2015 AAO Annual Session Milo Hellman Research Award, Harry Sicher Research Award, Thomas M. Graber Awards of Special Merit

The Milo Hellman Research Award, Harry Sicher Research Award and Thomas M. Graber Awards of Special Merit lectures will be held on Saturday May 16 and Monday May 18 in the Moscone Center. Consult the listing below for room number and time of lecture. Continuing education credit is available for attending these lectures.

Milo Hellman Research Award

Lecture Information: Saturday, May 16; 1:15pm-1:35pm; Moscone Center Room 104
Attenuation of articular cartilage degeneration progression by inhibition of Tgf-b1 signaling in a mouse model of osteoarthritis
Rebecca Chen, BDS
Harvard School of Dental Medicine

The goal of this study is to determine whether inhibition of transforming growth factor beta 1 (Tgf-b1) signaling prevents the articular cartilage of adult mature joints from being degenerated in a mouse model of osteoarthritis (OA). Although Tgf-b1 is believed to be essential for normal bone growth, studies have found increased expression of Tgf-b1 in the articular cartilage of human and mouse OA joints. In this study, the Tgfb receptor II (Tgfbr2) gene was conditionally knocked out from the articular cartilage of joints in mice at the age of 2 months old. Tgfbr2-deficient mice lived to the age of 12 months old and were sacrificed for collection of temporomandibular (TM) and knee joints. Tgfbr2-deficient mice were also subjected to destabilization of the medial meniscus (DMM) knee surgery. Joints were then collected from the mice at 8 and 16 weeks after the surgery. In addition, wild-type mice, C57BL, at the age of 8 to10 weeks old were subjected to DMM. Immediately following the surgery, these mice were treated with a Tgfbr2 inhibitor, Losartan, for 8 weeks and then sacrificed for collection of knee joints. All of the joints were characterized for evidences of articular cartilage degeneration. We did not find initiation and acceleration of articular cartilage degeneration by the genetic inactivation of Tgfbr2 in knee and TM joints of mice at the age of 12 months. We found that the removal of Tgfbr2 or the treatment of Losartan delayed the progression of articular cartilage degeneration induced by DMM, compared to that in wild-type littermates. Therefore, we conclude that inhibition of Tgf-b1 signaling protect articular cartilage of adult joints against the development of OA.

Harry Sicher Research Award

Lecture Information: Saturday, May 16; 1:35pm-1:55pm; Moscone Center Room 104
Harry Sicher Research Award
Candidate gene analysis of dental malocclusions
Cole A. Weaver, DDS, MS
University of Iowa

Introduction: According to the National Health and Nutrition Examination Survey III, the prevalence of malocclusions in the United States is approximately 20%. Our understanding of the etiology for most of these malocclusions is strikingly deficient.

Objectives: This study sought to reveal the underlying genetic basis for malocclusions. Specifically, this study explored potential correlations between three dimensional malocclusion phenotypes and craniofacial development genes.

Methods: Landmarks from CBCTs (124) and digital casts (161) were obtained from 285 subjects with skeletal Class I (n=60), Class II (n=143) and Class III (n=82) malocclusions. Genotypes were obtained from saliva taken of each subject. Three dimensional coordinate landmark superimposition, followed by Principal Component Analysis (PCA), was used to identify symmetric and asymmetric aspects of shape variation related to malocclusion. PCs explaining 51%-68% of total shape variation were regressed on 197 variants genotyped within 72 genes or loci adjusting for race, gender, age, and data source.

Results: Significant correlations ($p<0.01$) were found between malocclusion phenotypes and SNPs on genes BMP3, PITX2, MAFB, SNAI3, FGF8, ABCA4-ARHGAP29, FOXL2, PAX7, TBX1, LEFTY1, SATB2, TP63, SOX2 and the 400Kb region containing D1S435. Malocclusion phenotypes included, sagittal discrepancies (Class II versus Class III malocclusions), vertical discrepancies (deep bites versus open bites), Class II Division 1 versus Division 2 malocclusions, left to right asymmetries, dental cants, and malpositioned teeth.

Conclusion: Specific genetic pathways associated with malocclusions in all three facial dimensions were identified.

Thomas M. Graber Awards of Special Merit

Lecture Information: Saturday, May 16; 1:55pm-2:15pm; Moscone Center Room 104
ACTN3 R577X genotypes associate with Class II and deepbite malocclusions
Brian Zebrick, DDS, MS
Temple University

Introduction: Alpha-actinins are myofibril anchor proteins that influence the contractile properties of skeletal muscles. ACTN2 is expressed in slow type I and fast type II fibers, whereas ACTN3 is expressed only in fast fibers. ACTN3 homozygosity for the 577X stop codon (ie, changing 577RR to 577XX, the R577X polymorphism) results in the absence of α-actinin-3 in about 18% of Europeans, diminishes fast contractile ability, enhances endurance performance, and reduces bone mass or bone mineral density. We have examined ACTN3 expressions and genetic variations in the masseter muscles of orthognathic surgery patients to determine the genotype associations with malocclusion.

Methods: Clinical information, masseter muscle biopsies, and saliva samples were obtained from 60 subjects. Genotyping for ACTN3 single nucleotide polymorphisms, real time polymerase chain reaction quantitation of muscle gene message, and muscle morphometric fiber type properties were compared to determine statistical differences between genotype and phenotype.

Results: Muscle mRNA expression level was significantly different for ACTN3 single nucleotide polymorphism genotypes ($P<0.01$). The frequency of ACTN3 genotypes was significantly different for the sagittal and vertical classifications of malocclusion, with the clearest association being elevated 577XX genotype in skeletal Class II malocclusion ($P=0.003$). This genotype also resulted in significantly smaller diameters of fast type II fibers in masseter muscles ($P=0.002$).

