



PITT DENTAL MEDICINE

EIGHTEENTH ANNUAL
**Research
Symposium**

MAY 16, 2018

Pitt Dental Medicine is ranked **number four** for National Institute of Dental and Craniofacial Research (NIDCR).

The profound research performed at Pitt Dental Medicine maintained their rank in the top 10 for nearly two decades—validation of our commitment to exploration, investigation and analysis, and to the quality of the innovation being created here.

“This ranking is reflective of our alignment with the goals for research set forth by the NIH. Pitt Dental Medicine has been ranked in the top 10 for about a decade, but this move into the top 5, at number 4, is significant. It reflects a long-term approach to becoming one of the premiere dental research institutions in the country—in the world. It is a powerful statement of our staying power and the decades of hard work toward international acclaim.”

B.J. **Costello** DMD MD Dean

“Pitt Dental Medicine has been engaged in top-notch, world-class research for many years. Being in the top 5 of NIDCR funding is particularly rewarding, though, because it is the major metric of U.S. Dental School research strength. Pitt is now shoulder-to-shoulder with other particularly strong research dental schools. Our research is at the cutting edge and applies state-of-the-art approaches to establish major research programs that, as evidenced by the success in getting grants, are widely recognized by other researchers outside of Pitt. Contributing to our research strength are the many productive collaborations with faculty investigators at Pitt, across the country and worldwide.”

Mary **Marazita** PhD Director of the Center for Craniofacial and Dental Genetics

This ranking is important to our clinical faculty as the new knowledge generated will improve patient care and the health of the whole population health. Our cutting-edge research is important to patient comfort: the knowledge that they will receive the best possible contemporary care. Our students and alumni should feel a sense of pride in their Pitt Dental Medicine home.”

Charles **Steir** DDS PhD Director of the Center for Craniofacial Regeneration

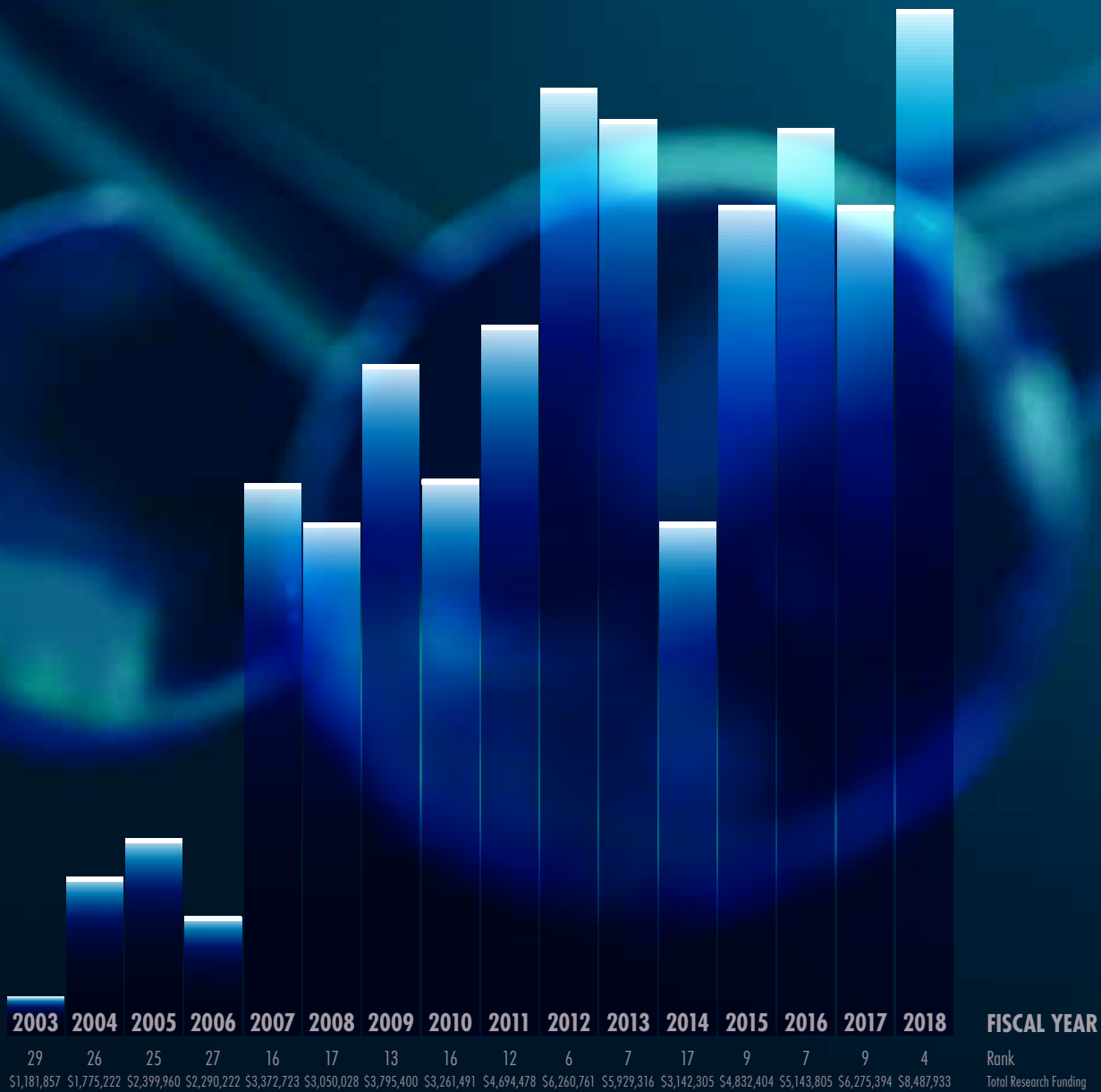
“The rankings validate the effort and talent of our faculty and staff and also demonstrate that we, as an institution, are “all in” with our support of the research missions of the dental profession and the University of Pittsburgh. Unquestionably, the new knowledge that our research generates will be important to improving patient care and population health. The “top 5” ranking, while arbitrary, is certainly something that brings attention to our school and will support our efforts to establish a sustainable research infrastructure. Maintaining that status is a worthy goal and one that, ideally, will continue to motivate us to continue achieving at the highest level.”

Robert **Weyant** MS DMD DrPH Associate Dean for Dental Public Health and Community Outreach

“The School of Dental Medicine’s ranking is an indication of its prominence in both dental research and in the training of new dental professionals. The school’s success reflects our campus-wide commitment to excellence at the University of Pittsburgh. I congratulate Dean BJCostello and all of the school’s leadership, faculty, staff and students on this achievement.”

Arthur S. **Levine** MD Senior Vice Chancellor for the Health Sciences and John and Gertrude Petersen Dean, School of Medicine

PITT DENTAL MEDICINE IN THE TOP FIVE FOR NIDCR FUNDING





Mary **Marazita** PhD
Director of the Center for Craniofacial and Dental Genetics



Charles **Sfeir** DDS PhD
Director of the Center for Craniofacial Regeneration

RESEARCH SYMPOSIUM HISTORY

In 2000, Dr. Mary Marazita became the Associate Dean for Research at the School of Dental Medicine. At that time, the research taking place at the school was not necessarily reflective of a school of this size. Additionally, many clinical researchers were working hard without sharing or learning about other research at the school.

Her vision to encourage research efforts was to set aside a day to celebrate and bring attention to the high-quality research going on “just down the hall” at the dental school. So, in 2001 she coordinated the first School of Dental Medicine Research Symposium in Scaife Hall. After 17 years, it has become the longest-running symposium at Pitt—and with good reason.

In 2002, while still focusing on research performed here at the School of Dental Medicine, she invited Raymond White from the University of North Carolina to be the keynote speaker. By expanding the event to include significant speakers from outside of Pitt, she began a tradition of inspiring faculty and student researchers through presentations by academics from other schools and institutions, as well as introducing research taking place at the school to researchers outside of the school.

2004 The Symposium broadened to include a luncheon for attendees. Student attendance became required for the event.

2012 The event continued to grow in attendance and significance. Concurrently, NIH funding increased from about \$2.5 million to over \$10 million by 2013. The School of Dental Medicine had become a significant force in dental medicine research.

2013 Dr. Charles Sfeir became Associate Dean for Research and continued to improve the event, which is the premier research event at Pitt. New funding is influencing the importance of translational research—the process focusing on the development of treatments based on research findings—and the School of Dental Medicine is influencing research worldwide.

DEAN'S MESSAGE

Dear colleagues and friends,

It is my great privilege to welcome you to our Research Symposium at Pitt Dental Medicine. This event is one that I look forward to each year. I see this occasion not only as a celebration of our successes in research but also as a jumping-off point for the great things our researchers will achieve in the future. We have much to celebrate and look forward to, as evidenced by the fact that we have achieved our highest ranking yet in the NIDCR rank list of funding to dental institutions, climbing to number four!

This accomplishment is a testament to the dedication of our researchers and the vision they hold for the future. Though their research ranges from core basic science, translational research, genetic studies to public health initiatives, it all shares an innovative spirit that sets it apart. By gathering together to see and support the progress of our researchers, we recognize the potential at Pitt Dental Medicine for even greater research achievements in the future.

Recently, becoming the Dean of our school has given me opportunity to view our research programs in a new way, and I am eager to expand our impact and scope. Our research is key to achieving preeminence as a school. We are well on our way to making that vision a reality, and this is due to the substantial innovations and discoveries made by our team of exceptional researchers. Those efforts not only solidify our peer status among top institutions but show the great promise for improving the oral and craniofacial health for individuals throughout the world. We are creating an impact worldwide.

Our work not only sets a standard for advancing science and growing programs that focus on discovery, but also presents an opportunity for our school to become a premiere school of dental medicine—one that strives to produce innovation in the lab and for our patients. As one example, this year Pitt Dental Medicine received an \$11.7 million NIDCR grant with our partners at the University of Michigan and the Weiss Institute to substantially change the way we commercialize innovations. Thru this grant our researchers have taken the additional step to accelerate the most promising ideas from many institutions into real patient solutions and products. At Pitt Dental Medicine, we believe that this progress is essential to the advancement of the dental profession as a whole.

I encourage each of you to explore the richness of our research programs and all of the exciting developments this work brings to the field. To participate in our research, as this symposium attests, not only allows you to share in our current, notable successes, but to become part of an effort to reach our tremendous potential. It is my honor to support this symposium and all that it represents for Pitt, and the health of all of us.

Sincerely,



B.J. Costello DMD, MD
Dean and Professor
University of Pittsburgh School of Dental Medicine

“We have much to celebrate and look forward to, as evidenced by the fact that we have achieved our highest ranking yet in the NIDCR rank list of funding to dental institutions, climbing to number four!”

B.J. Costello DMD MD
Dean





Charles **Sfeir** DDS PhD
Associate Dean for Research

Dear Pitt Dental Medicine friends,

It is a great honor to welcome you to the Eighteenth Annual Pitt Dental Medicine Research Symposium. Each year, we share and celebrate the accomplishments of the members of the School of Dental Medicine research community through this prestigious event. This year we are especially proud of being in the top 5 for National Institute of Dental and Craniofacial Research funding, placing fourth among dental institutions receiving NIDCR support. This is a reflection of the dedication to and innovative research being performed by our faculty, who are at the forefront of dental research. These research achievements, which hold great promise for the future of dental medicine and overall health, garner national and international recognition and demonstrate significance of our position among noteworthy dental institutions.

This event is designed to showcase the depth and breadth of our research programs—from genetic studies of orofacial birth defects to advances in craniofacial regeneration. The Center for Craniofacial and Dental Genetics (CCDG) continues its studies of oral health in Appalachia and the cleft and lip palate studies, which are inter-University and international collaborations that focus on genetic variants that influence facial features and their development. In the Center for Craniofacial Regeneration, various regenerative therapies are being developed for the pulp, periodontium,

ASSOCIATE DEAN'S MESSAGE

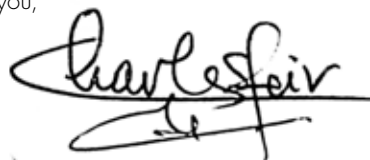
bone and soft tissues. The School of Dental Medicine, with the University of Michigan and Harvard University's Wyss Institute, is leading the Michigan-Pittsburgh-Wyss Resource Center: Supporting Regenerative Medicine in Dental, Oral and Craniofacial Technologies. This resource center is actively supporting promising projects from the clinical, academic and private sectors thereby bringing new technologies one step closer to patients. These research efforts truly illustrate our dedication and commitment to both the translational and basic science-focused spheres of research. While the pursuit of science itself is an admirable one, Pitt Dental Medicine looks not only to science, but beyond, to the patient-centered clinical applications where our research will benefit our friends, family and our whole community, now and in the future. To change one person's life through dental advancements is worth our effort.

Our symposium speakers share our dedication. This year's keynote speaker, Dr. Kenneth Hargreaves, DDS, PhD, Chair and Professor of the Department of Endodontics at the University of Texas Health Science Center San Antonio, will discuss the epidemic of opioid and substance use disorders, and research strategies in play to develop non-opioid pain killers to combat this epidemic. Three members of our faculty, Drs. Anitha Potluri, Timothy Erdle and Juan Taboas, will co-present on an exciting, innovative and rapidly evolving topic: Digital Dentistry. I am delighted that this topic, which I believe embodies the advancement and innovations in the dental field, is included in our program.

The innovative efforts embodied by these speakers are the type that permeate our entire school. The success of our research extends well beyond our researchers and their labs, into success in education and advances in patient care. Our dental students, residents and students in our masters and PhD programs benefit from the cutting-edge discoveries made within our school and usher in new generations of dentists who can embrace research to make them better clinicians and lifelong learners. Further, the success of our research means success for our patients because it enables us to provide the best dental treatment possible throughout the region and elevates our standard of care to a level that sets the bar for clinical advancement nationwide.

Our success in research brings us ever closer to our vision of excellence and innovation—a vision that encompasses all components of the school, from basic science to dental education to clinical care. As I look toward the future, I see how the fruits of all of our research endeavors benefit many through pioneering technologies, improved clinical practices and the increased understanding of genetics. As always, I am honored to be a part of this institution and glad to have the opportunity, year after year, to share with you all our progress and success.

Thank you,

A handwritten signature in black ink that reads "Charles Sfeir". The signature is stylized with a large, sweeping underline that loops back under the name.

Charles Sfeir
Associate Dean for Research


CCR UPDATE




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CENTER FOR CRANIOFACIAL AND DENTAL GENETICS



The Center for Craniofacial and Dental Genetics (CCDG) is an innovative University of Pittsburgh Center of Excellence, located in the School of Dental Medicine and directed by Professor Mary L. Marazita. From its inception in 2001, the CCDG has grown to a team of about 40 faculty, staff, and students, and currently is housed in the Bridgeside Point 1 building, near the Hot Metal Bridge, not far from the University of Pittsburgh Oakland campus.



Current research priorities of the CCDG include: genomic and phenotypic studies of orofacial clefting in populations around the world, studies of the etiologic factors contributing to dental caries and other oral health issues affecting Northern Appalachian populations, and identification of the genes that impact variation in specific facial features. These priorities are spearheaded by CCDG faculty including Dr. Marazita and Dr. Seth Weinberg, plus an extensive network of collaborators within the University of Pittsburgh and at many other universities, world-wide.

“I have been dedicated to research that eventually will elucidate the causes of orofacial clefts and other facial birth defects,” –Dr. Mary Marazita

Several recent developments distinguish the CCDG research program. Most notably, new grant funding has been received for the oral health disparities projects, for genomic studies of orofacial clefts, and for facial variation research. Furthermore, numerous important publications were completed in the last year in each of these areas.

Dr. Marazita received her PhD in genetics with an emphasis on biostatistics, from the University of North Carolina, Chapel Hill, followed by a postdoctoral fellowship in craniofacial biology at the University of Southern California. After holding faculty positions at UCLA and the Medical College of Virginia, Dr. Marazita joined the University of Pittsburgh in 1993 as Director of the Cleft Palate-Craniofacial Center’s Clinical Services team.

