



# The Explorer

Journal of Dental Student and Faculty Research

11<sup>th</sup> Edition | 2017

**UCLA**

School of Dentistry

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# A Letter from Dean Krebsbach



Dear Readers,

Thank you for taking the time to read this message. Dental and oral health research has been one of my greatest passions throughout my career. To become the dean of a dental school that is so heavily invested in dental research is inspiring. I have had the opportunity to meet several of our bright and talented D.D.S. students this past year, and they have shared their research passions and what they hope to achieve in their career. It makes me proud to think that the future of dental research will surely be in the hands of UCLA Dentistry alums.

As dentists and oral health specialists, we have a responsibility to our communities to provide the best possible care available. It is my belief that research moves the dental field forward. New clinical advancements and technology start in a research lab.

One of the ways that we celebrate our research achievements is at our annual Research Day, where we showcase research projects from our pre-doctoral, MS and PhD students, and our post-doctoral scholars. This past year, we

welcomed keynote presenter, Dr. Brian Schmidt, a professor and surgeon from NYU, who discussed The Neurobiology of Oral Cancer Pain. It gives me great pride to see how the dental school is contributing to the dental research field.

As our fourth year dental students embark on their different paths, I hope that they continue to incorporate research into their careers and practices. I also encourage our current dental students to continue and explore new avenues of research.

Sincerely,  
Paul Krebsbach, D.D.S., Ph.D.  
Dean

## A Letter from the Editors

Dear Readers,

We are extremely excited to present to you the 11<sup>th</sup> Edition of *The Explorer* Journal of Dental Student and Faculty Research. The UCLA School of Dentistry remains at the forefront of both dental and oral biological breakthroughs, with total research funding that exceeded \$23.2 million this past academic year. Thousands of hours have been put into hundreds of research projects throughout the school and we hope this journal provides a glimpse into the immense number of innovative technological advancements and discoveries taking place on a daily basis at the UCLA School of Dentistry.

Our amazing team of authors, editors, and designers has done an incredible job this entire year making this issue possible. We would like to thank them for their hard work and dedication. In addition, we would like to express our deep appreciation to Dean Paul Krebsbach for not only his continual support of research programs at the university, but also for being a tremendous advocate for our fellow dental students, faculty, and staff. We are eager and excited to see what the future holds with Dr. Krebsbach as our new Dean.

Lastly, with the start of a new school year in our midst, we would like to wish everyone the best of luck this year. Your tireless efforts both academically and clinically never cease to amaze and inspire us. Go Bruins!

Sincerely,  
Armin Miresmaili  
Darron Miya  
Sina Banankhah  
*The Explorer* Editors-in-Chief

Written by Ryan Gaw '19



Similar to many choices in healthcare, providers and patients often face the risk of encountering associated issues when attempting to remedy a problem. Dr. Tingxi Wu, a current Orthodontic Resident-PhD dual degree student, is working on a research project to investigate how to prevent the accumulation of plaque and

inflammation in patients with orthodontic brackets. To accomplish this, Dr. Wu developed an effective screening assay, which led to the discovery of several chemical compounds with strong inhibitory effects against bracket-induced plaque formation. The ultimate goal is to provide an effective and safe compound that can be integrated into toothpaste to be used by orthodontic patients to prevent bracket-associated plaque formation. She devised the idea for the research project by coupling her training background in oral microbial pathogenesis with the observation that gingivitis during orthodontic treatment is quite common.

The accumulation of biofilm can lead to a multitude of negative consequences such as white spot lesions, caries, and gingival inflammation. Today, there are many products that are offered to remove biofilm in orthodontic bracket patients after it has formed. These include products such as inter proximal brushes, threader floss, specialized toothbrushes, and Waterpik systems. Instead, Dr. Wu is trying to prevent initial formation of biofilm before it even forms. The working hypothesis is that

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*“polysaccharides and polypeptides on bacterial surfaces play major roles in microbial adherence and biofilm formation during bracket-induced plaque formation, which could be potentially inhibited by specific sugar or amino acid monomers”.*

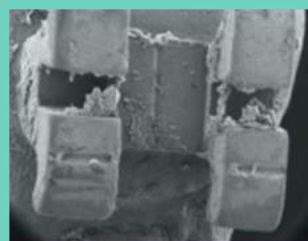
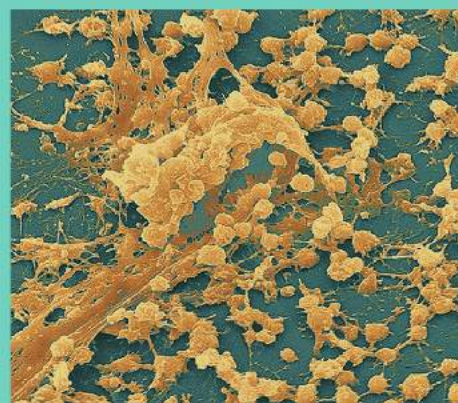
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The aim of the study is to discover sugars/amino acids, formulate them, and evaluate the safety and anti-plaque efficacy of the formula in-vitro and in-vivo. A panel of sugar/amino acids with inhibitory effects against in-vitro biofilm formation has been found and formulated. The formula showed strong inhibitory effects against bracket-induced biofilm formation in-vitro. A clinical study of the efficacy of this formula is now under evaluation in-vivo.

The pilot clinical study will be randomized, double-blinded, placebo-controlled and involve 60-subjects to evaluate the in-vivo safety and efficacy of this newly formulated paste on managing bracket induced plaque formation. The study covers two specific aims: evaluating the safety of administering this newly formulated toothpaste in adolescent subjects, and assessing the efficacy of this newly formulated toothpaste in reducing bracket-induced plaque formation among adolescent subjects. If successful, this study would validate the clinical safety and efficacy of this newly formulated toothpaste against bracket-induced plaque accumulation. The toothpaste can be especially helpful against bracket-induced dental diseases in adolescents; an age group that often neglects oral hygiene due to their hectic schedules. Lastly, by preventing biofilm associated problems such as gum recession or white spot lesions, the patient's satisfaction in the aesthetic result of orthodontic treatment can be further improved.

