Herman Ostrow School of Dentistry of USC

2019 ANNUAL RESEARCH DAY
WINNING POSTERS

Poster #82

Title: Advanced platelet-rich fibrin for soft tissue augmentation

Authors: Nathan A. Nourian, Micah Tabanfar, Neema Bakhshalian, & Alexandre-Amir Aalam

Faculty advisor: Neema Bakhshalian

Background: Connective tissue graft is the gold standard for soft tissue augmentation and root coverage procedures. However, morbidity of the donor area is a concern. Therefore, several other materials have been used for soft tissue augmentation. Advanced platelet-rich fibrin (A-PRF) is a type of platelet concentrate which can be used as an autogenous graft material for this procedure. **Purpose**: The aim of this retrospective study was to evaluate the efficacy of A-PRF in root coverage procedure using a 2D image analysis protocol. **Methods**: Twelve patients who underwent full-mouth gingival augmentation procedure using A-PRF were included in the study. The digital intra-oral photographs from pre- and 24 months post-therapy were superimposed in Adobe Photoshop. The areas of denuded root surfaces were measured in each picture and compared between the 2 time-points. To assess the percentage of root coverage, a non-parametric longitudinal model was run. **Results**: The model found a highly significant difference ($p<0.0001$) between the deluded root surface pre- and post-operative. The pre values were found to be significantly higher (median of 10056.00 pixels) as compared to post (median of 1295.00 pixels). **Conclusion**: The present study revealed that A-PRF can effectively decrease the denuded root surface when used in gingival augmentation procedures. Hence, it can be an ideal alternative to connective tissue graft. Additionally, with this new technique patients experienced decreased pain, swelling and recovery time. Longer term follow-ups and controlled clinical trials are necessary to compare A-PRF and connective tissue graft efficacy.

Poster #12

Title: Effect of different barriers on output of light curing units

Authors: Fares Albalawi & Jin-Ho Phark

Faculty advisor: Jin-Ho Phark

Background: Sufficient light output is essential for proper polymerization for dental restorations. However, barrier materials for infection control purposes could lead to compromised quality of light output emitted from light curing units. **Purpose**: To assess the effect of different barriers on light output emitted from LED light curing units. **Methods:** Five units (LED, Valo, Ultradent) were tested for light output using a radiometer (Bluephase Meter II). Each unit was measured 10 times under nine different barrier conditions: G1-without any barrier (control group), G2-single layer barrier tape , G3- double layer barrier tape, G4-single layer syringe cover, G5-double layer syringe cover, G6-single layer kitchen wrap, G7-double layer kitchen wrap, G8-single layer Valo sleeve, G9-double layer Valo sleeve. **Results:** The highest light output measurements (1460.8 mW/cm^2) was recorded for the control group (G1). Light output was decreased in groups with one layer of barrier material (G6, G8, G4, G2), ranging from 1387.2 mW/cm^2 to 1367.4 mW/cm^2. The lowest light output measurements were measured for groups with double layers of barrier material (G3, G9, G5, G7), ranging from 1315.0 to 1340.8 mW/cm^2. **Conclusion**: Barrier materials for infection control purposes decrease the light output of light curing units. Light output decreases even more when barriers are placed in double layers. Thus, type and thickness of barrier materials need to be considered for effective polymerization of dental restorations.

Poster #51

Title: Antagonistic interaction between Ezh2 and Arid1a coordinates dental root patterning via Cdkn2a

