Faculty Research Programs

in

the Division of Constitutive and Regenerative Sciences

Section of Endodontics
Section of Periodontics
Section of Restorative Dentistry

January 2016
I. ENDODONTICS

1) Kang, Mo K., DDS, PhD

Areas of Interest: Oral Keratinocyte Biology, Epithelial Plasticity, Mechanisms of Oral Inflammation, and Pulp-Dentin Regeneration

Our laboratory has three main interests in research. First is on “epithelial plasticity.” We have been working on the basic molecular mechanism of oral keratinocyte senescence, differentiation, immortalization, and tumorigenic conversion. In recent years, we discovered a novel transcription regulator called Grainyhead-Like 2 (GRHL2), which plays a pivotal role in keratinocyte proliferation and differentiation. We have uncovered the molecular targets genes of GRHL2 that include hTERT, PCNA, p63, miR-200 family genes, and epidermal differentiation complex (EDC) genes, as well as several reprogramming factors. In addition, GRHL2 is required for epithelial barrier function. At present, we are investigating the involvement of GRHL2 in normal oral epithelial function and in oral carcinogenesis.

Secondly, we are interested in the basic molecular mechanism of oral inflammation. Our main goal here is to elucidate the novel upstream regulators of the inflammatory process in the dental pulp and periodontium using cell culture and animal models, with long-term goal to develop new therapeutics to control inflammation and inflammation-associated alveolar bone loss.

Thirdly, we have on-going preclinical clinical studies in pulp-dentin regeneration. Preclinical model involves the use of pulpal and other dental mesenchymal stem cells (MSCs) for bone fide regeneration of pulp-dentin complex to restore the vitality and physiological functionality to otherwise necrotic pulp. Clinically, we are studying the efficacy of revascularization on pulp revitalization on patients in the Endo clinic. Our long-term goal here is to develop innovative, effective, and clinically feasible approach to fully regenerate pulp-dentin complex in immature teeth with necrotic pulp so as to retain pulp vitality in patients.
II. PERIODONTICS

1) Camargo, Paulo M., DDS, MS, MBA

I currently serve the school in two administrative functions, and therefore have a limited research program. While my commitment to administration is intense at the moment, it may not be permanent in nature and I may be re-intensifying my research efforts in the near future. The areas in which I have research interests are as follows.

Periodontal and bone regeneration

I have conducted numerous human clinical trials on regenerative approaches for periodontal lesions and extraction sockets. They included the execution of primary surgical procedures, reentry surgeries and the utilization of standardized methodology to evaluate clinical parameters and radiographs. My interest in this area continues and currently resides on evaluating novel agents that can enhance periodontal and bone regeneration, and to collaborate in the improvement of research instruments (imaging in particular) that are less invasive than surgical reentries in human clinical trials.

Pathogenesis and treatment of peri-implantitis

Working with Flavia Pirih, we have developed a murine model of peri-implantitis. The model includes upper molar extractions, placement and integration of titanium implants, and induction of peri-implant bone loss by installing silk ligatures around the fixtures or injecting LPS in the gingival tissues surrounding the implants. We are currently interested in identifying the differences between periodontitis (which can be similarly induced in mice) and peri-implantitis, as the two diseases are similar but not equal. We hope that understanding the clinical, cellular and molecular mechanisms of peri-implantitis will provide us with information leading to the development of preventive and treatment alternatives for the disease.

Salivary diagnostics for gingival and periodontal diseases

The use of saliva for the early, sub-clinical diagnosis of gingival and periodontal diseases and as a tool to predict the progression of periodontitis is attractive. I have collaborated with David Wong in this project. While I have no substantial knowledge about the techniques used to analyze such saliva samples (preteomics, transcriptomics and the like), my expertise in the project relates to the clinical selection of patients presenting with various forms and degrees of gingival and periodontal diseases. Perhaps more importantly, we have found a mechanism to utilize patients who present for treatment in our pre-doctoral clinics as research subjects, which greatly facilitates recruitment in clinical trials. Therefore, tapping into an existing pool of patients to conduct research trials without having to conduct extensive directed recruitment programs is an approach that our divisional group could further explore in the context of other studies.
2) Klokkevold, Perry R., DDS, MS, FACD

My research interests are focused on periodontal, alveolar and peri-implant bone. Projects have included studies designed to assess bone loss, remodeling and/or regeneration as well as studies designed to evaluate the effect of implant design on bone formation and implant stability. My current and future research activities are primarily aimed at developing and conducting patient based clinical studies. I welcome the opportunity to collaborate with colleagues, especially when our mutual interests and combined contributions are complimentary offering the potential for stronger research.

