Research and Clinical Excellence Day

Thursday, Oct. 10, 2019
Cole Hall – Medical Sciences
Reception follows at Millberry Union

KEYNOTE SPEAKER
Paul H. Krebsbach, DDS, PhD
Dean and Professor
School of Dentistry
University of California, Los Angeles

FACULTY RESEARCH LECTURER
Yvonne L. Kapila, DDS, PhD
Chair and Professor
Division of Periodontology
Diplomate American Board of Periodontology
Department of Orofacial Sciences

SPOTLIGHT ON CLINICAL EXCELLENCE
Arun B. Sharma, BDS, MSc.
Health Sciences Clinical Professor
Diplomate American Board of Prosthodontics
Director Graduate Prosthodontics

For more information, contact Roger Mraz at roger.mraz@ucsf.edu
dentistry.ucsf.edu/research
AGENDA

UCSF School of Dentistry Research and Clinical Excellence Day
October 10, 2019

8:00 – 9:00 Breakfast – lobby outside Cole Hall

9:00 – 9:15 Welcome and Opening Remarks
Sarah Knox, PhD
Co-Chair, Research and Clinical Excellence Day Committee

Michael Reddy, DMD
Michael Reddy, DMD, DMSc
Dean and Professor
UCSF School of Dentistry

Daniel Lowenstein, MD
Executive Vice Chancellor & Provost

9:15 – 10:00 Plenary Speaker
Paul Krebsbach, DDS, PhD
Dean and Professor
UCLA School of Dentistry
“Pluripotent Stem Cells: opening a new avenue for skeletal regeneration”

10:00 – 10:15 Break

10:15 – 11:30 Oral Presentations
Kyle Jones, DDS, PhD
Morning Session Chair

Daniel Kim (Mentor: Sunita Ho)
“Spatiotemporal Maps of Implant-Bone Biomechanics In situ”

Mai Zong Her (Mentors: Kristin Hoeft, Deborah Helsel)
“Alternative and Biomedical Oral Health Approaches: Central Valley Hmong Community”

Susan Keefe (Mentor: Ophir Klein)
“The cellular dynamics of intersphenoid synchondrosis (ISS) abnormal fusion in Costello syndrome”

Kevin Rivera (Mentor: Tejal Desai)
“Local Injections Of Nerve Growth Factor Accelerates Endochondral Fracture Repair”

Yushi Bai, PhD (Mentor: Stefan Habelitz)
“Evidence of Amelogenin Ribbons as Templates Guiding Enamel Apatite Growth”

11:30 – 12:00 Spotlight on Clinical Excellence
Arun Sharma, BDS, MS
Health Sciences Clinical Professor
“The role of Osseointegrated implants in reconstruction following treatment of oral cancer”

12:00 – 1:30 Lunch and poster session in the Millberry Union Gym

1:30 – 2:45 Oral Presentations
Eni Obadan-Udoh, DDS, MPH, Dr.Med.Sc.
Afternoon Session Chair

Phuong-Anh Giao (Mentor: Stephen Connelly)
“Efficacy of Botox in PTSD Patients Being Treated for Chronic TMD”

Kevin Hahn (Mentors: Andrei Goga, Sarah Knox)
“Understanding Nerve-Cancer Interactions in Perineural Invasion by Adenoid Cystic Carcinoma”

Tsu-Shuan Wu (Mentor: Benjamin Chaffee)
“Associations of Household Rules and Parental Awareness with Youth Tobacco Use”

2:45 – 3:35 Faculty Research Lecturer
Yvonne Kapila, DDS, PhD
Chair and Professor
“Microbes and the Microbiome – Unlocking their Potential to Address Oral Diseases”

3:35 – 3:45 Mentor of the Year Award
Presented by the John C. Greene Society

3:45 – 4:00 Announcement of Winners
Thomas Lang, PhD
Associate Dean for Research

4:00 – 5:00 Closing Remarks
Sarah Knox, PhD
Co-Chair, Research and Clinical Excellence Day Committee

Reception Millberry Union Gym
Paul H. Krebsbach, DDS, PhD | Plenary Speaker | Dr. Paul Krebsbach was appointed dean of the UCLA School of Dentistry on June 30, 2016. He also holds a professor appointment in the school’s Section of Periodontics.
Prior to his appointment at UCLA, he was a member of the faculty at the University of Michigan for 20 years. He was the Roy H. Roberts Professor of Dentistry and a Professor of Biomedical Engineering. He also served as Chair of the Department of Biologic and Materials Sciences and Division of Prosthodontics for over 10 years.
He is a fellow of the American Association for the Advancement of Science and the American Institute for Medical and Biological Engineering. He was awarded the William J. Gies Award by the International Association for Dental Research/American Association for Dental Research and was also the recipient of the International Association for Dental Research’s 2010 Distinguished Scientist Award for Basic Research in Biological Mineralization. In 2016, he completed a term as president of the AADR.

Presentation: “Pluripotent Stem Cells: opening a new avenue for skeletal regeneration”

Abstract: Current practices to maintain induced pluripotent stem cells (iPS) and human embryonic stem cells (hES) in an undifferentiated state typically require the support of mouse embryonic feeder cells (MEFs) or an undefined, animal extracellular matrix products such as Matrigel. These culture conditions that depend on animal contaminants, severely limit our ability to interpret mechanistic studies designed to resolve how human pluripotent stem cells interact with their extracellular environment to: 1) remain in a unique undifferentiated state and 2) make fate-changing lineage decisions. Likewise, the xenogeneic components of MEFs and Matrigel will ultimately hinder our ability to use these stem cells to treat debilitating human diseases.

We have overcome these obstacles by developing a synthetic matrix system that supports iPS (and hES) cell expansion and self-renewal within completely defined culture conditions that are free from xenogeneic contamination. The establishment of this synthetic matrix now allows us to probe the molecular basis of pluripotent stem cell self-renewal and differentiation, and will pave the way for clinical applications.

Arun B. Sharma, BDS, MSc | Spotlight on Clinical Excellence | Dr. Sharma is a Clinical Professor in the Division of Prosthodontics at the University of California, San Francisco School of Dentistry. Dr. Sharma is a Diplomate of the American Board of Prosthodontics. He maintains a private practice, and is the Director of the graduate program in prosthodontics at UCSF. He serves as the prosthodontist for the Center for Craniofacial Anomalies and the Head and Neck Reconstruction team. Dr. Sharma received his dental degree from the University of Bombay in 1983 and a Masters in Prosthetic Dentistry from the University of London. He then completed a prosthodontic residency from UCSF and a maxillofacial prosthetic residency from UCLA. Dr. Sharma has contributed to seven textbooks and authored many articles. He has served as the Assistant Editor of the Journal of Prosthetic Dentistry and is currently the Chair of the Editorial Council of the JPD. Dr Sharma is a Past president of the Pacific Coast Society for Prosthodontics and the American Prosthodontic Society and President-Elect of the American Academy of Maxillofacial Prosthetics. He has been the recipient of the Thomas Curtis award for excellence in teaching from the prosthodontic residents on 13 occasions.

Presentation: “The role of Osseointegrated implants in reconstruction following treatment of oral cancer.”

Abstract: Title: The field of maxillofacial prosthetics has benefitted most from osseointegrated implants. Patients who were left with a compromised quality of life even though the cancer was cured were really not able to be part of society. Implants have helped the prosthodontist provide restorations that significantly improve function, speech and appearance. This presentation will present patients who were treated for maxillary and mandibular tumors with a resection and then reconstructed with the help of implants.
Yvonne L. Kapila, DDS, PhD | Faculty Research Lecturer | Dr. Yvonne L. Kapila is Professor and Chair of the Division of Periodontology at UCSF. She has over 25 years of experience as a Periodontist, Academician, Teacher/Mentor, and Clinician Scientist. She served as the inaugural Director of Global Initiatives at the University of Michigan School of Dentistry for 5 years. She has authored over 90 peer reviewed publications in high impact journals, including Biochimica et Biophysica Acta Cancer Reviews, Cell Death and Differentiation, Cancer, JBM, Molecular Biology of the Cell, Journal of Proteome Research, Journal of Biological Chemistry, Genes and Cancer, PLOS one, Journal of Periodontology, and over 90 abstracts and book chapters. She has been continuously funded by NIH for over 25 years for her scientific work. She serves at the local and national level on NIH study sections for the NIDCR and NCI and at several UC-wide and UCSF grant review/funding committees. Dr. Kapila also serves as Chair of the Research Submissions Committee for the American Academy of Periodontology. She has been recognized by the American Academy of Periodontology with the Distinguished Scientist Award in 2019 and by the American Association for Dental Research with the Irwin D. Mandel Distinguished Mentoring Award in 2019.

Presentation: “Microbes and the Microbiome – Unlocking their Potential to Address Oral Diseases”

Abstract: Dr. Kapila will discuss the impact of microbes and the microbiome in relation to oral diseases, including periodontal disease and oral cancer. New research in her lab and in the field of the microbiome and host-microbial interactions point to the potential for harvesting and utilizing bacterial biomolecules for mitigating oral diseases. She will discuss the potential role of bacteriocins, probiotics, and reseeding our microbiomes/promoting optimal colonization for healthy oral microbiomes to prevent disease and promote health.
#01 Title: 3-D Analysis of Skeletal Expansion in Clear Aligner Patients

R AZIZOLLAHI, K KAI, S OBEROI

Division of Orthodontics, UCSF School of Dentistry

Objectives: In the past, clear aligners were used for simple tooth movements, leaving more complex cases to traditional orthodontic treatment. Clear aligners have become exponentially advanced and have recently been used to treat Phase I cases. Historically, skeletal expansion has only been seen in rapid and slow treatment modalities with traditional orthodontics. There is controversy on the effectiveness of aligners; and there is little evidence of their effects on skeletal expansion. Our study will aim to investigate the effects of these aligners on skeletal expansion to determine if aligners affect not only the dental arch, but also the craniofacial skeleton.

Methods: This is a retrospective study analyzing CBCT scans of Phase 1 orthodontic patients. Using the Invivo5 (Anatomage) software, we measured frontonasal suture, intermaxillary suture, trans-palatal suture, mid-palatal suture (between premolars, at canine, and at most anterior point of maxillary arch), angulation of first molars, maxillary and mandibular intermolar and inter-canine distance, airway total volume, and minimal cross-sectional airway area. Pre- and post-aligner treatment CBCT scans are analyzed and compared for seventeen patients. In addition, using iTero OrthoCAD software, we compared intermolar and inter-canine width for four Phase 1 patients undergoing aligner therapy. The scans analyzed are pre-treatment, refinement, and post-treatment.

Results: No refinement or post treatment CBCTs have been taken for the seventeen Phase 1 patients. Our analysis with Anatomage is on hold until these scans are available. Although the final scans for our analysis with OrthoCAD are not yet available, the refinement scans show an average of 2.5mm increase in inter-canine width and 1.8mm increase in intermolar width.

Conclusions: Although this study is still a work in progress, the results thus far demonstrate that skeletal expansion is possible in Phase 1 orthodontic patients treated with clear aligners.

Support: Buchannan Dental Clinic

#02 Title: Evaluating the Efficacy of the Biomaterials Curriculum at UCSF SoD

D BUI, S HABELITZ

UCSF SoD School of Dentistry

Objectives: The biomaterials curriculum at UCSF SoD is designed to teach dental students the basics of material science focusing on the materials used in dentistry. This study surveyed student satisfaction, perceived comfort level with curriculum topics, as well as the strengths and weaknesses of the curriculum.

Methods: Data were collected using a Qualtrics survey (collected: Spring and Summer 2019) polling dental students, including domestic and international, of all years. Participants were divided into preclinical (Year 1 and 2) and clinical (Year 3 and 4) categories and asked to answer 19 questions regarding satisfaction with the biomaterials curriculum, perceived comfort level with various concepts and materials taught in the course, as well provide suggestions to improve the course.

Results: A total of 126 responded of which 65 were underclassmen and 61 were upperclassmen. Despite the perceived importance of the biomaterials curriculum, the majority of UCSF dental students polled reported that they were unsatisfied with the biomaterials curriculum at UCSF to some degree (N=60/114). Students reported feeling somewhat unconfident regarding their knowledge of most dental materials and biomaterials concepts. However, confidence in biomaterials knowledge tended to increase with each increasing year of dental school (p<0.05 for 6/12 materials). Further, upperclassmen reported a need for advanced biomaterials education to supplement the clinical experience in the third and fourth year (N=32/40).

Conclusions:
• Biomaterials curriculum does not correlate with the skills taught in the simulation lab.
• Students better appreciate and understand the material as they gain clinical dental experience.
• Biomaterials education should be expanded to the curriculum in the later years of DDS program.
• Hands-on clinical experience may help to contextualize the information presented in the biomaterials curriculum.

Support: This project was possible due to support from Dr. Stefan Habelitz and ADEA.
#03 Title: IGF1 Signaling via mTOR Pathway Impacts Salivary Gland Organogenesis

K CHANG CHIEN, P. KAMARAJAN, C LE, Y KAPILA, L ZHAN

Department of Orofacial Sciences, UCSF School of Dentistry

**Background:** Recent studies have implicated the oral microbiome in the pathogenesis of oral squamous cell carcinoma (OSCC); the most common oral cancer for which the five-year survival rates have not changed significantly in decades. Streptococcus mutans (SM) antimicrobial peptide genes (NN2 and PNS1) contribute to SM’s pathogenicity and interactions within the oral environment. Our study aimed to assess the role of SM NN2 and PNS1 genes on OSCC cell proliferation and migration.

**Methods:** Overnight cultures of NN2 and PNS1 wild-type and counterpart knock-out SM strains grown in BHI broth were harvested and added to OSCC cancer cells (HSC-3) for treatment at 10, 50, 100 multiplicity of infection (MOI) for 2 hrs. For proliferation assays, the bacteria-treated cancer cells were washed and cultured in DMEM medium for 18hrs before assayed using the CyQUANT NF Cell Proliferation Assay Kit. A scratch assay was similarly used to evaluate changes in cell migration. The migration distance was evaluated using NIS-Elements BR4.14.04 imaging software. Unchallenged cells were used as a negative control and set at 100% of relative effects. All assays were performed in triplicate and were repeated 3 times (n=9).

**Results:** All SM challenged OSCC cells exhibited significantly reduced proliferation and migration compared to unchallenged controls (p<.05). The PNS1 knockout strain mediated significantly more inhibition of OSCC cell proliferation than its wildtype strain, whereas there was no difference between the NN2 knockout and its wild-type counterpart. However, the NN2 knockout triggered significantly more inhibition of OSCC cell migration than the wild-type strain, and there was no difference regarding the PNS1 gene.

**Conclusion:** SM inhibits OSCC cell properties, and the specific genes PNS1 and NN2 are in part responsible for the inhibition of OSCC cell proliferation and migration, respectively. Thus, SM virulence factor genes NN2 and PNS1 may be involved in OSCC pathogenesis via different mechanisms.

