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| **Table 1. Characteristics of included supragingival plaque studies (n = 13)** | | | | | | | | |
| **First Author, Year (REF)** | **Sample Type** | **Storage of Sample** | **Study Population** | **Caries Definition** | **Sample Size** | **Method of Analysis** | ***Caries-Active Taxa*** | ***Caries-Free Taxa*** |
| Jiang W, 2011 (8) | Healthy subjects: pooled Supragingival Plaque from buccal surfaces and accessible proximal surfaces of primary molars. Caries subject: pooled Supragingival Plaque from buccal and accessible proximal surfaces of intact enamel adjacent to carious lesions in primary molars. | The collected plaque samples were wiped onto endodontic paper, was immediately transported on ice to the microbiology laboratory and stored at -20 C before extraction of the genomic DNA. | Children; Ages 3-5 | Caries-Susceptible: dmfs >10; Caries Moderate: 4 <dmfs < 6; Caries Free: dmfs = 0 | n = 45; 15 Caries-Susceptible; 15 Caries Moderate; 15 caries free | 16s rDNA PCR-DGGE combined with primers specific for oral streptococci; V3-V5; Statistical Significance: p<0.05 | *NONE FOUND* | *Streptococcus mitis, Streptococcus oralis, Streptococcus sanguinis* |
| Zhang M, 2015 (26) | Supragingival Plaque from surface of intact enamel and surface of a deep caries lesion in non healthy subjects, and from at least three sites (including posterior and anterior teeth) in healthy samples. | The samples were transported on ice to the laboratory and stored at−80°C until used. | Children; Ages 3-6 | Caries group subjects: had more than 3 cavitated caries teeth which includes at least one carious primary molar(codes 5 or 6 based on the classification of the carious status of the ICDAS); Healthy group subjects: did not have caries in any teeth (code 0 based on the classification of the carious of the ICDAS) | n = 20 (10 twin pairs); healthy individuals: n = 10; Caries Individuals: n = 10 | Pyrosequencing of the 16s rRNA gene amplicons; V3-V5; Pyrosequencing; Statistical Significance: p<0.05 | *NONE FOUND* | *NONE FOUND* |
| Ihara Y, 2019 (27) | In Vivo Dental Plaque formed on hydroxyapatite disks | The disks were retrieved from the oral cavity 6 h later and placed in a microcentrifuge tube after rinsing with phosphate-buffered saline. | Adults; Ages 20-32 | Subjects with no caries-experienced teeth; Subjects with a moderate  number of caries-experienced teeth (1 to 7); Subjects with a high number of caries-experienced teeth (>=8) | n=74; No caries-experienced teeth: n = 20; Moderate  number of caries-experienced teeth n = 36; High number of caries-experienced teeth: n = 18 | Full length16S rRNA gene sequences of plaque, V2-V2 from saliva and plaque, and quantitative PCR to determine total bacterial amounts; V1-V9 (full length) and sequencing of V1-V2; PacBio Sequel for full length sequencing, Ion PGM for V1-V2 region of 16S rRNA; Statistical Significance: ---- | *NONE FOUND* | *NONE FOUND* |