#### Background:

MS, Oral Biology, UCLA School of Dentistry  
BDS, Wenzhou Medical University  
Sichuan University, School of Stomatology



# THE MANY LAYERS OF ORTHODONTICS

Written by Allie Larios '18

The dental profession is generally considered a facet of health which focuses on treating teeth. However, the general public tends to overlook the fact that dentists are trained to be head and neck specialists. Beyond the hard and soft tissues of the mouth, dental professionals are responsible for recognizing and diagnosing conditions of the nasal cavity, sinuses, oropharyngeal tract, and even the cervical region of the spine. Though these areas may seem like a dentist's uncharted territory to the average person, pioneers in our field such as Dr. Audrey Yoon are defying that notion.

Dr. Yoon is a highly regarded Orthodontist based in the Downtown Los Angeles area who has perfected the craft of creating beautiful smiles. She can be found tending to her patients at her practice during the week, yet Dr. Yoon still travels twice a month to Stanford to assume her alternative role as a member of the Sleep Surgery Team. Dr. Yoon and her team's research focuses on optimizing the Distraction Osteogenesis Maxillary Expansion technique and developing a surgery-first orthodontic protocol for Distraction Osteogenesis Maxillary Expansion, which was recently published in the latest Otorhinolaryngology (Ear-Nose-Throat) text book. Because of their research, an orthodontic approach is now considered a viable option for sleep apnea treatment. While Dr. Yoon has found that there is generally a surprising amount of disconnect between medical and dental professionals, her involvement with the Stanford Sleep Study group has shown the positive impacts of sharing knowledge and collaboration among health care professionals.

Other areas of interest to Dr. Yoon include the customization of oral appliance/distractor device design, craniofacial growth modification, frenulum inspection, and myofunctional therapy. She also recently became a part of a human genome project to identify three dimensional facial morphology characteristics and to predict obstructive sleep apnea in patients. What pushes Dr. Yoon to be committed to so many projects? "Most of my research is clinical research working with patients and I feel honored when they entrust me with their health and treatment welfare. When patients...give me their trust with the most personal and intimate matters, I am able to help them and see their life change after treatment." These experiences, along with the opportunity to work alongside people who she calls trustworthy and dedicated, has kept Dr. Yoon adamant with progressing her research aims even in the face of criticism. She notes that one of the main challenges in research is facing the politics of various groups, yet it is obvious that these obstacles have yet to prevent her and her team from turning their vision of optimizing sleep apnea treatment into a reality.

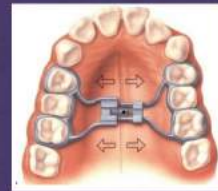
Although research may seem out of touch with the day-to-day happenings of most dental practitioners, Dr. Yoon believes her engagement with research has improved her clinical skills as an Orthodontist. "As a clinician, I see not the current trends but also see the limitations of knowledge and find many areas of curiosity which sets up new research questions to pursue." By keeping up with the latest advancements in research, Dr. Yoon feels more confident with her abilities and realm of knowledge when interacting with her patients. Her enthusiasm for patient care combined with her inquisitive nature to advance that care demonstrate how we, as clinicians, can be the people who both create and deliver treatment.

Leaders like Dr. Audrey Yoon, who are expanding the sphere of our profession in cutting edge ways, remind us through the power of research that the scope of dentistry is, in fact, not limited to teeth.

## Sleep Apnea Treatments

### RAPID PALATAL EXPANDER

We expand the upper jaw to be wider and the floor of the nose is expanded as well to create more nasal volume. It is an effective way for treating sleep apnea and sometimes this expander therapy is combined with tonsillectomy to achieve maximum results for children.



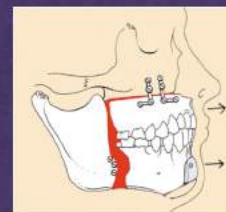
### ORAL APPLIANCES

For people who have small and retruded lower jaws, pushing the tongue backward, we re-position the lower jaw forward using orthodontic appliances. If you prefer not to have the full brace treatment, we can use a simple oral appliance that can be applied just during the night time.



### ORTHOGNATHIC SURGERY

For severe cases, we recommend orthognathic surgery in conjunction with braces, which has been proven to be the most effective surgical treatment for sleep apnea.



AUDREY YOON, DDS

From Dr. Audrey Yoon's website

# DR. JIN HEE KWAK

Written by Richard Song '19

"As exciting and fulfilling as it may be to provide great therapies and technologies to patients as an end-user, I feel the most passionate and intellectually stimulated developing scientifically invented platforms for new therapies that contributes to the advancement of healthcare," says Dr. Kwak, a board-certified orthodontist who is also an established scientist in the field of skeletal regenerative medicine. "In order to achieve this, I formulate research questions in clinic and then focus on catering innovation back to patient care here at UCLA, where world-renown faculty and clinical infrastructures are readily available to help me transform my ideas to reality."

In order to pursue her dream of becoming a dual clinician-scientist who could invent new clinical technology and apply them to patients needing novel treatment modalities, Dr. Kwak pursued the academic track in her dental school at Yonsei University, South Korea. Immediately following graduation, she joined the UCLA School of Dentistry as a research fellow in the laboratory of Dr. Kang Ting, a distinguished scientist in craniofacial and skeletal research and the discoverer of the novel osteogenic molecule, NELL-1. After orthodontic training at UCLA, Dr. Kwak joined the UCLA faculty to fulfill her dream as a clinician-scientist.