Conclusion: ACTN3 577XX is overrepresented in subjects with skeletal Class II malocclusion, suggesting a biologic influence during bone growth. ACTN3 577XX is underrepresented in subjects with deepbite malocclusion, suggesting that muscle differences contribute to variations in vertical facial dimensions.

Lecture Information: Monday, May 18; 8:00am-8:20am; Moscone Center Room 135
Cephalometric analysis and long-term outcomes of orthognatic surgical treatment for obstructive sleep apnea
Elizabeth Dela Cruz Ubaldo, DDS, MS
University of Washington

Purpose: Describe skeletal and posterior airway changes after orthodontics and surgical jaw advancement and to evaluate if there is a correlation between increasing advancement and long-term reduction in obstructive sleep apnea.

Methods: Lateral cephs and polysomnography (apnea-hypopnea index, AHI) from patients treated by bilateral sagittal split osteotomy (BSSO) or maxillomandibular advancement (MMA) in combination with orthodontics were collected. Patients completed a questionnaire and Epworth Sleepiness Scale (ESS) to assess long-term outcomes. Descriptive statistics for cephalometric measurements and linear regressions

were performed to find estimates for the final OSA (AHI and ESS) as a function of mandibular advancement.

Results: 43 patients with surgically advanced maxilla and mandible (5.2 mm and 8.3 mm) increased posterior airway 4mm. 33 patients completed the long-term survey (6.3 years ± 2.6 after treatment); 90% reported reduction of OS A and were pleased with facial appearance.

Conclusions: Maxillomandibular and posterior airway increased. There was no evidence of a linear relationship between greater amounts of mandibular advancement and improvement of OSA. Patients with less than10 mm advancement had successful objective short-term and subjective long-term OSA reduction.

Lecture Information: Monday, May 18; 8:20am-8:40am; Moscone Center Room 135
Miniscrew assisted slow expansion of mature sutures
Ross Jeffrey Pulver, DDS, MS
Texas A&M University Baylor College of Dentistry

Introduction: This study experimentally evaluated whether complex, mature, sutures can be separated using skeletal anchorage and light, continuous forces.

Methods: Twelve adult, 8 to 9 months old, female New Zealand White (NZW) rabbits were randomly assigned to one control and two experimental groups. Open-coil nickel-titanium springs delivered constant forces of 100 g across the sagittal suture to miniscrew implants (MSI's) placed bilaterally in the frontal bone. Sutural separation was measured bi-weekly. Bone formation (mineral apposition) on both the endocranial and ectocranial surfaces was measured with fluorescent labels and micro-computed tomography (µCT). Qualitative histologic analyses of the suture tissues were performed using H&E staining; osteoclasts were evaluated using tartrate resistant acid phosphatase (TRAP) staining.

Results: All 24 MSIs remained stable throughout the experiment. There was no statistically significant sutural separation in the control group. In the experimental groups, sutural separation was significant ($p < .05$) at all time points up to 42 days. The rate of separation was linear during the first 42 days, and decreased between 42 to 105 days. There were moderate correlations ($R=0.59-0.89$; $p=<.05$) between MSI separation and bone marker separation. Mineral apposition rate (MAR), which was not measureable in the control group, was significant in the experimental group. MAR was greater between 14-28 days than between 28-38 days, and it was greater on the ectocranial than endocranial surface. Based on the µCT analysis, 3D sutural volume of the experimental group increased significantly ($p=0.02$), but surface area did not ($p=0.26$).

Conclusions: It is possible to separate the sagittal suture of mature rabbits. Sutural separation is limited, indicating involvement of other sutural articulations.

Lecture Information: Monday, May 18; 8:40am-9:00am; Moscone Center Room 135
Genetic and treatment related risk factors associated with external apical root resorption (EARR) concurrent with orthodontia
Lina Sharab, DDS, MS
University of Kentucky

Objective: Determine the genetic and treatment-related factors associated with external apical root resorption (EARR) concurrent with orthodontic treatment.

Setting and Sample population: This case-control study of 134-unrelated, orthodontically-treated Caucasian individuals was conducted in part at an Indiana Private Practice, Indiana University and the University of Kentucky.

Methods: Utilizing a research databank containing information from over 1,450 orthodontically-treated patients, pre- and post-treatment radiographs from 460 individuals were evaluated for EARR of the

permanent maxillary incisors. Sixty-seven unrelated Caucasians with moderate-severe EARR were identified, and were age/sex-matched with orthodontically-treated Caucasian controls yielding 38 females and 29 males per group. Factors tested for an association with EARR included: 1) treatment duration, 2) extraction of maxillary premolars, 3) numerous cephalometric measurements, and 4) DNA polymorphisms within the interleukin-1beta (IL1B; rs1143634), interleukin-1alpha (IL1A; rs419598), interleukin-1 receptor antagonist (IL1RA; rs419598), and caspase-1 (CASP1; rs530537, rs580253 and rs554344) genes. Stepwise logistic regression was utilized to identify the factors significantly associated ($p<0.05$) with the occurrence of EARR.

Results: A long length of treatment, presence of the GA&AA-genotypes for IL1B SNP rs1143634, extraction of the maxillary first premolars, and a large change in maxillary incisor angulation during treatment were significantly associated with EARR. Conclusion: EARR occurrence was associated with both genetic and treatment-related variables, which together explained 24% of the total variation associated with EARR in the sample tested.