| Xiao J, 2018 (28) | Supragingival dental plaque was collected from the whole dentition with a standard dental scaler. | Previously established methods (Grier et al., 2017; Merkley et al., 2015) were used to perform oral microbiome sequencing and related bioinformatics analysis. Total genomic DNA from clinical samples (100ul saliva and 200ul plaque suspension) was extracted using Quick- DNATM Fecal/Soil Microbe Miniprep Kit (ZymoResearch, Irvine, CA) (Dardas et al., 2014; Merkley et al., 2015; Zhu et al., 2013) | Children Ages Unspecified: Average Age Children SECC = 4.0 +- 0.9, CF = 3.8 +- 1.6; | S-ECC was diagnosed per criteria of the American Academy of Pediatric Dentistry. The number of carious teeth and surfaces was charted with index variables of decayed, missing due to decay, or filled, according to the codes proposed by the World Health Organization’s Oral Health Surveys Basic Methods (1997). Plaque status for mothers and children were assessed separately according to criteria modified from Silness and Löe (1964) and Ribeiro Ade et al. (2002) | n = 36 plaque samples; children S-ECC: n = 21 and children CF: n = 15 | 16s rRNA amplicon sequencing; V1-V3 ; Illumina; Statistical Significance: p<0.05 | *Candida albicans, Streptococcus mutans,  Veillonella atypica, Veillonella dispar,  Veillonella parvula* | *S. oral taxon B66,  Actinomyces viscosus, Actinomyces naeslundii, Actinomyces oris,  Leptotrichia BU064* |
| de Jesus VC, 2020 (29) | Supragingival plaque | Samples were dislodged into 1 mL of RNAprotect Bacteria Reagent (Qiagen) and immediately frozen at –80 °C until further analysis. | Children; Ages <72 months | All children with S-ECC were recruited at the Misericordia Health Centre on the day of their dental rehabilitative surgery; Caries-free: dmft index equal to 0; no decayed, missing, or filled primary tooth surface | n=80; Severe Early Childhood Caries: n = 40; Caries Free: n = 40 | 16S rRNA and ITS1 rRNA gene amplicon sequencing; V4; Illumina MiSeq; Statistical Significance: p < 0.05 | *Streptococcus mutans, Veillonella dispar, Veillonella sp. oral taxon 780* | *Candida dubliniensis, Corynebacterium durum, Lautropia mirabilis* |
| Schoilew K, 2019 (30) | Pooled Supragingival Plaque | The collection site was isolated with cotton rolls and gently air dried. Sterile curettes were used for sampling of supragingival plaque from healthy enamel on the buccal surface of the first and second maxillary molars. The samples were pooled in an empty and sterile 1.5 ml microcentrifuge tube and frozen (−25°C) until further analysis. | Adults; Ages 18-80 | Active Caries Lesions: cavitated lesions as well as white spot lesions with an opaque, chalky surface. Inactive Caries Lesions: white spots with an intact, smooth and glossy surface and brown spots. | n = 46; n = 19 subjects without caries experience (NH; DMFT = 0); n = 27 subjects with ‘caries experience’ (CE; DMFT > 0 [F(T)> 0; D(T)= 0]) | 16s rRNA Amplicon Sequencing; V4; Illumina Miseq; Statistical Significance: p < 0.05; Benjamini-Hochberg corrected | *NONE FOUND* | *Capnocytophaga ochracea , Corynebacterium matruchotii, Porphyromonas pasteri, Selenomonas noxia* |
| Zheng Y, 2018 (31) | Supragingival plaque; Caries group samples were pooled from the lingual and proximal surfaces of decayed teeth were pooled and samples from the dental plaque in caries lesions were pooled. Samples from the caries-free group and the mothers group were collected from the labial, lingual and proximal surfaces of healthy teeth (including anterior and posterior teeth). | All supragingival plaque samples were obtained by scraping the tooth surfaces with a sterile metal excavator. The metal excavator was immersed in a sterile 1.5 ml eppendorf tube containing 1 ml of Ringer’s solution. The samples were transported on ice to the laboratory, and stored at −20◦C until genomic DNA extraction. | Children; Ages 3-6 | Caries group: had two or more cavitated teeth; Caries-free group: did not have any