: inactive non-cavitated lesion; CF: caries-free subjects: S: sound; Med: Median, Q1: first quartile; Q3: third quartile).

Taxonomic levels	CA									CI			CF		
	ANCL			INCL			S			INCL			S		
	Med	Q1	Q3	Med	Q1	Q3	Med	Q1	Q3	Med	Q1	Q3	Med	Q1	Q3
Domain	4	4	5	5	4	5	4	4	5	5	5	5	5	5	5
Phylum	38	36	41	40	39	41	36	33	39	41	39	42	38	36	40
Class	79	70	85	81	77	86	73	62	82	84	78	87	77	74	82
Order	150	141	165	157	148	168	146	126	163	169	159	171	147	143	160
Family	274	264	285	277	262	296	265	230	298	300	283	303	263	258	283
Genus	623	539	660	646	603	688	622	514	706	699	647	702	594	572	639

The relative abundance of OTUs for Phylum considering at least 1% of microbiome presence (abundant phylotype), are detailed in table 6. Of 29 phyla recovered, seven was considered predominant taxa, belonging to Actinobacteria, Firmicutes, Bacteroidetes, Fusobacteria, Proteobacteria, Spirochaetes. Actinobacteria, Firmicutes and Bacteroidetes were the phylum that showed the highest relative abundance while Proteobacteria and Spirochaetes were less abundant. Bacteroidetes was the only phylum that showed statistical difference between inactive sites from caries active (CA) and caries inactive (CI) subjects. The phyla Bacteroidetes had statistically significant lower relative abundance in CI-INCL compared to the other supragingival microbiomes ($p < 0.05$). All 29 recovered phyla from supragingival microbiome are presented in figure S1.

Table 6. Relative abundance of operational taxonomic units (OTUs) from most abundant recovered Phylum (more than 1%) from supragingival biofilm microbiome, in Bacteria domain. CA: caries active subjects: ANCL: active non-cavitated lesion; INCL: inactive non-cavitated lesion; S: sound; CI: caries inactive subjects: INCL: inactive non-cavitated lesion; CF: caries-free subjects: S: sound.

Domain	Phylum	CA			CI	CF
		ANCL	INCL	S	INCL	S
	Actinobacteria	35.4309	31.9129	22.6330	37.3696	38.0435
	Firmicutes	16.3471	13.8534	11.0226	18.3013	15.7665
	Bacteroidetes	13.3583 ^{ab}	22.9888 ^a	18.2013 ^{ab}	9.2105 ^b	21.7997 ^{ab}
Bacteria	Fusobacteria	9.1938	9.8397	10.3640	5.6750	9.4207
	Proteobacteria	4.9799	4.4026	7.6617	4.3596	2.8903
	Spirochaetes	0.0288	0.2212	0.4143	0.0914	1.6060
	unclassified (from Bacteria)	20.5139 ^{ab}	16.6955 ^a	29.6014 ^b	24.8521 ^b	10.2466 ^a

Cut off point of 1% of the microbiome.

Font: SILVA database/MG-RAST

Different lowercase letters indicate statistical difference between groups by Friedman test with Nemenyi post-hoc, 95% confidence level.

A total of 915 different genera were originated from all supragingival biofilm samples analyzed (table S1). The summary of total genus abundance observed on supragingival microbial communities from all groups are shown in table 7.

Table 7. Summary of total genus abundance (total reads) observed in supragingival biofilm microbiome. (Min: minimum; Max: maximum; Q1: first quartile; Q3: third quartile; CA: caries active subjects; ANCL: active non-cavitated lesion; INCL: inactive non-cavitated lesion; S: sound; CI: caries inactive subjects; INCL: inactive non-cavitated lesion; CF: caries-free subjects; S: sound.)

	CA			CI	CF
	ANCL	INCL	S	INCL	S
Min	0	0	0	0	0
Max	11713765	5039161	16418033	6874324	7405700
Median	40	18	33	28	30
Q1- Q3	2-844	1-419	2-684	1-659	2-1303

The relative abundance of OTUs for abundant genera are detailed in table 8. Considering abundant genera if it contributed with at least 0.1% of the microbiome, 74 genera (8.09%) could be recovered. The higher relative abundance (>10%) was found for *Actinomyces*, *Corynebacterium* and *Capnocytophaga*. There was no statistical difference considering the genus relative abundance among groups, except for genera *Capnocytophaga* that show significant less relative abundance ($p<0.05$) in inactive non-cavitated lesion from caries inactive subjects (CI-INCL) compared to caries active subjects (CA-INCL).

Table 8. Relative abundance of operational taxonomic units (OTUs) for most abundant recovered Genus (more than 0.1%) from supragingival biofilm microbiome. CA: caries active subjects; ANCL: active non-cavitated lesion; INCL: inactive non-cavitated lesion; S: sound; CI: caries inactive subjects; INCL: inactive non-cavitated lesion; CF: caries-free subjects; S: sound.

Phylum	Genus	CA			CI	CF	CA
		ANCL	INCL	S	INCL	S	all sites
Actinobacteria	<i>Actinomyces</i>	17.6759	15.4198	8.4770	14.7328	15.0821	13.6247
	<i>Corynebacterium</i>	8.9143	13.1498	11.2405	14.8008	14.8642	10.7137
	<i>Atopobium</i>	2.2203	0.3732	0.0876	0.9844	0.5232	1.0011
	<i>Micrococcus</i>	0.8611	0.1058	0.0607	0.2288	0.3766	0.3904
	<i>Rothia</i>	0.6261	0.5908	1.3912	3.2411	1.0165	0.9159
	<i>Propionibacterium</i>	0.5755	0.3158	0.3376	0.5374	1.3709	0.4281
	<i>Bifidobacterium</i>	0.4264	0.1297	0.1251	0.2074	0.6669	0.2466
	<i>Mobiluncus</i>	0.4067	0.2315	0.0169	0.1183	0.3378	0.2182
	<i>Arthrobacter</i>	0.3584	0.3503	0.2843	0.6506	0.2790	0.3279
	<i>Mycobacterium</i>	0.3541	0.1316	0.0816	0.2461	0.3300	0.2012
	<i>Slackia</i>	0.3536	0.0739	0.0012	0.1580	0.0451	0.1576
	<i>Enterorhabdus</i>	0.1908	0.0335	0.0004	0.0741	0.0119	0.0836
	<i>Catenuloplanes</i>	0.1431	0.0358	0.0050	0.0036	0.0392	0.0667
	<i>Nesterenkonia</i>	0.1230	0.1372	0.1570	0.1035	0.1574	0.1392
<i>Amycolatopsis</i>	0.1142	0.0043	0.0521	0.0262	0.1423	0.0668	

Phylum	Genus	CA			CI		CF	CA
		ANCL	INCL	S	INCL	S	all sites	
Actinobacteria	<i>Conexibacter</i>	0.1093	0.0166	0.0003	0.0384	0.0081	0.0473	
	<i>Saccharomonospora</i>	0.0979	0.0205	0.0002	0.0184	0.1564	0.0436	
	<i>Cellulomonas</i>	0.0913	0.0030	0.0006	0.0384	0.2200	0.0374	
	<i>Streptomyces</i>	0.0907	0.0629	0.0139	0.0721	0.1196	0.0550	
	<i>Streptacidiphilus</i>	0.0894	0.1309	0.0037	0.0472	0.1928	0.0649	
	<i>Arcanobacterium</i>	0.0796	0.0165	0.0033	0.0396	0.1255	0.0366	
	<i>Nocardiosis</i>	0.0745	0.0400	0.0020	0.0273	0.3150	0.0391	
	<i>Actinobacillus</i>	0.0637	0.1017	0.1197	0.1239	0.0882	0.0935	
	<i>Actinobaculum</i>	0.0592	0.0070	0.0216	0.0409	0.1098	0.0335	
	<i>Pseudonocardia</i>	0.0547	0.0148	0.0082	0.0372	0.2297	0.0282	
Bacteroidetes	<i>Capnocytophaga</i>	8.6725 ^{ab}	14.8779 ^a	12.246 ^{ab}	4.8726 ^b	7.1525 ^{ab}	11.373 ^{ab}	
	<i>Prevotella</i>	2.4165	3.2285	2.4940	3.0591	8.1100	2.6183	
	<i>Porphyromonas</i>	1.2355	3.0656	1.7348	0.4424	1.6741	2.0119	
	<i>Tannerella</i>	0.5841	0.7551	0.3890	0.4731	2.8055	0.5445	
	<i>Parabacteroides</i>	0.1721	0.2741	0.1463	0.1316	0.6872	0.1836	
	<i>Bacteroides</i>	0.0762	0.2879	0.2434	0.0448	0.3159	0.1859	
	<i>Coenonia</i>	0.0285	0.1142	0.1133	0.0055	0.0177	0.0796	
	<i>Chryseobacterium</i>	0.0155	0.0372	0.1106	0.0257	0.0252	0.0570	
Firmicutes	<i>Veillonella</i>	6.5915	6.4021	4.4722	4.5419	2.4343	5.7280	
	<i>Streptococcus</i>	2.8966	1.7017	2.5254	5.7529	1.8979	2.4997	
	<i>Eubacterium</i>	2.4502	2.0217	1.4262	2.0994	2.8780	1.9617	
	<i>Selenomonas</i>	1.6210	0.7978	0.6447	2.0360	2.9777	1.0676	
	<i>Clostridium</i>	0.4740	0.5115	0.3332	0.5793	0.9530	0.4272	
	<i>Lactobacillus</i>	0.3294	0.0448	0.0351	0.0708	0.0421	0.1549	
	<i>Enterococcus</i>	0.2634	0.0489	0.0201	0.1161	0.0309	0.1235	
	<i>Finegoldia</i>	0.2085	0.0495	0.0114	0.0613	0.1591	0.0983	
	<i>Gemella</i>	0.1495	0.4236	0.1410	0.2881	0.4446	0.2042	
	<i>Granulicatella</i>	0.1330	0.2678	0.2792	0.4923	0.3645	0.2183	
	<i>Megasphaera</i>	0.1277	0.0230	0.0489	0.1889	0.0757	0.0749	
	<i>Oribacterium</i>	0.1120	0.1379	0.0492	0.1790	0.2085	0.0931	
	<i>Butyrivibrio</i>	0.1080	0.2337	0.0697	0.1304	0.3995	0.1197	
	<i>Abiotrophia</i>	0.1046	0.1570	0.4553	0.5017	0.2621	0.2520	
	<i>Desulfotomaculum</i>	0.0582	0.0606	0.0392	0.0872	0.1469	0.0513	
	<i>Mitsuokella</i>	0.0521	0.0114	0.0049	0.0687	0.1819	0.0251	
	<i>Bacillus</i>	0.0500	0.1067	0.0415	0.0614	0.1646	0.0587	
	<i>Dialister</i>	0.0312	0.0114	0.0088	0.0405	0.1119	0.0183	
<i>Erysipelothrix</i>	0.0058	0.0192	0.0047	0.0768	0.1275	0.0082		
<i>Peptostreptococcus</i>	0.0013	0.0011	0.0081	0.0311	0.1782	0.0039		
Fusobacteria	<i>Leptotrichia</i>	7.2803	6.3517	7.2414	4.4706	6.3591	7.0688	
	<i>Fusobacterium</i>	1.6678	3.3468	2.9591	0.9872	2.8772	2.5245	
	<i>Sebaldella</i>	0.2204	0.1084	0.1295	0.1839	0.1271	0.1614	
Proteobacteria	<i>Neisseria</i>	3.3419	2.2566	3.6599	1.9023	0.6250	3.2360	
	<i>Haemophilus</i>	0.3747	0.4737	1.2741	0.4270	0.4379	0.7451	
	<i>Kingella</i>	0.2922	0.2723	0.4855	0.3916	0.1944	0.3631	
	<i>Campylobacter</i>	0.1724	0.4113	0.3869	0.5580	0.7641	0.3063	
	<i>Eikenella</i>	0.0982	0.0852	0.2390	0.0669	0.0516	0.1502	
	<i>Aggregatibacter</i>	0.0541	0.1209	0.3186	0.1767	0.0600	0.1710	
	<i>Mannheimia</i>	0.0541	0.0870	0.1680	0.0326	0.0335	0.1053	
	<i>Burkholderia</i>	0.0461	0.0723	0.1105	0.0376	0.0097	0.0767	

Phylum	Genus	CA			CI		CF	CA
		ANCL	INCL	S	INCL	S	all sites	
Spirochaetes	<i>Treponema</i>	0.0270	0.1853	0.4098	0.0868	1.5909	0.2092	
	<i>derived from Bacteria</i>	20.5139	16.6955	29.6014	24.8521	10.2466 ^b	23.2374	
	<i>Collinsella</i>	0.2805	0.0481	0.0029	0.1310	0.0211	0.1235	
	<i>derived from Actinobacteria (class)</i>	0.2094	0.0879	0.0087	0.0316	0.1292	0.1057	
	<i>derived from Clostridiales</i>	0.1627	0.2423	0.1141	0.1578	0.3797	0.1606	
Unclassified sequences	<i>derived from Gammaproteobacteria</i>	0.0636	0.1156	0.1622	0.0539	0.1350	0.1129	
	<i>derived from Propionibacteriaceae</i>	0.0565	0.0375	0.0356	0.0391	0.1749	0.0444	
	<i>derived from Pasteurellaceae</i>	0.0396	0.0528	0.1677	0.0811	0.0349	0.0921	
	<i>derived from Bacteroidetes</i>	0.0375	0.0221	0.1124	0.0166	0.5379	0.0633	
	<i>derived from Clostridiales Family XI. Incertae Sedis</i>	0.0168	0.0083	0.0093	0.0182	0.2489	0.0121	

Cut off point of 0.1% of the microbiome.

Font: SILVA SSU database/MG-RAST

Different lowercase letters indicate statistical difference between groups by Friedman test with Nemenyi post-hoc, 95% confidence level.

Nine genera were higher than 1% relative abundance for all subjects (*Actinomyces*, *Corynebacterium*, *Capnocytophaga*, *Prevotella*, *Veillonella*, *Streptococcus*, *Eubacterium*, *Leptotrichia*, and unclassified genera (derived from Bacteria)). Despite no significant difference among groups, *Atopobium* was higher than 2% in ANCL sites from CA subjects, showing less than 0.1% relative abundance for the other sites and subjects. In the same way, only for CF subjects, the genera *Propionibacterium* and *Tannerella* presented higher than 1% of relative abundance; and, *Haemophilus*, higher than 1% of relative abundance only for sound dental conditions from caries active subjects (CA-S) (table 8). Instead, *Porphyromonas* and *Fusobacterium* were less abundant than 1% only for caries inactive subjects (CI-INCL), and *Neisseria*, only for caries-free subjects (table 8).

Unclassified sequences (n=60) contributed with 6.56% of genera of all samples. Of all 915 genera, 17.38% (n=159) were less abundant than 0.0001%. The genera with relative abundance between $\geq 0.0001\%$ and $< 0.1\%$ corresponded to 74.54% (n=682) of all dental biofilm microbiome and contributed for the major genera diversity in supragingival microbial communities. A total of 123 (13.44%) genera were shared among supragingival biofilm microbiome from all sites and all subjects included in the study, representing a common core microbiome of supragingival plaques. The proportion of unclassified, shared and exclusive

genera (richness) observed into each subjects and sites are shown in table 9. The exclusive genera identified by sites from supragingival biofilm presented relative abundance lower than 0.0001%.

Table 9. Mean genus richness and proportion of richness, unclassified, shared and exclusive genera identified in supragingival biofilm microbiome for caries active group (CA) in different dental health conditions (ANCL: active non-cavitated lesion; INCL: inactive non-cavitated lesion; S: sound); for caries inactive group (CI) (INCL: inactive non-cavitated lesion); and for caries-free group (CF) (S: sound).

Groups	Sites (n)	Genus Richness	% genus richness in all microbiome	% unclassified genus sequences	% shared genus richness among all sites of all subjects (123 genus)	% exclusive genus by sites (n)
CA	ANCL (6)	531	58.03	0.38	23.73	2.19 (20)
	INCL (4)	559	61.10	0	22.00	2.19 (20)
	S (6)	538	58.80	0	22.86	2.30 (21)
CI	INCL (3)	569	62.19	0.18	21.62	3.17 (29)
CF	S (6)	534	58.36	0.56	23.03	3.10 (28)

As shown in figure 4, the 123 shared genera represent 4493 OTU abundances shared among the five dental health conditions; at the same time, the OTU exclusive abundance for each group can be observed in the figure.

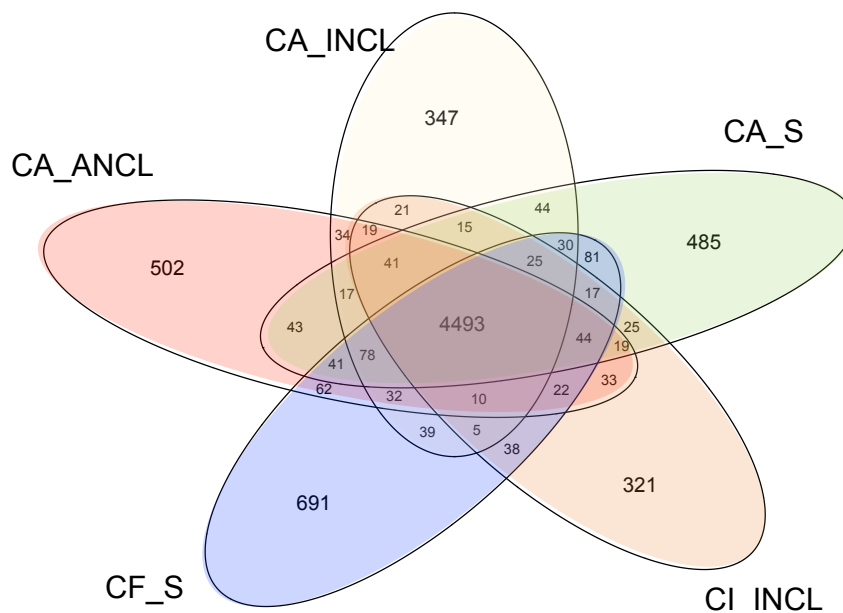


Figure 4. Venn diagram showing shared and unique OTU abundances at 97% identity, for genus taxonomic level, among supragingival biofilm from caries active subjects (CA_ANCL: active non-cavitated lesion; CA_INCL: inactive non-cavitated lesion; CA_S: sound); caries inactive subjects (CI_INCL: inactive non-cavitated lesion); and, caries-free subjects (CF_S: sound).

Paired analysis was conducted including only the caries active subjects (CA) with all dental conditions sequenced (ANCL, INCL and S). Comparing these sites from CA subjects, *Actinomyces* genera showed significantly higher abundance in supragingival microbiome from active non-cavitated lesion sites (CA-ANCL) (relative abundance = 20.83%) compared to sound sites (CA-S) (relative abundance = 9.63%) (Friedman test; Nemenyi post-hoc; $p < 0.05$). The genera *Capnocytophaga* showed significant higher abundance in supragingival microbiome from inactive non-cavitated lesion sites (CA-INCL) (relative abundance = 14.88%) compared to active non-cavitated lesion sites (CA-ANCL) (relative abundance = 4.82%) (Friedman test; Nemenyi post-hoc; $p < 0.05$). No statistical difference was observed for other genera in these group (CA), considering relative abundance cutoff point of 0.1%.

5.3 ALPHA DIVERSITY ANALYSIS

5.3.1 Diversity analysis for caries active subjects

The alpha diversity estimators Chao1, ACE (Abundance-based Coverage Estimator), and Fisher-alpha; and, the alpha diversity indices Shannon-Wiener, Simpson, Simpson Inverse, and Pielou-Shannon was calculated for caries active subjects (CA) (paired analysis: ANCL vs INCL vs S).

The observed richness of microbial supragingival biofilm communities at genus level was similar among different sites from the same subjects ($p = 0.54$) (figure 5).

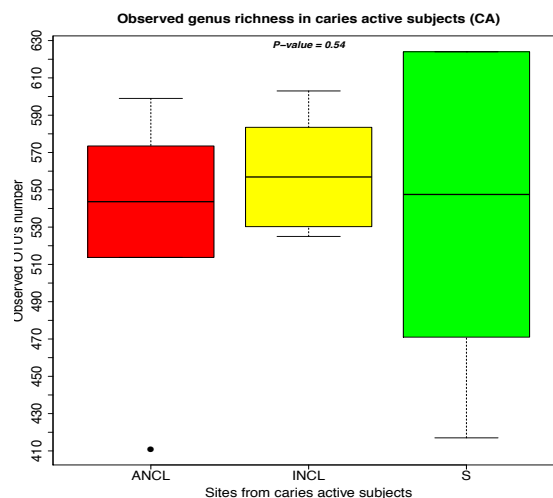


Figure 5. Total number of operational taxonomic units (OTUs) observed (richness) for genus taxonomic level in microbial communities of caries active subjects (CA) (paired analysis) in different sites (ANCL: active non-cavitated lesion; INCL: inactive non-cavitated lesion; S: sound). Friedman test with Nemenyi post-hoc, 95% confidence level.

The supragingival microbiome in ANCL had lower average of observed richness (531 genera) compared with supragingival microbiome in INCL (559 genera) and in sound dental sites (538 genera), despite no statistical significance observed. The table 10 presents a summary of observed genus richness, considering the total number of OTUs observed for caries active subjects (CA).

Table 10. Summary for observed genus richness in supragingival biofilm microbiome for caries active group (CA) in different sites (ANCL: active non-cavitated lesion; INCL: inactive non-cavitated lesion; S: health surface) (Min: minimum; Max: maximum; Q1: first quartile; Q3: third quartile).

	CA		
	ANCL	INCL	S
Min	411	525	417
Max	599	603	624
Median	557	555	557
Q1- Q3	514-574	530-584	471-624

Alpha diversity measures of microbial supragingival biofilm communities at genus level for caries active subjects (CA) are shown below.

The table 11 and figure 6 present the alpha diversity estimators for different dental health conditions (sites).

Table 11. Alpha diversity estimators of supragingival microbial communities (taxonomic level genus) in caries active subjects (CA) in different sites (ANCL: active non-cavitated lesion; INCL: inactive non-cavitated lesion; S: sound) (paired analysis). (Chao1 = Chao 1 richness estimator (se = standard deviation); ACE = Abundance-based Coverage Estimator (se = standard deviation); Fisher-alpha estimator).

CA subjects	Chao 1(se)			ACE(se)			Fisher-alpha		
	ANCL	INCL	S	ANCL	INCL	S	ANCL	INCL	S
1	614.28(20.01)	658.92(17.17)	678.56(17.24)	613.56(11.71)	659.38(12.10)	677.73(12.18)	45.79	48.77	48.17
2	503.04(29.63)	587.5(19.26)	482.17(20.73)	481.16(10.46)	583.75(11.56)	477.56(10.71)	32.76	43.33	32.80
3	615.73(16.52)	638.62(18.19)	703.00(23.56)	613.78(11.61)	647.58(12.09)	691.93 (12.56)	46.36	49.38	52.01
4	682.42(25.16)	624.94(27.87)	585.28(29.19)	669.05(11.91)	600.53(11.95)	563,75(11,53)	47.68	45.89	40.78
mean	603.87(22.83)	627.51(20.62)	612.25(22.68)	594.39(11.42)	600.53(11.95)	602.74(11.75)	43.14	46.84	43.33

Friedman test with Nemenyi post-hoc, 95% confidence level

The estimators from richness did not show statistical difference among sites from the same subjects (Friedman test with Nemenyi post-hoc; $p>0.05$).

Richness estimators among different sites from caries active subjects

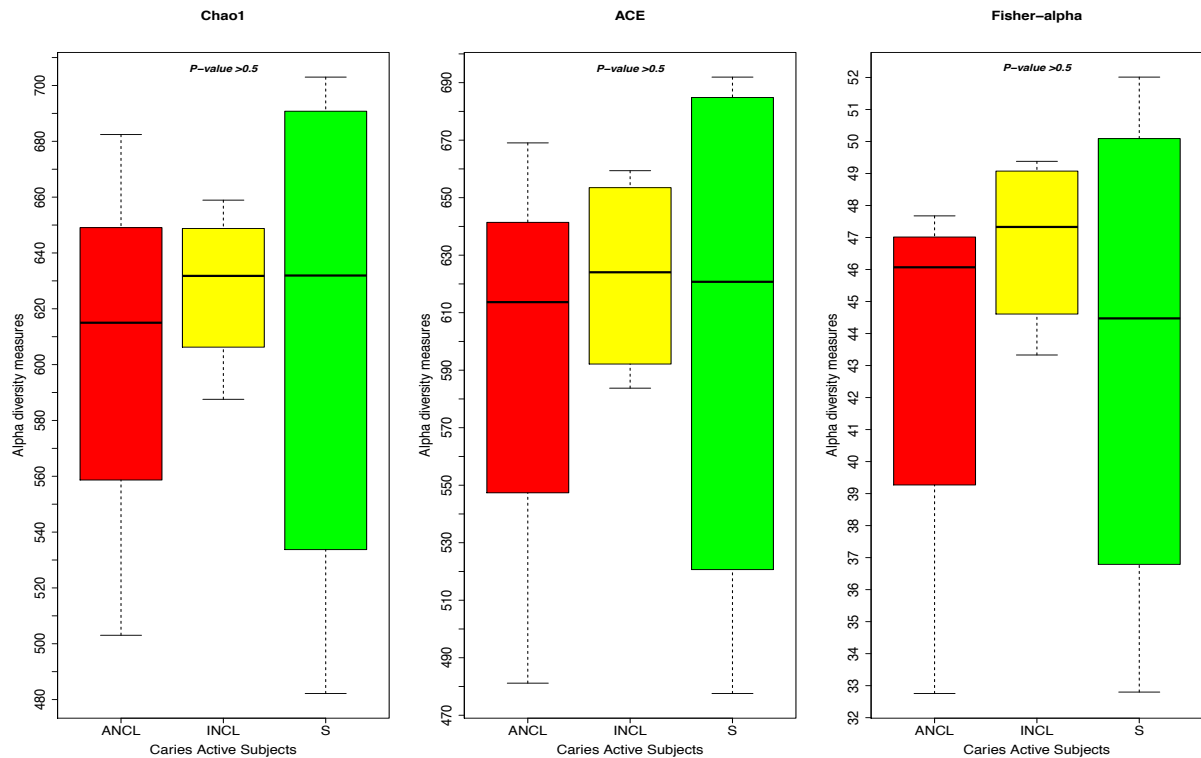


Figure 6. Richness estimators Chao 1, ACE (Abundance-based Coverage Estimator), and Fisher-alpha for genus taxonomic level in supragingival biofilm communities in caries active group (CA) in different sites (ANCL: active non-cavitated lesion; INCL: inactive non-cavitated lesion; S: health surface). Friedman test with Nemenyi post-hoc, 95% confidence level.

The table 12 and figure 7 present the alpha diversity indexes for caries active subjects (CA) in different dental health conditions (sites). No statistical difference was observed among alpha diversity indexes (Shannon-Wiener, Simpson, Simpson Inverse, Pielou-Shannon) for all dental sites (ANCL vs INCL vs S) in caries active subjects (CA) (paired analysis) (Friedman test with Nemenyi post-hoc; $p > 0.05$).

Table 12. Alpha diversity indexes of microbial communities (taxonomic level genus) in caries active subjects (CA) in different dental sites (ANCL: active non-cavitated lesion; INCL: inactive non-cavitated lesion; S: sound) (Shannon = Shannon-Wiener diversity index; Simpson = Simpson diversity index; Invsimpson = Inverse of Simpson diversity index; and Pielou = Pielou-Shannon equitative index).

CA subjects	Shannon			Simpson			Invsimpson			Pielou		
	ANCL	INCL	S	ANCL	INCL	S	ANCL	INCL	S	ANCL	INCL	S
1	2.455	2.548	2.468	0.849	0.875	0.835	6.6334	8.0252	6.0639	0.386	0.419	0.393
2	2.400	2.512	2.166	0.864	0.861	0.833	7.3527	7.1772	5.9746	0.375	0.416	0.342
3	1.940	2.741	2.536	0.704	0.851	0.839	3.3833	6.7290	6.2131	0.304	0.441	0.394
4	3.003	2.158	1.804	0.886	0.768	0.654	8.8042	4.3021	2.8897	0.475	0.359	0.307
mean	2.450	2.490	2.240	0.826	0.839	0.790	6.543	6.560	5.290	0.385	0.409	0.359

Friedman test with Nemenyi post-hoc, 95% confidence level

Alpha diversity indexes between caries active and caries-free subjects

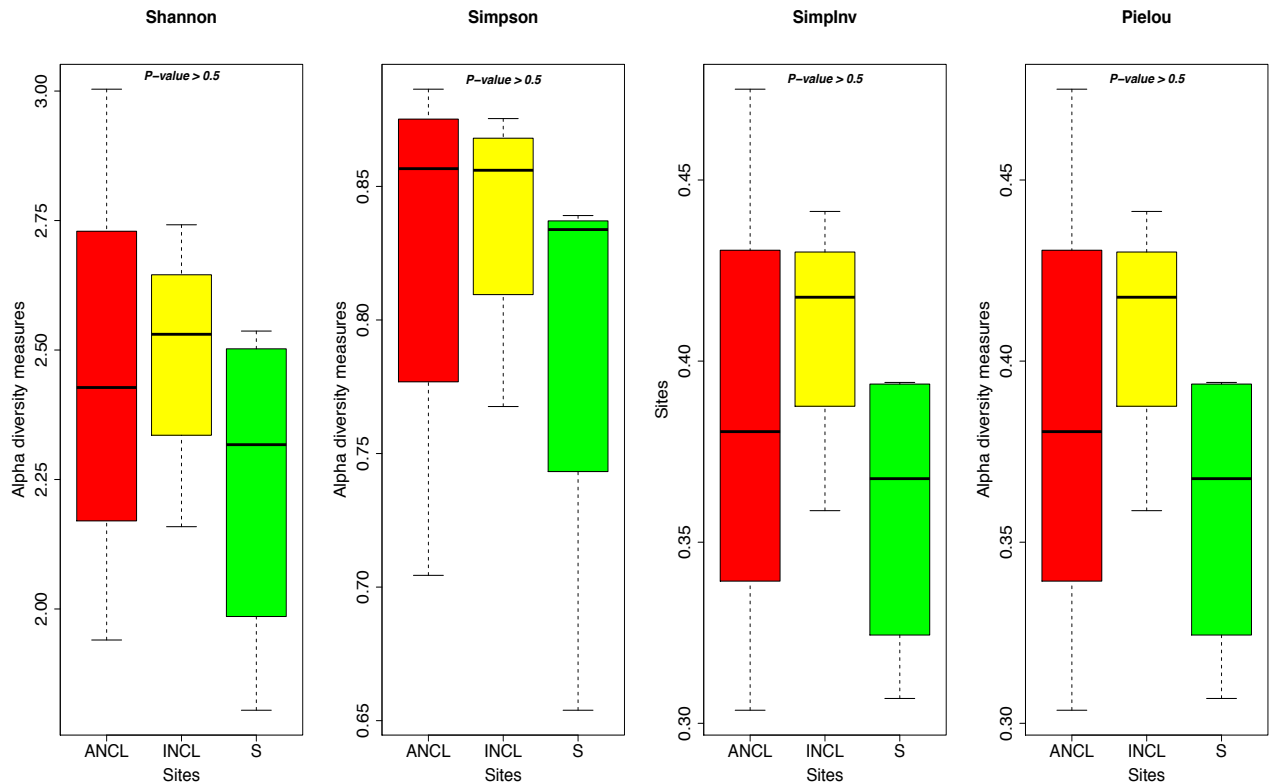


Figure 7. Alpha diversity indexes Shannon-Wiener, Simpson, Simpson Inverse, and Pielou-Shannon for genus taxonomic level in supragingival biofilm communities in caries active subjects (CA) in different sites (ANCL: active non-cavitated lesion; INCL: inactive non-cavitated lesion; S: sound) (paired analysis). Friedman test with Nemenyi post-hoc, 95% confidence level.

5.1.2 Diversity analysis between identical dental health conditions from different groups

The further alpha diversity analysis was made comparing specific sites from different groups. The INCL site from CA subjects was analyzed *versus* INCL site from CI subjects (CA-INCL *vs* CI-INCL). The sound site from CA subjects was analyzed *versus* sound sites from CF subjects (CA-S *vs* CF-S). These results are show below.

The observed genus richness for both comparisons are presented in figure 8. The statistical analysis by Mann-Whitney U test did not show statistical difference between observed richness among the same dental conditions from different subjects ($p=0.72$, and $p=0.38$ for CA-INCL *vs* CI-INCL, and CA-S *vs* CF-S, respectively).

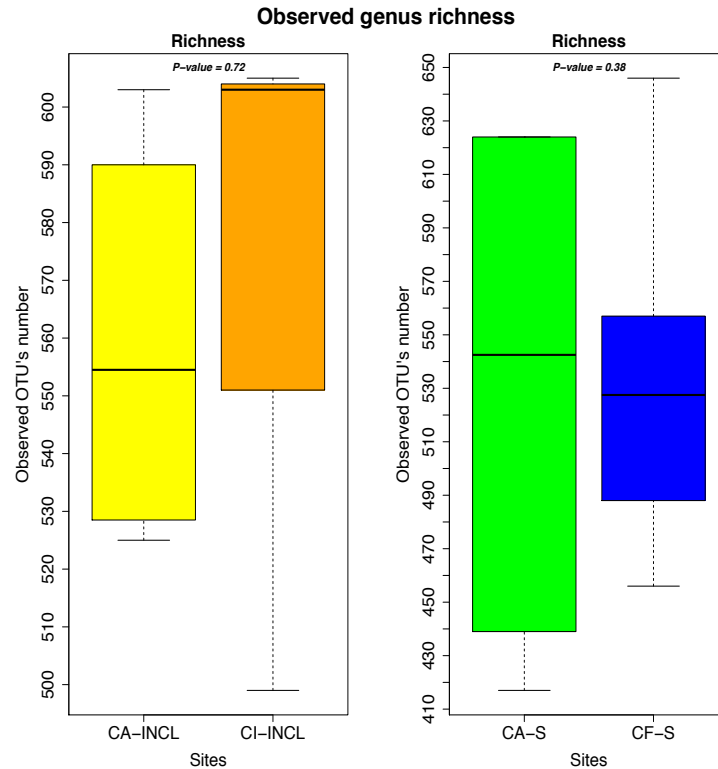


Figure 8. Total number of operational taxonomic units (OTUs) observed (richness) for genus taxonomic level in microbial communities between the same dental conditions from different subjects. *In the left:* inactive non-cavitated lesion from caries active subjects *versus* inactive non-cavitated lesion from caries inactive subjects (CA-INCL *vs* CI-INCL); *in the right:* sound dental surface from caries active subjects *versus* sound dental surfaces from caries-free subjects (CA-S *vs* CF-S). Mann-Whitney U test, 95% confidence level.

The table 13 presents the summary of observed genus richness for both comparisons (CA-INCL *vs* CI-INCL; CA-S *vs* CF-S).

Table 13. Summary for observed genus richness in supragingival biofilm samples between inactive non-cavitated lesion (INCL) from caries active subjects (CA), and inactive non-cavitated lesion (INCL) from caries inactive subjects (CI); and, between sound dental surface (S) from caries active subjects (CA) and sound dental surfaces (S) from caries-free subjects (CF) (Min: minimum; Max: maximum; Q1: first quartile; Q3: third quartile).

	CA	CI	CA	CF
	INCL	INCL	S	S
Min	525	499	417	456
Max	603	605	624	646
Median	554	603	464	528
Q1- Q3	530-584	551-604	428-569	493-554

The alpha diversity estimators observed between CA-INCL *versus* CI-INCL are presented below (figure 9). The Mann-Whitney U test did not show statistical difference between the same dental conditions from different subjects.

