MMP2 and Aquaporin, Whole Saliva pH and Treatment Needs

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Objectives: Salivary pH ranges from 6.2 to 7.4 and is kept near neutrality. We hypothesized that within the normal physiological limits of the saliva some people tend to show more susceptibility/ resistance towards dental conditions. We also hypothesized that genetics play a role in controlling the saliva pH of the mouth and individuals within a certain range of this pH variation may show more extensive and customized dental treatment needs due to difference in their oral environment pertaining to differences in the genetic makeup of all individuals. This can be the explanation of why some individuals are more or less susceptible to dental diseases. We investigated the potential association between saliva pH and various treatment needs with *MMP2* and the aquaporin locus.

Methods: Clinical data and saliva samples were obtained from the University of Pittsburgh Dental Registry and DNA Repository project. Analysis was performed by querying the medical and dental records of more than 6000 patients. A total of 189 patients were selected with almost equal number of males and females and assessed for their saliva pH values. pH was determined by the use of commercial strips. Some patients required stimulation to provide a saliva sample and it was done by the use of gum or candy to stimulate salivary secretion. Sex and ethnicity were also considered. Subjects were divided in two groups based on the pH of their saliva (above or below the mean pH of all subjects). Information was retrieved on positive/negative history for

hypertension, oral surgery treatment (as a surrogate for tooth loss), periodontitis, restorative treatment, and root canal therapy. Genetic association studies were also performed and the markers rs2241145, rs243865, rs243832, rs2285053, rs1163960 in *MMP2* and the marker rs461872 in the aquaporin locus were genotyped using TaqMan chemistry and end-point analysis. Chi-square and Fisher's exact tests were used in all comparisons with an alpha of 0.05.

Results: Out of the 189 subjects, 95 patients provided a saliva sample without the need for stimulation, 97 subjects were females, and 23 were African descendants. The mean pH of the saliva in all study participants was 7.16. We observed statistically significant differences in the distribution of saliva pH for the following genetic markers and phenotypes:

a. Periodontitis associated with rs11639960 and rs2285053.
b. Restorative treatment associated with rs243865, rs11639960, and rs2285053
c. Oral surgery treatment associated with rs11639960, rs2285053, rs243832, and rs461872
d. Root canal therapy associated with rs243865, rs11639960, rs11639960 and rs461872
e. Hypertension associated with rs243865 rs11639960, rs11639960, rs2285053, rs2241145 and rs461872

Conclusion: Our findings suggest that markers in *MMP2* and the aquaporin locus associate with specific dental and systemic conditions within a particular range of the expected normal salivary pH. These findings could help us predict dental treatment needs of individuals considering genotyping of markers in *MMP2* and the aquaporin locus.

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Preface

I would like to thank all of those who made my Master of Sciences degree possible. First and foremost, I would like to thank Dr. Alexandre Vieira, my advisor and mentor. Through his guidance I have been able to achieve greater heights in life. Thank you for all your support at all times and for always being there for me.

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I am blessed to have parents who have guided me at all steps and stand by me in every thick and thin. I wish I can be like my Dad someday.

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1.0 Introduction

1.1 Saliva and its functions

Saliva has been the focus of studies for a long time,[1] but its importance for chair side use has only been recognized recently. There is a bulk of research that aimed to understand the biochemical and physiological roles of saliva and defined its role in digestion, speech, lubrication and maintenance of overall health of the mouth[2]. Recent studies[28] have also shown that saliva can be used to detect biomarkers that help us predict the disease and health status of the body.

However, the use of saliva as research material may pose particular problems due to its complex biochemical and physical chemical properties and its inherent variability and instability.

The term whole saliva is used to describe the combined fluids present in the oral cavity released from major glands, i.e. parotid glands, submandibular glands, and sublingual glands, and minor salivary glands present in the mucosa of the tongue (Von Ebner glands), cheeks, lips and palate[3,4]. The composition of saliva includes water (99.5%), proteins (0.3%) and inorganic and trace substances (0.2%).[5-7]

Proteins (which concentrate at 1-2 mg/ml) in the saliva include:

a. glycoproteins,[3]
b. enzymes (e.g., α-amylase, carbonic anhydrase),
c. immunoglobulins, and
d. a wide range of peptides (cystatins, statherin, histatins, proline-rich proteins) with antimicrobial activities.[5,7]

The inorganic components of saliva include:

a. sodium,
b. potassium,
c. chloride and
d. bicarbonate

There are mainly two types of cells that control the consistency of the salivary secretion, the first being serous cells that can be found in parotid, submandibular, lingual and palatal glands and secrete a watery fluid, essentially devoid of mucus. The second cells are the mucous cells, present in submandibular, sublingual labial and palatal glands and produce thick elastic and viscous secretions, which have high content of mucus in them. Serous cells get activated and mainly release secretions in presence of stimulation via massage, gum, candy or smell and sight of food. Other than this saliva is also composed of food remnants, oral microorganisms, blood, oral tissues etc.

The quality and quantity of the secreted saliva is dependent on a lot of factors such as diet, drugs, age, sex, blood properties, activity and size of salivary gland [8, 9], flow rate and the circadian rhythm[10-13]. Salivary stimulation is increased by the smell of food but also by irritants in the mouth.

1.1.1 Saliva pH and diagnostic tests

Secretion of saliva ranges from 0.3 to 7 ml saliva per minute [14] with pH ranging from 6.2 to 7.4 and on consumption of food or drinks, the salivary pH changes but comes back to normal physiological range within 30 minutes due to buffering capacity of the saliva. However, even considering the fact that our oral cavity stays within the normal physiological range of the saliva

pH for most time of the day, still some people tend to show more susceptibility/resistance to dental diseases indicating a possible role of genetics in controlling the oral environment. Saliva has ease of collection and can be easily stored, and sufficient quantities can be obtained[15]. Saliva does not clot like blood and is full of biomarkers[16]. The non-invasive accessibility of saliva reduces the amount of stress and discomfort produced in patients. Since saliva can be used as an excellent diagnostic fluid due to being inexpensive, non-invasive and easy-to-use[15], it can be used as a biomarker and can be used as a chair side diagnostic test for the detection of the diseases and the treatment outcomes for various conditions. There are many parameters for which saliva samples can be tested due to abundance in their physio-chemical, biological and molecular properties. However, for this study we are interested in testing salivary pH and look for differences in the same based on variation in markers in *MMP2* and aquaporin locus. There is very scanty literature relating the saliva pH to the demographics of the patients and differentiating the disease conditions and treatment outcomes using genetic analyses, and our study aims to explore these possible relationships.

1.2 Periodontitis

Saliva pH also influences the periodontal health of the teeth. According to the study by Takahashi *et al*., [17, 18] saliva pH influences the growth of bacteria like *Porphyromonas gingivalis* (pH of 6.5-7.0), *Prevotella intermedia* (pH of 5.0-7.0) and *Fusobacterium nucleatum* (pH of 5.5-7.0). All these bacteria prefer acidic oral environment for their growth and in turn cause periodontal conditions. Calculation of saliva pH can help in predicting the prognosis of the periodontal conditions and in turn can affect the treatment planning [19]. We want to look at effects

of variation in markers in *MMP2* and aquaporin locus on dental conditions like periodontitis, and if this influence depends on certain salivary pH ranges that are within what is considered normal or demographic features such as sex and ethnicity.

1.2 Restorative treatment

According to Guggenheimer and Moore, 2003 and Dodds *et al.*, 2005 saliva performs function of buffering and its pH is particularly important in maintaining physiological oral environment. Various ions and substances like bicarbonate, phosphate, urea, amphoteric proteins, and enzymes etc. help in maintain the normal pH of the saliva[20,21]. The buffering capacity of saliva also affects the demineralization and remineralization of enamel and dentin; measurement of buffering is can be done by activity and the amount of the bicarbonate, which in turn affect the salivary pH.

Food and drink change the pH level of saliva. For example, bacteria in mouth break down the carbohydrates consumed, releasing lactic acid, butyric acid, and aspartic acid, which lower the pH level of saliva and this reduced pH of the saliva causes demineralization of the calcified structures of the tooth and destruction of the organic matter. This process starts the cavitation in the tooth leading to dental caries. Different individuals show different response to these acidic conditions, some people develop caries early in life even after serious efforts to maintain their oral health whereas others may show some protection against caries. Restorations are a treatment response to caries and cavitated tooth surfaces are restored with various restorative materials like resins, amalgam, gold, glass ionomer cements etc. It is an established fact that reduced salivary pH over the tooth surface leads to dental caries, and cavitated surfaces are restored with different

dental materials. Thus, restorative treatments can be considered as surrogate to dental caries. According to the National Health and Nutrition examination survey 2015-2016, about 57% of the American population suffers from dental caries and out of these about 45% individuals received restorative treatment. This study aims to evaluate the pH of saliva, determine its association to needs of the restorative treatments considering it a surrogate of dental caries and further divide subgroups on basis of demographics such as sex and ethnicity and thus evaluate its suitability as a diagnostic marker of disease using genetic variation in *MMP2* and the aquaporin locus. This may help us answer at least in part what makes some people more or less susceptible to dental caries and thereby different needs for restorative treatments.

1.3 Oral surgery treatment

Dental caries and periodontal disease are known to be the two major causes leading to tooth extractions in people[22].

Most dental pain and anxiety are a result of sequalae of dental caries, which starts from a painless decalcified area that mimics a white spot, followed by destruction of organic matter and demineralization of calcified structures leading to cavitation and brownish discoloration. Exposure of the dentin and subsequent infection in the pulp leads to severe pain situations[23].

The stimulus involved in pain can range from thermal to chemical stimulation. To overcome all the discomfort the only option left is to restore the tooth and if proper steps for filling the teeth are not taken well in time, pulp inflammation can start. As pulp is properly confined, inflammation can cause severe pressure inside a closed chamber leading to severe pain followed by necrosis of pulp if left untreated. Then infection can spread to periapical areas and can cause

abscess, granulomas or cysts. Not being able to maintain oral hygiene leads to accumulation of plaque and a change in the microflora may cause gingival inflammation (gingivitis). Gingivitis may progress to periodontitis causing damage to the periodontal apparatus and severe bone loss and eventually tooth loss will be the final outcome.

If no steps are taken in these stages, the only option left is to extract the tooth. Our study is involved at evaluating the pH of saliva, determine its relevance to the tooth extractions, dividing it on basis of demographics and thus evaluate its suitability as a diagnostic marker of disease using genetic analyses.

1.4 Root canal therapy

Mentioned above are the sequelae of dental caries, if infection reaches the pulp, the intervention in such conditions is root canal therapy.

Endodontic treatment is necessary when the pulp, the soft tissue inside the root canal, becomes inflamed or infected. Causes for the infection include deep decay, repeated dental procedures on the tooth or tooth trauma[24]. Our study aims to find if variation in markers in *MMP2* and the aquaporin locus cause have any effect in altering oral environment via saliva pH and if such changes have any effect on differences in need for root canal therapies for individuals. Demographic factors like sex and ethnicity are also considered.

1.5 Hypertension

Hypertension (high blood pressure) is one of the most common diseases related to lifestyle of humans. Hypertension is defined as systolic blood pressure (SBP) of ≥140 mmHg and/or diastolic blood pressure (DBP) of ≥90 mmHg. According to Yokokawa *et al.*, 2010 up to 30% of adults worldwide have hypertension. Hypertension is the leading cause of cardio-vascular conditions and in general systemic conditions affect oral health. Saliva plays a significant role in the maintenance of oral health (Dodds *et al.*, 2005)[21], so any change in systemic health should affect the properties of the saliva. A few studies have been done that evaluate the relationship between blood pressure and the saliva pH. A few of the studies suggested that the pH of unstimulated saliva was significantly lower in the subjects with hypertension compared to people with normal blood pressure regardless of any effect of medication[25]. It was observed that increased acidity in the oral cavity in unstimulated saliva is related to increasing levels of systolic and diastolic blood pressure. The blood pressure influences the general condition in several ways (Alonso *et al.*, 1993; Wong, 2006)[26,27] and we are interested in finding the relationship of the whole saliva pH with hypertension condition based on variation in markers in *MMP2* and aquaporin locus.

2.0 Genetic influences on characteristics of saliva, role of MMPs and aquaporins

Matrix metalloproteinases (*MMPs*) are proteolytic enzymes capable of degrading all of the extracellular matrix and basement membrane components[29]. *MMPs* also play an important role in normal tissue remodeling but also cause severe destructive inflammatory conditions[29]. *MMPs* are released as pre enzymes and require activation for its catabolic effects[30].

MMP's are present in the whole saliva[31], gingival crevicular fluid (GCF) and dental plaque[32]. They are also associated with periodontitis and dental caries[32-34]. The saliva pH changes characteristic of changes in blood pressure[25], growth of bacteria associated with periodontitis[17, 18], dental cavitation etc. cause activation of potent *MMP's* (acidic environment), followed by neutralization. This activates catalytic activity of these enzymes[33], suggesting that *MMPs* are crucial in altering the oral environment and for different dental processes through its regulation by saliva pH or its effects on it.

Even though *MMPs* are found in several inflammatory conditions, including oral diseases, very scanty literature has been published on their influence on saliva pH in causing different dental diseases.

Aquaporin family (*AQP*) plays crucial functions in salivary synthesis and secretion[35]. The expression of *AQP*1, 3 and 5 has also been described during mouse salivary gland development, suggesting that aquaporins may also have an important role in controlling properties of the saliva and maybe a role in altering the salivary pH and its composition[36-38].

3.0 Purpose of Research

Different dietary habits and the food items consumed by humans change the saliva pH of the mouth. Some food items like carbonated drinks render an acidic pH to mouth whereas items like baking soda or vegetables like broccoli make the pH of the mouth more alkaline. These differences in the saliva pH create a different dental environment and lead to different dental conditions. Saliva has a buffering potential due to presence of phosphate, bicarbonate ions etc. and the pH of the oral cavity returns back to normal within a time span of 30 minutes. Even after the buffering actions of the saliva to neutralize the saliva pH to get it within the normal physiological limits, people do get dental diseases. In addition to this there is a lot of variation seen in individuals for susceptibility towards dental diseases despite having the same dietary habits and shared environment. Some people tend to show more susceptibility to dental diseases like caries and periodontitis even after they take proper oral hygiene measures whereas some people tend to show an inherent protection against these dental diseases. We also believe that systemic health greatly alters the oral environment and has effects on the properties of the saliva.

It is often said that every human is unique. Above all this, humans are 99.99% identical to each other and what makes each individual unique is 0.1% of our genome, which is approximately three million base pairs. This may seem to be insignificant but in these three million differences lie the changes that gives one individual red hair instead of blonde and green eyes instead of blue. We believe that the same concept, when applied, answers to our question of why some individuals are more susceptible to certain dental conditions than others. This difference in susceptibility leads to different oral environment for all, which requires intervention with more

customized treatment needs for different individuals based on their genetic makeup, but it is very difficult to look for associations in the whole genome for different dental conditions at once.