carious teeth in their oral cavity | n = 31; Dental caries: n = 16 ; Caries-free: n = 15 | 16S rRNA amplicons; V3-V4 ; Illumina sequencing in the Human Oral Microbial Identification Next Generation Sequencing (NGS) HOMINGS Laboratory ; Statistical Significance: Benjamini-Hochberg, adjusted P-value <0.0001 | *Actinomyces massiliensis, Lactobacillus fermentum , Neisseria sicca, Prevotella oulorum,  Streptococcus mutans,  Veilonella dispar* | *Actinomyces israelii, Capnocytophaga sputigena, Fusobacterium periodonticum,  Haemophilus parainfluenzae, Leptotrichia sp ot 498, Porphyromonas sp ot 279* |
| Richards VP, 2017 (32) | Supragingival plaque | Each plaque sample was obtained by pooling material from at least two different tooth sites of similar health conditions using sterile periodontal curettes | Children; Ages 2-7 | Caries active with enamel lesions only (CAE) (no decayed teeth [DT] and ≥0 missing and filled teeth [MFT]), and caries active with at least two cavitated, unrestored dentin carious lesions (CA) (≥2 DT and ≥0 MFT) | n=55; | HOMINGS and 16s rRNA sequencing ; V3-V4;  Illumina Miseq Sequencing; Statistical Significance: p<0.05 | *Streptococcus mutans ST-15,  Bergeyella sp oral taxon 322 BE-02,  Veillonella parvula,  Streptococcus anginosus,  Prevotella salivae,  Prevotella maculosa,  Megasphaera micronuciformis,  Scardovia Genus probe GP-075,  Selenomonas sp oral taxon 149 SE-13,  Cryptobacterium curtum,  Lactobacillus fermentum,  Lactobacillus Genus probe 2 GP-045,  Lactobacillus Genus probe 4 GP-047* | *Ottowia sp oral taxon 894 OT-02,  Neisseria bacilliformis NE-01,  TM7[G-3] sp oral taxon 351,  Streptococcus Genus probe 3 GP-128* |
| Eriksson L, 2018 (33) | Supragingival biofilm collected from all accessible tooth surfaces; whole stimulated saliva | Supragingival biofilm was collected from all accessible tooth surfaces with sterile wooden toothpicks and pooled by subject into 100 µL of TE buffer (10mM Tris, 1mM ethylenediaminetetraacetic acid [EDTA], pH 7.6). Whole saliva collected for 3 min into ice-chilled sterile test tubes while subjects chewed paraffin wax. All samples were stored at –80 °C. | Adolescents; Age 17 | Numbers of tooth surfaces that had caries in the enamel or into the dentine, had a filling, or were missing were recorded from visual and radiographic examinations. Caries in the enamel was scored according to a visual color change or demineralization within the enamel on bitewing X-rays. Caries in the dentine was scored according to local breakdown in the enamel or a cavity or when demineralization extended into the dentine on bitewing X-rays. | n = 154; 71 present caries (46%); 82 no caries. | Multiplex 16S rDNA amplicon sequencing with HOMINGS protocol ; V3-V4;  Illumina Miseq Sequencing; Statistical Significance: P ≤ 0.005 | *Only S. mutans was significantly (p<=0.005) more abundant in saliva and toot biofilm samples from subjects with caries than those from caries-free adolescents* | *NONE FOUND* |
| Piwat S, 2015 (34) | Supragingival plaque | Supra-gingival plaque samples were taken with a sterile curette from the sites of 16M, 21D, 36M, and 41D. In case of missing teeth, the samples were taken from the next tooth distally. The plaque samples were transferred to sterile Eppendorf tubes containing 100 μl of TE-buffer to which 100 μl 0.1 M NaOH was added. The samples were stored in a refrigerator until they were transported and processed in the laboratory of Oral Microbiology, Institute of Odontology, University of Gothenburg, Sweden | Children; Age 12-14 | Caries free: DT=0; Low caries: DT 1–4; High caries: DT>4 | N = 100; Caries free: n = 34; Caries: n = 66 | Checkerboard; Statistical Significance: ---- | *NONE FOUND* | *NONE FOUND* |