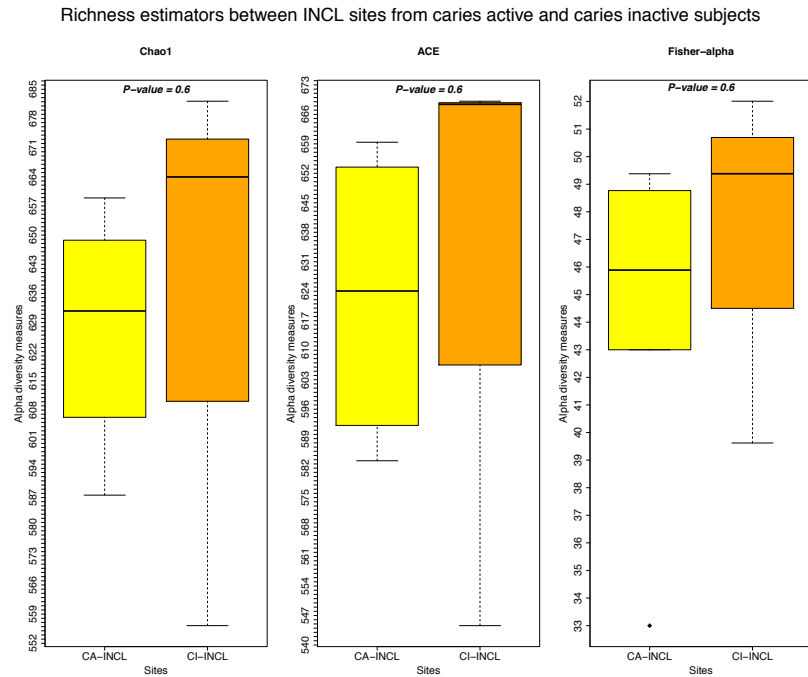


Figure 9. Richness estimators Chao 1, ACE (Abundance-based Coverage Estimator), and Fisher-alpha for genus taxonomic level in supragingival biofilm communities between inactive non-cavitated lesion from caries active subjects *versus* inactive non-cavitated lesion from caries inactive subjects (CA-INCL *vs* CI-INCL). Mann-Whitney U test, 95% confidence level.

The alpha diversity estimators observed between CA-S *versus* CF-S are presented below (figure 10). The Mann-Whitney U test did not show statistical difference between the same dental conditions from different subjects.

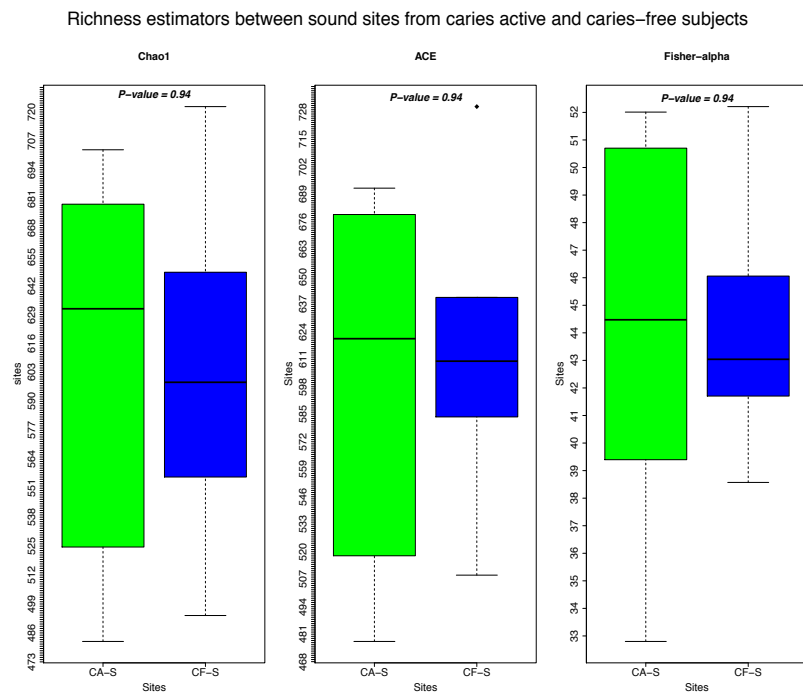


Figure 10. Richness estimators Chao 1, ACE (Abundance-based Coverage Estimator), and Fisher-alpha for genus taxonomic level in supragingival biofilm communities between sound dental surface from caries active subjects and sound dental surfaces from caries-free subjects (CA-S *vs* CF-S). Mann-Whitney U test, 95% confidence level.

The alpha diversity indexes observed between CA-INCL *versus* CI-INCL are presented below (figure 11). The Mann-Whitney U test did not show statistical difference between the same dental conditions from different subjects.

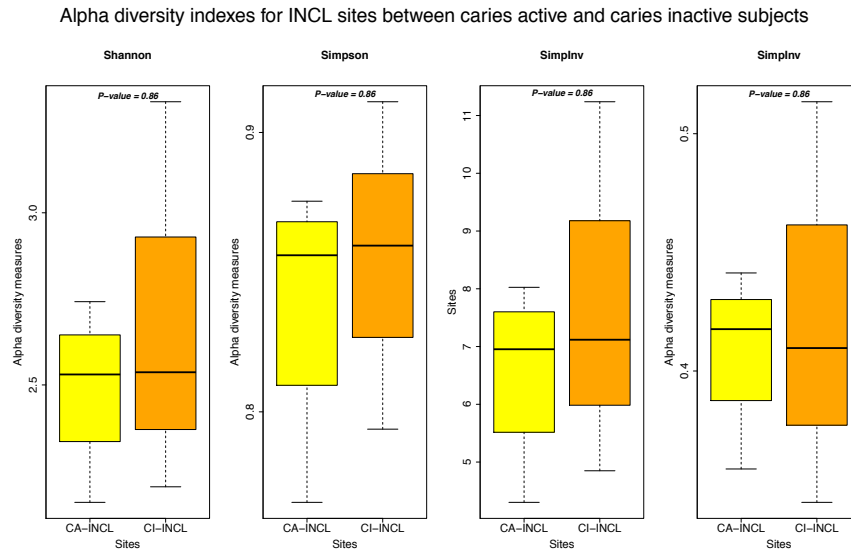


Figure 11. Alpha diversity indexes Shannon-Wiener, Simpson, Simpson Inverse, and Pielou-Shannon for genus taxonomic level in supragingival biofilm communities between sites inactive non-cavitated lesion from caries active subjects and inactive non-cavitated lesion from caries inactive subjects (CA-INCL *vs* CI-INCL). Mann-Whitney U test, 95% confidence level.

The alpha diversity indexes observed between CA-S *versus* CF-S are presented below (figure 12). The alpha diversity between these identical dental conditions from different subjects show statistical difference by Mann-Whitney U test.

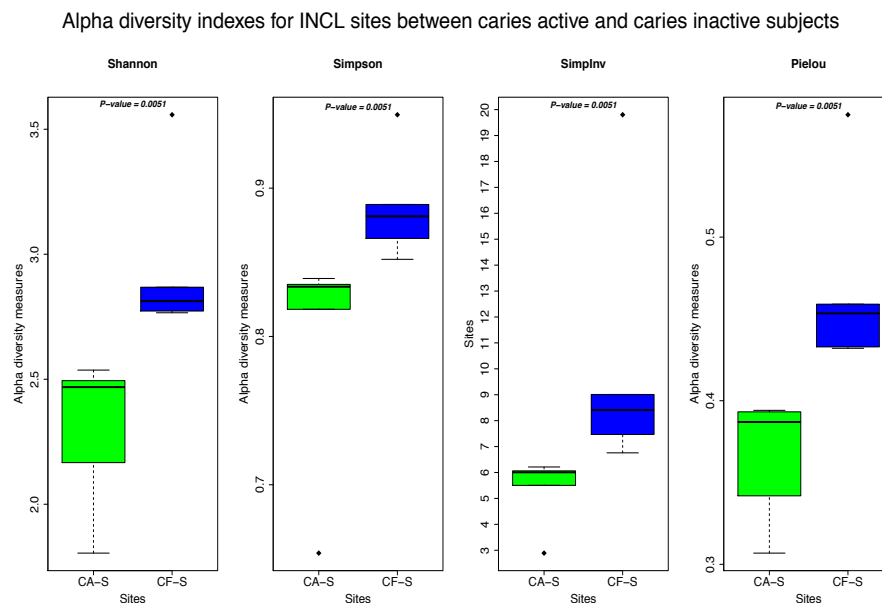


Figure 12. Alpha diversity indexes Shannon-Wiener, Simpson, Simpson Inverse, and Pielou-Shannon for genus taxonomic level in supragingival biofilm communities between sound dental surface from caries active subjects and sound dental surfaces from caries-free subjects (CA-S *vs* CF-S). Mann-Whitney U test, 95% confidence level.

Considering these comparisons, some inferences can be postulated for alpha diversity between sound surfaces from different subjects (CA-S vs CF-S):

1st the highest Shannon-Wiener index in sound sites from CF subjects represent that more rare genera were recovered in this condition and they had the higher diversity;

2nd the Simpson dominance and Simpson inverse index were higher in sound sites from CF subjects, indicating fewer common genera diversity for this condition compared to sound sites in CA subjects;

3rd Pielou-Shannon was higher in sound sites from CF subjects, indicating more equitative genus abundance in this microbiome.

5.2.3 Diversity analysis between caries active and caries-free subjects

The supragingival microbiome of subjects presenting caries activity (CA) was compared with that subjects that have never presented caries activity (caries-free subjects - CF). The figure 13 shows the observed genus richness for both subjects (CA vs CF). The statistical analysis by Mann-Whitney U test did not show statistical difference between observed richness among these sites compared between different subjects ($p=0.97$).

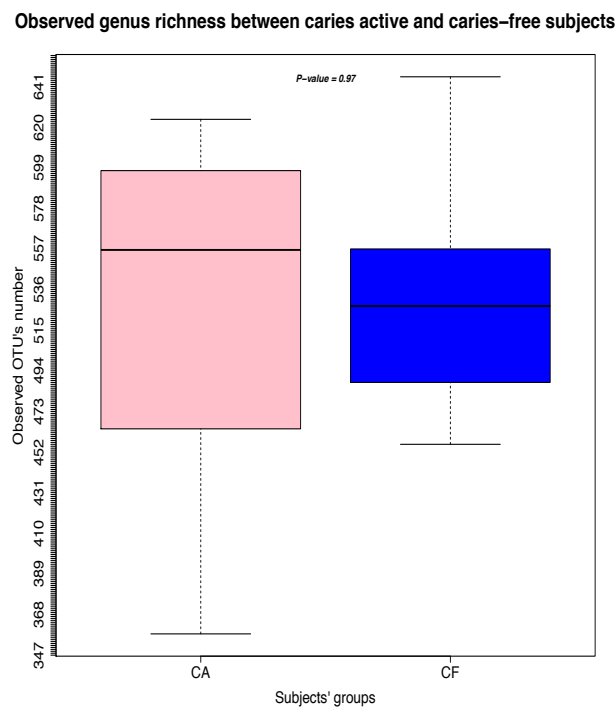


Figure 13. Total number of operational taxonomic units (OTUs) observed (richness) for genus taxonomic level in supragingival microbial communities between caries active subjects and caries-free subjects (CA vs CF). Mann-Whitney U test, 95% confidence level.

The alpha diversity estimators observed between CA *versus* CF subjects are presented in figure 14. The statistical analysis by Mann-Whitney U test did not show statistical difference among different subjects ($p>0.05$).

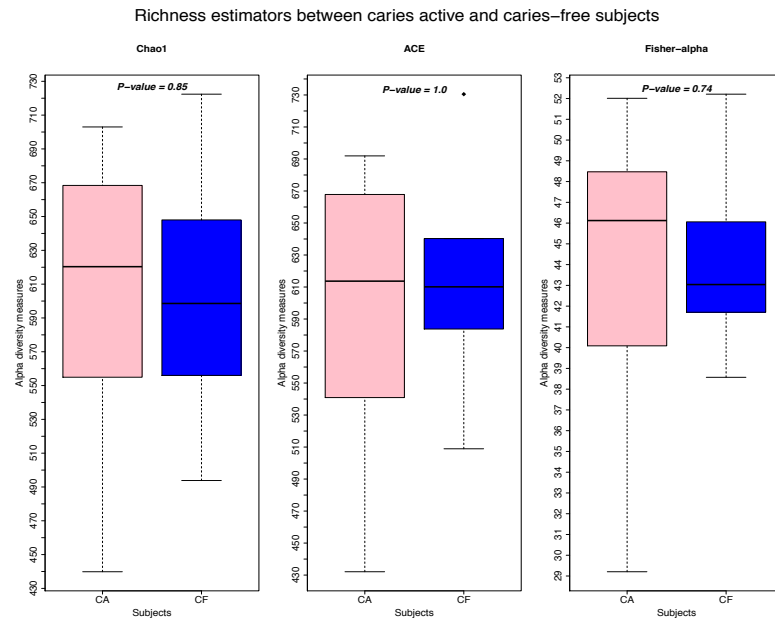


Figure 14. Richness estimators Chao 1, ACE (Abundance-based Coverage Estimator), and Fisher-alpha for genus taxonomic level in supragingival biofilm communities between caries active subjects and caries-free subjects (CA vs CF). Mann-Whitney U test, 95% confidence level.

The alpha diversity indexes observed between CA *versus* CF subjects are presented in figure 15. The alpha diversity between different subjects show statistical difference by Mann-Whitney U test.

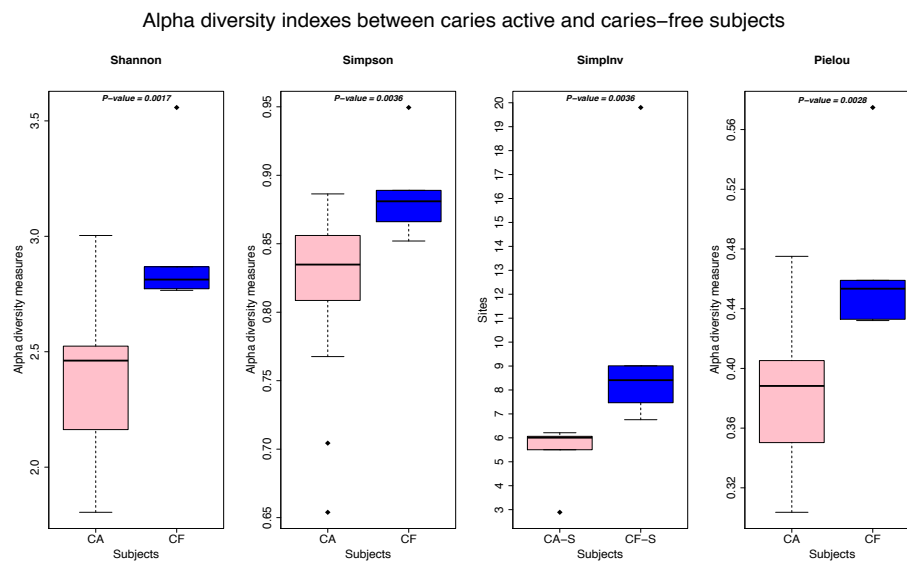


Figure 15. Alpha diversity indexes Shannon-Wiener, Simpson, Simpson Inverse, and Pielou-Shannon for genus taxonomic level in supragingival biofilm communities between caries active subjects and caries-free subjects (CA vs CF). Mann-Whitney U test, 95% confidence level.

Considering these comparisons, some inferences can be postulated for alpha diversity between caries active and caries-free subjects (CA vs CF):

1st the highest Shannon-Wiener index from CF subjects represent a higher diversity and more rare genera was recovered in this condition;

2nd the Simpson and Simpson inverse index were higher in CF subjects, indicating lower dominance from common genera compared to CA subjects;

3rd Pielou-Shannon was higher in CF subjects, indicating more equitative genus abundance in this microbiome.

5.4 BETA DIVERSITY ANALYSIS

Hierarchical clustering analysis was conducted to observe the dissimilarities (or similarities) between supragingival biofilm communities (beta diversity).

The figure 16 presents a dendrogram from supragingival biofilms communities from caries active (CA), caries inactive (CI) and caries-free (CF) subjects, obtained by UPGMA (Unweighted Pair Group Method with Arithmetic Mean) clustering method.

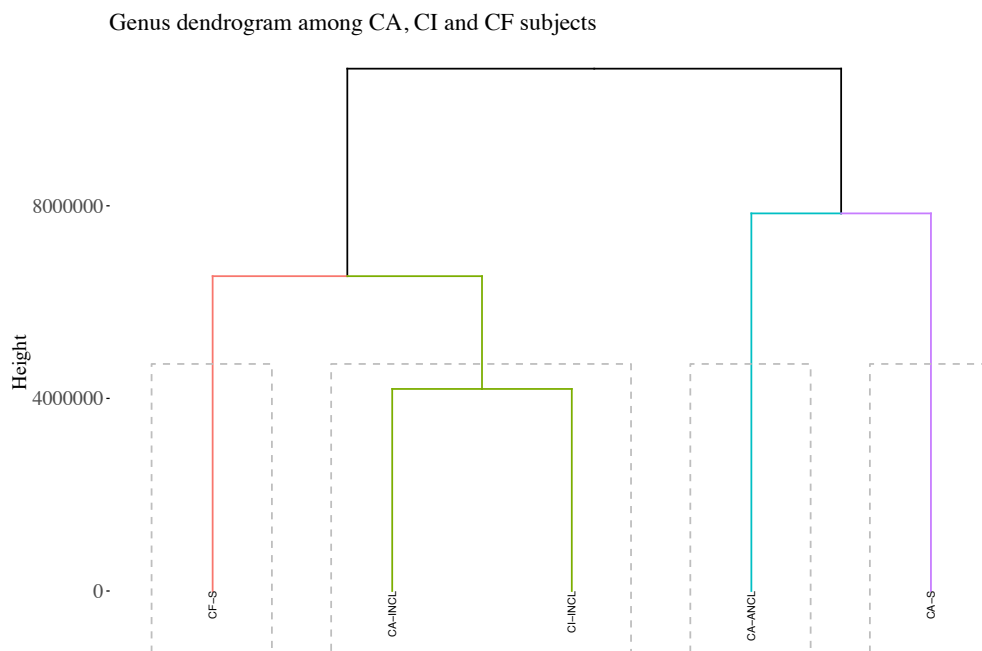


Figure 16. Hierarchical dendrogram representing the profiles of supragingival biofilms communities from caries active subjects in different dental sites (CA-ANCL: active non-cavitated lesion; CA-INCL: inactive non-cavitated lesion; CA-S: sound), caries inactive subjects (CI-INCL: inactive non-cavitated lesion), and caries-free subjects (CF-S: sound). UPGMA clustering method, with Euclidean distance. Cophenetic index = 0.8513354.

The genus with higher than 1% relative abundance were clustered using K-means cluster analysis. The K-means clusters between the same dental health conditions (sites) from different subjects are visualized in figures 17 (CA-INCL vs CI-INCL) and 18 (CA-S vs CF-S).

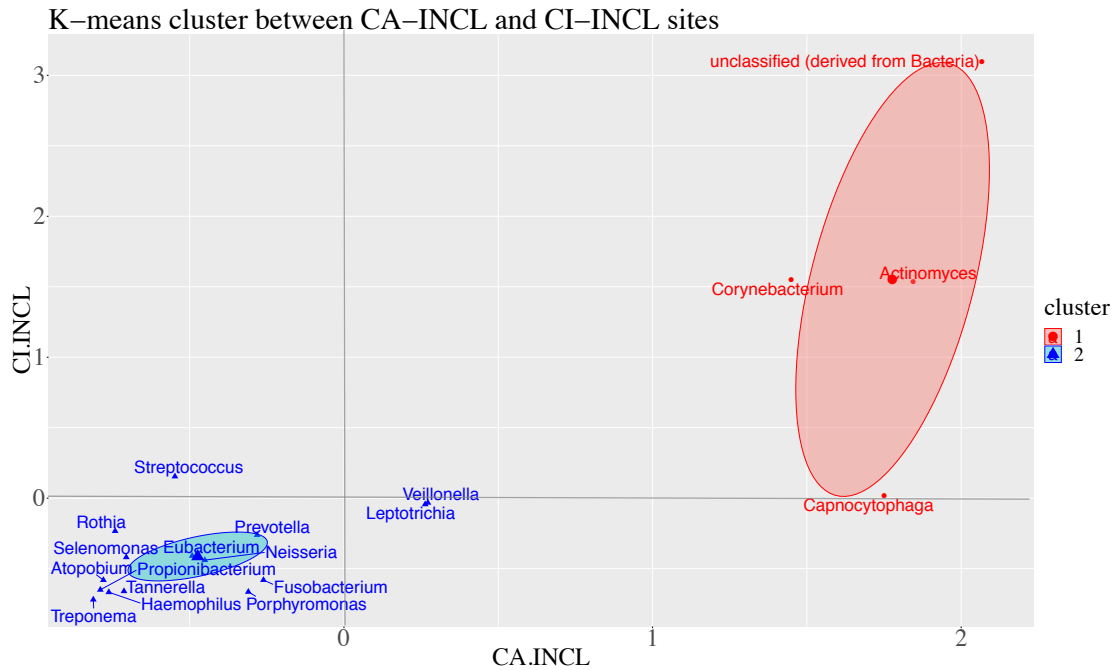


Figure 17. Hierarchical k-means cluster representing the profiles of genus with higher than 1% relative abundance in supragingival biofilms communities from inactive non-cavitated lesion in caries active subjects versus inactive non-cavitated lesion in caries inactive subjects (CA.INCL vs CI.INCL).

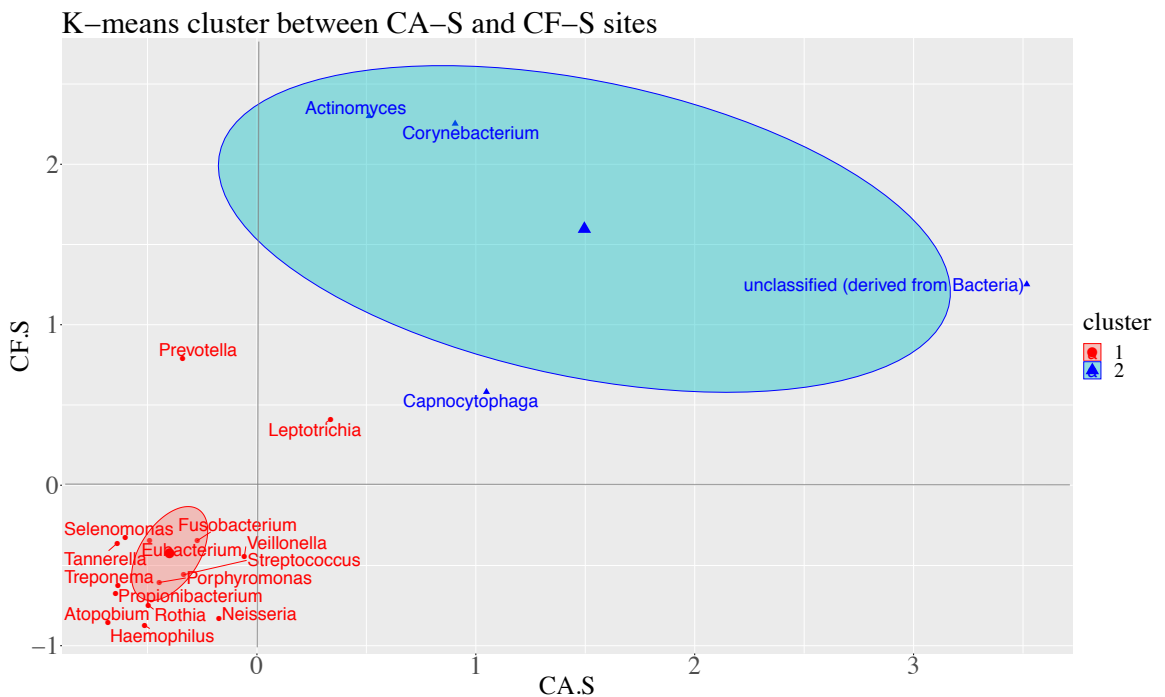


Figure 18. Hierarchical k-means cluster representing the profiles of genus with higher than 1% relative abundance in supragingival biofilms communities from sound dental surfaces in caries active subjects versus sound dental surfaces in caries-free subjects (CA.S vs CF.S).

The genus higher than 1% were clustering using K-means cluster analysis. The figure 19 and 20 shows the K-means clusters between the same dental health conditions from different subjects.

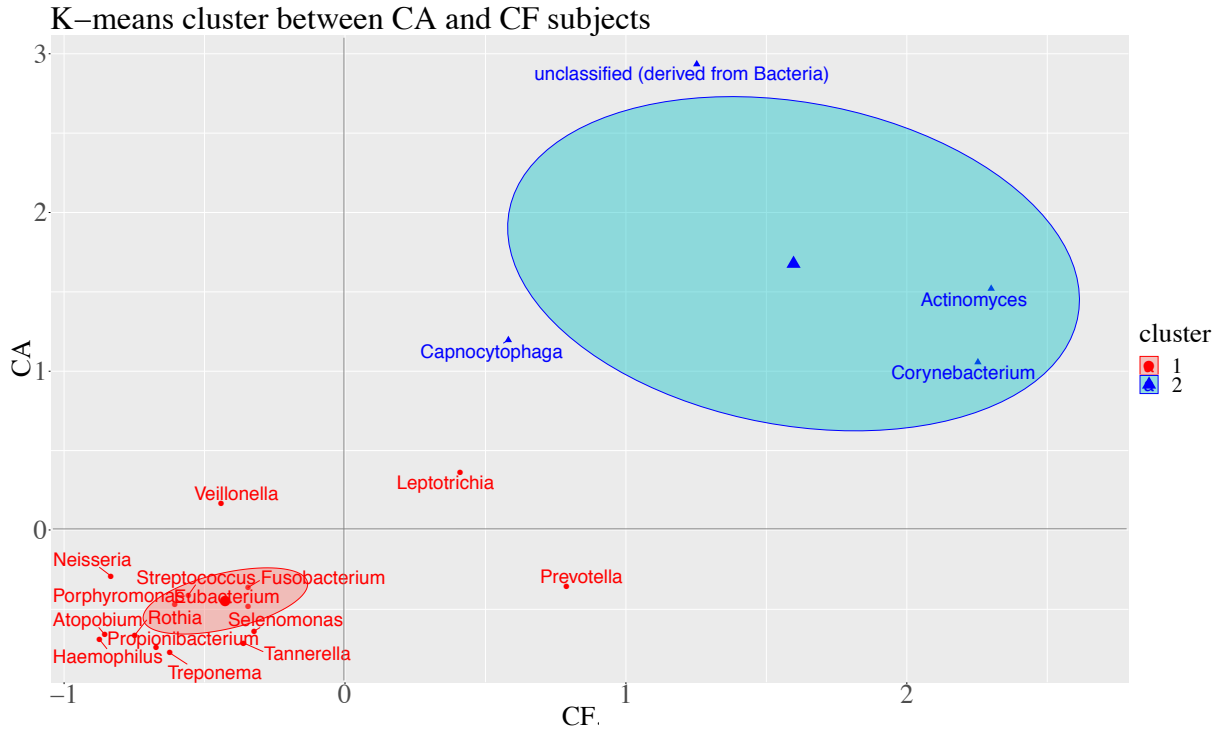


Figure 19. Hierarchical k-means cluster representing the profiles of genus with higher than 1% relative abundance in supragingival biofilms communities from caries active subjects *versus* caries-free subjects (CA vs CF).

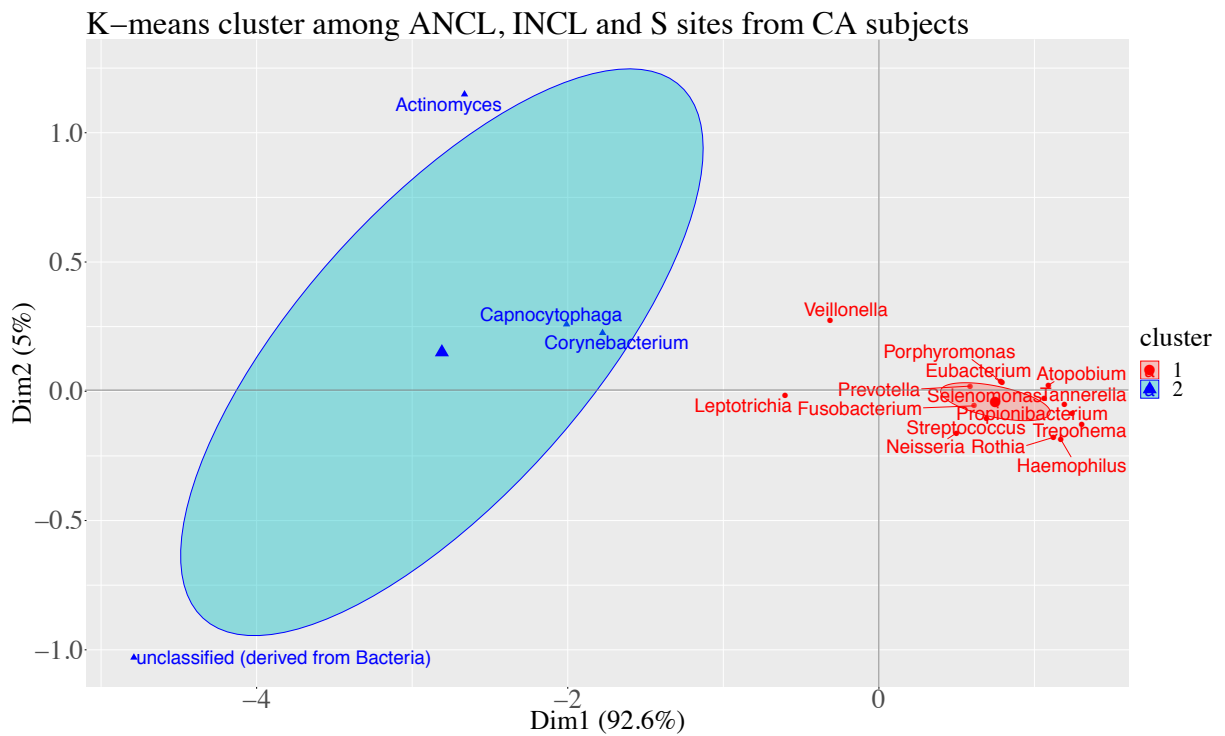


Figure 20. Hierarchical k-means cluster representing the profiles of genus with higher than 1% relative abundance in supragingival biofilms communities from caries active subjects in different dental health conditions ((ANCL: active non-cavitated lesion; INCL: inactive non-cavitated lesion; S: sound).

To gain insight into similarities in the bacterial community structures among the subjects included in this study, the Metric Multidimensional Scaling Ordination (MDS/ PCoA: Principal components analysis) was conducted using average of log2 fold change (avg(logFC)) (figure 21).

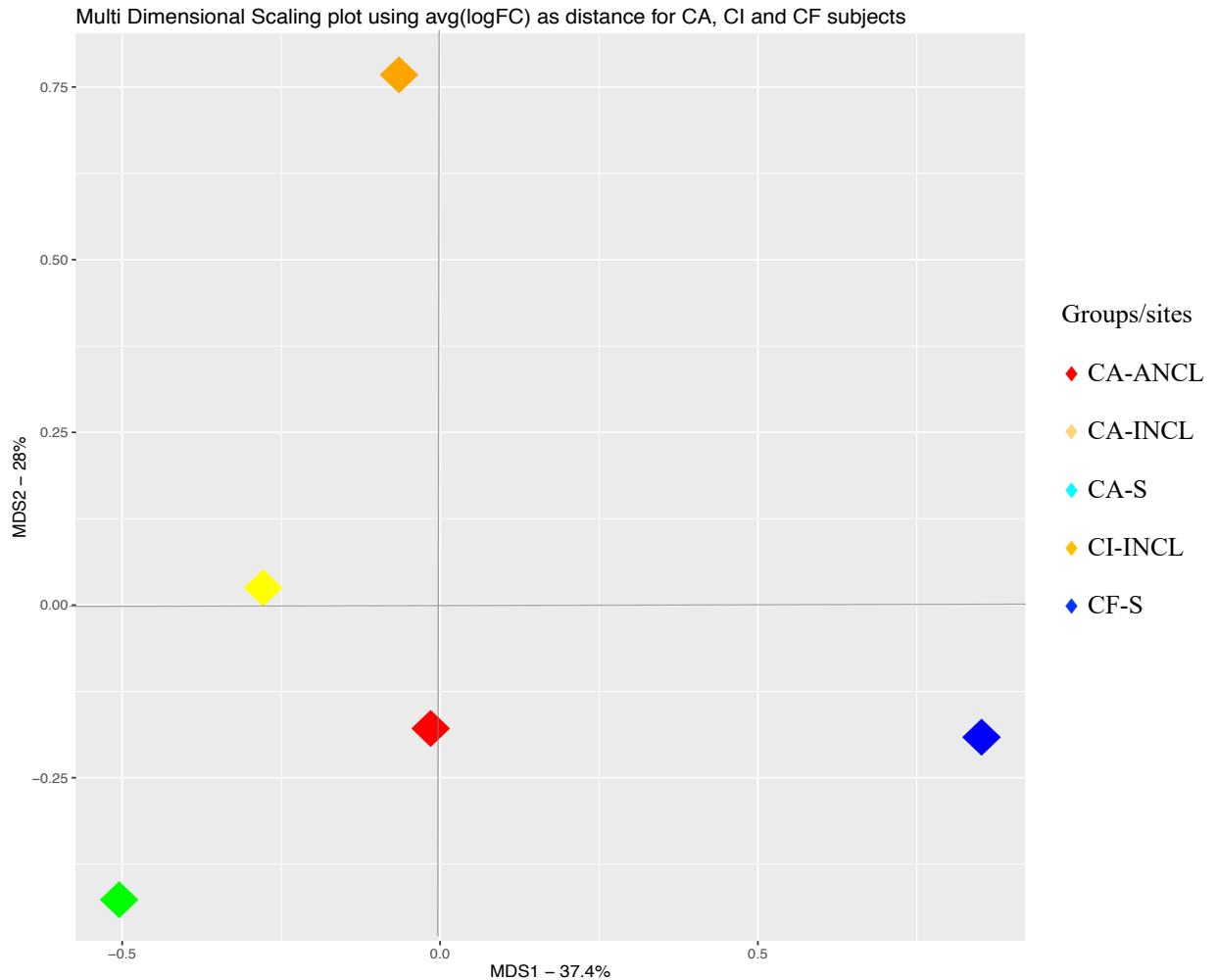


Figure 21. Metric Multidimensional Scaling Ordination (MDS/PCoA) among supragingival biofilms communities from all groups. Each sample is represented by a diamond. Red diamond represents the active non-cavitated lesions from caries active subjects (CA-ANCL). Yellow diamond represents the inactive non-cavitated lesions from caries active subjects (CA-INCL). Green diamond represents the sound surfaces from caries active subjects (CA-S). Orange diamond represents the inactive non-cavitated lesions from caries inactive subjects (CI-INCL). Blue diamond represents the sound surfaces from caries-free subjects (CF-S). MDS using average of log2 fold change (avg(logFC)).

The figure 21 reveals that MDS1 explain 37.4% of the variation observed, and MDS2 explain 28% of the variation. However, the samples did not form well-separated clusters corresponding to the five groups, suggesting that the bacterial structures in healthy and caries groups were similar.