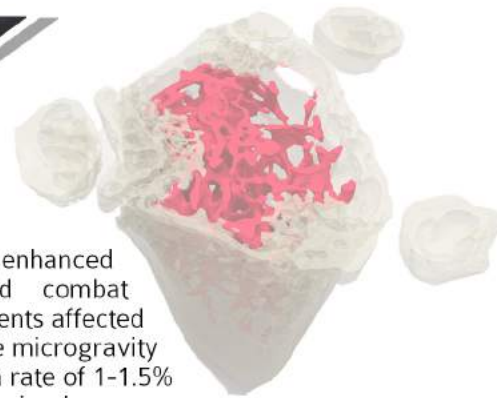
As the best example of an approach to start from a clinically important question to bringing a solution back chairside, Dr. Kwak explains the history of how the novel osteogenic protein NELL-1 was discovered and its path to clinical trials and FDA approval for medical application. Two decades ago, Dr. Ting and his research team investigated why there is overzealous bone formation in the cranial sutures of craniosynostosis patients who at the time were under the collaborative care of the UCLA Craniofacial Clinic and the Orthodontics clinic. The bones collected from these patients were analyzed and were found to have high expression of the NELL-1 gene. Since then, NELL-1 as a recombinant protein therapeutic was produced and has repeatedly proven in animal models to regenerate local defects of the bones without presenting the common side-effects of osteogenic growth factors in the market. NELL-1 is now approaching clinical trials in preparation for FDA approval for use in osteoporotic patients' spinal fusion therapy.

While working with Dr. Ting and his team members Dr. Chia Soo and Dr. Ben Wu, Dr. Kwak came to believe that NELL-1 has potential to be further developed as a systemic therapy to treat osteoporosis and associated bone loss in the alveolar bones and the mandibular condyles. This idea for a systemic NELL-1 therapy came to fruition when NASA and CASIS (the manager of the U.S. National Laboratory of the International Space Station [ISS]) collaborated to fund a nearly 140 million dollar research proposal centered on sending rodents up to space to study the effects of the therapy on space-flight induced osteoporosis.

The objective of this colossal study, called "Systemic NELL-1 Therapy for Spaceflight-induced Osteoporosis" is to see whether administration of PEGylated NELL-1,

a modified version of NELL-1 with enhanced pharmacokinetics, could combat extreme bone loss in rodents affected by microgravity. Because microgravity induces osteoporosis at a rate of 1-1.5% bone loss per month in humans as compared to the typical 2-3% bone loss per year experienced by millions of people on Earth, a successful NELL-1 therapy in space would have huge implications for treating not only astronauts, but also numerous osteoporotic patients on Earth complicated by disuse atrophy. To perform this experiment, 20 rodents will be sent up to space in a manned journey where they will be administered NELL-1 systematically once every 2 weeks, while another 20 rodents will serve as the control group in the Kennedy Space Center (KSC) in Florida, receiving the same exact drug and dosages. Half of the flight group animals will be returned from space to UCLA halfway through the experiment to continue receiving treatment on ground, and they will be compared with the full-flight and ground control group to give us insight into post-flight recovery and the retention of therapeutic effect. DXA bone scans will be used for longitudinal analysis of the bone mineral density and bone volume. After 9 weeks of experiments, rodents will finally be harvested and analyzed by a variety of methods such as fluorochrome label analysis, microCT/PET scans, organ pathology/toxicology tests, histology and immunohistochemistry to verify the safety and efficacy of the systemic NELL-1 therapy for osteoporosis.

The rocket carrying these 20 rodents will launch in mid-2017, making this a huge year for the research team as well as UCLA. Because of the magnitude of the project, Drs. Kwak, Ting, Wu, and Soo have been working diligently for the past two years, to ensure every little concern is identified and addressed. Although two years of planning for just one project may seem like an excessive amount of work, Dr. Kwak does not consider research as work. When asked if she had any advice for students pursuing research, she responded, "Don't do research for the sake of doing research. Do something you truly have a passion for - otherwise it will just feel like work." It was exactly this passion Dr. Kwak has for research that has led her to be so successful so early into her career.



# UNDERSTANDING OSTEONECROSIS

## UNRAVELING THE MYSTERIES OF ONJ

Written by Debbie Lee '18

**Osteonecrosis of the jaw (ONJ)** is a condition that exposes bone in the jaw and is unfortunately linked to dentists, as it often occurs after a dental extraction. It is associated with anti-resorptive medications such as bisphosphonates (BPs) or denosumab, and can be severe and debilitating, requiring surgical removal of affected bone. It is not a new disease as it has been described and documented extensively for over 150 years. However, our understanding of the ONJ at a molecular level is lacking, and thus the disease cannot be adequately prevented or treated at the clinical level.

Dr. Reuben Kim is an associate professor in the Section of Restorative Dentistry and the Director for Collaborative Research Programs in the Division of Constitutive & Regenerative Sciences. He has been a loyal Bruin for the entirety of his dental career as he received both his DDS in 2003 and PhD in 2008 from UCLA, started his professorship at UCLA in 2006, and became tenured in 2013. As a young practitioner at UCLA, he began to notice the frequency of ONJ patients in the clinic, and soon became interested in the disease process. He spent years researching ONJ development, and made great strides in expanding our understanding of the osteomucosal healing in ONJ.

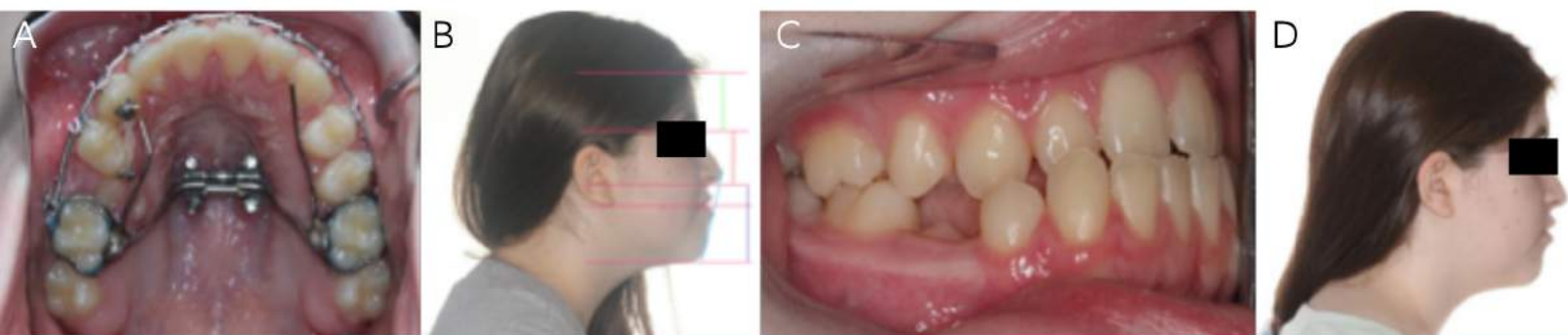
Having had a strong background in epithelial biology, Dr. Kim started looking at ONJ from a soft tissue perspective. The oral cavity is unique in that the soft tissue and hard tissues are in direct contact with each other. It was this interaction between soft and hard tissues that he explored further, looking specifically into the role of BPs in disrupting this interaction. To study this, he and his team developed animal models that recapitulate multiple disease entities, including ONJ lesions, to examine the underlying pathophysiology at the preclinical level.