Dr. Marazita has been involved in the studies of a wide variety of human traits and disorders over the years, including birth defects, oral diseases, premature birth, behavioral and psychiatric conditions, diabetes, and many others. She has two current major research projects: genomic and phenotypic studies of orofacial cleft birth defects, and studies of genetic, microbiological and behavioral factors impacting oral health in children.

Dr. Marazita’s involvement in orofacial cleft research traces its roots back to her time as a postdoctoral student in the 1980s, and partly results from her training in medical genetics, during which she logged many hours in medical genetics specialty clinics, including those involving birth defects. The most common facial birth defects are orofacial clefts, such as cleft lip and cleft palate. Orofacial clefts create feeding difficulties early in life and require numerous surgical and dental interventions, as well as speech therapy and other ongoing services. Moreover, these individuals face increased risk for mental health problems, certain types of cancer and overall, a higher mortality rate. Ever since her postdoctoral years in the 1980s, Dr. Marazita has been continuously funded for her orofacial cleft research by the National Institute for Dental and Craniofacial Research (NIDCR) of the NIH. Her studies have led her to collaborations

around the globe with research sites on every continent except Antarctica. Current collaborators include investigators in the Philippines, Colombia, Nigeria, Puerto Rico and various sites in the United States.

Recent new funding to support the CCDG's orofacial cleft research includes two new grants that were received from the Gabriella Miller Kids First Pediatric Research Initiative (GMKF) from the Office of the NIH Director (<https://commonfund.nih.gov/kidsfirst/overview>). These new grants add whole genome sequencing of African and Chinese populations to previously funded research that provided sequencing of Caucasian and Latin American populations. It has been known for a long time that there are multiple genes and environmental risk factors that contribute to clefting. Only recently, though, have researchers had enough data to leverage so they can determine the source and reasons for the complexity. In fact, in spite of its complexities, many researchers are finding genes and combinations of genes that make biological sense to separate clefts into different groups and further understand the patterns of risk factors.

Improving Lives in Appalachia

In addition to orofacial cleft research, Dr. Marazita and the CCDG are engaged in research aimed at determining sources of oral health disparities in high risk, Northern Appalachian populations in West Virginia and western Pennsylvania. The goal of this project is to design effective interventions to reduce these disparities by examining genetic, environmental, behavioral, and microbiological factors and patterns of transmission within families in Appalachia in order to understand the causes of these oral health disparities. This research began in 2000, in collaboration colleagues at West Virginia University and the University of Michigan. Since those collaborations began in 2000, multiple research grants have been received by the CCDG from the NIH. The currently-funded COHRA projects focus on following the development of the dentition and onset of oral diseases in a cohort of Caucasian mother-child pairs recruited during pregnancy and followed until the child reaches at least age 6.

Furthermore, in the past year the CCDG's Center for Oral Health Research in Appalachia (COHRA)

Research Study has received additional funding from the NIDCR to recruit a cohort of African-American pregnant women—the "COHRA Smile" cohort. "To gear up, we hired two new research staff (Tonya Dixon and Jill Beach) and began active recruiting in November. As of February, we have enrolled 20 moms, the first step toward developing a cohort of about 400 African-American women and their babies." These women follow the same protocol as the original COHRA2 cohort of Caucasian women. "Periodically, they bring their children to the CCDG research suite at Bridgeside Point for evaluations that include a brief medical history, caries assessment, and sampling of saliva and plaque for DNA and microbiome analysis. Additional demographic, diet, oral hygiene, and psychosocial data is collected via phone interviews. We plan to follow-up until the children are at least two years old." Our colleagues at West Virginia University, under the leadership of Dr. Daniel W. McNeil and Dr. Linda Alexander, are beginning to recruit a COHRA Smile cohort from West Virginia. We are excited about the opportunity to create the COHRA Smile cohort because it will enable us to determine if racial factors compound the oral health disparities observed throughout Northern Appalachia.



COHRA Smile research staff members, Tonya Dixon (left) and Jill Beach (right)



Evaluating patients for the COHRA Smile project includes collecting brief medical histories, caries assessments and samples of saliva and plaque for analysis.

Discovering the Genetic Basis for Facial Appearance

“All of our faces are unique and our facial features show a great deal of variation. Evidence points to the fact that much of this observable variation can be explained by genetic differences among individuals,” said Seth Weinberg, PhD, a CCDG researcher and Associate Professor in the Department of Oral Biology. “Our goal is to identify which parts of the genome are associated with specific facial features.” Studies like this can help researchers gain a better understanding of how particular genes and pathways influence facial development, improve knowledge of how genetic variation relates to the features in certain birth defects and syndromes, and eventually allow for creation of predictive models about how the face grows.

Not long after joining the School of Dental Medicine faculty in 2009, Dr. Weinberg received funding as part of the NIDCR FaceBase Consortium to investigate genetic influences on normal-range facial traits. As part of this effort, Dr. Weinberg led the effort to create the first web-based, public repository of normal human 3D facial images and measurements—the 3D Facial Norms Project.

Studies on the genetic basis of normal-range variation in human facial features were spurred initially by phenotypic studies of orofacial clefting. As a graduate student, Dr. Weinberg, helped

develop protocols that Dr. Marazita and her team use to study facial shape in OFC families. Dr. Weinberg, with a background in physical anthropology, has research interests in the etiology of craniofacial birth defects, the genetic basis of human craniofacial variation, and the application of morphometrics and imaging to the study of complex craniofacial traits.

Following an initial 2016 publication, where several novel links between genetic variants and facial measurements were identified, Dr. Weinberg and his team published two high-profile papers on this topic.

In late 2017, in a paper published in the *American Journal of Human Genetics*, exploded the myth that earlobe attachment is not a simple Mendelian trait, as so many of us learned in grade school. On the contrary, almost 50 regions in the genome appear to be associated with this trait. The study also showed that many of the implicated genes are expressed in the developing human and mouse ear.

This paper, which included almost 75,000 participants, was a joint collaboration led by Dr. Weinberg. It involved numerous collaborators around the world including faculty and students in Pitt’s Department of Human Genetics, colleagues at the University of Washington, the Shanghai Institutes for Biological Sciences, University College London, and the personal genomics company 23andMe.

“This study actually started as a side project with a few third-year dental students and grew into something much bigger,” Dr. Weinberg said. “You never know where these things will lead.”

While earlobe attachment may not seem like a particularly important trait, these findings can tell us about the genes and pathways involved in normal ear development – an area where our understanding is still poor. That is relevant because the outer ear is affected in many genetic syndromes. This study can help us understand why this is the case. Moreover, it shows how even seemingly simple traits can involve incredibly complex biology.

In early 2018, Dr. Weinberg and colleagues at Pitt, Katholieke Universiteit Leuven (in Belgium), Stanford University, and Penn State, published a major paper on human facial gene mapping in *Nature Genetics*. Using an innovative machine-learning



Dr. Seth Weinberg

approach to measuring the face, this work identified 15 well-replicated genetic regions associated with distinct aspects of facial morphology. Many of the implicated genes are known to be involved in craniofacial development or in syndromes where the face is affected. Moreover, the team was able to show that variants in or near these genes impact the behavior of cranial neural crest cells, which are critical for building the face during early development.

Commenting on this paper, Dr. Weinberg said, "This is probably the most work I have been involved with to date. It shows the true power of cross-disciplinary collaboration, melding together expertise in anthropology, computer science, genomics, bioinformatics, and cell biology."

Both the 2017 and 2018 publications received wide media attention, including coverage by NPR, NBC, Popular Science, The Scientist magazine, and the Pittsburgh Post-Gazette.

Despite these successes, Weinberg acknowledges that there is still much we do not know. At this time, he and his team of collaborators are working to apply their innovative approach to analysis to much larger datasets. This effort will be made possible by a recent \$1.7 million RO1 awarded to Dr. Weinberg and collaborator Dr. John Shaffer (secondary appointment in the Department of Oral Biology) to continue this line of investigation.



Members of the Center for Craniofacial and Dental Genetics in their Bridgeside Point location

INNOVATORS IN TMJ RESEARCH AND RECONSTRUCTION

In 2018, temporomandibular joint (TMJ) dysfunction is a common occurrence. Although performing a full replacement is a trusted and effective option, there are many patients who exist along a TMJ spectrum; not quite needing a full replacement, but struggling with discomfort. For many of these patients, a simpler disk replacement could improve quality of life. However, for years, a safe and effective replacement product has been out of reach.

“... the final trial surgeries and data analysis should be complete during the summer of 2019, ... the team would have a very strong case for FDA approval of their device for use in the general public.”

During the 1980s, surgeons were using a Proplast Teflon implant to replace the TMJ disk. However, the FDA soon banned this material when it became apparent that, for a subset of patients with the implant, the disk was causing erosion of the skull, ultimately endangering the patient's brain. Since then, the FDA has classified most TMJ devices as Class 3, a designation that indicates the highest level of complexity. Considered to carry the greatest potential risk to the patient, these devices demand the most stringent regulations in order to verify that they are both safe and effective.

The intensity of the FDA requirements has presented a special challenge for doctors seeking to innovate in this highly specialized field. However, that has not deterred a passionate team of doctors and researchers in our own backyard from pushing forward.

For the past eight years, Dr. William Chung and Dr. Alejandro Jose Almarza have been integral members of a team from the Pitt School of Dental Medicine who are working towards FDA approval of a TMJ disk replacement implant.

Dr. Chung, Professor in the Oral and Maxillofacial Surgery Department, came to the project early on, after hearing a lecture by Dr. Stephen Badylak, a Professor in the Department of Surgery and Deputy Director of the McGowan Institute for Regenerative Medicine, who has pioneered extra-skeletal implants for healing. Intrigued by Dr. Badylak's device, which was already approved for other parts of the body, he approached the doctor to ask if this could be a viable option for replacing the TMJ disk. Badylak suggested they do a study together, and before Dr. Chung could decline, the project was born.

With the help of Dr. Bryan Brown, Assistant Professor in the Department of Bioengineering, Dr. Chung prepared to conduct the initial trials. The team contacted Cornell University College of Veterinary Medicine and arranged to carry out a series of surgeries there in order to collect the data necessary to receive FDA approval for human trials.

Around this time, Dr. Alejandro Almarza, Associate Professor of Oral Biology, joined the team. With an extensive background in TMJ research, Dr. Almarza introduced quantitative measures into the data analysis, in order to determine how the remodeled tissues compared to the normal tissues. A key aspect of Dr. Almarza's work on the project has been measuring the compressive and tensile properties of the disk replacement implant in order to understand how the implant can be developed and altered for improved results in the patient. This tissue is extremely unique, due to the fact that it is better at resisting pulling forces than compressive forces. As a result, the team sought to confirm that the manufactured implant could replicate this highly specialized function.

After performing the trial implant surgeries at Cornell, the team used non-invasive MRIs to monitor the position of the implants for six months and determine whether they were remodeling as intended. According to the data collected during this phase, the properties of the remodeled tissues fully matched those of the native tissues in compression and matched at least half of the properties of the native tissues in tension. Never before have results for a manufactured TMJ insert looked so promising.

Despite incredible strides forward, the team understands that the challenges are far from over. One of the fundamental inhibitors of progress is the fact that not all TMJ surgeons agree on how to address the same patient. Because of this, it can be difficult to rally unanimous support for a single new implant or procedure. However, based on their findings thus far, Dr. Chung believes, "It's a no brainer. We'd be doing patients a disservice not to pursue this device in humans."

Dr. Almarza echoes this passion, saying, "It gets us up in the morning...knowing that the patient will be better for it." Although some may still require the full TMJ replacement later on, the implant could help others avoid this procedure all together. Either way, the implant offers patients greater comfort and long-term mobility than any other options currently available.

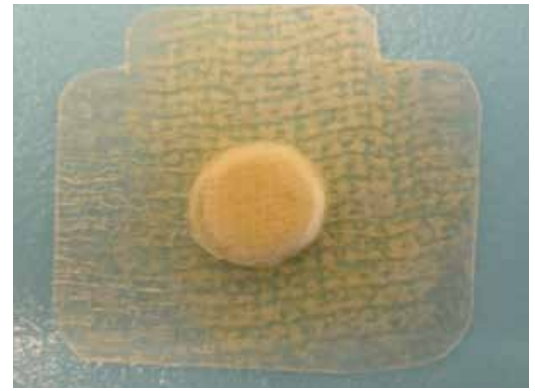
In the past 18 months, the doctors secured a FDA-certified biomedical company, Cook Biotech, to manufacture the implant—a key step toward receiving approval for human trials from the FDA. The team plans to begin the last round of trial

surgeries at Cornell with this high-quality device later this year. If all goes as expected, the final trial surgeries and data analysis should be complete during the summer of 2019, at which point, they would be ready to re-submit their data and results to the FDA.

If approved to begin human trials, the first surgeries would be performed on 10 patients in Pittsburgh. Once deemed to be safe and effective in those cases, the team plans to enlist three other universities to recruit 100 of their own patients to carry out the trials. Provided that there are no complications during this phase, the team would have a very strong case for FDA approval of their device for use in the general public.

Of course, at the heart of their research mission is the desire to better serve each patient that walks through the door. This journey has been a labor of love, and one that would not be possible if Dr. Chung, Dr. Almarza and their team did not fully believe in the potential benefit this procedure could provide.

After eight years, the doctors are poised to translate this research into human trials and publish their findings. This specific approach to the TMJ disk is the first of its kind, and the combined announcement of these developments could set Pittsburgh apart as a leader in TMJ research, not just in the country, but around the world.

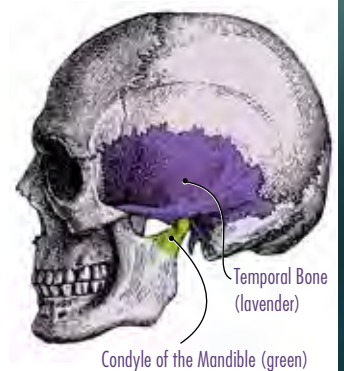


MatriDisc is supplied to surgeons ready to easily replace the patient's damaged meniscus after its removal.

TMJ Anatomy

The temporomandibular joint (TMJ) is the joint that connects the jaw to the skull. More specifically, the TMJ permits articulation of the condyle of the mandible with the temporal bone. In between the condyle and the temporal bone is the meniscus, sometimes referred to as the TMJ disk. When functioning properly, a healthy TMJ allows for easy, pain-free chewing and talking. However, a variety of factors including age, injury and autoimmune diseases can cause the meniscus to become thin and

the TMJ to no longer function as it should. Without the necessary cushion that the fibrous disk provides, the joint is forced to articulate bone-on-bone. This can cause pain not only in the jaw, but in the neck, ears and head, in the form of a migraine. Given the pivotal role that proper jaw function plays in nourishment, communication and overall quality of life, many patients require surgery in order to regain TMJ mobility and decrease what can often be debilitating discomfort.



Dr. Alexandre Vieira

BRIDGING THE GAP FROM RESEARCH TO TREATMENT

Thirteen years ago, Dr. Alexandre Vieira, Director of Clinical Research and Director of Student Research for the School of Dental Medicine, had a two-fold vision: to obtain DNA samples from patients with the goal of better understanding, diagnosing and treating dental conditions and diseases and to maintain these samples as a resource for fellow researchers.

“One of the greatest strengths of the DRDR is its ability to be used by other researchers and teams seeking to mine questions more specific to their unique disciplines.”

The inspiration for this came out of the belief that creating a comprehensive set of dental phenotypes linked to DNA samples here in Pittsburgh would allow for greater ease of exploration. The system in place at the time required researchers to gather their data from complicated external sources. So, assembling a database of DNA samples that could be studied over time at the School of Dental Medicine seemed like an important and necessary step.

Despite the potential for push back, Dr. Vieira developed a protocol that was approved by the ethics committee, and with this, the Dental Registry and DNA Repository (DRDR) was born. From the start, one of the major challenges was determining how to systematically invite participants. Fortunately, the School has always supported the project by employing a staff member to assist with recruitment. And in time, the DRDR created opportunities for students to become involved in both the research and recruitment efforts as well.