**Support:** This study was supported by contributions from Dr. John and Deborah Greenspan, faculty emeritus.

#04 Title: Age-related changes to periostin expression and the effect on fracture healing

E CHO, D CLARK, R MARUCIO

Department of Orthopedic Surgery, UCSF School of Medicine

**Objectives:** Elderly population demonstrate increased fracture healing delays and complications with an associated increase in morbidity and mortality. Macrophages are important in wound healing and manifest age-related changes that may be detrimental to fracture healing outcomes. We have previously demonstrated that macrophage-derived periostin expression, an important promoter of osteoblastic activity, is downregulated with age. This study aims to further elucidate the effect of age on periostin expression and its role in fracture healing in vivo and in vitro.

**Methods:** All animal experiments were approved by UCSF IACUC. Bone marrow stromal cells (BMSC) from young (3 months) and old (36 months) mice were isolated and cultured. BMSC were supplemented with old and young macrophages and recombinant periostin and stained via alizarin red. Additionally, bone marrow derived macrophages were grown in culture in osteoblastic or basal media and then collected for qPCR analysis. Closed non-stable tibia fractured were created in young, old and periostin-/- mice. After 5 days, callus were isolated and analyzed via qPCR. Or, fracture calluses were isolated after 10 days and analyzed via stereology (n=5/group).

**Results:** Bone marrow derived macrophages from old mice demonstrated decreased periostin expression compared to young. The addition of young macrophages or recombinant periostin did not increase mineralization in cultures of old BMSCs. Decreased periostin expression was demonstrated in the callus of old mice compared to young with an associated decrease in Col I, Col II and Col X. Old mice and periostin-/- mice demonstrated significantly decreased callus, bone and cartilage volume compared to young (p<0.05).

**Conclusion:** Expression of periostin is dysregulated as a function of age in vitro and in vivo. Decreased periostin with aging and its relation to bone fracture healing suggest it may have a role as a therapeutic target for the management of bone fractures in elderly.

**Support:** Summer Dental Student Research Fellowship Program, NIH/NIA (R01-AG046282)

#05 Title: IGF1 Signaling via mTOR Pathway Impacts Salivary Gland Organogenesis

K DILEO, S SUDIWALA, S KNOX

Program in Craniofacial Biology, UCSF School of Dentistry

**Objectives:** With only poor symptomatic therapies available to patients with salivary gland (SG) dysfunctions, as from radiation therapy or Sjörgen’s Syndrome, regenerative stem cell therapy offers a potential solution. However, SG organogenesis remains poorly understood. Here we investigate the impact of insulin-like growth factor-1 (IGF-1), a factor highly expressed during a period of extensive epithelial growth and differentiation, on SG size and shape and progenitor cell proliferation and differentiation.

**Methods:** To determine if IGF-1 signaling regulates glandular development, intact SGs from embryonic day (E)13 murine embryos were cultured with IGF receptor 1 (IGFR1) inhibitor picropodophyllin for 48h. To test if IGF-1 acts via mammalian target of rapamycin complex (mTORC) 1 and 2, major regulatory signaling complexes that can be activated by IGF/IGFR, we cultured SG with Torin-1 (inhibits mTORC1/2) or rapamycin (inhibits mTORC1). We determined if IGF-1 impacted the epithelium directly and via mTORC, by culturing E13 epithelia with IGF-1 or rapamycin/Torin-1 for 48h. Changes in tissue morphology and cell proliferation were assessed.
measured using brightfield and immunofluorescent microscopy, respectively. Changes in markers of progenitor cell differentiation/maturation and alterations in the mTOR pathway were measured using qPCR.

**Results:** IGFR1 inhibition increased end-bud (pre-acini) size, whereas mTORC1/2 inhibition significantly reduced end-bud and total gland size, suggesting IGFR1 modulation of end-bud size did not act via mTORC. However, IGF-1 significantly increased epithelial progenitor cell markers that were in some cases blocked by rapamycin and Torin-1.

**Conclusion:** Our findings suggest that IGF-1/IGF1R signaling is essential for SG development where it regulates the epithelial morphology, progenitor cell maintenance/expansion and tissue maturation, and does so, in part, through mTORC signaling. Future studies will aim to utilize IGF-1 in the generation of de novo salivary tissue to replace dysfunctional SGs.

**Support:** UCSF Summer Dental Student Fellowship Program

#05 Title: Effectiveness of Dental Screenings at Community Health Fairs for Increasing Access to Care

A ELIAS, E GROVER, J ESTRADA, S HYDE

UCSF School of Dentistry

**Objectives:** UCSF’s Registered Campus Organizations (RCOs) hold monthly community health fairs to increase access to care for at-risk populations. It is unknown whether community health fair participants who receive a recommendation to visit a dentist proceed to complete their dental visit. This study aims to (1) determine the percentage of participants who complete a dental visit within 4 months of receiving a referral at a UCSF RCO community health fair and (2) identify barriers and enablers influencing participants’ completion of a dental visit.

**Methods:** Participants were recruited from RCO community health fairs from 2018-2019. Dental screening, oral hygiene instruction, a referral list of local dentists, and a brief survey were completed at the time of the event and follow-up questions were asked via phone four months after each event.

**Results:** Sixty participants were recruited from ten health fairs. Fourteen participants completed both pre- and post-surveys (23%), of which half completed their recommended dental visit. Completing the recommended dental visit was associated with participants finding that the referral list of local dentists was helpful and that the dentists on the referral list were accessible by public transportation and had appointments available (all p<0.05). Dental insurance status, the cost of treatment, taking time off work, and dental fear were not associated with dental visit completion status (all p>0.05).

**Conclusion:** A referral list of local dentists, accessible by public transportation, with available appointments, enabled the completion of the recommended dental visit. Potential barriers of dental insurance status, treatment cost, taking time off work, and dental fear were not found to affect visit completion. Despite multiple phone call attempts, this study was limited by a low post-survey response rate and follow-up data will continue to be collected for a more conclusive outcome.

#06 Title: Effectiveness of Dental Screenings at Community Health Fairs for Increasing Access to Care

A ELIAS, E GROVER, J ESTRADA, S HYDE

UCSF School of Dentistry

**Objectives:** UCSF’s Registered Campus Organizations (RCOs) hold monthly community health fairs to increase access to care for at-risk populations. It is unknown whether community health fair participants who receive a recommendation to visit a dentist proceed to complete their dental visit. This study aims to (1) determine the percentage of participants who complete a dental visit within 4 months of receiving a referral at a UCSF RCO community health fair and (2) identify barriers and enablers influencing participants’ completion of a dental visit.

**Methods:** Participants were recruited from RCO community health fairs from 2018-2019. Dental screening, oral hygiene instruction, a referral list of local dentists, and a brief survey were completed at the time of the event and follow-up questions were asked via phone four months after each event.

**Results:** Sixty participants were recruited from ten health fairs. Fourteen participants completed both pre- and post-surveys (23%), of which half completed their recommended dental visit. Completing the recommended dental visit was associated with participants finding that the referral list of local dentists was helpful and that the dentists on the referral list were accessible by public transportation and had appointments available (all p<0.05). Dental insurance status, the cost of treatment, taking time off work, and dental fear were not associated with dental visit completion status (all p>0.05).

**Conclusion:** A referral list of local dentists, accessible by public transportation, with available appointments, enabled the completion of the recommended dental visit. Potential barriers of dental insurance status, treatment cost, taking time off work, and dental fear were not found to affect visit completion. Despite multiple phone call attempts, this study was limited by a low post-survey response rate and follow-up data will continue to be collected for a more conclusive outcome.

#07 Title: Applications of Novel Amelogenin Peptides in Tooth Whitening by Bleaching

X FAN, C LE, W LI, L ZHAN, L LI, H ZHAI, S HABELITZ

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

**Objectives:** Though composing less than 1% of the total enamel weight, the enamel protein remnants predominantly derived from amelogenin, may play important roles in binding hydroxyapatite (HAP) crystals together and sealing the inter-HAP-crystal spaces. Previous studies have identified P2 as a self-assembly domain and P4, P9 and P24 as HAP-binding domains. This study aimed to assess whether novel amelogenin peptides containing P2 assembly and one of HAP-binding domains (P4, P9 or P24) can re-strengthen weakened enamel after dental bleaching by functionally adhering the crystals as well as reduce enamel re-staining by sealing the inter-crystal gaps.

**Methods:** Bovine enamel blocks with 5x5mm window were bleached by 30% hydrogen peroxide for 30 minutes and then treated with 50µm/ml peptides with no peptide treatment as control. The microhardness of bovine enamel was determined by indentation width measured by Image Pro system for each sample at baseline, post-bleaching, and post-peptide treatment. For the effects of amelogenin peptides on enamel re-staining, bovine enamel blocks were bleached, treated respectively with P2P4, P4P9, P2P24 and control, and then immersed in coffee for 6 hrs, 1, 2, 3, 4 and 5 days. The enamel shade was recorded by two investigators blinded of treatment groups against Besy professional 3D R-20 dental tooth whitening shade guide at baseline, 6 hrs, 1, 2, 3, 4 and 5 days. Data was analyzed using ANOVA between the groups.

**Results:** Bleaching significantly reduced enamel microhardness (paired t-test, P<.05). P2P4 and P2P24 significantly restored enamel microhardness to baseline but P2P9 showed no effect. There was no significant difference on coffee staining of P2P4, P2P9, P2P24 post-bleaching compared to control at 6 hrs, 1, 2, 3, 4 and 5 days (P>.05).

**Conclusion:** Our study indicated that P2P4 and P2P24 significantly improved microhardness of bleached enamel but none of the amelogenin peptides showed effects on coffee staining at 6 hrs, 1, 2, 3, 4 and 5 days.

**Support:** UCSF Catalyst Award, UCSF Department of Orofacial Sciences and NIH/NIDCR R01DE025709
#08 Title: Efficacy of Botox in PTSD Patients Being Treated for Chronic TMD
P GIAO, S CONELLY
San Francisco Veteran Affairs Medical Center, UCSF School of Dentistry

**Objectives:** Chronic pain is the most common cause of long-term disability in the United States, and perhaps among the most difficult to treat due to its subjective nature. Two chronic disorders common in the veteran population, Temporomandibular joint disorder (TMD) and Post Traumatic Stress Disorder (PTSD), often present concomitantly and share negative synergistic relationships. Interestingly, Incobotulinum toxin (Botox) injections into the muscles of mastication as a treatment for chronic TMD pain is effective in reducing myalgia and arthralgia and as an added effect, reduces PTSD symptoms. The study observes the neurological mechanisms behind this effect to further understand the connection between PTSD and chronic pain conditions such as TMD.

**Methods:** This study is double-blinded, randomized, and placebo-controlled. It involves two clinical visits over a six-week period. Eligible patients have diagnoses of both PTSD and TMD. Both clinical visits include a TMJ clinical assessment, an fMRI of the brain, an EMG and ultrasound of the muscles of mastication, and an EKG. At the first visit, patients are given three bilateral Botox or saline injections into the masseter and two into the temporalis. In addition, patients are given a mobile application to monitor their levels of pain, stress, and sleep every day until the follow-up visit.

**Progress report:** Four patients with a diagnosis of TMD and PTSD who have completed the study have been unblinded and one patient is currently enrolled. Pre and post Botox/ saline injection fMRIs will be compared as well as masseter and temporalis muscle thickness.

**Future directions:** The self-reported daily pain management data over the six-week period of the five patients will be analyzed.

**Support:** San Francisco Veteran Affairs Medical Center

#09 Title: Understanding Nerve-Cancer Interactions in Perineural Invasion by Adenoid Cystic Carcinoma
K HAHN, B AVSAROGLU, M TALIEB, J LEE, D VAN DE MARK, M GRUNER, S KNOX, A GOGA
Department of Cell & Tissue Biology, Heme/Oncology, UCSF School of Dentistry, Department of Medicine,

**Objective:** This study evaluates whether impeding nerve-ACC tumor cell communication will improve radiation therapy sensitivity to diminish cancer cell survival and growth. Treating ACC cells with sympathetic and parasympathetic mimetics simulated the in-vivo cancer-nerve cell environment. Cell viability and differential gene expression were examined post-radiation to evaluate the drugs’ effects.

**Methods:** Ratiometric calcium imaging with Fura-2AM dye was used to determine the most effective concentration of drug mimetics with which to expose ACC cells. Spheroids were plated in 96-well plates and incubated with increasing concentrations of isoproterenol (100-1000nM) or carbachol (100-1000nM) and propidium iodide to tag dead cells. Some plates were treated with single 10Gy dose of radiation before imaging. Cells were analyzed via brightfield and fluorescent imaging. Differential gene expression for spheroids exposed to drug mimetics were analyzed with RNA sequencing.

**Results:** Ratio of Fura-2 emission intensities collected at 510nm of 340nm and 380nm excited Fura-2AM was measured to reveal the amount of free-to-bound calcium in ACC cells, a proxy for the activation signal in presence of mimetic drugs. Based on preliminary data, 100nM of each drug was determined as the appropriate concentration. To analyze differential gene expression of cancer spheroids upon mimetic drug treatment, ACC spheroids were treated at these concentrations for 4hr and RNA was isolated from drug-treated and control samples and sent for sequencing. Sequencing analysis is in progress. The effect of drug treatments on viability of irradiated cancer cells was measured by high-content time-lapse microscopy. Automated image analysis using Gen5 Software (Biotek Instruments) was used to determine cell viability.

**Conclusion:** Although results are not statistically significant, comparison of control and 100nM isoproterenol treatment groups suggest that this drug provides ACC cells with some resistance to irradiation. Our work is on-going, and further studies are required to further explore perineural invasion in nerve and ACC cells.

**Support:** Department of Cell & Tissue Biology

#10 Title: Three-Dimensional analysis of Cortical Bone Thickness in Individuals with Non-Syndromic Unilateral Cleft Lip and Palate
HJ HAN, J KO, W HOFFMAN, S OBEROI
Departments of Orofacial Sciences and Plastic and Reconstructive Surgery, UCSF School of Dentistry

**Objectives:** The aim of this study was to measure the cortical bone thickness of the infrazygomatic crest area in individuals with unilateral cleft lip and palate using cone beam computed tomography for placement of miniplates used for bone anchored maxillary protraction.

**Methods:** CBCT scans were obtained from 31 non-syndromic UCLP children diagnosed with maxillary hypoplasia (17 males, 14 females, mean age: 11.9 years). 5 horizontal and 5 vertical reference planes were drawn at the infrazygomatic crest area. The cortical bone thickness at 25 intersection points on the cleft side and the non-cleft side was measured.