His studies suggest that there is an underlying structural problem associated with ONJ development. For example, chronic inflammation due to chronic periodontitis or pulpal disease is a predisposing factor that can further exacerbate ONJ after a dental extraction when a patient is on anti-resorptive therapy. Dr. Kim demonstrated this direct link with both an extraction model and an inflammation model. He induced inflammation in mice by 1) performing pulp exposure to mimic periapical disease, and 2) fitting a ligature to mimic periodontitis. After inducing inflammation for a period of time, and administering BPs, the tooth was extracted. Evidently, after BP administration, higher incidences of ONJ development and more severe bone necrosis were observed in mice with pulp exposure and ligature placement. Similar results were demonstrated using a denosumab model. While Dr. Kim seeks to discover so much more with a number of ongoing studies in the field of osteomucosal healing and ONJ, the clinical implications for his studies so far have enormous significance. Periodontal and pulpal diseases must be controlled before performing tooth extraction in patients on anti-resorptive therapy in order to reduce the risk of developing ONJ.

In addition to running an active research lab in the Section of Oral Biology, Dr. Kim is currently the Course Chair for the 6-quarter long Direct Restoration courses for both first and second year dental students and an active practitioner in the UCLA Faculty Group Dental Practice as a restorative dentist.







# CHALLENGING THE ACCEPTED

## Post-puberty maxillary skeletal expansion with MARPE

Written by Chantal Hakim '18

The classical school of thought regarding maxillary skeletal expansion has always been that it is near impossible to achieve efficient and effective orthodontic movement post-puberty without invasive surgery. The two traditional modes of maxillary palatal expansion, the hyrax and jackscrew appliances, effectively accomplish this feat if the maxillary suture is still open. Between the ages of 12 and 15, a patient's intermaxillary suture becomes interdigitated and such skeletal movements become extremely difficult. Ideally, we would like to achieve skeletal expansion by separating the intermaxillary suture, however, after the interdigitation occurs, we mostly achieve dental expansion and bone bending rather than true skeletal expansion. In the past, if patients could not achieve results with a traditional expander, the only other option was surgically assisted rapid palatal expansion (SARPE) or orthognathic surgery (LeFort I) - both very invasive procedures.

Dr. Won Moon, the program director at the UCLA School of Orthodontics, and his team have challenged this notion through their development of the Miniscrew-Assisted Rapid Palatal Expander (MARPE). This appliance is an implant-assisted expander that achieves true skeletal expansion regardless of the growth stage of the patient. Dr. Cathy Lee, a third-year resident in the UCLA Orthodontic Program has used this cutting edge technology and achieved successful results on several of her patients and shared her experiences as well as more information on the mechanics of the MARPE. The mini-screws are each approximately 1-2 mm in diameter and 6-11 mm in length and work by engaging both layers of cortical bone in the palate (Figure A). This gives the appliance maximum anchorage to separate the palatal segments.

Lee attributes the superiority of the MSE to a conventional expander to three qualities. The first is being able to achieve skeletal expansion: "A conventional expander is a tooth borne expander but with an MSE you get true skeletal

expansion so you won't get tipping of the teeth like you would with the traditional expander." The second is improved vertical control of growth, "A traditional expander could open the bite, but by using MSE, vertical control could be possible, controlling the vertical pattern of the patient." And finally, she discusses effective anchorage, "MSE provides maximum anchorage, which controls the AP movement of teeth," she explains.

Dr. Lee has successfully achieved skeletal expansion in multiple pediatric and adult patients. In the case Dr. Lee has shared, a 13 year old female patient presented to the clinic with a chief complaint of having an underbite. Upon further examination, the patient was deemed to be a Skeletal class III with 6 mm of negative overjet (Figures A and B). Using a lateral cephalogram and hand wrist film to assess growth and maturity, Dr. Lee was able to determine that the patient's growth was almost complete. Since the patient has a dolichofacial pattern (steep mandibular angle), and needed maximum anchorage to create appropriate space for unerupted upper right 5, Dr. Lee decided to use an MSE rather than traditional expander which tends to open the patient's bite, worsening the patient's dolichofacial pattern. Through MARPE skeletal expansion, Dr. Lee was able to address the patient's chief complaint and achieve 4.5 mm of expansion.

Remarkably, the patient's facial esthetics had improved drastically. In Figure D, the Class III skeletal relationship seems to have disappeared completely. Through this method of expansion, the patient could avoid an invasive procedure or extractions and is completely satisfied with her treatment. Dr. Lee definitely acknowledges the advantages of this new technology, "compared to other orthodontics programs, by attending UCLA, I have had a great opportunity to get exposed to cutting edge technology, and MSE is a good example. I think I am very blessed that I have been here at UCLA learning many innovative techniques."

# GRANT NISHIMURA - PRE-DOC

Written by My Nguyen '18

Ever since Dr. Brånemark placed his first titanium implant in 1965, implants have become one of the most popular assets in modern day dentistry. The osseointegration of titanium to bone has allowed implants to become much more predictable and successful. From replacing a single missing tooth to reconstructing a resected mandible, implants have changed dentists' capabilities to rehabilitate the oral cavity. Every day, cutting edge research laboratories invest time toward improving stability and duration of implant placement. Grant Nishimura, a third-year dental student at the UCLA School of Dentistry, immediately realized the impact implants can have in restoring a patient's oral function and esthetic which motivated him to engage in the forefront of implant research.