Authors: Junjun Jing & Yang Chai

Faculty advisor: Yang Chai

Background: EZH2 is a key component of polycomb repressive complex 2 (PRC2), which is responsible for Histone 3 Lysine 27 trimethylation (H3K27Me3). Ezh2 is required for neural crest derived cartilage and bone formation. However, the role of Ezh2 in tooth development is unknown. **Purpose**: We aim to elucidate the role of Ezh2 in molar development and its function in patterning the tooth furcation. **Methods**: Multiple transgenic mouse models were generated in this study: *Osr2KI-Cre;Ezh2*$^{fl/fl}$, in which *Ezh2* expression is lost in the tooth mesenchyme; *DMP1-Cre;Ezh2*$^{fl/fl}$, in which *Ezh2* is knocked out in odontoblasts; *K14-Cre;Ezh2*$^{fl/fl}$, in which *Ezh2* is knocked out in epithelial cells; and *Gli1-CreER;Ezh2*$^{fl/fl}$, in which *Ezh2* is lost in root progenitor cells; *Osr2KI-Cre;Ezh2*$^{fl/fl}$*;Arid1a*$^{fl/+}$, in which haploinsufficiency of *Arid1a* is generated in *Osr2KI-Cre;Ezh2*$^{fl/fl}$ mice. MicroCT scanning and histological analysis were combined to analyze the phenotypes of these mice. **Results**: When *Ezh2* expression was lost in the tooth mesenchyme in *Osr2KI-Cre;Ezh2*$^{fl/fl}$ mice, only one root formed and the root furcation was defective. In contrast, inactivation of *Ezh2* in epithelial cells lead to delayed furcation development. Loss of *Ezh2* in odontoblasts and root progenitor cells resulted in normal furcation and molar development. Importantly, *Arid1a* haploinsufficiency rescues root patterning defect in *Osr2KI-Cre;Ezh2*$^{fl/fl}$ mice, indicating that Arid1a and Ezh2 may work antagonistically to control the tooth furcation development. **Conclusion**s: Our study provides evidence that Ezh2 in the tooth mesenchyme work antagonistically with Arid1a to determines the root number in mouse molars.

Poster #55

Title: Regenerating sutures in craniosynostosis

Authors: Mengfei Yu, Yuan Yuan, & Yang Chai

Faculty advisor: Yang Chai

Background: Craniosynostosis results in cranial deformities and other symptoms, which pose extensive and recurrent surgical management problems. For the past decade, tissue regeneration field has been greatly improved since the thriving of material science and stem cell biology. **Purpose**: In our study, we want to regenerate the coronal suture in *Twist*$^{+/-}$ mice using complex hydrogels with normal suture mesenchymal cells. **Methods**: Photo-cross-linkable gelatin methacrylate (GelMA) modified with matrigel/collagen I (MC-GM) were used as scaffolds. *Twist*$^{+/-}$ mice used in surgery were divided into five groups which treated with 1) blank control, 2) MC-GM control, 3) MC-GM + heat inactivated nomal suture cells, 4) MC-GM + nomal suture cells, 5) MC-GM + nomal suture cells. Samples are collected at different time points. **Results**: 2 months after we surgically removed the fused coronal suture structure of *Twist1*$^{+/-}$ mice, radiographic results showed that there were still some gaps between frontal and parietal bones in MC-GM + nomal suture cells group, however the gaps became narrower in group MC-GM + heat inactivated nomal suture cells and MC-GM control, and the two bones were almost fused in group MC + nomal suture cells and blank control. After 3 months, the gaps still retained in MC-GM + nomal suture cells group, while the gaps disappeared in all the other groups. Histomorphometric and immunofluorescence analysis also revealed the presence of Gli1+ cells between the bones only in MC-GM + nomal suture cells group 3 months after surgery, which implied the suture-liked structure formed. **Conclusion**: Thus, the complex hydrogels with normal suture cells may enhance suture regeneration and have a profound impact on regenerative medicine.

Poster #30

Title: Cranial pericytes derived from neural crest cells reveal a pericyte-specific functional defect in Alzheimer's disease