Vieira lab at School of Dental Medicine, University of Pittsburgh is interesting in finding the variables that become markers for different oral conditions and the outcomes of the treatment of these conditions. Our lab has been working on *MMP2* and aquaporin locus for several years now. We have shown that markers in *MMP2* are associated with periapical lesions[39] in deep carious conditions and failures in composite restorations[40]. We have also shown that variations in aquaporin locus are associated with TMJ disorders in periodontal conditions[46], erosive tooth wear[45] and a possible preventive effect in dental caries[42]. *MMP's* are present in the whole saliva[31], gingival crevicular fluid (GCF) and dental plaque[32]. They are also associated with periodontitis and dental caries[32-34]. The saliva pH changes characteristic of changes in blood pressure[25], growth of bacteria associated with periodontitis[17,18] or dental cavitation cause activation of potent *MMP's* (acidic environment), followed by neutralization. This activates catalytic activity of these enzymes[33], suggesting that *MMPs* are crucial in altering the oral environment and for different dental processes through its regulation by saliva pH or its effects on it. Even though *MMPs* are found in several inflammatory conditions, including oral diseases, very scanty literature has been published on their influence on saliva pH in causing different dental diseases. In addition, Aquaporin family (*AQP*) plays crucial functions in salivary synthesis and secretion[35]. The expression of Aqp1, 3 and 5 has also been described during mouse salivary gland development, suggesting that aquaporins may also have an important role in controlling properties of the saliva and maybe a role in altering the salivary pH and its composition[36-38]. Considering our research experience with *MMP2* and aquaporin, we are interested in finding if

variation in these genes have any effect on the oral disease depending on the saliva pH. Any differences in association of saliva pH to the markers in *MMP2* and the aquaporin locus may suggest differences in the oral conditions and thereby a need for more customized treatment plan for different individuals. Some individuals may require complex treatment interventions like root canal therapies or extractions, while some may have inherent protective effects.

We hypothesize that there are differences in the associations between saliva pH and different phenotypes like periodontitis, restorative treatment, root canal therapies, oral surgeries and systemic conditions like hypertension based on genetic differences in individuals for markers in *MMP2* and the aquaporin locus. We are also interested in looking at these differences in individuals dividing them on basis of demographic factors like sex and ethnicity.

4.0 Subjects and Methods

4.1 Study population and saliva sample collection

Dental Registry and DNA Repository (DRDR) is a database that was established in 2006 at the University of Pittsburgh. Clinical data and saliva samples were obtained from University of Pittsburgh Dental Registry and DNA Repository Project. For the purpose of this study a total of 6,222 subjects were screened and 189 patients were selected. Every patient that has been treated at the University of Pittsburgh, School of Dental Medicine receives an invitation to participate in the registry and sign a consent form authorizing the retrieval of information from their dental records. The study is approved by University of Pittsburgh Institutional Review Board (IRB approval #0606091). The subjects were recruited from DRDR and from the 6,222 subjects available in the project, 189 patients were selected and assessed for their saliva pH values.

4.2 Study participants and collection of saliva sample

The selected subjects were assessed for their saliva pH values. pH was determined by the use of commercial strips. Since some patients required stimulation to provide a saliva sample, having had stimulation using unsweetened gum was considered in the analysis. Sex and ethnicity were also considered. Subjects were divided in two groups based on the pH of the saliva (above and below the mean saliva pH of all subjects). Out of the 189 subjects, 95 subjects provided a saliva

sample without the need for stimulation. 97 subjects were females, and 23 were African descendants. The following figure shows the demographic characteristics of the study subjects:

Figure 1 Demographic Data on the sample population for saliva pH based on gender differences

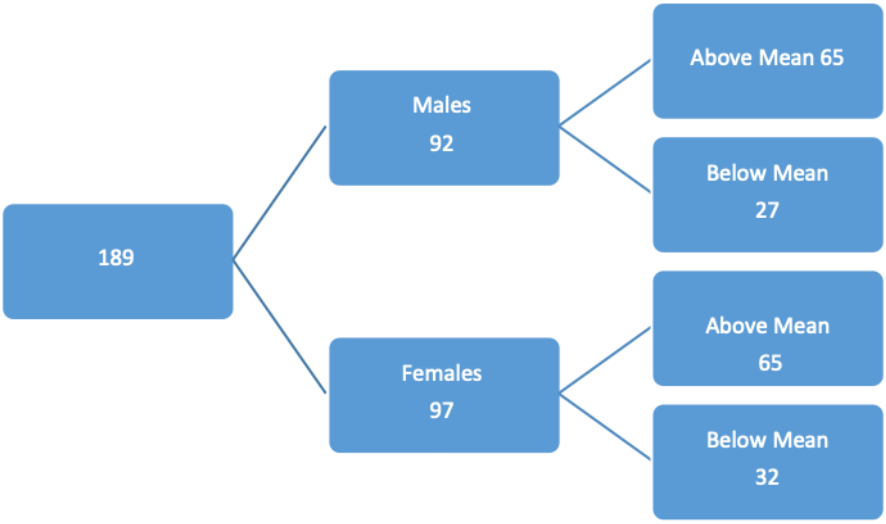

Figure 2 Demographic Data on the sample population for saliva pH based on ethnic differences

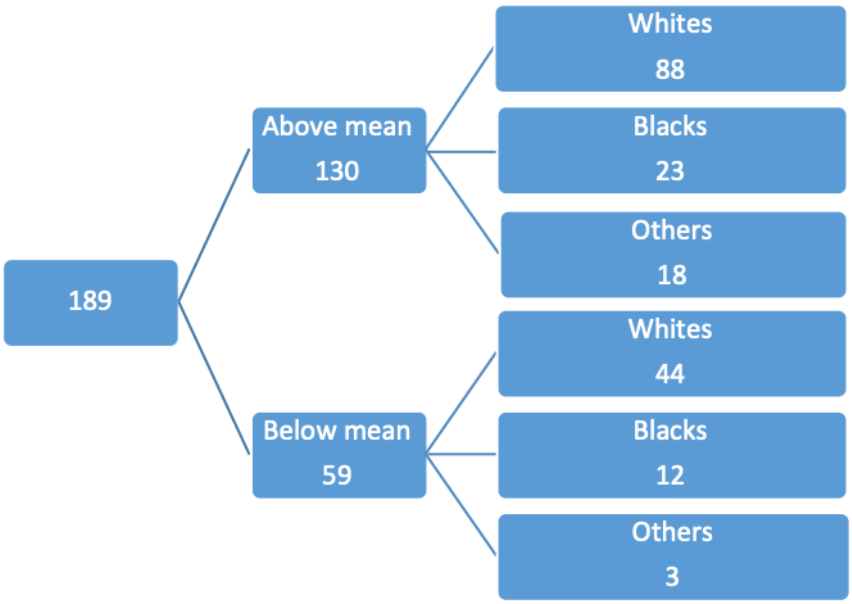

Figure 3 Histogram depicting the distribution of saliva pH in the sample population

Salivary pH	Number of people
4.5	2
5	4
5.5	1
5.75	3
5.88	3
6	6
6.13	1
6.25	2
6.5	2
6.75	16
6.88	1
7	18
7.25	29
7.38	10
7.5	53
7.55	22
7.88	4
8	11

The values of the saliva pH calculated for our sample ranged from as low as 4.5 to as high as 8 with all the continuous variables in between. Most of the saliva samples showed salivary pH within what is considered the normal physiological limits with some outliers. Since these data were not perfectly normally distributed as seen in the figure 3, we chose to calculate the mean of the saliva pH and compare two groups, individuals having their saliva pH above or below the mean pH of the cohort. The mean value of the saliva pH of the sample was 7.15 with 130 individuals with saliva pH above the mean and 59 with saliva pH below the mean. Eighty-eight individuals were White and 23 Black in the sample with saliva pH above the mean of the cohort and 44 White and 12 Black in the sample with saliva pH below the mean of the cohort as seen in figure 2.

Regarding sex, 92 individuals were males and 65 of those had saliva pH above the mean and 97 were females with 32 of them with saliva pH below the mean as seen in figure 1.

4.3 Selection of phenotypes

The following selection criteria was met for the phenotypes of periodontitis, restorative treatment, oral surgery treatment, root canal therapy, and hypertension:

Periodontitis: Subjects with periodontitis were defined as having 30% or more teeth with sites of clinical attachment loss of 5mm or more.

Restorative treatment: It was defined as having any surface of the tooth restored in the oral cavity by amalgam, glass ionomers or resins, and other less used materials.

Oral surgery treatment: Subjects who had undergone extractions of any tooth, which is a surrogate for tooth loss.

Root canal therapy: Subjects with any tooth with history of root canal therapy.

Hypertension: Subjects who had a systolic blood pressure (SBP) of 140 mm Hg or more, or a diastolic blood pressure (DBP) of 90 mm Hg or more.

4.4 *MMP2* and aquaporin locus genotypes

The genotyping data were in existence. Genomic DNA was extracted from saliva and the genotypes were generated using Taqman chemistry[62]. The reactions were carried out with the use of standard conditions as suggested by the manufacturer. Genotyping of five single nucleotide polymorphisms (rs2241145, rs243865, rs243832, rs2285053, rs1163960) in *MMP2*, located on chromosome 16 and one single nucleotide polymorphism (rs461872) in the aquaporin locus, located in chromosome 12, were generated.

Table 1 Details of all the tested markers

Mapping gene	Marker	Chromosome region	Common and rare alleles
MMP2	rs243865	16q12.2	CT
MMP2	rs11639960	16q12.2	AG
MMP2	rs2285053	16q12.2	CT
MMP2	rs2241145	16q12.2	CG
MMP2	rs243832	16q12.2	CG
aquaporin locus	rs461872	12q13.12	AG

4.5 Statistical analysis

All collected data were entered into Excel and Numbers applications and the comparisons were performed using Stata software.

Genetic analyses were performed using PLINK Whole Genome Association Analysis software version 1.9.

Fisher's exact and chi-squared tests were used to determine if there were differences between the clinical outcomes and variation in genetic markers and were stratified based on the saliva pH above or below the mean of the total group. Demographic factors were taken into consideration while performing the statistical analyses, but not if saliva was collected under stimulation or not. Alpha used was 0.5.

5.0 Overall results

The results for the study were divided in two sections:

The first section involves the association of saliva pH and the different phenotypes like periodontitis, restorative treatment, root canal therapy, oral surgery treatment, and hypertension. This was performed to find out trends in the saliva pH in our selected sample population.

The other section involves the genetic and allelic association tests for the same phenotypes to look for associations depending on the saliva pH range with markers in *MMP2* and the aquaporin locus.

5.1 Analysis of the cohort saliva pH and its association with different phenotypes

5.1.1 Saliva pH and Periodontitis

There were no significant differences in the distribution of saliva pH seen when subjects with saliva pH above and below the mean of the cohort were compared for their positive and negative phenotypes of periodontitis. No significant p- values were obtained as shown in the table below.

Table 2 Saliva pH and periodontitis based on sex and ethnicity

	Number of subjects with saliva pH above the mean pH	Number of subjects with saliva pH below the mean pH	P-value
Subjects with Periodontitis	56	28	0.6
Subjects without Periodontitis	72	31	
Males with Periodontitis	30	15	0.4
Males without Periodontitis	35	12	
Females with Periodontitis	26	13	1
Females without Periodontitis	37	19	
Whites with Periodontitis	40	21	0.8
Whites without Periodontitis	48	23	
Blacks with Periodontitis	8	5	0.7
Blacks without Periodontitis	15	7	

5.1.2 Saliva pH and restorative treatment

Whites were more likely to show saliva pH above the mean of the cohort when there was a positive history of restorations whereas Blacks showed a higher tendency to have saliva pH above the mean of the cohort when there was negative history for restorative treatment. We found saliva pH above the mean of the cohort to be associated with Whites without restorative treatment and saliva pH below the mean pH of the cohort to be associated with Blacks without any restorative treatment and the p-value for these associations were 0.03 and 0.05 respectively indicating that it is statistically significant.

Table 3 Saliva pH and restorative treatment based on sex and ethnicity

	Number of subjects with saliva pH above the mean pH	Number of subjects with saliva pH below the mean pH	P-value
Subjects with Restorations	96	39	0.3
Subjects without Restorations	33	19	
Males with Restorations	51	17	0.19
Males without Restorations	14	9	
Females with Restorations	45	22	0.87
Females without Restorations	19	10	
Whites with Restorations	70	27	**0.03**
Whites without Restorations	19	17	
Blacks with Restorations	13	9	**0.05**
Blacks without Restorations	10	1	

5.1.3 Saliva pH and oral surgery treatment

Individuals were more likely to have saliva pH above the mean of the cohort when they were not treated for any tooth extractions. Similar trends were observed when White individuals were analyzed separately. The p-value for these associations was 0.014 and 0.009, respectively.

Table 4 Saliva pH and oral surgery treatment based on sex and ethnicity

	Number of subjects with saliva pH above the mean pH	Number of subjects with saliva pH below the mean pH	P-value
Subjects with Oral surgery	53	36	**0.014**
Subjects without Oral surgery	74	23	
Males with Oral surgery	23	15	0.08
Males without Oral surgery	41	12	
Females with Oral surgery	30	21	0.09
Females without Oral surgery	33	11	
Whites with Oral surgery	33	28	**0.009**
Whites without Oral surgery	53	17	
Blacks with Oral surgery	13	9	0.35
Blacks without Oral surgery	9	3	

5.1.4 Saliva pH and root canal therapy

No significant differences in the distribution of the mean saliva pH were observed when subjects with saliva pH above and below the mean pH of the cohort were compared on the basis of having had a positive and negative history of root canal therapy. There were no statistically significant differences as shown in the table below.

Table 5 Saliva pH and root canal therapy based on sex and ethnicity

	Number of subjects with saliva pH above the mean pH	Number of subjects with saliva pH below the mean pH	P-value
Subjects with Root Canal Therapy	20	16	0.06
Subjects without Root Canal Therapy	108	43	
Males with Root Canal Therapy	9	6	0.33
Males without Root Canal Therapy	55	21	
Females with Root Canal Therapy	11	10	0.11
Females without Root Canal Therapy	53	22	
Whites with Root Canal Therapy	14	13	0.07
Whites without Root Canal Therapy	73	31	
Blacks with Root Canal Therapy	3	2	0.81
Blacks without Root Canal Therapy	19	10	

5.1.5 Saliva pH and hypertension

There were no significant differences in the distribution seen when subjects with saliva pH above and below the mean pH of the cohort were compared for their positive and negative phenotypes of hypertension.