Under the guidance and mentorship of Dr. Peter Moy, a world renown researcher in implant dentistry, Grant was motivated to investigate the biochemical factors and mechanical measurements that would improve the clinical loading of implants. In one of his research projects, Grant investigates the effects of Platelet Rich Fibrin (PRF) in different bone grating material. PRF is a second-generation platelet concentrate, similar to Platelet Rich Plasma (PRP), which can be used to promote wound healing, bone growth, graft stabilization, wound healing and hemostasis. It is superior to PRP because the processing technique is simplified and it doesn't require biochemical-additives.

By adding PRF to different types of bone graft materials, Grant attempts to find the best combination that would result in enhanced osseous healing. The clinical implication of his research involves the potential for earlier healing time and implant loading. Increasing the stability and reducing the duration of implant placement will benefit the patient functionally and esthetically.

Grant's second research project involves analyzing an additional 5 years of data regarding the Implant Stability Quotient (ISQ) values of implants. The ISQ is a scale of 1 to 100 and is a measure of the stability of an implant. Typically, higher values (> 70 ISQ) correlate with greater stability and lower values (< 60 ISQ) correlates with lower stability. The values are a potential indicator of the loading protocol of the implants, with higher values corresponding with immediate loading. With the additional set of 5 years of data containing thousands of implants measured with ISQ, this means more evidence to reinforce existing loading protocol measurements or establish new ones.

Grant is optimistic about the future of implants in dentistry and hopes to continue his research in view of pursuing Oral and Maxillofacial Surgery. Despite his dedication to research, he serves as the class Vice President for the class of 2018 and is actively involved in Basic Dental Principles teaching apprenticeship and Oral & Systemic Medicine Club. Although balancing the dental curriculum and research is a difficult task, Grant has gained a new definition of time efficiency. "Research is the most rewarding if you have a genuine interest in it and manage your time wisely."



southernimplant.us

# 2017 Research Day Abstracts

## MRONJ Clinical and Radiographic Presentation After Bisphosphonate v Denosumab Treatment

Chantal Hakim, Edwin Eshagzadeh, Kaycee C. Walton

**Background:** Medication Related Osteonecrosis of the Jaw (MRONJ) is a rare but significant side effect of antiresorptive therapy, and specifically Bisphosphonates or Denosumab. Both drugs are prescribed for conditions exhibiting bone fragility like osteoporosis and primary or metastatic bone cancer. Current literature contains few studies comparing the difference between the clinical and radiographic appearance of MRONJ caused by these medications.

**Objective:** To examine the existence and extent of clinical and radiographic differences between patients treated with only Bisphosphonates vs. patients treated with Denosumab.

**Methods:** We retrospectively analyzed the records of 70 patients being treated at the UCLA School of Dentistry for MRONJ caused by Bisphosphonate therapy or Denosumab. Age, gender, primary disease, inciting event, stage of disease at presentation and the presence and extent of radiographic changes associated with ONJ were obtained. Fisher's exact test was used to compare qualitative variables and Student's t-test to compare numeric variables. The data was analyzed to assess differences between the disease-causing medications.

**Results:** In the Denosumab group, more patients were treated for oncologic disease while in the BP group, the number of oncologic vs. osteoporotic patients was similar. Both groups had a higher incidence of females vs. males and of ONJ occurring in the mandible vs. the maxilla. There was no statistically significant difference regarding the clinical staging of MRONJ between the two groups. However, radiographically, the Bisphosphonate group demonstrated a significantly higher incidence of extensive and localized sclerosis, lytic changes and sequestration.

**Conclusions:** Although there was no difference in the appearance of clinical bone exposure upon presentation, a statistically significant difference in the radiographic presentation of disease was observed. Follow up outcome studies are needed to assess whether this diverse radiographic presentation results in differences in MRONJ progression and healing.

## Knowledge, Attitude, Beliefs, and Practices (KABP) Surveys on Special Needs Patients and their Student Dentist Providers.

Haejin Kang, Francisco Ramos-Gomez

**Objective:** 1) Evaluate dental students' level of understanding of the challenges presented by special needs patients and their clinical competency to treat these patients professionally. 2) Compare knowledge, experience, comfort, and competency by class year and by number of clinical experiences.

**Methods:** An email with a link to an anonymous 21-question knowledge, attitude, behavior, and practice (KABP) survey on special needs patients was sent to 255 dental students: third year, fourth year, and recently graduated dental students from UCLA SOD. The electronic mailing list included all the dental students enrolled in each class year. The KABP survey form explicitly stated that participation in the study was voluntary and that completing the survey will be considered respondent's consent to participate. The survey questions were based on American Academy of Pediatric Dentistry's (AAPD's) definition of special health care needs and guidelines on management of dental patients with special health care needs. Specific questions were asked to assess student's clinical competency, experience (# of special needs patients seen), comfort, and knowledge accordingly. One-way ANOVA was performed for the analysis of variance along with pair-wise comparisons of sample means through the Tukey HSD test.

**Results:** In general, the student dentists at UCLA SOD felt like they had a moderate level of knowledge (mean= 3.2) and very little clinical experience (mean=0.875) on special needs patients (add another chart or refer to table 3,4). When comparing the responses from different class years, 4th year and recent graduates had higher levels of knowledge than that of 3rd year dental students ( $p < 0.01$ ). Despite this trend, recent graduates did not have more experience in clinic nor feel more confident and competent treating special needs patients compared to the 4th year dental students. Out of the total respondents, approximately 41% (10) of the recent graduates and 52% (17) of the 4th year dental students reported that they had never provided any treatment for patients with special needs (See Figure 3). The rest of the respondents who did have clinical experience treating special needs patients showed higher levels of competency in treating these patients with increase in the number of clinical experiences ( $p < 0.001$ ; See Table 7).

**Conclusion:** Continuing effort to increase exposure and clinical experience in treating special needs patient is required to improve and maintain the level of knowledge and competency of student dentists in UCLA SOD.

## Chronic ethanol and tobacco treatment enhances CSC phenotype in oral cancer cells

Calvin Kieu, Sung Hee Lee, Ji Ho Han, No-Hee Park, Ki-Hyuk Shin

The Shapiro Family Laboratory of Viral Oncology and Aging Research at UCLA School of Dentistry

**Objective:** Cancer stem-like cells (CSCs or cancer-initiating cells) are subpopulations of cancer cells that possess self-renewal capacity, which is the driving force of tumorigenesis. CSCs are potentially responsible for metastasis, drug resistance, and recurrence of cancers. Despite compelling evidence that alcohol and tobacco are crucial risk factors for oral cancer, their effects on CSCs has not yet been well understood. In this study, we investigated the effect of ethanol and cigarette smoke condensate on various CSC phenotypes of tongue cancer cells.