| Mannaa A, 2013 (35) | Pooled supragingival plaque from posterior approximal sites | Each plaque sample was placed in an Eppendorf tube containing 150 μ l of sterile TE buffer (10 mM Tris–HCl, 1 mM EDTA, pH 7.6). Then 100 μ l of 0.5 M NaOH was added to the plaque pellet and the bacterial suspension was stored at -20°C pending further processing | Children and Adults; Ages 4–6, 12–16, and 17+ | Caries was registered clinically and radiographically at the D3 level | n = 258; 86 mothers and their children aged 4–6 years and 12–16 years old participated | Checkerboard DNA-DNA hybridization ; Statistical Significance: p<0.05 | *NONE FOUND* | *NONE FOUND* |
| Tanner AC, 2011 (36) | Plaque samples were taken with sterile wooden toothpicks from the buccal and interproximal surfaces of molars to include plaque from carious lesions in the severe ECC children. | Each plaque sample was put in a 5-ml airtight vial containing 2 ml prereduced anaerobically sterilized (PRAS) Ring- er’s solution (49) with 3-mm glass beads (44) and placed in insulated bags with frozen freezer blocks. Samples were transported to the microbiology laboratory and processed within 4 h of sampling. | Children; Ages 2-6 years old | Children with severe ECC (14) had extensive caries in the primary dentition that affected over 36% of tooth surfaces with an average of 4 pulpally involved teeth (21) and were scheduled for restorative treatment under general anesthesia. Caries-free children, determined by visual and radiographic examination, had no cavities or enamel white spot lesions, which can represent early stages of tooth enamel demineralization. | N = 82; Severe ECC: n = 42; caries-free children: n = 40 | Partial sequences for 16S rRNA gene. Isolate sequence compared with taxon sequences in HOMD; Statistical Significance: p<0.05 | *Actinomyces gerencseriae, Scardovia wiggsiae, Streptococcus cristatus, Streptococcus mutans, Veillonella parvula* | *NONE FOUND* |
| Teng F, 2015 (37) | Dental plaque biofilm |  | Children; Age around 4 | Microbiota with dmfs of zero were designated as ‘‘Healthy’’ (‘‘H’’); otherwise were as ‘‘Caries’’ (‘‘C’’), which consist of ‘‘low caries’’ (1 % dmfs < 6) and ‘‘severe caries’’ (dmfs R 6 | n = 50; (i) The ‘‘stay healthy’’ (H2H) group: n = 17 subjects (94 samples) maintained healthy state, with dmfs staying zero. (ii) The ‘‘caries-onset’’ (H2C) group: n = 21 subjects (120 samples) underwent the transition from healthy to caries-active state. (iii) The ‘‘caries-progression’’ (C2C) group: n = 12 subjects (70 samples) | 16S rRNA ; V1-V3; Pyrosequencing; Statistical Significance: p < 0.05 | *Streptococcus spp.,  Prevotella spp.,  Veillonella spp.,* | *NONE FOUND* |
| Agnello M, 2017 (38) | Plaque samples were collected from each subject by swabbing a sterile interdental brush on all available tooth surfaces | Samples were immediately frozen at −80 °C in 15% glycerol until used for analysis. | Children; Age <72 months | S-ECC: had severe tooth decay involving multiple primary teeth and were recruited from the Misericordia Health Centre in Winnipeg, Canada, on the day of their sched- uled dental rehabilitative surgery under general anesthesia. Caries-free: children were assessed to ensure that there was no evidence of caries (dmft = 0, no cavitations or white spot lesions) | n = 50; S-ECC: n = 30; Caries-free children: n = 20 | 16S rRNA ; V3-V4; Illumina; Statistical Significance: Benjamini Hochberg; p < 0.05 | *Streptococcus mutans,  Veillonella sp. HOT‐780,  Porphyromonas HOT 284* | *Streptococcus gordonii, Streptococcus sanguinis* |