**Results:** The mean cortical bone thickness of the 25 measured points was 1.19 mm on the cleft side and 1.17 mm on the non-cleft side with no significant difference. The greatest cortical bone thickness was found to be at the most superior, posterior point, which...
was 1.49 mm on the cleft side and 1.47 mm on the non-cleft side. The thinnest mean cortical bone thickness was measured at the most inferior, anterior point, which was 0.94 mm on the cleft side and 0.95 mm on the non-cleft side. There was no significant difference between males and females.

**Conclusion:** Our data suggests that miniplates should be placed superiorly and posteriorly at the infrazygomatic crest area, as the area has the greatest cortical bone thickness.

**Support:** Department of Orofacial Sciences

---

**#11 Title: California Older Adults Lack Dental Coverage and Access to Care**

M HAO, A KOTTEK, E MERTZ

Healthforce Center at UCSF, UCSF School of Dentistry

**Objectives:** Medical coverage is almost universal through Medicare when individuals reach age 65, but dental coverage is often lost for these older adults. This project describes the current state of dental coverage and access, examines the settings in which dental services are delivered, and investigates dental initiatives in the past 10 years with a focus on individuals ages 65 and over in California.

**Methods:** Quantitative data was collected from publicly available databases (i.e., California Health Interview Survey, Medical Expenditures Panel Survey, California Department of Health Care Services) and published literature. Qualitative data was collected from a literature review, secondary data, and interviews with key stakeholders.

**Results:** California’s older adults have lower dental insurance coverage (53.4% ages 65-84; 42.3% ages 85+) compared to adults ages 18-64 (68.1%) in 2017; however, adults ages 65+ have higher utilization rates (46.3%) compared to adults ages 21-64 (39.1%). Settings utilized by older adults vary depending on level of dependency, geographic residence, and insurance coverage. Many federal and state policies intend to help improve older adult oral care, but lack of direct services, oral health funding, and regulatory enforcement makes it difficult for older adults to have universal access to dental care.

**Conclusion:** There are critical gaps in federal and state policies that contribute to the low rate of oral health coverage and access for older adults in California. This analysis illustrates the need for supportive policy initiatives to provide adequate coverage, service delivery, and provider training for this population.

**Support:** West Health Policy Institute

---

**#12 Title: Investigating the Role of Adaptor Proteins Crk/Crkl in Craniofacial Development**

E HARRIS, J BUSH

Department of Cell & Tissue Biology, UCSF School of Dentistry

**Objectives:** Src homology 2 (SH2) domain adapters are critical for receptor tyrosine kinase (RTK) signal transduction. Crk (c10 regulator of tyrosine kinase), and its paralog Crkl are SH2 domain adaptors implicated in mediating signaling by RTKs, particularly EphB2, an RTK important for secondary palate development. Crk loss of function has been reported to result in cleft palate and vascular defects in mice and Crkl has been implicated in DiGeorge/del22q11 syndrome, demonstrating defects in craniofacial development. We sought to better understand Crk and Crkl signaling in its control of craniofacial development and contribute to orofacial clefting by examining both single and compound loss of function of Crk and Crkl.

**Methods:** Embryos used for histology studies were derived from crossing Crklox/+ ; Crkllox/+ ; Osr2 Irescre/+ mice with Crklox/lox; Crkllox/lox conditional floxed mice in order to generate different combinations of Crk; Crkl compound mutants. Embryos were dissected at E15.5 and obtained according to standard animal protocol. Histological analysis was then performed.

**Results:** While phenotypes like vascular defects and eye dysmorphology were observed upon loss of Crk or Crkl, loss of either Crk or Crkl alone did not result in a cleft palate. Complete loss of Crk and Crkl resulted in a dramatic cleft palate phenotype, with reduced/malformed palatal shelves and loss of epithelial adhesion to the palatal mesenchyme. In addition to vascular phenotypes, there was blebbing and loss of epithelial adhesion among both single and double knockouts.

**Conclusions:** Crk and Crkl play overlapping and redundant roles in multiple aspects of development, including epithelial adhesion and vascular development. Cleft palate was only observed when Crk and Crkl were both lost from the secondary palate mesenchyme, supporting redundancy between these genes in craniofacial development.

**Support:** Program in Craniofacial Biology, R01DE023337

---

**#13 Title: Alternative and Biomedical Oral Health Approaches: Central Valley Hmong Community**

MZ HER (1), KS HOEFT (1), D HELSEL (2)

(1) Department of Preventive and Restorative Dental Sciences, UCSF School of Dentistry, (2) Department of Sociology, CSU Fresno

**Objectives:** Previous research demonstrates continued use of local alternative healing in the Hmong community, such as herbal medicine and healing with shamans, but no research to date has looked at alternative healing practices for oral health concerns and how that interplays with care-seeking behaviors of biomedical dental care. This study seeks to understand how the Central Valley Hmong community uses alternative healing and biomedical dental care for their oral health needs.
Methods: Hmong adult community members and key informants (shamans) were recruited through flyer distribution, social media, and Hmong-affiliated non-profit organizations. Individual, semi-structured ethnographic interviews asked about participants’ oral health beliefs, use of alternative healing, and attitudes and behaviors toward biomedical dental care. Interviews were audio-recorded, transcribed, and coded for emerging themes with Dedoose software.

Results: 18 community members and 4 practicing shamans (30-75 years old, 63.6% female) were interviewed. Participants believed dental pain is a result of infections and poor oral health but some believe there are spiritual associations. Home remedies for general health were common among all community members but herbal medicine and shamans were used for dental pain mostly by elders. Younger members cited a stronger science understanding and lack of knowledge on herbal medicine and shamans as barriers for alternative approaches. Most participants viewed biomedical dental care as a quick remedy for dental pain instead of prevention. Both groups cited dental fears and language and financial barriers as major factors in the use of alternative approaches.

Conclusions: The continued use of alternative healing, especially among elders, toleration of dental pain, and language and financial barriers can delay seeking biomedical dental care, leading to more extensive and expensive dental procedures. This result can serve as a foundation for future research and guide service groups to better meet the oral health needs of the Hmong.

Support: Global Oral Health Program | UCSF School of Dentistry

#14 Title: Assessing Data Quality from Caries Risk Indices Captured in Electronic Health Record

N HWANG, A YANSANE, JM WHITE

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

Objective: The objective of this study was to assess how well dental clinicians chart findings in the Electronic Health Record (EHR) and how it affects a variety of caries indices calculated from Valid Electronic Health Record Dental Caries Indices Calculator Tool (VERDICT) in AxiUm.

Methods: Patients who had scheduled comprehensive or periodic oral examinations were recruited from the general dentistry faculty and resident clinic. Subjects received a complete clinical examination by their clinician. The VERDICT algorithm determined patients carries indices. Then, a trained calibrated assessor performed a clinical examination and a manual comparison of the EHR was performed (DMFT, DMFS, DT, MT, FT, DS, MS, FS, T and S). Discrepancies between any of the ten measures were noted. The correlation between the number of caries indices from what is determined by VERDICT and what is seen through clinical examination was then calculated (Lin's concordance correlation coefficient).

Results: Results are shown in the table below.

<table>
<thead>
<tr>
<th>Indices</th>
<th>LCC</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMFT</td>
<td>0.985</td>
<td>0.977</td>
<td>0.990</td>
</tr>
<tr>
<td>DMFS</td>
<td>0.996</td>
<td>0.994</td>
<td>0.997</td>
</tr>
<tr>
<td>DT</td>
<td>0.705</td>
<td>0.579</td>
<td>0.797</td>
</tr>
<tr>
<td>MT</td>
<td>1.000</td>
<td>1.000</td>
<td>1.000</td>
</tr>
<tr>
<td>FT</td>
<td>0.989</td>
<td>0.984</td>
<td>0.993</td>
</tr>
<tr>
<td>DS</td>
<td>0.969</td>
<td>0.952</td>
<td>0.980</td>
</tr>
<tr>
<td>MS</td>
<td>1.000</td>
<td>1.000</td>
<td>1.000</td>
</tr>
<tr>
<td>FS</td>
<td>0.997</td>
<td>0.995</td>
<td>0.998</td>
</tr>
<tr>
<td>T</td>
<td>0.992</td>
<td>0.987</td>
<td>0.995</td>
</tr>
<tr>
<td>S</td>
<td>0.874</td>
<td>0.813</td>
<td>0.917</td>
</tr>
</tbody>
</table>

Conclusions: Measures DMFT, DMFS, MT, FT, DS, MS, FS, and T have correlations above 0.900 which indicates excellent correlation. Measure S has a correlation between 0.750 and 0.900 which indicates good correlation. Measure DT has a correlation between 0.500 and 0.750 which indicates moderate correlation.

Support: Buchannan Dental Clinic

#15 Title: Availability and Affordability of Ready to Drink Beverages and Oral Hygiene Products in Kenya

A JAN (1,4), V KASAR (1,4), C SKACH (1,4), S LEWIS (1), P PATEL (1), D RAMACHANDRAN (1), D KIMATHI (3), L MUTHONI (3), T NTIMAMA (3), I WANJIRU (3), B CHAFFEE (1), K HOEFT (1), S KAPILA (2), R MUTAVE (3).

1) Department of Preventive and Restorative Dental Sciences, UCSF School of Dentistry 2) UCSF School of Dentistry, Department of Orofacial Sciences, 3) University of Nairobi School of Dental Sciences, 4) All authors contributed equally as first authors

Objective: Evaluate cost and availability of ready-to-drink-beverage (RDB) and oral-hygiene-product (OHP) in Kenyan stores.

Methods: This cross-sectional study investigated products at stores in Nairobi (n=4) and Meru (n=5), Kenya. A convenience sample of store locations was selected based on traffic and group safety considerations. A standardized intake form was used to record: 1) RDB: price, type of beverage, sugar content, number of brands, and numbers of products displayed on shelves, 2) common sized beverages: highest and lowest price, 3) OHP: price and number of different products available. Inclusion criteria for RDB were single bottles (<1000-mL). Photographs were taken of all RDBs in each store and later used to record beverage type and sugar content. The OHPs recorded were: adult and child toothbrushes, fluoridated and non-fluoridated mouthwashes and toothpastes. Descriptive statistics were calculated and compared using a paired t-test and Wilcoxon test.
Objective: To investigate how dental schools in the United States embed Oral Hygiene Instructions (OHI) into their pre-doctoral curriculum and to incorporate this information to develop an interactive education module to teach OHI to students in UCSF’s predoctoral program.

Methods: This research project will progress in three stages. The first stage will be to develop an online survey which will be distributed to all dental schools in the United States to understand how each school teaches OHI to their dental students and how they assess their students’ ability to give OHI to a patient. The second stage will be to gather and analyze insights from the other dental schools’ curriculum and determine the impact different teaching styles have on the efficacy of teaching OHI. The third stage will be to develop optimal curriculum enhancements to the way UCSF teaches OHI to dental students, and by proxy, how dental students teach OHI to patients.

Results: The results of our survey will illuminate the differences and similarities in predoctoral dental programs around the country and provide insight into how OHI is taught in different manners.

Conclusion: In this work-in-progress study, we plan on discussing how UCSF School of Dentistry can how their predoctoral students teach OHI to their patients. Based on the findings from other dental schools, we aim to create a hands-on, interactive module to enhance how UCSF students teach OHI that is patient-centered. In the future, we plan to measure how effective the UCSF curriculum change was to improving how dental students teach OHI and how patient behavior was modified.

Support: UCSF ADEA Academic Dental Careers Fellowship Program

#17 Title: The cellular dynamics of intersphenoid synchondrosis (ISS) abnormal fusion in Costello syndrome

S KEEFE, A SHARIR

Department of Orofacial Sciences, UCSF School of Dentistry

Objective: Costello syndrome (CS) is caused by a heterozygous de novo gain-of-function mutation in HRAS. CS patients exhibit dysmorphic craniofacial features including a prominent forehead, distinctive mid-facial features, and a variety of tooth malocclusions. While much is known about the causative gene for CS, far less is known about the mechanisms underlying craniofacial manifestations of the syndrome. We established a mouse model of CS that expresses a gain-of-function Hras variant specifically in neural crest-derived cells (Wnt1Cre;HrasG12V) and recapitulates the craniofacial abnormalities observed in CS individuals. In this model, we observed abnormal development of the intersphenoid synchondrosis (ISS), one of the main growth centers responsible for longitudinal growth of the cranial base. The aim of this project is to determine how hyperactivated HRAS affects the maturation and differentiation of the ISS, and whether the abnormal ISS fusion in CS is a cell-autonomous event.

Methods: Micro-CT and skeletal preparation. Single molecule RNA in-situ hybridization and fluorochrome injections were used to assess ISS differentiation and mineralization patterns. Lastly, ISS explants were cultured using Trowell’s method.

Results: Micro-CT analysis revealed significant differences in cranium shape and abnormal fusion of ISS at P21 in CS mice. In-situ hybridization showed similar expression of chondrocyte markers (Col2, ColX, and Ihh) in CS and control mice, while osteoblast markers (Col1, Spp1 and Sp7) were increased in CS mice at P3. Fluorochrome injections revealed an abnormal ossification of the lateral aspect of the ISS at P5 in CS mice. However, ISS explants exhibited normal growth.

Conclusion: Hyperactivated HRAS in CS causes abnormal closure of the ISS, which limits the elongation of the anterior skull base during postnatal development. Furthermore, the lack of ISS fusion in the CS explant suggests that this is not a cell-autonomous event.

Support: The Department of Orofacial Sciences and NIH Grant R35DE026602
#18 Title: UCSF DentiCal Experience of Preventative Dental Care from 2016-2018

T KHORASANI, AA LAZAR

Department of Preventive and Restorative Dental Sciences, UCSF School of Dentistry and the CAN DO (Center to Address Oral Health Disparities)

Objective: Despite the availability of federal dental coverage, utilization of dental benefits among those federally covered was 45%, and, of those that used federal benefits, 73% used it for preventative care. These results imply that federal dental coverage may not increase dental health utilization. This study’s objective was to assess preventative dental care utilization of patients who received DentiCal at the UCSF Predoctoral Clinic.

Methods: A retrospective chart review of the UCSF Axium patient database was used to extract DentiCal patients seen at the UCSF Clinic between 2016 to 2018. Exclusion criteria were edentulous patients and patients discontinued from the predoctoral clinic. Preventative care was defined as follows: Periodic oral exams (POE), comprehensive oral exams (COE), all CAMBRA products dispense, prophylaxis, caries risk assessment, periodontal maintenance, fluoride varnish and topical, preventative resin restorations, 1 month periodontal evaluations, sealants, caries arrest medication, de-sensitizing agents, and occlusal guards.

Results: The UCSF Predoctoral clinic’s preventative participation among DentiCal patients was 70% (3505/5008 patients), and the remaining 1,503 patients (30%) received non-preventative care between 2016-2018. Of those that received preventative care in 2016, 33% of those patients returned for preventative care in 2017 and 10% returned in 2017 and 2018. Among all patients seen for preventative care in 2018, 42% were previous patients with no preventative care for at least two years.