**Methods:** We treated human tongue squamous cell carcinoma cells with ethanol, cigarette smoke condensate, and the combination of ethanol with cigarette smoke condensate for extended periods and examined their effects on CSC properties. The following CSC phenotypes were compared between the untreated control and the treated tongue cancer cells: self-renewal capacity, expression of pluripotency transcription factors, migration, and anchorage independent growth ability.

**Results:** Chronic ethanol and cigarette smoke condensate treatment enhanced CSC phenotypes of tongue cancer cells, such as an increase in self-renewal capacity, stem cell-associated genes expression, migration potential, and in vitro tumorigenic potential. More importantly, the combination treatment of ethanol and cigarette smoke condensate resulted in the greatest impact on CSC phenotypes in the cells.

**Conclusion:** Our studies suggest that chronic consumption of alcohol and tobacco may promote malignant progression of tongue cancer by increasing CSC properties. These results point towards the importance of the cessation of alcohol and tobacco consumption by patients who are diagnosed with cancer.

## Heparin-mimicking Sulfonated Hydrogel to Stabilize BMP-2 activity for enhanced Osteogenesis

Paul Kim, Soyon Kim, Min Lee

**Objectives:** Sulfated polysaccharides such as heparin have been shown to form stable complexations with BMP-2 and have been widely used in controlled release systems to sustain the immature protein release. However, heparin's nature of variability, unpredictability, and difficulty in modification comes by as problems. Similar biological activities to heparin have been observed in small compounds that contain sulfate or sulfonate groups. This study aims to stabilize and augment BMP-2 activity and enhance osteogenesis in tissue engineering chitosan hydrogels by integrating photo-crosslinkable methacrylated glycol chitosan (MeGC) with heparin-mimicking sulfonic acid molecules, poly-vinylsulfonic acid (PVSA) and poly-4-styrenesulfonic acid (PSS).

**Methods:** The incorporation of PVSA or PSS in MeGC hydrogels was verified by toluidine blue staining. The protective effects of PVSA or PSS on BMP-2 stability were studied under various therapeutically relevant environments. Ability of the sulfonated hydrogels to bind BMP-2 was confirmed with immunostaining. Release kinetics of BMP-2 from hydrogels was also tested with ELISA. Ability of the developed hydrogels to enhance osteogenesis of encapsulated bone marrow stromal cells (BMSCs) was evaluated via qRT-PCR analysis and alizarin red staining.

**Results:** The homogeneous and stable incorporation of PVSA or PSS was observed in MeGC hydrogel's properties. Bioactivity of BMP-2 was well maintained in the presence of polysulfonates under various therapeutic stressors (thermal, acidic and enzymatic). Sulfonated MeGC hydrogels significantly increased osteogenic differentiation of encapsulated BMSCs without BMP-2 supplementation as observed by increased mineralization and upregulated osteogenic gene markers compared to unmodified hydrogel. This is likely due to the hydrogel surface that sequestered and augmented endogenous BMP activity as validated by immunostaining for BMP-2. Additionally, the sulfonated hydrogels supported sustained release of loaded BMP-2 with reduced initial burst compared to untreated MeGC.

**Conclusions:** Heparin-mimicking sulfonated hydrogel, through stabilization and augmentation of BMP-2 activity, enhances osteogenesis and could be a promising biomaterial for bone regeneration.

## Clastic cells absent around root surfaces in pulp-exposed periapical lesions

Deborah Lee, Avisha Shah, Minju Song, Sol Kim, Ki-Hyuk Shin, Mo Kang, No-Hee Park, and Reuben Kim

**Introduction:** Clastic cells, originating from the monocyte-macrophage lineage, resorb mineralized tissues. They can be activated to function through the binding of receptor activator of NF- $\kappa$ B ligand (RANKL) to its receptor (RANK), or can remain latent due to OPG, a RANKL antagonist secreted by osteoblasts preventing binding of RANKL to RANK. Odontoclasts are clastic cells specifically found in dental tissues (e.g., root surfaces). In periapical periodontitis, alveolar bone around the tooth apex becomes resorbed as osteoclastic activity is increased; yet the roots of the teeth are often left intact, presumably owing to the high resistance of root surface resorption from odontoclasts by yet unknown underlying mechanisms. Here, we aim to examine spatial patterns of clastic cells using a periapical periodontitis model in mice.

**Methods:** We induced periapical lesions in mice by exposing the pulp of the left maxillary first molar with a  $\frac{1}{4}$  round bur. The contralateral right maxillary first molar was used as a control. The maxillae were harvested, fixed, and subjected to  $\mu$ CT scanning and three-dimensional volumetric analysis. Morphological parameters of trabecular bone microarchitecture in femur were assessed using the CTAn software and bone volume fraction was measured. TRAP staining was performed and osteoclasts were quantified. Immunohistochemical staining was performed for RANKL, OPG, and F4/80, a marker for macrophages.

**Results:** At the apex of the tooth, pulp exposure resulted in periapical radiolucency with mineralized tissues at the surrounding bone surfaces but not on the root surfaces. Histologically, clastic cells were present on the bone surfaces but absent around the root surfaces. Expression of F4/80 and RANKL were not found at close proximity to the root surfaces, but OPG expression was globally expressed.

**Conclusion:** The lack of F4/80 and RANKL expression around the root of the tooth, in part, is associated with absent odontoclasts and intact root surfaces despite prominent bone resorption around the pulp-exposed tooth.

## Connective tissue formation proceeds epithelial closure and bone formation during osteomucosal healing

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**Objectives:** Osteomucosal healing is a simultaneous and interdependent healing process of the soft and hard tissues that typically occurs in the oral cavity following dentoalveolar trauma such as extraction. Although the concept of osteomucosal healing is well-known, the underlying cellular and molecular events that occur in this process are not clearly understood. Here, we aim to investigate the early temporal and spatial patterns of osteomucosal healing in the context of epithelial closure, connective tissue formation, and woven bone formation following tooth extraction in mice.