Applying a Mature DRDR

Today, there are more than 6,000 participants on the DRDR registry, which grows at the rate of roughly 400-600 new entries every year. With this large and growing number of DNA samples, Dr. Vieira is able to ask more sophisticated questions and obtain more comprehensive medical records—understanding each person as a whole. Although an ambitious concept, the DRDR allows researchers to evaluate issues of best practice and seek to understand if there are better ways to perform certain treatments.

One recent question involved looking into the correlation between mental health and common dental procedures such as fillings and root canals. What Dr. Vieira found was that while poor mental health had no impact on the success of amalgam fillings, it did greatly increase the potential for failed root canals or composite resin fillings. This offers a prime example of the relevance of these questions. If a patient with a mental health concern goes to the dentist and the dentist does not consider these risks, the patient might not receive the results they desire.

One of the greatest strengths of the DRDR is its ability to be used by other researchers and teams seeking to mine questions more specific to their unique disciplines. In this way, the database proves its worth in both breadth and depth of potential information.

A recent example of this arose when the Pitt Dental Medicine Department of Orthodontics expressed interest in probing what causes individuals to need braces. Using samples from the DRDR, the researchers identified that misalignment in the jaw that causes the need for braces could have

origins beyond the skeletal basis. Muscle force was examined to measure the amount of force applied when an individual was asked to seal their lips. Through these data, stored in the DRDR, it became clear that a genetic variation concerning unusual, muscle-related genes that are more frequently present in people with weaker muscle forces is associated with a need for braces. These findings added a degree of complexity into the discussion of orthodontics that was not previously considered.

This project is a striking example of what can be accomplished when different disciplines turn to the vast body of research available from the DRDR to push the limits of current or traditionally accepted knowledge in their field.

Growing the Future of the DRDR

For the past twelve years, the DRDR been the only project in the world to collect and maintain DNA samples for the purpose of long-term research related to oral health. As a result, researchers around the globe have become increasingly interested in understanding Dr. Vieira's approach. One of the most visible signs of enthusiasm for the project comes from Puerto Rico, where researchers are in the process of opening their own version of the DRDR. Although the Puerto Rico team has not yet determined whether they will seek Dr. Vieira's assistance for organizing their data, theirs is the most concrete step in the direction of replicating the DRDR model.

While Dr. Vieira and his primarily junior team have made incredible breakthroughs in understanding the root cause behind common dental issues, the project has merely scratched the surface of what is possible. The results from the evaluation of mental health's role in dental treatments and collaborations such as that with the orthodontics department illuminate not just how the DRDR can shed light on issues of oral health, but on conditions throughout the body.

Ultimately, the research conducted by the DRDR can provide dentists with a greater degree of knowledge on the less-understood impact of genetics. This insight allows medical professionals to broaden their perspective on the root causes of disease and seek innovative changes in procedures that can positively impact the delivery and success of care.



Dr. Alexandre Vieira



DRDR Facts

Sample Size	5 mL
Samples Per Container	100
Total Samples	5000
Publications Supported	18
Pitt Faculty Supported	22
Students Mentored	168

* Values are based on 5,000 total samples.

LEADERS IN INTERDISCIPLINARY RESEARCH AND EVIDENCE-BASED DENTISTRY

Since the 1940's, the University of Pittsburgh School of Dental Medicine has pioneered research into clinical prevention, behavioral dentistry, and population health.

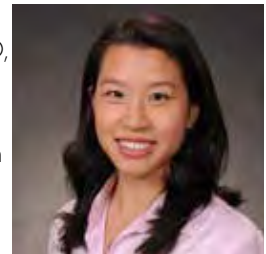
Dr. Robert J. Weyant, professor, chair and Associate Dean for Dental Public Health and Community Outreach, formed the Department of Dental Public Health in 1994 by combining the departments of Community Dentistry and Behavioral Sciences. As chairman of the new department he emphasized an interdisciplinary approach to education and research, creating a department that now comprises individuals with backgrounds and experience in behavioral science, epidemiology, biostatistics, educational research, community dentistry and more. The faculty members' varied backgrounds converge around a unifying theme of population health that motivates their approach to teaching and research. The overarching mission of the department is to improve the oral health of all, which is accomplished through community-based education and research, policy advocacy aimed at improving access to care, and an emphasis on prevention and health promotion in the dental curriculum.

“Evidence based practice is grounded in a belief that when a dentists are informed by the current best evidence of “what works” and uses that information as part of a treatment planning process with the patient ...”

The department operates a varied research program that is supported by both federal and foundation grants. One of the longest-running research program that the department participates in is the Center for Oral Health Research in Appalachia (COHRA.)

Since 2002, COHRA has examined how oral health disparities in Appalachian children develop and are sustained throughout their lives, leading to lifelong health consequences. This multidisciplinary study brings together researchers across disciplines as wide ranging as genetics, molecular biology, microbiology, behavioral and social sciences. To date, it has resulted in nearly 100 papers and abstracts published in the peer reviewed literature.

As an example, Dr. Jacqueline Burgette, DMD, PhD, the newest member of the department has incorporated her research in social network analysis into the COHRA study. She will be studying the impact of mothers' social networks on their children's oral health. Her project is currently funded by a Robert Wood Johnson training grant.



Dr. Jacqueline Burgette

Dr. Burgette's project along with all COHRA research has as its ultimate goal inform the development of interventions that will reduce oral health disparities in the region.

Other federally funded activities within the department include the Center of Excellence in Pain Education project, directed by Dr. Zsuzsa Horvath. Dr. Paul Moore, who is also supported by the center, is a nationally recognized leader in education for dentists on appropriate opioid use.



Dr. Zsuzsa Horvath

Evidence-Based Dentistry Guides and Improves Patient Treatment

Evidence-based practice is an important theme within the department's research and teaching mission. Evidence based practice is grounded in a belief that when a dentist is informed by the current best evidence of "what works" and uses that information as part of a treatment planning process with the patient, that will result in the best chance for optimal patient outcomes. Thus, at the heart of evidence-based teaching is the notion that each dentist should master the skills to efficiently search clinically relevant evidence, evaluate its quality and implement it in patient care. Beyond individual efforts, evidence-based practice also emphasizes changes to the actual structure of how clinical care is delivered. Identifying and addressing organizational and structural barriers to the provision of care based on current best evidence is



Dr. Deborah Polk

the domain of translational research. Departmental faculty member Dr. Deborah Polk, focus her research interests on this area and was recently awarded a National Institutes of Health (NIH)

U01 grant to identify the best way to influence dentists' clinical behavior through system-level changes. The importance of this research, states Dr. Weyant, is that it will "advance care delivery in ways that will improve both patient and population health".



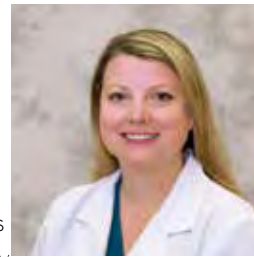
Dr. Robert Weyant

Dr. Weyant has been course director for the evidence-based dentistry program for over 15 years. During this time he has adapted his teaching of EBP to the changing needs of clinical

dentists and the ongoing advances in information technology. "Rather than go to the library," he explains, "we are now teaching students that you can find high quality evidence at your fingertips, when you need it, on a mobile phone."

A recent example of how new evidence can be used to improve patient care was a case involving a patient who requested new dentures. Due to a

hyper-responsive gag reflex, the patient was unable to tolerate any stimulation to the palate. The patient had been struggling to wear his current denture which was ill-fitting due to his difficulty tolerating the denture impression process. As Dr. Sarah Grafton, assistant professor of operative dentistry, explains, "the student researched a technique utilizing removable training plates of increasing thickness to effectively 'train' the patient to tolerate palatal stimulation for specified time intervals." The technique was published online at the in The Cochrane Library.



Dr. Sarah Grafton

By searching for an approach that would be more tolerable for the patient, evaluating the quality of the evidence attesting to its potential success and implementing the procedure, the student was able to conduct a successful impression, allowing new dentures to be made. According to Dr. Grafton, this same method used to make a successful impression allowed the patient to tolerate the new dentures, "within a period of about 6 months." One year later, the patient continues successfully to wear his new dentures. This is an excellent example of how challenging patient care situations can be addressed through accessing and applying high quality evidence.

The Department of Dental Public Health in collaboration with the Department of Pediatric Dentistry also manages a federal Health Resources and Services Administration training grant aimed at training pediatric dentistry residents in care to high risk, low access population such as commonly found in rural Pennsylvania. The training grant also supports the residents for completion of a Master's in Public Health degree.

As he looks to the future, Dr. Weyant anticipates that the Department of Dental Public Health will continue its tradition of high quality teaching and research in support of the School of Dental Medicine's overall mission.

FABRICATING THE FUTURE OF DENTISTRY



3D printing may seem mysterious, futuristic, the stuff of sci-fi. But many industries are employing the technology here and now to develop products, customize parts and products, and reduce manufacturing time and cost. Aerospace companies, medicine, even sneaker manufacturers—entire fields are evolving due to 3D printing.

Dentistry is no exception. Faculty at the University of Pittsburgh School of Dental Medicine are actively exploring ways that digital technology and 3D printing can improve outcomes in dental treatment, lower costs and increase patient satisfaction. Among the ground-breaking developments is a collaborative research project between Pitt Dental Medicine and Swanson School of Engineering that may “fabricate” the future of dentistry.

The research partners propose a new way: taking digital images of a patient’s mouth; using AI algorithms and computer programming to design a denture framework; then 3D printing the product ...

Research partners John Ference, DMD, MPH, a prosthodontist and assistant professor at Pitt Dental Medicine, and Markus Chmielus, PhD, an assistant professor in the University of Pittsburgh Department of Mechanical Engineering and Materials Science, are using additive manufacturing (AM, a 3D printing method) and generative design (the use of computer software and artificial intelligence[AI]) to create and test denture frameworks. AM uses computer-aided design and manufacturing (CAD/CAM) to rapidly produce a prototype and then accurately build up materials to fabricate a complex structure tailored to a specific patient.

Using additive manufacturing, these partnering Pitt faculty hope to make stronger products with more accurate fit at lower cost using a method that is radically different from traditional subtractive techniques.

“We still fabricate dentures the same way we’ve been doing it for 20 years or more,” Dr. Ference said. “Traditional methods of fabrication require numerous steps that include impression making, model fabrication, transporting models back and forth to the dental laboratory, casting metal, adding porcelain, finishing, polishing and storage of casts. Every step in the fabrication process requires a thorough understanding of the coefficient of thermal expansion and manipulation of materials to avoid ill-fitting prostheses. Whether it is contraction of impression materials, expansion of gypsum, the contraction of molten metal or zirconia, contraction of dental polymers—good technique dictates success or failure. Digital scanning and fabrication methods eliminate many of the changes metals, porcelain, and impression materials undergo.”

Dr. Chmielus agrees that the established method leaves much potential for error. “A metal partial dental framework normally gets cast from an imprint using a gummy material in your mouth, then they cast another shape, and then out of that shape, they produce the metal framework,” he said. “It is a fairly complex method and not extremely accurate because it gets wiggled around to be removed from the patient’s mouth, then they cast another shape and then another. There are a lot of steps involved where errors can be introduced.”

The research partners propose a new way: taking digital images of a patient’s mouth; using AI algorithms and computer programming to design a denture framework; then 3D printing the product

by selectively binding a powder together with a glue, layer by layer, then removing that glue.

They did exactly that for an in vivo proof-of-concept study recently published in the *Journal Additive Manufacturing*. Their team compared the mechanical and physical properties of a 3D-printed framework (made of Inconel 625 metal alloy) with traditionally manufactured frameworks. They tested for specific gravity, tensile strength, elongation, compressive strength, flexural strength, impact, and coefficient of linear thermal expansion—and found that the physical and mechanical properties of their denture were very similar.

Their work has been recognized by the American Dental Education Association (ADEA), which awarded Pitt Dental Medicine and Dr. Ference the 2016 ADEAGies Award for Outstanding Innovation by an Academic Dental Institution. The findings have been presented to an engineering audience at the Materials Science and Technology 2017 conference, and Dr. Ference is preparing to submit the work to the American College of Prosthodontics and the *Journal of Prosthetic Dentistry*.

“We’ve shown we can print these. They have very good structure, good strength, comparable dimensions,” Dr. Chmielus said. “The next step is to move toward the patient, use dental scanning capabilities, make a digital model of the denture framework of the implant, then print it.” Ultimately, Drs. Ference and Chmielus aim to create a denture framework out of a biocompatible material, test the mechanical properties and dimensional properties again with that new material, then print and place the dentures in patients. To facilitate the next stage, they recently submitted a request for funding from the National Institutes of Health (NIH) to cover materials and an engineering PhD student to work full-time on the research. They eventually hope to obtain approval from the University of Pittsburgh Institutional Review Board to conduct a pilot study in the School of Dental Medicine.



A 3D printed partial denture plate that is undergoing continued refinement and testing as part of Dr. Ference and Dr. Chmielus' research.

The Big Picture

“I think this is going to shake up the profession,” Dr. Ference said. “The future dental professional must be able to use a hand-held or cone-beam tomography scanner to create digital scans of a patient requiring a prosthesis, modify and digitally design it, fabricate it by printing, and deliver and adjust the prosthesis before the patient leaves the operator.”

“I think this is going to shake up the profession”

Potential benefits for patients are fourfold: The new method stands to save them time, reduce costs, reduce the weight of prostheses, and improve fit. Rather than scheduling and enduring six visits over time, patients would be scanned one day and have the prosthesis the next, as the process takes several hours rather than several days. Practitioners could use less expensive materials and would go through fewer steps to both acquire a model and to make a denture framework. Prostheses would be much stronger and longer lasting, requiring fewer replacement. And even when replacements would be necessary, digital models would already be on file for reproduction.

“To meet the growing expectations and patient demands in the United States will require dental professionals to make prostheses faster, use materials that are less expensive, lighter weight

and able to be produced more economically. Prototyping through additive and subtractive manufacturing allows the dental profession to treat diseased teeth and missing teeth in an efficient, productive manner while reducing cost," Dr. Ference said.

"There's really nothing you can do with 3D printing that you can't do another way,"

Dr. Tim Erdle, DMD, a clinical assistant professor at Pitt Dental Medicine, sees even more potential uses for digital dentistry and 3D printing in the future. He encourages his colleagues to imagine patients who have experienced trauma or neglect and need to restore function, bite and smile through surgery. He hopes dental surgeons will one day obtain a cone-beam/3D image of the patient, convert the data into a model using software, digitally augment the bone via a surgical guide, print a mandible or part of a maxilla for example, perform trial surgery, and then implant it into the patient. "It provides training and set-up for the surgery, and lowers the time, so surgery is easier, more predictable for the doctor and the patient," he said.

How Does Dentistry Get There?

The future is promising, but challenges and work lie ahead. Dr. Ference said the biggest hurdle is the dental field's tendency to be slow to embrace innovation.

"I think dentists have always been scared of technology," he said. "But if they don't get on board, they'll have empty practices. People

these days just don't have time to spend at six appointments to fabricate one full denture. People want things quicker and cheaper. So this is going to be very successful, and we've come a long way. The future of dentistry is very promising if we're willing to embrace and invest in technology."

Dr. Erdle says the investment to learn can be small at first. He started exploring the potential accuracy and efficiency of desktop 3D printers in dentistry in the spring of 2017 by buying a basic desktop printer on Amazon for \$300 and building it himself. He has since built a second printer to keep up with changing technology. Desktop printers can range from about \$1,000 for a do-it-yourself model to about \$4,000 for a commercial model, Dr. Erdle said, and they can produce products that are accurate to about 100 microns.

He has engaged online communities in other disciplines to learn along the way. "3D printing itself isn't new at all, and there are entire communities out there that have been printing little figurines and small tools," he said. In fact, dentistry itself has a growing community of people interested in incorporating the technology: For example, a Facebook group, 365 Digital Dentistry, has about 11,000 members.

