1. PREDOCTORAL CATEGORY

#01 Title: Elucidating the actions of Botox on TMD and PTSD symptoms
K AUDI (1) S CONNELLY (1), R SILVA (1,2)

(1) UCSF School of Dentistry, Department of Oral and Maxillofacial Surgery, (2) San Francisco Veteran Affairs Medical Center

Objectives: Temporomandibular Joint Disorder (TMD) is a poorly understood disease that affects 10-25% of Americans. Among the veteran population, it often co-present with Post Traumatic Stress Disorder (PTSD). We discovered Botox decreases TMD-related pain and reduces the symptoms of PTSD, particularly the anxiety and hypervigilance states. Further, the actions and time-course of Botox on the muscles is surprisingly ill-defined in relation to pain reduction. Our study aims are two-fold: one is to use the pain-relieving aspect of Botox as a tool to better understand the connection between chronic pain and PTSD, and second is to precisely define the actions of Botox on muscle volume and strength, change in pain scores, and PTSD symptoms.

Methods: In this pilot study, two patients met the requirements for a diagnosis of TMD and PTSD. They completed questionnaires to evaluate pain and PTSD symptoms, enrolled in a daily pain application, had Electromyelography (EMG) to evaluate muscle function, and an ultrasound of the Masseter, Temporalis, and Sternocecidomastoid muscles to measure muscle thickness before Botox injections. Lastly, they underwent a resting state evaluation and imaging of the trigeminal nucleus via fMRI. After preliminary testing was done, patients received onabotulinum toxin (Botox) injections (100 units/4cc saline) into the Masseter and Temporalis.

Results: Two patients have completed phase one of the study. Data compared before and after injections showed a decrease in average daily pain from a 6.5 to 3. We expect to see an alteration in the connectivity of regions of the brain involved in PTSD and TMD, a reduction in the pain severity questionnaires, and a decrease in muscle thickness of the massetter and temporalis with no change in the SCM. Clinically, patients should experience less pain from TMJ, and should see a reduction in PTSD symptoms.

Support: The Department of Oral and Maxillofacial Surgery

#02 Title: What we know about Peri-implantitis: review of all systematic reviews
S BAJAJ (1), S KAPOOR (1), P TAHIR (2), Y RAJENDRAN (3), Y KAPILA (3)

(1) UCSF School of Dentistry, International Dentist Program, (2) Education and Copyright Librarian (3) UCSF School of Dentistry, Department of Orofacial Sciences, Division of Periodontology

Objective: This work-in-progress review aims to summarize all the evidence available in the literature in the form of systematic reviews on Peri-implantitis.

Methods: Literature searches were performed to find systematic reviews on Peri-implantitis. PubMed, Embase, and Web of Science databases were searched. We collaborated with a medical librarian to help develop the search strategies and conducted searches from January 1st 1970-September 1st 2017. Searches used MESH (index) terms and keywords. Upon completion, data from three different databases were extracted using EndNote X8. Subsequently, after removing duplicates, 194 studies classified as systematic reviews were obtained. Systematic reviews with a focus on/or discussing Peri-implantitis in detail were included. Studies misclassified as systematic reviews that were commentaries, opinions, reports of plenary sessions, case reports and workshop consensus reports were excluded. Two reviewers independently reviewed the title and abstract of 194 studies and excluded 43 studies based on the exclusion criteria. Finally, 12 studies were removed based on the inclusion criteria and a total of 139 systematic reviews were included in the review. Any discrepancy at this stage in inclusion and exclusion of studies was solved through mutual consensus and moderated by a third reviewer.

Progress Report: An instrument was developed to abstract relevant information from 139 studies. Currently, the abstracted information is being summarized using an iterative process by four independent reviewers. Overarching themes are being developed to categorize available evidence on Peri-implantitis by diagnoses, etiology, distinctive treatment modalities; surgical and non-surgical, and perspectives of different dental specialties.

Future Directions: The results of the review will successfully identify gaps in knowledge about Peri-implantitis, and will open doors for future research to answer targeted questions that will be raised in the discussion section of the review.
The Program in Global Oral Health

#04 Title: Oral health education addressing early childhood caries: a systematic review

SE BALLARD, JC BARKER, KS HOEFT

UCSF School of Dentistry, Department of Preventive and Restorative Dental Sciences

**Objective:** Early childhood caries (ECC) is the most prevalent chronic childhood disease in the United States (US), can have long-term impacts on health and quality of life, and disproportionately affects disadvantaged populations. Theory-based, culturally appropriate oral health education (OHE) is one method of addressing ECC. Previous reviews of ECC OHE were international and/or had limiting inclusion criteria. Our objective was to identify and evaluate OHE programs for 5-year-olds or younger and/or their parents.

**Methods:** Programs were identified using keywords/search strings from Google and scientific literature databases like PubMed. Inclusion criteria: targeted 5-year-olds or younger and/or their parents, US-based, described ECC prevention OHE programs, published between September 2000-June 2017. Publications were assessed on characteristics including: target population, inclusion of theory, and type of evaluation.

**Results:** We identified 390 unique articles from scientific literature databases and 90 websites from the first 3 results pages of 3 Google searches. Fifty-four programs fit inclusion criteria for in-depth evaluation. Programs ranged from postcards to complex curricula in hospitals, schools, and communities. Fifteen programs targeted racial/ethnic minorities. Twenty-nine programs addressed low-income populations. Ten were theory-based. Twenty-two reported improvement in oral health knowledge, behavior, and/or health outcomes. Nineteen described outcome evaluations in detail (1 randomized controlled trial, 8 single-group pre-post, 2 two-group pre-post, 1 historical controlled trial, 1 retrospective controlled chart review).

**Conclusion:** The failure of implants is highly coincidental with the presence of periodontal disease and other factors. A holistic approach, which includes careful analysis of systemic conditions, emotional disorders, smoking, and endodontic history, should be practiced.

**Support:** UCSF Department of Orofacial Sciences/Division of Periodontology

#05 Title: The mixed trajectory of the feminization of U.S. dentistry

X BAO (1), E MERTZ (2)

(1) UCSF School of Dentistry, Healthforce Center (2) UCSF School of Dentistry, Department of Preventive and Restorative Dental Sciences

**Objectives:** Female enrollment in dental school has only recently reached parity, raising concerns about the impact of feminization on dentistry. This study identifies indicators to analyze the trajectory of feminizing professions in order to describe the trends of the feminization of the dental profession in the United States.
**#06 Title: Caries treatment, not experience, differs by acculturation among U.S. Hispanic/Latinos**

D BUl (1), B CHAFFEE (1), T FINLAYSON (2)

(1) UCSF School of Dentistry, Department of Preventive and Restorative Dental Sciences, (2) SDSU Division of Health Management and Policy

**Objectives:** Acculturation is a social-cultural process that may contribute to oral health outcomes in the U.S. Hispanic/Latino population. This study examined associations between acculturation and health behaviors, health insurance status, dental utilization, DMFT, and dental treatment modality among Hispanic/Latino adults.

**Methods:** Cross-sectional data were drawn from the baseline wave of the Hispanic Community Health Study/Study of Latinos (collected: 2008-2011), a cohort of adults (age 18-74) of diverse Hispanic/Latino heritage in four U.S. cities (N=13,556). Three groups to reflect acculturation level were defined according to scores on the Short Acculturation Scale for Hispanics language subscale and were used to compare sugar, alcohol, and tobacco consumption, health insurance coverage, dental utilization, DMFT and its components. Weighted negative binomial regression models were used to adjust for age, gender, income, and education attainment and to calculate adjusted marginal values for outcome variables.

**Results:** Alcohol and tobacco consumption were most frequent in the high acculturation group. Adjusted marginal probability of health insurance coverage was higher with greater acculturation (Low: 35% Medium: 48% High: 71%, p<0.0001). Adjusted marginal probability of a past-year dentist visit did not differ meaningfully between acculturation groups (Low: 46%, Medium: 50%, High: 50%, p=0.03). Unadjusted mean DMFT was lower with greater acculturation (Low: 11.8, Medium: 9.6, High: 6.9, p<0.001), but differences in DMFT were attenuated completely after adjustment for age, gender, education, and income. Despite similar adjusted DMFT scores, treatment modality differed among acculturation groups: higher acculturation groups had fewer decayed, fewer missing, and more filled teeth.

**Conclusion:** Unlike DMFT, treatment modality differed by acculturation group regardless of similar dental utilization frequencies. Insurance coverage and health literacy may determine whether dental disease experience results in restorations, extractions, or untreated decay by acculturation group.

**Support:** Drs. John and Deborah Greenspan

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**#07 Title: Taiwanese taxi drivers' perspectives on the effects of areca betel nut chewing on oral and systemic health: a pilot study**

CP CHANG (1), BP LIN (2)

(1) UCSF School of Dentistry, (2) UCSF School of Dentistry, Department of Orofacial Sciences, Division of Pediatric Dentistry

**Objective:** Areca nut is the fourth most commonly used psychoactive substance in the world. In Taiwan, approximately 10% of the population, or two million people chew betel nut. Although the prevalence of betel nut chewing is high among taxi drivers, limited data is available. This pilot study evaluated and compared the awareness of health effects of betel nut chewing, oral health routines, beliefs, and knowledge between betel nut chewing taxi drivers in Taiwan and those taxi drivers who are non-betel nut chewers.

**Methods:** One hundred and seventy six taxi drivers in Taiwan were interviewed. Cross-sectional data was collected over a three-week period in December 2016 in the form of simple survey questionnaire of taxi drivers waiting in lines to pick up customers. Analysis involved using categorical data and looking for correlation between variables of interest. Statistical significant (p ≤0.05) mean difference of the data collected between taxi drivers who are betel nut chewers (n=100) and taxi drivers who are non-betel nut chewers (n=76) were tested by the student two-tailed t-test.

**Results:** Stress relief and boredom were the most commonly cited reasons for chewing betel nut. Non-chewers brush their teeth statistically more per day (p=0.0068) and visit the dentist more often compared to chewers (p=0.0411). Non-chewers are statistically more satisfied with their oral hygiene routines compared to chewers (p=0.0110). Chewers are statistically less aware of the effects of betel nut chewing on oral (p=0.0018) and systemic (p=0.0029) health than those who are non-chewers.
Conclusions: Although 75% of taxi drivers in Taiwan who self-identify as betel nut chewers are aware of the potential detrimental effects chewing betel nut have on the oral and systemic health, nearly three quarters of betel nut chewing taxi drivers indicated that they would continue to chew betel nut.

Support: Program in Global Oral Health Research Fellowship

#08 Title: pH regulators in mechanobiologically active sites of the dentoalveolar complex

A CHEN (1), AM JENG, L CHEN (1), R HE (1), M KANG (1), Y ZHANG (2), SP HO (1)

(1) UCSF School of Dentistry, Department of Preventive and Restorative Dental Sciences, (2) UCSF School of Dentistry, Department of Orofacial Sciences

Objectives: pH is postulated to be a key mediating factor for mineralization events at mechanically active sites of the periodontal ligament (PDL-bone and PDL-cementum entheses and alveolar bone of the dentoalveolar complex (DC)). This study aims to generate spatiotemporal maps of pH regulators vacuolar-type H+-ATPase (V-ATPase) and anion exchanger 2 (AE2) in DC of mice subjected to experimental tooth movement.

Methods: Elastic spacers were placed between left maxillary molars of 8-week-old Scleraxis-Green fluorescent protein mice (SCX-GFP) fed hard food, creating 2 cohorts (n=3/cohort): hard diet with elastic spacer and an age-matched contra-lateral control. At 8 and 11 weeks (T0/T3), specimens were harvested, X-ray micro-CT scanned, processed for histology, and analyzed for PDL-space changes. Spatially-targeted expressions of V-ATPase and AE2 were colocalized with SCX, osteoclast-associated tartrate resistant acid phosphatase (TRAP), and matrix protein fibronectin. Biochemical expressions were correlated with physical perturbations (narrowed and widened regions [NR/WR] of PDL-space), mapped by using three-dimensional CT-scans.

Results: NR/WR of PDL-space were observed in experimental specimens (NR peak values: T0=66.1±8.6μm, T1=51.2±9.0μm, T3=52.7±8.9; WR peak values: T0=88.0±3.1μm, T1=115.1±18.2μm, T3=138.0±46.9) when compared to control specimens (peak values; T0=70.6±2.7μm, T1=66.8±0.9μm and T3=63.6±5.7μm). SCX and V-ATPase expression was observed along PDL-bone entheses. V-ATPase was also present in PDL fibroblasts and alveolar bone. Fibronectin was observed in alveolar bone, where expression increased with time. TRAP was observed at resorption sites. AE2 was not observed in the DC.