Authors: Casey Griffin & Ruchi Bajpai

Faculty advisor: Ruchi Bajpai

Background: Defects in or loss of functional forebrain pericytes leads to breakdown of the integrity of the blood brain barrier (BBB), causing leakage of toxins and pathogens into the brain and compromising the immune-privileged state of the brain. Leakiness of the BBB has recently been found to play a part in numerous neurodegenerative diseases, most notably Alzheimer's disease (AD). **Purpose**: My project focuses on understanding what defines forebrain pericytes as a unique pericyte population, with emphasis on their developmental source as well as their transcriptome and epigenome architecture, and the changes in these aspects associated with disease. **Methods**: I have developed a system of generating forebrain pericytes from neural crest cells in vitro. I have characterized these cells functionally and transcriptomically, comparing to primary brain pericytes across different species. I have also generated pericytes from AD patient cells and compared these to primary patient pericytes and controls to begin to characterize the pericyte-specific defects in AD. **Results**: I have identified pericyte defects that are common across different patients and mutations of AD, honing in on possible general pathways important to pericyte function at the BBB. I have also shown that the in vitro system I created is able to recapitulate in vivo conditions in both the wild type state and the disease state when compared to both primary human and primary rat samples. **Conclusion**: My in vitro method of generating forebrain pericytes is able to provide insights into the roles pericytes play in development and maintainence of the BBB, as well as the mechanisms of various defects associated with disease. This system can be used to study pericytes of different AD mutations, as well as be applied to other diseases involving pericytes, such as ALS and Parkinson's.

Poster #31

Title: Quantitative light-induced fluorescence for visualization and quantification of coronal dentin mineral density.

Authors: Garima Sandhu, Amrita Chakraborty, & Janet Moradian-Oldak

Faculty advisor: Janet Moradian-Oldak

Background: QLF has been routinely employed to study enamel defects, especially white spot lesions on teeth. Utilization of sodium fluorescein dye and QLF to monitor de- and re-mineralization of root dentin has also been recently reported (I.A. Pretty et al., 2003). **Purpose**: To employ QLF to quantify the changes in fluorescence of coronal dentin when subjected to demineralization and remineralization in the presence of amelogenin derived peptide (P26). P26 has been shown to be effective in growing enamel like apatite crystals on etched enamel surface (Mukherjee et al., 2017). **Methods**: Cross-sections (1.5mm thickness) of extracted mandibular third molars were used. Two windows measuring 1 mm x 1mm were created on every section using clear varnish and were examined under QLF for generating baseline values. Samples were demineralized for 72 hours and analyzed under QLF at intervals of 12, 48 and 72 hours. Samples were split into half, one half was used as an internal control being remineralized in artificial saliva, and the other half being remineralized in the presence of P26. Sodium fluorescein dye was used at every step of analysis to complement visualization under QLF. **Results:** Gradual loss in fluorescence of dentin with respect to baseline values was observed during demineralization and the reverse was seen after remineralization. Percentage loss in fluorescence (ΔF) was used for quantification of data. The results are in agreement with the results from Micro-CT. **Conclusion:** We conclude that QLF can be employed to study changes in dentin and be quantified for better understanding of remineralization process.

Poster #105

Title: Effect of exercise on endothelial function during breast cancer chemotherapy

Authors: Kyuwan Lee, Irene Kang, Joanne E. Mortimer, & Christina M. Dieli-Conwright

Faculty advisor: Christina M. Dieli-Conwright

Purpose: We sought to determine the effects of an 8-week HIIT intervention on vascular endothelial function in breast cancer patients undergoing anthracycline chemotherapy. **Background**: Anthracycline chemotherapy is a cardio-toxic regimen by nature and may contribute to cardiovascular disease mortality by reducing vascular endothelial function in breast cancer patients. High intensity interval training (HIIT) has been shown to increase endothelial function compared to moderate intensity exercise in patients with obesity. **Methods**: Thirty breast cancer patients were randomized to either HIIT or control (CON) groups. The HIIT group participated in an 8-week HIIT intervention occurring 3 times per week on a cycle ergometer. The CON group was offered the HIIT intervention after 8 weeks. At baseline and week 9, endothelial function was assessed using FMD. FMD was measured from the brachial artery diameter at baseline and 1min after cuff deflation. Repeated measures ANOVA was performed to assess changes in endothelial function. **Results**: At baseline, the HIIT group (n=15) and CON group (n=15) groups did not differ by age (46.9±9.8 years), BMI (31.0±7.5 kg/m2), and systolic/diastolic blood pressure (116.1±11.8/72.3.9±5.6 mmHg). Post-exercise, FMD significantly increased from baseline in the HIIT group (wk 0: 12.6±6.8%, wk 9: 16.9±8.1%; 19.8%) when compared to baseline and the CON group ($P<0.05$). FMD significantly decreased from baseline (wk 0: 13.0±4.3%, wk 9: 6.1±2.8%; -21.9%) in the CON group ($P<0.05$). **Conclusion**: HIIT improved endothelial function in breast cancer patients undergoing. Larger randomized trials are needed to establish the optimal exercise strategy to attenuate chemotherapy-induced cardio-toxicities on endothelial function.