"Dentistry is never going to be entirely digital because it is something you do with your hands. And we don't want to be entirely digital," Dr. Erdle said. "But it is a great tool to have in the toolbox." He hopes the school and its faculty can be "cautiously creative—giving students and residents time to play a little bit to see how they can use the technology in a new and innovative way, then run with it responsibly."

Dr. Juan Taboas, PhD, a researcher in the School of Dental Medicine, emphasizes the word responsibly. He is working to develop hydrogel scaffolds to study intracellular signaling, cell-to-cell communication, and tissue growth, and he aims to someday use 3D printing to create the scaffolds. Although he also is excited about the potential of digital and 3D technology in many facets of dentistry, he cautions the industry to make sure that any advancements are evidence based.

"There's really nothing you can do with 3D printing that you can't do another way," he said. "But is it something that dentistry needs or not? Is it

Dr. Steven Ference shown with the large, 3D printer that currently is being used as a part of his research.



something that benefits patients? Let's not just jump on the bandwagon only because it sounds cool."

He stressed the importance of evidence-based practice and comparative effectiveness research whenever dentistry implements such technology, as well as the importance of educating students along the way.

"Some of the students have played with 3D printers in their garages. It is not a difficult technology to comprehend," he said. But there is more to it than that. "We have to revamp our materials courses so they understand the limitations, how materials shrink as they are built layer by layer, how they shrink more between layers than within layers. Students need to understand why this happens and what to look for to choose the best materials. And they need a digital design background. They have one cursory exposure now. They need to develop experience with the software, how to draw on the computer."

Dr. Ference imagines a future where dentists who have such training can take images of a patient, digitally design the necessary product, then head to a local, large printing lab with very sophisticated and expensive equipment for accurate, cost-effective production.

Collaboration + Education = Creation

Pitt Dental Medicine's four-year dentistry program is designed to comply with the guidelines set forth by the Commission on Dental Accreditation (CODA). The curriculum is designed to graduate good dentists, to get students through their boards and clinical licensure examinations. The school's leaders are actively ways to continue success in those areas while also training dentists in digital dentistry and 3D printing.

"Changes in the curriculum have been happening, and there's an understanding of the need for further change in the curriculum," Dr. Ference said. "Administrators are open to those ideas. They know it's necessary if they want to be competitive."

He suggests further collaboration between the schools and departments right here at Pitt that can build upon his current partnership with engineering. In the same way dental students can concurrently



Dr. Timothy Erdle



Dr. Juan Taboas

pursue a master's of public health degree or a business degree through the Graduate School of Public Health or the Joseph M. Katz Graduate School of Business, perhaps future students can simultaneously complete their dental training and earn a master's degree in dental technology or a master's in dental materials through a collaboration with the Swanson School of Engineering.

"All of health care is in the midsts of moving to an interdisciplinary approach to making patients healthier these days. In the past, we were like missile silos: For example, the engineering school, dental school, and medical school would be distinct silos of information," he said. "But we're now on a horizontal collaboration and integration of everything we do—getting a lot of specialties involved to improve treatments for all of our patients."

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RESEARCH CLUSTERS

Center for Craniofacial and Dental Genetics

Genetics plays an increasingly critical role in modern biomedical science and clinical practice, including dental and craniofacial sciences. The University of Pittsburgh historically has been a leader in genetics, developing one of the first Departments of Human Genetics in the nation. Within the School of Dental Medicine, this tradition is embodied in the Center for Craniofacial and Dental Genetics (CCDG), which was established as a University Research Center of Excellence in 2001. Research at the CCDG is primarily focused on understanding the etiological basis of complex oral and craniofacial traits, notably dental caries and orofacial clefting, with an emphasis on genomic and phenotypic analyses.

Led by the Director, Dr. Mary L. Marazita, the CCDG currently comprises 4 faculty (plus 8 additional affiliated faculty), 28 staff, and 15 students and post-doctoral fellows. CCDG faculty have expertise in statistical genetics, molecular genetics, computational modeling, morphometrics, and imaging. The Center has had continuous National Institutes of Health funding since its establishment, currently about \$5 million annually.

CCDG Faculty

Mary L. Marazita, BS, PhD
Professor
CCDG Director

Katherine Neiswanger, BA, MA, PhD
Research Associate Professor

Petr Pancoska, BS, PhD
Research Associate Professor

Seth M. Weinberg, BA, MA, PhD
Associate Professor

**Center for Craniofacial
Regeneration**

Content yet to be delivered

Dental Public Health

Through a variety of research, teaching and outreach initiatives, the Department of Dental Public Health advances its primary mission of “improving population oral health.” The various domains of mission-related activities include the following:

- Conducting research aimed at identifying and reducing oral health disparities;
- Preparing students for non-traditional careers in academics, public health, and other areas of importance to society;
- Implementing of evidence-based practice in patient care;
- Advancing methodology for the study of population health issues of relevance to dentistry;
- Advocacy and policy development aimed at improving access to dental care; and
- Advancing service learning and interprofessional education.

Department Faculty

Robert Weyant, MS, DMD, DrPH

Professor

Chair

Associate Dean for Dental Public Health and Community Outreach

Joseph Ambrosino, BS, MS, MPM, DMD, FAGD

Instructor

Jacqueline Burgette, DMD, PhD

Assistant Professor

Zsuzsa Horvath, PhD

Assistant Professor

Anchal Malik, BDS, MHA

Assistant Professor

Nina Markovic, BSDH, MS, PhD

Associate Professor

Paul Moore, BS, DMD, MS, PhD, MPH

Professor

Louise Platt, RDH, BSDH, MHPE

Instructor

Deborah Polk, AB, PhD

Assistant Professor

Richard Rubin, BA, DDS, MPH

Assistant Professor

Nilesh Shah, PhD

Assistant Professor

The Dental Registry and DNA Repository (DRDR) was created in response to the need for large sample populations to act as a resource to researchers of complex oral diseases and conditions. The interplay between the host, its genetic background and the environment, where each component has a relatively small effect size, suggests that studies need to be robust and sample sizes should be in the magnitude of several hundreds, if not thousands, of observations.

The DRDR is an archive of clinical information linked to saliva samples from consenting individuals. Participants include both children and adults who have received treatment at the University of Pittsburgh School of Dental Medicine. Currently, approximately 6,200 subjects are part of the DRDR database, which is available to faculty and students for the development of clinical research projects.

The registry has supported several faculty and student projects, and more than 20 scientific papers and grants have been generated with this resource.

Dental Registry and DNA Repository Faculty

Alexandre R. Vieira, DDS, MS, PhD

Professor

Director of Clinical Research and Student Research
of the School of Dental Medicine

**Dental Registry and
DNA Repository**

GRADUATE OPPORTUNITIES

Dental Anesthesiology

The Department of Dental Anesthesiology is extremely active in teaching, research, and service. The department operates a 3-year dental anesthesiology residency program and is a training site for the School of Nursing's Student Nurse Anesthetist program.

Together, these residents, nurses, and our own selective dental students enable the department to provide clinical anesthesia services in the oral surgery, implant, phobia, pediatric, and special needs areas. The department maintains some of the most sophisticated equipment found in any dental school setting. This includes nine anesthesia machines, three fiberoptic videoscopes, and three videolaryngoscopes.

- Predoctoral teaching includes courses in local anesthesia, medical emergencies, pain and anxiety control, enteral sedation, and clinical medicine. The medical emergency management is accomplished at the University of Pittsburgh's Peter M. Winter Institute for Simulation, Education, and Research (WISER) Center, where students are assessed as they manage various office emergencies in real time using high-fidelity human simulators.
- Department of Dental Anesthesia faculty are involved in continuing education for the School of Dental Medicine, teaching courses in local

anesthesia for dental hygienists, medical emergencies and a 15-hour course in basic and advanced anesthesia management and simulation for licensure and permit renewal. In addition to their many activities and responsibilities, departmental faculty are actively engaged with many school-related committees while pursuing research and publication objectives.

- Dental Anesthesiology Residency Program
 - o The department operates a three-year, CODA-accredited, hospital-based dental anesthesiology residency program. The goal of this program is to prepare dentists to manage pain and anxiety in adult, pediatric, and special needs patients. Graduates receive a Certificate in Dental Anesthesiology and are eligible to take the board examination of the American Dental Board of Anesthesiology.
 - o All residents must be graduates of an accredited U.S. or Canadian dental school. The application is submitted through the ADEA Postdoctoral Application Support Service (ADEA PASS) website and the deadline for submission is September 15 of each year.

The Department of Dental Public Health provides high-quality education to first-professional dental students and residents, conducts scholarly research that advances knowledge in dentistry, and acts as a resource service unit not only within the School of Dental Medicine, but also to other areas throughout the University and surrounding community. Departmental faculty members engage in a variety of funded and non-funded basic, clinical, and population-based research. Research productivity is substantial and many faculty play leadership roles in local or national research organizations. Our faculty are working on important new methods for designing and analyzing dental data and advancing dental research. The

department currently is part of a large National Institutes of Health (NIH)-funded project on the causes and elimination of oral health disparities in Appalachian children and their families. A theme of understanding the causes of oral disease and developing effective interventions for vulnerable and underserved populations runs through much of the department's research activities. The department maintains active research collaborations with the University of Pittsburgh Cancer Institute (UPCI), Magee-Womens Hospital, the Clinical and Translational Science Institute (CTSI), and numerous other research universities in the United States and abroad.

Dental Public Health

The Department of Diagnostic Sciences in the School of Dental Medicine is responsible for the areas of oral radiology, oral medicine, oral pathology, and dental emergency medicine. The department has faculty that have achieved diplomate status ("boarded") in their specialties of oral medicine, oral and maxillofacial pathology, and oral and maxillofacial radiology, indicating their experience and expertise in their fields. All faculty teach pre-doctoral students, dental hygiene students, and residents either in clinical rotations or in foundational and clinical didactic courses, and provide continuing education to dentists, hygienists, and physicians. The department hosts a three-year residency program in oral and maxillofacial

pathology and houses a biopsy laboratory. The department has hosted several summer research scholars and participates in resident research projects. In addition, faculty have their own research areas of interest. Recent, current, and future projects include data-mining of the axiUm electronic record to assess treatment disparities of disadvantaged patients; quality assessment outcomes of consultation recommendations; genetic mutations in odontogenic tumors; cancer chemoprevention using lyophilized fruits; comparative radiographic features of ossifying fibromas; immunohistochemical features of salivary gland neoplasms; demographics and outcomes of the biopsy service; and demographics and outcomes of the oral medicine clinical practice.

Diagnostic Sciences

Graduates are required to take part in the American Board of Endodontics examination. When the program ends, all residents will be awarded a certificate in endodontics and be considered board-eligible.

Research Focus

- Pulp regeneration using scaffolds and growth factors
- Pulp regeneration using cellular approaches
- Understanding root anatomy through high-resolution micro-CT imaging
- Industry collaborations to assess and improve endodontic files

- Effectiveness of instrument systems to deliver disinfecting agents into the root canal

Clinical Training

- Treatment management, including surgery of diseases of the dental pulp and periapex, and trauma of the tooth root and pulp

Criteria

- Applicants must hold a DMD from a CODA-recognized dental school or its equivalent
- Applications are accepted May–August of each year
- Admissions are conducted using a rolling format

Endodontics

Certificate in Endodontics with Optional MDS

Oral Biology

MS or PhD Degree

Graduate study in this program covers a wide range of topics at the molecular, cellular, and organismic levels as well as translational and clinical studies. The mission of the graduate studies program in oral biology is to foster intellectual curiosity, excellence, and creative vision in students and to prepare them as future leaders in the field of academic dentistry and dental and craniofacial research.

Promising first-professional dental students and residents are encouraged to enter the PhD or MS graduate programs in oral biology and pursue both degrees simultaneously. First-professional dental students in the graduate program will follow all requirements for the PhD or MS programs, as well as complete research requirements toward an MS or PhD degree.

Research Focus

The focus of the program is on oral health and biomedical research and teaching. The program's scope encompasses studies of fundamental

biological phenomena related to the development, structure, and function of the craniofacial region and the development of new therapies, biomaterials, and diagnostic tools for the treatment of diseases and disorders in the craniofacial area with the aim of improving health and well-being. Currently, faculty in the Department of Oral Biology are focused on two areas of research concentration (ARCOs): craniofacial regeneration and craniofacial genetics. These form the basis of graduate training in this program.

According to the U.S. Bureau of Labor Statistics, craniofacial tissue engineers and craniofacial geneticists have excellent job prospects and earning potential in the next decade. Of the 30 fastest-growing occupations, biomedical engineer is ranked number one and genetic scientist is ranked number six. It is projected that 28,000 biomedical/craniofacial tissue engineers and 154,000 medical scientist/craniofacial geneticist positions will be needed by the year 2018.

Oral and Maxillofacial Surgery

The Department of Oral and Maxillofacial Surgery (OMS) at the University of Pittsburgh offers a six-year, dual-degree program and a four-year program. Three residents are accepted each year as well as one pediatric craniomaxillofacial fellow.

Research Focus

- Regenerative medicine of craniomaxillofacial defects
- TMJ reconstruction with tissue engineering
- Stem cell-mediated regeneration of lost tissues
- Sleep apnea outcomes
- Virtual surgical planning outcomes
- Resorbable metal technologies
- Cleft and craniofacial anomalies

Training

The program is designed to be truly integrated and allow for the maximal benefit of coordinated medical training and the progression of knowledge and skill in oral and maxillofacial surgery.

Residents are exposed to the full scope of oral and maxillofacial surgery throughout their training, including interdisciplinary care. From the outset, new residents work with first-professional dental students in a training and supervisory role in the undergraduate OMS clinic. Residents also are required to attend the Department of Oral and Maxillofacial Surgery Grand Rounds, Journal Club, treatment planning conferences in the Dentofacial Deformities Program (in conjunction with the Orthodontic Program), and the weekly Surgical Treatment Planning, Implant, and Trauma Conferences.

Criteria

- All residents must be graduates of a CODA-accredited U.S. or Canadian dental school.
- Fellows must be graduates of a CODA-accredited OMS residency program.
- Application deadline is September 15 of each year.

Graduates are required to take the qualifying examination of the American Board of Pediatric Dentistry at the end of the second year of training.

Research Focus

- Prenatal counseling for oral health
- Oral health promotion for disadvantaged children
- Infant oral health
- Early childhood caries
- Obesity and its relationship to dental development and physical growth
- Etiology, microbiology, prevention, and control of dental caries
- Dental trauma and its prevention
- Adolescent dentistry

- Behavior guidance and management for the pediatric dental patient

Clinical Training

- Advanced diagnostic and clinical training necessary to provide specialty care to infants, children, adolescents, and individuals with special needs.
- Clinical rotations at Children's Hospital of Pittsburgh of UPMC in anesthesiology, pediatric medicine, and hospital grand rounds.
- Teaching component in the predoctoral, preclinical, clinical, and didactic courses.

Criteria

- Applicants must be graduates of a U.S. or Canadian dental school.
- Application deadline is October 1, 2018.

Pediatric Dentistry
Certificate in Pediatric Dentistry with Optional MDS

Graduates will be eligible to take the examination for specialty certification in orthodontics offered by the American Board of Orthodontics.

Research Focus

- Craniofacial morphology and function in different populations
- Efficiency and efficacy of treatment modalities
- Craniofacial molecular and cellular control mechanisms
- Impact of biomaterials on delivering orthodontic mechanics

Clinical Training

- Diagnosis, prevention, and treatment/management of abnormal congenital or developmental relationships of the dentofacial anatomy, from infancy to adulthood, in diverse populations

Criteria

- Applicants must hold a DMD or its equivalent.
- Application deadline is September 15, 2018.

Orthodontics and Dentofacial Orthopedics
Certificate in Orthodontics with Optional MDS

Periodontics and Preventive Dentistry

Content yet to be delivered

Prosthodontics

Certificate in Prosthodontics with Optional MDS Degree

Senior Residents must challenge the written portion of the examination for certification in prosthodontics offered by the American Board of Prosthodontics. In addition, they must complete at least 1 of the 3 cases required by the Board. Other funded opportunities include: ACP annual meeting and Prosthodontic Board Review Course, 5 session Misch Institute Course (Las Vegas, Nev.), ACP Pa. Chapter annual meeting, Tri-annual M. D. Anderson Cancer Center update course (Houston, Tex.)