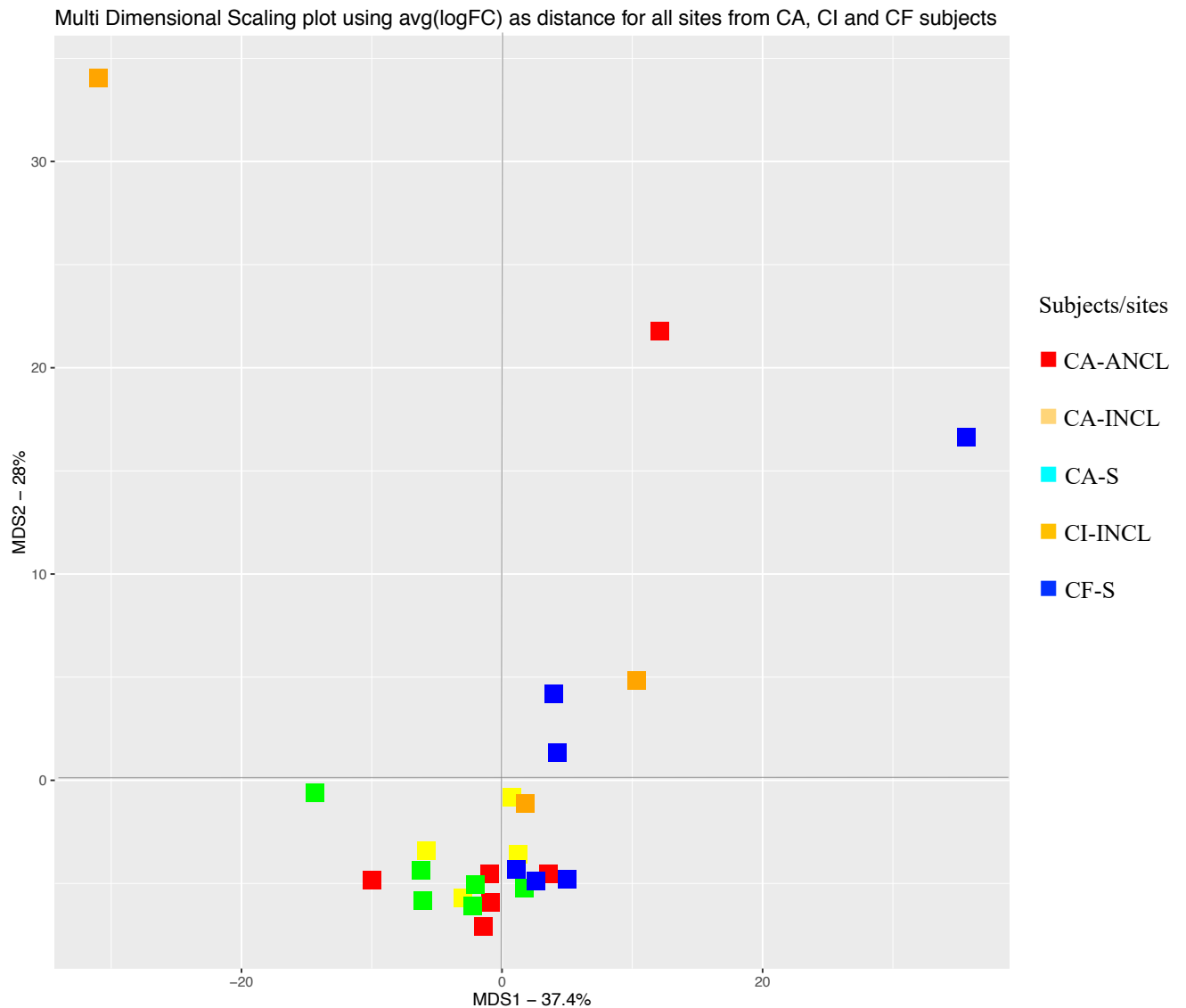


Figure 22. Metric Multidimensional Scaling Ordination (MDS/PCoA) among supragingival biofilms communities from all subjects and sites. Each sample is represented by a square. Red square represents the active non-cavitated lesions from caries active subjects (CA-ANCL). Yellow square represents the inactive non-cavitated lesions from caries active subjects (CA-INCL). Green square represents the sound surfaces from caries active subjects (CA-S). Orange square represents the inactive non-cavitated lesions from caries inactive subjects (CI-INCL). Blue square represents the sound surfaces from caries-free subjects (CF-S). MDS using average of log₂ fold change (avg(logFC)).

The figure 22 reveals that MDS1 explain 37.4% of the variation observed, and MDS2 explain 28% of the variation. However, the individual samples did not form well-separated clusters corresponding to the five groups and 25 sites, suggesting that the bacterial structures in all subjects were similar.

6 DISCUSSION

Investigation of whole microbial communities that actively engage the biofilm formation in dental health and disease is essential to understand the relationships between microbial communities in these conditions and for a better understanding of caries etiology (Mager et al., 2003; Jekinson; Lamont, 2005; Benítez-Páez et al., 2014; Henne et al., 2016; Nascimento et al., 2017). The present study revealed and compared the active bacterial composition profile and diversity from supragingival biofilm obtained from caries-free subjects, inactive non-cavitated lesions from caries inactive subjects, and active and inactive non-cavitated caries lesions, as well as sound dental surfaces from caries active subjects.

Dental biofilms comprise metabolically active, metabolically inactive and dead cells (Peterson et al., 2014). We performed RNA-Seq analysis of RNA isolated from supragingival biofilms, therefore our results show a taxonomic profile from the microbiome in alive and in metabolically active condition. Benítez-Páez et al. (2014), and Simón-Soro et al. (2014) showed that when DNA-based bacterial composition of a lesion was compared to RNA-based composition of the same individual lesion, a clear difference in pattern of bacterial genera was observed, with less recovered genera from RNA-based analysis. Yu and Zhang (2012) showed different profiles of microbial community using DNA and cDNA datasets in a study comparing metagenomic and metatranscriptomic analysis of microbial community structure of an activated sludge (AS) community from a municipal wastewater treatment plant in Hong Kong. The percentage of bacterial sequences in AS shifted from 92.2% (DNA) to 68.2% (cDNA), evidencing that metagenomic DNA comes from cells that are viable or not (higher proportion) not reflecting the actual metabolic activity (Sorek; Cossart, 2010; Kressirer et al., 2018). In 2017, Belstrøm et al. performed a metagenomic and metatranscriptomic characterization of the saliva from disease-associated microbiota in patients with periodontitis and dental caries. Metagenomic analysis showed significantly different beta diversity between groups, whereas metatranscriptomic did not. A relevant outcome from this study was the higher recovered *Streptococcus* from RNA- than DNA-based analysis, suggesting that *Streptococcus* was the most active genera in saliva microbiome.

The introduction of high-throughput pyrosequencing has provided new insights into the compositions and structures of microbial communities. We used Illumina HiSeq 3000 pyrosequencing to explore the microbial diversity and community structure of 25 supragingival biofilm samples by sequencing the 16S rRNA from seven subjects with dental caries, three

subjects with past caries experience, and six subjects that had never developed caries disease. The RNA-based approach from *in vivo* oral samples presents some methodologic limitations, including RNA instability and amounts of sampling material (Frias-Lopez; Duran-Pinedo, 2012; Benítez-Páez et al., 2014; Solbiati; Frias-Lopez et al., 2018). The sequencing of cDNA is an important stage for reduce these restrictions. Even, high-coverage sequencing technologies generate short read lengths, that could compromise accurate taxonomic assignment of the sequences (Benítez-Páez et al., 2014). We minimize potential errors in taxonomic assignment mapping the reads to rRNA genes at maximum for genus taxonomic level (Benítez-Páez et al., 2014). We used matches against 16S rRNA database of 97% sequence identity (Yarza et al., 2008; Zaura et al., 2009).

We obtained an average of 21,855,554 high-quality sequences from all groups, which was much higher than reported in previous studies (Benítez-Páez et al., 2014; Simon-Soro et al., 2014). The Good's coverage estimator of >97% suggested that our sequencing depth was sufficient to reflect the full microbial diversity of supragingival biofilm, indicating that some extremely low abundance of rare genera could be detected. The significance of the long tail distribution in the population structure is unclear but may represent a reservoir of species that may modulate their abundance over time, enhancing the complementarity of functions encoded within the dental biofilm community, with mutualistic relationships (Benítez-Páez et al., 2014). It is plausible that the maintenance of such reservoirs is evolutionarily favorable and contribute to the interpersonal variability of microbial communities (Mager et al., 2003; Belda-Ferre et al., 2012; Mark Welch et al., 2016). Our study agrees with this theory, once we observed low genera with high relative abundance in all groups (18 genera higher than 1% of relative abundance) and a big portion of the identified genera are present at very low abundance. The feature of the microbiota presents a functional redundancy inherent to related species that may explain the observed subject-to-subject variability in human microbiomes. The extent of the interpersonal variability in microbial composition of dental plaque within and across varied niches is largely uncharacterized but these factors are likely to directly contribute to the disparate results obtained by various association studies examining dental caries (Benítez-Páez et al., 2014; Simon-Soro et al., 2014; Mark Welch et al., 2016, Xiao et al., 2016).

The differences in abundance observed in the microbial communities may result from real differences among individuals, fluctuations within a single individual over time, or a combination of the two (Mark Welch et al., 2016). The discovery of “hedgehog” consortia from dental plaque, by Mark Welch et al. (2016), argues that the consistency of the composition and structure of the “hedgehog” across many individuals suggests that organisms are highly relevant to understand the roles, organization, and dynamics of the members of the consortium,

disagreeing with the concept that the lack of a consistently abundant microbial “core” has led to the idea that perhaps it is not organisms but genes and functions that are conserved within the microbiome, distributed across a variety of organisms whose identities are irrelevant. They suggest that an understanding of the ecology and physiology of the organisms in the bacterial consortium will provide an organizing principle to understand and interpret metagenomic and metatranscriptomic data. Shared genus from all subjects and sites was observed in the supragingival microbiome analyzed in our study. A “core microbiome” was formed for 123 common genera, representing 4493 OTU abundance. The existence of a “core microbiome” was first proposed by Turnbaugh et al. (2007) and referred to the organisms, genes, or functions shared by all or most individuals in a given human habitat, such as the oral cavity, nasal cavity, skin, and intestinal tract. Most studies conducted to date have found a core microbiome. Zaura et al. (2009) found within an individual oral cavity, over 3600 unique sequences, over 500 different OTUs or "species-level" phylotypes (sequences that clustered at 3% genetic difference) and 88 to 104 higher taxa (genus or more inclusive taxon). Xiao et al. (2016) described a core microbiome representing 72.6% of all OTUs recovered (7522 OTUs abundance). Johansson et al. (2015) observed a core microbiome with 24 species. The studies have been found shared organisms among all subjects, but it is not clear if these communities are contributing to health or disease. Considering the polymicrobial aspect of caries we can suggest that a shared community should be modulated during metabolic alterations in the host and in the local niche driving to healthy or diseased conditions, corroborating with the ecological plaque hypothesis proposed by Marsh (1991) and its extended concept proposed by Takahashi and Nyvad (2011).

Bacteria was the predominant domain from supragingival biofilm, also observed from majority of studies from dental plaque microbiome (Keijsers et al., 2008; Gross et al., 2010; Johansson et al., 2015; Xiao et al., 2016; Eriksson et al., 2017; 2018). Eukaryota represented the second more abundant domain recovered (figure S1), and Archaea domain was recovered from caries inactive and caries-free subjects in very low relative abundance, not allowing a conclusion about its correlation with caries. Moraes (2016) recovered Archaea from human root canal samples, constituting less than 1% of the total OTUs. Archaea are found in extreme environmental conditions that resemble the environment of the early appearance of life. They are able to develop under conditions of high or low temperatures, the total absence of oxygen, osmotic conditions and extreme pHs, and their cells have chemical, structural and specific metabolic pathways, not fully characterized (Tominaga, 2013). Actually, various archaeal species have been shown to inhabit distinct human body ecosystems such as the intestine, the oral cavity, the vagina, and skin (Dridi et al., 2011; Probst et al., 2013; Bang; Schmitz, 2015).

The majority of the, so far, detected archaea in humans, particularly from the gut and mouth, are methanoarchaea (Bang; Schmitz, 2015).

Corresponding with previous studies (Keijser et al., 2008; Peterson et al., 2011; Benítez-Páez et al., 2014; Xiao et al., 2016; Eriksson et al., 2017) our survey supports the view that supragingival ecological niche is a highly selective environment as we observe only four distinct phyla at an appreciable abundance (higher than 10%), despite the presence of 29 phyla with less relative abundance in these microbiomes. The Actinobacteria, Firmicutes, Bacteroidetes and Fusobacteria are the dominant phyla. Of all, Bacteroidetes show significant higher abundance in INCL from CA subjects, compared to INCL from CI subjects. All other phyla did not show statistical difference among the groups. He et al. (2017) showed abundance levels of Bacteroidetes and Spirochaetes significantly higher in carious patients than in healthy individuals. Bacteroidetes had been recovered among the four higher abundant phyla from dental plaque microbiome, but shows a variable abundance distribution, sometimes presenting the first or second higher abundance of total dental microbiome (Johansson et al., 2015; Xiao et al., 2016; Eriksson et al., 2017), sometimes presenting moderate or low abundance (Gross et al., 2010; He et al., 2017), suggesting a high adaptability of genera and species that make up this phylum.

Of all 915 recovered genera in this study, we observed only three genera presenting higher than 10% of relative abundance for all supragingival microbiome (Actinobacteria: *Actinomyces* and *Corynebacterium*; Bacteroidetes: *Capnocytophaga*). *Capnocytophaga* was present with statistically higher abundance in INCL from CA subjects compared to INCL from CI subjects. *Capnocytophaga* has been recovered more frequently in health conditions from DNA-based approaches (Aas et al., 2008; He et al., 2017). He et al. (2017) observed similar abundance of *Capnocytophaga* between CA and CF subjects, but with a tendency to higher abundance in health. Eriksson et al. (2018), however, demonstrate that members of the dental plaque can be related with disease in microbiome with extreme low or no detectable *S. mutans*, indicating *Fusobacterium*, *Actinomyces*, *Neisseria*, *Tannerella*, *Treponema*, *Peptostreptococcus*, *Dialister*, *Corynebacterium*, *Capnocytophaga*, *Selenomonas*, *Gracilibacteria*, *Leptotrichia*, *Porphyromonas*, *Bacteroidetes* and *Gemella* with a mutualistic relationship into the microbial community. Microbiomes with high abundance of *S. mutans* show less numbers of associated bacteria, founding sometimes *Actinomyces* sp HOT 448, *Scardovia wiggisiae*, *Stomatobaculum longum* and *Veillonella atipica* with low abundances in the same microbiome (Eriksson et al., 2018). In the oral biofilm the nutrients for bacteria are provided by saliva, gingival crevicular fluid, food containing sugars, food debris, and metabolic products from other bacteria (Hojo et al., 2009). When the excretion of a metabolite is used by

a different microorganism, a metabolic communication that drives to a positive or negative regulatory effect into the microbiome is generated (Hojo et al., 2009). *Capnocytophaga* requires CO₂ for growth. In the biofilms structure, it is abundant just inside the corncob shell suggesting that it is making use of a CO₂-rich environment generated by *Streptococcus* (Hojo et al., 2009; Mark Welch et al., 2016; Marsh; Zaura, 2017). The fact that biofilms are found in health and disease, the presence of commensal bacteria playing important role for the equilibrium of the microbiome is suggested. This fact can be an important explanation for high abundance of *Capnocytophaga* in both, diseased or healthy oral conditions.

Corynebacterium has been considered important for oral health (Benítez-Páez et al., 2014; Mark Welch et al., 2016; Xiao et al., 2016). *Corynebacterium*, *Actinomyces* and *Neisseria* were the most abundant genera in the RNA-based community from Benítez-Páez et al. (2014). Our RNA-based study recovered *Corynebacterium* with high abundance in health subjects. Only ANCL from CA subjects had less than 10% of relative abundance of *Corynebacterium*. Aas et al. (2008), found *Capnocytophaga* in healthy, and *Corynebacterium* in diseased ones. March Welch et al. (2016) suggests that *Corynebacterium* is the foundation taxon of the bacterial consortium in dental plaque, structuring the environment, and creating habitat for other organisms and nucleating a plaque-characteristic consortium. Nyvad and Fejerskov (1987) observed the structure of microbial community colonizing removable enamel chips worn inside the mouth. They showed scattered filamentous cells oriented perpendicularly to the primarily coccus-covered surface at 24 hours and a mixed community of abundant filamentous organisms by 48 hours, suggesting that colonization with *Corynebacterium* may take place around the 24-hour stage in plaque development. Our samples recovered high abundance of *Corynebacterium* from all sites, and can represent a microbial community well established, once the subjects were oriented to remain 12 hours without dental hygiene.

Actinomyces was significantly high represented in ANCL sites compared to INCL sites from CA subjects. Considering the total supragingival microbiome of CA subjects compared to CF subjects, *Actinomyces* presented higher abundance in the latter (CF). Benítez-Páez et al. (2014), found *Actinomyces* overrepresented in healthy conditions from DNA-based metagenome, and *Actinomyces*, *Corynebacterium* and *Neisseria* the most abundant genera in the RNA-based community from a 24 hours dental plaque in one dental healthy subject. Other studies using DNA-based sequencing analysis have found *Actinomyces* higher abundant in healthy sites (Eriksson et al., 2017). In another study of Eriksson et al. (2018), the microbiome analysis from extreme low or no detectable *S. mutans* showed *Actinomyces* related with disease. These results can indicate that these genera have an important capability for metabolic modulation, adapting in different host conditions. *Streptococcus* and *Actinomyces* are among

the early colonizers in dental biofilm formation (Keijser et al., 2008; Dige et al., 2009; Marsh; Zaura, 2017). Mark Welch et al. (2016) demonstrated that *Actinomyces* can be found near the base of hedgehog structures, and that *Corynebacterium* attaches in sites with preexistent biofilm consisting of *Streptococcus* and *Actinomyces*, and not directly on the tooth surfaces. This observation can be explaining a high abundance of *Actinomyces* in both diseased and healthy conditions. In root caries, the levels of *Actinomyces* gene expression were found similar either in health how in disease (RNA-based analysis), suggesting that it is a commensal bacterium in root surfaces sites, but showing survival mechanisms that allow them to survive in acidic environments (Dame-Teixeira et al., 2016).

Fifteen genera presented higher than 1% and less than 10% of relative abundance in supragingival biofilm microbiome in our study. *Leptotrichia*, *Veillonella*, *Streptococcus*, *Atopobium*, *Neisseria*, *Porphyromonas* and *Haemophilus* were more abundant in CA subjects. Johansson et al. (2015) showed *Porphyromonas*, *Streptococcus* and *Neisseria* increased in high-caries Romanian adolescents. We recovered *Prevotella*, *Tannerella*, *Propionibacterium* and *Treponema* with an increased amount of relative abundance in CF subjects. *Eubacterium*, *Selenomonas*, *Rothia* and *Fusobacterium* were related with health subjects, as well. *Leptotrichia*, *Rothia* and *Streptococcus* (*S. sanguinis* and *S. mitis*) were related with disease in RNA-based study from Simón-Soro et al. (2014). We observed the genera *Streptococcus* with increased abundance in CA subjects, but *Rothia* was recovered with similar amount from CA and CF subjects, with slight tendency for higher abundance in healthy sites. *Atopobium* had higher than 2% of relative abundance only in ANCL from CA subjects, with less than 1% of relative abundance for the other groups. Xiao et al. (2016), described *Atopobium* how a possible biomarker for dental disease, besides *Tenericutes*, *Desulfomicrobium*, *Veillonellaceae_G_1*, *Mycoplasma* and *Clostridiales_F_1_G_1*. In other study, He et al. (2017) suggested *Atopobium*, *Selenomonas* and *Treponema* with high occurrence in disease conditions. Simón-Soro et al. (2014) found *Atopobium*, *Tannerella* and *Treponema* exclusive in dentin lesions. In our study *Tannerella* was not related to disease. Xiao et al. (2016), described *Tannerella* as a possible biomarker for oral health, along with *Fusobacterium*, *Aggregatibacter*, *Corynebacterium*, *Cardiobacterium*, *Lachnoanaerobaculum* and others. However, *Selenomonas* was present in ANCL sites with >1% abundance and could be implicated in caries disease, agreeing with Xiao et al., 2016. Tanner (2016) demonstrated that some species were suppressed by the acidic agar included *Streptococcus sanguinis*, *Actinomyces*, *Selenomonas*, *Campylobacter*, *Prevotella*, *Fusobacterium* and *Campylobacter* species. This would suggest that these species would not fit into species of the advanced aciduric phase of dental caries. In contrast *S. mutans*, *Streptococcus anginosus*, *Streptococcus salivarius*, *Lactobacillus gasseri*,

Scardovia wiggisiae, *Parascardovia denticolens* and *Bifidobacterium dentium* were detected more frequently from the acid agar and could be candidates for the advanced aciduric stage of caries progression.

Comparations between INCL from CA and CI subjects (CA-INCL vs CI-INCL) presented similar alpha diversity. However, composition was different in these two microbiomes. In spotlight, we observed that *Fusobacterium* and *Porphyromonas* were recovered in much smaller amounts (0.6%, and 0.4%, respectively) in INCL from CI subjects, presenting higher than 3% of relative abundance for the INCL from CA subjects. Eriksson et al. (2017), had found higher *Actinomyces* in health sites, also recovered more abundant *Fusobacterium* and *Porphyromonas* in these health conditions. We found *Fusobacterium* and *Porphyromonas* related with health. *Porphyromonas*, *Fusobacterium*, *Tannerella* and *Leptotrichia* are considered late colonizers from dental biofilm and were found in significative more abundance in dental plaque from caries subjects compared to health in the study of Benítez-Páez et al. (2014). *Fusobacterium* has been implicated with healthy in other studies (Aas et al., 2008, Johansson et al., 2015). The role of *Fusobacterium* as a central bacterium in the biofilm development physically linking early and late colonizers (Kolenbrander; London, 1993; Lancy et al., 1983) was questioned by Mark Welch et al. (2016). In the structural analysis of dental biofilms, *Corynebacterium* was the most abundant taxon and showed a physical link among the colonizers into the biofilm structure and not *Fusobacterium*. The authors discuss that *Fusobacterium* may contribute to consortium organizations, being one of four filamentous taxa in hedgehogs, but it is not the most abundant neither the most spatially extensive organism in the biofilm structure. We found *Corynebacterium* higher than 10% of relative abundance for all sites, except in CA-ANCL, where the abundance was 8.9%. *Fusobacterium* was higher than 1% of relative abundance but reached a maximum of 3.35% in CA-INCLsites. Our results from active microbiome in supragingival biofilms corroborate with the higher importance of *Corynebacterium* in biofilm structure and function.

Comparations between sound sites from CA and CF subjects (CA-S vs CF-S) revealed markedly differences from diversity. The sound sites from CA subjects presented significative less diversity, higher dominance and were less equitable than sound surfaces from CF subjects. Higher diversity has been described for health sites for several ecologic studies (Gross et al., 2010; Benitez-Paez et al., 2014; Simón-Soro et al., 2014; Xiao et al., 2016). According Xiao et al. (2016), more diverse bacterial community represents a healthier and more stable ecosystem in supragingival biofilms. The carbohydrate-driven lowering of the pH from lactate produced by acid-producing species could lead to suppression of acid-sensitive species and overgrowth of acid-tolerant species, resulting in decreased bacterial diversity in

supragingival plaques as caries progresses, as well as a decreasing number of species capable of surviving harsh conditions (Gross et al., 2010).

These observations were confirmed when caries active subjects were compared to caries-free subjects (CA vs CF). Supragingival microbiome, from CA subjects, presented significant less diversity, higher dominance and were less equitable than sound surfaces from CF subjects. The bacterial diversity between caries active and caries-free subjects presented statistical differences, suggesting interpersonal variability. *Prevotella* was higher represented in CF subjects and *Veillonella* in CA subjects. Eriksson et al. (2017) found similar *Veillonella* distributions in caries active and caries-free individual, with a tendency for higher abundance in health conditions. Aas et al. (2008) revealed *Veillonella* and *Selenomonas* in all dental conditions (health and disease). Simón-Soro et al. (2014) found *Veillonella* in CA enamel lesion. Our study shows a tendency for higher abundance of *Capnocytophaga*, *Veillonella* and *Neisseria* in CA subjects, and for *Corynebacterium*, *Prevotella*, *Tannerella*, *Propionibacterium* and *Treponema* in CF subjects. *Veillonella* uses lactate as an essential carbon and energy source (Takahashi, 2015; Marsh; Zaura, 2017). Gross et al. (2012) found higher proportions of *Veillonella* spp. in samples from caries lesions compared to healthy enamel. The explain are due the increased glycolytic activity and higher levels of lactate in caries sites. Mixed cultures have been demonstrated de symbiotic relationship between *S. mutans* and *Veillonella* (Liu et al., 2011). Liu et al., (2011) demonstrate that *V. parvula* inhibits sugar metabolism of *S. gordonii* (antagonistic with *S. mutans*) favoring *S. mutans* growth.

We found that the supragingival microbiome shows similar intrapersonal diversity, but different consortia of genera recovered from different dental health conditions. The diversity analysis did not find statistical differences in bacterial diversity among different sites from caries active subjects (ANCL vs INCL vs S), showing that the supragingival microbiome present similar structure from each subject. However, the composition and abundance were not the same. Specifically, we found that *Actinomyces* was highly represented in ANCL sites, compared to INCL sites; contrarily, *Capnocytophaga* presented lower abundance in ANCL sites compared with INCL, from caries active subjects. Benítez-Páez et al. (2014), found *Actinomyces* overrepresented in health conditions from DNA-based and RNA-based metagenome analysis from a 24 hours dental plaque in one dental health subject. Other studies DNA-based sequencing has found *Actinomyces* higher abundant in health sites (Eriksson et al., 2017), discording with our results. However, how discussed above, *Actinomyces* is an important early colonizer for tooth and, besides *Streptococcus*, has a relevant implication in the *Corynebacterium* fixation during bacterial succession.

We performed the hierarchical cluster analysis from all supragingival microbiome using Euclidean distance and UPGMA clustering method for beta diversity comparisons among all groups. Two principal clusters were formed from supragingival microbiome, one showing INCL sites from CA and CI subjects the closest microbial community and related to CF subjects. The ANCL and S sites from CA subjects clustered together and were farther from another cluster. This analysis presented a high cophenetic index (0.8513354) indicating a good quality of the built dendrogram, being the similarity obtained representative of all supragingival communities. Comparing specific dental conditions between subjects, we conducted a K-means hierarchical cluster analysis using genera with higher than 1% of relative abundance. For CA-INCL vs CI-INCL two clusters were clearly formed, one by *Actinomyces*, *Corynebacterium* and *Capnocytophaga*. Mark Welch et al. (2016) observed *Corynebacterium* an essential genus in the plaque structure with strong plaque specificity in healthy subjects; in addition, they included *Capnocytophaga*, which was 10-fold more abundant in plaque than at nonplaque sites, as well as *Lautropia* and *Rothia*. The authors described *Actinomyces*, *Porphyromonas*, and *Veillonella* as equally abundant. Our results found the closest approximation between *Corynebacterium* and *Actinomyces* in this cluster. Both genera were positively related with INCL sites from caries active and caries inactive subjects. *Capnocytophaga* was farther than both and did not show a clear position between the same conditions from different subjects. The other 15 genera clustered together. *Veillonella* and *Leptotrichia* was farther from the center of the cluster, and positively related with INCL from CA subjects; *Streptococcus* was far too, but positively related with INCL from CI subjects. In the Mark Welch et al. (2016) analysis, *Streptococcus* was substantially more abundant at nonplaque sites than in plaque on average. This wide-ranging habitat preference likely reflects the capacity of *Streptococcus* to be an efficient colonizer of multiple oral surfaces. Additional genera with broad habitat range in the mouth included *Haemophilus* and *Veillonella*. Comparing sound surfaces from CA and CF subjects (CA-S vs CF-S) by K-means hierarchical cluster analysis, *Prevotella* loses its proximity to the cluster center, and moves positively in relation to the caries-free subject. This tendency is maintained when analyzing the subject's caries active versus subject's caries-free (CA vs CF). In this condition, *Veillonella* also moves away from the center of the cluster, but in direction to the disease condition (CA subjects). In both comparisons, *Corynebacterium* and *Actinomyces* show closer approximation than with *Capnocytophaga* although belonging to the same cluster. The important structure referred like a "hedgehog" was described by Mark Welch et al. (2016) to describe a complex microbial consortium detected in plaque. They observed the presence of a mass of *Corynebacterium* filaments with *Streptococcus* at the periphery, with radially oriented filaments. More nine taxa were observed as regular participants in that structure:

Corynebacterium, *Streptococcus*, *Porphyromonas*, *Haemophilus/Aggregatibacter*, *Neisseriaceae*, *Fusobacterium*, *Leptotrichia*, *Capnocytophaga*, and *Actinomyces*. Other genera were detected rarely or inconsistently in the hedgehog structures. We found the same genera with higher abundance in our supragingival microbiome analysis, proving that our analysis obtained a good picture of the active microbiome of the supragingival biofilm.

The metric multidimensional scaling ordination (mMDS) is similar to PCoA analysis. In the present study, although there is a tendency for CA sites clustered together and distant from CI and CF subjects, there are not a clearly dissimilarity among them. The mMDS could explain only 37,4% of distance between groups, by the “x” axis, and only 28% by the “y”-axis. This result demonstrated that the community’s structures are very similar. However, it is important to analyze the composition of genera into different microbiomes.

Our study is the first to reveal a metabolically active bacterial microbiome from whole supragingival biofilm from different dental healthy and diseased conditions. We could demonstrate the bacterial composition profile and diversity from microbiome in active non-cavitated lesions, inactive non-cavitated lesions and sound surfaces in caries active subjects, as well as inactive non-cavitated lesions in caries active subjects, and sound dental biofilm from caries-free subjects. Our study confirms the affirmation from Simón-Soro et al. (2014) that the existence of a high level of diversity in the active fraction of the bacterial community (RNA-based approach) is related with the high number of organisms detected in supragingival biofilm and not due to dead or inactive species, highlighting that dental caries is a polymicrobial disease, where multispecies microbial consortia are metabolically active in the lesions. The present study shows that the supragingival microbial communities profile presents an intrapersonal similarity. The interpersonal diversity and microbial composition profile were different and revealed that the healthy/diseased status matters more than sites. Furthermore, the core microbiome of caries inactive patients, despite being in a health condition, are not similar to caries free patients. We suggest that alterations from supragingival microbial communities should be analyzed from a longitudinal way in caries diseased subjects for a better comprehensive understanding of this ecological process.

7 CONCLUSIONS

This study revealed that bacterial composition at genus level in the supragingival biofilm microbiome from active and inactive caries and caries-free subjects has a high richness of genera, showing a genus diversity decreasing in caries active subjects in relation to caries-free subjects. The different dental conditions from caries active subjects (ANCL, INCL, S) are similar in diversity. Caries inactive subjects did not differ from bacterial diversity comparing to the same dental condition in caries-active subjects, although *Capnocytophaga* genera was higher represented in caries-active than caries-inactive subjects. The biofilm microbiome from sound surfaces was less diverse in caries subjects compared to health subjects, suggesting a more restrictive environment conditions in disease.

The present study shows that the supragingival microbial communities profile presents an intrapersonal similarity. The interpersonal diversity and microbial composition profile were different and revealed that the healthy/diseased status matters more than sites.

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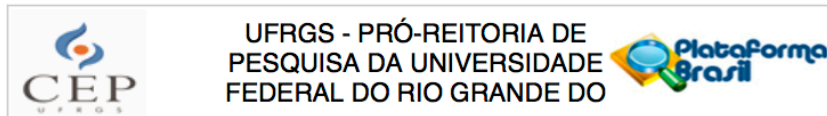
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ANNEXES

Annex 1 Ethics Committee Report



PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: ALTERAÇÕES NO BIOFILME EM DECORRÊNCIA DA INATIVAÇÃO DE LESÕES DE CÁRIE

Pesquisador: Clarissa Cavalcanti Fatturi Parolo

Área Temática:

Versão: 5

CAAE: 56583316.8.0000.5347

Instituição Proponente: Faculdade de Odontologia

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 2.094.686

Apresentação do Projeto:

Trata-se de um projeto de pesquisa da Faculdade de Odontologia da UFRGS.

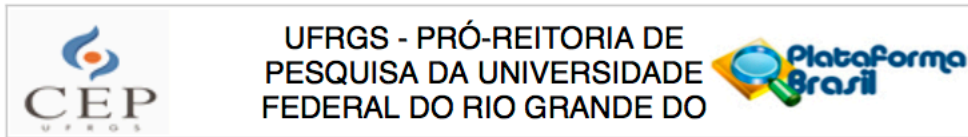
Objetivo da Pesquisa:

Objetivo Primário: Avaliar as alterações metabólicas que ocorrem no biofilme em função da inativação das lesões de cárie.

Objetivo secundário:

1. Avaliar as espécies bacterianas metabolicamente ativas no biofilme dental em resposta ao processo de inativação de lesões de cárie não cavidadas em esmalte;
2. Avaliar a expressão gênica do biofilme dental em resposta ao processo de inativação de lesões de cárie não-cavidadas em esmalte;
3. Avaliar a expressão diferencial do biofilme nas condições de saúde (biofilme coletado de superfície hígida), lesão ativa e inativa;
4. Identificar as rotas metabólicas mais ativas nas espécies bacterianas mais relevantes,

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determinadas pelo

objetivo específico 1, nas diferentes condições do biofilme (cárie-ativo, cárie, inativo, hígido);

5. Identificar genes de virulência que possam ser usados como alvo para reconhecimento de atividade metabólica relacionada a lesões de cárie em esmalte.

Avaliação dos Riscos e Benefícios:

No que diz respeito a riscos e benefícios, os pesquisadores esclareceram que não serão necessárias consultas adicionais para as coletas relacionadas a esta pesquisa. Todos os procedimentos relacionados a este estudo serão realizados durante o atendimento normal dos pacientes nas Clínicas da Faculdade de Odontologia da UFRGS. Desde o recrutamento e esclarecimentos sobre a pesquisa até as coletas de biofilme, serão realizadas nos mesmos dias e horários de atendimento normal destes pacientes. Mesmo aqueles pacientes que se enquadram no grupo onde haverá coleta após a inativação das lesões de cárie não haverá necessidade de deslocamento extra até a faculdade, uma vez que as consultas finais de manutenção fazem parte do tratamento da doença cárie.

No parecer anterior do CEP, foi questionado se a solicitação de um participante

que já apresenta atividade de cárie, permanecer 24 horas sem realizar higienização bucal não poderia agravar a doença. Em resposta a esta solicitação, os autores afirmaram que a doença cárie é resultado de um desequilíbrio homeostático complexo na microbiota que envolve diferentes fatores, como a dieta, a higiene, o acesso ao flúor, o fluxo salivar, a capacidade da saliva de neutralizar os ácidos bucais e outros fatores. Além disso, enfatizaram que mesmo que o acúmulo de biofilme seja um fator determinante para o surgimento e manutenção da doença cárie, é importante ressaltar que alterações subclínicas em superfície de esmalte somente são observadas após duas semanas de acúmulo de biofilme e que as alterações clinicamente detectáveis (e ainda reversíveis) são detectadas após quatro semanas de acúmulo de biofilme. Apesar disso, modificaram o período de 24h para 12h conforme alterações assinaladas na nova versão do projeto.

Por fim, os autores afirmaram que o direito ao atendimento será assegurado a todos os pacientes, independentemente de sua participação na pesquisa, seguindo os princípios éticos, o que não estava claro na análise anterior do projeto pelo CEP e que agora foi devidamente explicada no TCLE.

Os pesquisadores informaram que não será feita análise do DNA humano e reclassificaram o projeto, passando de projeto da Área Temática Especial de Genética Humana para projeto sem

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temática especial, atendendo à solicitação do CEP (PENDÊNCIA ATENDIDA).

Comentários e Considerações sobre a Pesquisa:

Estudo clínico observacional com coleta de biofilme (placa dentária) de voluntários com e sem atividade de cárie, seguido de análise do RNA mensageiro de bactérias presentes nestes biofilmes. O biofilme dentário será coletado antes e após o tratamento para inativação de lesões não cavitadas ativas.

Para a coleta de biofilme inicial (amostra cárie-ativa), os pacientes serão orientados a não realizar higiene bucal 12 horas e não ingerir alimentos 2 horas antes da consulta, de modo a permitir o acúmulo de biofilme. Biofilme de uma superfície contralateral hígida do mesmo paciente será coletado (amostra biofilme hígido).