Conclusion: At UCSF predoctoral clinic, utilization of preventative care was high at 70% among DentiCal patients seen each year. This usage was comparable to the national utilization rate at 73%. However, continuation of preventative care was low over the three years. Longer follow-up is needed to assess whether utilization of preventative care changes over time.

Support: Delta Dental Community Care Foundation

#19 Title: Spatiotemporal Maps of Implant-Bone Biomechanics In situ

D KIM (1), B WANG (1), S WHEELIS (2), D RODRIGUES (2), M KANG (1), S HO (1)

(1) Department of Preventive and Restorative Dental Sciences, UCSF School of Dentistry, (2) Department of Bioengineering, University of Texas at Dallas

Objective: Physical and chemical characteristics of craniofacial bone adjacent to implant were correlated in three-dimensional space and time to gather insights into functional osseointegration of dental implant using a rat model.

Methods: 0.76 mm titanium-based rat dental implants were placed in the maxillary bone of 12 male Lewis rats divided into three groups (N =3/group; 3, 11, and 24 days). After implant placement, all rats were subjected to hard diet (hard pellet food), and euthanized at time points of 3, 11, and 24 days. Biomechanical testing was performed to extract stiffness of implant-bone complex and load to failure. The complex was scanned by X-ray-micro CT for 3D imaging. Digital volume correlation was performed to map localization of strain within bone. Spatial maps and colocalization of calcium, phosphorus and zinc using microprobe X-ray fluorescence spectroscopy was performed.

Results: Figure – Volume rendered X-ray tomograms of implants with bone are shown in row 1 (R1). Virtual slices indicated changes in spatial proximity of bone with implants. Three days of implantation illustrated contact between implant and bone, indicative of mechanical interlocking (R2C1, R3C1). However, 11 days of implantation illustrated an increased compressive strain profile within an organic matrix (R2, R3&R5, C2) around the implant. The load to failure and stiffness of the implant-bone complex initially decreased, but over time, increased significantly (R6). Higher levels of Zn were observed at the implant-bone interface and were analogous to the ligament-cementum interface.
Conclusion: The initially observed compressive strains could resorb bone resulting in an organic construct in close proximity to the implant. However, prolonged function (chewing) could alter the compressive strain profile to tension with increased mineralization of the organic matrix around the implant.

Support: This project was supported by Delta Dental Community Care Foundation and NIH/NIDCR R01 NIH/NIDCR - R01 DE022032 (SPH).

#20 Title: A Direct-to-Consumer split may be an alternative to traditional splint therapy

R LE. R SILVA

Department of Oral & Maxillofacial Surgery, UCSF School of Dentistry, and San Francisco VA Health Care System Department of Veteran Affairs

Objectives: Bruxism is a common dental malady, causing dental damage, muscular pain, and headache. There are no studies comparing traditional dentist-made splints to direct-to-consumer splints, where patients make their own impressions. This study seeks to establish the characteristics of patients seeking splint treatment and to determine the factors that influence satisfaction and thus would be predictive of a positive outcome with either a traditional or direct-to-consumer splint.

Methods: Adult subjects (N=38) with a history of bruxism were recruited at the San Francisco VA Medical Center. All subjects underwent pre-treatment assessment consisting of a clinical exam, panoramic radiograph, and questionnaire. Patients underwent impressions for a traditional splint and made their own impressions for the direct-to-consumer splint after viewing an online tutorial and reading the product instructions. Following delivery of each splint, patients were reassessed after a minimum of a 2 week period of use. Traditional splints were adjusted by the dentist and direct-to-consumer splints were delivered without adjustment. Subjects were queried on their experience with each splint and asked to compare both devices.

Results: The average patient age was 56 (range 31-80). The most common objective finding was dental wear (97%), with most patients reporting muscular pain (45%). Most patients completing the study preferred the traditional splint (71%) over the direct-to-consumer splint, and this preference was no different among younger age groups. When using the direct-to-consumer kit, many patients required assistance due to errors in selecting tray size, mixing the putty material, and assessing impression quality.

Conclusions: Splint therapy is beneficial for patients who brux and a direct-to-consumer splint may be suitable for those with good manual dexterity who can follow online instructions and those who cannot afford a traditional splint that is delivered and adjusted by a dentist.

Support: Summer Research Fellowship Program and Dental Service, San Francisco VA Health Care System
#21 Title: Fluoride Levels in Drinking Water Sources of Urban and Rural Kenya: A Preliminary Study

S LEWIS, P PATEL, D RAMACHANDRAN, A JAN, V KASAR, C SKACH, D KIMATHI, N TATIYIA, I WANJIRU, L MUTHONI, C LE, L ZHAN, S KAPILA, B CHAFFEE

Departments of Preventive Restorative Sciences and Orofacial Sciences at UCSF School of Dentistry, and University of Nairobi School of Dental Sciences

Objectives: Dental fluorosis, a factor contributing to early enamel defects and caries risk, is a known public health concern in various parts of Kenya. Fluoride is reported as a natural pollutant of drinking water sources in Kenya. However, few studies report fluoride concentration of drinking water sources from urban and rural regions in Kenya. The primary objective of this study is to determine the fluoride concentration of water sources supplying houses, schools, and stores in provinces near Meru and Nairobi. Additionally, the study aims to determine whether fluoride levels in available toothpaste products are as advertised and can serve as a reliable supplement.

Methods: Fourteen samples were collected at convenient roadside sites ranging from Meru to Nairobi provinces of Kenya (10 Meru, 3 Ruiru, 1 Kamdini) during the dry season (March-April 2019). Samples were collected in polypropylene vessels and analyzed using a fluoride assay. Thirty four toothpaste samples were collected, 15 were analyzed and the remaining are in-progress. Fluoride concentrations were determined using a fluoride ion selective electrode. A calibration with fluoride standards was used for fluoride estimation. Total fluoride (TF) was analyzed for water and toothpaste samples, in addition to total soluble fluoride (TSF) for toothpaste samples.

Results/Conclusions: The fluoride concentration in drinking water ranged from 0.08-0.70ppm, with only one sample reaching 0.70ppm. TF for 14 of 15 toothpaste samples and TSF for 13 of 15 toothpaste samples were within 10% of advertised fluoride levels. Results indicate soluble fluoride in most available toothpaste products match labeled values, but there is a broad range of fluoride levels in drinking water. Future studies can assess water fluoride levels throughout Kenya, in addition to evaluating whether toothpaste products can be used as a source of fluoride for areas with inadequate water fluoride levels.

Support: UCSF School of Dentistry Research and Clinical Excellence Day 2019 Program

#22 Title: Sugar Industry Involvement in Cyclamate Research: A Historical Analysis of Internal Documents, 1962-1970

K LOVELL, CE KEARNS

UCSF School of Dentistry, Philip R. Lee Institute for Health Policy Studies, UCSF

Objectives: Over 130 countries have approved cyclamates, a class of artificial sweeteners, for use in foods and beverages; however, the U.S. Food and Drug Administration (FDA) banned them in 1970. The Sugar Research Foundation (SRF), a sugar industry trade group, funded research on cyclamates between 1962-1970 that contributed to the FDA’s decision. The objective of this study was to describe the planning and implementation of SRF’s cyclamate research program.

Methods: We searched the University of California, San Francisco Library Food Industry Documents Archive for internal sugar industry documents that pertained to SRF’s cyclamate research program. We used a snowball strategy to identify related documents and external sources to triangulate and contextualize findings. We chronologically organized relevant documents and identified emerging themes.

Results: Faced with the economic threat of the popularity of cyclamates in the 1960s, SRF’s position was that cyclamates were neither safe nor therapeutic. SRF supported this position by: 1) hiring a public relations firm, 2) engaging scientific advisors to plan a research program, and 3) funding 64 research projects at 14 universities in the US and internationally between 1962-1970. SRF disseminated their position through: 1) 29 scientific publications, 2) press releases, 3) sending spokesman to engage with FDA leadership, 4) correspondence with the FDA, and 5) an advertising campaign.

Conclusion: SRF conducted a sophisticated public relations program with the aim to discredit evidence of the safety of cyclamates and of their efficacy in weight loss, obesity, and cardiovascular disease. Further scrutiny of bias in sugar industry funded studies of artificial sweeteners is warranted to ensure that regulatory decisions have been made in the public’s best interest.

Support: John C. Greene Fund

#23 Title: Differential Regulation of Mmp13 by Runx2 Isoforms

A LUCENA, S SMITH, D CHU, R SCHNEIDER

Department of Orthopaedic Surgery, UCSF School of Medicine

Objective: Runx2 is an important transcription factor that binds numerous target genes and plays many roles, from inducing osteogenesis to promoting collagenases (e.g., Mmps) during bone resorption, ultimately regulating jaw length. In the developing jaw skeleton of birds, eight isoforms of Runx2 are expressed, consisting of two promoter regions (1 or 2), an alternatively spliced variable exon (A or B), and alternative C-termini (1 or 2). The goal of this project is to determine if each Runx2 isoform is activating or repressive when binding to its generic target sequence and when binding to the promoter of a known Runx2 target gene, Mmp13.

Methods: DF-1 (chick) and CCL-141 (duck) fibroblast cells were transfected with three Runx2 isoforms as well as a synthetic promoter containing Runx2 binding sites (OSE2), or Mmp13 promoter sequences (with/without a Runx2 binding site). Promoter
activity was measured by luciferase. Mmp13 mRNA and protein levels were measured in response to Runx2 isoform over-expression. Statistical significance was established using a t-test.

**Results:** 1A1 and 2A1 isoforms induced OSE2 activity while 2B2 was repressive. When transfected with the endogenous Mmp13 promoter, 1A1 diminished activity in DF-1 cells while 2A1 and 2B2 increased activity. In CCL-141 cells, all isoforms increased activity compared to controls. Mmp13 mRNA and protein data corroborate the luciferase results. Statistical analysis was done using a Student's t-test.

**Conclusion:** Comparing 2B2 to other isoforms reveals that exon (A) and/or interchangeable C-terminus 1 could be important for affinity to the binding site. 2B2 induced high Mmp13 activity in both cell types, indicating that adjacent promoter elements to the binding site are important for Mmp13 expression. Comparing activity of 1A1 to 2A1/2B2 isoforms shows that promoter 1 variants are repressive in DF-1 cells but activating in CCL-141. More isoforms need to be tested to strengthen the support of these trends.

**Support:** The Associate Dean for Research Student Research Fund, NIH Grants R01DE025668 and R01DE016402 to RAS, and F32DE027283 to SSS.

#24 Title: Polymicrobial-Induced Periodontal Disease Triggers a Wider Radius of Effect

A.MARTINEZ, L GAO, M. KANG, R. KURAJI, C. YE, K PACHIYAPPAN, C LE., L ZHAN, H RANGÉ, S HO, YL KAPILA.

Department of Orofacial Sciences, School of Dentistry, UCSF, Department of Periodontology, Guanghua School of Stomatology, Hospital of Stomatologie, Sun Yat-sen University, Guangzhou, China, Department of Preventive and Restorative Dental Sciences, School of Dentistry, UCSF, Department of Life Science Dentistry, The Nippon Dental University, Tokyo, Japan, Department of Periodontology, The Nippon Dental University School of Life Dentistry at Tokyo, Tokyo, Japan, State Key Laboratory of Oral Diseases, National Clinical Research Center for Oral Diseases, Department of Periodontology, West China School of Stomatology, Sichuan University, Chengdu, China, Université de Paris, Department of Periodontology, U.F.R. of Odontology, F-75006 Paris France; Service of Odontology, AP-HP, Rothschild Hospital; Laboratory Orofacial Pathologies, Imaging and Biotherapies, EA 2496, Montrouge France

**Objectives:** Periodontal disease is a microbially-mediated inflammatory disease of the tooth-supporting tissues. This polymicrobial infection triggers a host-immune response and proteolytic tissue destruction that leads to bone, periodontal ligament, cementum, and gingiva loss around teeth. Although the bacterially-mediated mechanisms of alveolar bone destruction have been widely studied, the effects of the microbial challenge on the periodontal ligament have not been well explored. Therefore, the current investigation introduced a new mouse model of periodontal disease to examine the effects of a polymicrobial infection on periodontal ligament properties, changes in bone loss, and the host immune response.

**Methods:** Periodontal pathogens, namely Porphyromonas gingivalis, Treponema denticola, Tannerella forsythia, and Fusobacterium nucleatum were used as the polymicrobial oral inoculum in a common mouse strain. Alveolar bone loss measured morphometrically, serum antibody response to the bacterial challenge as assessed by ELISAs, immune gene profiling, and changes in periodontal ligament width dimensions as determined by micro-CT were evaluated following bacterial challenge.

**Results:** The polymicrobial infection triggered significant alveolar bone loss, a heightened antibody response to the pathogens, an elevated cytokine immune response, and a widening of the periodontal ligament space; the latter has not been previously reported in disease models.

**Conclusions:** These changes in the periodontal ligament space were present at sites farther away and apically from the site of insult, indicating that the polymicrobial radius of effect extends beyond the bone loss areas and site of initial infection. This new polymicrobial mouse model of periodontal disease in a common mouse strain is useful for evaluating the features of periodontal disease.

**Support:** This study was supported by an NIH R01 DE025225 grant and AAP Sunstar Innovation grant to YLK and NIH R21 DE027138 and R01 DE022032 to SPH. Additional support provided by the UCSF School of Dentistry Dean's Office.

#25 Title: Assessing UCSF Health Trainees' Preparedness to Address LGBTQIA+ Health

B MORGAN, G ESSEX

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

**Objectives:** Lesbian, gay, bisexual, transgender, and queer (LGBTQ) populations face health disparities linked to discrimination and social stigma that can limit access to healthcare. This project expands a 2018 study at UPenn investigating healthcare trainees' preparedness to treat LGBTQ patients which found that dental students at UPenn were significantly less interested in receiving formal LGBTQ health education than their peers in medicine. Our survey aims to assess UCSF predoctoral health professions students' comfort level, attitudes, and preparedness to care for LGBTQIA+ patients in order to investigate how well UCSF is preparing its students to address this community's health needs.

**Methods:** Survey questions were adapted from the Greene et al. (2018) study to arrive at a seventeen-item questionnaire. We expanded the scope of the original study from dental, medical, and nursing students to also include students in UCSF pharmacy and physical therapy programs. The new Qualtrics survey was sent to students via UCSF Listservs. Basic demographic information was collected but the survey was otherwise anonymous. 218 responses were compared across program and gender/sexual minority status.