Conclusion: V-ATPase and SCX expressions were higher in PDL and at the PDL-bone enthesis, indicating that regions experiencing higher strain could also be subjected to acidification. Individual presence and association of SCX and V-ATPase was not observed at TRAP positive resorting sites in the DC suggesting that V-ATPase acidification precedes macroscopically observable mineral resorption events, supporting the theory that pH may be a key activator for mechanically induced mineralization events.

Support: Presidential Chair Fund, Dr. Thomas Lang, Associate Dean for Research, School of Dentistry, UCSF; NIH/NIDCR R01DE022032 (SPH); Biomaterials and Bioengineering Correlative Microscopy Core (https://www.bbcmc.ucsf).

#09 Title: Utilization of pediatric dental care in China

M CHEN (1) , L ZHAN (1) , J ZOU (2), J PENG (2), J CHENG (1)

UCSF School of Dentistry (1), (2) West China School of Dentistry Sichuan University (3)

Objectives: With dietary change with increased consumption of sweet snacks and drinks in the new generation, dental caries has been an emerging public health problem in children in China. This work-in-progress project aims to assess children’s utilization of dental care in China and its association with demographics, parents’ attitude and experience, children’s dental fear and dental status.

Methods: This will be a cross-sectional study with 500 children aged 0-12 years old and their parents who visit pediatric primary care and dental care clinics at West China Medical Center. The consented parent-children dyads will be interviewed for their demographics, parents’ attitude and experience, and children’s dental status, dental fear, dental utilization and possible treatments through a tested questionnaire. Descriptive statistics such as mean, standard deviation, frequency and percentage and their 95% confidence intervals will be used to summarize the children’s dental fear and utilization. The associations of dental fear and utilization with demographics, dental status, possible treatment, and parents’ attitude and experience will be evaluated with general linear models.

Progress Report: We are currently in the process of collecting data.

Contributions: Through literature review on PubMed, no study has ever published for systematically investigation on children’s dental fear and dental utilization and other associated factors in China. Thus, this research project will provide us with a better understanding of factors related children’s dental utilization in China and guide policy makers and clinical professional to make better interventions to improve children’s oral health in China.

Support: Program in Global Oral Health Research Fellowship
#10 Title: Characterizing axon guidance in mouse palate

M CHEN (1), A O’NEILL (2), J BUSH (2)

UCSF School of Dentistry, Program in Craniofacial Biology (1), UCSF School of Dentistry, Department of Cell and Tissue Biology (2)

**Objectives:** The secondary palate is a sensory organ housing the nasopalatine, greater palatine, and lesser palatine nerves, which are critical for general and taste sensation, and are anesthetic targets for maxillary dental procedures. However, nerve development in the palate has not been studied extensively. Hence, this study aims to characterize axonal phenotypes and their interactions with Ephs/ephrins, which are signaling cues that have been shown to be involved in axon guidance in other parts of the body. We aim to characterize the architecture of palatal axons in wildtype and mutant murine embryos at various embryonic stages.

**Methods:** Wildtype and mutant embryos of various stages were harvested at various stages (E11.5-E15.5). The palates were dissected, stained with a 2H3 (anti-neurofilament) antibody, an anti-ephrin-B1 antibody, and DAPI, cleared in SeeDB, and visualized using confocal microscopy.

**Results:** Wildtype E11.5 embryos lack any branches. Wildtype E12.5 embryos exhibit small lateral branches. In wildtype E13.5 embryos, the greater palatine nerve has parallel lateral branches and lacks branches at the anterior-medial border, where ephrin-B1 is strongly expressed. At E14.5 and E15.5, the greater palatine nerve branches into the anterior-medial palate. Efnb1 heterozygous mutants display fewer parallel branches and ephrinB1 patches that axons seem to track along. EphA3;EphA7 double mutants appear similar to controls.

**Conclusion:** In wildtype mice, the greater palatine nerve first branches laterally and then medially. This could be due to high ephrin-B1 expression in the anterior-medial palate acting as a repulsive force for axon guidance. Consistent with this, disorganized ephrin-B1 expression leads to disorganization of the axon tree. Though EphA3 and EphA7 are expressed in the palate, they appear not to affect axon guidance. Elucidating these cellular mechanisms could enhance our understanding of axon guidance mechanisms in secondary palate development and improve diagnosis of failed axon patterning, which is important for understanding dental anesthesia.

**Support:** Dr. Caroline Damsky and Dr. Peter Sargent and R01DE0258767

#11 Title: Developing oral health literacy instruments for Chinese speakers

K CHONG, SA GANSKY

UCSF School of Dentistry, Department of Preventive and Restorative Dental Sciences

**Objectives:** Health literacy has been found to correlate with health outcomes, and different oral health literacy assessments have been developed to assess literacy in dentistry. San Francisco has one of the largest Chinese immigrant communities in North America. This work-in-progress aims to develop oral health literacy assessment tools in Cantonese and Mandarin for basic screening purposes and improve clinical interaction between provider and patient.

**Methods:** The Oral Health Literacy Assessment in Cantonese (OHLA-C) and OHLA-Mandarin (OHLA-M) tools will include a word recognition and comprehension portion. The HKREALD-30 will be utilized in the OHLA-C word recognition portion, while bilingual dental providers and bilingual health educators will be consulted in developing the comprehension portion. Another set of experts will help assess face validity. The English Language Acculturation Scale (ELAS) will assess basic, survival and social involvement English skills. The Oral Health Impact Profile (OHIP-14) in Chinese is a measure of oral health related quality of life (OHRQOL). 50 Cantonese and 50 Mandarin participants will be recruited over 3 months at UCSF medical center. Bi-lingual adults who use Chinese as a primary language will qualify for participation, with a five dollar gift card as appreciation for participation. Each participant will complete both OHLA and either OHLA-C or OHLA-M in a random sequence. Difference between OHLA and OHLA-C/OHLA-M scores will be compared with paired t-tests.

**Preliminary Data:** Literature review and survey design has been completed. A human subjects research studies application has been drafted to submit to the UCSF Institutional Review Board.

**Future Directions:** A Chinese Oral Health Literacy Assessment, comprising separate Cantonese and Mandarin versions (OHLA-C/OHLA-M), will be developed and validity established. By understanding patients’ oral health literacy, dental providers can personalized information to match comprehension level of patients to improve oral health education and outcome.

**Support:** Program in Global Oral Health Research Fellowship

#12 Title: Functional remineralization of dentin lesions using PILP-Releasing glass-ionomer cements

H FATHI-KELLY (1), M BACINO (1), S ENGELBERTH (1), G MARSHALL (1), S MARSHALL (1), TQ LE (2), S HABELITZ (1)

(1) UCSF School of Dentistry, Department of Preventive and Restorative Dental Sciences, (2) UCSF School of Dentistry, Department of Orofacial Sciences

**Objective:** Remineralization of dentin lesions not only requires recovery of apatite mineral, but also incorporation of the mineral within collagen fibrils for mechanical reinforcement of the dentin matrix to achieve functional remineralization (FR). The polymer-induced liquid precursor (PILP) process induces FR, by applying treatments of artificial lesions in solutions comprised of poly-Aspartic acid (pAsp). Here we developed glass-ionomer cements (GICs) that set in clinically relevant times and release PILP ingredients to induce FM.
**Methods:** A Box-Behnken experimental design was used to evaluate setting characteristics of novel GICs from bioactive glass, polyacrylic acid (PAA), maleic acid (MA), pAsp, and/or phosvitin (PV). Artificial lesions (n=3) were created by a 66h demineralization followed by rinsing, drying, and rehydrating before restoring with experimental GICs (n=3) and sealing with resin. The remineralization treatments were performed by soaking in simulated-body-fluid (SBF) for 2 weeks. The lesion shrinkage after dehydration (indicating remineralization) and elastic modulus (indicating FM) were measured and compared to cement controls (n=3) using Analysis of Variance (ANOVA).

**Results:** About 50 PILP-cement systems were evaluated and enabled finding PILP-GICs that set quickly (3-10min). Treatments with pAsp- or PV-containing cements significantly reduced shrinkage (p ≤ 0.05, CI=95%), while no substantial improvement was observed without these molecules. The elastic modulus of the demineralized zone (E=0.5GPa) increased when these PILP-releasing cements were applied. A PV-based cement improved the mechanical properties in the demineralized zone (E=13±3GPa), which is insignificantly different from sound dentin (E=14±4GPa, p=0.46, CI=95%) and indicates complete FM of the lesions.

**Conclusion:** Novel PILP-releasing GICs have been designed that could function in a clinical setting and provide minerals that reinforce the dentin matrix. These GICS have the potential to become an intricate part of minimally invasive dental treatments that repair natural caries lesions and thus conserve more of the natural tissue.

**Support:** This project was supported by the National Institute of Health/National Institute of Dental and Craniofacial Research under grant R01DE016849 and the Presidential Chair Fund at the University of California, San Francisco

**#13 Title:** Evaluating quality of clinic and hospital treatments for odontogenic infections

M FORGHANY, J PERKINS

UCSF School of Dentistry, Department of Oral and Maxillofacial Surgery

**Objectives:** In an era of limited healthcare resources and uncertain future access to care for dentally underserved patients, evaluation of healthcare quality is critical to healthcare delivery systems. Safety net hospitals, like ZSFG (Zuckerberg San Francisco General) Hospital, provide care to many patients with odontogenic pain and infections, which occurs at significant cost to the Department of Public Health. Patients typically are treated through two pathways: Emergency Department and outpatient Oral and Maxillofacial Surgery Clinic. Our objective was to determine whether healthcare value, types of care and outcomes vary between these two pathways.

**Methods:** Data was extracted from charts of patients who visited ZSFG due to an odontogenic infection in 2016. Two patient cohorts were created: those who received care in the clinic and those who received treatment in the hospital, defined as the emergency department and operating room. Quality of care was determined by the following variables: imaging ordered, hospital admission, duration of stay, and cost. Other outcome variables include: gender, age, medical issues, reason for treatment, and surgical intervention.

**Results:** Of the 64 patients from the cohorts, 37 patients were seen in the hospital and 27 in the clinic. 66.7% of the hospital patients received a CT scan, while 11.8% of clinic patients received a CT scan. 13.3% of hospital patients received both a CT scan and a panoramic radiograph while 0% of clinic patients received both types of imaging (p-value<0.0001). Of the hospital cohort, 37.8% had a hospital stay. No clinic patient had a hospital stay. Average cost of treatment per patient encounter in the hospital, clinic, and both pathways was $33,222, $1166, and $5,206, respectively.

**Conclusions:** Patients treated for odontogenic infections in the outpatient clinic at ZSFG receive higher quality of treatment, as defined by our parameters, than patients who are treated in the hospital.

**Support:** Buchanan Dental Clinic

**#14 Title:** Intra- articular injections of amniotic fluid for temporomandibular joint disorder

N GABRIEL, S CONNELLY, R SILVA

UCSF School of Dentistry, Department of Oral and Maxillofacial Surgery, San Francisco Veteran Affairs Medical Center

**Objectives:** Currently, there is no injectable that has proven to be effective in relieving clinical symptoms associated with temporomandibular disorder (TMD). Amniotic fluid has the potential as a novel anti-inflammatory, pain reducing intra-articular injectable. The goal of this study was to assess the effectiveness of amniotic fluid in the reduction of pain and clinical symptoms experienced by patients who suffer from TMD.

**Methods:** Eleven patients were enrolled. A clinical examination obtained a baseline pain score, assessment of joint noise, and measurement of maximal incisal opening (MIO). Patients were injected with 1cc of amniotic fluid into the TMJ space. Follow up calls were made every week to note level of pain via a visual analog system (VAS) following the injections.

**Results:** Amniotic fluid injections had a significant effect on TMD measures. Injections resulted in a decreased pain score and increased MIO in nine out of eleven patients. In the responders, pre and post pain score results showed a significant decrease in pain (two sample t test, p<0.000049), as well as a significant increase in MIO (two sample t test, p<0.026). For example, one patient has experienced pain relief that pre-injection was an 8/10 which decreased to a 1/10 for 10 months and counting. Other patients have experienced similar results; however there have been a small proportion that has been non-responsive.