O mesmo procedimento será realizado para a coleta final de biofilme (amostra cárie-inativa), que será realizada após a inativação das lesões cariosas dos indivíduos (aproximadamente 3 meses de tratamento), sendo que para a inativação das lesões será realizada controle da atividade cariogênica. Também será coletado biofilme de 12 voluntários cárie inativos. Para controle interno, uma superfície hígida do mesmo paciente de ambos os grupos será avaliada. Os biofilmes serão armazenados para análise laboratorial (sequenciamento de RNA bacteriano). Serão selecionados 12 indivíduos com lesões não cavitadas ativas (LNCA), nas clínicas da Faculdade de Odontologia da Universidade Federal do Rio Grande do Sul. O biofilme dentário será coletado antes e após o tratamento para inativação dessas lesões. Para a coleta de biofilme inicial (amostra cárie ativa), os pacientes serão orientados a não realizar higiene bucal 12 horas e não ingerir alimentos 2 horas antes da consulta, de modo a permitir o acúmulo de biofilme. Biofilme de uma superfície contralateral hígida do mesmo paciente será coletado (amostra biofilme hígido). O mesmo procedimento será realizado para a coleta final de biofilme (amostra cárie-inativa), que será realizada após a inativação das lesões cariosas dos indivíduos (aproximadamente 3 meses de tratamento), sendo que para a inativação das lesões será realizada controle da atividade cariogênica. Para controle interno, uma superfície hígida do mesmo paciente de ambos os grupos será avaliada. O mRNA das amostras de biofilme será isolado e utilizado para preparo das bibliotecas genômicas de cDNA, que serão sequenciadas na máquina de alto rendimento Illumina HiSeq2500, disponível na Universidade de Leeds. As sequências geradas serão mapeadas contra genomas de mais de 100 espécies bacterianas relacionadas com a cavidade oral. Será avaliado e comparado o metatranscriptoma do biofilme bacteriano nas três condições (cárie-

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ativo, cárie inativo, hígido), buscando a atividade gênica que esteja relacionada com o processo de inativação de lesões cariosas. Os níveis de expressão gênica serão calculados. Para análise de dados, o pacote estatístico DESeq2 será utilizado para calcular a expressão diferencial entre as diferentes condições.

Considerações sobre os Termos de apresentação obrigatória:

O termo de assentimento foi incluído e redigido de maneira apropriada.

Conclusões ou Pendências e Lista de Inadequações:

O parecer é favorável a aprovação do projeto.

Considerações Finais a critério do CEP:

Aprovado.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_712016.pdf	17/05/2017 12:01:49		Aceito
Outros	Termodocolaboracao.pdf	17/05/2017 12:01:24	DANIELA JORGE CORRALO	Aceito
Outros	Termodeanuencia.pdf	17/05/2017 12:01:02	DANIELA JORGE CORRALO	Aceito
Outros	CartarespostaCLARISSA.doc	17/05/2017 11:59:11	DANIELA JORGE CORRALO	Aceito
Projeto Detalhado / Brochura Investigador	Projetoatualizado.doc	17/05/2017 11:56:05	DANIELA JORGE CORRALO	Aceito
Folha de Rosto	FolharostoAssinada.pdf	17/05/2017 11:51:30	DANIELA JORGE CORRALO	Aceito
Declaração de Pesquisadores	Justificativadoc.pdf	08/02/2017 17:08:06	Láís Daniela Ev	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TERMOASSENTIMENTO_projetobiofilme.pdf	08/02/2017 11:35:29	DANIELA JORGE CORRALO	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TERMOCONSENTIMENTO_projetobiofilme.pdf	08/02/2017 11:35:00	DANIELA JORGE CORRALO	Aceito

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Outros	CARTACEPSET2016.pdf	20/09/2016 16:56:57	NAILE DAME TEIXEIRA	Aceito
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Declaração de Instituição e Infraestrutura	ANUENCIALEEDS.pdf	06/05/2016 17:30:34	NAILE DAME TEIXEIRA	Aceito
Declaração de Instituição e Infraestrutura	ANUENCIALABIM.pdf	06/05/2016 17:30:24	NAILE DAME TEIXEIRA	Aceito

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

PORTO ALEGRE, 01 de Junho de 2017

Assinado por:
MARIA DA GRAÇA CORSO DA MOTTA
(Coordenador)

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APPENDIX

Appendix 1 Figure S1: Phylum relative abundance

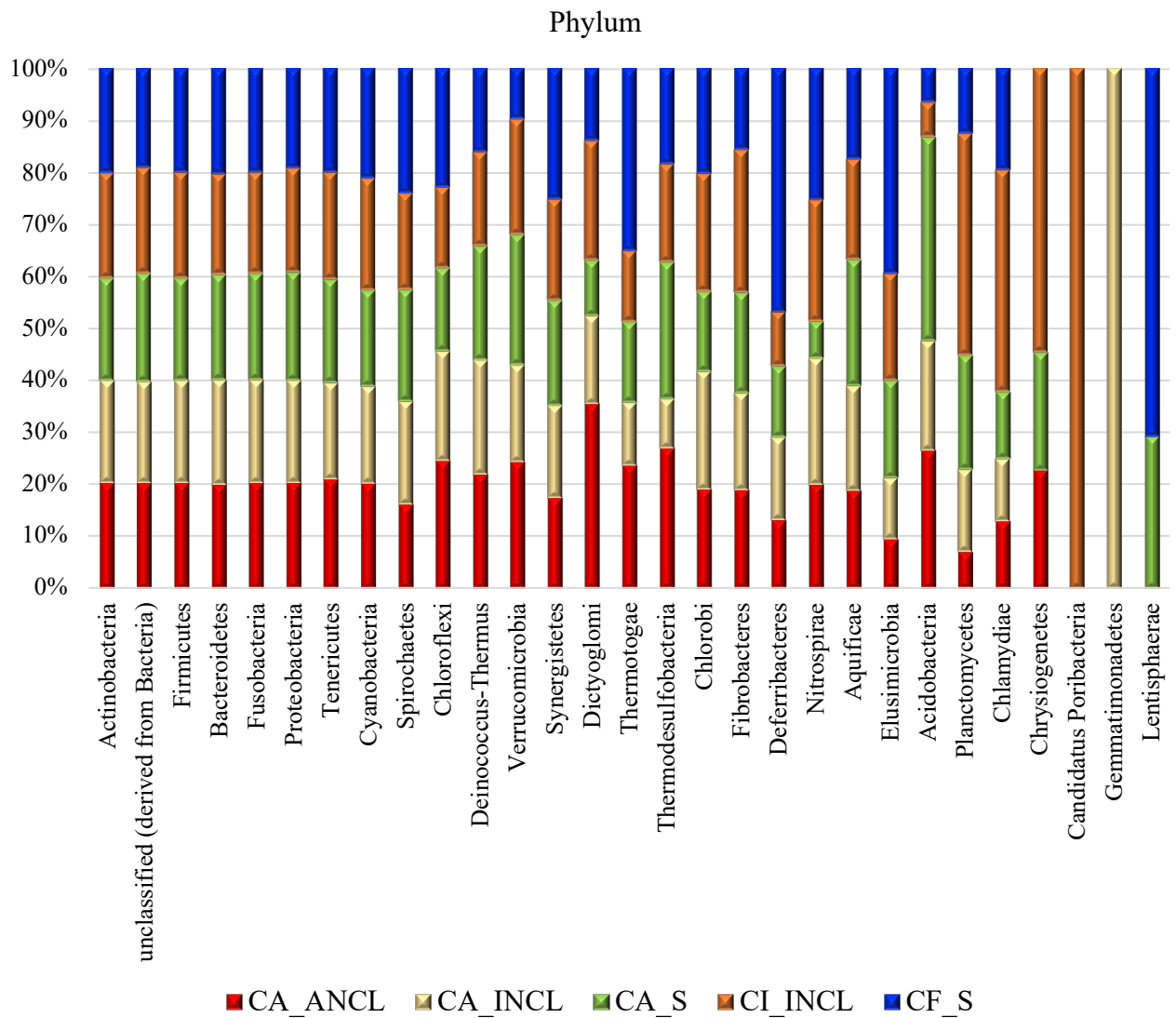


Figure S1. Relative abundance of operational taxonomic units (OTUs) from the 29 recovered Phylum from supragingival biofilm microbiome, in Bacteria domain. CA: caries active subjects: ANCL: active non-cavitated lesion; INCL: inactive non-cavitated lesion; S: sound; CI: caries inactive subjects: INCL: inactive non-cavitated lesion; CF: caries-free subjects: S: sound.

Appendix 2 Table S1: Total genera recovered from all subjects' sites and groups.

Table S1. Relative abundance of all genera observed in supragingival biofilms communities from all sites and groups of subjects included in the study (CA-ANCL: active non-cavitated lesions from caries active subject; CA-INCL: inactive non-cavitated lesions from caries active subjects; CA-S: sound surfaces from caries active subjects; CI-INCL: inactive non-cavitated lesions from caries inactive subjects; CF-S: caries-free subjects).

GENUS	SUBJECTS' SITES																								SUBJECTS' GROUPS					
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF
unclassified (derived from Bacteria)	28,6756	15,7646	29,5371	2,4547	50,9265	3,4642	20,4643	6,3529	9,2558	33,2935	33,9749	34,1992	2,8338	27,3022	56,3729	35,5195	40,2052	24,9113	7,4670	7,5303	8,2057	8,2961	5,4786	15,7734	14,5341	20,5139	16,6955	29,6014	24,8521	10,2466
Actinomyces	26,0839	30,0686	2,7586	23,9179	2,3891	26,1661	8,7796	23,4968	29,9767	0,6339	10,9311	1,9636	18,2177	1,7343	1,5175	4,3299	9,4873	9,8402	23,3305	9,1464	1,9067	23,3248	6,1515	21,0770	24,1779	17,6759	15,4198	8,4770	14,7328	15,0821
Corynebacterium	4,0366	3,7545	4,6178	15,1630	8,0436	13,9082	8,4138	22,3254	20,5822	0,6424	14,3140	3,2508	24,8477	3,8668	0,9040	0,6114	12,7880	1,7440	24,1986	3,4625	8,6698	24,8143	7,0327	18,8477	18,5177	8,9143	13,1498	11,2405	14,8008	14,8642
Capnocytophaga	0,0406	12,8475	26,0414	0,3447	8,8029	0,9300	21,1283	1,1414	5,5587	33,3993	10,4260	23,2246	0,2546	26,1839	11,9853	5,2064	4,9432	2,7690	5,9402	3,3525	24,0444	3,4681	3,8518	4,1798	5,5675	8,6725	14,8779	12,2461	4,8726	7,1525
Leptotrichia	0,0186	3,3135	7,5864	13,4129	2,4149	11,4980	4,4472	14,5332	1,5441	3,3611	2,6309	2,6035	22,7546	8,5470	0,9788	1,7297	3,1369	5,5624	5,3825	1,4749	14,2775	6,2043	9,1129	3,2136	2,8367	7,2803	6,3517	7,2414	4,4706	6,3591
Veillonella	14,5338	9,3560	3,2621	15,3537	2,0958	1,4936	11,9268	5,6903	1,8247	0,2425	3,0299	3,3732	11,6523	0,3529	0,8966	10,5529	0,7450	2,1608	10,1324	2,1409	0,9813	3,8443	2,3246	2,5699	1,8718	6,5915	6,4021	4,4722	4,5419	2,4343
Neisseria	0,0480	0,7630	4,5998	0,0247	14,0191	0,2204	2,1649	0,6418	0,4604	7,1595	2,0429	3,8568	0,0251	7,2349	9,9553	3,5234	3,2548	2,2884	0,1629	0,1608	0,8621	0,3088	0,1515	1,2729	0,5922	3,3419	2,2566	3,6599	1,9023	0,6250
Streptococcus	16,3511	4,3739	0,5151	1,0761	1,1642	0,4836	1,2781	2,6183	2,0820	0,7659	3,3490	0,3161	1,5707	0,4053	4,5379	7,1373	10,2509	3,5500	1,8706	2,2786	0,2493	1,4009	0,9164	3,2791	3,2881	2,8966	1,7017	2,5254	5,7529	1,8979
Eubacterium	0,0032	1,4342	1,7800	7,3708	0,3321	2,7586	1,1621	3,7595	2,7502	0,3679	0,3219	0,6697	5,7365	0,2706	0,4578	0,1549	1,1443	3,0386	2,6665	0,6621	2,7540	2,8835	5,6220	2,4761	1,8708	2,4502	2,0217	1,4262	2,0994	2,8780
Prevotella	0,5666	2,3519	3,0972	5,3814	0,3814	2,0540	3,2952	4,0472	3,2496	1,7458	1,1463	4,7086	4,7376	2,9360	0,3245	2,2134	0,1528	4,1729	5,7363	34,8492	3,7439	2,1169	9,8295	5,5050	2,9967	2,4165	3,2285	2,4940	3,0591	8,1100
Atopobium	0,6282	0,0175	0,5166	0,3370	0,0210	8,3153	0,0032	0,0257	1,8159	0,0753	0,0026	0,0673	0,3691	0,0354	0,0071	0,0023	0,0002	4,0586	0,4199	0,4073	0,3243	0,2201	1,5599	0,2980	0,4408	2,2203	0,3732	0,0876	0,9844	0,5232
Fusobacterium	0,0142	6,7471	1,4040	0,8656	1,1309	0,8520	6,1570	1,0290	1,3432	2,9474	3,5724	4,6439	0,4092	2,8856	0,9166	9,7484	0,6213	2,0708	0,8095	5,5898	5,0194	1,0929	2,6085	2,2734	2,4041	1,6678	3,3468	2,9591	0,9872	2,8772
Selenomonas	0,0120	0,0704	1,0125	6,9195	0,1298	1,1074	0,3733	0,9189	1,8105	0,3853	0,0220	0,8810	1,8418	1,0537	0,0902	0,0209	0,0536	6,2011	2,0046	1,3409	2,1005	1,1356	9,4741	1,5994	2,6460	1,6210	0,7978	0,6447	2,0360	2,9777
Porphyromonas	0,0035	1,6619	3,8623	0,1105	0,6100	0,4800	3,6289	3,2755	0,4582	4,5128	1,5902	2,4190	0,1893	2,4025	0,6793	7,8591	0,3267	0,9639	0,2886	0,9909	5,1250	0,6195	1,3640	1,4893	0,2534	1,2355	3,0656	1,7348	0,4424	1,6741
Micrococcus	0,0885	0,0365	0,2088	0,0500	0,0425	3,3035	0,0901	0,0492	0,2953	0,0086	0,0461	0,1839	0,0221	0,0866	0,0069	0,0817	0,0229	0,9755	0,0543	0,2978	0,0626	0,4806	0,3791	0,5538	0,2854	0,8611	0,1058	0,0607	0,2288	0,3766
Rothia	0,9472	0,5637	0,4152	0,0156	1,2995	0,6590	0,2413	0,3894	1,8761	0,1986	2,8479	0,0689	0,0593	0,2037	2,4446	0,1001	6,0690	1,6753	0,8990	0,1485	0,1823	1,5930	0,7040	1,0507	2,4249	0,6261	0,5908	1,3912	3,2411	1,0165
Tannerella	0,0015	0,2648	1,6404	0,3742	0,1384	0,5455	0,1072	2,0057	0,4926	0,5606	0,0785	0,6864	0,4163	1,1409	0,1478	0,1482	0,0924	1,0316	0,5988	2,6418	9,7401	0,6022	3,1695	1,0743	0,5840	0,5841	0,7551	0,3890	0,4731	2,8055
Propionibacterium	0,2502	0,1057	0,3417	0,2473	0,2746	1,5953	0,2005	0,4937	0,4971	0,0831	0,3714	0,5877	0,0284	0,5120	0,0513	0,8813	0,1054	2,1242	0,1600	0,4130	0,0977	4,2128	1,3159	0,3806	0,9047	0,5755	0,3158	0,3376	0,5374	1,3709
Clostridium	0,0070	0,3271	0,3300	1,4102	0,0788	0,5178	0,2418	0,7359	0,7544	0,4867	0,0962	0,4321	0,8657	0,4160	0,0829	0,0882	0,0902	1,7274	0,5057	0,5173	0,9669	0,5390	2,3557	0,6886	0,6078	0,4740	0,5115	0,3332	0,5793	0,9530
Bifidobacterium	1,6488	0,1441	0,1769	0,0476	0,0917	0,7191	0,0862	0,1790	0,2370	0,0246	0,1180	0,2796	0,0227	0,2238	0,0158	0,1789	0,0132	0,6934	0,1617	0,1090	0,0567	1,7266	1,0460	0,2076	0,4784	0,4264	0,1297	0,1251	0,2074	0,6669
Mobiluncus	0,0423	0,0678	0,0530	0,0829	0,0126	1,5374	0,0577	0,0307	1,0368	0,0011	0,0116	0,0124	0,0335	0,0275	0,0035	0,0010	0,0482	0,3452	0,0739	0,0566	0,0621	0,5505	0,2621	0,5416	0,2345	0,4067	0,2315	0,0169	0,1183	0,3378
Haemophilus	0,0189	0,4919	0,5026	0,0125	0,8859	0,2661	0,6238	0,2267	0,2656	0,7680	1,9059	1,4262	0,0090	2,0468	0,4564	0,8322	0,4438	0,4383	0,4020	0,1826	0,8028	0,2347	0,1049	0,5763	0,7736	0,3747	0,4737	1,2741	0,4270	0,4379
Arthrobacter	0,8434	0,2942	0,0928	0,3203	0,2375	0,5089	0,1759	0,2500	1,0896	0,0385	0,5610	0,0282	0,0865	0,0712	0,3715	0,0632	1,0916	0,4271	0,2741	0,0315	0,0491	0,5945	0,1568	0,2068	0,6079	0,3584	0,3503	0,2843	0,6506	0,2790
Mycobacterium	0,5214	0,1573	0,0408	0,2134	0,0461	0,9537	0,1084	0,0829	0,3227	0,0371	0,0652	0,0770	0,1318	0,1316	0,0150	0,0206	0,0804	0,4129	0,3423	0,0695	0,1703	0,5051	0,5873	0,2770	0,1911	0,3541	0,1316	0,0816	0,2461	0,3300
Slackia	0,0006	0,0012	0,0649	0,0001	0,0039	1,4210	0,0003	0,0002	0,3684	0,0133	0,0003	0,0054	0,0001	0,0020	0,0010	0,0004	0,0001	0,7459	0,0157	0,0580	0,0431	0,0005	0,1042	0,0560	0,0043	0,3536	0,0739	0,0012	0,1580	0,0451
Lactobacillus	2,7715	0,0180	0,0185	0,0859	0,0356	0,0214	0,0432	0,0234	0,0657	0,0579	0,0141	0,0401	0,0153	0,0213	0,1469	0,0324	0,0701	0,1348	0,0367	0,0224	0,0158	0,0132	0,0977	0,0550	0,0411	0,3294	0,0448	0,0351	0,0708	0,0421
Kingella	0,0235	0,0617	0,4601	0,0014	1,1471	0,0166	0,2183	0,1104	0,1281	0,8242	0,3037	1,1432	0,0056	0,5522	1,2204	0,2216	0,8203	0,0848	0,0745	0,0732	0,3157	0,1333	0,0876	0,2712	0,2485	0,2922	0,2723	0,4855	0,3916	0,1944
Collinsella	0,0134	0,0009	0,0450	0,0058	0,0024	1,1235	0,0005	0,0015	0,2345	0,0121	0,0001	0,0042	0,0091	0,0029	0,0012	0,0002	0,0002	0,6127	0,0161	0,0045	0,0244	0,0025	0,0566	0,0252	0,0042	0,2805	0,0481	0,0029	0,1310	0,0211
Enterococcus	0,0501	0,0248	0,0272	0,0064	0,0060	1,0350	0,0054	0,0226	0,1946	0,0190	0,0167	0,0064	0,0095	0,0138	0,0573	0,0496	0,0348	0,4711	0,0142	0,0132	0,0227	0,0130	0,0519	0,0541	0,0086	0,2634	0,0489	0,0201	0,1161	0,0309
Sebaldella	0,0001	0,2379	0,0755	0,1364	0,0659	0,5954	0,2125	0,0628	0,0264	0,0384	0,1801	0,0721	0,0999	0,1303	0,0279	0,2485	0,0000	0,1640	0,4027	0,0121	0,2267	0,1458	0,1465	0,1260	0,0266	0,2204	0,1084	0,1295	0,1839	0,1271
unclassified (derived from Actinobacteria (class))	0,0070	0,0007	0,0511	0,0048	0,0012	0,8251	0,0121	0,0003	0,4282	0,0001	0,0002	0,0300	0,0013	0,0222	0,0126	0,0000	0,0003	0,1401	0,0077	0,0148	0,0347	0,1532	0,0097	0,1433	0,5043	0,2094	0,0879	0,0087	0,0316	0,1292

GENUS	SUBJECTS' SITES																					SUBJECTS' GROUPS								
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF
unclassified (derived from Actinobacteria (class))	0,0070	0,0007	0,0511	0,0048	0,0012	0,8251	0,0121	0,0003	0,4282	0,0001	0,0002	0,0300	0,0013	0,0222	0,0126	0,0000	0,0003	0,1401	0,0077	0,0148	0,0347	0,1532	0,0097	0,1433	0,5043	0,2094	0,0879	0,0087	0,0316	0,1292
Finegoldia	0,1060	0,0067	0,0545	0,0307	0,0122	0,7456	0,0416	0,0069	0,1612	0,0039	0,0059	0,0195	0,0029	0,0392	0,0026	0,0018	0,0022	0,1237	0,0941	0,1209	0,0338	0,1975	0,1658	0,2342	0,1158	0,2085	0,0495	0,0114	0,0613	0,1591
Enterorhabdus	0,0001	0,0001	0,0274	0,0000	0,0010	0,7743	0,0001	0,0001	0,1676	0,0054	0,0001	0,0016	0,0000	0,0009	0,0005	0,0001	0,0000	0,3538	0,0053	0,0078	0,0128	0,0001	0,0340	0,0130	0,0005	0,1908	0,0335	0,0004	0,0741	0,0119
Campylobacter	0,0184	0,2489	0,3399	0,0864	0,0990	0,1644	0,2850	0,4273	0,7223	0,3087	0,0575	1,2472	0,0874	0,9279	0,1479	0,9073	0,1991	0,1789	1,1706	1,2596	0,8353	0,8797	0,2772	0,5718	1,1629	0,1724	0,4113	0,3869	0,5580	0,7641
Parabacteroides	0,0007	0,0964	0,4586	0,1210	0,0350	0,1686	0,0816	0,6430	0,1411	0,2856	0,0701	0,2369	0,1349	0,3499	0,0429	0,1647	0,0053	0,3491	0,1557	1,0048	1,9770	0,2643	0,6690	0,3309	0,1627	0,1721	0,2741	0,1463	0,1316	0,6872
unclassified (derived from Clostridiales)	0,0006	0,1459	0,2903	0,2454	0,0256	0,1705	0,0736	0,2930	0,4761	0,2733	0,0448	0,1925	0,2248	0,1514	0,0408	0,0640	0,0034	0,4753	0,1590	0,0875	0,4144	0,1364	1,3589	0,1332	0,1443	0,1627	0,2423	0,1141	0,1578	0,3797
Gemella	0,0098	0,4731	0,1670	0,0736	0,0183	0,1650	0,1324	0,9342	0,5989	0,0722	0,2085	0,0836	0,0885	0,0389	0,0645	0,4849	0,4168	0,4691	0,0438	0,5474	0,0574	0,0209	0,3358	0,8402	1,0244	0,1495	0,4236	0,1410	0,2881	0,4446
Catenuloplanes	0,0247	0,0143	0,0332	0,0000	0,0063	0,5475	0,0885	0,0000	0,0062	0,0069	0,0034	0,0167	0,0000	0,0090	0,0013	0,0047	0,0000	0,0000	0,0097	0,3004	0,0037	0,0000	0,0036	0,0229	0,0011	0,1431	0,0358	0,0050	0,0036	0,0392
Granulicatella	0,2864	0,2281	0,0549	0,2250	0,1034	0,0384	0,1230	0,4188	0,5011	0,0844	0,4068	0,0655	0,2410	0,0340	0,4173	0,4122	0,7542	0,3054	0,2983	0,0288	0,0264	0,1064	0,0586	1,0698	0,5446	0,1330	0,2678	0,2792	0,4923	0,3645
Megasphaera	0,0024	0,0134	0,1898	0,3931	0,0051	0,0937	0,0306	0,0277	0,0121	0,0111	0,0015	0,0417	0,1890	0,0311	0,0112	0,0061	0,0041	0,2427	0,3684	0,0364	0,0747	0,0442	0,1820	0,0504	0,0727	0,1277	0,0230	0,0489	0,1889	0,0757
Nesterenkonia	0,2298	0,1823	0,0418	0,0688	0,0395	0,2058	0,2485	0,0395	0,1412	0,0324	0,3452	0,0170	0,0707	0,0261	0,0857	0,0053	0,0000	0,2652	0,1323	0,2113	0,0183	0,2656	0,0215	0,1085	0,4305	0,1230	0,1372	0,1570	0,1035	0,1574
Amycolatopsis	0,0734	0,1910	0,0097	0,3484	0,0015	0,0989	0,0032	0,0072	0,0011	0,0058	0,0671	0,0276	0,1123	0,0099	0,0050	0,0012	0,0014	0,0187	0,0582	0,0001	0,0087	0,3634	0,0314	0,2248	0,0128	0,1142	0,0043	0,0521	0,0262	0,1423
Oribacterium	0,0009	0,0519	0,1059	0,1196	0,0066	0,2642	0,0248	0,1348	0,4138	0,0775	0,0076	0,1642	0,0896	0,0507	0,0151	0,0041	0,0040	0,7074	0,0886	0,0139	0,1627	0,1193	0,7736	0,0383	0,1623	0,1120	0,1379	0,0492	0,1790	0,2085
Conexibacter	0,0001	0,0001	0,0195	0,0000	0,0006	0,4401	0,0001	0,0000	0,0819	0,0043	0,0001	0,0011	0,0000	0,0006	0,0003	0,0000	0,0000	0,1829	0,0030	0,0000	0,0105	0,0001	0,0257	0,0083	0,0000	0,1093	0,0166	0,0003	0,0384	0,0081
Butyrivibrio	0,0005	0,0902	0,1967	0,1245	0,0188	0,1378	0,0446	0,1953	0,6892	0,1923	0,0291	0,0974	0,0960	0,1535	0,0252	0,0492	0,0018	0,4157	0,1203	0,1067	0,3786	0,1435	1,5007	0,1556	0,0708	0,1080	0,2337	0,0697	0,1304	0,3995
Abiotrophia	0,0694	0,2639	0,0839	0,0887	0,1312	0,0471	0,0688	0,2227	0,1555	0,2569	0,2260	0,0798	0,1364	0,1272	1,9778	1,6749	0,1709	1,9796	0,0693	0,3169	0,0420	0,0332	0,4434	0,4647	0,2284	0,1046	0,1570	0,4553	0,5017	0,2621
Eikenella	0,0020	0,0251	0,2173	0,0003	0,2898	0,0159	0,0954	0,0100	0,0471	0,2268	0,1947	0,1608	0,0007	0,2452	0,8723	0,1591	0,0796	0,1463	0,0093	0,0576	0,0848	0,0264	0,0419	0,0333	0,1075	0,0982	0,0852	0,2390	0,0669	0,0516
Saccharomonospora	0,0041	0,0010	0,0119	0,0001	0,0045	0,3940	0,0403	0,0168	0,0041	0,0002	0,0004	0,0002	0,0001	0,0001	0,0001	0,0001	0,0002	0,0807	0,0048	0,0003	0,0195	0,1865	0,0839	0,3949	0,0008	0,0979	0,0205	0,0002	0,0184	0,1564
Cellulomonas	0,0081	0,0930	0,0005	0,0008	0,0004	0,3281	0,0006	0,0098	0,0009	0,0003	0,0004	0,0010	0,0005	0,0005	0,0014	0,0001	0,0002	0,1561	0,0174	0,0065	0,0289	0,3154	0,7327	0,0957	0,0037	0,0913	0,0030	0,0006	0,0384	0,2200
Streptomyces	0,0156	0,0422	0,0217	0,0895	0,0092	0,2649	0,0439	0,0962	0,1077	0,0009	0,0117	0,0051	0,0319	0,0136	0,0024	0,0090	0,0384	0,1543	0,0653	0,0152	0,0605	0,2469	0,0952	0,1021	0,1360	0,0907	0,0629	0,0139	0,0721	0,1196
Streptacidiphilus	0,0001	0,0060	0,0428	0,0053	0,0044	0,3279	0,0615	0,0002	0,5533	0,0006	0,0009	0,0075	0,0061	0,0081	0,0009	0,0001	0,0000	0,1202	0,0606	0,0167	0,0662	0,1613	0,0129	0,3934	0,4387	0,0894	0,1309	0,0037	0,0472	0,1928
Arcanobacterium	0,0092	0,0502	0,0043	0,0016	0,0469	0,2665	0,0086	0,0349	0,0205	0,0006	0,0059	0,0007	0,0031	0,0007	0,0024	0,0008	0,0383	0,0800	0,0192	0,0037	0,0145	0,2056	0,2745	0,1280	0,0059	0,0796	0,0165	0,0033	0,0396	0,1255
Bacteroides	0,0041	0,2101	0,1794	0,0209	0,0186	0,0248	0,3471	0,1719	0,0186	0,6546	0,2697	0,3191	0,0121	0,2459	0,0290	1,3029	0,0029	0,1688	0,0246	0,6166	0,2115	0,0506	0,9296	0,1657	0,0816	0,0762	0,2879	0,2434	0,0448	0,3159
Nocardiosis	0,0088	0,0017	0,0143	0,0016	0,0038	0,2911	0,0345	0,0076	0,1280	0,0007	0,0003	0,0072	0,0039	0,0017	0,0006	0,0001	0,0010	0,0488	0,0451	0,0532	0,0410	0,4099	0,0327	0,5866	0,6065	0,0745	0,0400	0,0020	0,0273	0,3150
Thermobispora	0,0002	0,0065	0,0498	0,0001	0,0058	0,2530	0,0487	0,0001	0,0229	0,0053	0,0026	0,0207	0,0001	0,0187	0,0009	0,0020	0,0008	0,0267	0,0115	0,3737	0,0015	0,0090	0,0114	0,0606	0,0011	0,0724	0,0238	0,0064	0,0101	0,0594
Spiroplasma	0,0002	0,0843	0,0203	0,0286	0,0215	0,1929	0,0510	0,0052	0,0191	0,0121	0,0714	0,0138	0,0165	0,0291	0,0115	0,0977	0,0000	0,0824	0,1127	0,0204	0,0142	0,0497	0,0779	0,0270	0,0095	0,0690	0,0264	0,0417	0,0589	0,0359
Actinobacillus	0,0015	0,0655	0,1467	0,0020	0,1047	0,0335	0,1606	0,0595	0,0298	0,1183	0,0784	0,1070	0,0018	0,4609	0,0396	0,0649	0,1937	0,0099	0,1072	0,0369	0,2854	0,0143	0,0176	0,0846	0,1176	0,0637	0,1017	0,1197	0,1239	0,0882
unclassified (derived from Gammaproteobacteria)	0,0006	0,0934	0,1592	0,0024	0,0795	0,0246	0,2202	0,0335	0,0524	0,0805	0,1524	0,4423	0,0033	0,3203	0,0220	0,0560	0,0278	0,0470	0,0871	0,3027	0,2391	0,0567	0,0951	0,0602	0,2118	0,0636	0,1156	0,1622	0,0539	0,1350
Actinobaculum	0,0108	0,0710	0,0005	0,0010	0,0022	0,2027	0,0056	0,0132	0,0068	0,0005	0,0093	0,0004	0,0910	0,0005	0,0014	0,0007	0,0258	0,1165	0,0166	0,0057	0,0139	0,2261	0,2511	0,0633	0,0063	0,0592	0,0070	0,0216	0,0409	0,1098
Desulfotomaculum	0,0017	0,0547	0,0305	0,1757	0,0119	0,0609	0,0284	0,1063	0,0723	0,0481	0,0204	0,0451	0,0623	0,0868	0,0037	0,0111	0,0030	0,2852	0,0745	0,1164	0,2098	0,0856	0,3066	0,0899	0,0893	0,0582	0,0606	0,0392	0,0872	0,1469