**Results:** Dentistry, Nursing, and Pharmacy students rated their program’s culture as significantly less welcoming toward members of the LGBTQIA+ community than Medicine and Physical Therapy students (p<0.05), with Dentistry being least welcoming (62.5 on
D Patel, C Santa Maria, W Chang, D Nguyen, M Bacino, E Babaie, S Habelitz

Lesions. Subsequently, specimens were immersed in remineralization solution with fluoride (0.1, 2.5ppm) for 14 or 28d and analyzed with optical microscopy, SEM, and Energy-Dispersive-X-Ray-Spectroscopy (EDX). Intrafibrillar mineralization was evaluated by measuring resistance to tissue removal from bleaching with 7% NaOCl and statistically analyzed (Tukey, p<0.05).

Methods: Dentin slices were sectioned from human molars and deminerlized to create shallow (140um) or deep (700um) artificial lesions. Subsequently, specimens were immersed in remineralization solution with fluoride (0.1, 1.2, 2.5ppm) for 14 or 28d and analyzed with optical microscopy, SEM, and Energy-Dispersive-X-Ray-Spectroscopy (EDX). Intrafibrillar mineralization was evaluated by measuring resistance to tissue removal from bleaching with 7% NaOCl and statistically analyzed (Tukey, p<0.05).

Results: Optical microscopy suggested that lesions shrink minimally after remineralization for all treatment groups (p>0.05). SEM images for lesions remineralized with fluoride showed mineral precipitate (>100um) on the lesion surface. EDX analysis indicated that the main mineral phase was a mixture of hydroxyapatite and fluorapatite. The lesion zone disintegrated when exposed to bleach, indicating that remineralization failed to protect the tissue. Conversely, lesions remineralized with PILP and fluoride were resistant to bleach treatments and did not show signs of disintegration at 24h NaOCl exposure. SEM microscopy of PILP-treated specimens displayed fully remineralized dentin structurally similar to sound dentin. No surface precipitate of mineral was observed. Calcium and phosphate analysis by EDX showed full recovery of ions throughout the entire lesion comparable to sound dentin.

Conclusion: Fluoride in calcium phosphate solution creates predominantly surface precipitation, but is unable to induce intrafibrillar mineral in collagen. Functional remineralization of dentin lesions requires the presence of pAsp. Therefore fluoride-based strategies to remineralize enamel cannot be translated for repair of carious dentin.

Support: Center for Dental, Oral & Craniofacial Tissue & Organ Regeneration (C-DOCTOR), Department of Preventative and Restorative Dental Sciences, UCSF School of Dentistry, and UCSF Catalyst Award "PILP Treatment for the Repair of Dental Caries"
#28 Title: Adipocytes Emerge in Salivary Glands Post Irradiation

E PEREIRA, D SCHEEL, Z BROWN, Y OGURI, S. MOHABBAT, S KNOX, S KAJIMURA

UCSF School of Dentistry, Diabetes Center, Diabetes Center, Center, Dept. of Cell and Tissue Biology, Dept. of Cell and Tissue Biology

Objective: Treatments for head and neck cancers often incorporate radiation therapy, which can lead to salivary gland dysfunction. We seek to understand this phenomenon by determining whether salivary gland irradiation leads to the adipocyte emergence, thereby causing dysfunction.

Methods: The salivary glands (SGs) of 6 mice−n=2 aged 7, 9, and 10 weeks−were irradiated with 5 Gy; n=2 mice aged 7 and 10 weeks were not irradiated. At day 14 and 30, submandibular glands (SMG) and sublingual glands (SLG) were harvested, fixed, washed, dehydrated in sucrose, and frozen in OCT at -80°C. Glands were cryo-sectioned at 12μm and stained via H&E. For IHC, after permeabilizing the SG’s with 0.5% Triton X-100 in PBS for 10min, samples were blocked in PBST containing 5% BSA, 10% donkey serum for 2h, followed by incubation with primary antibodies against Sox2(1:200) or perilipin(1:200) overnight at 4°C. Staining was then done with primary antibodies against KRT8(1:200), perilipin(1:200), or UCP1(1:200). The slides were stained with secondary antibodies(1:300) for 2h at room temperature, then treated with Hoechst 33342(1:1000).

Results: SLG harvested from irradiated 14-week old mice 30 days post-exposure displayed abnormal acini morphology and irregular duct formation via H&E. IHC for adipocyte marker perilipin indicated lipid droplet emergence in cells surrounding ducts. Furthermore, co-staining for SG progenitor marker Sox2 indicated no co-localization. A second round of IHC was done with KRT8 and UCP1. Perilipin was noted in the irradiated and control mice, but co-staining with KRT8 and UCP1 indicated no perilipin co-localization.

Conclusion: We found that after irradiation, a small subset of cells adjacent SLG ducts exhibit lipid droplets. Further research should test the hypothesis with more mice to understand adipocyte emergence frequency and to test the effect of age.

Support: This project was supported by the Summer Dental Student Fellowship Program

#29 Title: Perceived Dental Provider Communication and Treatment Comprehension Among Mexican-origin Adults

G QUINTERO, KS HOEFT, GX AYALA, M SCHIAFFINO, A PATRON, TL FINLAYSON

Department of Preventive and Restorative Dental Sciences, UCSF School of Dentistry; School of Public Health, San Diego State University; and the Institute for Behavioral and Community Health

Objectives: Mexican-origin adults experience higher oral health diseases than non-Hispanic whites, including root and untreated caries. This study explores comprehension of oral health information (health literacy) and communication in the dental clinic which could be protective factors, but are underexplored in this population.

Methods: This is a secondary data analysis of 71 semi-structured interviews (both English and Spanish) about individuals’ oral health behaviors and dental experiences from an existing study. Adults age 21-40 were recruited from two clinics and surrounding communities in northern San Diego and Imperial Counties, California. Interviews were transcribed in original language and thematically analyzed using Dedoose Software.

Results: Participants’ average age was 31±7, 54% men, 49% single, 54% Spanish-language dominant, and 56% U.S.-born. Though most participants were able to name dental treatments, such as “filling” and “root canal”, many did not describe their treatment in detail beyond the procedure title. Negative Encounters with providers revolved around themes related to: participants feeling their pain was disregarded; fear/ anxiety; treatment plans not being well-communicated; and lack of information. Negative Encounters sometimes led to participants refusing to return to that provider (or seek dental care at all). Positive Encounters shared a theme of comfort, and described providers who listened, were responsive to pain, answered questions, were informative, and were perceived as trustworthy. Those with Positive Encounters were more likely to go back to the same provider and trust them with their dental care. Most participants claimed language was not a barrier in their interactions since offices usually had Spanish language interpreters.

Conclusion: Participants reported communication deficits, beyond a language barrier deficit, as a factor in poor dental encounters among Mexican-origin adults. Provider listening, patience, explanation, and pain management influenced perception of dental encounter and regular care. Effective communication skills should be considered part of standard of care.

Support: This project was supported by NIH/NIDCR DE026742 and the UCSF Program in Global Oral Health

#30 Title: Oral manifestations of HIV/AIDS: a pilot interprofessional health education module

S SAINI, AR LERMAN, L DORAN-GARCIA, K JONES, S HYDE

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

Objectives: HIV/AIDS is a global health concern impacting oral and systemic health. There are few programs within the U.S. focused on interprofessional oral health education related to HIV/AIDS. This study aims to (1) develop a training module to educate health professional learners to identify common oral signs of HIV/AIDS and (2) measure levels of comfort with self-assessed skills.

Methods: A training module provided UCSF interprofessional health learners with an introduction to oral health and its significance to systemic health, the disease process of HIV/AIDS, and recognition of oral disease indicators of HIV. Pre- and post-module evaluations were administered via Qualtrics and analyzed using non-parametric methods.
Results: Sixty-three pre- and 35 post-module evaluations were completed. Respondents were primarily female (68%), 25-29 years-old (56%), from the School of Pharmacy (60%), and second-year learners (56%). There was significant improvement between pre- and post-scores for being comfortable screening for oral diseases related to HIV, describing oral findings, and describing the common clinical oral manifestations of HIV/AIDS (all p<0.0001). No significant improvement was found in the scores for oral health being an important aspect of overall health (p=0.9844) or learning about oral health being a valuable part of education for health professional learners (p=0.1049). Seventy-seven percent of learners agreed-to-strongly agreed that the module substantially improved their knowledge of oral health in the HIV disease process.

Conclusion: A ceiling effect of high scores pre-module for oral health being an important aspect of overall health, and learning about oral health being a valuable part of education, resulted in no significant improvement in these scores. Learners post-module felt more comfortable performing oral health screenings, describing oral findings, and identifying oral manifestations of HIV/AIDS. Further training resources should be developed to increase the oral health knowledge of health professional learners and practitioners.

Support: Global Oral Health Community Partnership, UCSF School of Dentistry

#31 Title: Community Information and Oral Health

S SOOFIAN, J CHENG, S GANSKY

Division of Oral Epidemiology & Dental Public Health, Department of Preventive and Restorative Dental Sciences, UCSF School of Dentistry

Objectives: This project seeks to evaluate the value of patients’ social determinants of health in understanding patients’ dental outcomes, in addition to individual-level factors collected in electronic health records (EHR), in order to develop strategies for incorporating such factors into dental care.

Methods: Data was extracted from 2008-2018 EHR from UCSF dental clinics, including patients’ demographics, oral hygiene behaviors, carries risk, dental outcomes, and residential ZIP code. ZIP code-specific variables, including but not limited to, median household income, race/ethnicity composition, employment/population ratio, and educational composition were obtained from US Census archives.

Generalized linear mixed-effect models were used to examine community-level variables for their roles in understanding oral health in addition to individual-level EHR variables in EHR.

Results: At their first visit, 17,094 out of 60,735 (28.15%) patients had at least one untreated decayed lesions, with a mean 1.76 (SD: 4.75). Around 50%, 26%, and 15% of patients had one, two, and three exam follow-ups respectively. In addition to all significant individual-level variables (demographics, enrollment year, insurance, tobacco use, time points, high sugar diet, inadequate saliva, fluoride level, etc.), several community-level variables were significantly and individually associated with the number of untreated decayed lesions, including: percent Hispanic or Latino, percent of families below poverty, percent of households using food stamps, percent of those ≥ 25 years holding a graduate degree, and Gini Index. When all the significant variables were included in the same model, community Gini Index (ranging between 0.1414 and 0.6494) remains a significant predictor (P = 0.0060).

Conclusions: Community-level variables, in particular Gini Index, are valuable predictors of patients’ dental outcomes, in addition to individual-level variables. Future research should explore how these community-level variables can be incorporated into the dental care delivery system in order to provide patients with additional care and public resources to improve their oral health.

Support: Summer Dental Student Research Fellowship Program and the Delta Dental Community Foundation Research Award

#32 Title: Determining pH-dependence of Recurrent Cancer-associated SMAD4-R361H Mutation in TGF-β Signaling

B THANASUWAT, K KISOR, D BARBER

Department of Cell & Tissue Biology, UCSF School of Dentistry

Objectives: A distinct enabling feature of most cancer cells is an increased intracellular pH (pHi), which promotes metastasis and cancer progression. The Barber lab determined that some charge-changing somatic mutations, such as arginine to histidine, confer a gain in pH-regulated protein functions. SMAD4, a transcriptional mediator of TGF-β signaling, is mutated in many cancers with SMAD4-R361H being recurrent. We hypothesize that the R361H mutant gains pH sensing with reduced binding to the transcriptional activators SMAD2 and 3 at the higher pH of cancer cells.

Methods: Recombinant SMAD4-WT and R361H with a GST-tag were generated in E coli, purified on Sepharose, and confirmed using SDS-PAGE. A549 lung cancer cells were treated +/- TGF-β. Cells were lysed in RIPA buffer and incubated with SMAD4 fusion proteins at pH 7.0 or 7.8. After 2 h, binding complexes were isolated on Sepharose resin, separated by SDS-PAGE and the abundance of bound phosphorylated and total SMAD2 and SMAD3 was determined by immunoblotting.

Results: We first analyzed the crystal structure of SMAD4-WT in complex with SMAD3 (PDB-1U7F) and observed a salt-bridge between Arg361 of SMAD4-WT and Asp408 of SMAD3. We reasoned that a deprotonated, neutral His substituted for a positive Arg might confer a lower binding affinity to SMAD2 and 3 at the higher pH of cancer cells. We found that binding of SMAD2 and 3 to WT SMAD4 was robust with lysates from TGF-β treated A549 cells but absent in untreated cells. With TGF-β-treated samples, binding was similar with WT SMAD4 at pH 7.0 and 7.8; therefore, it was pH-independent. Although binding of SMAD2 and 3 to the mutant SMAD4-R361H was similar to WT with incubations at 7.0 there was no detectable binding at pH 7.8. Hence, a higher pH decreased SMAD2 and 3 to SMAD4-R361H, in agreement with our prediction that SMAD4-WT binding to SMAD2 and 3 would be...
pH-independent between pH 7.0 and 7.8, but the His substitution would confer pH-sensitive binding, with less binding at the higher pH of a cancer cell.

Conclusions: Based on our results, the positive charge of Arg and His at position 361 is essential to SMAD4 binding. Substitution of His at this position disrupts binding to SMAD3 in a pH-sensitive manner, resulting in a loss of tumor suppressor function of SMAD4.

Support: This project was supported by a donation Faculty Emeritus Caroline Damsky and Peter Sargent

#33 Title: The role of Yap/Taz in palatal shelf mesenchyme during palatogenesis

N VO, C CHEN, A GOODWIN

Department of Orofacial Sciences, Division of Craniofacial Anomalies, UCSF School of Dentistry

Objectives: The cellular and molecular mechanisms underlying secondary palate development, particularly changes in tissue tension and remodeling, remain elusive. We explored the Hippo pathway, a known mechanosensory signaling pathway that regulates proliferation, apoptosis, and differentiation in palatogenesis, and found that deletion of its downstream effectors Yes-associated protein (Yap) and transcriptional co-activator with PDZ-binding motif (Taz) in palatal shelf (PS) mesenchyme caused a delay in elevation, resulting in cleft palate. Next, we determined Yap/Taz gene targets in the PS during elevation by performing RNA-Seq. The goal of this summer research project was to 1) determine the role of Yap/Taz in PS growth and morphogenesis by quantifying proliferation and cell death and 2) verify Yap/Taz gene targets in vivo.

Methods: Yap and Taz were deleted in a subset of PS mesenchymal cells using Col2Cre and Osr2Cre drivers in mouse embryos. We injected pregnant dams with BrdU, collected embryos, and performed immunofluorescence with antibody against BrdU and TUNEL staining. RNA Scope was performed with probes against Inhba, Phex, and Loxl4, which were identified as differentially expressed genes by RNA-Seq on RNA from E14.5 Yapfl/fl;Tazfl/fl;Col2Cre and control palatal shelves.