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| **Table 2. Characteristics of included salivary studies (n = 9)** | | | | | | | | |
| **First Author, Year (REF)** | **Sample Type** | **Storage of Sample** | **Study Population** | **Caries Definition** | **Sample Size** | **Method of Analysis** | ***Caries-Active Taxa*** | ***Caries-Free Taxa*** |
| Wang Y, 2019 (39) | Saliva (To minimize stimulation of salivation, saliva needed to be kept in the mouth for 3 min. Subjects were then instructed to drool into sterile cryogenic vials for 3 min) | Each saliva sample was pipetted into a sterile 1.5-ml Eppendorf tube, which wassnap-frozen in liquid nitrogen and stored at80°C | Children; Ages 3-5 months; Unspecified | Severe ECC: dmfs ≥ 8; Caries-Free: dmfs =0 | n = 44; Severe early childhood caries (ECC): n = 25; Caries-free: n = 19 | Metagenomics Analysis (gene cataloging); Illumina HiSeq/TruSeq; Statistical Significance: FDR < 0.1 | *Anaeroglobus geminatus, atopobium rimae, Bifidobacterium dentium, Cryptobacterium curtum, Dialister invisus, Eubacteriaceae bacterium ACC19, Lactobacillus salivarius, Olsenella uli, Oribacterium sp. Oral taxon 078, Parascardovia denticolens,  Prevotella amnii, prevotella buccae, Prevotella denticola, prevotella multiformis, Prevotella multisaccharivorax, prevotella nigrescens, prevotella oris,  prevotella sp. Oral taxon 317, Shuttleworthia satelles, Streptococcus mutans* | *Candidatus Nitrospira defluvii, Erysipelotrichaceae bacterium 5\_2\_54FAA, Neisseria lactamica, Streptococcus australis* |
| Hurley E, 2019 (5) | Unstimulated Saliva and layers of dentinal caries | Caries samples were placed in a sterile 1.5-ml micro-centrifuge tube and transported to the laboratory, where they were frozen until further analysis and stored at −80 °C. Salivary swabs were placed in a collection tube, and stored at−80 °C. | Children; Age <60 months; Primary | For the caries-active group, caries was recorded at the level of cavitation into dentine (cavitation level), using the WHO criteria, with the addition of visible non cavi- tated dentine caries as referenced by Whelton et al.; Caries-free children did not show clinical evidence of early pre-cavitation of caries or white spot lesions and had no history of treatment on any tooth surfaces | n=138; Severe Early Childhood Caries: n = 68; Caries Free: n = 70 | 16S rRNA amplicon sequencing; V4-V5; Illumina MiSeq; Statistical Significance: Benjamini and Hochberg correction; p<0.05 | *Prevotella histicola, Streptococcus mutans,  Veillonella dispar* | *Alloprevotella tannerae , Haemophilus parainfluenzae,  Leptotrichia buccalis, Prevotella salivae* |