**Conclusion:** The results of the study support the hypothesis that amniotic fluid is an effective treatment in the reduction in pain and clinical symptoms experienced by patients who suffer from TMD. Because of this, it has the potential to decrease opioid medication use, decrease the need for invasive surgery, and result in a higher quality of life.

**Support:** The Department of Oral and Maxillofacial Surgery
#15 Title: Three-dimensional analysis of the effect of expansion and/or protraction on oropharyngeal volume and MCA in nonsyndromic CLP/CLCP children

J GAO, N ALREJAYE, S OBEROI

UCSF School of Dentistry, Cleft and Craniofacial Orthodontic Program

Objectives: Cleft lip and palate (CLP) is the most common birth defect in the United States and is known to be associated with many airway problems. There are limited studies in the literature evaluating the effect of maxillary expansion and/or protraction on oropharyngeal airway in children with non-syndromic cleft lip and palate. The aim of this study was to evaluate and compare oropharyngeal airway volume and minimal cross-sectional area (MCA) in individuals with non-syndromic CP/L using CBCT before and after Phase I orthodontic maxillary expansion with or without protraction.

Methods: A retrospective study of CBCT data of preadolescent individuals (ages, 8.7 ± 2.6 years) with cleft palate with or without cleft lip (n=18) who underwent Phase I orthodontic maxillary expansion with or without protraction at University of California, San Francisco (UCSF) was conducted. A control group of 9 preadolescent individuals (ages, 8.7 ± 2.6 years) with cleft palate with or without cleft lip was used for comparison. Measurements were conducted by 3DMD Vultus with cross-sectional areas calculated for each 2-mm entire length of the airway. The oropharyngeal area was defined inferiorly from vallecula and superiorly by the palatal plane.

Results: The measurement method proved reliable as the intraclass correlation coefficients between the double measurements were all over 0.9 in 5 sample groups. There was a statistically significant increase in pharyngeal airway volume after phase I orthodontic treatment, however, there was no statistically significant change in minimal cross-sectional area.

Conclusion: The findings indicate that maxillary expansion may increase oropharyngeal volume and but may not reduce airway problems as the minimal cross sectional area is not reduced.

Support: UCSF Program in Craniofacial Biology

#16 Title: The effect of age on inflammatory regulation in periodontal disease.

E HSU (1), M NAKAMURA (3), R MARCUCIO, D CLARK (2)

(1) UCSF School of Dentistry, (2) UCSF/ZSFGH Orthopaedic Trauma Institute, (3) San Francisco Veteran Affairs Medical Center

Objectives: Periodontal disease is an inflammatory process that affects nearly fifty percent of the US population. The burden of periodontal disease falls disproportionally on the elderly population and may be associated with systemic dysregulation of the inflammatory response associated with aging. This study aims to elucidate the age-related effects on inflammatory regulation in the periodontium, specifically investigating mesenchymal stem cell (MSC) regulation of inflammation through activation of triggering receptor expressed on myeloid cells-2 (TREM2), a negative regulator of inflammation on macrophages.

Methods: Maxillas were isolated from old (24 months) and young (3 months) mice. Alveolar bone loss was measured from the cementoenamel junction to the alveolar bone crest at each molar. Maxillary gingiva was isolated and prepared for quantitative polymerase chain reaction (qPCR) analysis. Additionally, MSCs were harvested from bone marrow of old and young mice and cultured. MSCs were co-incubated with a BWZ/TREM2 reporter cells line, which expressed LacZ upon TREM2 activation. A LacZ absorbance assay was used to assess TREM2 activation by MSCs.

Results: Bone loss was greater in old mice (0.24±0.024mm) compared to young (0.12±0.011mm) (p<0.05). Pro-inflammatory genes IL-1β, TNF-α, and IL-6 demonstrated a greater than 10 fold increase in expression within the gingiva of old mice compared to young. MSCs were able to activate TREM2 and young MSCs activated TREM2 to a greater degree than old but this was not statistically significant.

Conclusion: These findings indicate that there is increased bone loss in old mice and this may be associated with dysregulated production of inflammatory cytokines locally. Additionally, inflammatory regulation by MSCs may be partially due to MSC/TREM2 interactions, and age-related defects in MSCs may have resulted in decreased activation of TREM2. These findings demonstrate dysregulation of inflammation associated with increased age and suggest a novel target, TREM2, for treating age-related changes to the inflammatory response.

Support: Presidential Chair Fund

#17 Title: Insights into sialoliths: a materials perspective

S IRIBARREN (1), N JABER (1), M KANG (1), S WIENER (2), M STOLLER (2), J CHANG (3), S HO (1)

(1) UCSF School of Dentistry, Department of Preventive & Restorative Dental Sciences, (2) UCSF School of Medicine, Department of Urology, (3) UCSF School of Medicine, Department of Otolaryngology

Objectives: Salivary stones, known as sialoliths, affect 1 in 100 individuals and their etiology is not fully understood. Sialoliths are primarily made of calcium and phosphate; these elements are also found in supra- and sub-gingival tooth calculus. The aim of this study is to map structural, elemental, and mineral density profiles with an end goal to determine the origins of salivary stones.
Methods: Intact submandibular salivary stones (n=5) were imaged using a light microscope, X-ray micro-computed tomography unit, and a scanning electron microscope (SEM) (Zeiss, Pleasanton, CA). Back-scattered energy (BSE) from electrons was used to identify lower and higher atomic number regions within stones. Electron dispersive X-ray spectroscopy was used to determine chemical composition of stones. Datasets, mainly mineral densities as per the X-ray attenuation, atomic number as per the BSE and structural variation from electron micrographs were correlated to establish relationships between structure, density, and chemical composition of stones.

Results: Salivary stones illustrated three volumes/zones of low (674 ±35 mg/cc), medium (1155±69 mg/cc), and high (1627±17 mg/cc) mineral densities (MD). Microstructures identified by SEM in lower MD zones were plate-like, and in medium MD zones were agglomerates of nanospherulitic structures. In higher density areas there were zones of packed nanoparticles. The mineral densities of sub- and supra-gingival calculus were 1290–1770 (1525±40) mg/cc*.

Conclusion: Results illustrate nature’s hierarchical archetype is conserved in tooth calculi and salivary stones since both are predominantly formed by spherulitic nanoparticles. Furthermore, higher order morphology of salivary stones occurs layer-by-layer in both structure and chemical composition maps, indicating stratified biominerals are not anatomy-specific.

Support: UCSF School of Dentistry, Department of Preventive & Restorative Dental Sciences, UCSF School of Medicine Department of Urology and Department of Otolaryngology

#18 Title: Integrins and matrix proteins within functionally active dentoalveolar fibrous joint

AM JENG, A CHEN, M KANG, R HE, L CHEN, SP HO

UCSF School of Dentistry, Department of Preventive and Restorative Dental Science

Objective: The periodontal ligament (PDL), an adaptive connective tissue responds to mechanical forces. To shed light on mechano responsiveness of the PDL, this study seeks to colocalize integrin β3, a mechanically sensitive signal transducing molecule, with remodeling associated extracellular-matrix (ECM) proteins—bone sialoprotein (BSP), osterix (OSX), and fibronectin (FBN).

Methods: Systematic studies were performed to evaluate PDL-bone and PDL-cementum enthesial adaptations in specimens harvested periodically from Scleraxis-Green fluorescence protein mice (SCX-GFP, N=6) fed hard food and raised for 8- and 11-weeks (T0/T3). Architectural changes at the PDL-bone and PDL-cementum entheses were detected by analyzing X-ray micro-CT three dimensional (3D) scans, and correlating them with spatially targeted immunocolocalized integrin and ECM proteins.

Results: Narrow and widened regions (NR/WR) of the PDL-space were seen in experimental specimens when compared to control specimens. In control and experimental specimens, BSP and FBN expression increased over time in interradicular bone and PDL but remained constant throughout cementum. OSX expression varied with location and increased over time. In distal roots, T0 control and experimental specimens expressed OSX in distal regions and with time, experimental OSX expression shifted to mesial regions. Integrin β3 expression shared similar patterns with FBN in the PDL and increased in areas with high OSX expression. SCX was expressed predominantly at the PDL-bone entheses.

Conclusion: Among the three matrix proteins, OSX expression was closely correlated with integrin β3. This implies that integrin β3 may have significant influence in activating upstream proteins, such as OSX, and be influential in mediating downstream proteins, BSP and FBN, that carry out roles of forming and resorbing mineral. Knowing how integrins influence matrix proteins will provide insights into the PDL’s adaptive abilities including its entheses with bone and cementum.

Support: Dr. Thomas Lang, Associate Dean for Research, School of Dentistry, UCSF; NIH/NIDCR R01DE022032 (SPH); Biomaterials and Bioengineering Correlative Microscopy Core (https://bbcmc.ucsf.edu).

#19 Title: Oral health-related quality of life in Cambodian children and adolescents

R KONG, S PI, H CHIU, G TAYLOR

UCSF School of Dentistry, Department of Preventive and Restorative Dental Sciences

Objectives: Few studies have investigated Cambodian oral health. This work-in-progress aims to describe changes in oral-health-related quality of life (OHRQoL) following intervention with oral hygiene instruction (OHI) to Cambodian children and adolescents ages 8-14 in the SF Bay Area. Following baseline measures, data will be collected at 6- and 12-months to assess the effects of OHI on participants’ OHRQoL.

Methods: The project design is a randomized controlled trial that includes two groups, with 50 participants randomized to either control or OHI intervention groups. The Short Form Child Perceptions Questionnaire will be administered for both groups before the intervention for baseline scores. An immediate post-intervention survey and follow-up surveys at 6- and 12-months will be administered to both groups to record changes in these measures. Differences in OHRQoL between pre- and post-questionnaires will be evaluated, as well as differences across the three post-questionnaires will be assessed with χ² test and tests for trends. Cronbach’s α values will assess internal reliability. To assess other factors that may have an effect on the bivariate comparisons between the two groups, multivariable analyses will be conducted, controlling for other demographic characteristics including gender, household income, parent’s education, parent’s immigration status, and SF Bay area location.

Progress Report: Currently, we are working with our community partners to organize a Cambodian Health Symposium to gather the population together for the study to be performed and to translate all forms and questionnaires into the Cambodian language.

Future Directions: The symposium will be held 10/01/2017 to collect initial visit data, followed by the 6- and 12-month visits to collect additional post-intervention data. Results of this study may provide future investigations with preliminary data for developing further interventions in this under-resourced population.
Near-Infrared (NIR) imaging can accurately detect carious lesions under sound enamel well before they are apparent on radiographs. Commercially-available NIR systems for intra-oral applications operate at approximately 780 & 850-nm, but stains interfere considerably at these wavelengths. This study aims to compare the contrast of occlusal lesions under stain at wavelengths from the visible to 2200-nm to determine the optimal NIR wavelength for diagnosing dental decay.

Methods: Fifty teeth with stained occlusal surfaces were imaged with visible light, quantitative light fluorescence, and NIR reflectance at wavelengths from 850 to 2200nm. The intensity values of stained and sound regions on the occlusal surface were measured to determine the lesion contrast ratios. Samples were sectioned at the region of interest, examined with polarized light microscopy, and sorted into three groups based on lesion depth: outer half of enamel (E1), inner half of enamel (E2), and dentin (D).

Results: Lesions visible in reflectance at 850nm were heavily masked by stains as indicated by negative contrast values. Near-IR reflectance imaging at and above 1300nm yielded significantly higher contrast of the demineralization on the occlusal surface compared with visible reflectance imaging. NIR reflectance imaging at wavelengths beyond 1700nm yielded the highest lesion contrast in all three groups, and contrast increased correspondingly with lesion depth.

Conclusion: This study demonstrates that NIR reflectance imaging performed at or above 1300nm is more effective for detecting occlusal lesions through stained surfaces.

Support: This Summer Fellowship project was funded by a contribution from The Department of Orofacial Sciences.
**#23 Title: Cartilage Grafts Completely Bridge Bone in Critical-Sized Mandibular Defects**

M NGUYEN (1,2), S WONG (1,2), D HU (2), T MICLAU (2), R MARCUCIO (1,2), C BAHNEY (2)

(1) UCSF School of Dentistry, (2) UCSF/ZSFGH Orthopedic Trauma Institute, Department of Orthopaedic Surgery

**Objectives:** Autologous bone grafts are the current standard for dental surgeries such as mandibular reconstructions and implants. Limited bone availability, donor site morbidity, and graft resorption continue to pose problems for these grafts. In search of a viable alternative, this study tests the efficacy of cartilage grafts in promoting bone regeneration in mandibular defects and determines the origin of the newly formed bone.