GENUS	SUBJECTS' SITES																							SUBJECTS' GROUPS						
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-INCL	CA-INCL	CA-S	CI-INCL	CF
unclassified (derived from Propionibacteriaceae)	0,0006	0,0144	0,0360	0,0110	0,0207	0,1763	0,0230	0,0653	0,0513	0,0101	0,0354	0,0873	0,0042	0,0488	0,0031	0,0778	0,0000	0,1755	0,0088	0,0488	0,0123	0,4821	0,2346	0,0499	0,1230	0,0565	0,0375	0,0356	0,0391	0,1749
Gordonibacter	0,0001	0,0000	0,0157	0,0000	0,0007	0,2206	0,0001	0,0001	0,0686	0,0022	0,0000	0,0012	0,0000	0,0008	0,0001	0,0000	0,0000	0,1374	0,0025	0,0000	0,0097	0,0000	0,0331	0,0081	0,0001	0,0560	0,0137	0,0003	0,0290	0,0091
Kocuria	0,0224	0,0102	0,0274	0,2259	0,0079	0,0357	0,0114	0,0623	0,0587	0,0021	0,0237	0,0337	0,1860	0,0077	0,0105	0,0051	0,1337	0,0930	0,0045	0,1046	0,0080	0,3318	0,0253	0,0334	0,0343	0,0556	0,0324	0,0518	0,0771	0,0997
Pseudonocardia	0,0857	0,0310	0,0183	0,0043	0,0070	0,1506	0,0136	0,0196	0,0229	0,0004	0,0029	0,0019	0,0325	0,0021	0,0018	0,0003	0,0158	0,0681	0,0446	0,0052	0,0332	0,2586	0,4753	0,2767	0,1889	0,0547	0,0148	0,0082	0,0372	0,2297
Aggregatibacter	0,0011	0,0291	0,0427	0,0060	0,1610	0,0623	0,0787	0,1171	0,0682	0,2858	0,4032	0,3259	0,0049	0,8288	0,0132	0,0803	0,1624	0,0933	0,2383	0,0809	0,0857	0,0385	0,0252	0,0467	0,1333	0,0541	0,1209	0,3186	0,1767	0,0600
Mannheimia	0,0008	0,0669	0,0626	0,0003	0,1928	0,0077	0,0988	0,0061	0,0465	0,2367	0,2961	0,1409	0,0007	0,1633	0,0843	0,1598	0,0210	0,0761	0,0221	0,0022	0,0743	0,0459	0,0080	0,0406	0,0018	0,0541	0,0870	0,1680	0,0326	0,0335
Mitsuokella	0,0004	0,0032	0,0433	0,1862	0,0015	0,0519	0,0044	0,0018	0,0470	0,0008	0,0003	0,0201	0,0048	0,0083	0,0018	0,0002	0,0000	0,2354	0,0554	0,0247	0,0307	0,0461	0,9070	0,0375	0,0312	0,0521	0,0114	0,0049	0,0687	0,1819
Cryptobacterium	0,0000	0,0001	0,0024	0,0007	0,0000	0,2099	0,0000	0,0007	0,0222	0,0001	0,0000	0,0014	0,0005	0,0000	0,0002	0,0000	0,0000	0,1164	0,0035	0,0001	0,0001	0,0003	0,0052	0,0023	0,0000	0,0508	0,0045	0,0003	0,0250	0,0015
Bacillus	0,0385	0,0963	0,0340	0,0239	0,0119	0,0876	0,1366	0,0806	0,1377	0,0428	0,0557	0,0151	0,0419	0,0476	0,0157	0,0393	0,0471	0,1093	0,0515	0,0485	0,1619	0,0793	0,1483	0,1292	0,5820	0,0500	0,1067	0,0415	0,0614	0,1646
Bogoriella	0,0048	0,0030	0,0330	0,0013	0,0049	0,1651	0,0793	0,0003	0,0115	0,0052	0,0041	0,0149	0,0003	0,0149	0,0020	0,0012	0,0012	0,0121	0,0093	0,2857	0,0022	0,0061	0,0230	0,0868	0,3251	0,0481	0,0332	0,0059	0,0064	0,0912
Burkholderia	0,0135	0,0413	0,0312	0,0012	0,1769	0,0193	0,0667	0,0059	0,0911	0,1684	0,1862	0,0513	0,0003	0,0475	0,2287	0,0360	0,0547	0,0541	0,0091	0,0016	0,0169	0,0112	0,0122	0,0091	0,0018	0,0461	0,0723	0,1105	0,0376	0,0097
Exiguobacterium	0,0044	0,0108	0,0421	0,1324	0,0090	0,0490	0,0328	0,0608	0,0682	0,0339	0,0049	0,0320	0,0582	0,0738	0,0057	0,0115	0,0002	0,2674	0,0895	0,0528	0,0774	0,0606	0,1808	0,0793	0,0777	0,0450	0,0472	0,0294	0,0881	0,0890
Jonesia	0,0001	0,0456	0,0017	0,0001	0,0014	0,1517	0,0021	0,0013	0,0120	0,0005	0,0009	0,0010	0,0001	0,0015	0,0005	0,0008	0,0123	0,0560	0,0543	0,0283	0,0053	0,1081	0,0585	0,0421	0,1295	0,0426	0,0035	0,0008	0,0369	0,0607
Glaciibacter	0,0000	0,1105	0,0001	0,0001	0,0000	0,1137	0,0000	0,0029	0,0001	0,0001	0,0001	0,0003	0,0000	0,0000	0,0002	0,0001	0,0004	0,0811	0,0027	0,0009	0,0103	0,1330	0,0745	0,0428	0,0000	0,0412	0,0008	0,0001	0,0177	0,0534
unclassified (derived from Pasteurellaceae)	0,0002	0,0175	0,0091	0,0002	0,1153	0,0713	0,0774	0,0077	0,0448	0,0776	0,3000	0,1304	0,0005	0,2632	0,0043	0,0336	0,0516	0,2713	0,0106	0,0025	0,1918	0,0064	0,0114	0,0043	0,0014	0,0396	0,0528	0,1677	0,0811	0,0349
unclassified (derived from Bacteroidetes)	0,0000	0,0003	0,0006	0,0003	0,0068	0,1514	0,0003	0,0004	0,0011	0,1318	0,0002	0,1939	0,0001	0,5894	0,0001	0,0004	0,0008	0,0793	0,0004	3,0748	0,1395	0,3786	0,3950	0,1554	0,0051	0,0375	0,0221	0,1124	0,0166	0,5379
Gordonia	0,0061	0,0347	0,0273	0,0098	0,0311	0,0807	0,0295	0,0333	0,0373	0,0055	0,0202	0,0521	0,0099	0,0184	0,0062	0,0238	0,0094	0,0584	0,0631	0,0102	0,0136	0,1908	0,1513	0,0403	0,1023	0,0365	0,0281	0,0201	0,0394	0,0901
Cardiobacterium	0,0000	0,0254	0,0451	0,0006	0,0991	0,0263	0,0291	0,0042	0,0229	0,0512	0,0343	0,1670	0,0048	0,1818	0,0145	0,0226	0,0921	0,0405	0,0099	0,1239	0,1130	0,1107	0,0208	0,0329	0,2073	0,0347	0,0250	0,0635	0,0509	0,0878
Glycomyces	0,0014	0,0414	0,0003	0,0037	0,0066	0,1149	0,0046	0,0115	0,0133	0,0005	0,0018	0,0007	0,0004	0,0037	0,0006	0,0006	0,0109	0,0488	0,0203	0,0027	0,0080	0,0732	0,1392	0,0216	0,0021	0,0346	0,0075	0,0015	0,0221	0,0462
Brachymonas	0,0000	0,0001	0,1639	0,0000	0,0001	0,0000	0,0001	0,0000	0,0001	0,0047	0,0000	0,0338	0,0000	0,0034	0,0000	0,0103	0,0040	0,0001	0,0000	0,0000	0,0253	0,0000	0,0002	0,0000	0,0000	0,0338	0,0008	0,0050	0,0017	0,0040
Acidothermus	0,0001	0,0333	0,0002	0,0001	0,0009	0,1221	0,0001	0,0020	0,0055	0,0001	0,0001	0,0001	0,0004	0,0003	0,0002	0,0027	0,0381	0,0041	0,0015	0,0035	0,0925	0,0648	0,0236	0,0003	0,0336	0,0016	0,0002	0,0104	0,0373	
Aeromonas	0,0001	0,0001	0,0040	0,1765	0,0014	0,0088	0,0006	0,0496	0,0018	0,0007	0,0004	0,0040	0,0579	0,0014	0,0010	0,0018	0,0015	0,0124	0,0105	0,0099	0,0001	0,0025	0,0051	0,0048	0,0057	0,0317	0,0137	0,0124	0,0071	0,0043
Dialister	0,0080	0,0084	0,0065	0,0292	0,0013	0,0963	0,0026	0,0033	0,0425	0,0077	0,0009	0,0521	0,0066	0,0069	0,0002	0,0017	0,0008	0,0753	0,0663	0,6385	0,0044	0,0343	0,1342	0,0466	0,0129	0,0312	0,0114	0,0088	0,0405	0,1119
Myroides	0,0001	0,0156	0,1141	0,0282	0,0028	0,0009	0,0702	0,0056	0,0201	0,1332	0,0823	0,1264	0,0154	0,0136	0,0145	0,0012	0,0005	0,0056	0,0561	0,0456	0,1370	0,0143	0,0936	0,0135	0,0291	0,0307	0,0539	0,0518	0,0223	0,0515
Ruminococcus	0,0002	0,0211	0,0514	0,0611	0,0028	0,0288	0,0116	0,0433	0,1264	0,0428	0,0045	0,0856	0,0199	0,0280	0,0101	0,0271	0,0043	0,0819	0,0469	0,0051	0,0245	0,0509	0,1118	0,0091	0,0410	0,0305	0,0474	0,0223	0,0360	0,0405
Megamonas	0,0052	0,0050	0,0279	0,1061	0,0036	0,0219	0,0114	0,0202	0,0232	0,0058	0,0008	0,0176	0,0687	0,0230	0,0014	0,0263	0,0051	0,1199	0,0470	0,0207	0,0420	0,0372	0,3521	0,0279	0,0638	0,0299	0,0151	0,0208	0,0441	0,0893
Paenibacillus	0,0005	0,0038	0,0092	0,1479	0,0043	0,0090	0,0078	0,0591	0,0361	0,0163	0,0023	0,0174	0,0515	0,0300	0,0034	0,0032	0,0013	0,1336	0,0314	0,0347	0,0290	0,0228	0,0782	0,0233	0,0174	0,0291	0,0282	0,0181	0,0395	0,0339
Sanguibacter	0,0013	0,0010	0,1234	0,0049	0,0121	0,0018	0,0017	0,0025	0,0231	0,0003	0,0002	0,0690	0,0018	0,0448	0,0033	0,0003	0,0004	0,4223	0,0040	0,0358	0,0001	0,0012	0,1136	0,2726	0,0007	0,0288	0,0058	0,0157	0,0878	0,0917
Coenonia	0,0001	0,0893	0,0598	0,0002	0,0271	0,0024	0,1696	0,0014	0,0249	0,2724	0,1237	0,1741	0,0006	0,2720	0,0410	0,0246	0,0000	0,0080	0,0103	0,0111	0,0758	0,0088	0,0058	0,0039	0,0070	0,0285	0,1142	0,1133	0,0055	0,0177
unclassified (derived from Betaproteobacteria)	0,0062	0,0119	0,0481	0,0023	0,0766	0,0132	0,0043	0,0250	0,0085	0,0138	0,0109	0,0435	0,0004	0,1376	0,0276	0,0087	0,0088	0,0204	0,0055	0,0002	0,0310	0,0047	0,0083	0,0222	0,0005	0,0278	0,0121	0,0338	0,0099	0,0129

GENUS	SUBJECTS' SITES																								SUBJECTS' GROUPS					
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF
unclassified (derived from Lachnospiraceae)	0,0002	0,0281	0,0115	0,0641	0,0083	0,0393	0,0157	0,0588	0,0471	0,0270	0,0049	0,0389	0,0074	0,0192	0,0037	0,0037	0,0025	0,0742	0,0269	0,0080	0,0644	0,0124	0,1164	0,0101	0,0398	0,0270	0,0350	0,0113	0,0262	0,0398
Treponema	0,0054	0,0046	0,0129	0,0004	0,0006	0,0961	0,0079	0,0010	0,1277	0,9549	0,0137	1,7328	0,0009	1,3270	0,0031	0,0089	0,0015	0,3613	0,0336	5,4164	0,5913	0,0008	5,0271	0,2955	0,0151	0,0270	0,1853	0,4098	0,0868	1,5909
Roseburia	0,0002	0,0122	0,0672	0,0393	0,0016	0,0099	0,0072	0,0438	0,1364	0,0073	0,0026	0,0045	0,0424	0,0073	0,0085	0,0017	0,0002	0,0355	0,0377	0,0045	0,0372	0,0271	0,1098	0,0184	0,0063	0,0244	0,0419	0,0120	0,0214	0,0358
Syntrophococcus	0,0001	0,0619	0,0222	0,0205	0,0163	0,0233	0,0413	0,0216	0,0703	0,0057	0,0163	0,0132	0,0038	0,0156	0,0045	0,0115	0,0000	0,0289	0,0041	0,0209	0,0721	0,0594	0,1390	0,0294	0,0879	0,0239	0,0359	0,0117	0,0074	0,0660
Streptobacillus	0,0004	0,0209	0,0199	0,0438	0,0099	0,0331	0,0246	0,0681	0,0194	0,0068	0,0208	0,0137	0,0497	0,0291	0,0039	0,1912	0,0031	0,0511	0,0566	0,0164	0,0940	0,0249	0,1831	0,0082	0,0166	0,0233	0,0321	0,0332	0,0329	0,0563
Geobacillus	0,0002	0,0026	0,0167	0,0693	0,0021	0,0307	0,0098	0,0026	0,0111	0,0002	0,0008	0,0043	0,0362	0,0049	0,0023	0,0002	0,0010	0,1293	0,0432	0,0237	0,0251	0,0205	0,0416	0,0299	0,0677	0,0226	0,0066	0,0089	0,0429	0,0323
Skermania	0,0000	0,0179	0,0000	0,0002	0,0000	0,0785	0,0001	0,0015	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0012	0,0342	0,0031	0,0018	0,0041	0,0992	0,1095	0,0227	0,0000	0,0210	0,0005	0,0000	0,0086	0,0461
Acidaminococcus	0,0096	0,0160	0,0106	0,0675	0,0011	0,0115	0,0144	0,0050	0,0043	0,0069	0,0090	0,0081	0,0439	0,0109	0,0003	0,0141	0,0008	0,0374	0,0260	0,0413	0,0185	0,0195	0,0287	0,0083	0,0334	0,0191	0,0087	0,0153	0,0177	0,0218
Parascardovia	0,0817	0,0053	0,0013	0,0004	0,0006	0,0353	0,0007	0,0006	0,0046	0,0001	0,0001	0,0005	0,0000	0,0014	0,0002	0,0000	0,0000	0,0033	0,0014	0,0063	0,0001	0,0064	0,0024	0,0017	0,0013	0,0183	0,0013	0,0003	0,0012	0,0030
Dietzia	0,0005	0,0028	0,0072	0,0012	0,0021	0,0655	0,0143	0,0034	0,0494	0,0013	0,0066	0,0025	0,0006	0,0017	0,0015	0,0049	0,0005	0,0124	0,0046	0,0242	0,0055	0,0153	0,0010	0,0387	0,0112	0,0181	0,0161	0,0035	0,0045	0,0178
unclassified (derived from Clostridiales Family XI, Incertae Sedis)	0,0110	0,0148	0,0029	0,0756	0,0001	0,0037	0,0019	0,0013	0,0298	0,0085	0,0086	0,0329	0,0081	0,0043	0,0001	0,0009	0,0005	0,0284	0,0325	1,5256	0,0018	0,0068	0,2907	0,1191	0,0515	0,0168	0,0083	0,0093	0,0182	0,2489
Cytophaga	0,0002	0,0333	0,0157	0,0013	0,0227	0,0177	0,0637	0,0028	0,0199	0,0642	0,0501	0,0349	0,0006	0,0890	0,0218	0,0261	0,0177	0,0232	0,0197	0,2430	0,0423	0,0316	0,0291	0,0188	0,0104	0,0155	0,0393	0,0400	0,0196	0,0501
Chryseobacterium	0,0003	0,0393	0,0087	0,0001	0,0521	0,0016	0,0476	0,0072	0,0127	0,0897	0,2502	0,0308	0,0000	0,0652	0,0192	0,0609	0,0334	0,0343	0,0124	0,0067	0,0653	0,0286	0,0025	0,0247	0,0140	0,0155	0,0372	0,1106	0,0257	0,0252
Helcococcus	0,0001	0,0268	0,0092	0,0149	0,0058	0,0270	0,0117	0,0552	0,0098	0,0200	0,0067	0,0236	0,0144	0,0453	0,0007	0,0062	0,0000	0,0384	0,0084	0,0124	0,1213	0,0254	0,1665	0,0165	0,0117	0,0151	0,0241	0,0153	0,0110	0,0591
Geobacter	0,0000	0,0013	0,0626	0,0113	0,0000	0,0000	0,0125	0,0969	0,0003	0,0001	0,0067	0,0000	0,0156	0,0002	0,0033	0,0001	0,0002	0,0277	0,0007	0,0001	0,0002	0,0010	0,0399	0,0002	0,0000	0,0149	0,0302	0,0060	0,0060	0,0070
unclassified (derived from Proteobacteria)	0,0069	0,0270	0,0163	0,0039	0,0268	0,0085	0,0087	0,0058	0,0369	0,0668	0,0857	0,0216	0,0108	0,0058	0,1529	0,0130	0,0217	0,0935	0,0066	0,0033	0,0018	0,0179	0,0155	0,0092	0,0142	0,0145	0,0230	0,0558	0,0307	0,0108
Dehalococcoides	0,0001	0,0017	0,0026	0,0000	0,0012	0,0559	0,0151	0,0000	0,0024	0,0015	0,0005	0,0010	0,0000	0,0034	0,0005	0,0029	0,0002	0,0001	0,0018	0,0696	0,0000	0,0000	0,0008	0,0109	0,0000	0,0143	0,0065	0,0010	0,0008	0,0103
Scardovia	0,1280	0,0006	0,0004	0,0000	0,0000	0,0001	0,0001	0,0000	0,0002	0,0000	0,0000	0,0002	0,0000	0,0001	0,0000	0,0001	0,0000	0,0001	0,0009	0,0000	0,0000	0,0130	0,0325	0,0030	0,0111	0,0140	0,0001	0,0001	0,0004	0,0101
Staphylococcus	0,0005	0,0102	0,0185	0,0401	0,0013	0,0085	0,0066	0,0162	0,0567	0,0116	0,0024	0,0089	0,0115	0,0101	0,0083	0,0028	0,0009	0,0630	0,0167	0,0117	0,0277	0,0174	0,1395	0,0137	0,0296	0,0139	0,0197	0,0068	0,0195	0,0392
Halanaerobium	0,0002	0,0001	0,0031	0,0629	0,0003	0,0103	0,0018	0,0002	0,0411	0,0001	0,0000	0,0014	0,0009	0,0026	0,0005	0,0000	0,0000	0,0509	0,0122	0,0106	0,0087	0,0029	0,0273	0,0145	0,0162	0,0133	0,0087	0,0008	0,0149	0,0130
Stenoxybacter	0,0025	0,0030	0,0069	0,0002	0,0676	0,0010	0,0058	0,0221	0,0128	0,0572	0,0041	0,0233	0,0006	0,0043	0,0078	0,0098	0,0015	0,0019	0,0075	0,0013	0,0105	0,0072	0,0048	0,0061	0,0294	0,0131	0,0199	0,0064	0,0038	0,0087
Gallibacterium	0,0001	0,0027	0,0010	0,0000	0,0688	0,0051	0,0026	0,0008	0,0008	0,0015	0,0066	0,0056	0,0000	0,0179	0,0004	0,0040	0,0032	0,0080	0,0015	0,0075	0,0012	0,0005	0,0003	0,0069	0,0011	0,0127	0,0016	0,0060	0,0036	0,0030
Terrabacter	0,0001	0,0298	0,0001	0,0000	0,0003	0,0363	0,0001	0,0010	0,0004	0,0002	0,0005	0,0006	0,0001	0,0001	0,0005	0,0001	0,0010	0,0277	0,0010	0,0006	0,0024	0,0249	0,0573	0,0103	0,0002	0,0125	0,0004	0,0004	0,0064	0,0180
Rhodococcus	0,0100	0,0156	0,0008	0,0081	0,0063	0,0283	0,0281	0,0087	0,0257	0,0033	0,0135	0,0013	0,0033	0,0016	0,0047	0,0025	0,0210	0,0087	0,0389	0,0036	0,0095	0,0027	0,0040	0,0088	0,0028	0,0123	0,0185	0,0067	0,0252	0,0056
Acidimicrobium	0,0141	0,0169	0,0012	0,0013	0,0024	0,0325	0,0050	0,0040	0,0176	0,0007	0,0011	0,0045	0,0010	0,0009	0,0007	0,0014	0,0010	0,0094	0,0049	0,0029	0,0246	0,0035	0,0010	0,0061	0,1373	0,0123	0,0065	0,0014	0,0042	0,0207
Mycoplasma	0,0000	0,0008	0,0082	0,0005	0,0004	0,0427	0,0004	0,0011	0,0055	0,0312	0,0006	0,0195	0,0001	0,0334	0,0003	0,0004	0,0004	0,0168	0,0056	0,0043	0,0076	0,0246	0,0402	0,0029	0,0011	0,0121	0,0067	0,0077	0,0057	0,0145
Riemerella	0,0003	0,0285	0,0105	0,0001	0,0338	0,0022	0,0274	0,0115	0,0080	0,0594	0,2107	0,0417	0,0001	0,0529	0,0140	0,0469	0,0140	0,0233	0,0147	0,0182	0,0953	0,0180	0,0357	0,0156	0,0125	0,0117	0,0247	0,0942	0,0162	0,0320
Pasteurella	0,0001	0,0143	0,0116	0,0000	0,0352	0,0075	0,0172	0,0007	0,0109	0,0350	0,0726	0,0108	0,0000	0,0390	0,0397	0,0824	0,0299	0,0239	0,0027	0,0007	0,0215	0,0072	0,0014	0,0056	0,0060	0,0116	0,0146	0,0426	0,0185	0,0073
Elizabethkingia	0,0005	0,0298	0,0096	0,0001	0,0206	0,0103	0,0310	0,0031	0,0069	0,0543	0,2002	0,0382	0,0002	0,0687	0,0147	0,0423	0,0069	0,0260	0,0054	0,1047	0,0426	0,0201	0,0464	0,0184	0,0104	0,0116	0,0229	0,0923	0,0102	0,0357
Nocardia	0,0013	0,0080	0,0038	0,0014	0,0032	0,0370	0,0105	0,0055	0,0139	0,0006	0,0078	0,0030	0,0009	0,0046	0,0006	0,0028	0,0040	0,0057	0,0095	0,0046	0,0010	0,0222	0,0052	0,0051	0,0125	0,0115	0,0082	0,0043	0,0064	0,0089

GENUS	SUBJECTS' SITES																						SUBJECTS' GROUPS							
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF
Desulfitobacterium	0,0161	0,0277	0,0006	0,0248	0,0043	0,0041	0,0303	0,0102	0,1636	0,0036	0,0069	0,0057	0,0017	0,0073	0,0009	0,0203	0,0020	0,0298	0,0356	0,0299	0,0095	0,0008	0,1028	0,0095	0,0120	0,0110	0,0465	0,0057	0,0202	0,0257
unclassified (derived from Flavobacteriaceae)	0,0005	0,0297	0,0088	0,0001	0,0320	0,0011	0,0323	0,0013	0,0094	0,0484	0,1931	0,0412	0,0001	0,0228	0,0169	0,0502	0,0256	0,0237	0,0040	0,0042	0,0170	0,0108	0,0008	0,0151	0,0087	0,0110	0,0224	0,0836	0,0172	0,0103
Beutenbergia	0,0750	0,0061	0,0002	0,0022	0,0009	0,0060	0,0014	0,0045	0,0121	0,0001	0,0011	0,0015	0,0002	0,0001	0,0028	0,0004	0,0017	0,0196	0,0440	0,0002	0,0001	0,0009	0,0010	0,0033	0,0169	0,0108	0,0041	0,0010	0,0212	0,0030
Francisella	0,0001	0,0209	0,0051	0,0079	0,0038	0,0216	0,0088	0,0498	0,0105	0,0149	0,0033	0,0048	0,0078	0,0249	0,0009	0,0051	0,0000	0,0209	0,0083	0,0113	0,0658	0,0268	0,0270	0,0146	0,0041	0,0107	0,0209	0,0074	0,0074	0,0259
Laribacter	0,0005	0,0016	0,0018	0,0001	0,0604	0,0004	0,0031	0,0032	0,0053	0,0150	0,0012	0,0145	0,0001	0,0259	0,0673	0,0077	0,0274	0,0037	0,0006	0,0013	0,0008	0,0006	0,0003	0,0005	0,0008	0,0104	0,0055	0,0145	0,0125	0,0007
unclassified (derived from Alphaproteobacteria)	0,0002	0,0018	0,0086	0,0006	0,0003	0,0287	0,0005	0,0032	0,0004	0,0057	0,0008	0,0170	0,0003	0,0024	0,0003	0,0339	0,0001	0,0011	0,0005	0,0063	0,0064	0,0007	0,0219	0,0079	0,0005	0,0090	0,0021	0,0044	0,0004	0,0075
Promicromonospora	0,0030	0,0161	0,0005	0,0027	0,0021	0,0241	0,0059	0,0048	0,0236	0,0004	0,0060	0,0003	0,0021	0,0010	0,0006	0,0019	0,0062	0,0040	0,0335	0,0005	0,0006	0,0080	0,0004	0,0043	0,0081	0,0090	0,0082	0,0030	0,0160	0,0039
Oscillatoria	0,0001	0,0003	0,0082	0,0323	0,0015	0,0066	0,0034	0,0104	0,0083	0,0061	0,0001	0,0068	0,0239	0,0062	0,0009	0,0002	0,0001	0,0571	0,0175	0,0184	0,0073	0,0072	0,0310	0,0036	0,0206	0,0088	0,0066	0,0066	0,0182	0,0129
Dermatophilus	0,0113	0,0037	0,0011	0,0012	0,0064	0,0229	0,0095	0,0012	0,0071	0,0020	0,0226	0,0025	0,0006	0,0010	0,0103	0,0011	0,0007	0,0074	0,0031	0,0074	0,0002	0,0243	0,0024	0,0025	0,0069	0,0086	0,0056	0,0101	0,0030	0,0078
Tetrasphaera	0,0004	0,0001	0,0001	0,0002	0,0002	0,0353	0,0004	0,0016	0,0024	0,0000	0,0005	0,0001	0,0004	0,0001	0,0001	0,0000	0,0003	0,0027	0,0033	0,0002	0,0001	0,0019	0,0001	0,0036	0,0013	0,0086	0,0011	0,0003	0,0019	0,0015
Actinocorallia	0,0006	0,0014	0,0013	0,0000	0,0231	0,0168	0,0014	0,0023	0,0466	0,0048	0,0380	0,0003	0,0002	0,0033	0,0344	0,0018	0,0007	0,0273	0,0086	0,0001	0,0003	0,0420	0,0002	0,0005	0,0032	0,0082	0,0110	0,0187	0,0090	0,0095
Paraprevotella	0,0000	0,0137	0,0105	0,0016	0,0007	0,0151	0,0149	0,0037	0,0028	0,0108	0,0179	0,0292	0,0004	0,0518	0,0004	0,0245	0,0000	0,0153	0,0037	0,2878	0,0154	0,0339	0,1265	0,0365	0,0021	0,0079	0,0089	0,0192	0,0045	0,0711
Brucella	0,0000	0,0065	0,0016	0,0047	0,0274	0,0066	0,0147	0,0044	0,0059	0,0111	0,0029	0,0245	0,0017	0,0371	0,0079	0,0066	0,0002	0,0019	0,0031	0,0037	0,0047	0,0046	0,0016	0,0043	0,0239	0,0079	0,0097	0,0111	0,0016	0,0059
Blautia	0,0004	0,0054	0,0038	0,0102	0,0019	0,0180	0,0028	0,0119	0,0333	0,0172	0,0028	0,0227	0,0055	0,0060	0,0015	0,0059	0,0034	0,0691	0,0076	0,0026	0,0053	0,0044	0,0922	0,0064	0,0140	0,0078	0,0135	0,0061	0,0184	0,0205
Dichelobacter	0,0000	0,0051	0,0036	0,0009	0,0260	0,0085	0,0124	0,0065	0,0074	0,0091	0,0032	0,0316	0,0009	0,0789	0,0023	0,0065	0,0329	0,0454	0,0046	0,0109	0,0115	0,0127	0,0018	0,0448	0,0173	0,0077	0,0093	0,0176	0,0249	0,0190
Meiothermus	0,0000	0,0416	0,0028	0,0000	0,0070	0,0027	0,0251	0,0020	0,0005	0,0021	0,0182	0,0088	0,0000	0,0013	0,0011	0,0011	0,0000	0,0034	0,0008	0,0018	0,0031	0,0002	0,0004	0,0022	0,0015	0,0076	0,0105	0,0081	0,0010	0,0015
Kitasatospora	0,0311	0,0021	0,0011	0,0149	0,0014	0,0044	0,0035	0,0061	0,0427	0,0007	0,0002	0,0006	0,0050	0,0047	0,0005	0,0001	0,0135	0,0069	0,0124	0,0014	0,0042	0,0085	0,0021	0,0072	0,0014	0,0075	0,0113	0,0019	0,0118	0,0049
Kytococcus	0,0000	0,0105	0,0007	0,0004	0,0000	0,0247	0,0001	0,0007	0,0001	0,0000	0,0001	0,0000	0,0001	0,0000	0,0003	0,0000	0,0000	0,0153	0,0008	0,0001	0,0008	0,0353	0,0326	0,0041	0,0001	0,0074	0,0002	0,0001	0,0034	0,0142
Frankia	0,0001	0,0002	0,0010	0,0002	0,0007	0,0281	0,0041	0,0002	0,0766	0,0001	0,0002	0,0002	0,0001	0,0005	0,0002	0,0001	0,0029	0,0526	0,0013	0,0007	0,0010	0,0014	0,0011	0,0028	0,0014	0,0071	0,0165	0,0002	0,0124	0,0016
Eggerthella	0,0003	0,0000	0,0004	0,0000	0,0000	0,0283	0,0001	0,0000	0,0021	0,0002	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0083	0,0004	0,0005	0,0028	0,0003	0,0005	0,0004	0,0000	0,0069	0,0005	0,0000	0,0019	0,0007
Anabaena	0,0001	0,0016	0,0022	0,0110	0,0003	0,0182	0,0008	0,0038	0,0270	0,0001	0,0001	0,0080	0,0061	0,0001	0,0007	0,0000	0,0000	0,0523	0,0049	0,0001	0,0034	0,0063	0,0624	0,0010	0,0149	0,0068	0,0066	0,0023	0,0125	0,0141
Flavobacterium	0,0001	0,0149	0,0136	0,0003	0,0090	0,0023	0,0227	0,0024	0,0080	0,1725	0,1219	0,0550	0,0022	0,0240	0,0163	0,0082	0,0128	0,0042	0,0055	0,0117	0,0270	0,0051	0,0251	0,0022	0,0015	0,0067	0,0392	0,0576	0,0083	0,0115
Brevibacterium	0,0001	0,0125	0,0004	0,0008	0,0013	0,0195	0,0003	0,0008	0,0032	0,0001	0,0023	0,0003	0,0001	0,0003	0,0007	0,0002	0,0050	0,0124	0,0018	0,0005	0,0006	0,0199	0,0110	0,0053	0,0020	0,0067	0,0010	0,0010	0,0053	0,0078
Renibacterium	0,0004	0,0010	0,0006	0,0010	0,0197	0,0125	0,0011	0,0045	0,0021	0,0002	0,0027	0,0006	0,0016	0,0007	0,0009	0,0000	0,1108	0,0003	0,0031	0,0005	0,0019	0,0030	0,0008	0,0013	0,0213	0,0066	0,0020	0,0016	0,0480	0,0036
Hespellia	0,0000	0,0015	0,0190	0,0027	0,0008	0,0080	0,0026	0,0062	0,2050	0,0874	0,0017	0,0086	0,0025	0,0069	0,0012	0,0091	0,0000	0,0610	0,0230	0,0037	0,0332	0,0017	0,2363	0,0060	0,0031	0,0066	0,0569	0,0038	0,0210	0,0474
Yersinia	0,0002	0,0040	0,0004	0,0000	0,0362	0,0006	0,0086	0,0006	0,0030	0,0081	0,0160	0,0203	0,0000	0,0143	0,0044	0,0087	0,0001	0,0003	0,0030	0,0000	0,0001	0,0001	0,0000	0,0003	0,0019	0,0065	0,0053	0,0113	0,0012	0,0003
Akkermansia	0,0127	0,0315	0,0001	0,0056	0,0002	0,0005	0,0032	0,0008	0,0020	0,0002	0,0226	0,0009	0,0007	0,0002	0,0001	0,0001	0,0000	0,0004	0,0099	0,0000	0,0005	0,0001	0,0001	0,0001	0,0000	0,0064	0,0018	0,0086	0,0038	0,0001
Gardnerella	0,0461	0,0006	0,0002	0,0011	0,0001	0,0029	0,0001	0,0002	0,0007	0,0000	0,0000	0,0001	0,0000	0,0032	0,0003	0,0002	0,0001	0,0005	0,0006	0,0068	0,0000	0,0021	0,0141	0,0024	0,0074	0,0060	0,0003	0,0005	0,0004	0,0049
Nocardioides	0,0001	0,0017	0,0010	0,0002	0,0027	0,0206	0,0026	0,0067	0,0083	0,0014	0,0052	0,0009	0,0003	0,0038	0,0016	0,0240	0,0080	0,0407	0,0010	0,0048	0,0005	0,0908	0,0025	0,0047	0,0043	0,0058	0,0046	0,0040	0,0120	0,0221
Erysipelothrix	0,0001	0,0018	0,0027	0,0205	0,0009	0,0066	0,0015	0,0095	0,0708	0,0145	0,0034	0,0141	0,0054	0,0043	0,0003	0,0009	0,0000	0,3285	0,0264	0,6012	0,0070	0,0034	0,1854	0,0993	0,0520	0,0058	0,0192	0,0047	0,0768	0,1275
Synechococcus	0,0000	0,0010	0,0020	0,0003	0,0004	0,0214	0,0017	0,0002	0,0007	0,0008	0,0006	0,0003	0,0037	0,0016	0,0006	0,0001	0,0018	0,0012	0,0017	0,0002	0,0015	0,0129	0,0026	0,0105	0,0224	0,0057	0,0010	0,0013	0,0017	0,0084

GENUS	SUBJECTS' SITES																								SUBJECTS' GROUPS					
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF
unclassified (derived from Burkholderiales)	0,0000	0,0000	0,0278	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0008	0,0000	0,0031	0,0000	0,0007	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0106	0,0000	0,0001	0,0000	0,0000	0,0057	0,0001	0,0005	0,0000	0,0017
Shuttleworthia	0,0000	0,0010	0,0181	0,0041	0,0001	0,0036	0,0014	0,0043	0,1215	0,0541	0,0022	0,0278	0,0005	0,0077	0,0008	0,0000	0,0001	0,0221	0,0270	0,0004	0,0124	0,0039	0,1356	0,0031	0,0041	0,0054	0,0341	0,0054	0,0146	0,0267
Turicella	0,0000	0,0002	0,0001	0,0005	0,0003	0,0214	0,0002	0,0015	0,0035	0,0000	0,0004	0,0001	0,0002	0,0003	0,0001	0,0001	0,0000	0,0092	0,0015	0,0005	0,0000	0,0021	0,0003	0,0008	0,0004	0,0053	0,0012	0,0003	0,0024	0,0008
Peptococcus	0,0000	0,0403	0,0001	0,0001	0,0001	0,0004	0,0158	0,0000	0,0073	0,0088	0,0163	0,0016	0,0002	0,0217	0,0000	0,0045	0,0000	0,1215	0,0001	0,0752	0,0215	0,0000	0,1133	0,0261	0,0240	0,0052	0,0089	0,0097	0,0248	0,0395
Prolixibacter	0,0021	0,0066	0,0138	0,0006	0,0066	0,0006	0,0053	0,0072	0,0020	0,0299	0,0168	0,0376	0,0001	0,0348	0,0017	0,0715	0,0131	0,0112	0,0038	0,0444	0,0160	0,0023	0,0847	0,0065	0,0071	0,0052	0,0092	0,0196	0,0092	0,0243
Thermincola	0,0000	0,0002	0,0001	0,0001	0,0000	0,0209	0,0003	0,0001	0,0001	0,0008	0,0001	0,0001	0,0000	0,0000	0,0000	0,0004	0,0000	0,0004	0,0009	0,0009	0,0090	0,0017	0,0014	0,0002	0,0001	0,0051	0,0003	0,0001	0,0004	0,0022
Pseudochrobactrum	0,0000	0,0064	0,0058	0,0000	0,0096	0,0055	0,0151	0,0000	0,0005	0,0112	0,0108	0,0320	0,0000	0,0183	0,0027	0,0015	0,0009	0,0132	0,0030	0,0109	0,0323	0,0297	0,0000	0,0163	0,0005	0,0049	0,0077	0,0109	0,0042	0,0168
Pectobacterium	0,0000	0,0006	0,0003	0,0000	0,0290	0,0001	0,0027	0,0018	0,0011	0,0066	0,0004	0,0075	0,0000	0,0048	0,0015	0,0038	0,0246	0,0002	0,0012	0,0000	0,0001	0,0000	0,0000	0,0002	0,0001	0,0048	0,0028	0,0021	0,0109	0,0001
Coprococcus	0,0000	0,0015	0,0121	0,0127	0,0000	0,0001	0,0008	0,0033	0,0439	0,0000	0,0004	0,0000	0,0079	0,0001	0,0024	0,0000	0,0004	0,0035	0,0051	0,0001	0,0003	0,0028	0,0146	0,0016	0,0005	0,0048	0,0097	0,0020	0,0028	0,0036
Thermoanaerobacter	0,0000	0,0006	0,0008	0,0017	0,0002	0,0171	0,0011	0,0002	0,0051	0,0001	0,0014	0,0000	0,0000	0,0005	0,0001	0,0002	0,0001	0,0007	0,0021	0,0107	0,0004	0,0008	0,0002	0,0183	0,0059	0,0046	0,0015	0,0006	0,0010	0,0066
Microbacterium	0,0005	0,0044	0,0004	0,0005	0,0018	0,0143	0,0016	0,0013	0,0030	0,0006	0,0030	0,0005	0,0006	0,0009	0,0003	0,0004	0,0030	0,0094	0,0106	0,0064	0,0002	0,0038	0,0044	0,0022	0,0007	0,0045	0,0016	0,0015	0,0071	0,0029
Methylococcus	0,0000	0,0000	0,0182	0,0001	0,0020	0,0012	0,0000	0,0001	0,0100	0,0027	0,0001	0,0456	0,0002	0,0747	0,0019	0,0076	0,0000	0,0149	0,0038	0,0458	0,0080	0,0264	0,0152	0,0017	0,0578	0,0044	0,0024	0,0173	0,0045	0,0207
Agromyces	0,0001	0,0007	0,0001	0,0010	0,0007	0,0164	0,0032	0,0040	0,0032	0,0001	0,0010	0,0002	0,0026	0,0002	0,0002	0,0082	0,0000	0,0046	0,0041	0,0036	0,0001	0,0216	0,0006	0,0041	0,0123	0,0043	0,0029	0,0014	0,0025	0,0074
unclassified (derived from Rhodocyclaceae)	0,0000	0,0000	0,0193	0,0000	0,0001	0,0013	0,0000	0,0001	0,0000	0,0001	0,0003	0,0014	0,0000	0,0012	0,0000	0,0002	0,0006	0,0001	0,0000	0,0000	0,0011	0,0000	0,0001	0,0008	0,0029	0,0043	0,0000	0,0005	0,0003	0,0007
Zymomonas	0,0000	0,0002	0,0183	0,0001	0,0012	0,0009	0,0080	0,0004	0,0053	0,0029	0,0001	0,0108	0,0000	0,0024	0,0010	0,0091	0,0000	0,0062	0,0000	0,0539	0,0173	0,0080	0,0120	0,0206	0,0237	0,0042	0,0046	0,0022	0,0013	0,0198
unclassified (derived from Deltaproteobacteria)	0,0001	0,0029	0,0019	0,0123	0,0010	0,0054	0,0022	0,0044	0,0188	0,0061	0,0093	0,0061	0,0054	0,0112	0,0005	0,0056	0,0015	0,0453	0,0036	0,0186	0,0189	0,0036	0,1092	0,0151	0,0074	0,0042	0,0067	0,0072	0,0112	0,0286
Pseudomonas	0,0003	0,0030	0,0040	0,0001	0,0157	0,0016	0,0065	0,0009	0,0037	0,0087	0,0011	0,0087	0,0001	0,0141	0,0057	0,0105	0,0037	0,0019	0,0028	0,0015	0,0012	0,0022	0,0005	0,0010	0,0027	0,0042	0,0049	0,0048	0,0030	0,0014
Tenacibaculum	0,0000	0,0125	0,0004	0,0003	0,0133	0,0007	0,0242	0,0007	0,0064	0,0188	0,0008	0,0100	0,0000	0,0305	0,0106	0,0035	0,0075	0,0002	0,0050	0,0014	0,0008	0,0001	0,0020	0,0002	0,0019	0,0040	0,0137	0,0075	0,0051	0,0009
unclassified (derived from Epsilonproteobacteria)	0,0000	0,0011	0,0046	0,0002	0,0008	0,0114	0,0005	0,0075	0,0182	0,0038	0,0003	0,0024	0,0004	0,0068	0,0002	0,0209	0,0002	0,0065	0,0091	0,0662	0,0021	0,0116	0,0047	0,0175	0,0063	0,0040	0,0063	0,0026	0,0048	0,0157
Tsakumurella	0,0000	0,0025	0,0002	0,0000	0,0009	0,0141	0,0017	0,0003	0,0018	0,0002	0,0037	0,0000	0,0000	0,0003	0,0023	0,0001	0,0018	0,0024	0,0059	0,0001	0,0001	0,0080	0,0007	0,0001	0,0000	0,0039	0,0011	0,0017	0,0034	0,0019
Vibrio	0,0001	0,0028	0,0007	0,0000	0,0203	0,0004	0,0054	0,0002	0,0031	0,0085	0,0008	0,0064	0,0000	0,0035	0,0084	0,0216	0,0347	0,0008	0,0018	0,0001	0,0002	0,0004	0,0000	0,0003	0,0005	0,0039	0,0041	0,0036	0,0155	0,0003
Providencia	0,0024	0,0075	0,0005	0,0026	0,0106	0,0017	0,0096	0,0032	0,0046	0,0062	0,0023	0,0070	0,0005	0,0045	0,0044	0,0089	0,0519	0,0006	0,0060	0,0003	0,0004	0,0008	0,0001	0,0013	0,0031	0,0038	0,0064	0,0034	0,0243	0,0009
Aromatoleum	0,0000	0,0004	0,0020	0,0001	0,0165	0,0021	0,0007	0,0004	0,0040	0,0034	0,0007	0,0218	0,0001	0,0308	0,0102	0,0195	0,0100	0,0019	0,0016	0,0095	0,0019	0,0008	0,0039	0,0006	0,0121	0,0036	0,0017	0,0097	0,0052	0,0035
Bavariicoccus	0,0197	0,0030	0,0006	0,0050	0,0005	0,0003	0,0024	0,0052	0,0087	0,0014	0,0067	0,0008	0,0048	0,0003	0,0161	0,0088	0,0076	0,0064	0,0027	0,0012	0,0000	0,0011	0,0008	0,0124	0,0313	0,0036	0,0042	0,0059	0,0055	0,0068
Weeksella	0,0001	0,0077	0,0024	0,0001	0,0118	0,0007	0,0113	0,0034	0,0046	0,0172	0,0548	0,0047	0,0000	0,0202	0,0038	0,0166	0,0000	0,0057	0,0062	0,0042	0,0186	0,0101	0,0005	0,0052	0,0066	0,0035	0,0089	0,0250	0,0035	0,0076
Alloscardovia	0,0234	0,0004	0,0004	0,0002	0,0000	0,0032	0,0022	0,0002	0,0004	0,0000	0,0000	0,0001	0,0011	0,0007	0,0000	0,0000	0,0001	0,0405	0,0007	0,0000	0,0000	0,0054	0,0014	0,0001	0,0005	0,0035	0,0010	0,0003	0,0085	0,0015
Chromobacterium	0,0001	0,0007	0,0065	0,0001	0,0105	0,0011	0,0026	0,0021	0,0026	0,0165	0,0055	0,0060	0,0001	0,0064	0,0827	0,0030	0,0104	0,0060	0,0005	0,0014	0,0017	0,0018	0,0020	0,0009	0,0002	0,0034	0,0048	0,0136	0,0058	0,0014
Micromonospora	0,0003	0,0025	0,0004	0,0014	0,0004	0,0110	0,0020	0,0016	0,0433	0,0002	0,0012	0,0003	0,0005	0,0011	0,0005	0,0005	0,0020	0,0049	0,0019	0,0007	0,0001	0,0031	0,0003	0,0050	0,0017	0,0033	0,0096	0,0008	0,0026	0,0022
IsotERICOLA	0,0001	0,0001	0,0000	0,0002	0,0000	0,0135	0,0001	0,0002	0,0002	0,0000	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0002	0,0002	0,0000	0,0000	0,0001	0,0002	0,0013	0,0001	0,0033	0,0001	0,0001	0,0001	0,0004
Prausserella	0,0000	0,0242	0,0000	0,0000	0,0008	0,0003	0,0000	0,0109	0,0134	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0050	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0033	0,0055	0,0003	0,0001	0,0016