1) Preservation of Alveolar Bone Dimension following Tooth Extraction
Extraction socket / ridge preservation as well as ridge augmentation is an important consideration when teeth are lost and implant(s) placement is the desired outcome. A recently completed clinical study entitled Radiographic Analysis of Tooth Extraction Sites Grafted with Anorganic Bovine Bone with or without a Collagen Matrix and a Collagen Membrane for Implant Site Development evaluated the effect of bone graft materials on alveolar bone preservation. A variety of methods were used to measure the results including three dimensional imaging and histology. Although I do not have any current studies evaluating the surgical management of extraction sockets, evaluation of materials and techniques to preserve alveolar bone following tooth extraction continues to be an area of interest.

2) Effect of Implant Design on Peri-Implant Bone
Evaluation of implant design, including surface micro-topography as well as macro-geometry features, on peri-implant bone remodeling and implant stability has been a research interest for many years. Most of my previous work was conducted with animal models using reverse torque testing and histomorphometric analysis to measure outcomes. A recently completed clinical study entitled Effect of Implant Thread Design on Bone Remodeling and Implant Stability evaluated the effect of macro thread design on implant stability in the early healing period. Another ongoing clinical study entitled Prospective Randomized-Controlled Evaluation of Implant Abutment Platform Switching for the Preservation of Crestal Bone will evaluate the effect of healing abutment dimensions on early bone remodeling (bone loss versus preservation).

3) Effect of Laser Therapy on Periodontal Regeneration
Evaluation of laser therapy is a relatively recent research interest that was spurred by the surging popularity of lasers in dentistry, especially periodontics. There are many claims citing laser therapy as a better alternative to surgical therapy and that laser therapy promotes periodontal regeneration but there is a paucity of research to support these claims. My interest is to design and conduct studies that facilitate a better understanding of the role of laser therapy in periodontics. A current clinical study entitled Clinical Evaluation of Laser Therapy used as an Adjunct to Non-Surgical Treatment of Chronic Periodontitis: A Randomized, Controlled, Split-Mouth Clinical Study will evaluate the effect of laser therapy on chronic periodontitis including an assessment of periodontal bone regeneration.
3) Lux, Renate, PhD

Areas of Interest: Oral Microbial Interspecies Interactions, Oral Microbial Surface Colonization and Oral Microbial Communities in Health and Disease
The overall research interest of our laboratory revolves around the understanding of oral microbial communities on different levels. The lab is equipped for aerobic and anaerobic planktonic as well as biofilm growth of a variety of cultivable oral microorganisms including biofilm formation. We are experienced in the genetic manipulation of a number of oral bacterial species as well as their transcriptional analysis, and are set up to perform oral bacterial community profiling.

1) One major research interest in Dr. Lux' laboratory is the understanding of the factors involved in interspecies interactions of the oral opportunist pathogen Fusobacterium nucleatum with other oral microorganisms on a molecular level. We have discovered and characterized several adhesins of this important bridging organisms that mediate attachment to a number of oral streptococci as well as the periodontal pathogen Porphyromonas gingivalis. We also investigated the transcriptional changes triggered in F. nucleatum and T. denticola upon interaction with a variety of relevant partner strains using microarray and transcriptome sequencing approaches. We are currently in the process of analyzing the regulatory processes involved in controlling the expression and production of RadD, one of the adhesins of F. nucleatum that is involved in interaction with oral streptococci, some strains of P. gingivalis and mediates the induction of apoptosis in lymphocytes.

2) Another research area in Dr. Lux' laboratory is the investigation of microbial biofilm formation on dental restorative surfaces including titanium implant and acrylic denture materials. We collaborated with Dr. Tak Ogawa’s laboratory to discover that UV-treatment of titanium greatly reduces oral bacterial attachment for extended periods of time. Currently, we are working with Dr. Ben Wu’s laboratory to investigate how different surface modifications of acrylic denture materials affect attachment and viability of oral bacterial microorganisms including Candida albicans.

3) As additional research area, Dr. Lux' laboratory has investigated the microbial community structure of different oral diseases including endodontic infections and periodontitis. We are collaborating with Dr. Flavia Pirih’s laboratory to determine the genetic factors influencing the oral microbiome in periodontal health and disease using a well-established mouse model system.

4) Pirih, Flavia, DDS, PhD

My main research interests are:

Periodontitis:

A) We are interested in understanding the genetic mediators of periodontitis utilizing a genome-wide association approach with the Hybrid Mouse Diversity Panel (HMDP).
B) In collaboration with Renate Lux, we are interested in identifying the differences in microbial colonization utilizing the HMDP.
C) In parallel, we intend to initiate a human study to validate our findings in a clinical setting. Our long-term goal is to identify patients at risk for developing periodontitis and ultimately prevent the disease.