Table 6 Saliva pH and hypertension based on sex and ethnicity

	Number of subjects with saliva pH above the mean pH	Number of subjects with saliva pH below the mean pH	P-value
Subjects with Hypertension	26	12	1
Subjects without Hypertension	102	47	
Males with Hypertension	17	5	0.41
Males without Hypertension	47	22	
Females with Hypertension	9	7	0.36
Females without Hypertension	55	25	
Whites with Hypertension	19	9	0.85
Whites without Hypertension	68	35	
Blacks with Hypertension	4	3	0.63
Blacks without Hypertension	18	9	

5.2 Genotyping analysis of different markers for the selected phenotypic conditions

Our genotyping results for association of salivary pH to different conditions depicted various significant associations when tested for different markers. In the following subsections, the significant association results have been tabulated for rs243865, rs11639960, rs2285053, rs2241145, rs243832 and rs461872 for the conditions and treatments studied: periodontitis, restorative treatment, oral surgery treatment, root canal therapy and hypertension.

5.2.1 Statistically significant results for genotyping analysis for association of periodontitis with saliva pH tested for different markers

Tables 7 and 8 show an excess of rs243865 heterozygotes for subjects without periodontitis with saliva pH above the mean of the cohort. Additionally, male individuals without periodontitis were less likely to have the less common allele T when their saliva pH was below the mean of the cohort when tested for the same marker. Significant p-values suggest that there are differences in distribution of the saliva pH for different genotypes and different alleles whether a C or a T, in overall cohort and for males respectively when tested for the marker rs243865 of *MMP2* for subjects without periodontitis.

Table 7 rs243865 genotyping analysis of subjects for association between salivary pH and periodontitis

Subjects without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	26	14	**0.04**
CT	32	4	
TT	3	2	

Table 8 rs243865. Allele frequency analysis of subjects for association between salivary pH and periodontitis

Males without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	40	15	**0.03**
T	18	1	

Tables 9 and 10 show that individuals without periodontitis were more likely to be heterozygotes and have the less common allele G of rs11639960 when their saliva was below the mean of the cohort. Significant p-value showed that there are significant differences in distribution of the saliva pH for different genotypes of marker rs11639960 of *MMP2* for subjects without periodontitis. Significant differences in the distribution of the saliva pH for different alleles whether an A or a G, was also found in all subjects when tested for the same marker.

Table 9 rs11639960 genotyping analysis of subjects for association between salivary pH and negative history of periodontitis

Subjects without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	56	21	**0.04**
AG	4	6	
GG	0	0	

Table 10 rs11639960 allele frequency analysis of subjects for association between salivary pH and negative history of periodontitis

Subjects without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	116	48	**0.04**
G	4	6	

Tables 11 and 12 showed that females were more likely to have T allele independent of their periodontal health status when their saliva pH was above the mean pH of the cohort.

Table 11 rs2285053 allele frequency analysis of female subjects for association between salivary pH and periodontitis

Females with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	42	26	**0.03**
T	8	0	

Table 12 rs2285053 allele frequency analysis of female subjects for association between salivary pH and negative history of periodontitis

Females without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	65	37	**0.05**
T	11	1	

5.2.2 Statistically significant results for genotyping analysis for association of tooth restorative treatment with saliva pH tested for different markers

Tables 13, 14 and 15 showed that individuals without restorative treatment were less likely to have the less common allele T of rs243865 when their saliva pH was below the mean of the cohort. Similar trends were seen in the white and male population of our study population.

Table 13 rs243865 allele frequency analysis of subjects for association between salivary pH and restorative treatment

Subjects without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	35	29	**0.04**
T	19	5	

Table 14 rs243865 allele frequency analysis of male subjects for association between salivary pH and negative history of restorative treatment

Males without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	11	15	**0.03**
T	7	1	

Table 15 rs243865 allele frequency analysis of white subjects for association between salivary pH and negative history of restorative treatment

Whites without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	15	25	**0.01**
T	13	5	

Tables 16 and 17 showed that there was an excess of heterozygotes of rs11639960 for female subjects without restorations when their saliva pH was below the mean of the cohort. The results of the allelic association of rs11639960 show an excess of rare allele G in subjects without restorative history when their saliva pH was below the mean of the cohort. Our result showed that there are significant differences in distribution of the saliva pH for different genotypes of rs11639960 of *MMP2* for female subjects without restorations. We also found that there is a significant difference in the distribution of the saliva pH for different alleles whether an A or a G, in all subjects without restorations when tested for the same marker.

Table 16 rs11639960 genotyping analysis of female subjects for association between salivary pH and negative history of restorative treatment

Females without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	11	6	**0.03**
AG	0	3	
GG	0	0	

Table 17 rs11639960 allele frequency analysis of subjects for association between salivary pH and negative history of restorative treatment

Subjects without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	46	27	**0.03**
G	0	3	

Tables 18 and 19 showed that in females, independent of having restorations, the rare allele T was not present for subjects with saliva pH below the mean of the cohort and an excess of homozygotes of common allele C of rs2285053 was seen for subjects with saliva pH above the mean pH of the cohort. Our result showed that there are significant differences in distribution of

the saliva pH for different genotypes of rs2285053 of *MMP2* for female subjects with restorations.

We also found that there is a significant difference in the distribution of the saliva pH for different alleles whether a C or a T, in all female subjects with restorations when tested for the same marker.

Table 18 rs2285053 genotyping analysis of female subjects for association between salivary pH and restorative treatment

Females with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	34	22	**0.05**
CT	8	0	
TT	2	0	

Table 19 rs2285053 allele frequency analysis of female subjects for association between salivary pH and restorative treatment

Females with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	76	44	**0.01**
T	12	0	

5.2.3 Statistically significant results for genotyping analysis for association of oral surgery treatment with saliva pH tested for different markers

Tables 20 and 21 showed that there was an excess of rs11639960 heterozygotes for subjects with saliva pH below the mean of the cohort and excess of rs11639960 homozygotes of major allele A for subjects with saliva pH above the mean. Additionally individuals with oral surgery treatment were less likely to have the less common allele G when their saliva pH was above the mean of the cohort when tested for the same marker. Our results showed that there are significant

differences in distribution of the saliva pH for different genotypes of rs11639960 of *MMP2* for subjects that received oral surgery treatment. We also found that there is a significant difference in the distribution of the saliva pH for different alleles whether an A or a G, in all subjects with a positive history of Oral Surgery when tested for the same marker.

Table 20 rs11639960 genotyping analysis of subjects for association between salivary pH and having received oral surgery treatment

Subjects that received oral surgery treatment	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	36	22	**0.03**
AG	0	3	
GG	0	0	

Table 21 rs11639960 allele frequency analysis of subjects for association between salivary pH and having received oral surgery treatment

Subjects that received oral surgery treatment	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	72	47	**0.03**
G	0	3	

Table 22 showed that there was no rs2285053 rare allele T in female subjects with oral surgery treatment when their saliva pH was below the mean and an excess when the saliva pH was above the mean pH of the cohort. Our results showed that there are significant differences in distribution of the saliva pH for different alleles of rs2285053 of *MMP2* for females that did not receive oral surgery treatment. Thus, having a specific allele for rs2285053 of gene *MMP2* associated with having a specific saliva pH if you are a female with negative history of oral surgery.

Table 22 rs2285053 allele frequency analysis of female subjects for association between salivary pH and negative history of having had oral surgery

Females that did not receive oral surgery treatment	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	56	22	**0.01**
T	12	0	

Tables 23 and 24 showed that there was an excess of rs243832 minor allele G homozygotes in females and excess of minor allele G for subjects without the oral surgery treatment when their saliva pH was above the mean of the cohort. Our results showed that there are significant differences in distribution of the saliva pH for different genotypes of rs243832 of *MMP2* for all female subjects that did not receive oral surgery treatment. We also found that there is a significant difference in the distribution of the saliva pH for different alleles whether a C or a G, in all female subjects with negative history of oral surgery when tested for the same marker.

Table 23 rs243832 genotyping analysis of female subjects for association between salivary pH and negative history of having had oral surgery

Females that did not receive oral surgery treatment	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	9	5	**0.05**
CG	25	6	
GG	14	0	

Table 24 rs243832 allele frequency analysis of female subjects for association between salivary pH and negative history of having had oral surgery

Females that did not receive oral surgery treatment	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	43	16	**0.018**
G	53	6	

Tables 25 and 26 showed that there was an excess of rs461872 heterozygotes for subjects without history of oral surgery treatment with saliva pH above the mean of the cohort and similar ratio patterns were seen for males without any history of tooth extraction. Our results showed that there are significant differences in distribution of the saliva pH for different genotypes of rs461872 in the aquaporin locus for all subjects and especially males that did not receive oral surgery treatment.

Table 25 rs461872 genotyping analysis of subjects for association between salivary pH and negative history of having had oral surgery

Subjects that did not receive oral surgery treatment	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	21	4	**0.04**
AG	26	15	
GG	21	3	

Table 26 rs461872 genotyping analysis of male subjects for association between salivary pH and negative history of having had oral surgery

Males that did not receive oral surgery treatment	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	11	3	**0.04**
AG	14	9	
GG	11	0	

5.2.4 Statistically significant results for genotyping analysis for association of root canal therapy with saliva pH tested for different markers

Tables 27 and 28 showed that there was an excess of rs243865 heterozygotes for male subjects with root canal therapy with saliva pH above the mean of the cohort and excess of rs243865 homozygotes of major allele C with saliva pH below the mean of the cohort. An excess of minor allele T was also seen when their saliva pH was above the mean pH of the cohort, Our results showed that there are significant differences in distribution of the saliva pH for different genotypes of rs243865 of *MMP2* for all male subjects with a history of root canal therapy. We also found that there is a significant difference in the distribution of the saliva pH for different alleles whether a C or a T, in all male subjects with root canal therapy when tested for the same marker.

Table 27 rs243865 genotyping analysis of male subjects for association between salivary pH and having had root canal therapy

Males with root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	0	3	**0.02**
CT	6	1	
TT	1	0	

Table 28 rs243865 allele frequency analysis of male subjects for association between salivary pH and negative history of having had root canal therapy

Males with root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	6	7	**0.04**
T	8	1	

Tables 29 and 30 showed that there was an excess of rs11639960 heterozygotes and excess of rare allele G for subjects without root canal therapy with saliva pH below the mean of the cohort. An excess of homozygotes and higher allele frequency for the common allele A were also seen for subjects without root canal therapy when their saliva pH was above the mean pH of the cohort. Our results showed that there are significant differences in distribution of the saliva pH for different genotypes of rs11639960 of *MMP2* for all subjects without root canal therapy. We also found that there is a significant difference in the distribution of the saliva pH for different alleles whether an A or a G, in all subjects with negative history of root canal therapy when tested for the same marker.

Table 29 rs11639960 genotyping analysis of subjects for association between salivary pH and negative history of having had root canal therapy

Subjects without root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	77	28	**0.03**
AG	4	6	
GG	0	0	

Table 30 rs11639960 allele frequency analysis of subjects for association between salivary pH and negative history of having had root canal therapy

Subjects without root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	158	62	**0.03**
G	4	6	

Table 31 and 32 showed that females were less likely to have the less common rs2285053 allele T when their saliva pH was below the mean of the cohort and more likely to have it when their saliva pH was above the mean pH of the cohort independent of individual root canal status.

Table 31 rs2285053 allele frequency analysis of female subjects for association between salivary pH and having had root canal therapy

Females with root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	18	20	**0.04**
T	4	0	

Table 32 rs2285053 allele frequency analysis of female subjects for association between salivary pH and negative history of having had root canal therapy

Females without root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	89	43	**0.03**
T	15	1	

Table 33 showed that Blacks have excess of rs461872 heterozygotes for subjects without root canal therapy when their saliva pH was below the mean pH of the cohort and excess of homozygotes of less common allele G when their saliva pH was above the mean pH of the cohort. Our results showed that there are significant differences in distribution of the saliva pH for different genotypes of rs461872 in the aquaporin locus for Blacks without root canal therapy.

Table 33 rs461872 genotyping analysis of black subjects for association between salivary pH and negative history of having had root canal therapy

Blacks without root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	2	0	**0.04**
AG	2	5	
GG	15	5	

5.2.5 Statistically significant results for genotyping analysis for association of hypertension with saliva pH tested for different markers

Tables 34 and 35 showed that individuals without hypertension were more likely to have the less common rs243865 allele T when their saliva pH was above the mean of the cohort. Similar trends for the allele frequency were seen specifically for male individuals without hypertension. Our results showed that there are significant differences in distribution of the saliva pH for different alleles of rs243865 of *MMP2* for overall cohort and especially males without any history of hypertension.

Table 34 rs243865 allele frequency analysis of subjects for association between salivary pH and negative history of hypertension

Subjects without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	117	62	**0.04**
T	53	14	

Table 35 rs243865 allele frequency analysis of male subjects for association between salivary pH and negative history of hypertension

Males without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	52	32	**0.03**
T	28	6	

Tables 36 and 37 showed that for hypertensive patients, an excess of rs11639960 heterozygotes was seen when their saliva pH was below the mean pH of the cohort. Additionally, they were also more likely to have the less common allele G when their saliva pH was below the mean of the cohort. Our results showed that there are significant differences in distribution of the saliva pH for different genotypes of rs11639960 of *MMP2* for all subjects with hypertension. We also

found that there is a significant difference in the distribution of the saliva pH for different alleles whether an A or a G, in all subjects with hypertension when tested for the same marker.

Table 36 rs11639960 genotyping analysis of subjects for association between salivary pH and hypertension

Subjects with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	18	8	**0.05**
AG	0	2	
GG	0	0	

Table 37 rs11639960 allele frequency analysis of subjects for association between salivary pH and hypertension

Subjects with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	36	18	**0.05**
G	0	2	

Table 38 shows excess of rs11639960 heterozygotes for males with hypertension when their saliva pH was above the mean pH of the cohort. In addition to this excess of homozygotes of common allele A are seen when their saliva pH was above the mean pH of the cohort.

Table 38 rs11639960 genotyping analysis of male subjects for association between salivary pH and hypertension

Males with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	14	3	**0.05**
AG	0	1	
GG	0	0	

Table 39 shows that females without hypertensive history, show an excess of rs2285053 minor allele T, when the saliva pH of the subjects was above the mean of the cohort. Our results showed that there are significant differences in distribution of the saliva pH for different alleles of rs2285053 of *MMP2* for females without hypertension.

Table 39 rs2285053 allele frequency analysis of female subjects for association between salivary pH and negative history of hypertension

Females without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	91	49	**0.01**
T	17	1	

Tables 40 and 41 shows that there was an excess of rs2241145 heterozygotes for males and females without hypertension when their saliva pH was below and above the mean of the cohort respectively. Our result showed that there are significant differences in distribution of the saliva pH for different genotypes of rs2241145 of *MMP2* for all male and female subjects with a negative history of hypertension.