Poster #101

Title: The learning process and neural substrates linked to a discovery task and a future for modulation

Authors: Andrew Hooyman, Jason J. Kutch, Nicolas Schweighofer, Beth E. Fisher, James Gordon, & Carolee J. Winstein

Faculty advisor: Carolee J. Winstein

Background: Discovery tasks are an under investigated area of motor learning which may be highly relevant to our overall understanding of how humans learn motor skills. **Purpose**: The purpose of our research into complex discovery tasks is three-fold: First, we aimed to better understand the learning processes associative with successful learning of a discovery task. **Results:** Our results indicate that optimal performance on the task requires initial high levels of exploration followed by adequate exploitation to acquire and then retain maximum success. Second, we wished to better understand where the processes of exploration, exploitation and retention of a discovery task exist within the human brain. Using resting-state Electroencephalography (rs-EEG) we performed a whole brain analysis of every feasible rs-EEG functional connectivity pair to predict exploration, exploitation and retention of the discovery task. We were able to identify three distinct and predictive networks for each phase. Finally, to better understand the plasticity underlying the predictive functional connectivity of the discovery task, we developed a novel intracortical Paired Associative Stimulation (iPAS) paradigm aimed at increasing connectivity along a specific rs-EEG intracortical circuit. Results of our paradigm demonstrated feasibility that iPAS can significantly increase functional connectivity of a specific resting-state fronto-motor circuit compared to two separate controls. **Conclusion:** Overall, we were able to uncover the learning processes and neural substrates associated with a discovery task and develop a future neuromodulatory method that may better define the causal relationships between the brain and behavior in relation to the learning of a motor skill.

Poster #116

Title: Determining brain-behavior changes secondary to an internal focus during standing

Authors: Alexander J. Garbin, Stephanie N. Yassa, & Beth E. Fisher

Faculty advisor: Beth E. Fisher

Background: Previous research has shown that adopting an internal focus of attention (IFA) results in a nonoptimal neuromuscular pattern consisting of reduced motor cortical inhibition and increased muscle co-contraction during simple force production tasks. However, neither of these variables of have been examined during a more ecologically valid task such as standing. IFA instructions are commonly utilized in clinical practice and the concomitant neural and biomechanical changes may lead to increased fall risk. **Purpose**: To characterize the neural (motor cortical inhibition) and biomechanical (co-contraction) changes following internal vs. external focus of attention (EFA) instructions delivered during different standing postures. Our results will support future work that aims to understand how focus of attention may impact older adults with an excessive concern of falling. **Methods**: 2 healthy adult participants stood with a narrow-base-stance or single-limb-stance while being instructed to stand quietly with an IFA or EFA. While standing, motor cortical inhibition was quantified via the combined use of peripheral electrical stimulation and transcranial magnetic stimulation. Co-contraction index was measured via electromyography placed on the Soleus and Tibialis Anterior of the dominant limb. **Results**: In our participants, adoption of an IFA resulted in reduced motor cortical inhibition relative to adoption of an EFA during narrow and single-limb-stance. Furthermore, the participants exhibited greater co-contraction while focusing internally during single-limb-stance. **Conclusion**: Our preliminary findings suggest that adoption of an internal focus of attention may reduce cortical inhibition and increase lower extremity muscular co-contraction during stance, particularly in the most challenging standing posture.