GENUS	SUBJECTS' SITES																								SUBJECTS' GROUPS					
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF
Cyanobium	0,0000	0,0006	0,0126	0,0016	0,0000	0,0012	0,0006	0,0028	0,0076	0,0000	0,0001	0,0003	0,0008	0,0000	0,0006	0,0000	0,0000	0,0050	0,0073	0,0000	0,0011	0,0021	0,0305	0,0010	0,0005	0,0032	0,0024	0,0003	0,0037	0,0060
Azospirillum	0,0235	0,0007	0,0018	0,0003	0,0007	0,0002	0,0002	0,0007	0,0040	0,0007	0,0002	0,0015	0,0000	0,0031	0,0002	0,0001	0,0004	0,0003	0,0122	0,1560	0,0005	0,0036	0,0017	0,0108	0,0124	0,0032	0,0012	0,0007	0,0048	0,0218
Thermobifida	0,0017	0,0008	0,0001	0,0005	0,0003	0,0112	0,0012	0,0061	0,0061	0,0000	0,0001	0,0002	0,0004	0,0004	0,0001	0,0000	0,0001	0,0005	0,0017	0,0013	0,0002	0,0009	0,0002	0,0021	0,0013	0,0031	0,0032	0,0002	0,0008	0,0010
Vagococcus	0,0111	0,0036	0,0006	0,0051	0,0017	0,0007	0,0013	0,0087	0,0091	0,0012	0,0078	0,0020	0,0107	0,0003	0,0069	0,0055	0,0177	0,0049	0,0052	0,0007	0,0001	0,0019	0,0010	0,0282	0,0129	0,0031	0,0047	0,0064	0,0104	0,0091
Aminobacterium	0,0000	0,0001	0,0076	0,0053	0,0002	0,0018	0,0010	0,0003	0,0044	0,0002	0,0000	0,0044	0,0002	0,0011	0,0001	0,0000	0,0000	0,0010	0,0039	0,0003	0,0001	0,0044	0,2545	0,0002	0,0004	0,0029	0,0013	0,0007	0,0017	0,0437
Micrococcus	0,0015	0,0006	0,0004	0,0013	0,0004	0,0095	0,0138	0,0021	0,0039	0,0011	0,0223	0,0005	0,0242	0,0029	0,0002	0,0024	0,0001	0,0024	0,0222	0,0003	0,0004	0,0006	0,0123	0,0021	0,2422	0,0029	0,0067	0,0136	0,0088	0,0276
Alcaligenes	0,0009	0,0020	0,0004	0,0000	0,0134	0,0007	0,0012	0,0002	0,0033	0,0054	0,0010	0,0026	0,0000	0,0079	0,0140	0,0024	0,0040	0,0008	0,0006	0,0000	0,0000	0,0001	0,0000	0,0001	0,0007	0,0028	0,0020	0,0037	0,0021	0,0001
Actinomyces	0,0001	0,0010	0,0001	0,0002	0,0016	0,0094	0,0012	0,0019	0,0052	0,0002	0,0028	0,0001	0,0004	0,0003	0,0011	0,0000	0,0069	0,0030	0,0030	0,0001	0,0000	0,0018	0,0012	0,0011	0,0006	0,0027	0,0020	0,0013	0,0046	0,0010
Cellulomicrobium	0,0004	0,0031	0,0007	0,0022	0,0021	0,0060	0,0029	0,0056	0,0131	0,0003	0,0278	0,0000	0,0023	0,0008	0,0048	0,0007	0,0121	0,0062	0,0077	0,0005	0,0004	0,0074	0,0012	0,0041	0,0019	0,0027	0,0052	0,0114	0,0093	0,0031
Arcobacter	0,0001	0,0085	0,0016	0,0000	0,0074	0,0002	0,0089	0,0003	0,0031	0,0162	0,0603	0,0042	0,0000	0,0038	0,0051	0,0165	0,0015	0,0117	0,0006	0,0009	0,0021	0,0015	0,0001	0,0026	0,0008	0,0026	0,0067	0,0246	0,0032	0,0015
Candidatus Desulforudis	0,0003	0,0000	0,0000	0,0000	0,0000	0,0108	0,0000	0,0000	0,0086	0,0000	0,0000	0,0004	0,0000	0,0000	0,0000	0,0000	0,0000	0,0070	0,0167	0,0150	0,0001	0,0047	0,0416	0,0018	0,0094	0,0026	0,0017	0,0001	0,0077	0,0110
Lactococcus	0,0100	0,0056	0,0010	0,0014	0,0006	0,0007	0,0025	0,0014	0,0048	0,0039	0,0029	0,0004	0,0005	0,0013	0,0143	0,0023	0,0119	0,0813	0,0017	0,0004	0,0005	0,0198	0,0020	0,0170	0,0014	0,0025	0,0029	0,0032	0,0222	0,0091
Thiomonas	0,0005	0,0003	0,0003	0,0003	0,0052	0,0059	0,0004	0,0001	0,0043	0,0010	0,0042	0,0033	0,0001	0,0005	0,0078	0,0005	0,0075	0,0015	0,0003	0,0000	0,0000	0,0002	0,0000	0,0003	0,0000	0,0024	0,0012	0,0030	0,0036	0,0001
Tetragenococcus	0,0001	0,0010	0,0007	0,0008	0,0001	0,0084	0,0004	0,0003	0,0192	0,0000	0,0002	0,0016	0,0012	0,0005	0,0027	0,0002	0,0247	0,0222	0,0020	0,0008	0,0005	0,0030	0,0133	0,0010	0,0044	0,0024	0,0039	0,0009	0,0157	0,0037
Collimonas	0,0015	0,0033	0,0003	0,0000	0,0095	0,0011	0,0013	0,0002	0,0042	0,0034	0,0015	0,0146	0,0000	0,0011	0,0222	0,0015	0,0060	0,0028	0,0005	0,0000	0,0000	0,0001	0,0000	0,0002	0,0000	0,0024	0,0019	0,0051	0,0033	0,0001
Trichococcus	0,0082	0,0029	0,0025	0,0015	0,0018	0,0005	0,0014	0,0055	0,0092	0,0009	0,0018	0,0003	0,0019	0,0003	0,0062	0,0047	0,0048	0,0065	0,0044	0,0001	0,0001	0,0004	0,0012	0,0041	0,0028	0,0024	0,0039	0,0021	0,0050	0,0016
Caldicellulosiruptor	0,0000	0,0041	0,0007	0,0026	0,0011	0,0047	0,0017	0,0105	0,0031	0,0030	0,0012	0,0018	0,0016	0,0090	0,0003	0,0006	0,0000	0,0119	0,0013	0,0020	0,0151	0,0129	0,0279	0,0040	0,0016	0,0024	0,0045	0,0024	0,0029	0,0112
Pseudobutyviribrio	0,0000	0,0012	0,0037	0,0017	0,0007	0,0045	0,0012	0,0102	0,0073	0,0006	0,0006	0,0003	0,0003	0,0010	0,0044	0,0004	0,0004	0,0077	0,0014	0,0022	0,0005	0,0053	0,0064	0,0025	0,0011	0,0024	0,0047	0,0010	0,0023	0,0033
Leifsonia	0,0013	0,0016	0,0004	0,0004	0,0011	0,0071	0,0033	0,0019	0,0068	0,0001	0,0008	0,0003	0,0005	0,0005	0,0006	0,0001	0,0012	0,0012	0,0038	0,0003	0,0001	0,0012	0,0004	0,0018	0,0009	0,0024	0,0031	0,0006	0,0022	0,0009
Tissierella	0,0025	0,0077	0,0003	0,0034	0,0002	0,0020	0,0010	0,0005	0,0150	0,0014	0,0022	0,0022	0,0010	0,0050	0,0002	0,0004	0,0000	0,0551	0,0142	0,1219	0,0010	0,0032	0,0496	0,0125	0,0064	0,0024	0,0037	0,0020	0,0165	0,0260
Aeriscardovia	0,0195	0,0000	0,0008	0,0000	0,0000	0,0003	0,0012	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0027	0,0001	0,0001	0,0002	0,0023	0,0005	0,0000	0,0001	0,0006
Variovorax	0,0004	0,0006	0,0067	0,0000	0,0043	0,0005	0,0009	0,0002	0,0012	0,0049	0,0004	0,0025	0,0000	0,0039	0,0062	0,0032	0,0010	0,0001	0,0003	0,0000	0,0002	0,0000	0,0000	0,0001	0,0001	0,0023	0,0014	0,0019	0,0006	0,0001
Cupriavidus	0,0008	0,0013	0,0050	0,0000	0,0047	0,0006	0,0008	0,0002	0,0039	0,0029	0,0034	0,0029	0,0000	0,0022	0,0100	0,0002	0,0082	0,0028	0,0004	0,0002	0,0002	0,0044	0,0001	0,0005	0,0002	0,0022	0,0016	0,0031	0,0042	0,0011
Butyricimonas	0,0000	0,0002	0,0011	0,0059	0,0006	0,0037	0,0006	0,0010	0,0075	0,0017	0,0002	0,0103	0,0004	0,0020	0,0002	0,0008	0,0000	0,0026	0,0233	0,0194	0,0267	0,0023	0,0182	0,0177	0,0001	0,0022	0,0022	0,0017	0,0092	0,0143
Agrococcus	0,0000	0,0000	0,0000	0,0000	0,0000	0,0091	0,0000	0,0001	0,0000	0,0004	0,0000	0,0041	0,0000	0,0000	0,0001	0,0000	0,0001	0,0002	0,0001	0,0000	0,0001	0,0001	0,0025	0,0000	0,0000	0,0022	0,0001	0,0005	0,0001	0,0005
Kineococcus	0,0000	0,0147	0,0000	0,0000	0,0001	0,0005	0,0001	0,0001	0,0002	0,0000	0,0005	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0012	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0020	0,0001	0,0002	0,0005	0,0000
Carnobacterium	0,0033	0,0038	0,0009	0,0032	0,0017	0,0008	0,0018	0,0067	0,0114	0,0040	0,0115	0,0028	0,0032	0,0010	0,0090	0,0048	0,0086	0,0121	0,0046	0,0004	0,0002	0,0024	0,0064	0,0162	0,0018	0,0020	0,0053	0,0066	0,0078	0,0059
Alicyclobacillus	0,0000	0,0004	0,0005	0,0005	0,0000	0,0069	0,0001	0,0000	0,0142	0,0002	0,0001	0,0028	0,0000	0,0000	0,0000	0,0000	0,0002	0,0151	0,0002	0,0022	0,0006	0,0021	0,0100	0,0002	0,0038	0,0019	0,0028	0,0004	0,0032	0,0029
Phocoenobacter	0,0000	0,0012	0,0015	0,0000	0,0064	0,0015	0,0010	0,0019	0,0034	0,0014	0,0081	0,0015	0,0000	0,0102	0,0069	0,0220	0,0025	0,0144	0,0024	0,0016	0,0010	0,0059	0,0000	0,0040	0,0038	0,0019	0,0018	0,0066	0,0049	0,0030
Microscilla	0,0056	0,0095	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0004	0,0001	0,0000	0,0009	0,0000	0,0001	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0018	0,0003	0,0018	0,0000	0,0003	0,0001	0,0005
Photorhabdus	0,0000	0,0006	0,0049	0,0000	0,0045	0,0000	0,0015	0,0001	0,0007	0,0002	0,0009	0,0020	0,0000	0,0007	0,0005	0,0004	0,0011	0,0003	0,0003	0,0000	0,0000	0,0003	0,0000	0,0010	0,0002	0,0018	0,0008	0,0008	0,0006	0,0003
Actinoplanes	0,0000	0,0006	0,0000	0,0000	0,0000	0,0072	0,0095	0,0015	0,0015	0,0012	0,0062	0,0000	0,0008	0,0001	0,0008	0,0000	0,0002	0,0683	0,0013	0,0002	0,0000	0,0071	0,0000	0,0006	0,0496	0,0018	0,0045	0,0025	0,0145	0,0068
Xenophilus	0,0000	0,0000	0,0084	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0006	0,0000	0,0006	0,0000	0,0003	0,0000	0,0062	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0017	0,0001	0,0004	0,0000	0,0000

GENUS	SUBJECTS' SITES																										SUBJECTS' GROUPS				
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF	
Bulleidia	0,0001	0,0005	0,0010	0,0056	0,0001	0,0022	0,0001	0,0005	0,0097	0,0003	0,0009	0,0053	0,0003	0,0004	0,0000	0,0001	0,0000	0,0777	0,0062	0,1414	0,0005	0,0002	0,0927	0,0314	0,0198	0,0017	0,0021	0,0011	0,0182	0,0407	
Delftia	0,0000	0,0000	0,0080	0,0000	0,0003	0,0000	0,0000	0,0000	0,0001	0,0002	0,0000	0,0006	0,0000	0,0003	0,0003	0,0014	0,0006	0,0002	0,0000	0,0000	0,0010	0,0005	0,0000	0,0000	0,0000	0,0017	0,0001	0,0002	0,0003	0,0003	
Microtetraspora	0,0011	0,0005	0,0003	0,0005	0,0048	0,0025	0,0017	0,0041	0,0056	0,0001	0,0013	0,0002	0,0018	0,0021	0,0004	0,0001	0,0028	0,0002	0,0043	0,0001	0,0001	0,0006	0,0001	0,0096	0,0024	0,0017	0,0028	0,0012	0,0028	0,0028	
Legionella	0,0000	0,0009	0,0003	0,0001	0,0074	0,0014	0,0020	0,0004	0,0010	0,0015	0,0006	0,0068	0,0000	0,0113	0,0010	0,0005	0,0033	0,0004	0,0007	0,0002	0,0007	0,0002	0,0002	0,0002	0,0027	0,0017	0,0013	0,0029	0,0017	0,0005	
Candidatus Aquiluna	0,0000	0,0129	0,0000	0,0001	0,0000	0,0001	0,0005	0,0001	0,0003	0,0001	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0002	0,0003	0,0000	0,0000	0,0000	0,0027	0,0000	0,0000	0,0017	0,0003	0,0000	0,0001	0,0005	
Kribbella	0,0075	0,0005	0,0005	0,0004	0,0011	0,0019	0,0009	0,0008	0,0080	0,0002	0,0053	0,0002	0,0002	0,0011	0,0002	0,0011	0,0041	0,0089	0,0009	0,0007	0,0002	0,0158	0,0004	0,0010	0,0026	0,0017	0,0022	0,0022	0,0039	0,0041	
Halothermothrix	0,0000	0,0008	0,0068	0,0000	0,0001	0,0004	0,0001	0,0001	0,0001	0,0001	0,0000	0,0023	0,0001	0,0001	0,0000	0,0001	0,0003	0,0031	0,0013	0,0000	0,0001	0,0099	0,1886	0,0002	0,0003	0,0016	0,0001	0,0003	0,0012	0,0338	
Kinetoplastibacterium	0,0004	0,0015	0,0000	0,0000	0,0075	0,0007	0,0008	0,0001	0,0042	0,0007	0,0004	0,0014	0,0000	0,0006	0,0148	0,0007	0,0047	0,0004	0,0003	0,0000	0,0000	0,0001	0,0017	0,0001	0,0000	0,0016	0,0013	0,0022	0,0022	0,0003	
Propionigenium	0,0000	0,0017	0,0005	0,0059	0,0002	0,0012	0,0007	0,0006	0,0001	0,0004	0,0002	0,0005	0,0004	0,0009	0,0001	0,0004	0,0000	0,0006	0,0004	0,0001	0,0024	0,0005	0,0015	0,0001	0,0003	0,0016	0,0005	0,0004	0,0003	0,0008	
Basfia	0,0001	0,0010	0,0004	0,0000	0,0038	0,0031	0,0008	0,0001	0,0008	0,0018	0,0009	0,0033	0,0000	0,0018	0,0009	0,0029	0,0013	0,0052	0,0005	0,0002	0,0004	0,0005	0,0001	0,0003	0,0010	0,0016	0,0008	0,0012	0,0018	0,0004	
Acidovorax	0,0000	0,0000	0,0074	0,0000	0,0000	0,0001	0,0001	0,0003	0,0002	0,0005	0,0001	0,0026	0,0000	0,0003	0,0003	0,0021	0,0001	0,0001	0,0000	0,0000	0,0079	0,0000	0,0002	0,0000	0,0000	0,0015	0,0002	0,0005	0,0001	0,0013	
Thiobacillus	0,0001	0,0011	0,0010	0,0000	0,0067	0,0005	0,0022	0,0003	0,0009	0,0317	0,0040	0,0028	0,0000	0,0030	0,0048	0,0024	0,0047	0,0019	0,0003	0,0001	0,0001	0,0001	0,0000	0,0007	0,0001	0,0015	0,0063	0,0030	0,0025	0,0002	
Janthinobacterium	0,0002	0,0014	0,0000	0,0000	0,0070	0,0008	0,0008	0,0004	0,0027	0,0022	0,0000	0,0043	0,0000	0,0010	0,0122	0,0014	0,0022	0,0018	0,0004	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0015	0,0013	0,0022	0,0014	0,0001	
unclassified (derived from Erysipelotrichaceae)	0,0000	0,0016	0,0015	0,0036	0,0004	0,0014	0,0003	0,0008	0,0023	0,0053	0,0004	0,0055	0,0019	0,0094	0,0006	0,0006	0,0005	0,0155	0,0018	0,0065	0,0019	0,0018	0,0264	0,0022	0,0030	0,0015	0,0016	0,0027	0,0041	0,0067	
Aquitalea	0,0000	0,0009	0,0008	0,0001	0,0069	0,0003	0,0027	0,0009	0,0003	0,1132	0,0032	0,0481	0,0000	0,0022	0,0030	0,1564	0,0000	0,0857	0,0000	0,0000	0,0000	0,0000	0,0000	0,0011	0,0001	0,0015	0,0200	0,0151	0,0175	0,0003	
Shewanella	0,0000	0,0015	0,0004	0,0001	0,0071	0,0002	0,0054	0,0001	0,0017	0,0029	0,0032	0,0028	0,0000	0,0062	0,0020	0,0044	0,0245	0,0007	0,0007	0,0002	0,0005	0,0002	0,0000	0,0004	0,0007	0,0015	0,0029	0,0029	0,0107	0,0003	
Leptospira	0,0002	0,0039	0,0003	0,0014	0,0008	0,0019	0,0027	0,0005	0,1704	0,0052	0,0023	0,0017	0,0011	0,0107	0,0007	0,0008	0,0016	0,0170	0,0003	0,0140	0,0113	0,0011	0,0205	0,0101	0,0034	0,0014	0,0351	0,0030	0,0042	0,0099	
Robinsoniella	0,0000	0,0100	0,0002	0,0002	0,0001	0,0002	0,0034	0,0001	0,0026	0,0028	0,0034	0,0005	0,0003	0,0087	0,0000	0,0015	0,0000	0,0219	0,0001	0,0280	0,0057	0,0000	0,0277	0,0083	0,0091	0,0014	0,0022	0,0028	0,0045	0,0115	
Leptolyngbya	0,0000	0,0000	0,0000	0,0000	0,0000	0,0056	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0036	0,0009	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0014	0,0000	0,0000	0,0011	0,0001	
Methylophaga	0,0000	0,0000	0,0018	0,0000	0,0016	0,0029	0,0001	0,0000	0,0006	0,0009	0,0012	0,0148	0,0001	0,0029	0,0001	0,0066	0,0002	0,0005	0,0000	0,0045	0,0322	0,0023	0,0030	0,0023	0,0243	0,0013	0,0003	0,0030	0,0002	0,0096	
Rathayibacter	0,0001	0,0021	0,0002	0,0010	0,0001	0,0033	0,0004	0,0081	0,0039	0,0000	0,0091	0,0000	0,0056	0,0001	0,0001	0,0001	0,0015	0,0016	0,0093	0,0001	0,0002	0,0014	0,0000	0,0139	0,0828	0,0013	0,0030	0,0045	0,0044	0,0123	
Weissella	0,0026	0,0008	0,0004	0,0016	0,0024	0,0007	0,0008	0,0070	0,0036	0,0004	0,0013	0,0015	0,0022	0,0008	0,0010	0,0017	0,0432	0,0109	0,0023	0,0095	0,0004	0,0001	0,0119	0,0091	0,0025	0,0013	0,0029	0,0014	0,0214	0,0056	
Peptostreptococcus	0,0000	0,0080	0,0002	0,0007	0,0001	0,0004	0,0006	0,0008	0,0013	0,0027	0,0098	0,0304	0,0013	0,0048	0,0002	0,0005	0,0000	0,1247	0,0150	1,0559	0,0024	0,0129	0,2565	0,0022	0,1809	0,0013	0,0011	0,0081	0,0311	0,1782	
Thalassospira	0,0000	0,0000	0,0000	0,0000	0,0080	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0013	0,0000	0,0000	0,0000	0,0000	
Caloramator	0,0046	0,0002	0,0005	0,0020	0,0004	0,0009	0,0003	0,0012	0,0013	0,0004	0,0000	0,0005	0,0021	0,0013	0,0001	0,0000	0,0000	0,0050	0,0019	0,0014	0,0140	0,0003	0,0005	0,0003	0,0011	0,0012	0,0008	0,0007	0,0017	0,0027	
Labrenzia	0,0000	0,0000	0,0040	0,0000	0,0002	0,0016	0,0000	0,0000	0,0006	0,0000	0,0000	0,0089	0,0000	0,0000	0,0000	0,0046	0,0004	0,0000	0,0000	0,0000	0,0011	0,0000	0,0000	0,0000	0,0093	0,0012	0,0001	0,0013	0,0002	0,0011	
Odoribacter	0,0000	0,0005	0,0053	0,0000	0,0001	0,0002	0,0058	0,0002	0,0007	0,0128	0,0042	0,0129	0,0001	0,0019	0,0002	0,0246	0,0000	0,0004	0,0002	0,0013	0,0059	0,0000	0,0187	0,0012	0,0000	0,0012	0,0045	0,0046	0,0002	0,0045	
Globicatella	0,0001	0,0036	0,0007	0,0006	0,0024	0,0004	0,0006	0,0029	0,0009	0,0034	0,0021	0,0003	0,0010	0,0009	0,0362	0,0638	0,0000	0,0497	0,0000	0,0000	0,0000	0,0000	0,0001	0,0016	0,0000	0,0012	0,0017	0,0086	0,0102	0,0004	
Salinivibrio	0,0000	0,0000	0,0000	0,0000	0,0001	0,0049	0,0000	0,0000	0,0000	0,0020	0,0000	0,0055	0,0000	0,0052	0,0000	0,0000	0,0000	0,0015	0,0000	0,1466	0,0035	0,0087	0,0017	0,0032	0,0000	0,0012	0,0003	0,0014	0,0003	0,0192	
Thauera	0,0000	0,0001	0,0009	0,0000	0,0060	0,0002	0,0006	0,0012	0,0003	0,0008	0,0005	0,0009	0,0000	0,0016	0,0020	0,0009	0,0002	0,0009	0,0000	0,0000	0,0001	0,0001	0,0001	0,0131	0,0001	0,0012	0,0007	0,0008	0,0003	0,0033	
Alistipes	0,0000	0,0005	0,0022	0,0005	0,0006	0,0020	0,0007	0,0066	0,0007	0,0038	0,0018	0,0176	0,0011	0,0045	0,0000	0,0019	0,0000	0,0043	0,0002	0,0464	0,0297	0,0020	0,0243	0,0049	0,0026	0,0012	0,0028	0,0037	0,0010	0,0156	
Syntrophomonas	0,0000	0,0007	0,0001	0,0033	0,0012	0,0013	0,0011	0,0003	0,0004	0,0001	0,0001	0,0020	0,0001	0,0021	0,0000	0,0001	0,0001	0,0387	0,0015	0,0001	0,0009	0,0007	0,0149	0,0079	0,0018	0,0011	0,0006	0,0006	0,0085	0,0050	
Azospira	0,0000	0,0000	0,0005	0,0000	0,0064	0,0000	0,0000	0,0000	0,0001	0,0002	0,0000	0,0002	0,0000	0,0004	0,0001	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0011	0,0001	0,0001	0,0000	0,0000	

GENUS	SUBJECTS' SITES																								SUBJECTS' GROUPS					
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF
Oxobacter	0,0000	0,0000	0,0053	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0023	0,0013	0,0000	0,0000	0,0000	0,0000	0,0017	0,0009	0,0001	0,0000	0,0066	0,1816	0,0000	0,0000	0,0011	0,0000	0,0005	0,0007	0,0318
Alkalispirillum	0,0000	0,0001	0,0039	0,0016	0,0002	0,0000	0,0048	0,0076	0,0042	0,0006	0,0000	0,0018	0,0035	0,0070	0,0027	0,0006	0,0001	0,0000	0,0025	0,0013	0,0002	0,0000	0,0068	0,0085	0,0254	0,0011	0,0048	0,0023	0,0010	0,0060
Coprobacillus	0,0000	0,0000	0,0000	0,0000	0,0000	0,0044	0,0004	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0000	0,0000	0,0002	0,0000	0,0005	0,0025	0,0000	0,0011	0,0001	0,0000	0,0001	0,0008
Curtobacterium	0,0000	0,0004	0,0000	0,0000	0,0021	0,0028	0,0003	0,0006	0,0123	0,0003	0,0006	0,0002	0,0000	0,0003	0,0033	0,0001	0,0019	0,0011	0,0015	0,0000	0,0000	0,0032	0,0001	0,0001	0,0004	0,0011	0,0027	0,0007	0,0016	0,0008
unclassified (derived from Ruminococcaceae)	0,0000	0,0012	0,0036	0,0009	0,0000	0,0001	0,0038	0,0050	0,0001	0,0010	0,0003	0,0004	0,0026	0,0002	0,0001	0,0000	0,0000	0,0035	0,0006	0,0019	0,0084	0,0001	0,0038	0,0043	0,0001	0,0011	0,0029	0,0007	0,0009	0,0033
Alkaliphilus	0,0006	0,0021	0,0003	0,0005	0,0005	0,0020	0,0012	0,0004	0,0050	0,0076	0,0017	0,0017	0,0002	0,0125	0,0000	0,0018	0,0002	0,0330	0,0011	0,0438	0,0064	0,0004	0,0986	0,0103	0,0068	0,0010	0,0028	0,0028	0,0072	0,0256
Coxiella	0,0000	0,0000	0,0025	0,0001	0,0022	0,0006	0,0000	0,0001	0,0006	0,0012	0,0000	0,0031	0,0000	0,0067	0,0000	0,0050	0,0002	0,0003	0,0001	0,0205	0,0075	0,0115	0,0038	0,0001	0,0156	0,0010	0,0004	0,0016	0,0002	0,0081
Avibacterium	0,0001	0,0008	0,0023	0,0000	0,0007	0,0014	0,0007	0,0002	0,0001	0,0029	0,0016	0,0012	0,0000	0,0014	0,0011	0,0004	0,0032	0,0002	0,0021	0,0020	0,0022	0,0005	0,0015	0,0023	0,0017	0,0010	0,0008	0,0011	0,0022	0,0017
Mycetocola	0,0000	0,0001	0,0000	0,0000	0,0000	0,0041	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0007	0,0004	0,0000	0,0000	0,0004	0,0007	0,0002	0,0000	0,0010	0,0000	0,0000	0,0003	0,0002
Salinispora	0,0000	0,0003	0,0000	0,0001	0,0000	0,0039	0,0000	0,0001	0,0004	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0009	0,0004	0,0001	0,0000	0,0016	0,0004	0,0000	0,0011	0,0000	0,0010	0,0001	0,0000	0,0005	0,0006
unclassified (derived from Synergistetes)	0,0000	0,0002	0,0001	0,0002	0,0000	0,0037	0,0001	0,0001	0,0000	0,0296	0,0000	0,1002	0,0000	0,0077	0,0000	0,0000	0,0001	0,0335	0,0050	0,0000	0,0022	0,0001	0,2275	0,0079	0,0000	0,0010	0,0049	0,0129	0,0087	0,0405
Herbaspirillum	0,0000	0,0000	0,0000	0,0000	0,0001	0,0039	0,0000	0,0000	0,0001	0,0007	0,0001	0,0001	0,0000	0,0029	0,0000	0,0001	0,0037	0,0000	0,0000	0,0000	0,0038	0,0001	0,0006	0,0014	0,0000	0,0010	0,0001	0,0005	0,0015	0,0011
Arsenophonus	0,0016	0,0001	0,0000	0,0000	0,0001	0,0031	0,0018	0,0002	0,0010	0,0001	0,0001	0,0001	0,0001	0,0257	0,0000	0,0502	0,0532	0,0001	0,0106	0,0004	0,0000	0,0003	0,0002	0,0038	0,0014	0,0009	0,0010	0,0064	0,0264	0,0012
Faecalibacterium	0,0000	0,0000	0,0001	0,0000	0,0000	0,0037	0,0000	0,0000	0,0005	0,0002	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0002	0,0040	0,0002	0,0019	0,0000	0,0001	0,0036	0,0010	0,0000	0,0009	0,0002	0,0001	0,0010	0,0011
Candidatus Phytoplasma	0,0000	0,0031	0,0004	0,0000	0,0002	0,0017	0,0036	0,0003	0,0009	0,0010	0,0021	0,0005	0,0000	0,0030	0,0004	0,0009	0,0002	0,0103	0,0001	0,0091	0,0029	0,0024	0,0146	0,0019	0,0031	0,0009	0,0018	0,0014	0,0022	0,0052
Rhodospirillum	0,0001	0,0006	0,0004	0,0000	0,0045	0,0000	0,0037	0,0000	0,0010	0,0019	0,0009	0,0025	0,0000	0,0009	0,0008	0,0028	0,0043	0,0007	0,0003	0,0000	0,0008	0,0001	0,0001	0,0003	0,0003	0,0009	0,0019	0,0010	0,0021	0,0003
Acholeplasma	0,0000	0,0003	0,0012	0,0021	0,0004	0,0009	0,0003	0,0110	0,0016	0,0004	0,0002	0,0006	0,0040	0,0037	0,0002	0,0003	0,0001	0,0060	0,0080	0,0095	0,0228	0,0040	0,0116	0,0034	0,0024	0,0009	0,0034	0,0015	0,0043	0,0085
Leucobacter	0,0001	0,0009	0,0001	0,0002	0,0002	0,0028	0,0002	0,0004	0,0010	0,0001	0,0009	0,0001	0,0001	0,0002	0,0007	0,0051	0,0001	0,0088	0,0007	0,0002	0,0001	0,0028	0,0007	0,0028	0,0007	0,0009	0,0004	0,0007	0,0021	0,0015
Actinosynnema	0,0002	0,0002	0,0000	0,0010	0,0001	0,0028	0,0013	0,0012	0,0027	0,0001	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0113	0,0000	0,0017	0,0000	0,0000	0,0000	0,0001	0,0000	0,0002	0,0009	0,0013	0,0000	0,0054	0,0000
Ornithobacterium	0,0000	0,0012	0,0002	0,0000	0,0001	0,0026	0,0005	0,0002	0,0012	0,0072	0,0002	0,0033	0,0000	0,0077	0,0001	0,0001	0,0000	0,0020	0,0000	0,0484	0,0025	0,0052	0,0067	0,0013	0,0001	0,0008	0,0017	0,0016	0,0004	0,0081
Soehngenia	0,0000	0,0000	0,0004	0,0001	0,0000	0,0028	0,0000	0,0000	0,0083	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0021	0,0001	0,0001	0,0014	0,0000	0,0037	0,0000	0,0002	0,0008	0,0016	0,0000	0,0005	0,0009
Acidithiobacillus	0,0002	0,0010	0,0001	0,0000	0,0029	0,0005	0,0014	0,0000	0,0022	0,0017	0,0018	0,0008	0,0000	0,0004	0,0054	0,0005	0,0018	0,0015	0,0003	0,0001	0,0001	0,0001	0,0001	0,0001	0,0000	0,0008	0,0013	0,0015	0,0012	0,0001
Anaplasma	0,0000	0,0000	0,0000	0,0046	0,0000	0,0000	0,0000	0,0002	0,0000	0,0156	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0112	0,0001	0,0001	0,0000	0,0000	0,0004	0,0001	0,0000	0,0008	0,0026	0,0000	0,0023	0,0001
Smaragdicoscus	0,0000	0,0000	0,0000	0,0000	0,0000	0,0031	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0001	0,0000	0,0007	0,0000	0,0000	0,0002	0,0001
Thermosinus	0,0000	0,0002	0,0001	0,0006	0,0001	0,0024	0,0002	0,0002	0,0002	0,0004	0,0002	0,0004	0,0002	0,0015	0,0000	0,0001	0,0000	0,0117	0,0007	0,0000	0,0015	0,0000	0,0024	0,0006	0,0002	0,0007	0,0002	0,0004	0,0027	0,0008
Aerococcus	0,0000	0,0045	0,0001	0,0006	0,0001	0,0001	0,0011	0,0005	0,0010	0,0020	0,0015	0,0006	0,0004	0,0020	0,0026	0,0012	0,0006	0,0131	0,0003	0,0080	0,0018	0,0001	0,0110	0,0035	0,0061	0,0007	0,0011	0,0014	0,0031	0,0045
Tropheryma	0,0004	0,0006	0,0003	0,0006	0,0008	0,0013	0,0017	0,0029	0,0016	0,0000	0,0006	0,0004	0,0005	0,0005	0,0002	0,0006	0,0048	0,0007	0,0032	0,0044	0,0001	0,0021	0,0238	0,0006	0,0002	0,0007	0,0017	0,0005	0,0034	0,0051
Ralstonia	0,0000	0,0003	0,0008	0,0000	0,0029	0,0001	0,0004	0,0015	0,0006	0,0008	0,0011	0,0086	0,0000	0,0010	0,0040	0,0010	0,0093	0,0007	0,0000	0,0000	0,0000	0,0000	0,0002	0,0002	0,0001	0,0007	0,0008	0,0021	0,0041	0,0001
Brevibacillus	0,0011	0,0003	0,0001	0,0030	0,0001	0,0001	0,0011	0,0006	0,0004	0,0027	0,0020	0,0001	0,0008	0,0001	0,0002	0,0058	0,0002	0,0014	0,0003	0,0012	0,0001	0,0002	0,0029	0,0005	0,0013	0,0007	0,0011	0,0012	0,0005	0,0009
Saccharopolyspora	0,0005	0,0012	0,0001	0,0007	0,0010	0,0009	0,0003	0,0003	0,0022	0,0003	0,0008	0,0000	0,0001	0,0001	0,0019	0,0016	0,0173	0,0001	0,0008	0,0000	0,0002	0,1383	0,0002	0,0009	0,0009	0,0007	0,0007	0,0006	0,0076	0,0300
Sporanaerobacter	0,0008	0,0009	0,0000	0,0027	0,0000	0,0003	0,0001	0,0000	0,0015	0,0005	0,0006	0,0016	0,0003	0,0001	0,0000	0,0001	0,0000	0,0011	0,0025	0,0700	0,0000	0,0002	0,0113	0,0070	0,0035	0,0007	0,0004	0,0005	0,0012	0,0115
Brachybacterium	0,0013	0,0019	0,0000	0,0001	0,0009	0,0006	0,0002	0,0003	0,0026	0,0000	0,0001	0,0000	0,0000	0,0002	0,0007	0,0000	0,0053	0,0002	0,0005	0,0004	0,0000	0,0004	0,0004	0,0000	0,0003	0,0007	0,0007	0,0001	0,0025	0,0002