Table 40 rs2241145 genotyping analysis of male subjects for association between salivary pH and negative history of hypertension

Males without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	4	2	**0.05**
CG	2	12	
GG	2	5	

Table 41 rs2241145 genotyping analysis of female subjects for association between salivary pH and negative history of hypertension

Females without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	6	3	**0.006**
CG	34	12	
GG	9	16	

Table 42 shows that there is also an excess of the rs2241145 common allele C for female individuals with negative history of hypertension when their saliva pH was above the mean of the cohort. Our results showed that there are significant differences in distribution of the saliva pH for different alleles of rs2241145 of *MMP2* for females without hypertension.

Table 42 rs2241145 allele frequency analysis of female subjects for association between salivary pH and negative history of hypertension

Females without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	46	18	**0.02**
G	52	44	

To sum up, Genotypic analysis of rs243865 showed significant association for variation in saliva pH for:

1. Subjects without periodontitis
2. Males with root canal therapy

Allele frequency analysis of rs243865 showed significant association for variation in saliva pH

for:

1. Males without periodontitis
2. Subjects especially males and Whites without restorative treatment
3. Males with root canal therapy
4. Subjects and especially males without hypertension

2) Genotypic analysis of rs11639960 showed significant association for variation in saliva pH for:

1. Subjects without periodontitis
2. Females without restorative treatment
3. Subjects with oral surgery treatment
4. Subjects without root canal therapy
5. Subjects with hypertension
6. Males with hypertension

Allele frequency analysis of rs11639960 showed significant association for variation in saliva

pH for:

1. Subjects without periodontitis
2. Subjects without restorative treatment
3. Subjects with oral surgery treatment
4. Subjects without root canal therapy
5. Subjects with hypertension

3) Genotypic analysis of rs2285053 showed significant association for variation in saliva pH for:

1. Females with restorative treatment

Allele frequency analysis of rs2285053 showed significant association for variation in saliva pH

for:

1. Females with periodontitis
2. Females without periodontitis
3. Females with restorations
4. Females without oral surgery treatment
5. Females with root canal therapy
6. Females without root canal therapy
7. Females without hypertension

4) Genotypic analysis of rs2241145 showed significant association for variation in saliva pH for:

1. Males without hypertension
2. Females without hypertension

Allele frequency analysis of rs2241145 showed significant association for variation in saliva pH

for:

1. Females without hypertension

5) Genotypic analysis of rs243832 showed significant association for variation in saliva pH for:

1. Females without oral surgery treatment

Allele frequency analysis of rs243832 showed significant association for variation in saliva pH

for:

1. Females without oral surgery treatment

6) Genotypic analysis of rs461872 showed significant association for variation in saliva pH for:

   1. Subjects without oral surgery treatment
   2. Males without oral surgery treatment
   3. Blacks without root canal therapy

Allele frequency analysis of rs461872 showed no significant association for variation in saliva

pH for different phenotypes tested.

6.0 Discussion

The values of saliva pH calculated for our sample ranged from as low as 4.5 to as high as 8 with all continuous values ranging in between these two values. However, since the data for the samples obtained was not perfectly normally distributed over the entire range, we chose to calculate the mean of the saliva pH and make the data categorical as above and below the mean. One limitation of our study was that the DRDR project collects stimulated saliva when the patient is unable to provide a saliva sample without stimulation. In the cohort we studied, out of the 189 subjects, 95 patients provided a saliva sample without the need for stimulation. The mean pH of the saliva in all study participants was 7.16. The mean pH of saliva among the subjects that were stimulated was 7.23 and for the ones that did not need stimulation was 7.08. There is a chance that stimulating the saliva made it more likely that a subject had lower saliva pH and belonged to the group that was below the mean. Needing stimulation suggest some level of dehydration that can be consequence of medication used, including antihypertensives. Evaluating this methodological variation is warranted in future studies. However, in real life clinical settings, it is likely that many individuals would need stimulation to provide saliva samples.

Another aspect of our design was the decision to reduce the continuous variable into two categoric groups, using the mean pH of the cohort as the cutoff. We have used this approach in a number of our previous work[43,59-61]. The impact of this method is the potential loss of statistical power, although it makes it more manageable to perform comparisons. One questions that remains is what the results would look like if a different cutoff was used. We hope we can test these variations in future work.

When the numerical data of the saliva pH described in categorical fashion as above and below the mean of the saliva pH of the cohort was tested for association with different phenotypes, there were differences seen in the distribution of the saliva pH for the different phenotypical conditions based on demographics such as ethnicity. There was an association seen between the salivary pH and phenotypic conditions like restorative treatment based on ethnicity and for overall cohort of subjects with oral surgery treatment including the whites. Based on the literature[17,18], we would expect subjects with periodontitis to have low saliva pH as acidic saliva pH influences the growth of bacteria like *Porphyromonas gingivalis* (pH of 6.5-7.0), *Prevotella intermedia* (pH of 5.0-7.0) and *Fusobacterium nucleatum* (pH of 5.5-7.0). All these bacteria prefer acidic oral environment, but our results showed that there are no significant differences seen in the frequency of periodontitis depending on the saliva pH being above or below of the mean of the cohort. There were no differences based on demographic categories as well. Similar results with no significant associations were seen for the positive and negative phenotypes of root canal therapies and hypertension. This may be attributed to the fact that most subjects in our study had saliva pH within the normal physiological range and saliva pH in this range had no or minimalistic effect in causing these conditions to be detected within our alpha value of 0.5. We can say that saliva pH within the range of our sample population that did seem to associate with the diagnosis of periodontitis, hypertension or the treatment need of root canal therapies. If any effect were to be detected as one would expect, much more observations might be needed to find significant associations within statistically significant alpha values. It is also possible that the sample size of the study was relatively small, which may have led to an overestimation of magnitude of associations that have been found. We also know that the bacteria in the mouth break down the food consumed, releasing lactic acid, butyric acid, and aspartic acid, which lower

the pH level of saliva and this reduced pH of the saliva causes demineralization of the calcified structures of the tooth and destruction of the organic matter causing cavitation and eventually the need for the restorative treatment. Hence, restorations are a surrogate of dental caries experience. In our study, significant differences in the distribution of the saliva pH were seen for the subjects with positive and negative history of restorative treatments based on ethnicity. Our findings suggested that whites were able to maintain saliva pH above the mean pH of the cohort when they were treated with restorative therapy and blacks were able to do the same without any need for treatment intervention with restorative therapies. This may indicate that blacks were able to remain on the higher range of the physiological pH scale without any restorative treatments indicating less experience of caries in blacks. This finding also matches with the National Health and Nutrition examination survey 2015-2016, which shows less caries experience for Blacks in the American population[55]. The consequence of not treating teeth at a proper time calls for root canal therapies or at the worst-case scenario, the need for tooth extraction. In our results we found that subjects were more likely to have saliva pH above the mean pH of the cohort when they were not treated for any tooth extractions indicating that higher pH than the mean pH of the cohort associated with less likeliness of tooth loss. It was also observed that higher pH than the mean pH of the cohort was associated with the less need for oral surgery treatment particularly in Whites. As already mentioned, no associations were observed when root canal therapies and history of hypertension were considered in the analysis.

Our lab has been working with *MMP2* and the aquaporin locus for several years now[39-46]. We have shown that variations in *MMP2* are associated with periapical lesions [39] associated with deep carious lesions and failures in composite restorative treatments[40]. Similarly, we have been studying variations in the aquaporin locus and showed they associate with temporomandibular

joint disorders associated with periodontitis[46], erosive tooth wear [45] and less caries experience[42]. Hence, here we tested *MMP2*, which others showed associated with caries progression in dentin and bond stability of adhesive materials[47-49], periodontitis[50,51] and hypertension[52,53]. Our study is the first one to test for associations of *MMPs* or aquaporins with saliva pH variations depending on measures of caries experience, periodontitis or hypertension.

We found that markers in *MMP2* and the aquaporin locus were associated with periodontitis, need for restorative treatment, oral surgery, root canal therapy and hypertension depending on differences in the normal salivary pH. Matrix metalloproteinase 2, also known as gelatinase A, is a membrane-bound protein that is important for extracellular matrix turnover, preferentially cleaving collagen types IV, V, VII, and XI and gelatin[56]. *MMP2* gelatinolytic activity probably occurs both in partially demineralized dentin at the bottom of caries lesions and at the surface treated with either etch-and-rinse or self-etch adhesives in treatment cases[40]. The breakdown products released in the oral cavity due to the action of collagenases on tooth materials or gingival tissues may cause small alterations in the saliva pH, but enough that they could be used as a biomarker for risk to help specific dental treatment needs or hypertension. Aquaporins (*AQPs*) are the complex regulators of water permeability and there is some new evidence of the involvement of *AQPs* in other cellular processes, such as cell adhesion, signaling, volume regulation and proteins expression[57]. *AQPs* are also involved in the secretory function of lacrimal and salivary glands in humans. Proportionally as the salivary flow declines with age, the *AQP* levels decrease as well[58]. *AQPs* are important for the oral environment, as they effect the properties of the saliva and different kinds of protein expression by them may have an effect on the pH of the saliva. *AQP* roles that might impact risks for dental caries, not only include the control of saliva secretion, but also the control of water during enamel development[42].

Our work has generated data on several parameters that will allow for calculations of precise sample sizes for testing. Also, for the first time, it is suggested that variation of saliva pH within what is considered the normal range, may serve as a biomarker for disease and simply disregarding the nominal associations presented here may delay discovery by misleading the field to believe no true biological relationships exist.

It is important to ponder on the fact that, today's era is the era of customized treatment planning for individuals, keeping in mind their biology, genetics, lifestyle, environment etc. Studies like "All of Us" are in full force recruiting individuals to help researchers contribute to health care in terms of better treatment and disease prevention and designing the fundamental principles of Precision Medicine. Our study is a preliminary step on the same lines in contributing towards Precision Dentistry keeping in mind the genetics of the individuals before any dental treatment planning. Hopefully in the next decade we will have enough information on dental genetics and our study is a small step in the same direction.

7.0 Conclusion

Our study shows that there are associations between saliva pH and different phenotypes like periodontitis, restorative treatment, root canal therapies, oral surgeries and systemic conditions like hypertension based on genetic differences in individuals for markers in *MMP2* and aquaporin locus. There are specific associations seen when demographic factors like sex and ethnicity are considered.

Any differences in association of saliva pH to the above-mentioned phenotypes based on markers in *MMP2* and aquaporin locus may suggest differences in the oral conditions based on differences in the saliva pH and thereby a need for more customized treatment plan for individuals.

Our findings suggest that markers in *MMP2* and the aquaporin locus associate with specific dental conditions based on differences in the oral environment pertaining to the differences in the saliva pH and could help us predict customized treatment needs for different individuals.

8.0 Limitations and future work

No study is completely flawless and inclusive of all possible aspects. There were a few limitations to our study as well. For our study we considered, for all subjects, restorative treatment as surrogate to dental caries, although there may have been many cases where dental caries was not treated with restorative materials leading to underreporting of caries status. Differences in saliva pH based on treatment with various restorative materials like composites, glass ionomers, amalgam, gold fillings etc. can also be considered. The socio-economic factors for the individuals in the study were not considered. Differences in socio-economic factors can make some individuals not opt for complex treatment interventions like root canal therapies and tooth extractions etc. All this would have led to underreporting of the complex treatment needs for the subjects in this study. Also, the medication and medical history of patients was not considered, which may have had effects on the saliva pH. Since it was difficult for some patients at our dental school to provide saliva samples without stimulation, having had stimulation was used for the samples of this study. The need for stimulation may indicate dehydration in mouth, which can due to radiation effects on salivary glands, history of diabetes, Sjogren's syndrome, HIV AIDS, use of tobacco/alcohol, or use of medications like antihypertensives etc. Considering all the mentioned factors is warranted for the future studies.

Also, the sample size of this study was relatively small, leaving more margin for error and overestimate of magnitude of associations. To compensate for these, we have tried to use the Fisher's exact test for the cases where observations were less than five to reduce for the statistical association errors. We also performed multiple testing for testing hypothesis comparing genotypic and allelic distributions for several markers, also by sex and ethnicity,

which may have led to the possibility that true null hypothesis was rejected. Since there are different ranges of saliva pH for different dental conditions, we want to customize our testing range of saliva pH for different dental conditions, which may help us predict more accurate range of saliva pH as a biomarker for dental diseases based on genetic markers for our future work. Above all this, emphasis should be laid on the fact that our aim in this study was to explore data for evidence of frequency differences in population to help generate future hypothesis that can be tested with proper sample sizes. Our work has also generated data on several parameters that will allow for calculations of precise sample sizes for testing.

Appendixes

This section contains supplemental data on detailed genotypic analysis for all the markers tested for various conditions.