**Methods:** The maxillary first molar of C57/BL6 mice were extracted atraumatically, and the maxillae were harvested everyday from day 0 to 7 ( $n = 3$  per day). The size of the epithelial wound closure was evaluated by measuring the wound areas and perimeters. Woven bone formation in the tooth-extracted sockets was examined and quantified using  $\mu$ CT scan. Formation of new connective tissues was evaluated using Tri-Chrome and Picro Sirius Red staining methods followed by polarized microscopy for quantification of collagen type I and III. Osteoclasts formation was examined using TRAP staining.

**Results:** The epithelial wound area and perimeter progressively decreased over 7 days without complete closure. Woven bone formation was observed around day 5 in mesial, distobuccal, and distopalatal socket areas. In contrast, expression of Collagen Type 1 and III started appearing as early as day 2. TRAP+ osteoclasts also appeared around day 2. Interestingly, there were no osteoclasts observed around the newly formed woven bone.

**Conclusion:** Our study indicates that formation of connective tissues is the early event that proceeds and mediates epithelial wound closure of the soft tissues and the woven bone formation of the hard tissues. Further detail understanding in the osteomucosal healing process may help better managing intraoral traumatic lesions that include soft and hard tissues.

## Effects of UV Photofunctionalization on Osseointegration in Aged Rats

Kourosh Nakhael, et al.

**Objectives:** Healthy life expectancy has increased over the years and the demand for implant treatment in elderly patients has increased accordingly. Geriatric patients have distinct biological disadvantages with respect to bone healing, and have shown considerably reduced osteogenic function. The purpose of this study was to evaluate the effects of photofunctionalization on osseointegration under the biologically adverse conditions of aging.

**Materials and Methods:** The biological capability of bone marrow-derived osteoblastic cells from young (8-week old) and aged (15-month old) rats was evaluated. Osteoblasts from aged rats were seeded on titanium discs with and without photofunctionalization, and assessed for initial cell attachment and osteoblastic functions by measuring the expression of ALP and calcium deposition. Titanium mini-implants, with and without photofunctionalization, were placed in the femur of aged rats, and the strength of osseointegration was measured at week 2 of healing. Peri-implant tissue was examined morphologically and chemically using scanning electron microscopy (SEM) and energy dispersive x-ray spectroscopy (EDS), respectively.

**Results:** Cells from aged rats showed substantially reduced biological capabilities compared with those derived from young rats. The cells from aged rats showed significantly increased cell attachment and the expression of osteoblastic function on photofunctionalized titanium than on untreated titanium. In addition, the strength of osseointegration was increased by 40% in aged rats carrying the photofunctionalized implants. Robust bone formation was observed around the photofunctionalized implants with strong elemental peaks of calcium and phosphorus, whereas the tissue around untreated implants showed weaker calcium and phosphate signals.

**Conclusion:** These in vivo and in vitro results corroboratively demonstrate that photofunctionalization is effective for enhancing osseointegration in aged rats.

## Vitamin D Pathway Regulation in Oral Keratinocytes Over-Expressing Cyclin D1

Sanjay Mallya, Jessica Sea, Niraj Patel, Miriam Guemes

**Objectives:** Oral squamous cell carcinoma (OSCC) is a common form of oral cancer with a poor survival prognosis. Cyclin D1 is a gene involved in cell cycle regulation and is known to be amplified in 30-50% of OSCC cases. Cyclin D1 overexpression has been linked to metastases and tumor malignancy. The hormone 1,25-dihydroxyvitamin D 1,25 (OH)2D3 is a crucial regulator of proliferation and differentiation and has anti-proliferative effects associated with G0/G1 cell cycle arrest.

**Methods:** We have developed stable oral keratinocyte cell lines that overexpress cyclin D1 (OKF6-D1), or harbor an empty vector control (OKF6-E). Cells were treated with 1,25 (OH)2D3, 10<sup>-8</sup>M, or with vehicle alone (ethanol) for 6 and 24 hours. mRNA was isolated and used to examine expression of the vitamin D receptor (VDR) and CYP24A1. Metabolism effects of overexpressing cyclin D1 were assessed by quantifying the radiolabeled conversion of 3H-25(OH)D to 3H-1,25 (OH)2D3 by HPLC. Cellular localization of VDR was examined by immunofluorescence.

**Results:** Treatment with 1,25 (OH)2D3 significantly increased expression of CYP24A1 in OKF6-D1 cells compared with control cells. Analysis of VDR mRNA expression and immunoblotting confirmed a significant reduction of VDR in OKF6-D1 cells versus OKF6-E cells after 1,25 (OH)2D3 treatment. HPLC analysis for vitamin D metabolites demonstrated decreased synthesis of activated 1,25(OH)2D3. Immunofluorescence analysis showed weaker VDR immunostaining in OKF6-D1 cells compared with control cells after 1,25 (OH)2D3 treatment.

**Conclusion:** Our data demonstrates that overexpression of cyclin D1 causes deviations in the Vitamin D pathway in oral keratinocytes. Ongoing experiments will help define the function of the vitamin D pathway in oral cancers overexpressing cyclin D1.

## Abnormal Skeletal and Dental Development in Gnathodiaphyseal Dysplasia

Jonathan Wechter, Miriam Guemes, Hannah Duong, Sanjay Mallya

**Background:** Gnathodiaphyseal dysplasia (GDD) is a rare autosomal dominant syndrome characterized by fibro-osseous lesions of the jaw bones, overall bone fragility and diaphyseal sclerosis of the long bones. Several missense mutations in the Anoctamin 5 (ANO5) gene have been identified as the underlying cause of GDD. Our lab previously presented an undiagnosed familial case of GDD. By ANO5 sequencing, a novel missense mutation was revealed in the ANO5 gene, causing an alteration at p.Cys356Tyr.

**Objectives:** To characterize ANO5 expression during intramembranous and endochondral ossification throughout bone development and bone pathophysiology.