Research Focus

- Dental materials
- Industry collaborations to assess and improve restorative treatments
- Implant supported restorations
- Digital Dentistry fabricated restorations via CAD-CAM and 3-D printing

Clinical Training

- Comprehensive multidisciplinary treatment planning and restoration of teeth, supporting structures, speech, esthetics, function, and comfort following caries, periodontal disease, trauma, severe wear, neoplasms, and TMD conditions
- 20-25% of the residency is spent in the Implant Center
- There is a scheduled Maxillofacial Prosthodontic rotation for Senior Residents at Montefiore Hospital

Criteria

- Applicants must hold a DMD degree or its equivalent and have passed the examination of the National Board of Dental Examiners.
- Application must be made through the National Matching Service following all of their guidelines and deadlines: <https://www.natmatch.com/dentres/applicants/applications/html>





TRANSLATIONAL AND CLINICAL RESEARCH



Clinical research is usually defined as research with human subjects that is:

- patient-oriented research;
- epidemiologic and behavioral studies; and
- outcomes research and health services research.

But clinical research also includes:

- discoveries in research laboratory or in preclinical studies that will have an impact on human health and may lead to the development of studies in humans;
- the process of applying discoveries generated during research in the laboratory, and in preclinical studies, to the development of trials and studies in humans;
- research aimed at enhancing the adaption of best practices in the community; and
- cost-effectiveness of prevention and treatment strategies is also an important part of translational science.

There are an abundance of resources available at Pitt Dental Medicine and the University of Pittsburgh to facilitate activities in these areas—seen at only a handful of institutions. These include guidance with clinical studies, intellectual property regulations and collaboration across multiple specialties throughout the University, especially with the McGowan Institute for Regenerative Medicine.

At the Center for Craniofacial Regeneration the necessary infrastructure is present to carry out pre-clinical studies for FDA submissions following general laboratory practices (GLP). These quality systems of management controls for research ensure uniformity, consistency, reliability, reproducibility, quality and integrity of pre-clinical experiments.

In addition, Pitt Dental Medicine's Clinical Research Center offers faculty and students an infrastructure for the development of clinical research projects. The center has dedicated clinical space with two dental operatories, waiting room, interview rooms and storage. Also, imaging capabilities are available which includes portable three-dimensional-imaging for visualization of facial tissues, panoramic radiography and portable sonography. The center houses the Dental Registry and DNA Repository (DRDR), the only project in the world that keeps dental clinical information linked to saliva samples of individuals undergoing dental treatment. Currently, the DRDR has approximately 5,000 consented participants; has supported several faculty and student research efforts; and has supplied support to more than 20 scientific publications and grant submissions.

Pitt Dental Medicine's translational efforts are well supported and speak to the rich intellectual capital and resources at the University of Pittsburgh who are dedicated to moving transformative innovations forward to help and heal patients.

RESEARCH INTERESTS



Alejandro Almarza

Dr. Almarza is an assistant professor in the School of Dental Medicine with a secondary appointment in the Department of Bioengineering and the University of Pittsburgh McGowan Institute of Regenerative Medicine. His research interests are temporomandibular joint cartilage and bone regeneration and biomechanics; development of novel bioreactors to further enhance healing; identifying appropriate stem cell sources for tissue engineering approaches such as bone marrow, muscle, fat; genetic manipulation of cells seeded on scaffolds to promote regeneration; and quantitative assessment of joint movement and kinematics.

Richard E. Bauer

Dr. Bauer's research interests focus on tissue regeneration for oral and maxillofacial surgical applications. Dr. Bauer has been involved in research related to regenerative medicine for hard and soft tissue reconstruction in the oral cavity. He currently is working on the clinical application of various collagen matrices for oral connective tissue regeneration.

Dr. Bauer has been active in applications for computer assisted planning and surgical execution in reconstructive jaw surgery, sleep apnea and dental implants. He has worked on projects related to volumetric airway analysis and predictive outcomes for maxillomandibular advancement for the management of sleep apnea. He also has been working on projects related to dynamic navigation for intraoral and facial surgery.

Elia Beniash

Dr. Beniash's primary research interest is in the area of biomineralization and bioinspired materials design. He is trying to understand basic mechanisms of mineralized tissue formation and more specifically how the protein assemblies control mineral formation and organization at the nanoscale. He applies this knowledge to the design of bioinspired hierarchical nanocomposites for biomedical and other technological applications.

Elizabeth Ann Bilodeau

Dr. Bilodeau's research interests include the clinicopathologic, immunohistochemical and molecular characterization of odontogenic tumors. Dr. Bilodeau serves on the editorial board of the journal, *Head and Neck Pathology*, and is a reviewer for several journals including *The Journal of Maxillofacial Surgery* and *Oral Surgery Oral Medicine Oral Pathology Oral Radiology*. She has authored more than 30 peer-reviewed articles.

Andrew Brown

Dr. Brown's broad research interests are in bioengineering, medical device development, translational research and academic commercial translation. His specific research focus areas revolve around bone regeneration, tissue engineering and metallic magnesium for biomedical applications. In addition to his research work as a clinical assistant professor in the Department of Periodontics at the University of Pittsburgh, he is the Program Manager for Commercial Translation at sciVelo, a translational research acceleration program at the University of Pittsburgh.

Jaqueline Burgette

Dr. Burgette's research addresses oral health disparities in children through health services research. Specifically, Dr. Burgette is conducting research on the impact of mothers' social networks on children's oral health utilization, practices and dental caries experience. She also is examining how mother's social support influences children's oral health outcomes in Northern Appalachia and the relationship between personal and global social network characteristics and dental use among adolescents.

William Chung

Dr. Chung is a Professor in Oral & Maxillofacial Surgery at the School of Dental Medicine. He has a secondary appointment in the Department of Surgery at the University of Pittsburgh McGowan Institute for Regenerative Medicine. Dr. Chung is the co-investigator of a National Institutes of Health-funded grant, utilizing tissue engineering to help create a replacement meniscus for the temporomandibular joint. This project is culminating in the first in-human trial of the investigative device at the University of Pittsburgh Medical Center (UPMC). Dr. Chung also is involved in creating and implementing a pilot study for the American Association of Oral & Maxillofacial Surgeons that uses the art and science of simulation to recognize and treat airway emergencies in a more timely, standardized fashion.

Bernard J. Costello

Dr. Costello's primary research interests are tissue engineering, craniomaxillofacial deformities and surgical outcomes. As Associate Dean for Faculty Affairs at the School of Dental Medicine, he works to encourage faculty members toward clinically relevant research and grow interdisciplinary collaboration, particularly between basic scientists and clinicians.

Currently, Dr. Costello is primary and co-investigator on several grants involving a calcium phosphate bone putty as well as resorbable metal fixation devices to treat craniofacial defects and deformities.

He works closely with a number of basic and translational scientists in the Center for Craniofacial Regeneration (CCR) at the University of Pittsburgh

School of Dental Medicine to design clinical studies and find new ways to reconstruct challenging congenital or acquired problems in children and adults with craniofacial deformities. He also has been a clinical investigator for studies on tissue adhesives, helping to bring products to market for patient use.

Robert L. Engelmeier

Dr. Engelmeier's research interests include occlusion and biomechanics, computer-aided design and manufacturing (CAD/CAM), 3-D printing, and development of denture teeth historical research.

Pouran Famili

Dr. Famili's research interests include the clinical periodontal manifestations and the implications of the link between oral and systemic health; surgical technique in implant placement; systemic bone loss and implant success; periodontal epidemiology; and periodontal implant maintenance.

James Guggenheimer

Dr. Guggenheimer's research interests are focused on the analysis of electronic health records of patients at the School of Dental Medicine to characterize their sociodemographic and health attributes. Areas of particular interest include cigarette smoking and smoking-related diseases within the context of smoking interventions. Another study examines patterns associated with the use of hospital emergency departments for the treatment of painful dental emergency conditions and the inappropriate use of opioid pain relievers.

Additional studies examine the effects of the monoclonal antibody denosumab in conjunction with vascular endothelial growth factor inhibitors on alveolar bone and medication-related osteonecrosis of the jaw.

Zsuzsa Horvath

Dr. Horvath conducts research on best practices in dental education and faculty development. Her scholarly activities focus on three areas: 1) institutional surveys of dental schools in North America; 2) program evaluation; and 3) evaluation of educational materials. Her overarching aim is to

apply reflective practice in teaching and research in order to explore areas of improvement at the local or national level, share evidence-based recommendations to enhance dental education, and disseminate best practices in order to contribute to the broader dental education community. Currently, Dr. Horvath serves as the principal investigator on the University of Pittsburgh Center of Excellence in Pain Education: Pain Challenges in Primary Care (CoEPE), a five-year grant funded by the National Institute of Health/National Institute for Drug Abuse (NIDA). As part of the project, Dr. Horvath's team is creating online interactive educational materials in pain medicine to be implemented in the five health sciences schools at the University of Pittsburgh. These materials will then be disseminated by NIDA nationwide. Her team is currently administering the first round of implementation and planning evaluation and publications.

Thotalla Jayaraman

Dr. Jayaraman's long-term interests are in identifying and characterizing the role of phosphate-containing signaling molecules that are important for biomineralization. He specifically examines: 1) the structural elements in SIBLING proteins that promote biomineralization in bone and dentine; and 2) whether phospholipids effect mineralization by direct or indirect activation of signaling pathways. While intra- and extracellular lipids are known to play an important role in both physiological and pathological processes, detailed information on lipid composition at a local level, as well as the location of biochemical reactions that modulate calcium- signaling pathways in osteoblasts and odontoblasts, is crucial for understanding their roles in cellular function and dysfunction in bone and dentine.

Satish Kumar

Dr. Kumar's educational background includes periodontology and dental implantology, oral medicine, temporomandibular disorders and orofacial pain. His research training includes basic science research to understand oral carcinogenesis, clinical research design and management, and evidence-based medicine and dentistry. His primary research interests include clinical research on selected oral, periodontal and peri-implant

diseases and dental education. He also is interested in evaluating the reporting quality of published research that is directly relevant to clinical care such as randomized controlled trials and systematic reviews. Dr. Kumar has published several original articles, reviews, case reports, critical summaries, book chapters and online educational materials in periodontology and oral medicine, and conducts peer-review of scientific articles for leading journals.

Thomas Craig Kunkel

The area of digital dentistry is rapidly growing in the field of prosthodontics. CAD-CAM technology coupled with CEREC innovation has created numerous research opportunities. The marginal fit of CEREC materials in fixed prosthodontics is a current research interest. Also, the use of CEREC in evaluating students in a pre-clinical setting is being studied. PrepCheck (Sirona, Inc.) is being utilized to objectively evaluate pre-clinical tooth preparations. This will be compared to the evaluations given to students in a more subjective, instructor-oriented environment.

Anchal Malik

Dr. Malik is greatly involved and interested in the teaching of cariology to pre-doctoral DDS students, and her research interests relate primarily to caries management, including risk assessment, early caries development, detection and/or prevention, developmental defects of enamel, particularly enamel hypoplasia, early childhood caries, health disparities, and evidence based practice. She is currently co-director of the cariology course and co-coordinator for the discipline of cariology in the curriculum. She is also interested in developing and integrating new teaching methods to improve dental education especially in the area of caries disease management that will help develop competent dentists in the area of caries management, and use of evidence-based information in order to improve the oral health of patients and the community.

Mary L. Marazita

Dr. Marazita's primary research interest is in the genetics of cleft lip, cleft palate, and other craniofacial and dental anomalies, as well as the genetics of normal facial development. She is

applying a coordinated approach, exploiting both statistical and molecular tools to investigate the etiology of these common, complex, human traits. In addition, she is investigating families ascertained through several international collaborations (e.g., China, Colombia, India, Hungary, Denmark, Argentina, Turkey, India, Canada, the Philippines, and Nigeria), utilizing a rich phenotyping approach to inform etiologic studies.

Another major area of current investigation is genetic, microbiological and epidemiological factors that contribute to oral health and oral diseases such as dental caries, in Appalachia and other regions worldwide. Also, she has active research collaborations in the genetics of several behavioral and psychiatric traits, as well as several other human disorders (e.g., premature birth, autonomic nervous system dysfunction and otitis media). Dr. Marazita is involved in the NIDCR FaceBase Consortium (www.FaceBase.org), the NHGRI Consensus Measures for Phenotypes and Exposures Initiative (PhenX, www.PhenX.org), the NIH Director's Office Gabriella Miller Kids First Pediatric Research Initiative (Kids First, <https://commonfund.nih.gov/kidsfirst>), the NIH Director's Office All of Us Precision Medicine Research Program (All of Us, <https://allofus.nih.gov/>) and other national and international research initiatives.

Nina Markovic

Dr. Markovic is an Associate Professor in Dental Public Health and Co-Director of the Center for LGBT Health Research at the Graduate School of Public Health. Her research interests include health risks associated with minority status with a special focus on women, women's health during the reproductive years and psychosocial and social rank factors associated with risk factors for cardiovascular diseases.

Adriana Modesto-Vieira

Dr. Modesto-Vieira's research interests involve topics in two main areas: (1) pediatric dentistry with emphasis in cariology, and dental trauma; (2) oral microbiology with emphasis in bacterial adhesion models, antimicrobial activity analysis, biofilm models, and bacterial DNA fingerprinting.

Mark P. Mooney

Dr. Mooney's interests include the etiology and pathogenesis of craniofacial anomalies; the development of animal models to study craniofacial growth and development; and the effects of extreme environments on human growth, development and evolution.

Paul A. Moore

Dr. Moore's research interest continues in investigating dental therapeutics in dentistry and anesthesiology. He has initiated randomized controlled clinical research trials, practice surveys and comprehensive reviews of the safe and effective use of analgesics, sedatives and local anesthetics as used in dentistry for pain control. He has served as principal investigator on 40 sponsored awards throughout his career.

Dobrawa Napierala

Dr. Napierala's research is focused on molecular determinants of disturbed development and homeostasis of mineralizing tissues, and in regeneration and repair of these tissues. Dr. Napierala studies diseases associated with defective endochondral ossification, formation of dental tissues, bone mineral density and ectopic mineralization. She is interested in the role of the TRPS1 transcription factor in skeletal and dental development and homeostasis, and in the mineralization process. Related to this, Dr. Napierala studies the phosphate signaling pathway in mineralizing cells and the biogenesis of matrix vesicles, which play important role in the initiation of the mineralization process of bone, cartilage and dentin, and have been implicated in vascular calcification.

Andrea Nave

Dr. Nave's research interests include behavior management and personality, and sedation for pediatric dental patients.

Katherine Neiswanger

Dr. Neiswanger's research interests focus on the genetics of complex diseases affecting oral health,

especially dental caries in children and phenotypic development in nonsyndromic cleft lip with or without cleft palate. She serves as the program manager for the Center for Oral Health Research in Appalachia (COHRA), a collaboration between the University of Pittsburgh's Center for Craniofacial and Dental Genetics (Dr. Mary Marazita, director), West Virginia University, and the University of Michigan. COHRA is enrolling a large sample of pregnant women and their babies and collecting longitudinal data to study the genetics, microbiology, and environmental factors predisposing children to early childhood caries.

Marnie Oakley

Dr. Oakley's primary research interest includes topics related to leadership development and ethics. Dr. Oakley also has research interests in the use of social media in dental education, mentoring of the clinical academician in research-related activity, and prescription drug abuse.