Poster #115

Title: Gluteus maximus activation improves hip biomechanics in femoroacetabular impingement syndrome

Authors: Jordan Cannon & Christopher M. Powers

Faculty advisor: Christopher M. Powers

Purpose: To determine if targeted gluteus maximus activation influences transverse plane hip kinematics and kinetics in persons with femoroacetabular impingement syndrome (FAIS) during a deep squat task. **Background:** Symptomatic bony impingement is thought to occur during activities in which the hip is flexed to angles greater than 90^{o}. High hip flexion angles combined with hip internal rotation produce the highest contact pressures on articular surfaces. The gluteus maximus has been implicated as a muscle of interest in the FAIS population given its ability to produce hip external rotation during tasks requiring deep hip flexion. **Methods:** Kinematic, kinetic, and EMG data were collected from 3 patients with confirmed FAIS. Two different squat variations were performed. First, an unconstrained squat to maximum depth (self-selected stance width and foot position). Next, in the same unconstrained position, participants were instructed to increase gluteus maximus activation to approximately 15% of their maximum voluntary isometric contraction (MVIC). The hip internal rotation angle and hip external rotator moment were calculated at the point of maximum hip flexion. **Results:** Increasing gluteus maximus activation from 7.6% MVIC to 14.0% MVIC resulted in a reduction in peak hip internal rotation (4^{o} on average) and an increase in the hip external rotator moment (0.07 Nm/kg). **Conclusion**: These preliminary results suggest that cueing patients with FAIS to activate their gluteus maximus may be protective against femoroacetabular impingement and provide functional benefits in tasks requiring deep hip flexion.

Poster #141

Title: Comparison of two automated motion correction strategies in autism neuroimaging

Authors: Aditya Jayashankar, Laura Harrison, Christiana Butera, Emily Kilroy, Jonas Kaplan, & Lisa Aziz-Zadeh

Faculty advisor: Lisa Aziz-Zadeh

Background: Motion artifacts have a significant effect on the interpretation of functional MRI (fMRI) data, especially in children with ASD, who tend to move more than controls during scanning (Pardoe, Hiess & Kuzniecky, 2016). Manual classification of artifacts is time consuming; automated classification is a desirable motion-correction strategy. **Purpose**: To implement and compare the automated performance of (1) ICA-AROMA (Pruim, 2015) and (2) FIX (Salim-Khorshidi, 2014; Carone, 2017). ICA-AROMA works off a predefined training set, while FIX can be trained on acquired data. **Methods**: Data of 58 subjects ages 8-15 (22 ASD), each performing two passive tasks, were preprocessed using FSL (Jenkinson, 2012). After ICA of all preprocessed data, motion correction was done with the unalterable ICA-AROMA. Components of 47 participants were manually classified for signal and noise components (Griffanti et al, 2017) and compiled into a training data set using FIX. Trained automated identification of signal vs. noise components in the remaining data was then performed. **Results**: Qualitative analysis of the motion correction results showed higher accuracy in the detection of task-correlated motion and multi-band acquisition artifacts by FIX over ICA-AROMA. Cross-validation showed FIX maintained 94.2% detection accuracy. FIX significantly identified more signal in participants with minimal motion ($p=0.0215$), and more noise in those with high motion ($p=0.02$). **Conclusion**: Training FIX with manually classified data provides a more robust and flexible approach to filtering noisy signals in task-based fMRI data. While the hand classification is subjective, additional raters or blind sample rating could overcome the caveat of single-rater bias.