**Methods:** Cartilage grafts were harvested from the fracture callus of R26/LacZ+/+ mouse tibia fractures 7 days post-fracture and transplanted into critical-sized (1.5mm) mandibular defects (unstable fracture, N=3/timepoint) or 2 mm trephine defects (stable fracture, N=2/time point). Tissues were harvested at 14 and 28 days post-fracture. Defects were left empty in trephine controls to confirm that defects were critical-sized (N=2). Samples were decalcified, OCS embedded, sectioned (10 um), and stained with Brundt Quadruple Stain (HBQ, blue =cartilage, red=bone) to determine integration between graft and host and to assess bony bridging of the defect. X-gal staining was used to determine the origin of the newly formed bone.

**Results:** Cartilage graft integration was observed at 14 days post-fracture. At 28 days post-fracture, unstable and stable defects displayed successful bone bridging, and remodeling had begun to occur. Empty osteotomies did not display significant bridging. X-gal-positive chondrocytes confirmed the presence of cartilage graft within the defect site at 14 days post-fracture. X-gal-positive osteoblasts and bone-lining cells indicated that the newly-formed bone was donor-derived.

**Conclusions:** The data from this study demonstrate that cartilage grafting in critical-sized mandibular defects leads to successful bone regeneration. Furthermore, we demonstrate that chondrocytes from the donor cartilage directly contribute to the regeneration of bone. Future studies will identify clinically-relevant sources of cartilage for therapeutic use.

**Support:** F30 DE026359-01; T32 DE007306-19; NIH; UCSF Department of Orthopaedic Surgery; ARCS; AO Foundation; UCSF School of Dentistry

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**#24 Title: Are Dental Providers Adhering to Antibiotic and Analgesic Prescription Guidelines?**

T NGUYEN, E OBADAN-UDOH, AI YANSANE, J WHITE, E KALENDERIAN

UCSF School of Dentistry, Department of Preventive and Restorative Dental Sciences

**Objectives:** There is often a lag between evidence-based clinical guidelines and clinical practice. In recent years, the ADA released updated antibiotic prophylaxis and opioid prescribing guidelines. The objective of this study was to examine the prescribing patterns of university-based dental providers following tooth extractions as they compare to the ADA guidelines.

**Methods:** We conducted a cross-sectional study of providers at a US academic institution using data from the BigMouth Dental Data Repository. A retrospective chart review was performed on the electronic health records of patients (n=45) who met our inclusion criteria (received an examination CDT code or medication within 7 days of tooth extractions). Descriptive statistics and bivariate analyses were produced using STATA v15.

**Results:** Overall, the sample had a higher proportion of females (64.4%), Caucasians (28.9%), and a mean age of 47.7 ± 24. Most patients were classified as low or middle income, and Medi-Cal enrollees. Of the 123 tooth extractions, the majority (88.9%) were non-surgical, and involved molar teeth (40%). Almost half of all patients underwent multiple extractions and the most common indication for extraction was periodontal disease. Approximately 10% of patients received prophylactic antibiotic prescriptions. Post-operatively, only 17.8% of patients received post-treatment analgesic prescriptions (of which 50% were opioids), and over one-quarter (26.7%) received antibiotic prescriptions. Post-operative complications occurred in 22.2% of patients; however, all were classified as temporary or mild harm. Bivariate analyses revealed no significant associations between procedure type, provider type, or medical co-morbidities, and analgesic and antibiotic prescribing patterns.

**Conclusion:** Our study revealed that a significant proportion of patients still received opioid prescriptions when they require post-treatment analgesic medications, despite several studies highlighting its sub-optimal efficacy as the first line treatment following tooth extractions. Similarly, dental patients routinely received antibiotic prophylaxis when not medically indicated, and post-treatment antibiotics following surgical extractions.

**Support:** Dr. Stuart Gansky and the Lee Hysan Fund
#25 Title: Three-dimensional monitoring of root angulation and inclination during orthodontic treatment

J PARK, S PI, R LEE, G NELSON, D HATCHER, S OBEROI

UCSF School of Dentistry, Department of Orofacial Sciences, Division of Orthodontics

Objectives: Improper root placement during orthodontic treatment is common because panoramic radiographs, the most frequently used radiograph to monitor root position, has been demonstrated to inaccurately reflect the root position. The alternative and more accurate approach to monitor root position is to use cone-beam computed tomography (CBCT) scans. However, CBCT scans require larger doses of radiation, so multiple CBCT scans are often contraindicated. Thus, we developed a reliable method to visualize in three dimensions the whole teeth, including the roots, throughout treatment with no additional radiation after a pre-treatment CBCT scan.

Methods: We tested this method at the middle of orthodontic treatment during which an orthodontist will often reposition brackets to solve root angulation problems visualized by a panoramic radiograph or CBCT scan. In this study, CBCT and digital surface scans were taken at pre and mid-treatment for a single patient. The pre-treatment CBCT scan was superimposed onto the mid-treatment digital surface scan generating the expected root positions at mid-treatment.

Results: Color displacement maps were generated showing minimal differences between the expected and true root positions.

Conclusion: Therefore, this approach has the potential to accurately monitor the root angulation and inclination in three dimensions at mid-treatment which could lead to improved bracket repositioning during treatment.

Support: American Association of Orthodontists Foundation (AAOF): Research Aid Award

#26 Title: Nisin-producing Lactococcus lactis decreases biofilm formation and disrupts preformed biofilms

B PARKS, A RADAIC, E MALONE, C LE, Y KAPILA

UCSF School of Dentistry, Department of Orofacial Sciences

Objective: Oral biofilms present complex microenvironments that contribute to multitudes of oral maladies, including caries, periodontitis and endodontic infections. Biofilms exhibit resistance to antibiotics and antimicrobials; however, recent work has shown treatment with probiotics can lead to decreased oral biofilm density. Though this research is promising, discovery of probiotic organisms falls well short of the medical community’s need for ways to eliminate pathogenic biofilms. The aim of this study was to determine if nisin, a dynamic antimicrobial, and nisin-producing probiotic Lactococcus lactis, reduce oral biofilm biomass in vitro.

Methods: Salivary samples were collected from healthy individuals, pooled, and static biofilms were cultured at 37℃ using cell-free saliva (CFS) as culture media. Static biofilm formation was examined by adding cell-containing saliva to CFS, challenging the samples with varying concentrations of nisin and different cell densities of L. lactis at t=0. Additionally, 24h and 48h pre-formed biofilms were challenged with nisin and L. lactis. Biofilm biomass and DNA content were analyzed using gram-staining techniques and CyQUANT cell proliferation assays. Confocal microscopy was used to determine bacterial viability using BacLight LIVE/DEAD bacterial staining.

Results: Nisin significantly decreased biofilm formation at low concentrations (0.1-2ug/ml) in a dose dependent manner, yet did not decrease the total biomass of the 24h or 48h pre-formed biofilm at these same concentrations. Similarly, L. lactis significantly decreased biofilm formation in a CFU/mL dependent manner; however, it did significantly decrease 24h and 48h pre-formed biofilm biomass in a CFU/mL independent manner.

Conclusion: Though nisin was more effective at preventing biofilm formation than at decreasing the biomass of preformed biofilms at low concentrations, nisin-producing L. lactis was able to significantly decrease biofilm formation and disrupt biofilms. This work highlights the significant role Lactococcus lactis might have as a probiotic and its potential therapeutic use in the treatment of biofilm-associated oral diseases.

Support: AAP/Sunstar Innovation Grant; UCSF Summer Research Fellowship; CAPES Grant Number 88881.133124/2016-01

#27 Title: Predicting final root positions after orthodontic treatment via crown superimposition of pre-treatment cone-beam computed tomography scan and post-treatment digital scan

S PI, J PARK, R LEE, G NELSON, D HATCHER, S OBEROI

UCSF School of Dentistry, Department of Orofacial Sciences, Division of Orthodontics

Objectives: Accurate root angulation and inclination are important for successful orthodontic treatment and periodontal health. Current radiographic techniques to monitor and finalize root positions are either inaccurate or use relatively large amounts of radiation. The objective of this project is to assess the accuracy, reliability, and clinical feasibility of an alternative methodology to the conventional radiographic techniques that can potentially monitor root movement in three dimensions at any stage of orthodontic treatment with minimal radiation.

Methods: This alternative methodology takes a pre-treatment cone-beam computed tomography (CBCT) scan and isolates the pre-treatment CBCT teeth into individual surface files. These pre-treatment CBCT teeth surface files are then superimposed onto a digital scan of the teeth at the stage of orthodontic treatment of interest. After this superimposition process, the position of the roots of the pre-treatment CBCT teeth are now in the “expected root position” (ERP) setup, an approximation of the root position at the stage of interest. In this study, the pre-treatment CBCT teeth will be superimposed onto an extra-oral laser scan of a post-treatment study model yielding the ERP setup at post-treatment. The ERP setup at post-treatment will be compared to the post-treatment...
CBCT scan which serves as the gold standard. The mesiodistal angulation and buccolingual inclination of all teeth in both the ERP setup and post-treatment CBCT scan were measured and compared. **Results:** Strong agreement between the ERP setup and post-treatment CBCT scan was displayed using Bland-Altman plots. Previous studies have shown that variations in root angulation of 2.5° are clinically acceptable. Preliminary results have found that 91.94% and 91.04% of teeth in the ERP setup have a mesiodistal angulation and buccolingual inclination within this 2.5° threshold respectively. **Conclusion:** This alternative methodology has the potential to accurately monitor root movement in three dimensions during orthodontic treatment. **Support:** American Association of Orthodontists Foundation (AAOF): Research Aid Award

#28 Title: HIV-associated disruption of oral epithelium through TNF-α and TGF-β activation

K REN (1), R HERRARA (2), S TUGIZOV (2)

(1) UCSF School of Dentistry; (2) UCSF School of Medicine

**Objectives:** Human immunodeficiency virus (HIV) disrupts the oral mucosal epithelium, impairing the epithelial barrier and allowing for paracellular pathogen penetration. This study aims to understand the molecular mechanisms of this disruption through tumor necrosis factor-alpha (TNF-α) and transforming growth factor beta-1 (TGF-β) activation, which may reduce epithelial barrier function by induction of epithelial mesenchymal transition (EMT).

**Methods:** Primary tonsil epithelial cells were isolated from HIV-uninfected tonsil tissues. Polarized cells were established in Transwell two-chamber filters. Apical surfaces of polarized cells were treated with HIV-1 envelope protein gp120 (10ng/ml) with or without antibodies against gp120, toll-like receptor 2 (TLR2), TLR4, TNF-α and TGF-β for 4 days. Untreated cells served as controls. Epithelial disruption was evaluated by measuring paracellular permeability and immunofluorescence detection of tight junction proteins, zonula occludin (ZO-1) and occludin. EMT phenotype was examined by E-cadherin and vimentin immunostaining. Two-sample t-tests were used; p<0.05 was considered significant.

**Results:** Gp120 treatment of polarized tonsil epithelial cells reduced ZO-1 and occludin expression by 81.6% and 62.6%, respectively, and induced paracellular leakage. Anti-gp120 antibody neutralized gp120 effect on disruption of tight junctions by 79.5%. Gp120 also reduced E-cadherin and upregulated vimentin expressions leading to EMT induction. Anti-gp120 antibody abolished gp120-mediated reduction in E-cadherin and upregulation of vimentin expression. Antibodies against TLR2 and TLR4 had a protective effect against gp120-induced tight junction disruption, i.e., expression of ZO-1 and occludin was increased approximately 4 and 2 folds, respectively. Similar effects were observed by antibodies against TNF-α. Gp120-induced EMT was inhibited by TGF-β antibody, i.e., vimentin expression was reduced by 74.8%.

**Conclusion:** HIV-1 gp120 protein interaction with TLR2 and TLR4 activates TNF-α and TGF-β, reducing E-cadherin and upregulating vimentin expression leading to EMT. Understanding the mechanisms of HIV-induced disruption of oral epithelium by EMT may open new avenues to inhibit EMT and preserve the barrier function.

**Support:** This project was supported by NIH grant R01 (1R01DE023315-01), the AADR Student Research Fellowship, and the UCSF Summer Research Fellowship.