Appendix Table 1 Detailed rs243865 genotyping analysis of subjects for association between salivary pH and periodontitis

Subjects with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	21	14	0.37
CT	21	12	
TT	3	0	
Subjects without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	26	14	**0.04**
CT	32	4	
TT	3	2	
Males with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	9	8	0.34
CT	13	6	
TT	2	0	
Males without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	12	7	0.68
CT	16	1	
TT	1	0	
Females with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	12	6	0.63
CT	8	6	
TT	1	0	
Females without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	14	7	0.29
CT	15	3	

TT	2	2	
Whites with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	16	11	0.37
CT	17	9	
TT	3	0	
Whites without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	15	9	0.14
CT	23	4	
TT	3	2	
Blacks with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	4	2	0.19
CT	1	3	
TT	0	0	
Blacks without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	8	4	0.18
CT	4	0	
TT	0	0	

Appendix Table 2 Detailed rs11639960 genotyping analysis of subjects for association between salivary pH and periodontitis

Subjects with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	36	16	-
AG	0	0	
GG	0	0	
Subjects without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	56	21	**0.04**
AG	4	6	
GG	0	0	
Males with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	23	10	**0.02**
AG	0	0	
GG	0	0	
Males without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	28	7	0.06

AG	1	2	
GG	0	0	
Females with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	13	6	0.10
AG	0	0	
GG	0	0	
Females without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	28	14	0.22
AG	3	4	
GG	0	0	
Whites with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	27	13	**0.02**
AG	0	0	
GG	0	0	
Whites without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	39	15	0.09
AG	4	5	
GG	0	0	
Blacks with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	5	2	0.25
AG	0	0	
GG	0	0	
Blacks without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	13	6	0.16
AG	0	1	
GG	0	0	

Appendix Table 3 Detailed rs2285053 genotyping analysis of subjects for association between salivary pH and periodontitis

Subjects with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	43	24	0.76
CT	9	3	
TT	2	1	
Subjects without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value

CC	48	25	0.36
CT	20	6	
TT	2	0	
Males with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	24	11	0.35
CT	5	3	
TT	0	1	
Males without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	20	7	0.76
CT	11	5	
TT	1	0	
Females with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	19	13	0.15
CT	4	0	
TT	2	0	
Females without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	28	18	0.16
CT	9	1	
TT	1	0	
Whites with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	32	17	0.34
CT	8	3	
TT	0	1	
Whites without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	18	19	0.18
CT	11	4	
TT	1	0	
Blacks with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	8	5	0.40
CT	0	0	
TT	0	0	
Blacks without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	8	6	0.19
CT	6	1	
TT	0	0	

Appendix Table 4 Detailed rs2241145 genotyping analysis of subjects for association between salivary pH and periodontitis

Subjects with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	6	4	0.33
CG	30	11	
GG	11	9	
Subjects without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	13	3	0.26
CG	35	19	
GG	13	3	
Males with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	3	2	0.10
CG	4	6	
GG	7	4	
Males without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	6	1	0.43
CG	15	7	
GG	7	1	
Females with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	3	2	0.33
CG	16	5	
GG	5	5	
Females without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	7	2	0.60
CG	20	12	
GG	6	2	
Whites with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	5	2	0.70
CG	23	9	
GG	9	6	
Whites without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	10	3	0.20
CG	18	13	
GG	10	2	

Blacks with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	1	0.85
CG	4	2	
GG	2	2	
Blacks without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	1	0	0.78
CG	10	5	
GG	2	1	

Appendix Table 5 Detailed rs243832 genotyping analysis of subjects for association between salivary pH and periodontitis

Subjects with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	10	3	0.59
CG	22	14	
GG	17	9	
Subjects without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	13	7	0.68
CG	41	17	
GG	14	4	
Males with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	8	1	0.24
CG	9	7	
GG	11	6	
Males without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	5	2	0.87
CG	22	7	
GG	5	1	
Females with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	2	0.82
CG	13	7	
GG	6	3	
Females without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	8	5	0.76
CG	19	10	

GG	9	3	
Whites with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	8	1	0.28
CG	16	10	
GG	13	8	
Whites without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	12	7	0.85
CG	25	11	
GG	10	4	
Blacks with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	2	0.76
CG	3	2	
GG	3	1	
Blacks without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	0	0	0.19
CG	10	6	
GG	3	0	

Appendix Table 6 Detailed rs461872 genotyping analysis of subjects for association between salivary pH and periodontitis

Subjects with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	17	3	0.08
AG	20	16	
GG	16	9	
Subjects without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	18	6	0.95
AG	26	15	
GG	22	8	
Males with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	7	1	0.24
AG	12	10	
GG	8	4	
Males without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	9	4	0.74

AG	12	5	
GG	9	2	
Females with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	10	2	0.32
AG	8	6	
GG	8	5	
Females without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	9	2	0.38
AG	14	10	
GG	13	6	
Whites with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	16	3	0.11
AG	16	12	
GG	8	6	
Whites without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	14	6	0.86
AG	22	10	
GG	8	5	
Blacks with periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	1	0	0.65
AG	2	2	
GG	5	3	
Blacks without periodontitis	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	2	0	0.09
AG	2	4	
GG	10	3	

Appendix Table 7 Detailed rs243865 genotyping analysis of subjects for association between salivary pH and restorative treatment

Subjects with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	35	15	0.73
CT	42	13	
TT	2	1	
Subjects without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value

CC	12	13	0.11
CT	11	3	
TT	4	1	
Males with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	17	8	0.43
CT	26	6	
TT	1	0	
Males without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	4	7	0.22
CT	3	1	
TT	2	0	
Females with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	18	7	0.79
CT	15	7	
TT	1	1	
Females without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	8	6	0.50
CT	8	2	
TT	2	1	
Whites with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	26	9	0.87
CT	35	10	
TT	2	1	
Whites without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	5	11	0.10
CT	5	3	
TT	4	1	
Blacks with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	6	5	0.58
CT	2	3	
TT	0	0	
Blacks without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	6	1	0.49
CT	3	0	
TT	0	0	

Appendix Table 8 Detailed rs11639960 genotyping analysis of subjects for association between salivary pH and restorative treatment

Subjects with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	69	25	0.35
AG	4	3	
GG	0	0	
Subjects without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	23	12	0.1
AG	0	3	
GG	0	0	
Males with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	39	11	0.08
AG	1	2	
GG	0	0	
Males without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	12	6	0.15
AG	0	0	
GG	0	0	
Females with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	30	14	0.77
AG	3	1	
GG	0	0	
Females without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	11	6	**0.03**
AG	0	3	
GG	0	0	
Whites with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	53	17	0.62
AG	4	2	
GG	0	0	
Whites without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	13	11	0.07
AG	0	3	
GG	0	0	
Blacks with restorations	Subjects with saliva pH	Subjects with saliva pH	P-value

	above the mean	below the mean	
AA	11	7	0.22
AG	0	1	
GG	0	0	
Blacks without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	7	1	**0.03**
AG	0	0	
GG	0	0	

Appendix Table 9 Detailed rs2285053 genotyping analysis of subjects for association between salivary pH and restorative treatment

Subjects with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	69	34	0.38
CT	21	5	
TT	3	1	
Subjects without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	22	15	0.66
CT	8	4	
TT	1	0	
Males with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	35	12	0.74
CT	13	5	
TT	1	1	
Males without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	9	6	0.67
CT	3	3	
TT	0	0	
Females with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	34	22	**0.05**
CT	8	0	
TT	2	0	
Females without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	13	9	0.41
CT	5	1	
TT	1	0	

Whites with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	55	22	0.62
CT	15	4	
TT	1	1	
Whites without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	13	14	0.67
CT	4	3	
TT	0	0	
Blacks with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	10	10	0.35
CT	3	1	
TT	0	0	
Blacks without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	6	1	0.49
CT	3	0	
TT	0	0	

Appendix Table 10 Detailed rs2241145 genotyping analysis of subjects for association between salivary pH and restorative treatment

Subjects with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	16	6	0.35
CG	49	15	
GG	18	11	
Subjects without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	3	1	0.14
CG	16	15	
GG	7	1	
Males with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	7	3	0.77
CG	24	6	
GG	11	4	
Males without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	0	0.20
CG	5	7	

GG	3	1	
Females with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	9	3	0.24
CG	25	9	
GG	7	7	
Females without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	1	1	0.25
CG	11	8	
GG	4	0	
Whites with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	13	4	0.52
CG	35	9	
GG	14	7	
Whites without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	1	0.06
CG	6	13	
GG	5	1	
Blacks with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	1	0.89
CG	8	6	
GG	3	3	
Blacks without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	1	0	0.89
CG	6	1	
GG	1	0	

Appendix Table 11 Detailed rs243832 genotyping analysis of subjects for association between salivary pH and restorative treatment

Subjects with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	20	6	0.5
CG	44	19	
GG	24	11	
Subjects without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	3	4	0.24
CG	19	12	

GG	7	2	
Males with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	12	3	0.82
CG	22	8	
GG	12	5	
Males without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	1	0	0.72
CG	9	6	
GG	3	2	
Females with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	8	3	0.90
CG	22	11	
GG	11	6	
Females without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	4	0.10
CG	10	6	
GG	4	0	
Whites with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	18	4	0.41
CG	29	10	
GG	19	10	
Whites without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	4	0.50
CG	12	11	
GG	4	2	
Blacks with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	2	0.70
CG	8	7	
GG	3	1	
Blacks without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	0	0	0.45
CG	5	1	
GG	3	0	

Appendix Table 12 Detailed rs461872 genotyping analysis of subjects for association between salivary pH and restorative treatment

Subjects with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	25	5	0.1
AG	37	23	
GG	25	10	
Subjects without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	10	4	0.6
AG	9	8	
GG	13	7	
Males with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	11	3	0.44
AG	20	11	
GG	12	3	
Males without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	4	2	0.79
AG	4	4	
GG	5	3	
Females with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	13	2	0.16
AG	17	12	
GG	13	7	
Females without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	6	2	0.69
AG	5	4	
GG	8	4	
Whites with restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	22	5	0.42
AG	31	15	
GG	12	5	
Whites without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	8	4	0.44
AG	7	7	
GG	4	6	
Blacks with restorations	Subjects with saliva pH	Subjects with saliva pH	P-value

	above the mean	below the mean	
AA	1	0	0.22
AG	3	6	
GG	9	5	
Blacks without restorations	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	2	0	0.78
AG	1	0	
GG	6	1	

Appendix Table 13 Detailed rs243865 genotyping analysis of subjects for association between salivary pH and having received oral surgery treatment

Subjects that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	23	16	0.63
CT	21	9	
TT	2	1	
Subjects that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	24	12	0.29
CT	32	7	
TT	4	1	
Males that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	9	8	0.24
CT	10	3	
TT	1	2	
Males that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	12	7	0.35
CT	19	4	
TT	2	1	
Females that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	14	8	0.75
CT	11	6	
TT	1	0	
Females that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	12	5	0.59
CT	12	3	
TT	2	0	
Whites that had oral surgery	Subjects with saliva pH	Subjects with saliva pH	P-value

	above the mean	below the mean	
CC	11	11	0.39
CT	16	7	
TT	2	1	
Whites that did have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	20	9	0.63
CT	23	6	
TT	4	1	
Blacks that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	9	4	0.24
CT	1	2	
TT	0	1	
Blacks that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	3	2	0.30
CT	4	1	
TT	0	1	

Appendix Table 14 Detailed rs11639960 genotyping analysis of subjects for association between salivary pH and having received oral surgery treatment

Subjects that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	36	22	**0.033**
AG	0	3	
GG	0	0	
Subjects did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	56	15	0.19
AG	4	3	
GG	0	0	
Males that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	16	8	0.17
AG	0	1	
GG	0	0	
Males that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	35	9	0.32
AG	1	1	
GG	0	0	

Females that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	20	14	0.10
AG	0	2	
GG	0	0	
Females that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	21	6	0.39
AG	3	2	
GG	0	0	
Whites that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	23	16	0.10
AG	0	2	
GG	0	0	
Whites that did have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	43	12	0.22
AG	4	3	
GG	0	0	
Blacks that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	10	6	0.21
AG	0	1	
GG	0	0	
Blacks that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	8	2	**0.05**
AG	0	0	
GG	0	0	

Appendix Table 15 Detailed rs2285053 genotyping analysis of subjects for association between salivary pH and having received oral surgery treatment

Subjects that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	38	29	0.63
CT	13	6	
TT	1	1	
Subjects that did not oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	53	20	0.42
CT	14	3	

TT	3	0	
Males that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	15	9	0.45
CT	8	5	
TT	0	1	
Males that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	29	9	0.82
CT	8	3	
TT	1	0	
Females that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	23	20	0.26
CT	5	1	
TT	1	0	
Females that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	24	11	0.12
CT	8	0	
TT	2	0	
Whites that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	25	19	0.52
CT	7	6	
TT	0	1	
Whites that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	43	17	0.24
CT	12	1	
TT	1	0	
Blacks that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	10	9	0.12
CT	3	0	
TT	0	0	
Blacks that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	6	2	1
CT	3	1	
TT	0	0	

Appendix Table 16 Detailed rs2241145 genotyping analysis of subjects for association between salivary pH and having received oral surgery treatment

Subjects that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	9	6	0.93
CG	25	17	
GG	11	6	
Subjects that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	10	1	0.42
CG	40	13	
GG	14	6	
Males that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	4	3	0.57
CG	12	7	
GG	5	1	
Males that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	5	0	0.37
CG	17	6	
GG	9	4	
Females that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	5	3	0.93
CG	13	10	
GG	6	5	
Females that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	5	1	0.87
CG	3	7	
GG	5	2	
Whites that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	7	4	0.72
CG	13	12	
GG	7	4	
Whites that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	8	1	0.62
CG	28	10	
GG	12	4	
Blacks that had oral surgery	Subjects with saliva pH	Subjects with saliva pH	P-value

	above the mean	below the mean	
CC	1	1	0.966
CG	7	5	
GG	3	2	
Blacks that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	0	0.49
CG	7	2	
GG	1	1	

Appendix Table 17 Detailed rs243832 genotyping analysis of subjects for association between salivary pH and having received oral surgery treatment

Subjects that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	7	4	0.94
CG	26	18	
GG	15	11	
Subjects that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	16	6	0.38
CG	37	13	
GG	16	2	
Males that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	3	2	0.84
CG	8	7	
GG	4	5	
Males that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	10	1	0.52
CG	23	7	
GG	12	2	
Females that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	1	2	0.49
CG	7	11	
GG	1	6	
Females that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	9	5	**0.05**
CG	25	6	
GG	14	0	
Whites that had oral surgery	Subjects with saliva pH	Subjects with saliva pH	P-value

	above the mean	below the mean	
CC	4	3	0.37
CG	10	11	
GG	4	10	
Whites that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	16	5	0.35
CG	31	10	
GG	19	2	
Blacks that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	0	1	0.68
CG	3	6	
GG	1	1	
Blacks that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	1	0.42
CG	10	2	
GG	5	0	

Appendix Table 18 Detailed rs461872 genotyping analysis of subjects for association between salivary pH and having received oral surgery treatment

Subjects that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	14	5	0.35
AG	20	16	
GG	17	14	
Subjects that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	21	4	**0.047**
AG	26	15	
GG	21	3	
Males that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	5	2	0.50
AG	10	6	
GG	5	6	
Males that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	11	3	**0.04**
AG	14	9	
GG	11	0	
Females that had oral surgery	Subjects with saliva pH	Subjects with saliva pH	P-value

	above the mean	below the mean	
AA	9	3	0.37
AG	10	10	
GG	11	8	
Females that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	10	1	0.32
AG	12	6	
GG	10	3	
Whites that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	11	5	0.27
AG	14	11	
GG	6	9	
Whites that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	19	4	0.37
AG	24	11	
GG	10	2	
Blacks that had oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	1	0	0.44
AG	3	4	
GG	9	5	
Blacks that did not have oral surgery	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	2	0	0.14
AG	1	2	
GG	6	1	

Appendix Table 19 Detailed rs243865 genotyping analysis of subjects for association between salivary pH and root canal therapy

Subjects that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	3	6	0.15
CT	11	4	
TT	1	1	
Subjects that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	44	22	0.33
CT	42	12	
TT	5	1	
Males that had root canal therapy	Subjects with saliva pH	Subjects with saliva pH	P-value

	above the mean	below the mean	
CC	0	3	**0.02**
CT	6	1	
TT	1	0	
Males that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	13	12	0.06
CT	23	6	
TT	2	0	
Females that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	3	3	0.48
CT	5	3	
TT	0	1	
Females that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	23	10	0.86
CT	19	6	
TT	3	1	
Whites that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	1	4	0.08
CT	10	3	
TT	1	1	
Whites that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	30	16	0.47
CT	30	10	
TT	5	1	
Blacks that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	1	1	0.38
CT	0	1	
TT	0	0	
Blacks that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	11	5	0.89
CT	5	2	
TT	0	0	