Poster #136

Title: The anatomy of oral care habits of children with autism spectrum disorders

Authors: Dominique H. Como, Daniella C. Floríndez, Sharon A. Cermak, & Lucía I. Floríndez

Faculty advisor: Sharon A. Cermak

Background: Dental care is the most prevalent unmet health need in the US. Underrepresented and underserved groups (i.e., Latinos, Autism Spectrum Disorders (ASD)) are at increased risk for oral health disparities. Little research centers on factors like diet, culture, systemic barriers that contribute to successful home-based oral care and that may affect oral health. **Purpose:** To explore the factors that serve as barriers or facilitators to oral care practices of Latino children with Autism (cASD). **Methods:** This qualitative study of Latino families with cASD (6-12 years) (n=10) included interviews to identify the factors influencing oral health, videos of the child's oral care routines, and a photo food journal of the child's meals. Interviews were transcribed verbatim and thematically analyzed, videos were blindly coded, and photos were analyzed for content and overlapping food patterns. **Results:** The interviews yielded three themes: "*Estoy sóla*" described parents' feelings of isolation, "*Wait, there's more*" portrayed tooth-brushing as the only routine often performed by the child, and "*It's a Battle*" described parents relationship with their child's oral care habits due to disagreements related to enforcing self-care activities. Two themes pertaining to oral care practices were observed in the videos: *Parents-as-Partners* who facilitate activities and *Modifications* described changing the environment or activity to meet the child's needs. Lastly, the food journals revealed that cariogenic beverages were consumed more frequently than water. **Conclusion:** This research is novel in considering the influence of culture, family, diet, performance patterns and systemic restrictions on oral care practices for Latino cASD.

Poster #80

Title: 3D printing of custom nasal stents for babies with cleft lip and palate

Authors: Lauren Yen, Yasumura Toshihiko, Jeff Hammoudeh, Lori Howell, William Magee, Mark Urata, & Stephen Yen

Faculty advisor: Stephen Yen

Background: After primary repair of the lip and nose in infants with cleft lip and palate, nasal stents are used to support the nose after the repair. Currently, generic nasal stents are being used in the United States. **Purpose**: This pilot project will test whether we can design a custom nasal stent to improve nasal symmetry and 3D print it out of FDA approved materials. **Methods**: A model of a nasal stent was carved out in dental stone and scanned with the 3Shape dental scanner. Orthoanalyzer software was used to smooth out surface irregularities and add an extra bump layer to overcorrect the nasal projection and compensate for post-treatment shrinkage. The file was converted to STL format and modified with Fusion 360 software to add a connector and nasal holes to the virtual stent. The custom nasal stent was printed on a Moonray printer using NextDent Ortho IBT resin (Sprintray, Los Angeles, CA). **Results**: The printed stent is soft and flexible, has a connector to prevent accidental inhalation of the stent, and has the additional bump of material to support the nose. to ensure that the breathing hole The nasal hole is wide enough to insert a suction bulb. **Conclusion**: It is possible to 3D print custom nasal stents. Our next step is to scan the nose and create a mirror of the image of the good side without a cleft deformity to provide a model for creating the nasal stent.

Poster #71

Title: Microvasculature defects recapitulated in tooth pulp of rate AD model

Authors: Simon Youn, Casey Griffin, Ariana Rodriguez, Edmond Onwukwe, Brian Leung, Terrence Town, & Ruchi Bajpai

Faculty advisor: Ruchi Bajpai

Purpose: To test whether human tooth pulp can serve as a diagnostic tool to identify patients predisposed to getting Alzheimer's disease **Background:** Alzheimer's disease (AD) is a progressive neurodegenerative disease that is most often characterized by the accumulation of amyloid plaques and neurofibrillary tangles. There is no cure, but there are treatments that can slow the progression. However, there is no early diagnostic tool available to start treatments as early as needed. Furthermore, amyloid plaques and neurofibrillary tangles are late signs of Alzheimer's disease. In recent research, pericyte defects have become an important focus of AD. Pericytes of the blood-brain-barrier are neural crest derived cells that wrap around the endothelial cells of blood vessels and are critical for stabilization of blood vessels. However, a brain biopsy would not be ideal for patients to look for pericytes defects. Interestingly, neural crest cell derived pericytes also infiltrate craniofacial tissue including the tooth pulp. **Methods:** Analysis of rat brain at different ages from wild-type and AD model rats. Analysis of rodent tooth pulp from wild-type and AD model rats. Analysis of patient teeth at different ages and disease statuses. **Results:** Microvasculature defects in brains of AD rats predicted from our stem cell studies and consistent with microvasculature defects in patient brain samples. Microvascular defects and reduced pericyte coverage in isolated root pulp and oral cavity from the same animal models. **Conclusion:** Tooth pulp of AD rat serves as a powerful tool to identify pericyte defects that predispose patients to Alzheimer's disease.