GENUS	SUBJECTS' SITES																								SUBJECTS' GROUPS					
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF
Azoarcus	0,0000	0,0001	0,0013	0,0000	0,0003	0,0015	0,0002	0,0000	0,0007	0,0062	0,0001	0,0003	0,0000	0,0004	0,0006	0,0679	0,0001	0,0004	0,0009	0,0000	0,0002	0,0000	0,0016	0,0000	0,0008	0,0007	0,0012	0,0035	0,0005	0,0004
Rarobacter	0,0000	0,0001	0,0000	0,0000	0,0000	0,0026	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0040	0,0002	0,0059	0,0007	0,0000	0,0001	0,0000	0,0013
Enterobacter	0,0000	0,0002	0,0024	0,0000	0,0007	0,0000	0,0002	0,0000	0,0002	0,0002	0,0001	0,0033	0,0000	0,0002	0,0001	0,0003	0,0072	0,0016	0,0000	0,0000	0,0000	0,0001	0,0000	0,0006	0,0000	0,0007	0,0002	0,0005	0,0034	0,0002
Cellulophaga	0,0000	0,0004	0,0013	0,0000	0,0017	0,0002	0,0026	0,0001	0,0013	0,0730	0,0270	0,0118	0,0000	0,0258	0,0101	0,0003	0,0006	0,0001	0,0006	0,0006	0,0064	0,0008	0,0001	0,0000	0,0005	0,0007	0,0133	0,0164	0,0005	0,0013
Streptosporangium	0,0000	0,0006	0,0000	0,0001	0,0000	0,0023	0,0002	0,0002	0,0012	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0002	0,0020	0,0004	0,0149	0,0003	0,0055	0,0282	0,0008	0,0000	0,0007	0,0004	0,0000	0,0007	0,0077
Flexibacter	0,0000	0,0027	0,0003	0,0000	0,0015	0,0000	0,0109	0,0000	0,0004	0,0010	0,0003	0,0044	0,0000	0,0025	0,0016	0,0018	0,0031	0,0001	0,0011	0,0004	0,0005	0,0000	0,0040	0,0010	0,0013	0,0006	0,0044	0,0013	0,0017	0,0012
Chelatorans	0,0000	0,0000	0,0018	0,0000	0,0011	0,0004	0,0000	0,0000	0,0001	0,0000	0,0000	0,0009	0,0000	0,0031	0,0001	0,0004	0,0007	0,0002	0,0002	0,0004	0,0047	0,0005	0,0002	0,0002	0,0005	0,0006	0,0000	0,0006	0,0004	0,0010
Lonepinella	0,0000	0,0004	0,0003	0,0000	0,0005	0,0018	0,0002	0,0001	0,0002	0,0001	0,0009	0,0013	0,0000	0,0001	0,0009	0,0003	0,0001	0,0003	0,0002	0,0031	0,0001	0,0001	0,0003	0,0003	0,0002	0,0006	0,0002	0,0006	0,0002	0,0005
Halorhodospira	0,0000	0,0008	0,0002	0,0001	0,0004	0,0016	0,0010	0,0005	0,0003	0,0000	0,0011	0,0003	0,0001	0,0003	0,0001	0,0002	0,0000	0,0006	0,0007	0,0003	0,0001	0,0012	0,0000	0,0007	0,0005	0,0006	0,0006	0,0005	0,0004	0,0005
Escherichia	0,0001	0,0007	0,0003	0,0000	0,0019	0,0005	0,0013	0,0004	0,0005	0,0048	0,0010	0,0006	0,0000	0,0010	0,0016	0,0017	0,0098	0,0010	0,0002	0,0002	0,0001	0,0001	0,0002	0,0003	0,0001	0,0006	0,0015	0,0009	0,0044	0,0002
Aminobacter	0,0000	0,0001	0,0000	0,0001	0,0007	0,0018	0,0004	0,0002	0,0002	0,0004	0,0001	0,0002	0,0000	0,0007	0,0000	0,0000	0,0010	0,0000	0,0001	0,0000	0,0002	0,0002	0,0000	0,0003	0,0001	0,0006	0,0003	0,0002	0,0005	0,0002
Thiorhodovibrio	0,0000	0,0002	0,0008	0,0001	0,0014	0,0004	0,0008	0,0001	0,0005	0,0003	0,0002	0,0009	0,0000	0,0016	0,0001	0,0001	0,0000	0,0002	0,0001	0,0232	0,0002	0,0002	0,0001	0,0003	0,0003	0,0005	0,0005	0,0004	0,0001	0,0027
Pseudoclavibacter	0,0000	0,0005	0,0004	0,0000	0,0003	0,0013	0,0004	0,0002	0,0005	0,0003	0,0005	0,0000	0,0002	0,0004	0,0001	0,0034	0,0002	0,0051	0,0003	0,0002	0,0000	0,0109	0,0007	0,0012	0,0003	0,0005	0,0004	0,0005	0,0012	0,0028
Moraxella	0,0001	0,0001	0,0001	0,0000	0,0001	0,0019	0,0003	0,0002	0,0007	0,0000	0,0001	0,0001	0,0002	0,0000	0,0000	0,6841	0,0008	0,0000	0,0001	0,0000	0,0001	0,0001	0,0002	0,0001	0,0000	0,0005	0,0003	0,0337	0,0004	0,0001
Pelistega	0,0000	0,0000	0,0016	0,0000	0,0012	0,0000	0,0000	0,0000	0,0000	0,0000	0,0025	0,0003	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0005	0,0000	0,0010	0,0000	0,0000
Bergeriella	0,0000	0,0001	0,0012	0,0000	0,0015	0,0001	0,0001	0,0001	0,0003	0,0256	0,0001	0,0007	0,0000	0,0005	0,0042	0,0000	0,0196	0,0001	0,0002	0,0001	0,0000	0,0008	0,0000	0,0001	0,0005	0,0005	0,0043	0,0007	0,0083	0,0003
Alicyclophilus	0,0000	0,0000	0,0024	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0002	0,0000	0,0006	0,0000	0,0000	0,0000	0,0028	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0005	0,0000	0,0002	0,0000	0,0000
Achromobacter	0,0001	0,0005	0,0003	0,0000	0,0022	0,0001	0,0003	0,0000	0,0003	0,0002	0,0004	0,0016	0,0000	0,0002	0,0021	0,0001	0,0134	0,0005	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0005	0,0002	0,0006	0,0058	0,0000
Thermanaerovibrio	0,0000	0,0001	0,0010	0,0016	0,0000	0,0000	0,0000	0,0004	0,0052	0,0000	0,0001	0,0001	0,0000	0,0000	0,0002	0,0000	0,0000	0,0001	0,0005	0,0000	0,0000	0,0002	0,0007	0,0001	0,0000	0,0005	0,0011	0,0001	0,0002	0,0002
Pyramidobacter	0,0000	0,0000	0,0000	0,0000	0,0000	0,0020	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0002	0,0000	0,0000	0,0000	0,0024	0,0005	0,0000	0,0000	0,0001	0,0003
Thiobacter	0,0000	0,0002	0,0005	0,0000	0,0022	0,0000	0,0001	0,0000	0,0000	0,0002	0,0010	0,0006	0,0000	0,0001	0,0076	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0005	0,0001	0,0013	0,0001	0,0000
Phascolarctobacterium	0,0001	0,0025	0,0002	0,0005	0,0001	0,0001	0,0008	0,0002	0,0003	0,0002	0,0003	0,0001	0,0001	0,0006	0,0001	0,0003	0,0000	0,0038	0,0005	0,0009	0,0003	0,0001	0,0009	0,0006	0,0003	0,0005	0,0004	0,0003	0,0010	0,0005
Curvibacter	0,0000	0,0000	0,0000	0,0000	0,0027	0,0001	0,0003	0,0000	0,0001	0,0014	0,0000	0,0009	0,0000	0,0015	0,0021	0,0001	0,0027	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0005	0,0003	0,0006	0,0012	0,0000
Candidatus Riesia	0,0000	0,0011	0,0000	0,0000	0,0014	0,0003	0,0006	0,0002	0,0001	0,0057	0,0002	0,0014	0,0000	0,0007	0,0010	0,0019	0,0022	0,0001	0,0010	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0005	0,0012	0,0005	0,0013	0,0000
Holdemania	0,0004	0,0005	0,0002	0,0012	0,0003	0,0002	0,0011	0,0004	0,0011	0,0000	0,0002	0,0010	0,0001	0,0001	0,0001	0,0008	0,0000	0,0085	0,0009	0,0166	0,0002	0,0001	0,0069	0,0029	0,0019	0,0005	0,0007	0,0003	0,0021	0,0039
Streptoalloteichus	0,0000	0,0000	0,0000	0,0000	0,0000	0,0018	0,0000	0,0015	0,0001	0,0000	0,0001	0,0000	0,0002	0,0000	0,0000	0,0000	0,0012	0,0004	0,0000	0,0000	0,0000	0,0006	0,0001	0,0000	0,0000	0,0004	0,0004	0,0001	0,0006	0,0001
Lutiella	0,0000	0,0002	0,0000	0,0000	0,0026	0,0000	0,0003	0,0000	0,0003	0,0006	0,0003	0,0005	0,0000	0,0023	0,0093	0,0004	0,0002	0,0002	0,0002	0,0001	0,0000	0,0000	0,0000	0,0000	0,0001	0,0004	0,0003	0,0017	0,0002	0,0000
Thermocrispum	0,0008	0,0026	0,0000	0,0000	0,0000	0,0001	0,0000	0,0002	0,0028	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0006	0,0000	0,0000	0,0000
Macrococcus	0,0012	0,0020	0,0001	0,0001	0,0001	0,0000	0,0006	0,0002	0,0004	0,0000	0,0008	0,0001	0,0001	0,0001	0,0001	0,0008	0,0017	0,0007	0,0004	0,0000	0,0000	0,0000	0,0024	0,0002	0,0000	0,0004	0,0004	0,0004	0,0010	0,0004
Halothiobacillus	0,0000	0,0015	0,0004	0,0001	0,0006	0,0002	0,0012	0,0009	0,0054	0,0024	0,0010	0,0022	0,0003	0,0112	0,0001	0,0004	0,0000	0,0266	0,0000	0,0002	0,0126	0,0002	0,0735	0,0085	0,0026	0,0004	0,0021	0,0024	0,0054	0,0168
Bartonella	0,0000	0,0003	0,0004	0,0001	0,0010	0,0005	0,0008	0,0003	0,0008	0,0001	0,0002	0,0020	0,0002	0,0021	0,0001	0,0005	0,0034	0,0003	0,0001	0,0004	0,0006	0,0002	0,0001	0,0005	0,0021	0,0004	0,0005	0,0007	0,0016	0,0005
Aeromicrobium	0,0000	0,0000	0,0000	0,0000	0,0000	0,0018	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0005	0,0000	0,0000	0,0000	0,0004	0,0000	0,0001	0,0000	0,0001
Bergeyella	0,0000	0,0002	0,0002	0,0000	0,0017	0,0003	0,0001	0,0022	0,0007	0,0035	0,0003	0,0009	0,0000	0,0069	0,0000	0,0005	0,0000	0,0001	0,0031	0,0024	0,0110	0,0040	0,0003	0,0016	0,0013	0,0004	0,0013	0,0013	0,0012	0,0034

GENUS	SUBJECTS' SITES																								SUBJECTS' GROUPS						
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF	
Dorea	0,0000	0,0010	0,0000	0,0009	0,0002	0,0005	0,0006	0,0009	0,0006	0,0001	0,0001	0,0002	0,0000	0,0004	0,0003	0,0002	0,0010	0,0002	0,0001	0,0000	0,0000	0,0002	0,0000	0,0001	0,0002	0,0004	0,0006	0,0002	0,0005	0,0001	
Pleurocapsa	0,0000	0,0000	0,0000	0,0023	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0063	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0000	0,0000	0,0014	0,0000	
Pantoea	0,0000	0,0002	0,0004	0,0001	0,0014	0,0002	0,0046	0,0004	0,0005	0,0114	0,0005	0,0019	0,0000	0,0018	0,0003	0,0052	0,0226	0,0002	0,0004	0,0004	0,0003	0,0016	0,0000	0,0004	0,0005	0,0004	0,0038	0,0010	0,0098	0,0006	
Williamsia	0,0000	0,0000	0,0000	0,0000	0,0000	0,0017	0,0000	0,0000	0,0006	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0001	0,0000	0,0000	0,0000	
Ilyobacter	0,0000	0,0020	0,0001	0,0000	0,0002	0,0004	0,0004	0,0001	0,0000	0,0001	0,0002	0,0001	0,0000	0,0003	0,0000	0,0034	0,0000	0,0001	0,0001	0,0001	0,0002	0,0000	0,0001	0,0001	0,0002	0,0004	0,0002	0,0003	0,0001	0,0001	
Methylobacillus	0,0002	0,0003	0,0003	0,0000	0,0014	0,0002	0,0002	0,0002	0,0096	0,0004	0,0105	0,0006	0,0000	0,0003	0,0014	0,0003	0,0001	0,0031	0,0002	0,0001	0,0001	0,0002	0,0000	0,0001	0,0000	0,0004	0,0021	0,0041	0,0008	0,0001	
unclassified (derived from Peptococcaceae)	0,0006	0,0008	0,0007	0,0003	0,0001	0,0001	0,0011	0,0003	0,0001	0,0002	0,0003	0,0000	0,0003	0,0001	0,0001	0,0003	0,0002	0,0022	0,0005	0,0002	0,0000	0,0000	0,0012	0,0003	0,0000	0,0004	0,0005	0,0002	0,0007	0,0003	
Dictyoglomus	0,0000	0,0002	0,0001	0,0000	0,0000	0,0015	0,0001	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0001	0,0001	0,0000	0,0000	0,0000	0,0001	0,0000	0,0004	0,0001	0,0000	0,0001	0,0000	
Nicoletella	0,0000	0,0011	0,0003	0,0000	0,0010	0,0002	0,0037	0,0003	0,0039	0,0026	0,0064	0,0013	0,0000	0,0016	0,0000	0,0017	0,0000	0,0000	0,0004	0,0000	0,0006	0,0001	0,0001	0,0001	0,0002	0,0004	0,0027	0,0028	0,0002	0,0002	
Moorella	0,0000	0,0001	0,0000	0,0001	0,0001	0,0015	0,0002	0,0001	0,0002	0,0000	0,0001	0,0004	0,0001	0,0002	0,0000	0,0001	0,0000	0,0018	0,0003	0,0034	0,0005	0,0001	0,0011	0,0008	0,0005	0,0004	0,0001	0,0001	0,0005	0,0009	
Stenotrophomonas	0,0001	0,0000	0,0001	0,0012	0,0003	0,0004	0,0001	0,0000	0,0000	0,0000	0,0003	0,0000	0,0000	0,0001	0,0000	0,0001	0,0001	0,0000	0,0001	0,0000	0,0001	0,0001	0,0138	0,0003	0,0000	0,0004	0,0001	0,0001	0,0001	0,0024	
Borrelia	0,0000	0,0002	0,0015	0,0000	0,0002	0,0001	0,0001	0,0000	0,0004	0,0032	0,0012	0,0052	0,0000	0,0008	0,0006	0,0002	0,0001	0,0003	0,0001	0,0010	0,0020	0,0001	0,0257	0,0002	0,0000	0,0004	0,0006	0,0012	0,0001	0,0048	
Anaeromyxobacter	0,0010	0,0008	0,0000	0,0001	0,0002	0,0005	0,0003	0,0006	0,0015	0,0001	0,0003	0,0001	0,0000	0,0001	0,0007	0,0023	0,0003	0,0005	0,0005	0,0002	0,0000	0,0001	0,0000	0,0005	0,0003	0,0004	0,0006	0,0004	0,0004	0,0002	
Georgfuchsia	0,0000	0,0000	0,0018	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0079	0,0000	0,0000	0,0000	0,0000	0,0004	0,0000	0,0000	0,0000	0,0012	
Citrobacter	0,0000	0,0005	0,0001	0,0000	0,0016	0,0002	0,0010	0,0001	0,0002	0,0028	0,0001	0,0006	0,0000	0,0007	0,0006	0,0024	0,0499	0,0001	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0009	0,0004	0,0212	0,0000	
Rikenella	0,0000	0,0003	0,0013	0,0004	0,0001	0,0000	0,0006	0,0024	0,0001	0,0056	0,0018	0,0185	0,0005	0,0019	0,0000	0,0001	0,0000	0,0010	0,0003	0,0029	0,0052	0,0001	0,0780	0,0005	0,0001	0,0004	0,0018	0,0032	0,0003	0,0144	
Stanieria	0,0000	0,0000	0,0002	0,0000	0,0005	0,0010	0,0000	0,0000	0,0006	0,0002	0,0000	0,0015	0,0000	0,0094	0,0000	0,0000	0,0000	0,0026	0,0003	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0004	0,0002	0,0016	0,0006	0,0000	
Microbispora	0,0001	0,0003	0,0000	0,0004	0,0002	0,0009	0,0007	0,0010	0,0010	0,0000	0,0000	0,0001	0,0000	0,0001	0,0001	0,0000	0,0005	0,0005	0,0009	0,0001	0,0000	0,0003	0,0001	0,0000	0,0001	0,0004	0,0007	0,0000	0,0006	0,0001	
Microcystis	0,0000	0,0002	0,0001	0,0018	0,0001	0,0000	0,0002	0,0000	0,0003	0,0028	0,0001	0,0053	0,0011	0,0010	0,0001	0,0000	0,0000	0,0255	0,0005	0,0000	0,0006	0,0002	0,0165	0,0006	0,0001	0,0004	0,0006	0,0010	0,0054	0,0031	
Couchioplanes	0,0006	0,0005	0,0000	0,0001	0,0000	0,0009	0,0001	0,0005	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0011	0,0000	0,0009	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0002	0,0000	0,0008	0,0000	
Aneurinibacillus	0,0000	0,0007	0,0002	0,0002	0,0005	0,0005	0,0005	0,0013	0,0003	0,0017	0,0006	0,0001	0,0002	0,0003	0,0043	0,0039	0,0000	0,0343	0,0008	0,0000	0,0000	0,0001	0,0021	0,0008	0,0000	0,0004	0,0009	0,0010	0,0073	0,0006	
Acinetobacter	0,0001	0,0000	0,0002	0,0000	0,0018	0,0000	0,0003	0,0000	0,0004	0,0003	0,0002	0,0003	0,0000	0,0020	0,0003	0,0117	0,0022	0,0002	0,0019	0,0000	0,0032	0,0000	0,0002	0,0003	0,0000	0,0003	0,0002	0,0010	0,0017	0,0006	
Coraliomargarita	0,0005	0,0014	0,0000	0,0002	0,0000	0,0003	0,0001	0,0001	0,0002	0,0001	0,0004	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0001	0,0002	0,0002	0,0000	
Epulopiscium	0,0001	0,0002	0,0009	0,0002	0,0000	0,0004	0,0001	0,0006	0,0002	0,0004	0,0001	0,0002	0,0000	0,0013	0,0001	0,0000	0,0003	0,0021	0,0003	0,0000	0,0001	0,0001	0,0119	0,0003	0,0001	0,0003	0,0003	0,0003	0,0007	0,0021	
Derxia	0,0000	0,0000	0,0016	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0000	0,0000	0,0001	0,0000	
Desulfosporosinus	0,0002	0,0000	0,0001	0,0002	0,0001	0,0011	0,0001	0,0002	0,0004	0,0002	0,0000	0,0000	0,0002	0,0001	0,0000	0,0000	0,0000	0,0008	0,0003	0,0001	0,0018	0,0001	0,0038	0,0002	0,0001	0,0003	0,0002	0,0001	0,0003	0,0010	
Salmonella	0,0000	0,0003	0,0001	0,0000	0,0016	0,0000	0,0005	0,0000	0,0002	0,0010	0,0001	0,0004	0,0000	0,0004	0,0008	0,0008	0,0012	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0004	0,0003	0,0005	0,0000	
Gloeobacter	0,0000	0,0022	0,0001	0,0000	0,0002	0,0000	0,0010	0,0003	0,0016	0,0001	0,0000	0,0000	0,0005	0,0018	0,0000	0,0000	0,0003	0,0001	0,0000	0,0001	0,0002	0,0000	0,0001	0,0000	0,0000	0,0003	0,0008	0,0004	0,0001	0,0001	
Sporomusa	0,0000	0,0001	0,0009	0,0002	0,0002	0,0004	0,0007	0,0067	0,0012	0,0007	0,0000	0,0008	0,0007	0,0014	0,0001	0,0001	0,0000	0,0051	0,0007	0,0011	0,0006	0,0005	0,0083	0,0006	0,0049	0,0003	0,0024	0,0005	0,0013	0,0024	
Barnesiella	0,0000	0,0008	0,0002	0,0007	0,0001	0,0001	0,0007	0,0002	0,0004	0,0167	0,0012	0,0096	0,0004	0,0009	0,0001	0,0282	0,0001	0,0184	0,0026	0,4756	0,0003	0,0006	0,0282	0,0215	0,0095	0,0003	0,0031	0,0032	0,0048	0,0622	
Acetobacterium	0,0000	0,0002	0,0000	0,0013	0,0000	0,0002	0,0000	0,0004	0,0004	0,0000	0,0000	0,0001	0,0005	0,0000	0,0003	0,0000	0,0004	0,0084	0,0003	0,0022	0,0001	0,0001	0,0100	0,0012	0,0008	0,0003	0,0002	0,0002	0,0020	0,0023	
Nostoc	0,0000	0,0001	0,0006	0,0002	0,0000	0,0004	0,0004	0,0006	0,0001	0,0002	0,0001	0,0002	0,0002	0,0002	0,0001	0,0004	0,0000	0,0041	0,0004	0,0007	0,0011	0,0002	0,0007	0,0006	0,0001	0,0003	0,0003	0,0002	0,0010	0,0006	
Dolichospermum	0,0000	0,0000	0,0000	0,0000	0,0017	0,0000	0,0001	0,0000	0,0000	0,0004	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0002	0,0026	0,0001	0,0000	0,0003	0,0001	0,0000	0,0000	0,0005

GENUS	SUBJECTS' SITES																							SUBJECTS' GROUPS						
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF
Clavibacter	0,0001	0,0001	0,0000	0,0001	0,0007	0,0005	0,0003	0,0001	0,0013	0,0000	0,0001	0,0000	0,0002	0,0002	0,0000	0,0016	0,0002	0,0007	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0003	0,0004	0,0001	0,0010	0,0000	
Nakamurella	0,0000	0,0001	0,0000	0,0000	0,0003	0,0009	0,0001	0,0000	0,0005	0,0001	0,0001	0,0000	0,0000	0,0001	0,0003	0,0001	0,0069	0,0001	0,0019	0,0000	0,0000	0,0001	0,0003	0,0001	0,0031	0,0003	0,0002	0,0001	0,0037	0,0004
Gramella	0,0000	0,0003	0,0003	0,0000	0,0010	0,0001	0,0021	0,0000	0,0001	0,0003	0,0001	0,0004	0,0000	0,0040	0,0002	0,0005	0,0014	0,0000	0,0005	0,0002	0,0002	0,0002	0,0000	0,0001	0,0000	0,0003	0,0009	0,0007	0,0007	0,0001
Oceanimonas	0,0000	0,0007	0,0000	0,0003	0,0006	0,0001	0,0010	0,0002	0,0003	0,0000	0,0002	0,0001	0,0000	0,0039	0,0000	0,0000	0,0004	0,0000	0,0004	0,0001	0,0000	0,0000	0,0000	0,0002	0,0001	0,0003	0,0005	0,0007	0,0003	0,0001
Comamonas	0,0000	0,0000	0,0001	0,0000	0,0001	0,0010	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0008	0,0000	0,0000	0,0000	0,0008	0,0000	0,0000	0,0002	0,0000	0,0003	0,0000	0,0000	0,0003	0,0002
Sideroxydans	0,0000	0,0000	0,0007	0,0000	0,0007	0,0000	0,0001	0,0000	0,0001	0,0004	0,0015	0,0001	0,0000	0,0002	0,0008	0,0000	0,0003	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0001	0,0007	0,0002	0,0000
Syntrophobacter	0,0000	0,0002	0,0001	0,0001	0,0009	0,0003	0,0007	0,0001	0,0003	0,0002	0,0001	0,0009	0,0000	0,0009	0,0000	0,0003	0,0009	0,0001	0,0001	0,0000	0,0004	0,0001	0,0001	0,0002	0,0002	0,0003	0,0004	0,0003	0,0004	0,0002
unclassified (derived from Enterobacteriaceae)	0,0000	0,0001	0,0001	0,0000	0,0013	0,0000	0,0002	0,0001	0,0002	0,0005	0,0052	0,0019	0,0000	0,0014	0,0004	0,0023	0,0011	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0013	0,0000	0,0003	0,0002	0,0025	0,0005	0,0003
Thermoactinomyces	0,0000	0,0000	0,0000	0,0000	0,0000	0,0010	0,0000	0,0003	0,0001	0,0001	0,0000	0,0002	0,0001	0,0000	0,0000	0,0000	0,0000	0,0143	0,0006	0,0008	0,0000	0,0000	0,0180	0,0031	0,0002	0,0002	0,0001	0,0001	0,0031	0,0039
Candidatus Azobacteroides	0,0000	0,0005	0,0005	0,0000	0,0003	0,0002	0,0012	0,0004	0,0002	0,0011	0,0000	0,0008	0,0001	0,0007	0,0003	0,0006	0,0002	0,0002	0,0001	0,0002	0,0007	0,0001	0,0002	0,0003	0,0001	0,0002	0,0008	0,0003	0,0002	0,0003
Dethiosulfovibrio	0,0000	0,0000	0,0012	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0002	0,0004	0,0000	0,0001	0,0000	0,0006	0,0000	0,0001	0,0005	0,0000	0,0000	0,0004	0,0385	0,0037	0,0000	0,0002	0,0000	0,0002	0,0002	0,0075
Bordetella	0,0000	0,0006	0,0001	0,0000	0,0003	0,0004	0,0002	0,0000	0,0002	0,0001	0,0032	0,0001	0,0000	0,0001	0,0043	0,0005	0,0172	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0001	0,0017	0,0073	0,0000
Rhizobium	0,0000	0,0000	0,0002	0,0003	0,0001	0,0005	0,0002	0,0004	0,0005	0,0003	0,0001	0,0007	0,0003	0,0005	0,0000	0,0010	0,0004	0,0006	0,0018	0,0001	0,0002	0,0001	0,0056	0,0003	0,0003	0,0002	0,0003	0,0003	0,0010	0,0011
Thiothrix	0,0000	0,0001	0,0000	0,0012	0,0001	0,0000	0,0001	0,0002	0,0001	0,0001	0,0001	0,0001	0,0002	0,0001	0,0001	0,0000	0,0000	0,0010	0,0001	0,0007	0,0001	0,0000	0,0062	0,0001	0,0004	0,0002	0,0001	0,0001	0,0002	0,0012
Tolomonas	0,0000	0,0007	0,0001	0,0000	0,0006	0,0001	0,0026	0,0000	0,0002	0,0000	0,0010	0,0012	0,0000	0,0013	0,0000	0,0005	0,0006	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0011	0,0007	0,0003	0,0000
Catonella	0,0000	0,0003	0,0003	0,0001	0,0005	0,0001	0,0002	0,0006	0,0003	0,0010	0,0004	0,0001	0,0002	0,0003	0,0077	0,0122	0,0000	0,0055	0,0003	0,0000	0,0000	0,0000	0,0001	0,0009	0,0000	0,0002	0,0005	0,0017	0,0013	0,0002
Actinotalea	0,0000	0,0000	0,0005	0,0000	0,0000	0,0005	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0019	0,0005	0,0002	0,0001	0,0000	0,0000	0,0005
Sagittula	0,0000	0,0000	0,0000	0,0000	0,0013	0,0001	0,0000	0,0000	0,0001	0,0002	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000
Geitlerinema	0,0000	0,0001	0,0001	0,0011	0,0000	0,0001	0,0002	0,0017	0,0011	0,0001	0,0001	0,0002	0,0012	0,0004	0,0002	0,0000	0,0000	0,0025	0,0000	0,0001	0,0007	0,0001	0,0013	0,0007	0,0000	0,0002	0,0008	0,0004	0,0005	0,0005
Cellulosilyticum	0,0000	0,0000	0,0001	0,0000	0,0000	0,0009	0,0000	0,0000	0,0002	0,0001	0,0000	0,0006	0,0000	0,0006	0,0000	0,0000	0,0000	0,0010	0,0003	0,0000	0,0005	0,0000	0,0016	0,0005	0,0001	0,0002	0,0001	0,0002	0,0003	0,0005
Cylindrospermopsis	0,0000	0,0002	0,0002	0,0001	0,0002	0,0005	0,0002	0,0001	0,0005	0,0006	0,0005	0,0004	0,0001	0,0008	0,0004	0,0009	0,0000	0,0009	0,0008	0,0005	0,0003	0,0151	0,0002	0,0004	0,0002	0,0002	0,0003	0,0005	0,0005	0,0035
Desulfovibrio	0,0000	0,0001	0,0001	0,0000	0,0001	0,0008	0,0000	0,0001	0,0001	0,0001	0,0000	0,0000	0,0000	0,0002	0,0003	0,0016	0,0008	0,0004	0,0000	0,0002	0,0002	0,0002	0,0002	0,0001	0,0001	0,0002	0,0001	0,0002	0,0004	0,0002
Polaribacter	0,0000	0,0000	0,0000	0,0000	0,0002	0,0007	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0002	0,0000	0,0000	0,0002	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0001	0,0001	0,0000
Leuconostoc	0,0001	0,0002	0,0000	0,0005	0,0000	0,0004	0,0001	0,0002	0,0005	0,0005	0,0001	0,0028	0,0001	0,0001	0,0002	0,0001	0,0015	0,0073	0,0001	0,0000	0,0001	0,0000	0,0083	0,0006	0,0000	0,0002	0,0002	0,0004	0,0021	0,0016
Thiohalocapsa	0,0000	0,0002	0,0001	0,0000	0,0008	0,0001	0,0003	0,0000	0,0003	0,0002	0,0002	0,0001	0,0000	0,0015	0,0003	0,0001	0,0001	0,0001	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0002	0,0004	0,0001	0,0000
Nonomuraea	0,0005	0,0000	0,0003	0,0000	0,0002	0,0002	0,0000	0,0000	0,0003	0,0000	0,0001	0,0002	0,0000	0,0002	0,0000	0,0001	0,0000	0,0013	0,0004	0,0000	0,0000	0,0004	0,0002	0,0001	0,0001	0,0002	0,0001	0,0001	0,0004	0,0002
Vitreoscilla	0,0000	0,0000	0,0003	0,0000	0,0008	0,0001	0,0002	0,0003	0,0004	0,0020	0,0003	0,0002	0,0000	0,0003	0,0018	0,0000	0,0047	0,0021	0,0000	0,0000	0,0000	0,0001	0,0000	0,0003	0,0001	0,0002	0,0005	0,0004	0,0024	0,0001
Taylorella	0,0000	0,0000	0,0000	0,0000	0,0013	0,0000	0,0001	0,0002	0,0002	0,0003	0,0001	0,0003	0,0000	0,0003	0,0008	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0002	0,0002	0,0002	0,0000	0,0000
Massilia	0,0000	0,0003	0,0001	0,0000	0,0007	0,0002	0,0007	0,0001	0,0008	0,0005	0,0000	0,0003	0,0000	0,0016	0,0040	0,0005	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0005	0,0008	0,0001	0,0000
Peptoniphilus	0,0001	0,0003	0,0000	0,0000	0,0001	0,0005	0,0001	0,0001	0,0045	0,0036	0,0001	0,0048	0,0000	0,0011	0,0000	0,0001	0,0000	0,0546	0,0043	0,0090	0,0001	0,0018	0,0387	0,0169	0,0036	0,0002	0,0015	0,0008	0,0127	0,0125
Volucrobacter	0,0000	0,0002	0,0001	0,0000	0,0011	0,0000	0,0003	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0001	0,0001	0,0001	0,0000
Helicobacter	0,0000	0,0002	0,0003	0,0000	0,0002	0,0003	0,0005	0,0003	0,0009	0,0005	0,0001	0,0006	0,0002	0,0008	0,0003	0,0004	0,0015	0,0020	0,0013	0,0005	0,0002	0,0004	0,0156	0,0015	0,0003	0,0002	0,0005	0,0003	0,0015	0,0032