Jean A. O'Donnell

Dr. O'Donnell's research interest in teaching and learning reflects her role as Associate Dean for Academic Affairs, managing the predoctoral curriculum at the School of Dental Medicine. A former nurse, she also is interested in tobacco cessation research and currently is the SDM site PI on an NIH-funded grant in collaboration with the University of Sydney, Indiana University, and Health Partners Institute to assess the utility of an electronic clinical decision support system for improving dental providers' delivery of brief tobacco interventions. Additionally, she is interested in interprofessional education and collaborative practice to improve patient outcomes through teamwork. She is a member of the Schools of the Health Sciences Working Group on Interprofessional Education and has collaborated with members of the group to pilot interprofessional experiences for students involving two or more professions working together. Her interest in prescription drug abuse led to a collaborative publication with faculty at the Schools of Dental Medicine and Pharmacy and to co-mentoring a first-year dental student on a project of the same topic.

Deborah E. Polk

Dr. Polk studies how broader social factors create disparities in health behaviors and indicators of health at the individual level. Examples of social determinants she is interested in include social norms and public policies. Examples of health behaviors include smoking and oral hygiene behaviors. The health outcomes she studies include dental caries and periodontal disease. In addition, she identifies social and behavioral contexts in which genetic variants increase the probability of disease.

Anitha Potluri

Dr. Potluri's research interest includes utilizing electronic health records (EHR) to assess the frequency of fibro-osseous conditions in western Pennsylvania populations. She also is involved in analyzing and quantifying the changes around implants using digital subtraction radiography and CBCT imaging. Additionally her interests are in three-dimensional imaging with emphasis on cone beam volumetric imaging and analyzing the incidental findings and radiographic patterns of intraoral bone pathology.

Joanne L. Prasad

Dr. Prasad's research interests vary broadly from the clinical, radiologic, and histologic profile of oral lesions to topics of relevance to dental public health and dental education. Currently, she is involved in research projects focusing on fluoridation and caries prevalence in Appalachian children, the attitudes of health professionals towards opioids in dentistry, and innovative ways to enhance communication skills in students of dentistry.

Herbert L. Ray

Dr. Ray's research interests include conservative pulp therapies focusing on the resiliency of the dental pulp and the development of pulp dressings that promote dental pulp survival and dentinogenesis. Dr. Ray's other interests are in regenerative pulp therapies utilizing both dental pulp stem cells and novel materials to create a biological obturation of the root canal system.

Richard W. Rubin

Dr. Rubin's main interests are in exploring the interface of public health and oral health, and in developing culturally competent/community-minded dental students. His research explores the development of these attitudes and beliefs among dental students and the relationship of the effectiveness of our dental school's Student Community Outreach Program and Education (SCOPE) activities in this process. The SCOPE program also was mentioned in the American Dental Education Association (ADEA) Center for Policy and Research Best Practices in Dental Education 2004, and referenced in the 2006 ADEA Report of the Panel of the Macy Study. He also is interested in evaluating and implementing new approaches to teaching and learning. This includes techniques based on active adult-learning models, "learning communities" and applications of cognition theories. Dr. Rubin has been the liaison between the School of Dental Medicine (SDM) and the Graduate School of Public Health for the joint DMD/MPH program, and, in 2016, he designed and is currently directing the Certificate in Dental Public Health program at the SDM.

Charles Sfeir

Dr. Charles Sfeir is the Associate Dean for Research, Director of the Center for Craniofacial Regeneration and Chair of the Department of Periodontics and Preventive Dentistry. Dr. Sfeir also holds a faculty appointment in the Departments of Oral Biology, Bioengineering, and the McGowan Institute for Regenerative Medicine. He received a DDS degree from the Université Louis Pasteur in Strasbourg, France. He earned a degree in Periodontology and holds a PhD in Molecular Biology from Northwestern University in Chicago, Illinois.

Dr. Sfeir's research focus is:

- Bone and Dentin Tissue Engineering, utilizing biomaterials and cellular strategies to regenerate mineralized tissues:
 - o Biomimetic scaffolds development for bone/dentin tissue engineering using biomineralization principles.
 - o Biomaterials development such as calcium phosphates or polymeric materials to regenerate bone and dentin

- o Engineering cellular therapies for bone and dentin regeneration. Strategies involve scaffoldless systems as well as stem cells in combination with biomaterials.
- o Identifying the signaling pathways involved in stem cell differentiation to bone cells.
- Biomineralization, Post-translational modifications of non-collagenous proteins in bone and dentin
 - o Role of protein kinases in bone and dentin formation
 - o Role of phosphorylation in biomineralization
- Modulation of the immune system to develop therapies for periodontal disease,
 - o Strategies to modulate the immune system to develop therapies for periodontal disease. These strategies involve local peptide or molecular agent delivery to attract T-regulatory cells or a subset of macrophages to treat periodontal disease.
- Biodegradable metals, developing load bearing bone fixation devices
 - o Resorbable metals are attractive materials because of their 1) load bearing properties due to their initial mechanical strength; 2) modulus similar to native bone; 3) biocompatibility; and 4) ability to degrade in vivo.
- Pulp tissue regeneration, develop strategies to achieve better endodontic therapies using biomaterials versus cellular approaches
- Pre-clinical testing devices for FDA approval. Our laboratory operates in a GLP-like environment. Standard Operating Procedures (SOPs) are developed for every experiment carried out in the laboratory. We have also implemented quality control procedures.

Nilesh Shah

Dr. Shah's research interests include latent class modeling, longitudinal data analysis, survival analysis, and predictive modeling.

Sayuri Smith

Dr. Smith's goal is to make a new effective dental treatment method based on basic science, especially for periodontitis. She collaborates with chemical and bioengineers to explore new materials for dental treatments. Currently, she is working on the following projects: biological analysis of bone fixation devices made from biodegradable magnesium alloys; and periodontal treatment via recruiting regulatory T-cells using drug releasing microparticles. She believes that her unique expertise in dentistry/biology and collaboration with excellent engineers will advance the current dental treatment in the near future.

Deborah Studen-Pavlovich

Dr. Studen-Pavlovich's research interests include adolescent dentistry, behavior management, and sedation for pediatric dental patients.

Kurt F. Summersgill

Dr. Summersgill's research interests currently center on outcome assessments of the oral pathology biopsy laboratory service and the clinical oral medicine practice, which includes data-mining of the electronic health record (EHR). He has worked with residents on cancer preventive agents, pathologic features of dermal fillers, digital cytology and quality assessment of digital oral pathology.

Fatima Syed-Picard

Dr. Syed-Picard's research focuses on stem cells and tissue engineering for the following applications 1) implantable devices for craniofacial therapy, 2) models of craniofacial tissue development and regeneration, and 3) models of craniofacial disease. She is working to regenerate tissues including bone, dentin-pulp complex, and nerve for therapeutic use. Furthermore, Dr. Syed-Picard uses engineered tissues as a model to study basic developmental processes including tissue patterning. Her research utilizes predominately cell-based, scaffold-free tissue engineering where cells are able to generate and organize their own 3D structure and have the capacity to self-assemble into spatially organized multi-tissue structures. Dr. Syed-Picard uses a number of engineering tools to study these

constructs including advanced microscopy and microfluidic devices.

Heather Szabo-Rogers

The Szabo-Rogers laboratory is focused on understanding the embryological development of the face and skull. Using a combination of classical embryology and cell biological techniques, the laboratory is characterizing the signaling pathways and tissue interactions that are needed for normal development of the skull and face. We will use this information to determine how craniofacial anomalies including cleft lip and palate and craniosynostosis arise during embryogenesis. Additionally, our findings can be integrated into regenerative therapies being developed within the Center for Craniofacial Regeneration (CCR).

Juan M. Taboas

Dr. Taboas works to regenerate skeletal interfacial tissues, with a focus on cartilaginous tissues. His laboratory has created several tools to control the cellular microenvironment and guide tissue growth, including photopatterned biomaterial scaffolds, controlled drug delivery, microfluidic bioreactors, and real-time microscopy-based analysis of cell-material interactions. The laboratory's biomaterial and drug delivery technologies are funded for treatment of skeletal and craniofacial injuries and diseases.

Antonia Teruel

Dr. Teruel's current research interests are focused on the field of orofacial pain. She is interested in understanding the clinical characteristics and management of chronic orofacial conditions, such as temporomandibular disorders, chronic trigeminal neuropathy and trigeminal neuralgia. She currently is pursuing pain education research, particularly, how oral health care professionals learn about chronic orofacial pain and its treatment. Also, she is interested in improving the survivorship care of patients who have received treatment for head and neck cancer.

Konstantinos Verdellis

Dr. Verdellis's research interests include mineral and matrix changes in the dentin and enamel of developing teeth and the function of SIBLING proteins in the dentin, enamel and bone mineralization. For these studies he also has focused on the use of spectroscopy, Fourier Transform Infrared and Raman, imaging coupled with microcomputed tomography and histology. His research also has focused on the use of microcomputed tomography for analysis of bones and teeth morphometry and densitometry, as well as anatomically- and clinically-oriented studies in endodontics. He currently serves as the director for the microcomputed tomography core at the School of Dental Medicine and the scientific consultant at the microCT core of the Allegheny General Hospital Cardiovascular Institute.

Alexandre R. Vieira

Dr. Vieira's research interests include two main lines of investigations: 1) individual susceptibility to craniofacial, oral and dental diseases and conditions; and 2) the impact of overall health issues on oral health. The laboratory currently is developing projects on strategies to analyze genomics and oral microbiome data in combination with comprehensive clinical descriptions; the reasons why individuals born with clefts and/or dental anomalies are more susceptible to cancer later in life; and the impact of genetics on painful responses and resistance to certain drug treatments. His repository of clinical data linked to biological samples, the Dental Registry and DNA Repository, has allowed the development of investigations on a variety of oral health outcomes.

Christine Wankiiri-Hale

Dr. Wankiiri-Hale serves as the Associate Dean for Student Affairs at the University of Pittsburgh School of Dental Medicine. Her current research interests include evidence-based practice in dental education, research related to academic career paths in dental medicine, enhancing diversity in dental schools, and dental school admissions-related research. She is a member of several professional organizations, including ADEA, ADA, PDA and NDA, and she has presented nationally on her interests.

Seth Weinberg

The goal of Dr. Weinberg's research program is to leverage advanced 3D imaging, morphometrics, and genomics tools to better understand the biological determinants of quantitative craniofacial traits (e.g. cranial size and shape) and congenital anomalies that affect the head and face (e.g. cleft palate).

Robert J. Weyant

Dr. Weyant studies caries with an emphasis on early childhood caries. His other research interests include health disparities, social epidemiology, evidence-based practice and implementation science.

Samer H. Zaky

Dr. Zaky's research interest focuses on: (1) Osteoid-like substrate for bone engineering: While the selection criteria for bone engineering scaffolds are based chiefly on their relative mechanical comparability to mature bone, the Center for Craniofacial Regeneration (CCR) is challenging this preconception by studying and demonstrating that scaffolds with low stiffness would allow a load-transducing milieu in which osteogenesis, matrix deposition, and eventual bone maturation can take place. Such "soft" environment is considered to be mechanically closer to bone marrow and osteoid tissues as a common origin from which cortical as well as trabecular types of bone mature, each with its distinct mechanical properties. Dr. Zaky is investigating the molecular events and biomechanical cues that lead to progenitor/stem cell differentiation for osteogenesis and bone maturation on a soft substrate. His research would shed light on the molecular mechanisms involved in bone tissue development and would identify the best biomimetic approach to recapitulate its development. (2) Regenerative endodontics: It is of global consensus that the best replacement for dental pulp tissue in the root canal system is a genuinely cellularized, vascularized, and innervated pulp tissue. The regenerated tissue would create a biological obturation of the pulp space providing a host response to future bacterial invasion while permitting surrounding mineralized tissues the ability to maintain its normal physiological state. The CCR approach to dental pulp regeneration is by employing extracellular matrix as a scaffold to support cell homing from the periapical tissue to the pulp space.

KEYNOTE SPEAKER



Dr. Ken Hargreaves received his DDS from Georgetown University, his PhD in physiology from the Uniformed Services University of the Health Sciences in Bethesda, MD, and his certificate in Endodontics from the University of Minnesota. Ken spent 5 years at the Pain Clinic of the NIDCR and 7 years as an associate professor of Endodontics and Pharmacology at the University of Minnesota. He joined the University of Texas Health Science Center at San Antonio in 1997, as professor and Chair of the Department of Endodontics and is cross-appointed as professor in the Departments of Pharmacology, Physiology and Surgery in the Medical School. He maintains a private practice limited to endodontics and is a **Diplomate of the American Board of Endodontists**. Ken has received an **NIH MERIT Award** for research, two **IADR Distinguished Scientist Awards** and the **Louis I. Grossman Award** from the AAE. He has published more than 190 articles and, with Harold Goodis and Frank Tay, co-edited the 2nd edition Seltzer and Bender's Dental Pulp, and, with Lou Berman, co-edited the 11th edition of Cohen's Pathways of the Pulp. Ken also serves as editor of the *Journal of Endodontics*.

Kenneth Hargreaves DDS PhD

Professor and Chair of the
Department of Endodontics at
University of Texas in San Antonio

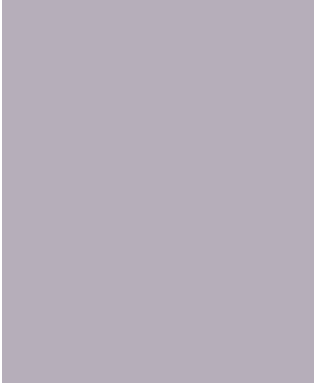


IRON IN THE FIRE: THE ROLE OF OXIDIZED LIPIDS IN PAIN CONDITIONS

Our country faces an epidemic of opioid and substance use disorders. One approach to address this problem is to develop non-opioid analgesics. The most common pain disorders treated by dentists are inflammatory in nature. Tissue injury leads to the local release of many inflammatory mediators, including oxidized linoleic acid metabolites (OLAMs). The OLAMs activate the so-called

“capsaicin receptor”, TRPV1, contributing to the development of inflammatory pain. Here, we will review the discovery of the OLAMs, their actions in activating TRPV1, and their role in inflammatory dental pain, as well as pain due to burns and other injuries. Discovery of these endogenous mediators has led to the development of a novel class of non-opioid analgesic drugs that treat pain at the source.

PRESENTERS



Presentation Title Here

Synopsis here

Name **Needed** DMD, PHD
Rank, Pitt Dental Medicine

Content yet to be delivered

A Chorioallantoic Culture Model to Evaluate Pulp Regeneration

Root canal therapy is a common dental procedure to treat carious teeth, with over 15 million procedures per year in the USA. The procedure comprises decay removal, root canal shaping, sterilization, and void filling with an inert material. Subsequently, the chamber is sealed and the crown restored. The therapy leaves a dead but otherwise mechanically functional tooth. Unfortunately, approximately 15%-30% will become re-infected or fail. Re-treatment is more costly and prone to failure. Hence, practitioners and patients opt for tooth extraction and dentures or implants. A living tooth would be able to sense temperature, injury, and infection, and thereby protect the tooth from damage and fight infection. Revascularization is a clinical method to regenerate the pulp, the living tissue, within a tooth. However, it is only successful in children because their teeth are still growing. Clinicians and scientists are developing numerous approaches to regenerate pulp, employing combinations of cells, drugs, and biomaterials. To date, no therapeutic method or commercial product exists to revitalize root canal treated teeth in adults.

We are developing a cell-free pulp regeneration device for root canal therapy in adults (Vital-Dent) that can be used without special training or facilities by practitioners in their clinics. Cell-free therapies require recruitment of cells and neurovascular tissue into the tooth to rebuild tissue, such as stem cells from the periodontal ligament that surrounds the tooth. In this work, I developed a porous collagen sponge scaffold to act as a scaffold for pulp regeneration using porogen leaching

and thermal denaturation for fabrication. The sponge mechanical and physical properties were measured, and toxicity to cells was evaluated. The sponges were then tested in a chorioallantoic membrane (CAM) model for their cell migration and blood vessel growth potential. Two sponge types were tested: 1) sponges soaked with drugs that promote cell migration, and blood vessel and nerve growth; and 2), sponges soaked in saline without drugs. These were inserted into the center of human tooth slices, placed on the CAM of 7 day old chicks, and cultured for 7 days.