Results: At E12.5, there was decreased proliferation in posterior (p=0.016, n=5) and increased cell death in middle (p=0.026, n=5) PS mesenchyme in Yapfl/fl;Tazfl/fl;Osr2Cre mutant embryos compared to control. Inhba, a known Yap target gene, was found to be expressed in the PS mesenchyme while Phex and Loxl4, genes encoding proteins involved in osteogenesis and collagen crosslinking, respectively, were expressed in mineralizing zones of the PS in 5 Yapfl/fl;Tazfl/fl;Col2Cre and control embryos at E14.5.

Conclusions: Deletion of Yap and Taz results in loss of PS mesenchymal cells due to regional decreased proliferation and increased apoptosis, which may contribute to the PS elevation delay. Yap/Taz target Inhba, Phex, and Loxl4 in the PS to regulate palatogenesis.

Support: Department of Orofacial Sciences; NIH/NIDCR K08DE028011

#34 Title: Associations of Household Rules and Parental Awareness with Youth Tobacco Use

TS WU, BW CHAFFEE

Division of Oral Epidemiology and Dental Public Health, Department of Preventive and Restorative Dental Sciences, UCSF School of Dentistry

Objectives: With recent public health concerns about the increasing popularity of non-cigarette tobacco products, it is important to reexamine parents’ roles in youth tobacco prevention. This study examined: (1) parental awareness of their children’s tobacco use, (2) household tobacco-free rules and youth initiation, (3) variations in awareness and initiation by tobacco product type.

Methods: Data came from youth (ages 12-17) who completed Waves 1-3 (collected 2013-2016) of the Population Assessment of Tobacco and Health Study, a nationally representative (USA) longitudinal household survey of tobacco use and health. Youth tobacco use was categorized as: cigarette only, e-cigarette only, smokeless tobacco only, non-cigarette combustible only, and poly-use. Pseudo cross-sectional time-series analysis (N=17,787) examined parent report of whether they know/strongly suspect their child uses tobacco. Longitudinal analysis among Wave 1 never-users examined household rules barring burned or non-burned tobacco use inside the home and whether parents talked with youth about not using tobacco as predictors of tobacco initiation. Survey-weighted logistic and multinomial logistic regression models adjusted for child and parent sociodemographic variables and other tobacco use risk factors. Multiple imputation accounted for missing covariate observations.

Results: Compared to youth cigarette use, parental awareness was lower for e-cigarettes (OR: 0.22), non-cigarette combustibles (OR: 0.18), and smokeless products (OR: 0.33, all p<0.001) among past 30-day users across Waves 1-3. Youth tobacco initiation by Wave 3 was lower when rules prohibited tobacco use throughout the home (OR: 0.78, 95%CI: 0.66, 0.93) compared to more permissive household rules. Parents’ advising youth against tobacco use was not associated with less initiation (OR: 1.14, 95%CI: 0.98, 1.33). Evidence did not strongly indicate household rules specifically about burned products more effectively prevented combustible tobacco initiation.

Conclusions: Many parents overlook their children’s non-cigarette tobacco use. Tobacco-free household environments appear more effective at preventing youth tobacco initiation than parents advising children not to use tobacco.

Support: UCSF School of Dentistry Summer Research Fellowship; Delta Dental Community Care Foundation; NIH Heart and Lung Blood Institute and FDA Center for Tobacco Products (grant number U54 HL147127)
#35 Title: Generation of large-scale chromosomal deletions in primary human keratinocytes

R FARHAD, V PLANELL-PALOP, C MOHIEU, AD TWARD

UCSF Oral and Craniofacial Sciences Graduate Program, UCSF School of Dentistry; and the Department of Otolaryngology, UCSF School of Medicine

Introduction: Large-scale chromosomal deletions frequently occur in the progression of head and neck squamous cell carcinoma (HNSCC). Many studies have linked the association of these deletions with particular patient outcomes. However, their precise contributions to tumorigenesis have yet to be elucidated. This gap in knowledge is partially due to limitations and difficulties associated with genome-editing techniques in the pre-CRISPR era. Here, we introduce an in vitro model for studying large-scale chromosomal deletions to establish their role as driver or passenger events in HNSCC progression.

Methods: CRISPR/Cas9 vectors coding for guide RNAs (gRNAs) that flank two of the commonly-deleted regions in HNSCC tumors were transfected into primary human keratinocytes. Genomic DNA was harvested 24 hours post-transfection and analyzed via endpoint PCR and TaqMan copy number assay qPCR. The endpoint PCR products were further analyzed via Sanger sequencing.

Conclusions: Chromosomal deletions occur at a high frequency in HNSCC tumors. However, there is no established model to determine whether these deletions exist as driver or passenger events. Here, we demonstrate the first successful large-scale deletion in a primary human cell culture system that can be further utilized to study the role of such events in HNSCC tumorigenesis.

Support: This study was supported by Program in Breakthrough Biological Research and UCSF School of Dentistry OHNRG pilot grant.

#36 Title: T. denticola Mediates Transcriptional Dysregulation of Tissue-Destructive Genes Through a TLR2-Dependent Pathway in Human Periodontal Ligament Cells

S GANTHER, P KAMARAJAN, L ZHAN, C FENNO, T DEFRANCO

Oral and Craniofacial Sciences Graduate Program and Department of Orofacial Sciences at UCSF School of Dentistry; Department of Microbiology and Immunology, UCSF School of Medicine; and the Biologic and Materials Sciences, University of Michigan

Objective: T. denticola, the best-studied oral spirochete, produces an acylated serine protease complex called Dentilisin, which has been shown to degrade cytokines, activate endogenous human MMPs and contribute to its adherence and penetration to epithelial and fibroblasts cells. While these behaviors are being studied by several groups, few direct links have been reported between T. denticola’s protease and the cellular and tissue processes that drive periodontal tissue destruction at the genetic or transcriptional level. Membrane localized pattern recognition receptors, such as TLR2, illustrate large plasticity in sensing an array of microbial components including acylated lipoproteins, such as T. denticola expressed Dentilisin. When Toll-Like Receptor (TLR) signaling is left unchecked, downstream genes such as MMPs can become significantly upregulated and constitutively activated, contributing to the overall destruction of the periodontium. This study aimed to better understand the extent of T. denticola’s ability to influence the regulation of tissue-destructive genes through a TLR2/Dentilisin-dependent pathway in human periodontal ligament cells (hPDL).

Methods: A human periodontal ligament TLR2 knockdown cell line was created using a lentiviral particle shRNA system and puromycin selection. Scramble shRNA was used as a negative control and validated using RT-qPCR across multiple clones. Both cell lines were challenged with wild-type and mutant T. denticola deficient for dentilisin expression (Td-P0760) for 2-hours followed by a 22-hour incubation and RNA extraction. Expression of candidate genes was measured using RT-qPCR.

Results: Scramble hPDL cells showed significant upregulation of MMPs 2, 14 and 28 while cells deficient for TLR2 maintained the same expression as the control group (no infection). Additionally, cells infected with Td-P0760 also did not induce upregulation of MMPs 2, 14 and 28.

Conclusion: We propose that T. denticola’s dentilisin activates TLR2, leading to subsequent activation of MAP Kinase signaling and dysregulation of MMPs 2, 14 and 28 in hPDL fibroblasts.

Support: NIH R01 DE025225 and NIH 2T32DE007306

#37 Title: Wnt Inhibition Decreases Established Trabecular Bone in a Mouse Model of Fibrous Dysplasia

H LUNG123, T MOODY2, K WENTWORTH2, M KANG1, S HO1, M SIROTA4, E HSIAO12

1Oral and Craniofacial Sciences Graduate Program, School of Dentistry, UCSF, 2Division of Endocrinology and Metabolism, Institute for Human Genetics, School of Medicine, UCSF, 3Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taiwan, 4Institute for Computational Health Sciences, UCSF

Objectives: Fibrous dysplasia (FD) is a common skeletal dysplasia where normal bone and bone marrow space are replaced by fibrous tissue and expansile trabecular bone lesions. The craniofacial bones are often involved, leading to pain and facial deformities. FD is a mosaic disease caused by a somatic mutation in the GNAS gene, which leads to constitutive activation of the Gs signaling pathway. FD has no effective treatments and surgery is often complex and associated with recurrence.
The Col1/Rs1 mouse model develops bone lesions that resemble FD in humans. Wnt signaling appears to be a major driver of the abnormal bone formation. Therefore, we used a Wnt inhibitor in Rs1 mice to test if the FD phenotype could be reversed.

**Methods:** We administered a porcupine inhibitor LGK974 in Rs1 and non-Rs1 mice with 3-4 mice in each group. We used a low dose (5mg/kg) for 8 weeks and high dose (30mg/kg) for 5 weeks. The mice were evaluated by dual-energy x-ray absorptiometry (DEXA), micro computed tomography (micro-CT) and histology. 

**Results:** In the low-dose group, the micro-CT scans and histology did not show significant differences between drug-treated and non-treated groups. In the high-dose group, the bone mineral density measured by DEXA significantly decreased in the drug-treated mice, both Rs1 and non-Rs1 groups. Histology showed resorption of the abnormal bone; however, the fibrous tissue in the Rs1 mice did not decrease.

**Conclusions:** Wnt inhibition can lead to decreased fibrous dysplastic bone, and separates two of the classical histologic phenotypes of FD (the abnormal bone and the fibrous tissue infiltrate). This suggests that different mechanisms drive these phenotypes. In addition, high dose Wnt inhibition also causes bone loss in control mice. These results provide us an insight into understanding bone formation and interaction between the Wnt and Gs signaling pathways, and identify potential drug targets for FD.

**Support:**
1. School of Medicine Startup Fund
2. Genentech Fellowship Award
3. Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine Doctoral Training Fellowship

---

**#38 Title:** Treponema denticola-disrupts actin reorganization and increases MMP-2 activation, leading to mechanical malfunction in human periodontal ligaments cells

E MALONE, S GANTHER, P KAMARAJAN, JC FENNO, Y KAPILA

Oral and Craniofacial Sciences Graduate Program, UCSF School of Dentistry; and University of Michigan, School of Dentistry

**Objective:** The aims of this study were to identify Treponema denticola’s (Td) influence on actin stress fibers, B-actin abundance, and the mechano-transducing functionality of human periodontal ligament (hPDL) cells. We hypothesize that 1) Td interactions with hPDL cells decrease filamentous stress fibers by decreasing the pool of available B-actin; 2) Td modulation of actin cytoskeleton functionality leads to increased MMP-2 activation and detachment of cells.

**Methods:** HPDL cells collected from extracted teeth were untreated or pretreated with Latrunculin B (a B-actin sequestering agent) and unchallenged or challenged with wildtype Td at an optimized multiplicity of infection (50) for 2hrs. Post-challenge, cultures were washed and incubated in MEMalpha medium for 24hrs. Post-incubation cultures were fixed for immunofluorescence staining or turned into lysates for western blotting analysis to determine shifts in stress fiber organization/abundance, B-actin pool, and MMP-2 expression, respectively. Additionally, cultured media was collected to determine MMP-2 activity via gelatin zymography and detachment assays were performed as functional readouts of the cellular response.

**Results:** Td challenged hPDL cells exhibited decreased actin stress fiber intensity, and B-actin protein levels compared to control. Increased MMP-2 activation resulted from sequestering free B-actin and enhanced due to Td challenge. Functionally, hPDL cells detached significantly from monolayer cultures due to Td challenge compared to control.

**Conclusions:** Td interaction with hPDL cells leads to disruption of the actin cytoskeleton by influencing stress fibers and the availability of B-actin monomers needed for actin dynamics. Td interaction and actin changes, result in MMP-2 activation and cellular detachment, mimicking the cellular and tissue changes observed in periodontal disease.

**Support:** This work was supported by grant funding from NIH; R01 DE025225 to YLK and JCF, F30DE027598 to ETM. We’d like to thank the OCS Program for support of EM.

---

**#39 Title:** Epithelial-Mesenchymal Interactions that Regulate Mandibular Osteogenesis

A NGUYEN, D CHU, Z VAVRUSOVA, J FISH, RA SCHNEIDER

Oral and Craniofacial Sciences Graduate Program and the Department of Orthopaedic Surgery, UCSF School of Dentistry

**Objectives:** Identifying molecular signals mediating the epithelial-mesenchymal interactions (EMI) would allow us to discover proteins that regulate mandibular osteogenesis, and which potentially could be used therapeutically to generate bone in cases of disease and injury.

**Methods:** An RNA-seq experiment was used to identify candidate genes involved in EMI in duck mandible. RNA in situ hybridization and RT-qPCR were used to characterize the spatiotemporal expression of these genes qualitatively and quantitatively on the mRNA levels in three avian species (duck, quail, and chicken). In vitro organ cultures were used to test if the expression of these genes in mandibular mesenchyme requires epithelial signaling. Gain and loss-of-function experiments tested if these genes regulate mandibular osteogenesis.

**Results:** Data from the RNA-seq experiment, RNA in situ, and RT-qPCR (n=16) reveal that spatiotemporal changes in members of the WNT and CXC signaling pathways are present at the right time, place, and levels to mediate the osteogenic EMI in the mandible. In vitro organ cultures (n=12) confirmed the expression of these genes in mandibular mesenchyme depends on epithelial signaling. Gain-of-function experiments showed mandibular osteogenesis significantly increases on the CXC overexpressed side compared to the non-treated side after 7 days of culture (n=10, p<0.05 paired t-test). Loss-of-function experiments showed inhibiting the WNT pathway completely blocks osteogenesis (n=16), whereas concurrently overexpressing CXC rescues the bone phenotype caused by inhibiting the WNT pathway (n=11). RT-qPCR showed altering the WNT pathway affects the expression of CXC (n=12), suggesting CXC acts downstream of WNT ligands.
Conclusions: Novel epithelial factors, including WNTs and CXC, involved in mandibular osteogenesis were identified. Especially, CXC and WNT have an osteogenic effect during EMI. This finding furthers our understanding of mechanisms underlying EMI in the mandible and leads to potentially novel therapeutic approaches to promote bone formation in the jaw following birth defects, disease, or injury.

Support: F30DE027616 to AN, Discovery Fellowship, R01DE016402 to RAS, S10OD021664 to RAS

#40 Title: The Role of TGFβ Signaling in Neural Crest-Mediated Jaw Bone Remodeling

T QU, SS SMITH, RA SCHNEIDER

Oral and Craniofacial Sciences Graduate Program, UCSF School of Dentistry

Objectives: Size-related malformations in the jaw are some of the most common human birth defects, including pro- and retrognathia, asymmetry, and clefting. To understand morphogenetic programs controlling jaw size during development, we take a comparative approach utilizing quail and duck, since duck jaws are proportionally much longer than quail. Previously, we have shown that bone resorption is a crucial step that establishes jaw length, and that bone resorption and jaw length can be altered by transplanting neural crest mesenchyme (NCM), the jaw progenitor population, from quail into duck. However, the molecular mechanisms through which NCM regulates bone resorption and jaw length remain unclear. We hypothesize that NCM differentially regulates TGFβ signaling in a species-specific manner, which in turn modulates expression of targets involved in bone remodeling such as Runx2 and Mmp13.