Appendix Table 20 Detailed rs11639960 genotyping analysis of subjects for association between salivary pH and root canal therapy

Subjects that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	15	9	-
AG	0	0	
GG	0	0	
Subjects that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	77	28	**0.03**
AG	4	6	
GG	0	0	
Males that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	9	3	0.08
AG	0	0	
GG	0	0	
Males that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	42	14	0.11
AG	1	2	
GG	0	0	
Females that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	6	6	-
AG	0	0	
GG	0	0	
Females that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	35	14	0.13
AG	3	4	
GG	0	0	
Whites that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	11	8	0.49
AG	0	0	
GG	0	0	
Whites that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	55	20	0.07
AG	4	5	
GG	0	0	
Blacks that had root canal therapy	Subjects with saliva pH	Subjects with saliva pH	P-value

	above the mean	below the mean	
AA	2	1	0.56
AG	0	0	
GG	0	0	
Blacks that did have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	16	7	14
AG	0	1	
GG	0	0	

Appendix Table 21 Detailed rs2285053 genotyping analysis of subjects for association between salivary pH and root canal therapy

Subjects that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	14	12	0.89
CT	5	3	
TT	1	1	
Subjects that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	77	37	0.21
CT	24	6	
TT	3	0	
Males that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	6	2	0.28
CT	3	3	
TT	0	1	
Males that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	38	16	0.80
CT	13	5	
TT	1	0	
Females that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	8	10	0.20
CT	2	0	
TT	1	0	
Females that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	39	21	0.11
CT	11	1	
TT	2	0	
Whites that had root canal	Subjects with saliva pH	Subjects with saliva pH	P-value

therapy	above the mean	below the mean	
CC	10	10	0.44
CT	4	2	
TT	0	1	
Whites that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	58	26	0.70
CT	15	5	
TT	1	0	
Blacks that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	1	0.70
CT	1	1	
TT	0	0	
Blacks that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	14	10	0.07
CT	5	0	
TT	0	0	

Appendix Table 22 Detailed rs2241145 genotyping analysis of subjects for association between salivary pH and root canal therapy

Subjects that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	5	3	0.13
CG	12	8	
GG	0	3	
Subjects that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	14	4	0.82
CG	53	22	
GG	25	9	
Males that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	1	1	0.49
CG	5	3	
GG	0	1	
Males that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	8	2	0.76
CG	24	10	
GG	14	4	
Females that had root canal	Subjects with saliva pH	Subjects with saliva pH	P-value

therapy	above the mean	below the mean	
CC	4	2	0.24
CG	7	5	
GG	0	2	
Females that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	6	2	0.95
CG	29	12	
GG	11	5	
Whites that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	3	2	0.17
CG	8	6	
GG	0	3	
Whites that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	12	3	0.44
CG	33	16	
GG	19	5	
Blacks that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	1	0	0.36
CG	2	2	
GG	0	0	
Blacks that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	1	0.81
CG	12	5	
GG	4	3	

Appendix Table 23 Detailed rs243832 genotyping analysis of subjects for association between salivary pH and root canal therapy

Subjects that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	6	3	0.18
CG	10	7	
GG	2	6	
Subjects that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	17	7	0.42
CG	53	24	
GG	29	7	
Males that had root canal therapy	Subjects with saliva pH	Subjects with saliva pH	P-value

	above the mean	below the mean	
CC	4	1	0.22
CG	4	2	
GG	1	3	
Males that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	9	2	0.59
CG	27	12	
GG	15	3	
Females that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	2	0.51
CG	7	5	
GG	1	3	
Females that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	8	5	0.40
CG	25	12	
GG	14	3	
Whites that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	5	3	0.19
CG	6	5	
GG	1	5	
Whites that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	15	5	0.74
CG	35	6	
GG	22	1	
Blacks that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	1	0	0.65
CG	1	1	
GG	1	1	
Blacks that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	1	2	0.12
CG	12	7	
GG	5	0	

Appendix Table 24 Detailed rs461872 genotyping analysis of subjects for association between salivary pH and root canal therapy

Subjects that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	6	3	0.68
AG	9	9	
GG	4	4	
Subjects that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	29	6	0.11
AG	37	22	
GG	34	13	
Males that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	4	1	0.42
AG	3	4	
GG	1	1	
Males that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	12	4	0.65
AG	21	11	
GG	16	5	
Females that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	2	2	0.97
AG	6	5	
GG	3	3	
Females that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	17	2	0.08
AG	16	11	
GG	18	8	
Whites that had root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	5	3	0.67
AG	6	7	
GG	2	3	
Whites that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	25	6	0.33
AG	32	15	
GG	14	8	
Blacks that had root canal therapy	Subjects with saliva pH	Subjects with saliva pH	P-value

	above the mean	below the mean	
AA	1	0	0.32
AG	2	1	
GG	0	1	
Blacks that did not have root canal therapy	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	2	0	**0.04**
AG	2	5	
GG	15	5	

Appendix Table 25 Detailed rs243865 genotyping analysis of subjects for association between salivary pH and hypertension

Subjects with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	9	3	0.52
CT	12	4	
TT	0	1	
Subjects without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	38	25	0.08
CT	41	12	
TT	6	1	
Males with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	6	2	0.52
CT	7	1	
TT	0	0	
Males without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	15	13	0.06
CT	22	6	
TT	3	0	
Females with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	3	1	0.38
CT	5	3	
TT	0	1	
Females without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	23	12	0.67
CT	5	3	
TT	0	1	
Whites with hypertension	Subjects with saliva pH	Subjects with saliva pH	P-value

	above the mean	below the mean	
CC	6	3	0.20
CT	9	2	
TT	0	1	
Whites without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	25	17	0.21
CT	31	11	
TT	6	1	
Blacks with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	0	0.22
CT	31	11	
TT	6	1	
Blacks without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	10	6	0.63
CT	3	1	
TT	0	0	

Appendix Table 26 Detailed rs11639960 genotyping analysis of subjects for association between salivary pH and hypertension

Subjects with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	18	8	**0.048**
AG	0	2	
GG	0	0	
Subjects without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	73	29	0.19
AG	4	4	
GG	0	0	
Males with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	14	3	**0.05**
AG	0	1	
GG	0	0	
Males without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	37	14	0.48
AG	1	1	
GG	0	0	

Females with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	4	5	0.38
AG	0	1	
GG	0	0	
Females without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	37	15	0.28
AG	3	3	
GG	0	0	
Whites with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	12	7	0.20
AG	0	1	
GG	0	0	
Whites without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	54	21	0.19
AG	4	4	
GG	0	0	
Blacks with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	4	1	0.12
AG	0	1	
GG	0	0	
Blacks without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	14	7	0.12
AG	0	0	
GG	0	0	

Appendix Table 27 Detailed rs2285053 genotyping analysis of subjects for association between salivary pH and hypertension

Subjects with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	19	9	0.94
CT	6	3	
TT	0	0	
Subjects without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	72	40	0.25
CT	23	6	
TT	4	1	

Males with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	12	2	0.14
CT	4	3	
TT	0	0	
Males without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	32	16	0.69
CT	12	9	
TT	1	1	
Females with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	7	7	0.18
CT	2	0	
TT	0	0	
Females without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	40	24	0.06
CT	11	1	
TT	3	0	
Whites with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	15	6	0.32
CT	11	1	
TT	3	0	
Whites without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	53	30	0.32
CT	16	4	
TT	1	1	
Blacks with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	3	0.34
CT	2	0	
TT	1	1	
Blacks without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	14	8	0.48
CT	4	1	
TT	0	0	

Appendix Table 28 Detailed rs2241145 genotyping analysis of subjects for association between salivary pH and hypertension

Subjects with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	7	2	0.71
CG	13	6	
GG	5	1	
Subjects without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	12	4	0.76
CG	52	24	
GG	20	11	
Males with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	3	1	0.52
CG	11	1	
GG	3	0	
Males without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	4	2	0.06
CG	2	12	
GG	2	5	
Females with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	4	1	0.18
CG	2	5	
GG	2	1	
Females without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	6	3	0.006
CG	34	12	
GG	9	16	
Whites with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	5	2	0.56
CG	10	4	
GG	3	0	
Whites without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	10	3	0.56
CG	31	18	
GG	3	0	
Blacks with hypertension	Subjects with saliva pH	Subjects with saliva pH	P-value

	above the mean	below the mean	
CC	1	0	0.64
CG	2	2	
GG	1	1	
Blacks without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	1	0.90
CG	12	5	
GG	3	2	

Appendix Table 29 Detailed rs243832 genotyping analysis of subjects for association between salivary pH and hypertension

Subjects with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	4	4	0.24
CG	15	4	
GG	5	4	
Subjects without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	19	6	0.38
CG	48	27	
GG	26	9	
Males with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	3	2	0.67
CG	8	2	
GG	4	1	
Males without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	10	1	0.25
CG	23	12	
GG	12	6	
Females with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	1	2	0.14
CG	7	2	
GG	1	3	
Females without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	9	5	0.32
CG	25	15	
GG	14	3	

Whites with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	4	3	0.55
CG	10	3	
GG	4	3	
Whites without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	16	5	0.55
CG	31	18	
GG	19	9	
Blacks with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	0	1	0.57
CG	3	1	
GG	1	1	
Blacks without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
CC	2	1	0.38
CG	10	7	
GG	5	0	

Appendix Table 30 Detailed rs461872 genotyping analysis of subjects for association between salivary pH and hypertension

Subjects with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	7	2	0.35
AG	8	5	
GG	9	5	
Subjects without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	28	7	**0.047**
AG	38	26	
GG	29	12	
Males with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	5	2	0.70
AG	4	2	
GG	6	1	
Males without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	11	3	0.47
AG	20	13	
GG	11	5	

Females with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	2	0	0.50
AG	4	3	
GG	3	4	
Females without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	17	4	0.19
AG	18	13	
GG	18	7	
Whites with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	5	2	0.86
AG	8	5	
GG	5	2	
Whites without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	25	7	0.19
AG	30	17	
GG	11	9	
Blacks with hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	1	0	0.34
AG	0	0	
GG	3	3	
Blacks without hypertension	Subjects with saliva pH above the mean	Subjects with saliva pH below the mean	P-value
AA	2	0	0.06
AG	4	6	
GG	12	3	

Appendix Table 31 Detailed rs243865 allele frequency analysis of subjects for association between salivary pH and periodontitis

Subjects with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	63	40	0.37
T	27	12	
Subjects without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	84	32	0.17
T	38	8	
Males with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	31	22	0.20
T	17	6	
Males without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	40	15	**0.04**
T	18	1	
Females with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	32	18	0.91
T	10	6	
Females without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	43	17	0.89
T	19	7	
Whites with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	49	31	0.29
T	23	9	
Whites without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	53	22	0.39
T	29	8	
Blacks with periodontitis	Allele frequency for subjects with saliva pH	Allele frequency for subjects with saliva pH	P-value

	above the mean	below the mean	
C	9	7	0.26
T	1	3	
Blacks without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	20	8	0.22
T	4	0	

Appendix Table 32 Detailed rs11639960 allele frequency analysis of subjects for association between salivary pH and periodontitis

Subjects with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	72	32	-
G	0	0	
Subjects without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	116	48	**0.04**
G	4	6	
Males with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	46	20	1
G	0	0	
Allele in males without Periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	57	16	0.07
G	1	2	
Females with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	26	12	-
G	0	0	
Females without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	59	32	0.25
G	3	4	
Whites with periodontitis	Allele frequency for	Allele frequency for subjects	P-value

	subjects with saliva pH above the mean	with saliva pH below the mean	
A	54	26	-
G	0	0	
Whites without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	82	35	0.11
G	4	5	
Blacks with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	10	4	-
G	0	0	
Blacks without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	26	12	0.15
G	0	1	

Appendix Table 33 Detailed rs2285053 allele frequency analysis of subjects for association between salivary pH and periodontitis

Subjects with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	95	51	0.54
T	13	5	
Subjects without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	116	56	0.16
T	24	6	
Males with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	53	25	0.26
T	5	5	
Males without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	51	19	0.96
T	13	5	
Females with periodontitis	Allele frequency for	Allele frequency for	P-value

	subjects with saliva pH above the mean	subjects with saliva pH below the mean	
C	42	26	**0.03**
T	8	0	
Females without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	65	37	**0.05**
T	11	1	
Whites with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	72	37	0.75
T	8	5	
Whites without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	47	42	0.07
T	13	4	
Blacks with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	16	10	n/a
T	0	0	
Blacks without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	22	13	0.24
T	6	1	

Appendix Table 34 Detailed rs2241145 allele frequency analysis of subjects for association between salivary pH and periodontitis

Subjects with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	42	19	0.56
G	52	29	
Subjects without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	61	25	1
G	61	25	

Males with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	20	10	1
G	28	14	
Males without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	27	9	0.895
G	29	9	
Females with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	22	9	0.50
G	26	15	
Females without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	34	16	0.88
G	32	16	
Whites with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	33	13	0.53
G	41	21	
Whites without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	38	19	0.78
G	38	17	
Blacks with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	8	4	0.62
G	8	6	
Blacks without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	12	5	0.795
G	14	7	

Appendix Table 35 Detailed rs243832 allele frequency analysis of subjects for association between salivary pH and periodontiti

Subjects with periodontitis	Allele frequency for subjects	Allele frequency for subjects	P-value

	with saliva pH above the mean	with saliva pH below the mean	
C	42	20	0.6
G	56	32	
Subjects without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	67	31	0.44
G	69	25	
Males with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	25	9	0.27
G	31	19	
Males without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	32	11	0.73
G	32	13	
Females with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	17	11	0.67
G	25	13	
Females without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	35	20	0.496
G	37	16	
Whites with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	32	12	0.23
G	42	26	
Whites without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	49	25	0.61
G	45	19	
Blacks with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	7	6	0.42
G	9	4	
Blacks without periodontitis	Allele frequency for subjects	Allele frequency for subjects	P-value

	with saliva pH above the mean	with saliva pH below the mean	
C	10	6	0.503
G	16	6	

Appendix Table 36 Detailed rs461872 allele frequency analysis of subjects for association between salivary pH and periodontitis

Subjects with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	54	22	0.15
G	52	34	
Subjects without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	62	27	0.95
G	70	31	
Males with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	26	12	0.47
G	28	18	
Males without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	30	13	0.47
G	30	9	
Females with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	28	10	0.20
G	24	16	
Females without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	32	14	0.58
G	40	22	
Whites with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	48	18	0.07
G	32	24	
Whites without periodontitis	Allele frequency for subjects with saliva pH	Allele frequency for subjects with saliva pH	P-value

	above the mean	below the mean	
A	50	22	0.63
G	38	20	
Blacks with periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	4	2	0.77
G	12	8	
Blacks without periodontitis	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	6	4	0.61
G	22	10	