#29 Title: pH sensitive cellular D-2-hydroxyglutarate levels: investigating IDH1-R132H mechanism

R SESANTO, K WHITE, B WEBB, D BARBER

UCSF School of Dentistry, Department of Cell and Tissue Biology

**Objectives:** The elevated intracellular pH (pHi) common to cancers can enhance tumorigenic functions of proteins with arginine to histidine (R>H) mutations. R>H mutations uniquely alter electrostatic interactions because histidine (pKa~7) titrates within physiological pH but arginine (pKa~12) is invariably positively charged. We sought to determine the possible gain in pH-sensing by isocitrate dehydrogenase-1 (IDH1-R132H), a highly recurrent R>H somatic cancer mutation. The R132H mutation enables a neomorphic reaction producing D-2-hydroxyglutarate (D2HG), an oncometabolite and epigenetic regulator. We tested the prediction that D2HG production by IDH1-R132H is pH-sensitive and increased at higher pH.

**Methods:** We generated NIH3T3 cells stably expressing IDH1-WT and IDH1-R132H, cultured them at higher (7.6) and lower (7.2) pH, and measured D2HG levels in lysates using a colorimetric assay. We generated and purified recombinant IDH1-WT and IDH1-R132H enzymes and measured activity using colorimetric assays for NADPH production (wild-type reaction) and consumption (neomorphic reaction).

**Results:** NIH3T3 cells demonstrated higher and pH-sensitive D2HG levels when expressing IDH1-R132H but not IDH1-WT. Contrary to our prediction, cells expressing IDH1-R132H had higher D2HG levels at lower pH compared with higher pH.

As expected, in vitro assays confirmed higher wild-type activity by IDH1-WT compared with IDH1-R132H and higher neomorphic activity by IDH1-R132H compared with IDH1-WT. Additionally, IDH1-R132H has lower wild-type activity at pH 7.0 compared to pH 7.5 but neomorphic activity was pH-insensitive. As expected, IDH1-WT was pH-insensitive under all conditions tested.

**Conclusions:** Cells expressing IDH1-R132H have pH-sensitive D2HG accumulation, with increased D2HG levels at lower pH. In vitro assays indicate that the neomorphic reaction is pH-insensitive. Currently ongoing work uses mass spectrometry analysis to determine the discrepancy in pH-sensitive D2HG production between in vitro and cell-based assays. Understanding the relationship between pH and IDH1-R132H neomorphic activity may inform new chemotherapeutic approaches and research into cancers with recurrent R>H mutations.

**Support:** Department of Cell and Tissue Biology and NIH CA197855
#30 Title: Self-assembly of modified amelogenin nanoribbons for templated mineralization

M SITLIN (1), S ENGELBERTH (1), J BONDE (2), L BULOW (2), S HABELITZ (1)

1) UCSF School of Dentistry, Department of Preventative and Restorative Dental Sciences, (2) Lund University, Department of Pure and Applied Biochemistry

**Objectives:** Amelogenin is an essential enamel matrix protein and self-assembles into a supramolecular framework that, combined with other proteins, facilitate the orientation and morphology of apatite crystal growth. However, the supramolecular matrix and the mechanisms by which such biomolecules control the nucleation, growth, and morphology of mineral is far from understood. Here we tested the hypothesis that extension to the amelogenin protein by amino acid sequences that are known to affect mineralization may facilitate guided-growth of apatite fibers on an organic template.

**Methods:** Recombinant full-length amelogenin (rH174) was modified by attaching aspartic acids (rH174-Asp), glutamic acid (rH174-Glu), and statherin (rH174-StC,-StN,-StLC) to its N- or C-terminal. Enamelin peptide with calcium and phosphate(Ca2+/PO43-) was added to existing rH174 nanoribbons at pH7 in various conditions, while other samples were incubated in various concentrations of Ca2+/PO43- in solution and buffers at pH5.5. Samples were prepared and imaged on mica and glass. Self-assembly and nanoribbon dimensions and mineralization were analyzed by atomic force microscopy(AFM) and transmission electron microscopy(TEM).

**Results:** Nanoribbons did not form for rH174-StLC, while all other modification self-assembled into ribbons within 2 weeks. They exhibited high organization and alignment (rH174-Asp,-Glu,-StN,-StLC), networked aggregation (rH174-Glu), and random orientation (rH174-Asp -StN) under various conditions. Analysis by TEM indicates the presence of randomly-oriented crystalline mineral in 8-week rH174-Asp.

**Conclusion:** The aspartic acid, glutamic acid, and statherin modifications, as well as Ca2+/PO43-concentrations significantly influenced the self-assembly of amelogenin in its organization, alignment, and distribution. rH174-Glu exhibited the most consisted nanoribbon structures, while rH174-Asp exhibited mineralization. This provides a platform to use other characterization techniques and assembly conditions to further examine the mechanical properties and mineralization of the nanoribbon matrix formed by these modifications. As such, more insight can be gained on the specific roles and mechanisms by which enamel proteins function in enamel development.

**Support:** Dr. Thomas Lang, DE025709

#31 Title: Oral microbiome and anthropometry changes following caries arrest using silver-nitrate/fluoride-varnish

H TAYLOR (1), J HORST (2), S DUFFIN (3), M DUFFIN (3), B CHAFFEE (4)

(1) UCSF School of Dentistry, (2) UCSF School of Medicine, Department of Biochemistry and Biophysics, (3) Shoreview Dental, LLC; (4) UCSF School of Dentistry, Department of Preventive and Restorative Dental Sciences, Division of Oral Epidemiology and Dental Public Health

**Objectives:** While studies have evaluated silver-fluoride combinations to arrest tooth decay, there is minimal information regarding the dental microbiome after intraoral silver use. Similarly, studies have evaluated the relationship between caries burden and anthropometric status, but the evidence is inconsistent. This study aimed to: 1. Evaluate changes in decayed tooth surfaces treated with SNFV over one year; 2. Assess associations between tooth decay and anthropometry, cross-sectionally and over time; 3. Compare the microflora of children treated and not treated with SNFV.

**Methods:** SNFV was applied to carious lesions in children ages 2-14 in rural Ghana (N=199). Tooth surfaces were re-assessed 12-months after application. Anthropometric status was calculated using WHO z-scores (height-for-age, BMI-for-age) at baseline and 12-months. Associations between z-scores and caries status were assessed using Spearman correlations. Stimulated saliva samples were collected from 38 children at 12-months for analyzing bacterial loads using rRNA gene sequencing.

**Results:** At baseline, 37% of children had ≥1 decayed tooth surface (mean: 5.3 surfaces). At 12-months, 69% of baseline decayed surfaces were arrested; 47% of children with baseline decay were free of active lesions. No meaningful association was found between baseline decay status and baseline anthropometry, nor change in height-for-age and decay reduction (all p>0.05). Correlation between change in BMI-for-age and decay reduction was weak but statistically significant (p=0.04). Bacterial ribosomal gene sequencing showed minimal differences in microbial abundances between children treated and not treated with SNFV, except children whose decay continued after treatment had significantly higher levels of S. mutans and Propionibacterium.

**Conclusions:** In this population, baseline tooth decay was not associated with baseline anthropometry, but reduction in decay was weakly associated with BMI-for-age increase. Treatment with SNFV reduced decay considerably and without differences in the natural microbiome 12-months after application, although children whose lesions completely arrested had significantly lower abundance of S. mutans.

**Support:** Program in Global Oral Health Research Fellowship
#32 Title: Effects of amyloid domains on the hydrolysis of amelogenin
L TIAN (1), L ZHU (2), H ZHAI (1), L LI (3), S HABELITZ (4), Y ZHANG(1), W LI (1)

(1) UCSF School of Dentistry, Department of Orofacial Sciences (2) Stanford University, (3) Nanjing Tech University (4) UCSF School of Dentistry, Department of Preventive and Restorative Dental Sciences

Objective: Amelogenin (AMG) is the dominant protein in developing enamel matrix and its removal by proteinase KLK4 is a key event in proper enamel mineralization. Recently, our lab discovered that certain domains within AMG protein could form amyloid-like structures, a type of aggregate that’s generally resistant to proteinase activity. The objective of this study is to determine the effects of assembly-related amyloid domains on the hydrolysis of AMG by KLK4.

Methods: Recombinant AMG proteins with deletions in bioinformatics-predicted amyloid forming regions P2, P3, P5, and P6 were expressed, purified and incubated with KLK4 in triplicate at zero, three, six, and twenty hours. SDS-PAGE and coomassie blue staining were used to compare the kinetic digestions of the full-length wild type AMG and mutant AMG with deletions of amyloid forming regions. The densities of the bands were analyzed by NIH ImageJ and compared by ANOVA.

Results: The purified AMG protein and its mutants show different digestion rate in the presence of KLK4. Only 9.6% of AMG was digested after three-hour incubation with KLK4 and 59.6% still remained intact after twenty-hour incubation. However, 41.9% of P2-deleted mutants were digested after three-hour incubation and only 13.3% remained after twenty-hour incubation. 30.5% of P3-deleted mutants were digested after three-hour incubation and 25.1% remained after twenty-hour incubation. P5 and P6’s digestion rates were similar to AMG.

Conclusions: The deletions of amyloid assembly sequences P2 or P3 significantly accelerated the hydrolysis of AMG by KLK4, which indicates that the existence of amyloid-mediated assembly may play an important role in regulating AMG degradation in tooth enamel development.

Support: UCSF Department of Orofacial Sciences

#33 Title: Effects of mandibular repositioning devices on airway of patients with obstructive sleep apnea: a computational fluid dynamics study
A TRAN, R GUPTA, S CONNELLY, R SILVA

UCSF School of Dentistry, Department of Oral and Maxillofacial Surgery, San Francisco Veteran Affairs Medical Center

Objectives: Mandibular repositioning devices (MRD) effectively and non-invasively treat patients with Obstructive Sleep Apnea (OSA). No studies have shown the ideal MRD characteristics in treating OSA for individual patients using computational fluid dynamics (CFD). This study focuses on utilizing sophisticated CFD modeling to analyze the change in several clinical parameters for patients with OSA, and to examine more specifically how the MRD leads to a reduction in OSA severity.

Methods: We gathered patients diagnosed with OSA based on prior polysomnography (PSG) results and had them obtain a repeat PSG with their custom MRD in place. Patients then underwent CT scan with and without the MRD. Engineering firm, SimuTec, utilized the scans to create three-dimensional models of the upper airway, and performed CFD analysis.

Results: A total of 81 patients were treated with MRD. 10 patients with pre- and post-MRD PSG results showed improvement in OSA from an average AHI of 23.26 to AHI of 5.55 (p=0.001022). All 10 patients underwent a CT scan with and without MRD. CFD analysis of 7 out of 10 patients showed airway improvement with an average increase of 34.5% in the airway volume and average decrease of 25.2% in maximum airway speed, 41.3% in overall total airway pressure, and 41.3% in airway resistance. CFD analysis of 3 patients with worsening airway flow parameters had an increase of 5mm or greater in vertical dimension of occlusion (VDO). Limiting the increase in VDO is important in preventing clockwise rotation of the mandible. CFD can be utilized as a predictive model in determining the optimal design of MRD necessary to provide ideal airway manipulation in a patient specific manner in order to alleviate OSA symptoms.

Support: UCSF Summer Dental Student Research Fellowship Program, SF VA Medical Center, Department of Oral and Maxillofacial Surgery

#34 Title: Assessing Factors Affecting Child Oral Health in Rural Nepal
T VARIMIZOVA (1), K SOKAL-GUTIERREZ (2), N ZAHID (3), M GANGULY (1), J BATCHELLER (3), L SPERO (4)

(1) UCSF School of Dentistry, (2) UC Berkeley-UCSF Joint Medical Program, (3) UC Berkeley, (4) Jevaia International

Objectives: Global oral health has transformed over the recent decades with the dietary invasion of junk food. While caries burden in industrialized countries has begun to decline, there has been an increase in the levels of tooth decay in developing countries, such as Nepal. This work-in-progress study aims to describe and determine associations between frequency of snack food, junk food, and sugary beverage consumption with caries prevalence, mouth pain, and malnutrition in children [0-12) years old in Nepali communities.

Methods: This study analyzed a convenience sample of 272 children [0-12) years old. Questionnaire regarding demographics and children’s dietary habits was given to caretaker accompanying the child. Dental screenings were conducted on the children by calibrated examiners according to WHO standards. Preliminary descriptive data analysis was conducted using Excel, Prism 7 and SPSS 23.0.
Support: powerful clinical implications for the possibility of fixing these defects in utero prior to their development.

Conclusions: The preliminary results support the hypothesis that increased consumption of junk food and sugary beverages may contribute to severe early childhood caries, dental abscesses, mouth pain and malnutrition, with the greatest risk in urban populations. Further exploring issues of oral and nutrition health will be accomplished through focus groups in Nepali communities.