Methods: Western Blot and RT-qPCR were used to address differences in TGFβ signaling between quail and duck. Immunohistochemistry (IHC) was used to characterize spatial distribution of RUNX2 and MMP13 protein.

Results: Western Blot and RT-qPCR analyses showed that quail have significantly higher levels of pSMAD3, Runx2, and Mmp13 during key stages when bone resorption is initiated. IHC also confirmed higher levels of RUNX2 and MMP13, and co-localization with TRAP (a bone resorption marker) in some mandible bones of quail but not duck. Strikingly, these higher levels and co-localization of MMP13, RUNX2, and TRAP are not observed in other bones.

Conclusions: Quail has greater activation of TGFβ signaling and upregulation of Runx2 and Mmp13 than duck at key developmental stages. MMP13 and RUNX2 are spatially regulated with higher levels in the angular bones in quail vs. duck, possibly creating zones of remodeling regulating jaw length. This project is significant for uncovering signals that regulate bone resorption in the mandible, which is essential for devising new therapies for birth defects.

Support: This research was funded by the National Institute of Health Grants R01DE025668 and R01DE016402 (to RAS) and 1F32DE027283-01A1 (to SSS).

#41 Title: Local Injections Of Nerve Growth Factor Accelerates Endochondral Fracture Repair

KO RIVERA (1), F RUSSIO (2) T MICLAU (3) TA DESAI (4) CS BAHNEY (5)

(1) Oral and Craniofacial Sciences Graduate Program, UCSF School of Dentistry, (2) Russio (Campus Bio-Medico University, Rome, Italy) (3) Orthopaedic Trauma Institute (4) Department of Bioengineering and Therapeutic Sciences (5) Steadman Philippon Research Institute, Vail, CO

Introduction: During endochondral fracture repair, the conversion of cartilage to bone in a fracture callus occurs adjacent to the invading neurovasculature. While angiogenic and osteogenic factors to promote fracture repair have been heavily studied, there is limited work exploring neurogenic factors. Therefore, we tested the therapeutic efficacy of Nerve Growth Factor to enhance fracture repair.

Objective: Establish NGF as a novel therapeutic for accelerating bone fracture repair and developing a clinically translational method of administration.

Methods: NGF effects on gene expression: NGF (0.5ug in 20uL DMEM) injections into calluses began either 4 or 7 days post-fracture for 3 consecutive days. Controls were injected with DMEM. Fracture calluses were then harvested 24 hours following the final NGF injection and prepared for RT-qPCR analysis of osteogenic and chondrogenic markers. NGF effects on tissue composition: NGF and control injections were done on days 7-9 post-fracture, and then tibias were harvested 14 days post-fracture. Samples were fixed in paraformaldehyde then decalcified for 14 days at 4oC then processed for paraffin embedding and stereological analysis. Another set of fractured tibia were similarly fixed then prepared for micro-computed tomography.

Results: Local NGF injections to the callus during the cartilaginous phase (days 3-5) promoted collagen I expression but reduced osteogenic markers osteocalcin (oc) and osteopontin (op). Interestingly, local NGF injections during the cartilaginous phase (days 7-9) resulted in an increase of osteogenic markers. Histology of fracture calluses 14 days post-fracture showed an increase in newly formed trabecular bone and less cartilage. Quantitative stereology revealed no difference in callus size between treated and controls, however, bone volume was significantly higher after local NGF injections. MicroCT data showed an increase in bone volume fraction and a significant increase in trabeculae connective density, trabecular number, and bone mineral density.

Conclusion: These data suggest NGF’s potential role during fracture repair. Moreover, our data further establishes NGF’s therapeutic efficacy in accelerating bone fracture repair.

Support: NIGMS R25-GM056847, NIDCR F31 DE 02848, UCSF Catalyst RAP Award
#42 Title: Variation in food particle size drives changes in oral biofilm abundance and architecture

L. SEDGHI (1), V BLAV ROGER (2), A RADIAC (3), S HO (4,5), Y KAPILA (1)

(1) Oral and Craniofacial Sciences Graduate Program, UCSF School of Dentistry (3) Dept. of Preventive and Restorative Dental Sciences (4) UCSF Department of Urology (5) UCSF School of Medicine

Objective: The effect of dietary nutritional properties to oral microbial communities is well-established. However, the impact of dietary structural properties remains unexplored. Recent studies in the field of food chemistry demonstrate that different food particle sizes, albeit having equivalent nutritional content, changes nutrient bio-availability. The objective of this study is to investigate if variation in food particle size induces changes in oral biofilm abundance.

Methods: Scanning electron microscopy (SEM) was performed on mandibular surfaces of mice fed a pellet vs. powder form of mouse chow for 6 weeks. Biofilms supplemented with small (fine) or large (coarse) wheat particle sizes were grown in vitro and were analyzed using SEM and growth curve analysis.

Results: SEM images of murine dental surfaces revealed striking differences, with exacerbated accumulation in the powder group (Fig.1). Biofilms grown in vitro demonstrated significant variation in biofilm abundance and surprisingly, biofilm architecture (Fig.2).

Conclusions: Excessive biofilm accumulation on the dental and gingival surfaces exists as the primary etiological factor in the onset and exacerbation of dental and periodontal diseases. As such, it is important to understand the mechanisms by which dietary structural properties control biofilm accumulation and shape microbial communities to advance dental disease prevention. Here, we demonstrate the first functional characterization of the influence of dietary particle size to microbial biofilm abundance and structure in the oral cavity.

Acknowledgments: This study was supported by NIH T32 # 2T32DE007306 (LMS), NIH R21 DE027138 (SPH), R01 DE022032 grant (SPH), NIH R01 DE025225 (YLK), and AAP Sunstar Innovation grant (YLK)

III. POSTDOCTORAL/RESEARCH SPECIALIST/VISITING SCHOLAR CATEGORY

#43 Title: Natural Carious Lesions in Dentin Remineralized by PILP-Treatments

E BABAIE, M BACINO, J WHITE, S HABELITZ

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

Objectives: It is believed that the polymer-induced liquid-precursor (PILP) induces remineralization. Herein, we examine the remineralization efficacy of different PILP-releasing methodologies on human dentin lesion with 1mm depth for up to 5 months.

Method: Extracted and sterilized molar teeth with cavitated dentin lesions (n = 15) were prepared following minimal invasive dentistry by removing only the infected area. pAsp (poly-Aspartic Acid, 27 kd) (PILP) was applied in two ways: A) as liner: mixed with a bioactive Bioglass and applied to lesion surface as a thin layer prior to sealing with fluoride and non-fluoride releasing resin modified glass ionomer (RMGI) and (B) as conditioner: pAsp was added at concentration of 5 mg/ml in calcium phosphate solutions to rehydrate lesions before restoring with RMGI. Lesions restored with RMGIs only, served as controls. Mineral density and residual caries volume was assessed using micro computed tomography (uCT).

Results: Our findings on mineral and residual caries demonstrated that use of different methodologies led to different increases of mineral content. The mineral recovery in general increased over time in all formulations, where the final mineral densities were higher in formulations that involved PILP compared to controls. Highest relative mineral density recovery of >90% and residual...
Objective: Enamel is comprised of a complex structural organization of nanofibrous apatite crystals. The nanostructure of enamel is believed to be guided by supramolecular assembly of the organic matrix. Amelogenin has shown the ability to assemble into ribbon structures in vitro. While these protein ribbons appear as an ideal template to guide ribbon-like formation of apatite, a direct association of organic nanostructure and apatite crystals has yet to be observed. Here we aim to obtain direct in-vivo evidence for amelogenin ribbons as templates guiding mineral growth.

Methods: 1. In vitro construction of amelogenin ribbons and structural characterization by TEM and AFM. 2. Perform ultra-thin sectioning on KLK4 knock-out mouse incisor followed by demineralization of the sections. 3. Characterize sections with TEM and compare with in-vitro constructed amelogenin ribbons. 4. Remineralization of the sections as well as in-vitro constructed amelogenin ribbons with pAsp solution and characterize the resulting organic-mineral complexes using structural and electron diffraction approaches.

Results: A network of amelogenin ribbons preserving the signature enamel textures can be observed on demineralized sections. Single amelogenin ribbons can be clearly resolved, matching perfectly with the dimensions of in-vitro constructed amelogenin ribbons. When immersing the sections in pAsp solutions, amorphous liquid precursor droplets associate with amelogenin ribbons and facilitate growth of amorphous mineral following the enamel texture. Similar protein-mineral association was also observed when mixing in-vitro amelogenin ribbons and pAsp solution. A transition into crystalline nanofibers of apatite was achieved after thermal treatment.

Conclusion: We obtained for the first time direct in-vivo evidence that the developing enamel matrix is comprised of amelogenin ribbons. Moreover, we demonstrated that such ribbons serve as templates for enamel biomineralization. This study challenges the current paradigm of amelogenin nanosphere guided mineralization and reinforces the model of ribbon-like assembly in the enamel matrix as prerequisites to enamel structure development.

Support: NIH/NIDCR Grant R21, the UCSF Catalyst Award “PILP Treatment for the Repair of Dental Caries” and by the Center for Dental, Oral & Craniofacial Tissue & Organ Regeneration (C-DOCTOR)

#44 Title: Evidence of Amelogenin Ribbons as Templates Guiding Enamel Apatite Growth
YS BAI 1, W LI 2, Y ZHANG 2, L. ACKERMAN 1, B. JOHAN 3 and S HABELITZ 1

1. UCSF School of Dentistry, Department of Preventative and Restorative Dental Sciences; San Francisco 2. UCSF School of Dentistry, Department of Orofacial Sciences 3. Center of Applied Life Science, Lund University, Sweden

Conclusion: The new PASP-bioglass cement liner and conditioner are capable of remineralizing the collagen as opposed to calcium-phosphate saturated solution and RMGI commercial controls, represent a promising approach in caries repair. These findings together emphasize the success of PILP methodologies potentially in clinical implementation.

Support: NIH/NIDCR R01-DE25709 Amyloids in Enamel Development

#45 Title: Developing the Persian Oral Health Literacy Assessment Scale with eDelphi
S BANAVA, SA GANSKY

Division of Oral Epidemiology & Dental Public Health, UCSF. Center to Address Disparities in Children's Oral Health (known as CAN DO), UCSF

Objectives: Functional oral health literacy is a risk indicator influencing oral health outcomes. In the United States (US), many immigrants face language barriers affecting communication with dental providers. Part one of a multiphase study aimed to develop a Persian oral health literacy assessment (POHLA) scale through the eDelphi method. The developed POHLA will be used to assess the oral health literacy.

Methods: To develop POHLA, the bilingual researcher (SB) translated three sets of dental terms (i.e. stem, similar, and distractor words) in the Rapid Estimate of Adult Literacy Dentistry (REALD-30) were translated from English to Persian. Then, the eDelphi method was implemented to capture an expert panel’s opinions and suggestions on translated Persian terms. The expert panel included five bilingual Iranian-born Persian-speaking dentists who moved to US after age 18+ with 2+ years as a dental practitioner, four bilingual laypeople, and one American-born, Persian reader and speaker. The eDelphi manager (SB) facilitated communication among panel members maintaining anonymity through multiple eDelphi rounds to reach consensus word translations. We used 75% agreement among panel members to accept translated words.

Results: Three eDelphi rounds were conducted in ~1 month to finalize POHLA. In the first round, the expert panel had 100% agreement on 49 terms, 78-89% agreement on 30 Persian terms, and 44-67% agreement on 11 terms. In the second round, the expert panel commented on terms with less agreement to reach consensus. In the third round, the expert panel had 100% agreement on 48 terms, 89% agreement on 33 terms, and 78% agreement on 9 terms. In the next study phase, POHLA will be used in semi-structured cognitive interviews for validation.

Conclusions: The eDelphi process effectively served to capture expert panel opinions anonymously. This platform could be advantageous for research studies for expert opinion and consensus.

Support: NIH/NIDCR T32DE007306, UCSF Center to Address Disparities in Oral Health (Known as CAN DO)
#46 Title: Assessment of Airborne Methicillin Resistant Staphylococcus Aureus (MRSA) in Dental Clinics

A BHALLA

Drexel School of Public Health

**Objective**: The propelling force and high speed of dental devices in combination with water spray can result in production of pathogenic aerosols derived from saliva, plaque, blood, calculus in patient’s mouth. There is a little known if these pathogenic aerosols could be a reservoir for Methicillin Resistant Staphylococcus Aureus (MRSA), one of the most common causes of healthcare associated infection. This study analyzed airborne MRSA concentration during different treatment procedures. These procedures were classified as high and low aerosol generating based on the duration of use of high speed dental devices.

**Methods**: The air sampling was performed for eleven treatment procedures using 400 hole Biostage Bioaerosol impactor calibrated to 28.3L/min for a period of 5 to 8 minutes. The air samples were collected side by side on the 100 x 15 mm petri dishes with antibiotic containing and no-antibiotic containing media, i.e. Oxacillin Resistant Staphylococcus Aureus Base (ORSAB) and Mannitol Salt Agar (MSA) respectively. Sample agar plates were transported to the laboratory within three hours of collection followed by incubation at 36°C, an optimal growth temperature for Staphylococcus Aureus. The colonies were counted after 72 hours.

**Results**: MRSA colonies were isolated in half of the high-aerosol generating procedures. The average concentration of MRSA during high aerosol generating procedures is 10 CFU/m3. No MRSA colonies were identified during low-aerosol generating procedures.

**Conclusions**: The isolation of MRSA in half of the sampled procedures is a safety concern for dental health care providers and patients. The results support our hypothesis that high aerosol generating procedures could result in higher average as well as higher MRSA concentration. This can be attributed to propelling force and high speed of the dental devices used and absence of rubber dam isolation during these procedures.

**Support**: Community Based Master's Project (Drexel School of Public Health)

#47 Title: Five-Year Comparative Analysis of Medicare Opioid Prescription Volume Among Oral and Maxillofacial Surgeons

NA PATEL (1,2), DA KEITH(3)

(1) Department of Oral and Maxillofacial Surgery, University of California San Francisco, (2) Department of Biomedical Informatics, Harvard Medical School, (3) Department of Oral and Maxillofacial Surgery, Massachusetts General Hospital

**Objectives**: To examine volume and variation in opioid prescribing practices among oral and maxillofacial surgeons (OMSs) serving Medicare beneficiaries from 2013 to 2017 and identify practice-level features that correlate with opioid prescription volume.