The sponges had appropriate mechanical properties for their intended use, with a dry dynamic modulus of 26 GPa and wet dynamic modulus of 10.5 kPa measured in unconfined compression. Over 75% of their pores were 400 μm or greater, with high interconnectivity measured using mercury porosimetry. The CAM model showed that cells migrated through the entire height of the sponges in 7 days, and that chemotactic agents enhanced the migration.

In conclusion, our scaffolds were found to promote cell infiltration and migration, and have sufficient mechanical properties to replace conventional root canal fillers. Vital-Dent development has continued, testing new drugs and materials, including hydrogel and combination hydrogel+sponge scaffolds that further enhance cell migration and angiogenesis. Experiments are underway that will evaluate living pulp-like tissue formation in root canals of treated teeth in animals.



Patrick E. **Donnelly** PhD
DMD Student Class of 2021, Pitt Dental Medicine



Yingci **Liu** DMD
Resident, Oral and Maxillofacial Pathology,
Pitt Dental Medicine

A retrospective analysis of clinicopathological factors associated with recurrence of early stage oral cancer

Oral squamous cell carcinoma (OSCC) is a life-threatening disease that can cause significant morbidity and mortality. OSCC recurrence occurs frequently, with the rates of recurrence varying between 12% and 40% depending on tumor stage. To date, little is known about which specific clinicopathologic factors are associated with increased risk of local recurrence in patients with early stage OSCC. A better understanding of the risk factors associated with recurrence will aid in improving follow-up protocols for oral cancer patients.

To address this question, we conducted a retrospective analysis of patient record data collected over the 9-year period spanning 2003 to 2012. We retrieved 50 cases of T1N0 stage OSCC, with 17 cases having experienced local recurrence within 5 years from the date of initial treatment ("recurrence group"), and 33 cases having experienced no recurrence ("control group"). Negative surgical margins were confirmed on all cases. Relevant clinicopathologic data included sex, age, oral site, history of dysplasia, and surgical treatment modality (excision +/- neck dissection).

We found that a significant portion of the tumors (17/50; 33%) experienced loco-regional recurrence. The vast majority (34/50; 68%) were classified as well-differentiated tumors. The lateral tongue was the most prevalent site (26/50; 52%) of the index lesion, but displayed the lowest rate of recurrence (13/26; 23.8%). The average age of the recurrence group was 64.4 years, while the average age of the control group was 62.4 years. Importantly, a higher risk of recurrence was found to be associated with a previous history of dysplasia (OR 16.3, $p < 0.05$) and cancer of a non-tongue site (OR 7.9). In addition, recurrence was noted to be similar in both genders as well as in both surgical treatment modalities.

As this research is ongoing, it would be premature to draw definitive conclusions at this time. Our present data, suggest that a history of dysplasia may be associated with a higher risk of recurrence while a lower rate of recurrence is observed with cancer of the tongue. Insofar as these findings generalize to other patients with OSCC, dental professionals hold a unique position in their proficiency of oral lesions and ability to follow up with patients with dysplasia at frequent intervals.

Measuring Microscopic Structures of Enamel Gives Insight on Caries Experience

The hierarchical structure of enamel gives insight on the properties of enamel and can influence the strength of enamel and ultimately caries experience. Presently, caries experience is measured using the DMFT/DMFS (dmft/dmfs) or ICDAS scores, but by analyzing the structure of enamel, a new measurement can be utilized to evaluate susceptibility to caries. The purpose of this study was to test the hypothesis that number of prisms and interprisms (particles) in enamel, density, and average gap distance between prisms and interprisms influence caries experience. SEM images of enamel from primary teeth were used to measure number of particles, density and gap distances between particles and the measurements were tested to verify a genetic association with variants of selected genes and correlations with caries experience and enamel microhardness.

Genetic associations were found between variants of genes including ameloblastin, amelogenin, enamelin, tuftelin, tuftelin interactive protein 11, beta defensin 1, and matrix metalloproteinase 20 and enamel structure (number of particles, density, gap distance). Significant correlations were found between caries experience and microhardness and enamel structure. In conclusion, our data support that genetic variation may impact enamel formation, and therefore influence susceptibility to dental decay and future caries experience. The approach presented here of evaluating enamel structure that may impact caries experience allows for hypothesizing that that identification of individuals at higher risk for dental caries and implementation of personalized preventative treatments may one day become a reality.



Ariana Kelly
DMD Student Class of 2021, Pitt Dental Medicine

Opioids in Dentistry: Attitudes and Beliefs of Dental Faculty

Objectives: Dentists are the second highest prescribers of immediate-release opioids in the United States. Yet, little is known of their attitudes and beliefs regarding the use of opioids in dentistry. Awareness of such attitudes and beliefs can assist in the development of programs aimed at reducing opioid abuse and misuse. The aims of this qualitative study are to determine the beliefs and opinions of clinical faculty at one U.S. dental school on the use of opioids in dentistry and to determine the feasibility of creating an opioid-free dental emergency clinic.

Although dentists are the second highest prescribers of immediate release opioids in the U.S., little is known about their attitudes and beliefs regarding the use of opioids in dentistry.

Methods. This study was approved for exempt status by our Institutional Review Board. Clinical faculty (DDS/DMD degree) were recruited via posted announcements and e-mails. Four one-hour long focus group sessions were conducted. Audio recordings of each focus group were transcribed verbatim and reviewed to identify recurrent themes.

A code book was developed and the data were analyzed and coded using QSR Nvivo10 software.

Results: A total of 27 faculty participated in the study (11 females and 16 males). Participants included general practitioners (n=13), surgical specialists (n=8), and non-surgical specialists (n=6). We found strong opposition to implementation of an opioid-free emergency clinic across all 4 focus groups. Several participants indicated disbelief that dentistry might play a significant role in the opioid crisis. Barriers and possible solutions related to controlling opioid abuse and misuse were also identified. Most of the solutions described by participants centered on patient and provider education.

Conclusion: Qualitative research is an effective way to determine attitudes that could impact the feasibility of an intervention. Our study revealed general resistance amongst clinical dental faculty to creation of an opioid-free emergency clinic. Alternative approaches should therefore be considered.



Thomas J. Robbins
DMD Student Class of 2020, Pitt Dental Medicine

POSTER SESSIONS

Dean's Scholars Prenatal Androgen Exposure and Tooth Development: Is There a Connection?

A. Bertot, M.K. Lee, J. Maurer, K. Neiswanger, M.L. Marazita, S.M. Weinberg

Objectives Prenatal androgens have been reported influence the development of craniofacial structures. While numerous genetic and environmental factors are known to affect dental development, the influence of such hormones is unknown. In this project we test whether 2nd:4th digit ratio (a proxy measure for prenatal androgen exposure level) is related to either the timing of first tooth appearance or the total number of teeth present in young children.

Methods A sample of 57 boys and girls had their hands scanned and digits measured at 2, 3, and 4 years of age. Digit ratios were then calculated and regression was used to investigate the relationship with dental traits.

Results In progress at the time of abstract submission

A Chorioallantoic Culture Model to Evaluate Pulp Regeneration Therapies

P.E. Donnelly, J. Chen, T. Swenson, R. Hasselbach, H.L. Ray, J.M. Taboas

Objectives Root canal therapy (RCT) replaces dental pulp tissue with an inert filler, rendering the tooth mechanically functional but non-vital. Acellular regenerative therapies require recruitment of cells and neurovascular tissue into the tooth canals. We have developed a chorioallantoic membrane (CAM) model to evaluate regenerative therapies and develop a potential acellular scaffold therapy that recruits vasculature and periodontal ligament stem cells (PDLSCs).

Methods Gelatin sponges were fabricated and mechanical properties were evaluated in unconfined compression. To simulate RCT, sponges were inserted into silicone rings and sealed with mineral trioxide aggregate on the top side. These were placed on seven-day-old chick CAMs (vasculature source). A full factorial design was used to evaluate the effects of a chemotactic agent ($\pm C$) and PDLSCs ($\pm P$) on cell and vascular infiltration. A human PDLSC pellet was placed between the constructs and CAM for +P groups. Sponges were

doped with medium with or without C. After seven days, constructs were harvested and stained with hematoxylin and eosin.

Results Gelatin sponges contained interconnected pores (~375 μm width). The sponges had a dynamic compressive modulus of 29 ± 3 kPa. The scaffolds were found to be cytocompatible, and supported cell adhesion and angiogenesis near the CAM.

Conclusion These scaffolds can promote cellular infiltration, and have sufficient mechanical properties to replace conventional fillers. Subsequent work will investigate vital pulp-like tissue formation in vivo. Due to infiltration of CAM fibroblasts, species-specific staining and longer time-points will be used to evaluate chemotactic effects on PDLSC migration.

Formation of Organized Periodontal Tissues Using Scaffold-Free Tissue Engineering

K. Frey, K. Rothermund, F.N. Syed-Picard

Objectives A major challenge in regenerating periodontal tissues is emulating its complex structure containing both mineralized tissues and ligament. The goal of this study was to determine if a multi-tissue construct resembling periodontium could be formed from human periodontal ligament stem/progenitor cells (PDLs) using scaffold-free tissue engineering. Scaffold-free tissue engineering allows cells to generate and organize a 3D structure without exogenous scaffold material. Previously, scaffold-free tissue engineering has facilitated the formation of spatially organized multi-tissue constructs. Here we hypothesized that scaffold-free tissues engineered from PDLs would result in a multi-tissue construct containing multiple organized tissues of the periodontium.

Methods Scaffold-free 3D tissues were engineered from human PDLs isolated from human third molars. PDLs were cultured in osteogenic differentiation media. After the cells became confluent, they contracted their tissue monolayer around two constraint points and formed a scaffold-free cylindrical tissue construct. The resulting constructs were sectioned and histologically characterized using hematoxylin and eosin

(H&E) staining, alizarin red staining to detect mineralization, and immunostaining against bone sialoprotein (BSP) as a marker of osteogenic cell differentiation and scleraxis as a marker of ligament formation.

Results H&E staining showed that the constructs formed from PDLs were solid and cellular. Positive alizarin red staining and the expression of BSP was localized to the center of the construct indicating the formation of mineralized tissue. Strong scleraxis expression was detected on the periphery of the construct demonstrating formation of ligament.

Conclusion Scaffold-free tissue engineering using PDLs resulted in spatially organized multi-tissue constructs with a mineralized bone/cementum core and a periodontal ligament periphery. These results are significant because the generated constructs can be used as a regenerative therapy to treat periodontal disease or serve as a functional model to study mechanisms of tissue patterning in an engineered tissue.

Evidence-Based Practice: Awareness and Application of Radiographic Selection Criteria

A.J. Herr, E.A. Bilodeau, A. Potluri

Objectives The Food and Drug Administration (FDA) has published guidelines for patient selection for prescribing dental radiographs. The objective of this study was to assess whether the dental faculty and students were aware of the FDA guidelines, their adherence to these guidelines, and their understanding of the principles of evidence-based dentistry (EBD). We hypothesized the faculty, as well as the students, would be aware of the guidelines and be aware of the term EBD.

Methods A survey on the prescribing practices of dental radiographs was developed from the FDA guidelines at the University of Pittsburgh School of Dental Medicine. The survey was sent to dental faculty and students. The participants were grouped into the categories of dental educators (DE), private practitioners (PP), dental educators/private practitioners (DE/PP), dental residents (DR), and 3rd and 4th year dental students (DS).

	DE	PP	DE/PP	DR	3rd Year DS	4th Year DS
Participants responded they aware of the FDA guidelines and correctly identified the appropriate guideline in 10 scenarios	36%	42%	35%	40%	51%	44%
Responded knew EBD Meaning	100%	100%	100%	100%	100%	100%
Identified Core Principles EBD Correctly	67%	17%	18%	40%	53%	40%

Table 1: Participant Awareness of FDA Guidelines

Results 67 participants completed the survey. Table 1, row 1 shows the average of the percentages of the participants who stated they were aware of the FDA guidelines and correctly identified the appropriate guideline in 10 different scenarios. Row 2 shows the percentage of participants who stated they knew what the term evidence-based dentistry meant, and row 3 shows the percentage of participants who correctly picked the core principles of evidence-based dentistry. (see Table 1, above)

Conclusion Our data reveals that most participants were not aware of the FDA published guidelines on radiographic selection criteria (range 36-51%). Furthermore, while 100% of those surveyed stated they knew what the term EBD meant, only 43% of all respondents correctly identified the core principles (range: 17% in private practitioners-67% in dental educators). Full-time dental educators performed the best on this with 67% correctly identifying the core principles of EBD.

Familiarity and Perception of Molar Incisor Hypomineralization (MIH)

J. Huyser, A. Modesto-Vieira

Objectives The purpose of this study was to assess the familiarization and perceptions of oral healthcare providers at the University of Pittsburgh School of Dental Medicine (UPSDM) regarding the knowledge, prevalence, diagnosis, treatment confidence, and etiology factors of Molar Incisor Hypomineralization (MIH).

Methods Surveys were distributed to 514 oral healthcare providers at the UPSDM. 243 surveys were distributed to licensed oral healthcare

providers including dental school faculty, hygiene faculty, and dental residents. 271 surveys were distributed to 2nd, 3rd, and 4th year dental students, and 2nd year hygiene students. All the participants were asked to fill out a 12-question survey via online or paper distribution. The MIH survey investigated general perception and knowledge, clinical experience, diagnosis, treatment confidence, views on etiology, and asked for any general comments.

Results A total of 51 (20.99%) licensed oral healthcare providers and 60 (22.14%) student oral healthcare providers completed the survey. The majority of providers who responded had 5 years or less of dental experience (63.96%) while the second largest group of respondents had 21 or more years (22.52%). A majority (53.09%) did not encounter MIH in practice and most (80.77%) observed 0-5% of their patients as having MIH. Despite the low number of patients seen with MIH, a majority (71.82%) of providers knew some or all the clinical features of MIH. Most respondents were aware that MIH differed from other enamel defects (62.16%). Most providers were unconfident or very unconfident with diagnosing MIH (68.22%) and even more were unconfident or very unconfident treating MIH (76.64%). The three etiological factors chosen most by the providers were genetic factors (34.39%), environmental contaminants (21.34%), and medical conditions (20.55%).

Conclusions Oral healthcare providers at the University of Pittsburgh School of Dental Medicine have a basic knowledge of MIH; however, most of these providers are not confident in the diagnosis or treatment of the disorder. Many reasons for the apparent lack of confidence may be the low occurrence seen in the patient population as well

as the majority of providers in this survey having 5 years or less of dental experience.

Measuring Microscopic Structures of Enamel Gives Insight on Caries Experience

A. Kelly, A.R. Vieira

Objectives The hierarchical structure of enamel gives insight on the properties of enamel and can influence the strength of enamel and ultimately caries experience. Presently, caries experience is measured using the decayed, missing, filled teeth/decayed, missing, filled surface (DMFT/DMFS for permanent teeth; dmft/dmfs for primary teeth) or international caries detection and assessment system (ICDAS) scores, but by analyzing the structure of enamel, a new measurement can be utilized to evaluate susceptibility to caries. The purpose of this study was to test the hypothesis that number of prisms and interprisms (particles) in enamel, density, and average gap distance between the particles influence caries experience.

Methods Scanning electron microscopy (SEM) images of enamel from primary molars were obtained and used to measure the number of particles, density and gap distances between particles and the measurements were tested to verify a genetic association with variants of selected genes and correlations with caries experience and enamel microhardness.

Results Genetic associations were found between variants of genes including ameloblastin, amelogenin, enamelin, tuftelin, tuftelin interactive protein 11, beta defensin 1, and matrix metalloproteinase 20 and enamel structure. Significant correlations (r values $\geq \pm 0.45$) were found between caries experience and microhardness and enamel structure. Further individual analysis showed that 94.25% of individuals with the minor allele and statistically significant associations to our phenotypes match our hypothesis regarding number of particles, density, and gap distance and caries experience.

Conclusion Our data support that genetic variation may impact enamel formation, and therefore influence susceptibility to dental decay and future

caries experience. The approach presented here of evaluating enamel structure that may impact caries experience allows for hypothesizing that the identification of individuals at higher risk for dental caries and implementation of personalized preventative treatments may one day become a reality.