Appendix Table 37 Detailed rs243865 allele frequency analysis of subjects for association between salivary pH and restorative treatment

Subjects with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	112	43	0.63
T	46	15	
Subjects without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	35	29	**0.035**
T	19	5	
Males with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	60	22	0.29
T	28	6	
Males without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	11	15	**0.025**
T	7	1	
Females with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	51	21	0.61
T	17	9	
Females without restorations	Allele frequency for subjects with saliva pH	Allele frequency for subjects with saliva pH	P-value

	above the mean	below the mean	
C	24	14	0.399
T	12	4	
Whites with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	87	28	0.91
T	39	12	
Whites without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	15	25	**0.01**
T	13	5	
Blacks with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	14	13	0.63
T	2	3	
Blacks without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	15	2	0.53
T	3	0	

Appendix Table 38 Detailed rs11639960 allele frequency analysis of subjects for association between salivary pH and restorative treatment

Subjects with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	142	53	0.36
G	4	3	
Subjects without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	46	27	**0.028**
G	0	3	
Males with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	79	24	0.085
G	1	2	
Males without restorations	Allele frequency for	Allele frequency for	P-value

	subjects with saliva pH above the mean	subjects with saliva pH below the mean	
A	24	12	1
G	0	0	
Females with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	63	29	0.78
G	3	1	
Females without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	22	15	**0.04**
G	0	3	
Whites with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	110	30	0.49
G	4	2	
Whites without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	26	25	0.085
G	0	3	
Blacks with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	22	15	0.23
G	0	1	
Blacks without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	14	2	-
G	0	0	

Appendix Table 39 Detailed rs2285053 allele frequency analysis of subjects for association between salivary pH and Restorative treatment

Subjects with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	159	73	0.19
T	27	7	

Subjects without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	52	34	0.43
T	10	4	
Males with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	83	29	0.57
T	15	7	
Males without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	21	15	0.70
T	3	3	
Females with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	76	44	**0.01**
T	12	0	
Females without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	31	19	0.16
T	7	1	
Whites with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	125	48	0.87
T	17	6	
Whites without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	30	31	0.69
T	4	3	
Blacks with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	23	21	0.38
T	3	1	
Blacks without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	15	2	0.53
T	3	0	

Appendix Table 40 Detailed rs2241145 allele frequency analysis of subjects for association between salivary pH and restorative treatment

Subjects with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	81	27	0.36
G	85	37	
Subjects without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	22	17	0.48
G	30	17	
Males with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	38	12	0.93
G	46	14	
Males without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	9	7	0.94
G	11	9	
Females with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	43	15	0.19
G	39	23	
Females without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	13	10	0.31
G	19	8	
Whites with Restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	61	17	0.46
G	63	23	
Whites without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	10	15	0.39
G	16	15	
Blacks with restorations	Allele frequency for	Allele frequency for	P-value

	subjects with saliva pH above the mean	subjects with saliva pH below the mean	
C	12	8	0.68
G	14	12	
Blacks without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	8	1	1
G	8	1	

Appendix Table 41 Detailed rs243832 allele frequency analysis of subjects for association between salivary pH and restorative treatment

Subjects with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	84	31	0.50
G	92	41	
Subjects without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	25	20	0.24
G	33	16	
Males with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	46	14	0.54
G	46	18	
Males without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	11	6	0.76
G	15	10	
Females with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	38	17	0.69
G	44	23	
Females without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	14	14	0.064
G	18	6	
Whites with restorations	Allele frequency for subjects with saliva pH	Allele frequency for subjects with saliva pH	P-value

	above the mean	below the mean	
C	65	18	0.16
G	67	30	
Whites without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	16	19	0.34
G	20	15	
Blacks with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	12	11	0.55
G	14	9	
Blacks without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	5	1	0.595
G	11	1	

Appendix Table 42 Detailed rs461872 allele frequency analysis of subjects for association between salivary pH and restorative treatment

Subjects with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	87	33	0.33
G	87	43	
Subjects without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	29	16	0.75
G	35	22	
Males with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	42	17	0.91
G	44	17	
Males without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	12	8	0.91
G	14	10	
Females with restorations	Allele frequency for subjects with saliva pH	Allele frequency for subjects with saliva pH	P-value

	above the mean	below the mean	
A	43	16	0.20
G	43	26	
Females without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	17	8	0.73
G	21	12	
Whites with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	75	25	0.35
G	55	25	
Whites without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	23	15	0.16
G	15	19	
Blacks with restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	5	6	0.51
G	21	16	
Blacks without restorations	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	5	0	0.39
G	13	2	

Appendix Table 43 Detailed rs243865 allele frequency analysis of subjects for association between salivary pH and having received oral surgery treatment

Subjects that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	67	41	0.42
T	25	11	
Subjects that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	80	31	0.19
T	40	9	

Males that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	18	19	0.30
T	12	7	
Males that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	43	18	0.38
T	23	6	
Females that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	39	22	0.72
T	13	6	
Females that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	36	13	0.35
T	16	3	
Whites that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	38	29	0.26
T	20	9	
Whites that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	63	24	0.399
T	31	8	
Blacks that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	19	10	0.06
T	1	4	
Blacks that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	10	5	0.67
T	4	3	

Appendix Table 44 Detailed rs11639960 allele frequency analysis of subjects for association between salivary pH and having received oral surgery treament

Subjects that had oral	Allele frequency for	Allele frequency for	P-value

surgery	subjects with saliva pH above the mean	subjects with saliva pH below the mean	
A	72	47	**0.035**
G	0	3	
Subjects that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	116	33	0.20
G	4	3	
Males that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	32	17	0.18
G	0	1	
Males that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	71	19	0.33
G	1	1	
Females that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	40	30	0.11
G	0	2	
Females that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	45	14	0.42
G	3	2	
Whites that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	46	34	0.11
G	0	2	
Whites that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	90	27	0.24
G	4	3	
Blacks that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	20	13	0.23
G	0	1	
Blacks that did not have	Allele frequency for	Allele frequency for	P-value

oral surgery	subjects with saliva pH above the mean	subjects with saliva pH below the mean	
A	16	4	-
G	0	0	

Appendix Table 45 Detailed rs2285053 allele frequency analysis of subjects for association between salivary pH and having had oral surgery

Subjects that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	89	64	0.52
T	15	8	
Subjects that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	120	43	0.16
T	20	3	
Males that ad oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	38	23	0.52
T	8	7	
Male that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	66	21	0.93
T	10	3	
Females that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	51	41	0.08
T	7	1	
Females that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	56	22	0.03
T	12	0	
Whites that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	57	44	0.48
T	7	8	
Whites that did not have	Allele frequency for	Allele frequency for	P-value

oral surgery	subjects with saliva pH above the mean	subjects with saliva pH below the mean	
C	98	35	0.09
T	14	1	
Blacks that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	23	18	0.14
T	3	0	
Blacks that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	15	5	1
T	3	1	

Appendix Table 46 Detailed rs2241145 allele frequency analysis of subjects for association between salivary pH and having had oral surgery

Subjects that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	43	29	0.79
G	47	29	
Subjects that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	60	15	0.29
G	68	25	
Males that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	20	13	0.38
G	22	9	
Males that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	27	6	0.28
G	35	14	
Females that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	23	16	0.75
G	25	20	

Females that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	33	9	0.695
G	33	11	
Whites that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	27	20	1
G	27	20	
Whites that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	44	12	0.57
G	52	18	
Blacks that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	9	7	0.86
G	13	9	
Blacks that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	11	2	0.35
G	9	4	

Appendix Table 47 Detailed rs243832 allele frequency of subjects for association between salivary pH and having had oral surgery

Subjects that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	40	26	0.77
G	56	40	
Subjects that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	69	25	0.27
G	69	17	
Males that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	14	11	0.57

G	16	17	
Males that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	43	9	0.82
G	47	11	
Females that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	9	15	0.45
G	9	23	
Females that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	43	16	**0.018**
G	53	6	
Whites that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	18	17	0.18
G	18	31	
Whites that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	63	20	0.25
G	69	14	
Blacks that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	3	8	0.56
G	5	8	
Blacks that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	14	4	0.25
G	20	2	

Appendix Table 48 Detailed rs461872 allele frequency analysis of subjects for association between salivary pH and having had oral surgery

Subjects that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	48	26	0.19

G	54	44	
Subjects that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	68	34	0.13
G	68	21	
Males that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	20	10	0.24
G	20	18	
Males that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	36	15	0.29
G	36	9	
Females that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	28	16	0.39
G	32	26	
Females that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	32	8	0.44
G	32	12	
Whites that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	36	21	0.09
G	26	29	
Whites that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	62	19	0.79
G	44	15	
Blacks that had oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	5	4	0.81
G	21	14	
Blacks that did not have oral surgery	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	5	2	0.795

G	13	4	

Appendix Table 49 Detailed rs243865 allele frequency analysis of subjects for association between salivary pH and having had root canal therapy

Subjects that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	17	16	0.23
T	13	6	
Subjects that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	130	56	0.16
T	52	14	
Males that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	6	7	**0.04**
T	8	1	
Males that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	49	30	**0.04**
T	27	6	
Females that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	11	9	0.795
T	5	5	
Females that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	65	26	0.63
T	25	8	
Whites that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	12	11	0.24
T	12	5	
Whites that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	90	42	0.24

T	40	12	
Blacks that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	2	3	0.44
T	0	1	
Blacks that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	27	12	0.91
T	5	2	

Appendix Table 50 Detailed rs11639960 allele frequency analysis of subjects for association between salivary pH and having had root canal therapy

Subjects that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	30	18	
G	0	0	
Subjects that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	158	62	**0.03**
G	4	6	
Males that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	18	6	-
G	0	0	
Males that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	85	30	0.12
G	1	2	
Females that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	12	12	-
G	0	0	
Females that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value

A	73	32	0.14
G	3	4	
Whites that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	22	16	-
G	0	0	
Whites that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	114	45	**0.08**
G	4	5	
Blacks that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	4	2	-
G	0	0	
Blacks that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	32	15	0.15
G	0	1	

Appendix Table 51 Detailed rs2285053 allele frequency analysis of subjects for association between salivary pH and having had root canal therapy

Subjects that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	33	27	0.83
T	7	5	
Subjects that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	178	80	0.07
T	30	6	
Males that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	15	7	0.13
T	3	5	
Males that did not have root canal therapy	Allele frequency for subjects with saliva pH	Allele frequency for subjects with saliva pH	P-value

	above the mean	below the mean	
C	89	37	0.69
T	15	5	
Females that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	18	20	**0.04**
T	4	0	
Females that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	89	43	**0.03**
T	15	1	
Whites that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	24	22	0.91
T	4	4	
Whites that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	131	57	0.46
T	17	5	
Blacks that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	5	3	0.75
T	1	1	
Blacks that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	33	20	0.9
T	5	0	

Appendix Table 52 Detailed rs2241145 allele frequency analysis of subjects for association between salivary pH and having had root canal therapy

Subjects that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	22	14	0.0000001
G	0	14	
Subjects that did not have	Allele frequency for	Allele frequency for	P-value

root canal therapy	subjects with saliva pH above the mean	subjects with saliva pH below the mean	
C	81	30	0.86
G	103	40	
Males that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	7	5	0.695
G	5	5	
Males that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	40	14	0.98
G	52	18	
Females that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	15	9	0.24
G	7	9	
Females that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	41	16	0.797
G	51	22	
Whites that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	14	10	0.23
G	8	12	
Whitesthat did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	57	22	0.88
G	71	26	
Blacks that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	4	2	0.598
G	2	2	
Blacks that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	16	7	0.697
G	20	11	

Appendix Table 53 Detailed rs243832 allele frequency of subjects for association between salivary pH and having had root canal therapy

Subjects that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	22	13	0.09
G	14	19	
Subjects that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	87	38	0.36
G	111	38	
Males that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	12	4	0.07
G	6	8	
Males that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	45	14	0.76
G	57	20	
Females that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	11	9	0.53
G	9	11	
Females that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	41	22	0.23
G	53	18	
Whites that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	16	11	0.08
G	8	15	
Whites that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	65	26	0.87
G	79	30	
Blacks that had root canal therapy	Allele frequency for subjects with saliva pH	Allele frequency for subjects with saliva pH	P-value

	above the mean	below the mean	
C	3	1	0.43
G	3	3	
Blacks that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	14	11	0.122
G	22	7	

Appendix Table 54 Detailed rs461872 allele frequency analysis of subjects for association between salivary pH and having had root canal therapy

Subjects that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	21	15	0.48
G	17	17	
Subjects that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	95	34	0.35
G	105	48	
Males that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	11	6	0.31
G	5	6	
Males that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	45	19	0.87
G	53	21	
Females that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	10	9	0.98
G	12	11	
Females that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	50	15	0.144
G	52	27	

Whites that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	16	13	0.40
G	10	13	
Whites that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	82	27	0.15
G	60	31	
Blacks that had root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	4	1	0.196
G	2	3	
Blacks that did not have root canal therapy	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	6	5	0.395
G	32	15	

Appendix Table 55 Detailed rs243865 allele frequency analysis of subjects for association between salivary pH and hypertension

Subjects with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	30	10	0.51
T	12	6	
Subjects without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	117	62	**0.037**
T	53	14	
Males with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	19	5	0.60
T	7	1	
Males without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value

C	52	32	**0.03**
T	28	6	
Females with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	11	5	0.34
T	5	5	
Females without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	65	30	0.43
T	25	8	
Whites with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	21	8	0.83
T	9	4	
Whites without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	81	45	0.09
T	43	13	
Blacks with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	6	2	0.39
T	2	2	
Blacks without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	23	13	0.66
T	3	1	

Appendix Table 56 Detailed rs11639960 allele frequency analysis of subjects for association between salivary pH and hypertension

Subjects with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	36	18	**0.053**
G	0	2	
Subjects without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value

A	150	62	0.20
G	4	4	
Males with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	28	7	0.07
G	0	1	
Males without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	75	29	0.49
G	1	1	
Females with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	8	11	0.40
G	0	1	
Females without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	77	33	0.30
G	3	3	
Whites with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	24	15	0.21
G	0	1	
Whites without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	112	46	0.21
G	4	4	
Blacks with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	8	3	0.14
G	0	1	
Blacks without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	28	14	1
G	0	0	

Appendix Table 57 Detailed rs2285053 allele frequency analysis of subjects for association between salivary pH and hypertension