Peri-implantitis:

We have developed a murine model of peri-implantitis and are currently interested in identifying the differences between periodontitis and peri-implantitis. In addition, we are interested in identifying effective treatment targets for peri-implantitis.
III. RESTORATIVE

1) Collaborative Research Projects

a) Fracture Resistance of Ceramic Crown with Various Composite Build-up Materials

Esteban D. Bonilla DDS, Richard G. Stevenson III DDS, Ms. Christine Khabaz, Shane N White DDS

Introduction: All build-up restorative materials, which are covered with indirect restorations are subjected to stress or strain over a period of time which eventually leads to failure. One of the most common modes of failures of dental materials over time is cyclic loading, causing microcracks and fractures. Modalities in restorative dentistry used to retain build up materials are self-threading pins and slots, countersinks in combination with adhesive systems. This in-vitro study will compare the catastrophic failures of ceramic crowns with different build-up materials and their use in restorative dentistry with or without pins.

Preliminary results: The pin-retained build-up had significantly less early failures when provisional crown is dislodged. The build-up with the microhybrid composite resins (Herculite XRV) supported by pins and 2mm step without pin on buccal and lingual surface showed the least catastrophic failures of e.max ceramic restorations followed by Core Flo and Ti-Core titanium reinforced composite resin. The Dual composite resin without pins showed the most catastrophic failures of the ceramic restorations.

b) Inlay leakage is strongly influenced by material, cement and tooth substrate

Vida Yousefi DDS, Esteban D. Bonilla DDS, Colby Smith DDS, Richard G Stevenson DDS, Kuei Chen, A Agnihotry, Shane White BDS, PhD.

Introduction: Although cast gold had long been the material of choice for indirect inlay restoration, a wide variety of materials and cements are now available. Resistance to leakage is key to long term clinical success. This may be influenced by the inlay material, cement, and tooth substrate, enamel or dentin. The purpose of this in vitro study was to evaluate the influence of inlay material, cement, and tooth substrate on microleakage.

Results: 3-way ANOVA found that the simple main effects of material, cement, and tooth substrate were all large and statistically significant (p<0.001). Cement type had the most important effect. All interaction terms were significant (p<0.05), indicating that different inlay, cement, and tooth substrate combinations behaved differently. Gold and e.max; Ketac Cem and Panavia; and enamel all leaked less than their alternatives (p<0.05).

Conclusions: Inlay material type; cement type; and tooth substrate, enamel or dentin, all profoundly influenced microleakage of indirect inlays. Cement type was most influential.

c) Influence of Core Buildup Materials in the Retention Form on Over-Prepared Teeth
**Colby Smith DDS, Esteban D. Bonilla DDS, Richard G. Stevenson III DDS, Hamid Azizi DDS, R. Aljammal, Shane N. White BDS, PhD**

**Introduction:** Occasionally, overpreparation of teeth resulting in excessively tapered preparations can contribute to this failure of the restoration. This should be corrected before fabricating the replacement restoration. A number of techniques have been suggested to improve retention of over-tapered crown preparations, including addition of retentive grooves, slots, or to use of adhesive system with core buildup materials to improve preparation form to hold the crown.

The present in vitro study will compare retention form of ceramic crowns with different build-up materials on over tapered preparations. The use of bonded core buildup materials to idealize overtapered preparations will result in improved retention and resistance form of crown restorations.

**Preliminary results:** The light cured microhybrid composite resin (Herculite XRV) with its corresponding 4th adhesive generation used as core build provide a better core foundation in the retention form on over-prepared teeth than the other core materials such as Bisfil-2B and Core Flo.

---

**d) The Effect of Using Various Materials to Support Undermined Cusps: A Comparison of Ultimate Strength**

**Richard G Stevenson III DDS, Natasha Lim DDS, Esteban D. Bonilla DDS, Janice A Lee, Shane N White BDS, PhD.**

**Introduction:** Numerous studies have shown that conservation of tooth structure is the primary factor to producing higher quality and longer lasting restoration. Preservation of unsupported occlusal enamel after removal of underlying carious dentin may result in the maintenance of aesthetics, cuspal reinforcement and resistance against the opposing enamel. The purpose of this investigation is to compare the ultimate strength and to examine the capacity of the tooth and the restorative materials to support the remaining undermined enamel.