| Xiao J, 2018 (28) | Nonstimulated whole saliva was collected from subjects through a saliva jet connected to a suction pump at least 2 h after any toothbrushing, eating, or drinking | Previously established methods (Grier et al., 2017; Merkley et al., 2015) were used to perform oral microbiome sequencing and related bioinformatics analysis. Total genomic DNA from clinical samples (100ul saliva and 200ul plaque suspension) was extracted using Quick- DNATM Fecal/Soil Microbe Miniprep Kit (ZymoResearch, Irvine, CA) (Dardas et al., 2014; Merkley et al., 2015; Zhu et al., 2013) | Children; Unspecified: Average Age Children SECC = 4.0 +- 0.9, CF = 3.8 +- 1.6; | S-ECC was diagnosed per criteria of the American Academy of Pediatric Dentistry. The number of carious teeth and surfaces was charted with index variables of decayed, missing due to decay, or filled, according to the codes proposed by the World Health Organization’s Oral Health Surveys Basic Methods (1997). Plaque status for mothers and children were assessed separately according to criteria modified from Silness and Löe (1964) and Ribeiro Ade et al. (2002) | n=39; Severe Early Childhood Caries: 19; Caries Free: 18 CF | 16s rRNA amplicon sequencing; V1-V3 ; Illumina; Statistical Significance: p<0.05 | *Streptococcus vestibularis,  Streptococcus salivarius, Veillonella atypica,  Veillonella dispar, Veillonella parvula* | *Streptococcus ET G 4d04* |
| Eriksson L, 2018 (33) | Supragingival biofilm collected from all accessible tooth surfaces; whole stimulated salive | Supragingival biofilm was collected from all accessible tooth surfaces with sterile wooden toothpicks and pooled by subject into 100 µL of TE buffer (10mM Tris, 1mM ethylenediaminetetraacetic acid [EDTA], pH 7.6). Whole saliva collected for 3 min into ice-chilled steril test tubes while subjects chewed paraffin wax. All samples were stored at –80 °C. | Adults; Age 17; Unspecified | Numbers of tooth surfaces that had caries in the enamel or into the dentine, had a filling, or were missing were recorded from visual and radiographic examinations. Caries in the enamel was scored according to a visual color change or demineralization within the enamel on bitewing X-rays. Caries in the dentine was scored according to local breakdown in the enamel or a cavity or when demineralization extended into the dentine on bitewing X-rays. | n = 154; 71 present caries (46%); 82 no caries. [This is confusing as the text says 154, but numbers in the table add to 153) | Multiplex 16S rDNA amplicon sequencing with HOMINGS protocol ; V3-V4 ;  Illumina Miseq Sequencing; Statistical Significance: P ≤ 0.005 | *Only S. mutans was significantly (p<=0.005) more abundant in saliva and tooth biofilm samples from subjects with caries than those from caries-free adolescents* | *NONE FOUND* |
| Belstrøm D, 2017 (40) | Stimulated Saliva | Participant was instructed to chew and spit continuously for 3 min into a sterile plastic cup, after which time the collected saliva from the cup was stored at –80°C | Adults ; Ages 18-76; Unspecified | Caries was registered according to Moller and Poulsen as manifest caries on tooth and surface level expressed as DMFT (decayed, missed, filled tooth) and DMFS (decayed, missed, filled surfaces) | n=88; Healthy: n = 57; Caries: n = 31 | HOMINGS; bacterial identification was performed using HOMINGS.; V3-V4;  Illumina Miseq Sequencing; Statistical Significance: Benjamini–Hochberg correction was used to control for multiple comparisons; For this analysis, an adjusted p-value of <0.0001 was considered statistically significant | *Bifidobacterium dentium,  Lactobacillus salivarius,  Streptococcus sp ot068,  Parascardovia denticolens* | *Fusobacterium periodonticum,  Porphyromonas sp ot279,  Bergeyella sp ot322,  Alloprevotella sp ot914,  Stomatobaculum sp ot097,  Leptotrichia sp ot223,  Lachnoanaerobaculum umeaense* |