Subjects with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	44	21	0.95
T	6	3	
Subjects without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	167	86	0.09
T	31	8	
Males with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	28	7	0.19
T	4	3	
Males without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	76	41	0.398
T	14	11	
Females with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	16	14	0.197
T	2	0	
Females without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	91	49	**0.011**
T	17	1	
Whites with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	33	15	0.36
T	3	3	
Whites without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	122	64	0.36

T	18	6	
Blacks with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	6	6	0.19
T	2	0	
Blacks without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	32	17	0.51
T	4	1	

Appendix Table 58 Detailed rs2241145 allele frequency analysis of subjects for association between salivary pH and hypertension

Subjects with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	27	10	0.91
G	23	8	
Subjects without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	76	32	0.53
G	92	46	
Males with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	17	3	0.34
G	17	1	
Males without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	10	16	0.17
G	6	22	
Females with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	10	7	0.49
G	6	7	
Females without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value

C	46	18	**0.02**
G	52	44	
Whites with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	20	8	0.498
G	16	4	
Whites without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	51	24	0.24
G	49	34	
Blacks with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	4	2	0.53
G	4	4	
Blacks without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	16	7	0.83
G	18	9	

Appendix Table 59 Detailed rs243832 allele frequency of subjects for association between salivary pH and hypertension

Subjects with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	23	12	0.86
G	25	12	
Subjects without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	86	39	0.97
G	100	45	
Males with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	14	6	0.47
G	16	4	
Males without hypertension	Allele frequency for subjects with saliva pH	Allele frequency for subjects with saliva pH	P-value

	above the mean	below the mean	
C	43	14	0.26
G	47	24	
Females with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	9	6	0.69
G	9	8	
Females without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	43	25	0.29
G	53	21	
Whites with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	18	9	1
G	18	9	
Whites without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	63	28	0.60
G	69	36	
Blacks with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	3	3	0.64
G	5	3	
Blacks without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
C	14	9	0.32
G	20	7	

Appendix Table 60 Detailed rs461872 allele frequency analysis of subjects for association between salivary pH and hypertension

Subjects with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	22	9	0.50
G	26	15	

Subjects without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	94	40	0.43
G	96	50	
Males with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	14	6	0.59
G	16	4	
Males without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	42	19	0.61
G	42	23	
Females with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	8	3	0.17
G	10	11	
Females without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	52	21	0.54
G	54	27	
Whites with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	18	9	1
G	18	9	
Whites without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	80	31	0.07
G	52	35	
Blacks with hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	2	0	0.19
G	6	6	
Blacks without hypertension	Allele frequency for subjects with saliva pH above the mean	Allele frequency for subjects with saliva pH below the mean	P-value
A	8	6	0.38
G	28	12	

Bibliography

1. Mandel, Irwin D. “A contemporary view of salivary research.” *Critical Reviews in Oral Biology & Medicine*, vol. 4, no. 3, Apr. 1993, pp. 599–604.

2. Silvers, A. R., & Som, P. M. (1998). Salivary glands. *Radiologic clinics of north America*, *36*(5), 941-966.

3. Young, John Atherton, and Ernest Willem Van Lennep. *The morphology of salivary glands*. Academic Press, 1978.

4. Van Nieuw Amerongen, Arie, Jan GM Bolscher, and Enno CI Veerman. "Salivary proteins: protective and diagnostic value in cariology?" *Caries research* 38.3 (2004): 247-253.

5. Zalewska, Anna, et al. "Structure and biosynthesis of human salivary mucins." *Acta Biochimica Polonica* 47.4 (2000): 1067-1079.

6. Humphrey, Sue P., and Russell T. Williamson. "A review of saliva: normal composition, flow, and function." *The Journal of prosthetic dentistry* 85.2 (2001): 162-169.

7. Troxler, R. F., et al. "Structural relationship between human salivary histatins." *Journal of Dental Research* 69.1 (1990): 2-6.

8. De Smet, Kris, and Roland Contreras. "Human antimicrobial peptides: defensins, cathelicidins and histatins." *Biotechnology letters* 27.18 (2005): 1337-1347.

9. Gusman, Heloisa, et al. "Human salivary gland-specific daily variations in histatin concentrations determined by a novel quantitation technique." *Archives of oral biology* 49.1 (2004): 11-22.

10. Veerman, E. C. I., et al. "Human glandular saliva: their separate collection and analysis." *European journal of oral sciences* 104.4 (1996): 346-352.

11. Dawes, C. "Circadian rhythms in human salivary flow rate and composition." *The Journal of physiology* 220.3 (1972): 529-545.

12. Ferguson, D. B., et al. "Circadian rhythms in human parotid saliva flow rate and composition." *Archives of Oral Biology*18.9 (1973): 1155-1173.

13. Ferguson, D. B., and C. A. Botchway. "A comparison of circadian variation in the flow rate and composition of stimulated human parotid, submandibular and whole saliva from the same individuals." *Archives of oral biology* 25.8-9 (1980): 559-568.

14. Castagnola, Massimo, et al. "Circadian rhythms of histatin 1, histatin 3, histatin 5, statherin and uric acid in whole human saliva secretion." *Biological rhythm research* 33.2 (2002): 213-222.

15. Edgar, William Michael. "Saliva and dental health. Clinical implications of saliva: report of a consensus meeting." *British dental journal* 169.4 (1990): 96-98.

16. Erdemir, Ebru Olgun, and Ali Erdemir. "The Detection of Salivary Minerals in Smokers and Non-Smokers with Chronic Periodontitis by the Inductively Coupled Plasma-Atomic Emission Spectrophotometry Technique." *Journal of periodontology* 77.6 (2006): 990-995.

17. Takahashi, N., and C. F. Schachtele. "Effect of pH on the growth and proteolytic activity of Porphyromonas gingivalis and Bacteroides intermedius." *Journal of dental research* 69.6 (1990): 1266-1269.

18. Takahashl, N., et al. "Acid tolerance and acid-neutralizing activity of Porphyromonas gingivalis, Prevotella intermedia and Fusobacterium nucleatum." *Oral microbiology and immunology* 12.6 (1997): 323-328.

19. Baliga, Sharmila et al. “Salivary pH: A diagnostic biomarker.” *Journal of Indian Society of Periodontology* vol. 17,4 (2013): 461-5. doi:10.4103/0972-124X.118317

20. Guggenheimer, James, and Paul A. Moore. "Xerostomia: etiology, recognition and treatment." *The Journal of the American Dental Association* 134.1 (2003): 61-69.

21. Dodds, Michael WJ, Dorthea A. Johnson, and Chih-Ko Yeh. "Health benefits of saliva: a review." *Journal of dentistry* 33.3 (2005): 223-233.

22. Jafarian, M, and A Etebarian. “Reasons for extraction of permanent teeth in general dental practices in Tehran, Iran.” Medical principles and practice: international journal of the Kuwait University, Health Science Centre vol. 22,3 (2013): 239-44. doi:10.1159/000345979

23. Holt, R et al. “Dental damage, sequelae, and prevention.” The Western journal of medicine vol. 174,4 (2001): 288-90. doi:10.1136/ewjm.174.4.288

24. https://www.aae.org/patients/root-canal-treatment/what-is-a-root-canal/root-canal-explained/

25. Nimma, V et al. Influence of hypertension on pH of saliva and flow rate in elder adults correlating with oral health status. *J Clin Diagn Res*. 2016;10(11): ZC34–ZC36. doi:10.7860/JCDR/2016/16799.8888

26. Alonso, Amalia, et al. "Erythrocyte anion exchanger activity and intracellular pH in essential hypertension." *Hypertension* 22.3 (1993): 348-356.

27. Wong, David T. "Salivary diagnostics powered by nanotechnologies, proteomics and genomics." *The Journal of the American Dental Association* 137.3 (2006): 313-321.

28. Segal, Alik, and David T Wong. “Salivary diagnostics: enhancing disease detection and making medicine better.” *European journal of dental education: official journal of the Association for Dental Education in Europe* vol. 12 Suppl 1 (2008): 22-9. doi:10.1111/j.1600-0579.2007.00477.x

29. Vuotila, T., et al. "The relationship between MMPs and pH in whole saliva of radiated head and neck cancer patients." *Journal of oral pathology & medicine* 31.6 (2002): 329-338.

30. da Silva Modesto, Karine Barros, et al. "Salivary flow rate and biochemical composition analysis in stimulated whole saliva of children with cystic fibrosis." *Archives of oral biology* 60.11 (2015): 1650-1654.

31. Rabelo Buzalaf, Marilia Afonso, Angelicas Reis Hannas, and Melissa Thiemi Kato. "Saliva and dental erosion." *Journal of Applied Oral Science* 20.5 (2012): 493.

32. Buijssen, Kevin JDA, et al. "Composition and architecture of biofilms on used voice prostheses." *Head & neck* 34.6 (2012): 863-871.

33. Rabelo Buzalaf, Marilia Afonso, Angelicas Reis Hannas, and Melissa Thiemi Kato. "Saliva and dental erosion." *Journal of Applied Oral Science* 20.5 (2012): 493.

34. Amado, Francisco, et al. "Salivary peptidomics." *Expert review of proteomics* 7.5 (2010): 709-721.

35. de Paula, Fernanda et al. “The expression of water channel proteins during human salivary gland development: a topographic study of aquaporins 1, 3 and 5.” *Journal of molecular histology* vol. 48,5-6 (2017): 329-336. doi:10.1007/s10735-017-9731-6

36. Larsen, Helga S., Ann-Kristin Ruus, and Hilde Kanli Galtung. "Aquaporin expression patterns in the developing mouse salivary gland." *European journal of oral sciences* 117.6 (2009): 655-662.

37. Akamatsu, Tetsuya, et al. "Expression and localization of aquaporins, members of the water channel family, during development of the rat submandibular gland." *Pflügers Archiv* 446.6 (2003): 641-651.

38. Aure, Marit H., et al. "Aquaporin 5 distribution pattern during development of the mouse sublingual salivary gland." *Journal of molecular histology* 42.5 (2011): 401.

39. Menezes-Silva, Renato et al. "Genetic susceptibility to periapical disease: conditional contribution of MMP2 and MMP3 genes to the development of periapical lesions and healing response." *Journal of endodontics* vol. 38,5 (2012): 604- doi:10.1016/j.joen.2012.02.009

40. Vieira, Alexandre R., et al. "A pragmatic study shows failure of dental composite fillings is genetically determined: a contribution to the discussion on dental amalgams." *Frontiers in medicine* 4 (2017): 186.

41. Leonardi, Denise P., and Alexandre R. Vieira. "From caries progression and restoration failures to periapical lesions in the era of precision." *JDR Clinical & Translational Research* (2020): 2380084419846436.

42. Anjomshoaa, Ida, et al. "Aquaporin 5 interacts with fluoride and possibly protects against caries." *PLoS One* 10.12 (2015).

43. Vieira, Alexandre R., et al. "In vitro acid-mediated initial dental enamel loss is associated with genetic variants previously linked to caries experience." *Frontiers in physiology* 8 (2017): 104.

44. Sezgin, Batın Ilgıt, et al. "Two-fold excess of fluoride in the drinking water has no obvious health effects other than dental fluorosis." *Journal of Trace Elements in Medicine and Biology* 50 (2018): 216-222.

45. Tulek, Amela, et al. "Aquaporins' influence on different dental erosive wear phenotypes in humans." *Caries Research* (2020): 1-11.

46. Bezamat, Mariana, et al. "Aquaporin locus (12q13. 12) might contribute to susceptibility of temporomandibular joint disorder associated with periodontitis." *PloS one* 15.3 (2020): e0229245.

47. Mazzoni, Annalisa, et al. "Role of dentin MMPs in caries progression and bond stability." *Journal of dental research* 94.2 (2015): 241-251.

48. Shimada, Yasushi, et al. "Localization of matrix metalloproteinases (MMPs-2, 8, 9 and 20) in normal and carious dentine." *Australian dental journal* 54.4 (2009): 347-354.

49. Mazzoni, Annalisa, et al. "Role of dentin MMPs in caries progression and bond stability." *Journal of dental research* 94.2 (2015): 241-251.

50. Makela, M., et al. "Matrix metalloproteinases (MMP-2 and MMP-9) of the oral cavity: cellular origin and relationship to periodontal status." *Journal of dental research* 73.8 (1994): 1397-1406.

51. Gürkan, Ali, et al. "Gene polymorphisms of matrix metalloproteinase-2,-9 and-12 in periodontal health and severe chronic periodontitis." *archives of oral biology* 53.4 (2008): 337-345.

52. Odenbach, Jeffrey, et al. "MMP-2 Mediates Angiotensin II–Induced Hypertension Under the Transcriptional Control of MMP-7 and TACE." *Hypertension* 57.1 (2011): 123-130.

53. Bosonea, Ana-Maria et al. “Metalloproteinases in hypertension and cardiac disease: differential expression and mutual regulation.” *Drug discovery today. Disease models* vol. 8,1 (2011): 29-35. doi:10.1016/j.ddmod.2011.02.001

54. De Carvalho, Flavia M., et al. "Aggressive periodontitis is likely influenced by a few small effect genes." *Journal of clinical periodontology* 36.6 (2009): 468-473.

55. Fleming, Eleanor, and Joseph Afful. "Prevalence of total and untreated dental caries among youth: United States, 2015–2016." (2018).

56. Price, Simon J., David R. Greaves, and Hugh Watkins. "Identification of Novel, Functional Genetic Variants in the Human Matrix Metalloproteinase-2 Gene ROLE OF Sp1 IN ALLELE-SPECIFIC TRANSCRIPTIONAL REGULATION." *Journal of Biological Chemistry* 276.10 (2001): 7549-7558.

57. Kitchen, Philip, et al. "Beyond water homeostasis: Diverse functional roles of mammalian aquaporins." *Biochimica et Biophysica Acta (BBA)-General Subjects* 1850.12 (2015): 2410-2421.

58. Pan Y, Iwata F, Wang D, Muraguchi M, Ooga K, Ohmoto Y, et al. Identification of aquaporin-5 and lipid rafts in human resting saliva and their release into cevimeline-stimulated saliva. Biochim Biophys Acta. 2009 Jan; 1790(1):49–56.

59. Shimizu, Takehiko, et al. "Enamel formation genes influence enamel microhardness before and after cariogenic challenge." *PloS one* 7.9 (2012).

60. Uhlen, Marte-Mari, et al. "Genetic variation may explain why females are less susceptible to dental erosion." *European journal of oral sciences* 124.5 (2016): 426-432.

61. Bayram, Merve, et al. "Genetic influences on dental enamel that impact caries differ between the primary and permanent dentitions." *European journal of oral sciences* 123.5 (2015): 327-334.

62. Ranade K, Chang MS, Ting CT, et al. High-throughput genotyping with single nucleotide polymorphisms. *Genome Res*. 2001;11(7):1262–1268. doi:10.1101/gr.157801