Support: Program in Global Oral Health Research Fellowship

II. GRADUATE CATEGORY

#35 Title: A primary cilia transition zone complex coordinates midfacial development

S ABRAMS (1), J REITER (2)

(1) UCSF School of Dentistry, Oral and Craniofacial Sciences Graduate Program, (2) UCSF School of Medicine, Department of Biochemistry & Biophysics

Objectives: Primary cilia are ubiquitous microtubule-based organelles that coordinate multiple signaling pathways critical for craniofacial development, including Hedgehog, Wnt, and PDGF. Ciliary dysfunction causes a range of disorders, collectively known as ciliopathies, many of which display craniofacial defects including cleft lip/palate, micrognathia, midface dysplasia, exencephaly and craniosynostosis. Despite the high prevalence of craniofacial abnormalities in ciliopathy patients, the molecular etiology underlying these defects are poorly understood. We previously found that the protein products of ciliopathy genes form a complex, termed the transition zone (TZ) complex, at the ciliary base to regulate ciliary membrane composition. Our current study utilizes multiple TZ mouse models to uncover the molecular mechanism underlying craniofacial dysmorphology.

Methods: We used morphometric analysis to quantify facial defects in multiple TZ mutants (Tctn2, Cc2d2a, and Tmem231). We utilized immunohistochemical approaches to analyze proliferation, apoptosis, and defects in ciliogenesis in mutant and control tissues. Finally, we used Cre-loxP technology to uncover tissue-specific requirements of the TZ complex in the various tissues comprising the craniofacial complex.

Results: 2D morphometric analysis uncovered a common set of craniofacial defects, including a collapse of the midface (hypotelorism). We confirmed that a defect in Hedgehog signaling drives the midface defect: decreasing Ptc1 gene dosage rescued the defect in both Tctn2 and Cc2d2a mutants. We found an early signaling defect in the head organizer- the prechordal plate (PrCP) – initiates the midface defect. This was evidenced by loss of the PrCP marker Gsc at E8.0. This led to reduced Hedgehog pathway activation in the basal forebrain at E9.0 resulting in widespread apoptosis in the neurectoderm and facial ectoderm culminating in midface collapse.

Conclusions: Our results have uncovered the molecular underpinnings for midface defects in transition zone ciliopathies and hold powerful clinical implications for the possibility of fixing these defects in utero prior to their development.

Support: NIH NIDCR grant F30DE024684 (to S.A.) and NIH NIGMS grant R01GM095941 (to J.R.)

#36 Title: Changes in the lesion dehydration rate with thickness of the surface layer formed during remineralization on enamel and dentin surfaces

NY CHANG, J JEW, D FRIED

UCSF School of Dentistry, Oral and Craniofacial Sciences Graduate Program, Department of Preventive and Restorative Dental Sciences

Objectives: A transparent highly mineralized outer surface zone is formed on caries lesions during remineralization that reduces the permeability to water and plaque generated acids. However, it has not been established how thick the surface zone should be to inhibit the penetration of these fluids. Near-IR (NIR) reflectance, which coincides with higher water absorption and manifests the greatest sensitivity to contrast changes in enamel, and thermal imaging, which manifests the greatest change for dentin, coupled with dehydration can be used to measure changes in the fluid permeability of lesions. Based on our previous studies, we postulate that there is a strong correlation between the surface layer thickness and the rate of dehydration. In this study, the rates of dehydration for simulated lesions in enamel and dentin with varying remineralization durations were measured.

Methods: Twenty enamel and 20 dentin bovine samples were subjected to 24 hours of surface-soften demineralization, followed by series of acidic remineralization at different time periods ranging from 0 hour to 192 hours. Reflectance dehydration imaging at NIR wavelengths from 1400-2300 nm was used to image simulated enamel lesions. Thermal imaging was used to measure dehydration changes on simulated dentin lesions. PS-OCT images were taken, and dehydration results were correlated to integrated reflectivity, lesion depth, and transparent surface layer thickness, respectively.

Results: From PS-OCT scans, the thickness of transparent surface layer was highly variable amongst both enamel and dentin samples throughout duration of remineralization. There is an apparent positive correlation between dehydration rate and integrated reflectivity and lesion depth, and a negative correlation compared to the transparent surface layer thickness, although non-linear.

Conclusion: The relationship between surface zone thickness and lesion permeability appears highly non-linear. Histology will be performed to validate the results here.

Support: NIH T32 Institutional Training Grant (UCSF) and F30 Individual Predoctoral NRSA Fellowship
#37 Title: TREM2/Dap12 activity in macrophages regulates fracture healing

D CLARK (1, 2), S BRAZINA (2), N ASONG (2), T MICLAU (2), M NAKAMURA (2), R MARCUCIO (2)

(1) UCSF School of Dentistry, Oral and Craniofacial Sciences Graduate Program (2) UCSF School of Medicine, Department of Orthopaedic Surgery

Objective: Fracture healing follows a strict temporal sequence characterized by an initial inflammatory phase followed by anabolic and catabolic processes. Perturbation of the inflammatory phase can have detrimental effects on the healing outcome. Older adults demonstrate increased pro-inflammatory cytokines, which is associated with a predisposition to a range of systemic diseases and conditions, including poorer fracture healing outcomes. Herein, we examine inflammatory regulation during fracture healing through the activity of the triggering receptor expressed on myeloid cells2 (TREM2) and DNAX-associated protein 12 kDa size (DAP12) in macrophages.

Methods: Tibia fractures were created in TREM2-/-, DAP12-/-, and wild type (WT) mice (n=6 mice/group). After healing, tibias were collected and stereological analysis was completed of the healing callus. At day 3 post-fracture macrophages were isolated from the bone marrow of young (14weeks) and old (24months) WT mice and analyzed via high-throughput mRNA sequencing (RNA-Seq).

Results: RNA-Seq data of bone marrow macrophages revealed a significant decrease in TREM2 expression in old mice compared to young with no significant change in other genes that comprise the TREM2 signaling pathway. Stereological analysis of total bone, cartilage and callus volume revealed delayed healing at early time points in TREM2-/- and DAP12-/- mice compared to WT. By day 10 there is a significantly smaller callus and significantly less bone in TREM2-/- and Dap12-/- compared to WT.

Conclusion: Activation of TREM2 in macrophages, and the resulting signaling through its co-receptor DAP12, results in downregulation of inflammation. Here, TREM2 expression was significantly downregulated in old macrophages compared to young. Delayed healing was demonstrated within the callus of TREM2-/- and DAP12-/- mice compared to the WT. The delayed healing is similar to delays reported in studies on fracture healing in old animals suggesting that TREM2 or DAP12 activity may become dysfunctional with age and negatively affect fracture healing.

Support: NIH/NIA R01AG046282

#38 Title: Interprofessional oral health education improves knowledge, confidence, and practice for pediatric healthcare providers

D COOPER (1), J KIM (1), K DUDERSTADT (2), R STEWART (1), B LIN (1), A ALKON (2)

(1) UCSF School of Dentistry, Department of Orofacial Sciences, Division of Pediatric Dentistry (2) UCSF School of Nursing

Background: Dental caries is the most prevalent childhood disease in the United States. Dental caries affects the health of 60–90% of school-aged children worldwide. The prevalence of untreated childhood dental caries is 19% for children 2–5 years of age in the U.S. Factors contributing to the progression of caries include socioeconomic status, access to care, and lack of anticipatory guidance. The prevalence of caries remains highest for children from specific ethnic or racial groups, especially those living in underserved areas where there is limited access to a dentist.

Objective: Researchers have acknowledged the links between oral health and systemic health, oral health care is not usually a component of pediatric primary health care. To address this public health crisis and oral health disparity in children, collaborative efforts among health professionals is critical for dental disease prevention and optimal oral health.

Method: This evaluation focused on a 10-week interprofessional practice and education course on children’s oral health involving dental, osteopathic medical, and nurse practitioner students at the University of California, San Francisco. The objective was to evaluate changes in knowledge, confidence, attitude, and clinical practice in children’s oral health of the students completed the course. Thirty-one students participated and completed demographic questionnaires and questionnaires before and after the IPE course: (1) course content knowledge, (2) confidence, (3) attitudes, and (4) clinical practice.

Results: There was statistically significant improvement in overall knowledge of children’s oral health topics, confidence in their ability to provide oral health services, and clinical practice. There was no statistically significant difference in attitude, but an upward trend toward positivity.

Conclusion: This IPE evaluation showed that offering an interprofessional course to graduate students in dentistry, nursing, and osteopathic medicine can improve their knowledge, confidence, and practice toward children’s oral health and expand their professional goals to include caring for underserved, minority children.

Support: Health Resources & Service Administration
#39 Personalizing orthodontics – precision health methods in orthodontic clinical trials

E EVE, S BALLARD, A LAZAR

UCSF School of Dentistry Departments of Orofacial Sciences and Preventive and Restorative Dental Sciences

**Background:** Precision orthodontics optimizes treatment for the individual rather than the average patient typically described in clinical trials. Statistical tests for heterogeneity of treatment effects (HTE) allow clinical investigators to report on how patients respond to treatment differently due to their unique genetics, anatomy, and history.

**Objectives:** To investigate the current prevalence, characteristics, and reporting practices of HTE methods in orthodontic publications.

**Methods:** Randomized clinical trials published in major orthodontic specialty journals in the year 2016 were identified and reviewed for HTE methods.

**Results:** 47 articles met the inclusion criteria. Of these, 4 contained keywords signaling HTE. Additional studies analyzed individual variations in treatment response without explicit mention of HTE.

**Conclusions:** Standardized reporting of HTE will enhance orthodontic clinical trials and facilitate meta-analysis so that clinicians may provide personalized, efficient treatment.

#40 Title: Functional remineralization of dentin with modified dental restorative materials

V GIRN (1), M BACINO (1), E SAEED (1), H FATHI-KELLY (2), R STEWART (1), T LE (1), S HABELITZ (2)

(1) UCSF School of Dentistry, Department of Orofacial Sciences, Division of Pediatric Dentistry, (2) UCSF School of Dentistry, Department of Preventative and Restorative Dental Sciences

**Objective:** Functional remineralization (FM) of dentin requires recovery of the mineral content and mechanical properties. FM by the polymer-induced liquid-precursor (PILP) process has been demonstrated in the laboratory by using pAsp. This study compares the ability of Biocem cement (NuSmile, Houston, Tx, USA), Biocem modified with polyaspartic acid (20% and 40%), and glass ionomer cements (GIC) Fuji I GI and Fuji IX (GC Corp., Tokyo, Japan) in their ability to restore the mechanical properties of demineralized dentin matrix in artificial lesions.

**Methods:** Artificial lesions were created by solution consisting of 0.05 M acetate buffer containing 2.2 mM calcium phosphate and adjusted to pH 5.0 for 66 hours. The lesions were rehydrated and treated in 5 groups: Biocem only, Biocem + 20% pAsp, Biocem + 40% pAsp, Fuji I, and Fuji IX (n=3) with and then left in SBF for 2 weeks prior to testing. The shrinkage after dehydration (indicating remineralization) was measured and compared.

**Results:** The shrinkage of the lesions treated with a Biocem + 40% pAsp was reduced (43%) compared to Fuji I and reduced (50%) compared to the control Biocem only group. The unmodified glass ionomer cements, Biocem, Fuji I and Fuji IX, appeared to form a superficial mineral layer on the top of the lesion which did not reinforce the dentin matrix.

**Conclusions:** Initial results from 2 week of treatment show addition of pAsp may enhance Biocem cement functionality by inducing FM. Non-modified GICs form mineral layer possibly due to fluoride release but do not mineralize dentin collagen. Further research is needed to apply PILP-releasing cements in a clinical setting.

#41 Title: Post-surgical antibiotic prescribing rationale of periodontists

JH HAI (1), Y KAPILA (1), B CHAFFEE (2)

(1) UCSF School of Dentistry, Department of Orofacial Sciences, Division of Pediatric Dentistry, (2) UCSF School of Dentistry, Department of Preventative and Restorative Dental Sciences

**Objectives:** Periodontal surgery, like other surgeries, carries with it the inherent risk of infection. Paradigm shifts have occurred in periodontics with the discontinuation of antibiotics in osseous surgery and mucogingival surgeries, however, this shift is a slower one with surgeries involving bone grafting. Protocols from the 1990’s for sinus augmentation recommend the use of antibiotics, but to date no randomized controlled trials have been performed to evaluate the effects on graft infection with and without antibiotics. With the incidence of infection being close to 3% for most periodontal surgeries, there is a need for standardized guidelines to prevent over-prescribing. This survey aims to evaluate post-surgical antibiotic prescribing habits of periodontists.