**Preliminary results:** The undermined cusps, which have been supported with dentin analogues such as either glass ionomer (GC Fuji IX) or composite resin, will retain strength similar to cusps which have not been undermined; maintaining occlusal relationships and potentially extend restoration survival.

---

**e) Fracture Resistance of Various CAD/CAM Onlay Restorations on Endodontically Treated Molars**

**Lilian Cheng DDS, Eric Scott DDS, Esteban D. Bonilla DDS, Richard G. Stevenson DDS, Shane N White BDS, PhD.**

**Introduction:** Studies have shown that endodontically-treated molars are generally debilitated due to loss of tooth structure and removal of the pulp. As a result of the weakness
of remaining tooth structure, pulpless posterior teeth are predisposed to fracture on function. Therefore, teeth treated by root canal therapy should be restored with any coronal full coverage restoration, minimally with a gold onlay. This study will assess fracture resistance of various CAD/CAM onlay restorations on endodontically treated molars.

**Expected results:** IPS e.max and Lava onlays will show better fracture resistance when compared to other CAD/CAM ceramic onlays (Vita Mark II, Lava Ultimate) in endodontically treated molars.

2) **Reuben H. Kim, DDS, PhD**

Areas of Interest: Osteomucosal healing, medication-related osteonecrosis of the jaw, HPV-associated oral carcinogenesis, dentin regeneration

First, Dr. Kim’s lab focuses on examining the role of osteomucosal healing – a simultaneous healing process of soft and hard tissues - in pathophysiology of medication-related osteonecrosis of the jaw (MRONJ). MRONJ is clinically defined as exposed necrotic bone with unhealed and open oral mucosa for more than 8 weeks, and is commonly occurs at the site of previous tooth extraction or other surgical interventions in long-term bisphosphonate (BP) or denosumab (Dmab) users undergoing therapy for bone-associated diseases. Dr. Kim’s lab uses both in vitro cell culture and in vivo mouse tooth-extraction models to elucidate molecular mechanisms of MRONJ induced by both BPs and Dmab specifically in the context of osteomucosal healing.

Second, Dr. Kim also focuses on studying the pathogenesis of HPV-associated carcinogenesis. HPV infection is critical event but not sufficient to cause HPV-associated cancer development, suggesting that additional genetic and/or epigenetic events are required. To investigate the molecular mechanisms, we use a multi-step process of oral epithelial carcinogenesis model both in vitro cell culture model and in vivo animal model with floxed mice systems.

Third, Dr. Kim’s lab also investigates the mechanisms of reparative dentin formation. Caries is the most prevalent infectious disease worldwide, and one of primary goals of dentistry after caries removal is to regenerate dentin formation at the pulpodentin complex (PDC) or pulomaterial complex (PMC). Dr. Kim’s lab utilizes both in vitro cell culture models using dental pulp stem cells (DPSCs) and in vivo mouse models using tooth preparation and restoration in order to elucidate fundamental mechanisms of dentin regeneration at the PDC or PMC.

3) **Esteban D. Bonilla, DDS**

Area of Interest: Importance of minimally invasive adhesive procedures preserving the biological integrity of the tooth during restorative treatment and better understanding of the pulp biology to prevent post-operative complications; Understanding the biomechanical concept of tooth restoration to restore proper function, esthetic and great longevity of the restoration; and Assessment of the behavior of different CAD/CAM restorative materials in relation with different tooth preparation design
As lecturer having a background in Prosthodontics, I have been involved in doing research at Restorative Dentistry for 20 years. Considering our passion and commitment in providing outstanding education, I and Dr. Richard G Stevenson have decided to start doing research projects with Dr. Shane N White through a Restorative Research Program (RRP). This is a unique program which is devoted to advancing the knowledge working together with dental students and faculties on a series of very interesting topics with clinical applications. From investigating the integrity of various dental materials, to evaluating the forte of familiar preparation designs, RRP researchers are exploring the topics that will ultimately further bolster our knowledge of restorative dentistry.

4) Marc R Hayashi, DMD

Areas of Interest: Osteoradionecrosis (ORN), medication-related osteonecrosis of the jaw (MRONJ), medical/dental management of ORN and MRONJ

Dr. Hayashi’s background is in restorative and hospital dentistry, with a current emphasis on the treatment of osteoradionecrosis (ORN). A restrospective study was conducted in the UCLA Hospital Dentistry clinic, evaluating the efficacy of Pentoxifylline/Tocopherol (PENTO) Combination in the treatment of ORN. A promising resolution rate of 84% was noted in the study. Dr. Hayashi’s research seeks to build upon these results to allow for a more direct comparison with other published research on this topic, along with evaluation of the PENTO combination efficacy in the treatment of MRONJ.