| Belstrøm D, 2016 (41) | Stimulated Saliva | The subjects expectorated for 1 min, and the saliva was discarded. For an additional 3 min, subjects continued to expectorate, and the saliva was collected in a plastic cup and stored at −80°C. | Adults; Ages 22-70; Unspecified | Dental caries was defined as manifest untreated ≥3 surfaces caries | n=30; Periodiontis: n = 10 ; Dental caries: n = 10; Orally healthy: n = 10 | HOMINGS; DNA isolation was performed following specifications of the protocol: Pathogen\_Universal\_200 (Roche, Mannheim, Germany) (26), and the HOMINGS technique was used for microbial analysis; V3-V4;  Illumina Miseq Sequencing; Statistical Significance: p<0.05 in combination with a FDR value of 0 was considered statistically significant | *Streptococcus mutans,  Streptococcus Genus probe 4,  Streptococcus Genus probe 1,  Lactobacillus Genus probe 1,  L. vaginalis, Actinomyces sp oral taxon 448,  Veillonella sp oral taxon 917* | *NONE FOUND* |
| Jiang S, 2016 (42) | Unstimulated saliva | The collected samples were quickly frozen on dry ice, transported to the laboratory within 2 h, and then stored at −80 ◦C until use | Children; Ages 3-4 ; Unspecified | The caries examination method and criteria recommended by the World Health Organization were followed. Decayed teeth were detected at the cavitation level. | N=40; Caries: n = 20; No Caries: n = 20 | 16S rRNA gene; V3‐V4; Illumina Miseq ; Statistical Significance: p < 0.05 | *Rothia dentocariosa,  Actinomyces graevenitzii,  Veillonella sp. oral taxon 780,  Prevotella salivae, Streptococcus mutans* | *Fusobacterium periodonticum, Leptotrichia sp. Oral clone FP036* |
| Yang F, 2012 (23) | Saliva | Samples were stored at -80°C before high-salt DNA extraction | Adults; Ages 18-22 | Caries-active: DMFT ≥ 6; Healthy: DMFT=0; | n=45; Healthy: n = 26; Caries Active: n = 19 | 16s rRNA Amplicon Sequencing; V4-V5; Illumina; Statistical Significance: p < 0.1 | *Actinomyces sp., Aggregatibacter paraphrophilus, Capnocytophaga granulosa, Catonella morbi, Eggerthella lenta,  Enterobacter sakazakii,  Fusobacterium periodonticum, Gemella sanguinis, Haemophilus parainfluenzae,  Haemophilus sp., Kingella denitrificans,  Lachnospiraceae [G-1] sp., Lachnospiraceae [G-2] sp.,  Lachnospiraceae [G-4] sp. , Lachnospiraceae [G-8] sp., Leptotrichia sp., Mobiluncus mulieris, Neisseria sp., Neisseria subflava,  Oribacterium sp.,  Peptococcus sp.,  Peptoniphilus sp.,  Peptostreptococcaceae [XI][G-5] sp., Peptostreptococcaceae [XI][G-7] sp.,  Porphyromonas sp.,  Prevotella histicola, Prevotella melaninogenica, Prevotella oris, Prevotella sp., Prevotella veroralis, Propionibacterium propionicum,  Treponema sp.,  Treponema vincentii,  Veillonella dispar, Veillonella parvula* | *NONE FOUND* |
| Luo AH, 2012 (43) | Saliva Sample | Bacterial DNA was extracted using the QIAampÒ DNA Mini Kit (Qiagen, GmbH, Hilden, Germany) according to the instructions of the manufacturer. The extracts were stored at )20°C until use | Children; Ages 6-8 ; Mixed | Caries-free: dmfs = 0; Caries-active: dmfs > 8 | n = 50; Caries-free: n = 20; Caries-active: n = 30 | 16S rRNA genes, sampled were assayed using HOMIM microarray; Statistical Significance: p<0.05 | *Bacteroidetes[G-2] sp \_ot274,  Capnocytophaga sputigena\_ot775,  Tannerella sp\_ot286,  Campylobacter showae\_ot763,  Campylobacter Cluster I\_ot580\_748\_763,  Selenomonas infelix \_ot126 and related species ot479\_ ot481\_ ot639\_ ot054,  Parvimonas micra\_ot111,  Leptotrichia hofstadii\_ot224* | *Gemella haemolysans\_ot626,  Granulicatella elegans\_ot596,  Streptococcus infantis and sp clone FN042\_ot065\_638,  Streptococcus mitis bv2 and sp clone FP064 \_ot069\_398,  Streptococcus sp clone F0042 \_ot067,  Rothia dentocariosa \_ot587* |