**Methods:** A brief 15-question survey will be distributed to members of the California Society of Periodontists. The survey includes questions about specific periodontal surgeries, prescribing rationale and demographic information.

**Results:** We anticipate that the results of the study will show that newer periodontists will prescribe antibiotics less often and use evidence-based guidelines as their rationale while more experienced periodontists will prescribe antibiotics more often based on their clinical knowledge.

**Conclusions:** Based on the anticipated results of the survey, evidence-based guidelines for prescribing antibiotics, particularly with bone grafting procedures, would be a beneficial addition to the periodontal and dental community and will aid in decreasing public health issues that arise from over-prescribing antibiotics.

**Support:** Program in Global Oral Health Research Fellowship
#42 Title: Characterization of treponema denticola-mediated interactions causing periodontal ligament tissue destruction

E MALONE (1), S GANTHER (1), C LE (2), JC FENNO (3), L ZHAN (2), Y KAPILA (2)

(1) UCSF School of Dentistry, Oral and Craniofacial Sciences Program, (2) UCSF School of Dentistry, Department of Orofacial Sciences, (3) University of Michigan School of Dentistry, Department of Biologic & Materials Sciences

Objectives: Periodontal disease is characterized by destruction of the periodontal hard and soft tissues along with their extracellular matrices (ECM). This destruction is mediated by many factors including, pathogenic microbes, which act as a catalyst for periodontal disease pathogenesis through the development of a dysbiosis of the microbiome. These pathogenic microbes also interact with host tissues, and thereby trigger adverse cellular events that lead to tissue destruction. One bacteria implicated in this dysbiosis and tissue destruction, is the oral spirochete, Treponema denticola (T. denticola), which is highly associated with periodontal disease.

The T.denticola outer membrane protein complex called dentilisin, contributes to the chronic activation of pro-MMP-2 in periodontal ligament (PDL) cells to ECM degradation. Despite these advances, there is little known about the T.denticola interactions with PDL cells that induce these cytopathic behaviors. Dentilisin may be a key factor in mediating these interactions. Understanding these mechanisms may help “reset” homeostatic conditions needed for repair, remodeling or regeneration of the periodontium.

The central hypothesis of this project is that T. denticola interactions with PDL cells mediate adverse effects on homeostasis and cellular functions leading to a compromised cellular phenotype.

Methods: The following methods were used to test this hypothesis. Human primary PDL cells (explanted from extracted teeth) were challenged with and without fluorescently (CFSE)-labelled wildtype T.denticola, and T.denticola mutant strains (lacking dentilisin activity) at different multiplicities of infections (10, 50 and 100) for 2hrs in the presence or absence of different concentrations of endocytosis inhibitors. Post-challenge, adhesion and migration assays were performed as functional readouts of the cellular response.

Results: Challenging PDL cells with wild type T. denticola disrupts PDL cell adhesion and migration dose-dependently.

Conclusions: T. denticola induces adverse responses in PDL cells consistent with characteristics observed in periodontal disease.

Support: NIH; R01 DE025225 to YLK and JCF, F30DE027598 to EM, and T32 to SG.

#43 Title: Wnt/beta-Catenin signaling regulates chondrocyte-to-osteoblast transformation during endochondral repair

SA WONG (1,2), T SHAO (2), D HU (2), T MICLAU (2), C BAHNEY (2), R MARCUCIO (1,2)

(1) UCSF School of Dentistry, Oral and Craniofacial Sciences Graduate Program (2) UCSF School of Medicine Orthopaedic Trauma Institute, Department of Orthopaedic Surgery

Objectives: Lineage tracing data demonstrate that chondrocytes contribute to the formation of bone by transforming into osteoblasts during endochondral ossification. However, the molecular mechanisms governing this process remain largely unknown. The canonical Wnt pathway is a prime regulatory candidate due to its role in directing skeletal development and promoting osteogenesis and fracture repair. A small number of callus chondrocytes have nuclear localization of beta-catenin, indicating that these cells undergo active canonical Wnt signaling. These cells lie adjacent to the invading vasculature, and we have previously demonstrated that secreted factors from endothelial cells drive osteogenesis. We hypothesized that the canonical Wnt pathway is a key regulator of chondrocyte transformation and that endothelial cells play an important role in stimulating chondrocyte Wnt activation through the secretion of Wnt ligands.

Methods: We inhibited and over-activated the canonical Wnt pathway in chondrocytes by conditionally deleting beta-catenin or over-expressing an indestructible form of beta-catenin. Fractures were made in the right tibia, and Cre recombination was induced with D6-10 injections of Tamoxifen. HBQ histology and stereology were performed to quantify tissue composition. Wnt reporter cells and qRT-PCR were used to assess endothelial expression of Wnts.

Results: Deletion of beta-catenin in chondrocytes significantly reduced bone formation and increased cartilage retention compared to controls, but did not affect absolute callus size. Conversely, conditional expression of an indestructible form of beta-catenin in chondrocytes significantly increased bone and reduced cartilage at early time points. HUVEC-conditioned media significantly increased luciferase activity of Wnt reporter cells compared to unconditioned media and qRT-PCR analysis of HUVECs confirmed expression of Wnt2b.

Conclusions: Our data demonstrate the critical role of canonical Wnt signaling during endochondral repair, particularly during chondrocyte-to-osteoblast transformation. Our data also indicate that endothelial cells secrete Wnt ligands and suggest that this may contribute to the osteogenic effects of endothelial cell conditioned media.

Support: NIDCR/NIH (F30DE026359 to SAW), AO Foundation, Orthopaedic Trauma Institute
#44 Title: Dental implant assessment and maintenance care: attitudes and practices of dental hygienists in the U.S.

I ZELLMER, L CHUNG, E COUCH, D CURTIS

UCSF School of Dentistry, Department of Preventive & Restorative Dental Sciences, MS Program in Dental Hygiene

Objectives: To investigate U.S. dental hygienists' attitudes and practices regarding dental implant assessment and maintenance care.

Methods: A 34-item quantitative, web-based survey was developed by study investigators and approved by the University of California, San Francisco Institutional Review Board. The survey was distributed nationally to a random sample of 10,000 dental hygienists from the American Dental Hygienists' Association membership database. All survey responses were analyzed and reported using frequency distributions for categorical variables.

Results: A total of 2033 dental hygienists responded to the survey for a 21% response rate. Among those respondents who practiced clinical dental hygiene, 98% reported providing care to patients with dental implants. Most respondents reported always assessing for bleeding/exudate (77%), mobility (71%), plaque/calculus (71%), and tissue color (69%) around implants. However, respondents reported never or rarely probing around implants (31%), checking for cement (34%), or evaluating occlusion (54%). A plastic/resin implant scaler was reported as the most commonly used instrument by 60% of the respondents, however only 7% felt it was effective. In contrast, while only 5% of the respondents reported using a subgingival air-polisher, 71% felt it was effective. The most commonly recommended oral hygiene aid for patients with implants was an oral irrigator. Continuing education courses (91%) and industry magazines (83%) were the most commonly reported sources of implant-related knowledge.

Conclusions: We identified substantial variability in dental implant assessment and maintenance care knowledge and practices among dental hygiene respondents. Therefore, future efforts should emphasize evidence-based implant care in continuing education and publications, and review dental hygiene program curricula, in an effort to provide optimal care to patients with dental implants.

Support: 1. Institute for Oral Health Research Grant, American Dental Hygienists' Association 2. American Dental Hygienists' Association, survey administration 3. Master of Science program in Dental Hygiene, UCSF

III. POSTDOCTORAL/RESIDENT CATEGORY

#45 Title: ABAIAP2L1/YAP interaction senses integrin disengagement and modulates response to EGFR inhibition in NSCLC

A BEARDSLEY (1,2,5), M FRANCISCO (1), B GINI (2), JM BARNES (2), R CAMARDA (1), O MOMCILOVIC (1), J ROHRBERG (1), D VAN DE MARK (1), A ATAKILIT (2), M TAILEB (1), A URISMAN (3), V WEAVER (4,5), T BIVONA (2,5), D SHEPPARD (2,5)

(1) School of Dentistry, Department of Cell & Tissue Biology, (2) School of Medicine, Department of Medicine, (3) School of Medicine, Department of Pathology, (4) School of Medicine, Department of Surgery, (5) UCSF Helen Diller Comprehensive Cancer Center

Objectives: The use of EGFR inhibitors (EGFRi) in non-small cell lung cancer (NSCLC) harboring EGFR mutations is characterized by robust yet transient responses. Studying the nature of persistent disease at time of best response to EGFRi therapy may yield insight on efficacious combinatorial therapy.

Methods: We use spheroid versus monolayer culture of EGFR mutated NSCLC lines to assess the acute response of EGFR mutated NSCLC to EGFRi monotherapy. In vitro phenotypes were corroborated by analyzing xenograft NSCLC tumor remnants following EGFRi treatment.

Results: We demonstrate that the acute response of EGFR-mutated NSCLC to EGFRi is dictated by adhesion context, such that matrix-attached NSCLC monolayers predominantly undergo growth arrest, whereas matrix-disengaged spheroids undergo apoptosis. Forced matrix disengagement via integrin knockdown or vinculin deletion sensitizes EGFR-mutated NSCLC to EGFRi-induced apoptosis. Both spheroid culture and integrin-matrix disruption in monolayers promote cytoplasmic sequestration of YAP, a morphology-responsive transcriptional co-activator and known mediator of resistance to MAPK-directed therapies. We demonstrate that YAP interaction with the I-BAR domain protein BAIAP2L1 is necessary for YAP cytoplasmic sequestration in NSCLC spheroids. Antagonism of YAP is disrupted by cortical sequestration of BAIAP2L1 in matrix-attached monolayers, implicating BAIAP2L1-YAP interaction as a novel sensor of integrin disengagement. Consistently, persistor cells in EGFRi-regressed tumors display nascent integrin-matrix engagement, YAP activation and BAIAP2L1 membranous sequestration. Moreover, resistance to EGFRi is markedly compromised in YAP- or vinculin-deleted xenografts. These findings implicate YAP activation via integrin-matrix adhesion and BAIAP2L1 cortical sequestration as a mechanism of resistance to EGFRi-induced cell killing in NSCLC.

Conclusions: We propose that combined inhibition of EGFR and the integrin/YAP axis is a plausible therapeutic approach in EGFR-mutated NSCLC.

Support: This work was supported, in part, by the Molecular Pathology of Cancer training grant T32 CA177555-02 (A.B.), the Uniting Against Lung Cancer/Lung Cancer Research Foundation Legacy Program (A.B.).
Support: indicates that both may be present in the organic matrix during amelogenesis. Physiological ion conditions and pH when investigating self-assembly. The simultaneous observation of both nanostructures in vitro in which nanospheres and nanoribbons have been stable concurrently. This study highlights the importance of considering dense concentration of spheres observed at one week, followed by the appearance of intermediate-length nanorods at two weeks. Closer examination revealed the simultaneous presence of nanospheres (20.6±1.3nm). Results: Eight homeless patients, three providers and two administrators completed interviews. Thirteen main concepts emerged during qualitative analysis of patient interviews. Common concepts discussed by patients were: patient satisfaction, length of care, program dissemination, community need, prior dental care and quality of life. All patients had positive OHIP scores, indicating their oral health had a negative impact on their quality of life prior to receiving dentures. The most commonly affected dimensions of oral health-related quality of life were functional limitation and physical disability. Each denture’s donated value was $482.50, requiring 18 hours of combined provider, laboratory technician and administrator time. Areas of improvement included improved continuity of care, adequacy of record keeping, and efficient use of volunteers. Key strengths of the program were fulfilling a community need, short length of time to complete care, and improving quality of life for edentulous homeless individuals. Support: UCSF School of Dentistry Global Oral Health Community Partnership.

#47 Title: Self-Assembly of amelogenin nanostructures in simulated enamel fluid

SA ENGELBERTH (1), S SANDHU (1), JS BONDE (2), S HABELITZ (1)

(1) UCSF School of Dentistry, Department of Preventive and Restorative Dental Sciences, (2) Lund University, Division of Pure and Applied Biochemistry, Center for Applied Life Sciences.