Poster #74

Title: 3D reconstruction of muscle defects in mouse cleft soft palate

Authors: Sara Kahng, Brian Song, Thach-Vu Ho, Xia Han, Jifan Feng, & Yang Chai

Faculty advisor: Yang Chai

Background: The soft palate is the posterior part of the secondary palate and is involved in important daily physiological functions such as speaking, swallowing, breathing, and hearing. Soft palate malformation or clefting, is a common congenital craniofacial defect in humans. Patients with soft palate malformations often have disorganized palatal muscles with reduced numbers of myofibers, which severely impair the normal functions of the soft palate. **Purpose**: 3D reconstruction of all the muscles of the soft palate provides improved spatial visualization of the muscle deformity and can help develop better clinical treatments of patients with soft palate malformation. **Methods**: *Osr2-KIcre;Runx2*$^{fl/fl}$ mutant mice show reduced muscle volume in the soft palate at newborn stage (unpublished data). Histological analysis of soft palate muscles of both control and mutant mice was performed by paraffin sectioning and MHC immunofluorescence staining. Images were taken from each section of the soft palate and imported into BioVis software for 3D reconstruction. **Results**: The levator veli palatini and palatopharyngeus muscle volumes are reduced in the mutants compared to control mice. In addition, the levator veli palatini reveals a cleft deformity compared to the continuous sling formation in the control mice. **Conclusion**: 3D reconstruction of soft palate muscles allows for better understanding of the anatomical defects in the mutant mice, which recapitulate those seen in humans, and can be utilized as a model to develop treatment strategies in the future.

Poster #64

Title: Real time monitoring of the formation and removal of biofilms from clinical-related pathogens using an impedance-based technology

Authors: Esmat Sodagar& Parish Sedghizadeh

Faculty advisor: Parish Sedghizadeh

Purpose: The aim of this work was to test the antimicrobial efficacy of novel bisphosphonate-antibiotic conjugates against clinically relevant bacterial bone biofilm pathogens using a rapid impedance-based real time cell analyzer. **Background**:Biofilms are described as surface-associated bacteria surrounded by a self-produced extracellular matrix. Many chronic infections, particularly bone infections, are caused by pathogenic bacteria growing as biofilms. Several methods are available to study such biofilms in vitro. However, these methods are limited by high labor intensity, intrusive sampling and/or long time lags from sampling. Therefore, sensitive, accurate, reproducible and faster methods are desirable for real time monitoring of biofilms. **Methods**: By using impedance measurements in microtitre plates with gold electrodes we assessed in real time the antimicrobial effects of bisphosphonate-antibiotic conjugates against bacterial biofilms. For experimental purposes, the following microbial strains were used: *S. aureus* ATCC 6538, *P. gingivalis* ATCC 33277 and *Aggregatibacter actinomycetemcomitans* (Aa) D7S1. Moxifloxacin and ciprofloxacin were tested as the parent or control antibiotics and the following experimental bisphosphonate-antibiotic conjugates were synthesized and tested: etidronate-carbamate-ciprofloxacin and etidronate-carbamate-moxifloxacin. **Results**: The MIC results using a 16-well plate real time cell analyzer show that these new conjugates have high antibiotic efficacy in comparison to the non-conjugated antibiotics in osteomyelitis preventative and eradication experiments in vitro. **Conclusion**: Real time biofilm analysis provides a promising tool to evaluate antibiotic therapy in clinical or clinically relevant biofilm-mediated infections. Furthermore, this class of chemical conjugates, incorporating osteoadsorptive bisphosphonates with high bone affinity, and fluoroquinolone antibiotics for bone-targeted delivery to treat osteomyelitis biofilm pathogens.