**Methods:** Murine femoral bone marrow stromal cells (BMSCs), mandibular bone marrow stromal cells and calvaria were harvested from wild-type mice, isolated, and stimulated to differentiate into osteoblasts. RNA was obtained at different time points to measure ANO5 expression throughout mineralization. Whole bone from femur, mandible, maxilla and calvaria was collected from 16.5-day mouse embryos, postnatal 2- day mice and 6-week old adult mice and used for ANO5 expression analysis and immunohistochemistry. ANO5 cellular localization was examined using immunofluorescence and confocal microscopy

**Results:** ANO5 expression increased as mineralization progressed in calvaria-derived osteoblasts and bone marrow stromal cells- derived osteoblasts during a 14-day period. Strong ANO5 immunoreactivity was detected in osteoblasts, odontoblasts, and periodontal ligament fibroblasts through development, in the jaws and long bones. Undifferentiated and differentiated osteoblasts show nuclear and cytoplasmic localization of ANO5.

**Conclusion:** Our data characterizes ANO5 expression in bone and teeth during development and in adult life. Ongoing experiments are evaluating a functional role for ANO5 in osteoblast differentiation and mineralization.

## Barriers to Accessing Dental Care for Patients in the UCLA School of Dentistry Special Patient Care Clinic

Allyson Wesman, Elham Nik, Eric C. Sung, Kathryn A. Atchison

**Objectives:** It is well known that inequalities exist in access to dental care for patients with a disability or requiring special care. The purpose of this project is to understand which barriers to care are the most difficult for patients at the UCLA Special Patient Care clinic to overcome.

**Methods:** A paper survey was distributed to patients and their caregivers in the UCLA School of Dentistry Special Patient Care clinic. 66 surveys were collected, with 88% completed by caregivers with reference to the patient, and 12% by patients themselves. The questions asked patients and caregivers about various barriers they might face in getting dental care, including finances, transportation, finding a dentist willing to treat the patient, long wait times, quality of care, relationship with the dentist, and fear of going to the dentist. Analysis included determination of mean response to questions using a visual analog scale, calculation of standard deviation, and determination of percentage of respondents rating various barriers as difficult.

**Results:** Respondents rate finding a dentist willing to treat them as the most difficult barrier to getting care. The second most difficult barrier to care is long wait time for an appointment. Over half of respondents report that it takes them more than one hour to reach the dental office, with 25% reporting it takes them over two hours. Only 39% of respondents state that they have a dentist they see regularly.

**Conclusion:** Routine dental care is very important to patients with special needs at UCLA, but these patients report that the greatest difficulty they have in accessing care is finding a dentist willing to treat them. Travel time to the dental office is also a significant burden to accessing care for many patients.

## Attenuation of Orthobunyavirus Protein Expression Through Manipulation of Untranslated Regions

Angel Wu, Yao Wang, Genhong Cheng

**Objective:** The Orthobunyavirus genus is part of the Bunyaviridae family. They are tripartite negative-sense RNA viruses associated with encephalitis in humans. Each strand is encapsulated by a nucleoprotein and is bound to viral RNA polymerase (L). In addition, the RNA segments are flanked by untranslated regions (UTRs) that display partial complementarity. It is known that the UTRs play a significant role in the viral life cycle, so we created a mini-genome system to study the significance of the length and sequence of the UTRs. Currently, there are no vaccines to protect against these viral infections but studying the role of UTRs could provide us with novel drug targets.

**Methods:** We flanked the bioluminescent reporter protein *Gussia Luciferase* with the 3' and 5' UTRs of Leayner virus, a member of the orthobunyavirus genus, to create a mini-genome system that models the viral life cycle. The vector was transfected into adenocarcinomic human alveolar basal epithelial cells (A549s) and the experiments were done *in vitro*. We first used PCR to create truncated UTRs to determine the critical length of the UTR. Then we used PCR (primer with single base changes) to introduce single nucleotide mutations to areas of the UTR that were well conserved between various genres in the bunyaviridae family.

**Results:** Our first experiment showed that only the first 26 nucleotides of the UTR are necessary for protein expression. Our second experiment showed that single nucleotide changes are poorly tolerated for nucleotides 1-7 in the UTR but are well tolerated after the 7th nucleotide.

**Conclusion:** We were able to show that the length and the specific sequence of the UTR are critical for the viral life cycle, possibly due to the sequence complementarity of 3' and 5' UTR. Knowing this gives us a target for anti-viral drugs that are specific to the bunyaviridae family.

## Histological Evaluation of Single Dose Bisphosphonates on Tooth Eruption

Timothy Yu, Richard Che, Jeffrey Olsen, Alison Quach, Reuben Kim

**Introduction:** Bisphosphonates (BP's) are anti-resorptive agents known to increase bone volume by inhibiting osteoclast activity. Though BPs have been extensively used to treat adults with a variety of bone diseases, recent clinical applications in children have been introduced to treat some genetic and acquired bone disorders, most notably Osteogenesis Imperfecta. The effect of BPs on the developing dentition is not well understood. In this study, we evaluated the effect of zoledronic acid (ZA), a potent BP, on the formation and eruption of molars in neonate rats.

**Methods:** 40 seven-day old rats were given a single injection of either ZA or saline control, and the eruption of their molars was observed clinically. Groups of rats were sacrificed at regular intervals and both maxilla and mandibles underwent MicroCT analysis, histological analysis, and bone density analysis.

**Results:** Eruption of 1st molars and 2nd molars in ZA-treated rats was significantly delayed, erupting at or around day 62 and day 41 respectively. The controls had molars that erupted normally at day 18 and day 22 respectively. Interestingly, 3rd molar eruption was not delayed in ZA-treated rats, erupting along with the controls at day 35. Histological analysis confirmed that the 1st and 2nd molars had already begun the eruption process at the time of ZA administration, while the 3rd molar tooth bud had not yet completed formation. Additionally, there was no evidence of abnormal root development or ankylosis in the histological specimens. Bone mineral density was shown to be higher in the alveolar bone of BP treated rats.

**Conclusions:** BP administration may result in a significant delay in tooth eruption in children. This inhibiting effect of BP appears to be in a developmental stage-dependent manner, with a preference for sites that are undergoing active eruption due to the increased bone turnover.





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