**Methods**: This cross-sectional study included Medicare Provider Utilization and Payment Data from 2013 to 2017. Providers were included if they were labelled as OMSs. The primary outcome variable was the opioid claim volume. The predictor variables included provider and beneficiary gender, beneficiary age, and beneficiary hierarchical condition category (HCC). The secondary outcome variables included mean opioid prescriptions per beneficiary and opioid days’ supply per claim. Descriptive statistics and regression analyses were computed at an alpha level of 0.05.

**Results**: The 5-year analysis cohort included 2071 distinct providers; 605,593 total opioid prescription claims were recorded for 516,217 Medicare beneficiaries, with an average supply of 3.54 days of opioids per patient. From 2013 to 2017, a significant increase had occurred in the number of mean opioid claims per provider (P < .001) and a significant decrease in both the mean opioid claims per beneficiary (P < .001) and the days’ supply per opioid claim per beneficiary (P < .001). Male provider gender (P < .001), lower beneficiary age (P < .001), percentage of female beneficiaries seen by a provider (P < .001), and lower HCC risk score (P < .001) all correlated with an increased opioid claim volume. Finally, a significant difference was found in the opioid claim volume among OMSs between the states (P < .001) and between OMS and other surgical subspecialties (P < .001).

**Conclusions**: Although the total number of opioids prescribed by OMSs has increased over time, the pre-scribing practices have, on the aggregate, become more responsible. The extreme cases of opioid prescribing and variations in state-level opioid claim volumes warrant additional investigation.

#48 Title: Selective Modulation of Pathogenic Oral Biofilms Towards Health with Nisin-Producing Probiotic and Nisin

A RADAIC, B PARKS; C YE, L GAO; E MALONE, L ZHAN, YL KAPILA

Department of Orofacial Sciences, UCSF School of Dentistry

**Background**: Oral biofilm dysbiosis is an imbalance in the oral microbiome and is associated with a variety of oral and systemic diseases, including periodontal diseases, caries, recurrent endodontic infections, and head and neck/oral cancer. Although antibiotics can be used to control this dysbiosis, use of antibiotics can lead to adverse side effects and superinfections. Thus, novel strategies have been proposed to address these shortcomings. Two new strategies are the use of probiotics and/or bacteriocins as antimicrobial agents, since they are considered safe for humans and the environment. Specifically, nisin is a naturally occurring bacteriocin produced by the gram-positive Lactococcus and Streptococcus genera, which are endemic to the oral and gut microflora. Nisin has been used worldwide with approval from the WHO and FDA for food preservation since 1988. Objective: Therefore, the objective of this work was to test whether nisin or the nisin-producing Lactococcus lactis bacteria can promote the formation of a healthier oral biofilm.
Methods: Biofilm were grown in vitro for 24h or 48h, treated with either Nisin or nisin-producer L. lactis for 24h. Then, the biofilms were either stained using Live/Dead Baclight and their structure visualized on confocal or directed to 16S sequencing were used for the biofilm species analyses.

Results: We found that nisin and nisin-producing L. lactis prevent oral biofilm formation and disrupt 24h and 48h pre-formed biofilms in vitro. Both treatments promote the diversity and richness of the oral biofilms, returning the indexes toward control levels or “healthy” biofilms. Finally, we demonstrate that both treatments decrease the levels of the pathogen F. nucleatum in the biofilms.

Conclusions: Nisin and nisin-producing L. lactis (functioning as a probiotic) can be used to promote a healthier oral biofilm, which may be useful for improving patient oral health.

Support: This work was supported by an AAP Sunstar Innovation Grant to YLK.

#49 Title: Oral Health Needs Assessment of Low-Income Pregnant Women/Mothers in Berkeley

K RAJU

University of California, San Francisco; University of California, Berkeley

Background: Maintaining good oral health during pregnancy is imperative for healthy mothers and infants. In addition to good daily nutrition and oral hygiene, a prenatal dental visit is recommended. Aim: The purpose of this study is to improve the oral health of low-income pregnant women/mothers in Berkeley.

Objectives: The objectives of the study are to (i) describe the prevalence of oral health problems, use of and barriers to dental care for pregnant women; (ii) examine the associations of predictor variables and prenatal dental visits; (iii) make recommendations for interventions to improve women’s oral health.

Material-Methods: An anonymous survey was completed by 57 women at Berkeley prenatal clinics serving low-income populations for City of Berkeley Oral Health Program Strategic Planning. Descriptive analysis was performed using SPSS 22.0, and logistic regression was used to examine the predictors associated with dental visits among pregnant women/mothers. One focus group transcript with African-American families was analyzed to identify themes regarding utilization and barriers to dental care.

Results: Forty percent of women reported currently suffering from dental problems. Overall, 39% of women did not visit a dentist during their pregnancy, and 25% of women were unaware that their health insurance covered dental care. Only 75% of women reported that their medical provider recommended a prenatal dental visit. The main barriers to dental care were financial (14%), lack of knowledge and awareness (9%), fear and anxiety (7%), time (7%), and not having a dentist (5%). Dental insurance (p<0.05) and recommendation by a medical provider (p<0.05) were significantly associated with having a prenatal dental visit.

Conclusion: There is a need for more dentists to accept Medi-Cal dental patients, and greater integration of medical and dental care to ensure that prenatal medical providers recommend prenatal dental visits.

IV. RESEARCH ASSOCIATES

#50 Title: Restorative options for dentin caries repair using the PILP-method

M BACINO, J WHITE, S HABELITZ

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

Objectives: It has been proven that PILP (Polymer-Induced Liquid Precursor) can repair artificial shallow lesions by guiding the remineralization of intertubular dentin, restoring both the mineral content and functionality of the tissue. This study is the continuation of previous work on shallow lesions (140 µm), whereas herein we examine the efficacy of different PILP delivery systems on lesions up to 700 µm deep. Poly-aspartic acid (pAsp) is used as the process-directing agent for PILP mineralization of collagen.

Methods: Artificial dental lesions were created using an acetic acid solution at pH 4.5 and incubated at 37°C on a 3-D rocker for one week 168 hours. Each set (n=3) was immersed in PILP solution, calcium phosphate solution, restored with a RMGIC control, or with a PILP-releasing liner or conditioner containing up to 5 mg/ml pAsp before RMGIC application. These samples were immersed in remineralizing solutions at 37°C on a 3-D rocker for 4 weeks. Specimens were analyzed using light microscopy, SEM, and nanomechanical testing.

Results: All delivery systems of pAsp increased the nanomechanical properties of dentin lesions when compared to commercially available RMGIC and saturated solutions. Dehydration shrinkage of lesions remineralized in PILP solutions was minimal and decreased significantly compared to all other groups (p<0.05). These specimens also had the highest recovery of the elastic modulus from 0.2GPa before to 10 GPa after remineralization (P<0.05).

Conclusions: The data shows that the PILP system is capable of creating functional remineralization in deeper lesion similar to previous observations on shallow lesions. The systems evaluated show promise of translating the PILP approach into clinical restorative dentistry for repair of dental caries as part of minimally invasive treatments.
#51 Title: Dental Therapists in the United States: Health Equity, Advancing?

A KOTTEK, C TORETSKY, M WERTS, E MERTZ

Healthforce Center at UCSF, School of Dentistry, UCSF (Kottek, Toretsky, Werts, Mertz); Philip R. Lee Institute for Health Policy Studies, School of Medicine, UCSF (Toretsky, Mertz); Preventive and Restorative Dental Sciences, School of Dentistry, UCSF

Objectives: Dental therapists (DTs) are primary care dental providers who practice in 54 countries worldwide. First adopted in 2006 in the United States (US), DTs have now been approved in 13 states. The objective of this study is to examine the drivers and outcomes of the US DT movement though a health equity lens.

Methods: A comprehensive document library on the DT movement, including published literature, internal grant documents, and grey literature, was compiled, and semi-structured interviews were conducted with key stakeholders. Dedoose software was used for qualitative coding across access, implementation, and community engagement conceptual models, and trends and findings were assessed within a model of oral health equity.

Results: The movement to spread DTs across the US is deeply rooted in the principles of health equity, and this focus has infused each step of the process, including community engagement, political coalition building, and sustainable structural change. Community engagement in legislative action has been evident in diverse statewide coalitions. Where DTs are fully deployed, improvements in access and patient outcomes have been documented for traditionally underserved populations. National education accreditation standards reduces educational barriers and improves workforce diversity, and model DT legislative language exists in alignment with these national standards.

Conclusions: The US DT movement is rooted in health equity. Advocacy has focused on legislative changes necessary to adopt DTs, and implementation efforts have developed the key regulatory and educational structural components. These efforts, along with preliminary evidence of safety and acceptability, have led to an increased pace of adoption. Having firmly taken root politically, the movement to scale DTs in the US to new states, and the subsequent short- and long- term health impacts of this spread, will depend on the path of implementation and a sustained commitment to the principles of health equity.

Support: W.K. Kellogg Foundation

#52 Title: Polyaspartic acid as a dentin conditioner: AFM study

P SHARMA M BACINO, E BABAIE, S HABELITZ

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

Objective: Conditioners are used to remove smear layer and to open dentin tubules to provide better bonding of cements and adhesives. In this study, we examined if a conditioner composed of polyaspartic acid at a certain pH can remove a smear layer in comparison to commercial GC America conditioner. Poly aspartic acid has shown potential to remineralize dentin collagen and may be able to repair caries in dentin.

Methods: Dentin slabs were prepared by cutting crown and root and polished using sand papers (400 and 600 grit) to imitate clinically relevant smear layer. Artificially created smear layer were randomly divided into two groups. One of the group was treated with commercial product (GC America conditioner made up of 20% polyacrylic acid and 3% aluminium chloride hexahydrate at pH 1.2) and other by our conditioner (20% polyaspartic acid at pH 1.2). Atomic Force Microscopy (AFM) was used to evaluate the removal of smear layer for both control and under test conditioner.

Results: Prepared specimens were treated with 20% polyaspartic acid (200 mg/ml) at pH 1.2 for two treatment times at 10 seconds and 30 seconds. After rinsing with water pH of conditioner and the control increase to 4.2 and 3.5, respectively. AFM images show that 30 seconds cause a change in dentin where tubules were wider than normal dentin compared to 10 seconds, same as control.

Conclusion: Polyaspartic acid works in a similar way to commercial GC conditioner based on poly-acrylic acid and is capable to remove dentin smear layer. Hence, we suggest to use polyaspartic acid for conditioning of dentin and are currently testing the efficacy of such conditioners on the remineralization of collagen and towards repair of caries-affected dentin.

Support: UCSF Catalyst Award “PILP Treatment for the Repair of Dental Caries” and by the Center for Dental, Oral & Craniofacial Tissue & Organ Regeneration (C-DOCTOR)
#53 Title: Interdisciplinary Treatment for Full mouth Implant Supported Rehabilitation: A Case report.

**Author:** Jonathan Bensoussan DDS University of California, San Francisco School of Dentistry, Division of Prosthodontics

**Author Affiliations:** Arun Sharma BDS, MS, University of California, San Francisco School of Dentistry, Director of Graduate Prosthodontics, Hoda Hai DDS, MS, University of California, San Francisco School of Dentistry, Division of Periodontics Stacey Lee DDS, MS, University of California, San Francisco School of Dentistry, Division of Periodontics, Pinelopi Xenoudi DDS, MS, University of California, San Francisco School of Dentistry, Director of Graduate Periodontics

**Abstract:** A multidisciplinary treatment between the prosthodontic and periodontal clinics at the UCSF dental center to rehabilitate a patient with a failing dentition. The patient's treatment sequence started with maxillary and mandibular complete dentures. After a three month healing period, the patient received a cone bean computed tomography dual scan using the Nobel Branemark protocol. From this information, a tissue borne guide was printed via additive manufacturing for implant guided surgery. In total, 6 Branemark implants were placed in the maxilla and 4 Branemark implants were placed in the mandible. Following osseointegration of the implants, a combination of patient clinical appointments and laboratory steps utilizing analog methods were taken to achieve a full wax try-in. The vertical dimension of occlusion, centric relation, esthetics and phonetics were verified before the final prescription was sent to Avadent. Computer aided designing and computer aided manufacturing and milling technology were used to produce the Montreal titanium bar, and the hybrid denture made from a pre-shrunken bio-hygienic, polychromatic acrylic puck. The final prostheses delivered to the patient were maxillary and mandibular implant supported fixed complete dentures.
Acknowledgements

Special thanks to the following faculty

Lisa Berens, DDS, MPH
Benjamin Chaffee, DDS, MPH, PhD
Kyle B. Jones, DDS, PhD
Sara Hughes, EdD
Sarah Knox, PhD
Thomas Lang, PhD
Eni Obadan-Udoh, DDS, MPH, Dr.Med.Sc.
Jennifer Perkins, DDS, MD

Research and Clinical Excellence Day Support Staff

Roger Mraz, Coordinator

Additional thanks to

Navita Kalair, BDS, MPH
Laurie Bercasio
Tiffany Criger
Dorian Hollis
Alyson Ng
Deepa Saha

Brennan Crilly
Tami Lam
Julia Martinez
Daliah Williams

Wesley Kao
Luan Tran

Eric Lee

John C. Greene Society
  • Susan Keefe, President
  • Sarah Wong, Vice President

Also:
Priscilla Castro
Brendan Co
Justin Donato
Forouzandeh Ghazi
Jai Ghotra
Trixe Illas
Zhaodong Liu
Calvin Maxwell
Brian Nguyen
Milan Shergill
Nimrita Singh
Pauline Tran
Ashley Zhang

Judges

Emilie Barruet, PhD
Elizabeth Couch, RDH, MS
Christine Hong, DMD, MS
Tyler Huycke, PhD
Tri Huynh, DDS, PhD
Andrew Jheon, DDS, PhD
Navita Kalair, BDS, MPH
Misun Kang, PhD
Cristin Kearns, DDS, MBA
Pauline Marangoni, PhD
Alison May, PhD
Elizabeth Mertz, PhD, MA
Jeffrey Nebenzahl, PhD
Marisol O'Neill, PhD
Neha Pincha, PhD
Amnon Sharir, PhD, DVM
Spenser Smith, PhD
Sonia Sudiwala, PhD
George Taylor, DMD, MPH, DrPH
Camilla Teng, PhD
Pinelopi Xenoudi, DDS, MS
The Research and Clinical Excellence Day Committee wishes to recognize the following for their generous financial support of the Summer Research Fellowship Program:

Delta Dental
The School of Dentistry Dean’s Office
The Department of Orofacial Sciences
The Department of Oral and Maxillofacial Surgery
The Department of Preventive and Restorative Dental Sciences
The Department of Cell and Tissue Biology
The Buchannan Dental Clinic
The Program in Global Oral Health
The Program in Craniofacial Biology
AADR Summer Fellowship Program
Associate Dean for Research Student Research Fund
Drs. Deborah and John Greenspan
Dr. Peter Sargent and Dr. Caroline Damsky
The Lee Hysan Fund
The John C. Greene Fund