Objectives: During amelogenesis (dental enamel formation) an organic matrix serves as the template for growth of nanofibrous mineral apatite crystals. 90% of the organic protein matrix is composed of amelogenin, which is then enzymatically degraded during tissue maturation. Due to this degradation, the exact configuration of amelogenin during amelogenesis is unknown. A long-held theory regarding its structure is that amelogenin forms nanospheres, as observed in vitro at alkaline pH, which align to form long chains for apatite growth. However, previous work in our laboratory indicates that in the presence of calcium and phosphate ions, amelogenin self-assembles into nanoribbons. In this study, we sought to elucidate amelogenin self-assembly in more physiologically relevant conditions.

Methods: Amelogenin was allowed to self-assemble in simulated enamel fluid (SEF) for up to 2 months. pH was monitored and morphology analyzed with microscopy.

Results: An unexpected rise in pH of the unbuffered SEF solutions was observed during incubation. Amelogenin in SEF (pH 6) formed nanoribbons within two weeks. Closer examination revealed the simultaneous presence of nanospheres (20.6±1.3nm). Assemblies conducted at more alkaline pH (initial pH 7.3 increasing to pH 9.0) demonstrated a more distinct progression with a dense concentration of spheres observed at one week, followed by the appearance of intermediate-length nanorods at two weeks, concluding with long nanoribbons decorated with nanospheres (20.1±1.4nm) at three weeks. These two structures remained stable together in solution for an additional five weeks.

Conclusions: This is the first time amelogenin nanoribbons have been observed at alkaline pH, as well as the only extended period in which nanospheres and nanoribbons have been stable concurrently. This study highlights the importance of considering physiological ion conditions and pH when investigating self-assembly. The simultaneous observation of both nanostructures in vitro indicates that both may be present in the organic matrix during amelogenesis.

Support: NIH/NIDCR R01DE025709

IV. RESEARCH ASSOCIATES

#48 Title: Natural caries lesions treated by polymer-induced liquid- precursor process (PILP) in vitro

R GOYAL (1), M BACINO (1), R GEHLOT (2), H FATHI- KELLY (1), S HABELITZ (1)

(1) UCSF School of Dentistry, Department of Preventive and Restorative Dental Sciences, (2) San Francisco Department of Public Health.

Objective: Chemomechanical methods which include papacarie (papain-based gel employing natural pepsin-like enzymes from papaya), polymeric smart burs when applied on extracted teeth containing natural lesions facilitate the removal of infected dentin and leave behind some of the affected tissue. We hypothesized that application of the PILP-process with poly-Asparatic acid of at
#49 Title: Periodontopathic bacteria enhance whereas oral commensals mitigate HNSCC cell migration via integrins

**J KAUR, P KAMARAJAN, C LE, L ZHAN, Y KAPILA**

UCSF School of Dentistry, Department of Orofacial Sciences

**Objective:** Resistance to conventional anticancer therapies in patients with advanced solid tumors has prompted the need for alternative cancer therapies. Many decades after the pioneering work by William Coley in the 1800s a variety of natural and genetically modified non-pathogenic bacterial species are being explored as potential anti-tumor agents. Some commensal bacteria, on which humans depend upon for nutritive, immune-modulating, and metabolic contributions may mitigate cancer. The purpose of this study was to explore the cancer modulatory potential of oral commensal and pathogenic bacteria in the context of head and neck squamous cell carcinoma (HNSCC).

**Methods:** The effects of three pathogenic oral bacteria, namely, Porphyromonas gingivalis, Treponema denticola, and Fusobacterium nucleatum, and two commensal bacteria Streptococcus mitis and Streptococcus sanguinis, on (HNSCC) cell migration were evaluated at bacteria24 hours after 2 hour bacterial challenge. Western blotting was used to evaluate integrin expression and Sstable viral-based shRNA approaches were used to suppress expression of specific integrins in this context of cell migration and bacterial challenge. Data were evaluated using t-tests and ANOVA.

**Results:** All three oral pathogenic bacteria enhanced HNSCC cell migration with concomitant increases in integrin alpha v expression. In contrast, the commensal bacteria, significantly inhibited HNSCC cell migration dose-dependently with concomitant decreases in integrin alpha v expression. Stable suppression of integrin alpha v abrogated the bacterially-enhanced migratory phenotype in HNSCC cells.

**Conclusion:** In summary, oral pathogenic bacteria promote HNSCC cell migration via integrin alpha v upregulation, whereas oral commensal bacteria abrogate this process. Furthermore Streptococcus mitis and sanguinis, may be useful as probiotics or therapeutic agents for HNSCC carcinogenic mechanisms.

**Support:** This project was supported in part by a Chancellor’s Mid-Career Faculty Recruitment Fund to YLK.

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#50 Title: UCSF dental office survey on patient safety culture

**K SINGH, E KALENDERIAN, E OBADAN-UDOH, J WHITE, A YANSANE**

UCSF School of Dentistry, Department of Preventive and Restorative Dental Sciences

**Objectives:** Investigators from several countries, regulatory bodies, and scientific institutions have published studies showing that significant numbers of patients are harmed while receiving health care, sometimes resulting in permanent injury, increased length of stay in health care facilities, or even death. Further, medical errors are among the leading cause of death within the US. In order to reduce the number of patient safety incidents and mitigate their effects, it is important to cultivate a robust patient safety culture. The primary objective of this study was to evaluate the patient safety culture among the students, residents, staff and faculty within UCSF School of Dentistry.

**Methods:** We conducted a cross-sectional study using a modified Medical Office Survey on Patient Safety Culture (MOSOPS) from September 2016 to January 2017 at UCSF. Faculty, residents, hygienists, dental students and staff were invited to complete electronic or paper-based versions of the questionnaire. Descriptive statistics were calculated for each survey item and the 10 underlying safety culture constructs using the STATA 14 statistical software.

**Results:** Of the 336 invited participants, 113 responded to the survey invitation (response rate: 32.4%). The construct receiving the highest composite percent positive scores was Teamwork (75%) while the “Work Pressure and Pace” category received the lowest score (46%). Compared to a previous survey conducted in 2012, there has been a decline in patient safety culture at UCSF, overall. Only 31% of UCSF respondents gave an overall safety rating of either “good” or “excellent” compared to 68% of medical office respondents in 2016.

**Conclusion:** These findings suggest that more work needs to be done to improve the patient safety culture within academic dental institutions. New policies and programs are needed, devoted to helping employees achieve better work-life balance and reduce the pressures that are a necessary part of delivering high quality dental care.

**Support:** This research was supported in part by UCSF School of Dentistry, Department of Preventive and Restorative Dental Sciences.
#51 Title: Spatial distribution of caries and periodontal disease in Sjögren syndrome and health

M RYDER (1), D RELMAN (2), D PROCTOR (3), S WALKER (1), T JUNG (1), J WENG (1), S SASTIEL (1), Y RAJENDRAN (1), Y KAPILA (1), (4) F CHEN

(1) UCSF School of Dentistry, Department of Oral and Maxillofacial Surgery, Division of Periodontology, (2)Stanford University, Department of Medicine, (3) Stanford University, Department of Microbiology, (4) Stanford Volunteer

Objectives: Sjögren’s Syndrome (SS) is a chronic autoimmune disease that can disrupt the function of salivary glands, resulting in hyposalivation. Studies have shown that hyposalivation is associated with an increased incidence of caries and periodontal disease. The purpose of this study is to examine the distribution of these diseases in the mouths of individuals suffering from hyposalivation.

Methods: Periodontal health and caries data were collected for 23 age-matched Healthy controls (HC) and 33 subjects suffering from SS. Periodontal health was evaluated by measuring CAL at three sites on the buccal and lingual surface of each tooth. Caries was measured using the DMFS index. UWS-FR (unstimulated whole saliva flow rate), age, and gender data were collected. The mean values were compared using unpaired t-tests. The distributions of caries and periodontal disease were examined using z-scores standardized against the total mouth mean values of the HC cohort.

Results: The mean UWS-FR of SS subjects (0.13 mL/min) was significantly lower (p < .05) than the mean UWS-FR of HC subjects (0.41 mL/min). The gender ratios between SS (30[F]: 2[M]) and HC subjects (11[F]: 12[M]) were significantly different (test of equal proportions, p < .05). Posterior teeth in the HC subjects showed a trend towards more periodontal disease compared to anterior teeth. The SS group only followed this trend in the maxilla, with a more random distribution in the mandible. The posterior teeth in HC and SS subjects were more vulnerable to caries compared to the anterior teeth. However, SS subjects showed an increased incidence of caries in the maxillary anterior teeth.

Conclusions: The data suggests that the distribution of caries and periodontal disease in SS subjects differs between the maxilla and mandible, and between SS and HC subjects.

Support: National Institute of Dental and Craniofacial Research; Stanford University School of Medicine; Palo Alto Institute for Research and Education

V. VISTING SCHOLAR

#52 Title: Leukemia inhibitory factor produced by fibroblasts within tumor stroma participates in invasion of oral squamous cell carcinoma

Y OHATA (1) K KAYAMORI (1), M TSUCHIYA (1), H HIRAI (2), S YAMAGUCHI (3), T AKASHI (4), K SAKAMOTO (1), A YAMAGUCHI (5), T IKEDA (1)

(1) Tokyo Medical and Dental University, Department of Oral Pathology (2) Tokyo Medical and Dental University, Department of Oral and Maxillofacial Surgery, (3) Tokyo Medical and Dental University, Department of Maxillofacial Surgery (4) Tokyo Medical and Dental University, Department of Surgical Pathology (5) Tokyo Dental College, Oral Health Science Center

Objectives: The interaction between cancer cells and cancer stroma plays a crucial role in tumor progression and metastasis in various types of malignancies, including oral cancer. However, the underlying mechanism has not been fully understood. The aim of this study was to investigate the interaction between oral cancer cells and fibroblasts, which are major tumor stromal components.

Methods: In vitro study using human oral squamous cell carcinoma (OSCC) cell lines and normal human dermal fibroblasts (NHDFs) was conducted. Immunohistochemical and clinicopathological analyses using 112 OSCC cases were also performed.

Results: The transwell assay revealed that migration and invasion of OSCC cell line, HO1-N-1 and HSC3 were significantly stimulated when co-cultured with NHDFs. To explore the factors that promote tumor invasion, we isolated NHDFs from co-culture with HO1-N-1, and performed microarray analysis. Among various upregulated genes, we focused on leukemia inhibitory factor (LIF) and confirmed that OSCC-derived conditioned medium significantly upregulated LIF expression in NHDFs. In vitro transwell analysis confirmed that NHDFs-induced OSCC migration and invasion were inhibited by LIF neutralizing antibody. Further, immunohistochemical analysis of OSCC cases revealed that 44 of 112 cases express LIF in the tumor stroma, especially in cancer-associated fibroblasts (CAFs). Clinicopathological analysis confirmed that the expression of LIF in CAFs was significantly correlated with increased tumor invasion depth.

Conclusions: Our results suggest that OSCC stimulates LIF production in fibroblasts, which participates in cancer cell invasion. This provides the potential therapeutic strategy targeting cancer stroma for OSCC patients.

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VI. CLINICAL CASE

Title: Aesthetic ceramic restorations of congenitally missing lateral incisors in the maxillary arch

JW KIM, V TAPALTSYAN
UCSF School of Dentistry

Background: From epidemiological studies in the past, it was found that 2% of the population displays congenitally missing one or both of maxillary lateral incisors. A patient in the predoctoral clinic presents with congenitally missing lateral incisors who is unhappy with her smile.

Aim: Assess and aesthetically restore missing lateral incisors without orthodontic and surgical procedures.

Materials and Methods: Patient was referred to the orthodontic clinic for an evaluation and treatment. However, patient desired to achieve aesthetic results without extended period of orthodontics and surgery. Casts of maxillary and mandibular arch were used to simulate the necessary reduction and mock wax-up was fabricated to assess the viability of FPD as a method of aesthetic restoration. The plan was to convert #6 and #11 to lateral incisors using porcelain veneers and #5 and #12 to cuspids using Emax porcelain restorations. 90-degree rotation of #12 presented additional complications in the treatment planning process.

Results: #5 and #12 were reduced to replicate the structure of cuspids and #6 and #11 were reduced to replicate the structure of lateral incisors. Ceramic veneers were fabricated for #6, 8, 9, 11 and Emax crowns were fabricated for #5 and #12. The veneers and crowns were placed using multi-link system. Patient is satisfied with her new smile.

Conclusion: In cases requiring aesthetic results to replace missing lateral incisors, use of FPD veneers and crowns present an alternative to orthodontic and surgical procedures.