| Ortiz S, 2019 (44) | Saliva | Non-stimulated saliva specimens (1–2 ml) were collected from the oral cavity of enrolled participants using the OMNIgene-ORAL collection and stabilization kit for microbial DNA (DNA Genotek; OM-501). In some cases, especially for young children, sterile bulbs or sterile swabs were used to collect saliva from the oral cavity, prior to placement of saliva within the OMNIgene- ORAL stabilization reagent. OMNIgene-ORAL stabilizes samples at the point of collection until transport to the laboratory, and permits long-term storage up to 1 year under ambient temperatures. | Children; Ages 2-12; Primary and Mixed | Caries-active: exhibited DMFT scores of 1–15 at the time of appointment. Caries-free individuals: demonstrated no apparent evidence of carious lesions. | n = 85; Caries-Active: n = 64; Caries-Free: n = 21 | PCR amplification using V3-V4 16S rDNA-specific primers and next-generation sequencing ; V3-V4 ; Illumina sequencing in the Human Oral Microbial Identification Next Generation Sequencing (NGS) HOMINGS Laboratory ; Statistical Significance: Fold changes larger than 1.5, with the FDR adjusted p-value of < 0.05 were considered statistically significant | *Actinomyces gerencseriae, Aggregatibacter actinomycetemcomitans, Alloprevotella tannerae, Bacteroidetes[G-5] Genus probe, Bacteroidetes[G-5] sp HOT 511, Butyrivibrio sp HOT 455, Capnocytophaga haemolytica, Capnocytophaga sp HOT 902, Fusobacterium nucleatum, Lachnospiraceae[G-2] sp HOT 096, Lactococcus lactis, Leptotrichia Genus probe 3, Leptotrichia sp HOT 218, Leptotrichia sp HOT 498, Moraxella Genus probe 2, Mycoplasma salivarium, Neisseria flavescens, Peptococcus sp HOT 167, Peptostreptococcaceae[XI][G-1][Eubacterium] infirmum, Porphyromonas sp HOT 930, Prevotella denticola, Prevotella pleuritidis, Prevotella veroralis, Streptococcus Genus probe 2, Streptococcus sobrinus, Treponema denticola, Treponema Genus probe 4, Treponema lecithinolyticum, Treponema maltophilum, Treponema sp HOT 237, Treponema sp HOT 257* | *Actinomyces Genus probe 3, Actinomyces johnsonii, Actinomyces lingnae, Actinomyces massiliensis, Actinomyces odontolyticus, Actinomyces sp HOT 170, Actinomyces sp HOT 178, Actinomyces sp HOT 877, Aggregatibacter paraphrophilus, Bacteroidales[G-2] sp HOT 274, Campylobacter concisus, Campylobacter curvus, Campylobacter gracilis, Capnocytophaga Genus probe 2, Capnocytophaga gingivalis, Capnocytophaga leadbetteri, Capnocytophaga sp HOT 332, Capnocytophaga sputigena, Cardiobacterium Genus probe, Cardiobacterium hominis, Cardiobacterium valvarum, Catonella Genus probe, Corynebacterium durum, Corynebacterium Genus probe, Corynebacterium matruchotii, Fusobacterium Genus probe 4, Fusobacterium periodonticum, Gemella Genus probe, Gemella haemolysans, Gemella sanguinis, Granulicatella adiacens, Granulicatella elegans, Haemophilus Genus probe 2, Haemophilus parainfluenzae, Haemophilus pittmaniae, Lachnoanaerobaculum sp HOT 083, Lachnoanaerobaculum umeaense, Lachnospiraceae[G-3] sp HOT 100,  Lactobacillus Genus probe 3, Lautropia mirabilis, Leptotrichia Genus probe 4, Leptotrichia sp HOT 219, Leptotrichia sp HOT 223, Leptotrichia sp HOT 392, Oribacterium sinus, Peptostreptococcaceae[XI][G-7] sp HOT 922, Porphyromonas catoniae, Porphyromonas pasteri* |