GENUS	SUBJECTS' SITES																										SUBJECTS' GROUPS				
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF	
Duganella	0,0000	0,0000	0,0000	0,0000	0,0012	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0012	0,0000	0,0001	0,0001	0,0000	0,0009	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0002	0,0004	0,0000	
Candidatus Regiella	0,0000	0,0000	0,0000	0,0001	0,0011	0,0000	0,0001	0,0000	0,0003	0,0002	0,0000	0,0001	0,0000	0,0004	0,0000	0,0000	0,0013	0,0002	0,0001	0,0000	0,0003	0,0000	0,0146	0,0001	0,0000	0,0002	0,0001	0,0001	0,0006	0,0025	
Dethiobacter	0,0000	0,0000	0,0000	0,0008	0,0000	0,0002	0,0000	0,0000	0,0000	0,0001	0,0001	0,0001	0,0000	0,0001	0,0001	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0002	0,0000	0,0001	0,0001	0,0000	
Dactylosporangium	0,0002	0,0013	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0001	0,0001	0,0000	0,0000	0,0028	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0002	0,0006	
Oligella	0,0000	0,0000	0,0002	0,0000	0,0006	0,0001	0,0003	0,0005	0,0005	0,0001	0,0000	0,0001	0,0001	0,0033	0,0002	0,0000	0,0015	0,0013	0,0001	0,0000	0,0003	0,0001	0,0015	0,0001	0,0000	0,0002	0,0003	0,0006	0,0009	0,0004	
Candidatus Blochmannia	0,0000	0,0000	0,0000	0,0000	0,0011	0,0000	0,0000	0,0000	0,0000	0,0000	0,0013	0,0000	0,0000	0,0005	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0006	0,0001	0,0000	
Thermotoga	0,0001	0,0001	0,0000	0,0000	0,0000	0,0006	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0001	0,0000	0,0000	
Photobacterium	0,0000	0,0002	0,0002	0,0000	0,0006	0,0001	0,0001	0,0000	0,0000	0,0004	0,0001	0,0014	0,0000	0,0012	0,0002	0,0003	0,0003	0,0001	0,0001	0,0000	0,0064	0,0000	0,0000	0,0001	0,0001	0,0002	0,0001	0,0004	0,0002	0,0010	
unclassified (derived from Flavobacteriales)	0,0000	0,0001	0,0005	0,0000	0,0004	0,0000	0,0003	0,0000	0,0002	0,0001	0,0006	0,0002	0,0000	0,0011	0,0000	0,0000	0,0002	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0002	0,0002	0,0004	0,0001	0,0000	
Oxalobacter	0,0000	0,0000	0,0001	0,0000	0,0010	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0002	0,0000	0,0001	0,0021	0,0000	0,0047	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0005	0,0002	0,0000	0,0003	0,0020	0,0001	
Idiomarina	0,0000	0,0005	0,0000	0,0000	0,0005	0,0000	0,0006	0,0001	0,0000	0,0002	0,0007	0,0002	0,0000	0,0001	0,0001	0,0000	0,0002	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0002	0,0002	0,0002	0,0003	0,0003	0,0001	0,0000
Vogesella	0,0000	0,0000	0,0001	0,0000	0,0009	0,0000	0,0001	0,0000	0,0000	0,0002	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0001	0,0000	0,0000	0,0000	
Xylanimicrobium	0,0000	0,0000	0,0001	0,0000	0,0001	0,0005	0,0000	0,0000	0,0005	0,0000	0,0001	0,0000	0,0000	0,0000	0,0003	0,0000	0,0009	0,0001	0,0000	0,0000	0,0000	0,0003	0,0000	0,0006	0,0001	0,0002	0,0001	0,0001	0,0004	0,0002	
Symbiobacterium	0,0000	0,0000	0,0000	0,0001	0,0000	0,0006	0,0000	0,0001	0,0001	0,0001	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0034	0,0006	0,0001	0,0002	0,0002	0,0004	0,0005	0,0001	0,0002	0,0001	0,0000	0,0009	0,0003	
unclassified (derived from Flavobacteria)	0,0000	0,0001	0,0003	0,0000	0,0006	0,0000	0,0011	0,0000	0,0001	0,0004	0,0001	0,0004	0,0000	0,0042	0,0002	0,0000	0,0000	0,0000	0,0001	0,0001	0,0004	0,0000	0,0000	0,0000	0,0000	0,0002	0,0005	0,0007	0,0001	0,0001	
Nitrosococcus	0,0012	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	
Psychroflexus	0,0000	0,0004	0,0002	0,0000	0,0003	0,0000	0,0010	0,0000	0,0000	0,1005	0,0542	0,0157	0,0000	0,0012	0,0057	0,0001	0,0003	0,0001	0,0000	0,0000	0,0011	0,0000	0,0077	0,0001	0,0000	0,0002	0,0169	0,0226	0,0001	0,0015	
Stackebrandtia	0,0000	0,0001	0,0000	0,0000	0,0000	0,0005	0,0000	0,0001	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0007	0,0000	0,0000	0,0000	0,0002	0,0000	0,0001	0,0000	0,0002	0,0001	0,0000	0,0001	0,0001	
Ureaplasma	0,0000	0,0008	0,0000	0,0000	0,0001	0,0001	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0094	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0006	0,0000	0,0001	0,0000	0,0001	0,0002	0,0000	0,0015	0,0000	0,0001	
Azorhizobium	0,0000	0,0000	0,0001	0,0000	0,0001	0,0005	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0001	0,0000	
Thermodesulfobium	0,0007	0,0000	0,0000	0,0004	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	
Carboxydotherrus	0,0001	0,0003	0,0001	0,0001	0,0000	0,0003	0,0003	0,0001	0,0039	0,0003	0,0001	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0028	0,0001	0,0002	0,0002	0,0104	0,0000	0,0007	0,0001	0,0001	0,0009	0,0001	0,0006	0,0025	
Heliobacterium	0,0000	0,0002	0,0001	0,0002	0,0002	0,0002	0,0003	0,0002	0,0002	0,0000	0,0001	0,0000	0,0001	0,0001	0,0000	0,0000	0,0005	0,0011	0,0001	0,0002	0,0002	0,0008	0,0023	0,0008	0,0000	0,0001	0,0002	0,0001	0,0005	0,0008	
Janibacter	0,0000	0,0001	0,0000	0,0000	0,0001	0,0004	0,0000	0,0001	0,0001	0,0000	0,0018	0,0000	0,0000	0,0000	0,0001	0,0006	0,0011	0,0001	0,0002	0,0000	0,0004	0,0014	0,0001	0,0000	0,0000	0,0001	0,0001	0,0007	0,0006	0,0004	
Croceibacter	0,0000	0,0005	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0000	0,0003	0,0009	0,0000	0,0004	0,0000	0,0000	0,0000	0,0000	0,0000	0,0031	0,0024	0,0000	0,0004	0,0000	0,0002	0,0001	0,0001	0,0003	0,0000	0,0008	
Rubrobacter	0,0000	0,0000	0,0001	0,0003	0,0000	0,0003	0,0000	0,0003	0,0004	0,0000	0,0000	0,0004	0,0003	0,0000	0,0002	0,0000	0,0000	0,0029	0,0001	0,0003	0,0000	0,0002	0,0046	0,0007	0,0003	0,0001	0,0001	0,0001	0,0007	0,0011	
Kutzneria	0,0000	0,0001	0,0000	0,0002	0,0004	0,0001	0,0005	0,0004	0,0002	0,0000	0,0019	0,0001	0,0001	0,0005	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0007	0,0001	0,0141	0,0000	0,0001	0,0003	0,0008	0,0000	0,0037	
Sedimentibacter	0,0000	0,0000	0,0006	0,0001	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0002	0,0001	0,0000	0,0000	0,0000	0,0002	0,0001	0,0008	0,0001	0,0000	0,0000	0,0001	0,0001	
Fusibacter	0,0000	0,0002	0,0000	0,0005	0,0000	0,0001	0,0000	0,0001	0,0002	0,0002	0,0001	0,0000	0,0003	0,0004	0,0001	0,0000	0,0000	0,0021	0,0003	0,0014	0,0001	0,0001	0,0075	0,0014	0,0004	0,0001	0,0001	0,0002	0,0005	0,0018	
Oerskovia	0,0000	0,0004	0,0000	0,0001	0,0001	0,0002	0,0008	0,0002	0,0001	0,0000	0,0002	0,0000	0,0001	0,0000	0,0000	0,0000	0,0004	0,0000	0,0002	0,0000	0,0000	0,0001	0,0000	0,0004	0,0000	0,0001	0,0004	0,0001	0,0003	0,0001	
Candidatus Accumulibacter	0,0000	0,0000	0,0000	0,0000	0,0000	0,0005	0,0000	0,0000	0,0000	0,0001	0,0003	0,0000	0,0000	0,0005	0,0000	0,0000	0,0088	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0002	0,0000	0,0001	0,0000	0,0002	0,0037	0,0001	

GENUS	SUBJECTS' SITES																								SUBJECTS' GROUPS					
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF
Zunongwangia	0,0000	0,0004	0,0002	0,0000	0,0002	0,0000	0,0009	0,0000	0,0000	0,0994	0,0516	0,0156	0,0000	0,0010	0,0056	0,0000	0,0000	0,0001	0,0000	0,0000	0,0011	0,0000	0,0000	0,0001	0,0000	0,0001	0,0167	0,0216	0,0000	0,0002
Flexithrix	0,0000	0,0002	0,0002	0,0000	0,0004	0,0000	0,0004	0,0000	0,0001	0,0007	0,0002	0,0013	0,0000	0,0031	0,0001	0,0003	0,0003	0,0000	0,0000	0,0002	0,0006	0,0000	0,0000	0,0002	0,0000	0,0001	0,0003	0,0007	0,0001	0,0002
Thermopolyspora	0,0000	0,0000	0,0000	0,0004	0,0000	0,0002	0,0000	0,0006	0,0003	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0005	0,0000	0,0000	0,0007	0,0000	0,0003	0,0002	0,0001	0,0002	0,0000	0,0002	0,0003
Pimelobacter	0,0000	0,0000	0,0000	0,0000	0,0000	0,0005	0,0018	0,0004	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0283	0,0000	0,0009	0,0001	0,0000	0,0006	0,0003	0,0002	0,0004	0,0001	0,0008	0,0000	0,0123	0,0003
Candidatus Hamiltonella	0,0000	0,0000	0,0004	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0003	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000
Xenorhabdus	0,0000	0,0001	0,0003	0,0000	0,0003	0,0000	0,0002	0,0000	0,0001	0,0001	0,0004	0,0002	0,0000	0,0000	0,0000	0,0001	0,0026	0,0003	0,0000	0,0000	0,0000	0,0006	0,0000	0,0002	0,0000	0,0001	0,0001	0,0002	0,0012	0,0002
Thermoleophilum	0,0000	0,0000	0,0001	0,0000	0,0000	0,0004	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0002	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000
Maricaulis	0,0001	0,0005	0,0000	0,0000	0,0000	0,0001	0,0002	0,0001	0,0001	0,0001	0,0005	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0002	0,0000	0,0000	0,0001	0,0001	0,0002	0,0000	0,0001	0,0001	0,0002	0,0001	0,0001
Metascardovia	0,0010	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0003	0,0000	0,0002	0,0001	0,0000	0,0000	0,0000	0,0001
Pectinatus	0,0000	0,0004	0,0001	0,0002	0,0000	0,0001	0,0001	0,0004	0,0001	0,0001	0,0001	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0008	0,0008	0,0004	0,0001	0,0002	0,0009	0,0003	0,0005	0,0001	0,0002	0,0001	0,0004	0,0004
Geodermatophilus	0,0000	0,0001	0,0001	0,0000	0,0000	0,0003	0,0001	0,0007	0,0006	0,0000	0,0001	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0005	0,0005	0,0020	0,0002	0,0002	0,0001	0,0001	0,0001	0,0001	0,0003	0,0001	0,0003	0,0003
Granulibacter	0,0000	0,0000	0,0005	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000
Cronobacter	0,0000	0,0002	0,0001	0,0001	0,0002	0,0001	0,0002	0,0003	0,0004	0,0001	0,0003	0,0005	0,0001	0,0001	0,0001	0,0001	0,0000	0,0000	0,0004	0,0000	0,0000	0,0001	0,0001	0,0001	0,0000	0,0001	0,0002	0,0002	0,0002	0,0001
Halochromatium	0,0000	0,0000	0,0004	0,0000	0,0001	0,0000	0,0001	0,0000	0,0005	0,0000	0,0001	0,0000	0,0000	0,0011	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0001	0,0003	0,0000	0,0000	0,0001	0,0002	0,0002	0,0001	0,0001
Persicobacter	0,0000	0,0006	0,0001	0,0000	0,0001	0,0000	0,0004	0,0000	0,0006	0,0002	0,0048	0,0001	0,0000	0,0001	0,0002	0,0035	0,0000	0,0001	0,0000	0,0000	0,0002	0,0000	0,0000	0,0001	0,0001	0,0001	0,0003	0,0020	0,0000	0,0001
Lysinibacillus	0,0002	0,0002	0,0001	0,0001	0,0000	0,0001	0,0005	0,0008	0,0001	0,0000	0,0000	0,0004	0,0000	0,0003	0,0001	0,0000	0,0002	0,0005	0,0043	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0004	0,0001	0,0018	0,0000
Edwardsiella	0,0000	0,0001	0,0000	0,0000	0,0005	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0002	0,0000	0,0001	0,0000	0,0000	0,0035	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0015	0,0000
Leeuwenhoekella	0,0000	0,0003	0,0001	0,0000	0,0002	0,0000	0,0003	0,0000	0,0002	0,0136	0,0023	0,0017	0,0000	0,0005	0,0010	0,0000	0,0003	0,0000	0,0000	0,0003	0,0001	0,0000	0,0000	0,0000	0,0000	0,0001	0,0024	0,0012	0,0001	0,0000
Synechocystis	0,0000	0,0003	0,0002	0,0000	0,0000	0,0000	0,0002	0,0003	0,0000	0,0001	0,0001	0,0002	0,0000	0,0003	0,0000	0,0000	0,0002	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0001	0,0002	0,0001	0,0001	0,0001
Thermoanaerobacterium	0,0000	0,0000	0,0000	0,0005	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0020	0,0001	0,0000	0,0002	0,0001	0,0024	0,0001	0,0000	0,0001	0,0001	0,0000	0,0000	0,0004	0,0005
Rhodospseudomonas	0,0005	0,0000	0,0001	0,0000	0,0001	0,0000	0,0001	0,0002	0,0001	0,0001	0,0000	0,0000	0,0000	0,0004	0,0002	0,0001	0,0000	0,0001	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0001	0,0001	0,0000
Thermodesulfator	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0002	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000
Pelobacter	0,0000	0,0001	0,0001	0,0000	0,0001	0,0002	0,0000	0,0002	0,0001	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0007	0,0001	0,0000	0,0000	0,0002	0,0001	0,0001	0,0000	0,0001	0,0001	0,0001	0,0002	0,0001
Methylocaldum	0,0000	0,0001	0,0000	0,0000	0,0005	0,0000	0,0004	0,0000	0,0000	0,0004	0,0003	0,0000	0,0000	0,0002	0,0004	0,0001	0,0007	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0002	0,0002	0,0003	0,0000
Oxalicibacterium	0,0000	0,0000	0,0001	0,0000	0,0005	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000
Catenulispora	0,0000	0,0000	0,0003	0,0000	0,0000	0,0001	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0013	0,0001	0,0005	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0007	0,0000
unclassified (derived from Chroococcales)	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0000	0,0001	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0001	0,0009	0,0002	0,0001	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0003	0,0000
Psychrobacter	0,0000	0,0000	0,0000	0,0001	0,0003	0,0001	0,0001	0,0001	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0428	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0021	0,0001	0,0002
Pseudoalteromonas	0,0000	0,0001	0,0001	0,0001	0,0001	0,0001	0,0004	0,0001	0,0013	0,0000	0,0004	0,0003	0,0000	0,0000	0,0000	0,0001	0,0004	0,0003	0,0004	0,0000	0,0000	0,0000	0,0020	0,0001	0,0003	0,0001	0,0004	0,0002	0,0004	0,0004
Desulfocaldus	0,0000	0,0000	0,0001	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0016	0,0000	0,0000	0,0000	0,0000	0,0004	0,0003	0,0000	0,0000	0,0000	0,0026	0,0006	0,0000	0,0001	0,0000	0,0000	0,0002	0,0002	0,0006
Klebsiella	0,0000	0,0001	0,0002	0,0000	0,0002	0,0000	0,0002	0,0000	0,0000	0,0008	0,0003	0,0000	0,0000	0,0002	0,0002	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0002	0,0002	0,0000	0,0000
Phormidium	0,0000	0,0001	0,0002	0,0000	0,0002	0,0000	0,0007	0,0000	0,0000	0,0000	0,0005	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0002	0,0001	0,0000	0,0001	0,0001	0,0001	0,0001	0,0001	0,0001	0,0003	0,0002	0,0001	0,0001
Dermaococcus	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000

GENUS	SUBJECTS' SITES																								SUBJECTS' GROUPS					
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF
Pseudanabaena	0,0000	0,0002	0,0000	0,0000	0,0000	0,0002	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000
Bermanella	0,0000	0,0000	0,0001	0,0000	0,0003	0,0000	0,0001	0,0001	0,0000	0,0000	0,0004	0,0000	0,0000	0,0003	0,0000	0,0006	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0002	0,0000	0,0000
Erwinia	0,0000	0,0000	0,0000	0,0000	0,0004	0,0000	0,0002	0,0000	0,0001	0,0001	0,0010	0,0002	0,0000	0,0009	0,0001	0,0008	0,0011	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0006	0,0005	0,0000
Verminephrobacter	0,0000	0,0000	0,0001	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0004	0,0002	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0005	0,0000	0,0001	0,0000	0,0001	0,0000	0,0001
Mesoplasma	0,0000	0,0000	0,0001	0,0000	0,0000	0,0003	0,0000	0,0000	0,0001	0,0000	0,0000	0,0004	0,0000	0,0000	0,0000	0,0000	0,0010	0,0005	0,0001	0,0000	0,0000	0,0000	0,0011	0,0008	0,0001	0,0001	0,0000	0,0001	0,0005	0,0004
Blattabacterium	0,0000	0,0002	0,0002	0,0000	0,0000	0,0000	0,0002	0,0001	0,0000	0,0306	0,0309	0,0075	0,0000	0,0003	0,0029	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0021	0,0001	0,0000	0,0001	0,0051	0,0126	0,0000	0,0004
Marinomonas	0,0000	0,0001	0,0000	0,0000	0,0003	0,0001	0,0003	0,0000	0,0000	0,0001	0,0004	0,0000	0,0000	0,0003	0,0000	0,0021	0,0017	0,0002	0,0001	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0001	0,0001	0,0003	0,0008	0,0001
Candidatus Glomeribacter unclassified (derived from Cyanobacteria)	0,0000	0,0000	0,0000	0,0000	0,0001	0,0003	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0001	0,0001	0,0000
Roseomonas	0,0000	0,0000	0,0001	0,0002	0,0002	0,0000	0,0000	0,0003	0,0000	0,0001	0,0000	0,0003	0,0001	0,0001	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0001	0,0000	0,0000
Oenococcus	0,0005	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000
Listeria	0,0000	0,0003	0,0000	0,0001	0,0000	0,0000	0,0007	0,0001	0,0001	0,0001	0,0001	0,0001	0,0001	0,0000	0,0008	0,0000	0,0045	0,0004	0,0001	0,0000	0,0000	0,0000	0,0017	0,0004	0,0001	0,0001	0,0003	0,0002	0,0020	0,0004
Congregibacter	0,0000	0,0000	0,0000	0,0000	0,0003	0,0001	0,0001	0,0001	0,0001	0,0000	0,0000	0,0002	0,0000	0,0004	0,0002	0,0001	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0001	0,0001	0,0000
Dokdonia	0,0000	0,0001	0,0002	0,0000	0,0002	0,0000	0,0003	0,0001	0,0000	0,0020	0,0002	0,0001	0,0000	0,0003	0,0001	0,0001	0,0000	0,0001	0,0001	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0001	0,0005	0,0001	0,0001	0,0001
Salegentibacter	0,0000	0,0001	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0002	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0001	0,0000	0,0009	0,0000	0,0001	0,0001	0,0000	0,0001	0,0000	0,0001	0,0000	0,0002
Microcoleus	0,0000	0,0000	0,0002	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0004	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000
Serratia	0,0003	0,0000	0,0000	0,0000	0,0001	0,0001	0,0001	0,0001	0,0002	0,0011	0,0001	0,0001	0,0000	0,0005	0,0001	0,0012	0,0064	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0011	0,0000	0,0001	0,0003	0,0002	0,0027	0,0003
Pediococcus	0,0001	0,0001	0,0000	0,0001	0,0001	0,0000	0,0004	0,0005	0,0005	0,0002	0,0005	0,0001	0,0002	0,0000	0,0002	0,0003	0,0007	0,0001	0,0001	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0001	0,0004	0,0003	0,0004	0,0001
Rickettsia	0,0000	0,0000	0,0001	0,0000	0,0003	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0004	0,0002	0,0002	0,0001	0,0012	0,0001	0,0001	0,0001	0,0064	0,0000	0,0018	0,0011	0,0000	0,0001	0,0001	0,0001	0,0016
Butyricoccus	0,0000	0,0000	0,0000	0,0000	0,0001	0,0002	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0001	0,0035	0,0000	0,0000	0,0000	0,0096	0,0001	0,0001	0,0013	0,0001	0,0301	0,0000	0,0000	0,0001	0,0000	0,0006	0,0020	0,0053
Cyclobacterium	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0001	0,0000	0,0001	0,0047	0,0000	0,0005	0,0000	0,0004	0,0000	0,0000	0,0000	0,0000	0,0000	0,0016	0,0000	0,0000	0,1824	0,0000	0,0000	0,0001	0,0008	0,0001	0,0000	0,0307
Azonexus unclassified (derived from Thermoanaerobacterales)	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000
Wigglesworthia unclassified (derived from Comamonadaceae)	0,0000	0,0001	0,0000	0,0000	0,0003	0,0000	0,0001	0,0001	0,0004	0,0002	0,0004	0,0002	0,0000	0,0002	0,0000	0,0000	0,0020	0,0002	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000
Chloroherpeton	0,0000	0,0004	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0003	0,0001	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000
Thermoflavimicrobium	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000
Desulfitibacter	0,0000	0,0000	0,0000	0,0000	0,0004	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000
Ktedonobacter unclassified (derived from Campylobacteraceae)	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000

GENUS	SUBJECTS' SITES																								SUBJECTS' GROUPS					
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF
Deinococcus	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000
Sodalis	0,0000	0,0001	0,0000	0,0000	0,0002	0,0001	0,0001	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0002	0,0007	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0003	0,0000
Candidatus Hemobacterium	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000
Roseiflexus	0,0000	0,0002	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0005	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0002	0,0000
Hymenobacter	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0001	0,0001	0,0008	0,0000	0,0001	0,0020	0,0000	0,0022	0,0000	0,0004	0,0000	0,0010	0,0001	0,0002	0,0003	0,0000	0,0001	0,0000	0,0000	0,0001	0,0002	0,0006	0,0002	0,0001
Natranaerobius	0,0000	0,0002	0,0000	0,0000	0,0001	0,0000	0,0004	0,0000	0,0001	0,0000	0,0000	0,0000	0,0006	0,0000	0,0000	0,0000	0,0000	0,0039	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0002	0,0001	0,0008	0,0000
Marinobacter	0,0000	0,0000	0,0000	0,0000	0,0001	0,0002	0,0001	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0002	0,0000	0,0001	0,0000	0,0003	0,0000	0,0000	0,0001	0,0000	0,0004	0,0002	0,0000	0,0001	0,0001	0,0000	0,0001	0,0001
Segniliparus	0,0000	0,0000	0,0001	0,0000	0,0001	0,0001	0,0001	0,0000	0,0002	0,0000	0,0002	0,0001	0,0000	0,0002	0,0000	0,0000	0,0006	0,0001	0,0001	0,0000	0,0000	0,0001	0,0001	0,0006	0,0002	0,0001	0,0001	0,0001	0,0003	0,0002
Desulfotignum	0,0005	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000
Histophilus	0,0000	0,0000	0,0001	0,0000	0,0002	0,0000	0,0001	0,0001	0,0000	0,0000	0,0001	0,0001	0,0000	0,0001	0,0001	0,0000	0,0009	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0004	0,0000
Tomitella	0,0000	0,0000	0,0000	0,0000	0,0001	0,0002	0,0000	0,0000	0,0006	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0007
Cryobacterium	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0006	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0002	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001
Tatumella	0,0000	0,0001	0,0000	0,0000	0,0002	0,0000	0,0000	0,0002	0,0000	0,0006	0,0000	0,0020	0,0000	0,0005	0,0005	0,0033	0,0009	0,0000	0,0005	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0002	0,0005	0,0006	0,0000
Gluconacetobacter	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0005	0,0000	0,0001	0,0000	0,0001	0,0000	0,0005	0,0001	0,0000	0,0004	0,0000	0,0002	0,0001	0,0000	0,0001	0,0000	0,0002
Sulfobacillus	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0006	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0001
Desulfatibacillum	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0001	0,0000	0,0001	0,0000	0,0002	0,0000	0,0002	0,0001	0,0000	0,0001	0,0000	0,0002	0,0000	0,0000	0,0000	0,0001	0,0001
Beggiatoa	0,0000	0,0000	0,0001	0,0000	0,0001	0,0001	0,0001	0,0000	0,0001	0,0000	0,0001	0,0001	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Thermaerobacter	0,0001	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0024	0,0001	0,0102	0,0000	0,0001	0,0088	0,0000	0,0000	0,0000	0,0000	0,0034
Brevundimonas	0,0000	0,0001	0,0001	0,0000	0,0001	0,0000	0,0002	0,0000	0,0000	0,0001	0,0001	0,0001	0,0000	0,0002	0,0000	0,0000	0,0002	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0001	0,0000
unclassified (derived from Nitrosomonadaceae)	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Fibrobacter	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0001	0,0001	0,0001	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0003	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000
Flammeovirga	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0003	0,0000	0,0000	0,0001	0,0000	0,0003	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0001	0,0001	0,0000	0,0000	0,0001	0,0001	0,0000	0,0001
Brochothrix	0,0001	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0002	0,0001	0,0002	0,0000	0,0000	0,0000	0,0000	0,0001	0,0003	0,0000	0,0000	0,0001	0,0001	0,0001	0,0001
Desulfotalea	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0002	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000
Dehalobacter	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0001	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001
Prochlorococcus	0,0000	0,0001	0,0001	0,0000	0,0001	0,0000	0,0003	0,0000	0,0000	0,0001	0,0001	0,0001	0,0000	0,0002	0,0000	0,0001	0,0000	0,0002	0,0002	0,0000	0,0001	0,0000	0,0007	0,0000	0,0000	0,0000	0,0001	0,0001	0,0001	0,0001
Thiomicrospira	0,0000	0,0001	0,0000	0,0000	0,0002	0,0000	0,0002	0,0004	0,0000	0,0003	0,0007	0,0002	0,0000	0,0000	0,0004	0,0001	0,0006	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0003	0,0003
Planobispora	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0002	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0001
Bibersteinia	0,0000	0,0002	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0001	0,0010	0,0021	0,0001	0,0000	0,0001	0,0000	0,0054	0,0001	0,0000	0,0002	0,0000	0,0000	0,0005	0,0000	0,0001	0,0001	0,0000	0,0002	0,0010	0,0001	0,0001
Nodularia	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0036	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0007	0,0000
Aphanizomenon	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Acaryochloris	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000

GENUS	SUBJECTS' SITES																							SUBJECTS' GROUPS							
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF	
Bowmanella	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0002	0,0000	0,0005	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0002	0,0001	0,0001	0,0001	0,0000
Lachnospira	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0002	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	
unclassified (derived from Thermomonosporaceae)	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0006	0,0000	0,0050	0,0000	0,0001	0,0007	0,0015	0,0001	0,0000	0,0000	0,0000	0,0001	0,0011	
Anaerostipes	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0002	0,0130	0,0005	0,0001	0,0000	0,0001	0,0002	0,0000	0,0009	0,0001	0,0069	0,0031	0,0002	0,0005	0,0003	0,1666	0,0001	0,0000	0,0000	0,0027	0,0001	0,0026	0,0281	
Actinospica	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	
Anaerobranca	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0016	0,0001	0,0004	0,0000	0,0000	0,0014	0,0001	0,0005	0,0000	0,0000	0,0000	0,0004	0,0004	
Pigmentiphaga	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	
Planomicrobium	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	
Allochromatium	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	
Dickeya	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0004	0,0000	0,0002	0,0014	0,0000	0,0003	0,0000	0,0002	0,0001	0,0000	0,0006	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0004	0,0001	0,0003	0,0000
Orientia	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0111	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	
Psychromonas	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0006	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	
Denitrovibrio	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0001	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0000	0,0049	0,0000	0,0000	0,0047	0,0049	0,0005	0,0000	0,0001	0,0000	0,0000	0,0026	
Proteus	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0011	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0011	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0000	0,0005	0,0000	
Cyanobacterium	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	
Hahella	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0002	0,0001	0,0001	0,0001	0,0001	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0012	0,0001	0,0000	0,0001	0,0001	0,0000	0,0002	0,0000	0,0000	0,0001	0,0001	0,0003	0,0001	
Candidatus Liberibacter	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0003	0,0000	0,0002	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0001	0,0001	0,0000	0,0000	0,0005	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	
Anaerococcus	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0002	0,0000	0,0003	0,0003	0,0000	0,0000	0,0127	0,0006	0,0000	0,0001	0,0000	0,0034	0,0001	0,0001	0,0001	0,0000	0,0028	0,0001	0,0000	0,0000	0,0002	0,0007	0,0005	0,0000	
Desulfoglaeba	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	
Piscirickettsia	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	
Thioalkalivibrio	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0003	0,0001	0,0000	0,0003	0,0001	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0001	0,0001	0,0001	0,0001	
Candidatus Rhodoluna	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0003	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0003	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	
Dyadobacter	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0001	0,0000	0,0005	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0004	0,0000	0,0000	0,0001	0,0001	0,0000	0,0001	
Marinilibalia	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0002	0,0003	0,0001	0,0002	0,0000	0,0000	0,0000	0,0006	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0011	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0001	0,0000	0,0002	
Thermacetogenium	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0002	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	
Nitrosovibrio	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	
Rhodobacter	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	
Heliobacillus	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0084	0,0001	0,0000	0,0000	0,0001	0,0000	0,0015	0,0000	
Elusimicrobium	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0002	0,0002	0,0000	0,0000	0,0000	0,0003	0,0000	0,0008	0,0000	0,0006	0,0000	0,0005	0,0146	0,0001	0,0000	0,0000	0,0001	0,0001	0,0002	0,0026	
Chelonobacter	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0003	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0001	0,0000	
Kibdelosporangium	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0001	
Salinibacterium	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0005	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0002	0,0000	
Sporolactobacillus	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	

GENUS	SUBJECTS' SITES																								SUBJECTS' GROUPS				
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL
Mariprofundus	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0001	0,0001	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Streptomonospora	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Laceyella	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0003	0,0000	0,0000	0,0000	0,0008	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001
Anaerotruncus	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0001	0,0000	0,0045	0,0000	0,0000	0,0000	0,0001	0,0000	0,0008
Methylocystis	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
unclassified (derived from Chromatiaceae)	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Ammonifex	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Anoxybacillus	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0001	0,0001	0,0000	0,0000	0,0000	0,0004	0,0000	0,0000	0,0000	0,0000	0,0001
Methylobacterium	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001
Brachyspira	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Wolbachia	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0018	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0007	0,0000
Desulfonospira	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0000
Oceanobacillus	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0022	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0009	0,0000
Halobacillus	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Heliorestis	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000
Spirochaeta	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0005	0,0001	0,0002	0,0000	0,0011	0,0000	0,0000	0,0001	0,0006	0,0001	0,0002	0,0007	0,0000	0,0011	0,0001	0,0000	0,0000	0,0001	0,0002	0,0003
Acetobacter	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0017	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0007	0,0000
Azovibrio	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Candidatus Kuenenia	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Desulfobulbus	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Hafnia	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Melissococcus	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Mesorhizobium	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000
Methylomonas	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Plesiomonas	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0006	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000
Schlegelella	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0004	0,0000	0,0052	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0022	0,0000
Terribacillus	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Thiolamprovim	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0002	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Wautersiella	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Desulfurella	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000
Pasteuria	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0022	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002
Thiohalorhabdus	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000
Zoogloea	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0001	0,0000	0,0000	0,0013	0,0001	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0006	0,0000

GENUS	SUBJECTS' SITES																								SUBJECTS' GROUPS					
	CA-ANCL1	CA-ANCL2	CA-ANCL3	CA-ANCL4	CA-ANCL5	CA-ANCL6	CA-INCL1	CA-INCL2	CA-INCL3	CA-INCL4	CA-S1	CA-S2	CA-S3	CA-S4	CA-S6	CA-S6	CI-INCL1	CI-INCL2	CI-INCL3	CF-S1	CF-S2	CF-S3	CF-S4	CF-S5	CF-S6	CA-ANCL	CA-INCL	CA-S	CI-INCL	CF
Desulforegula	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0012	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0002
Desulfocella	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0005	0,0000	0,0000	0,0000	0,0000	0,0009	0,0000	0,0000	0,0000	0,0000	0,0018	0,0000	0,0000	0,0000	0,0001	0,0002	0,0003	
unclassified (derived from Rickettsiaceae)	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0003	0,0076	0,0000	0,0000	0,0000	0,0001	0,0000	0,0001	0,0000	0,0000	0,0000	0,0000	0,0046	0,0000	0,0000	0,0000	0,0001	0,0010	0,0000	0,0008
Candidatus Cardinium	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0000	0,0035	0,0033	0,1315	0,0000	0,0000	0,0000	0,0000	0,0000	0,0003	0,0000	0,0000	0,0000	0,0000	0,0758	0,0000	0,0000	0,0000	0,0006	0,0165	0,0001	0,0127

Appendix 3 Table S2: Genera exclusive active non-cavitated lesions (CA-ANCL)

Table S2. Relative abundance of exclusive genera observed in supragingival biofilm samples for caries active subjects in active non-cavitated lesion sites (CA-ANCL).

Group	Phylum	Genus	Proportion
CA-ANCL	Actinobacteria	<i>Tetrasphaera</i>	0.0001
		<i>unclassified (derived from Ktedonobacteria)</i>	0.0001
		<i>unclassified (derived from Thermomonosporaceae)</i>	<0.0001
		<i>Skermania</i>	<0.0001
		<i>Metascardovia</i>	<0.0001
	Cyanobacteria	<i>Geminocystis</i>	<0.0001
	Firmicutes	<i>Pasteuria</i>	<0.0001
		<i>Thermoanaerobacterium</i>	<0.0001
		<i>Sedimentibacter</i>	<0.0001
		<i>Sarcina</i>	<0.0001
	Proteobacteria	<i>Rickettsiella</i>	<0.0001
		<i>Phyllobacterium</i>	<0.0001
		<i>Derxia</i>	<0.0001
		<i>Bibersteinia</i>	<0.0001
		<i>Beggiatoa</i>	<0.0001
	Betaproteobacteria	<i>Sterolibacterium</i>	<0.0001
		<i>Pandoraea</i>	<0.0001
	Fusobacteria	<i>Ilyobacter</i>	<0.0001
Verrucomicrobia	<i>Coralimargarita</i>	<0.0001	
Elusmicrobia	<i>Elusimicrobium</i>	<0.0001	