Assessment of Unique Gamification Strategies Across Multiple Higher Education Disciplines

D.A. Koval, D. Babichenko, L.B. Grieve, E.A. Bilodeau

Objectives The purpose of this study is to determine whether introduction of gamification strategies into course curricula positively impacts students' perception of that course, and whether it enhances their performance, as measured by improvement in final grades. Gamification is the utilization of game-like strategies and elements in a non-game setting. Its increasing incorporation into educational disciplines is theorized to improve student engagement and motivation, potentially resulting in better student learning outcomes.

Methods After obtaining IRB approval (PRO17030180), we examined class performance and anonymous end-of-semester surveys prior to and following implementation of distinct gamification strategies across courses from the University of Pittsburgh School of Computing and Information, School of Pharmacy, and School of Dental Medicine.

Sentiment analysis was first done by the authors for each student comment on a five point scale, where "0" was a strictly neutral comment, "-1" or "1" corresponded to a negative and positive comment respectively, and "-2" or "2" corresponded to the worst or best possible comments given, where students were most passionate in their reflections of the preceding semester. Means and standard deviations were used to determine where inter-rater reliability differed by more than a single unit on this five-point scale, and these comments that were flagged to be re-evaluated by reviews a second time in cohort. Automated sentiment analysis, a set of machine learning techniques for extracting overall emotional direction of a natural language phrase or

sentence, also scored the student feedback. Both a Python natural language processing (NLP) library called TextBlob and Semantria, a popular and well known sentiment NLP tool suite created by Lexalytics were utilized.

Results Automated sentiment analysis correlated with the authors manual ratings. Analysis of trends in final course grades, statistical analysis suggests that gamification tendencies benefit students learning. Additional analysis is pending.

Assessment of a Student Peer Tutoring Program in Dental Education

C. Maloney, C.R. Wankiiri-Hale, N. Seger, Z. Horvath

Objectives The University of Pittsburgh School of Dental Medicine incorporates a voluntary student peer tutoring program as one resource available to its pre-doctoral students. It specifically utilizes near-peer tutoring in both didactic and clinical courses in order to provide additional help to students who may be struggling. The goal of this research project is to conduct an initial program assessment, in terms of the benefits to both the tutors and the tutees.

Methods Data were collected using surveys from the tutors and the tutees, as well as reflective journals written by the tutors. Tutors were surveyed before their semester of tutoring and after its completion. Tutees were surveyed only after completion of the course. Responses to the surveys were analyzed using quantitative analysis, and content analysis was completed for open ended short responses. Reflective journals were analyzed using content analysis.

Results The data provided information on successful elements of the program and logistical problems to be addressed. It gave insight into what tutors hope to gain from the experience and what they were concerned about. Tutees commented on the effectiveness of their tutor and the extent to which tutoring helped their performance in the class.

Conclusion The assessment of the student peer tutoring program showed overall success, providing benefits not only to the tutees, but also to the tutors. In addition to academic credit, the tutors benefit from reviewing the course materials and practicing

skills that will help them in their future careers. Based on the initial program assessment, the understanding of the tutees has improved and the tutors gain a valuable experience.

Classical Autofluorescence Reduction Approaches are Ineffective for Human Enamel Tufts

M. Mehta, X. Yang, E. Beniash

Objective Non-specific fluorescence from demineralized enamel matrix can significantly compromise the immunofluorescence studies and lead to false positives. The goal of this study was to assess the effectiveness of autofluorescence reduction methods in mature human enamel matrix and forming dental tissues under different conditions.

Methods We compared two methods of background fluorescence elimination, Sodium borohydride (SBH) and Sudan Black (SBB) treatments on the sections of forming mouse incisor and human enamel tufts. Human enamel tufts were collected from demineralized healthy teeth, extracted for clinical reasons and embedded in paraffin. Mandibles were collected from 10 days old mice, demineralized and embedded in paraffin. Ten micron thick sections of both samples were treated with SBH and SBB according to standard protocols. Non-treated samples were used as controls. The samples were imaged in the epifluorescence mode and the fluorescence intensities were measured.

Results We demonstrated that SBB is far superior to SBH in reducing the background fluorescence in mouse forming dental tissues, including the forming enamel matrix, but that neither SBB nor SBH treatments were effective in reducing background fluorescence in mature human enamel tufts.

Conclusions The differences observed in the effects of the autofluorescence reduction methods might reflect the differences in the composition and amount of crosslinks between forming and mature enamel matrix. Further studies will be needed to optimize and standardize immunochemical procedures for the mature enamel matrix.

Reflective Journaling in Predoctoral Periodontology Education

E. Schwoegl, M. Rodgers, S. Kumar

Objectives The objective of this study was to improve future learning experiences in clinical education. The study examined dental students' ability to compose reflective journals during the periodontics clinic rotations.

Methods Each of 76 second-year dental students at the University of Pittsburgh School of Dental Medicine completed two reflective journaling exercises during their initial periodontics clinic rotations. They were provided a writing template with guiding, thought-provoking questions. A total of 144 journals were analyzed independently by two calibrated evaluators. Journals were analyzed using a rubric developed by Kember, which condensed Mezirow's seven levels of reflection into four categories: Habitual Action (HA), Understanding (U), Reflection (R), and Critical Reflection (CR). Individual, complete thoughts were identified in the students' journals, and each complete thought was then coded into one of Kember's reflection categories. Additionally, each journal's word count was calculated to explore any possible correlation between journal length and reflections (R and CR).

Results On average, 9.6 complete thoughts were identified in each journal, of which 16.1% contained non-reflections (0.2% HA, 15.9% U) and 83.9% contained reflections (73.8% R, 10.1% CR). The proportion of journals containing R dropped slightly between the first and second entries (85.2% vs. 82.7%), whereas the proportion containing CR increased from the first to the second entries (11.3% vs. 9.3%). The average word count was 527 words (204-1107) with no correlation between the word count and reflections.

Conclusion A high degree of reflection was observed in the second-year students' journals in periodontics clinic in a relatively short journal. Future research can look into whether the quality of students' journals changes as they progress through dental school and if there is any correlation between reflective journaling and improved clinical performance.

Educating Dentists on Treating Patients Under the Influence of Cannabis

R. Stephens, S.E. Grafton, K. Ryan Eddens

Objectives The goals of this study were to gather demographics and health statuses of a small patient sample of cannabis users at the University of Pittsburgh School of Dental Medicine and to use this information to understand the prevalence of cannabis use for dental anxiety/pain, the frequency of different methods of use in clinic patients, and how these patients should be treated.

Methods A survey was completed voluntarily by 79 patients (49 males and 30 females, aged 17-77) who reported cannabis use on a standard medical history form to gather information about their using habits. Demographic and health data were collected via axiUm. Fisher tests were performed to analyze correlations between sex, method of use, and dental anxiety/pain.

Results No statistical significance was found between sex and dental anxiety/pain ($P = 0.168$) and method of use and dental anxiety ($P = 0.170$). However, there was a larger percentage of men who reported using cannabis for dental anxiety/pain than women. Additionally, it appeared to be more common for joints and blunts to be used for dental anxiety/pain than other methods of use.

Conclusions Data from this study can be utilized by dentists to become more aware of cannabis use in their patients, as well as different methods of and reasons for use. It is important to note the differences in cognitive effects between methods of use and how more potent forms of cannabis could impair the ability for a patient to give informed consent. The implementation of mini-mental state examinations for these patients could be utilized to assess cognitive function prior to obtaining consent. Additionally, with the rise of medicinal marijuana sites in Pennsylvania, it is likely that cannabis use will be more widely reported. For these reasons, dentists must be knowledgeable on the subject and prepared to properly treat patients who report cannabis use.

An Expression Toolbox for the Retina, Muscles and Sclera of Fetal Mouse Eyes

Y. Wan, C. White, M.B. Rogers, H.L. Szabo-Rogers

Abstract Abnormal eye development is often associated with craniofacial anomalies. As an organ, the eye can be useful in identifying and understanding underlying craniofacial anomalies. Optic development involves sequential interactions between several different tissue types including the overlying ectoderm, adjacent mesoderm and neural crest mesenchyme and the neuroectoderm. In an ongoing expression screen in the lab, we identified several genes that are expressed in unique cell types in the optic region. Here, we describe the complimentary, coordinated patterns of expression of *Casq2*, *PENK*, *TFAP2 β* , *Zic1* and *Zic3* during mouse eye development. *Casq2* is a binding protein and *PENK* is a neurotransmitter. Neither *Casq2* nor *PENK* have a reported role in craniofacial development. *TFAP2 β* , *Zic1* and *Zic3* are transcription factors that are required for brain and craniofacial development. We found that these five genes are expressed in the major tissue types in the eye including the muscles, nerves, cornea and sclera. *PENK* expression is found in the sclera and perichondrium. The extra ocular muscles at E12.5 and E15.5 express *Casq2*. At those time points, the entire neural retina expresses *Zic1*. Between E12.5 and E15.5, *Zic3* is expressed in the optic disk and ciliary body. In contrast, the expression of *TFAP2 β* expanded from corneal epithelium to the outer layer of the neural retina between E12.5 to E15.5. The expression patterns of these five genes warrant further study to determine their functional role in eye morphogenesis.



Scaffold-free Dental Pulp Cell Sheets to Enhance Peripheral Nerve Regeneration

M. Ahmed, K. Rothermund, M. Dailey, T. Calabrese, F.N. Syed-Picard

Objectives Peripheral nerve damage is a commonly encountered clinical problem caused by trauma, disease, or surgical injury. The current gold standard treatment utilizes autologous nerve grafts; however, this requires a prolonged repair time and full functional recovery is not achieved. Neurotrophic factors (NTF) are proteins known to enhance axon regeneration and growth. Dental pulp tissue contains a population of stem/progenitor cells (DPC) that secrete NTFs, a characteristic likely due to their neural crest origin. Furthermore, these cells are easily accessible from autologous sources. The goal of this study was to develop and characterize scaffold-free DPC sheets as a NTF delivery system. We hypothesize that DPC sheets will express NTFs including brain-derived neurotrophic factor (BDNF), glial cell line-derived neurotrophic factors (GDNF) and neurotrophin-3 (NT-3), and will accelerate repair of damaged nerves and improve functional recovery.

Methods In this study, we fabricated scaffold-free cell sheets by culturing DPCs to super confluence with and without fibroblast growth factor 2 (FGF2). NTF gene expression of DPC sheets was assessed using qRT-PCR. DPC sheets secretome was used to culture SHSY-5Y neurons to test its effect on neurite extension in vitro.

Results DPC sheets were formed that are robust and can be easily handled. DPC sheets expressed high level of BDNF, GDNF, NT3 genes and this effect was enhanced by the addition of FGF2. DPC sheet secretome enhanced neurite extension in SHSY-5Y neurons indicating that DPC sheets have a positive functional effect on neurons.

Conclusion DPC sheets can be formed which secrete neurotrophic factors and enhance neurite extension in neurons. Scaffold-free DPC sheets show great promise as a new therapy to accelerate the regeneration of damaged peripheral nerves and improve functional recovery.

Correlation Between Arthritic Changes in the Cervical Vertebrae and TMJ

K. Babalola, A. Potluri, K. Rengasamy, A. Tadinada

Objectives The objective of this study was to retrospectively evaluate CBCT scans to study the relationship between the presence/absence of degenerative changes in the cervical vertebrae and the relationship between TMJ arthritic changes.

Methods Retrospective evaluation of 150 randomly selected CBCT scans of patients referred to The UCONN School of Dental Medicine's advanced Imaging facility was done.

The scans were evaluated using the invivo-5 software reconstruction program. Inclusion criteria were scans that had the TMJ bilaterally and at least the cervical vertebrae C-1-C3 in the field of view. The scans were scored for the presence or absence of osteoarthritis in both TMJs and their severity using Weishaupt/Pathria grading classification.

Grade1. normal facet joint space (24mmwidth); Grade2. narrowing of the facet joint space(<2mm) and/or small osteophytes, and/or mild hypertrophy of the articular process; Grade3. narrowing of the facet joint space and/or moderate osteophytes, and/or moderate hypertrophy of the articular process, and/or mild subarticular bone erosions; and Grade4. narrowing of the facet joint space and/or large osteophytes, and/or severe hypertrophy of the articular process, and/or severe subarticular bone erosions, and/or subchondral cysts.

Results Of the 150 scans analyzed, 112 (74.6%) had C-spine arthritis while 38(25.3%) did not have. 96 (64%) scans had TMJ arthritis while 54 scans (36%) did not have. 80 scans(53.3%) had both C-spine and TMJ arthritis, 32 scans (21.3%) had isolated spine arthritis, 16 (10.6%) had isolated TMJ arthritis while 38 scans (25.3%) had neither C-spine nor TMJ arthritis.

Conclusion: In this small sample size, a significant number of patients show both TMJ and cervical spine arthritis showing a correlation that must be explored further.

Sex Difference in the Numbers of Lateral Canals in Molars

S. Barna, A.R. Vieira

Objectives It is stated in the literature that the existence of bacteria within the root canal system is a leading cause of failure following endodontic treatment. There are a minimal number of studies that have evaluated the existence of lateral canals and the impact these untreated canals could have on the prognosis of treatment. Furthermore, there are limited studies that evaluate if there is a difference in the number of lateral canals between sexes. The purpose of this study was to evaluate the difference in the existence of lateral canals in molars between sexes in extracted teeth.

Methods Over a two-week period, extracted teeth were collected and separated by sex in 1:10 clorex solution. 18 teeth (8 molars and 8 premolars) were collected from females. 22 teeth (9 molars and 5 incisors) were collected from males. 24 teeth were not included because of restorations, broken roots, or were not molars. The teeth were accessed and iodine dye was placed into each canal system. The individual roots were then sectioned and the lateral canals identified.

Results Teeth included in this study were as follows: (a) Female; 1 mandibular molar, 3 third molars, and 4 maxillary molars. The number of lateral canals identified was 1, 0, and 0, respectively. (b) Male; 1 mandibular molar, 3 third molars, and 5 maxillary molars. The number of lateral canals identified was 0, 3, and 7, respectively.

Conclusions According to these results, there is a difference in the number of lateral canals in molars between sexes. This difference may explain, at least in part, distinct failure rates by sex of endodontic treatment in molars that have been reported.

Periodontal Disease and Periapical Pathology share similar Genetic Etiological Factors

M. Bezamat, H. Ouyang, A.R. Vieira

Objectives The purpose of this study was to identify associations between periodontal disease, periapical lesions and genes present in the

Mammalian target of rapamycin (mTOR) signaling, which is a central regulator for protein synthesis, and Endoplasmic Reticulum stress (ER stress), which is an essential pathway to maintain intracellular homeostasis.

Methods DNA samples extracted from saliva from 654 individuals were genotyped according to presence of periodontal disease and periapical lesions. Samples were obtained from the Dental Registry and DNA Repository project at the University of Pittsburgh. Twenty-seven polymorphisms in eight genes were selected for genotyping.

All samples were genotyped by the use of Taqman chemistry; allele frequencies were calculated and Hardy-Weinberg equilibrium confirmed. Analyses were performed comparing genotypes between affected and unaffected individuals for each phenotype, using the software PLINK with an alpha of 0.002.

Results We found association between the presence of periapical lesions and RHEB rs3753151 ($p=0.0002$), and also two SNPs in XBP1 (rs2097461, $p=0.04$; and rs2239815, $p=0.05$) and ERN1 (rs196929, $p=0.05$ OR=1.56; 95% C.I. 0.99-2.44; and rs196950, $p=0.02$; OR=1.65; 95% C.I. 1.07-2.53) showed a trend for association. For periodontal disease, we found association with two SNPs in ERN1 (rs196929 for both allele and genotype, $p=0.008$, OR=1.87; 95% C.I. 1.16-3.01 and $p=0.03$, respectively); rs196950, ($p=0.04$, OR=1.51; 95% C.I. 1.00-2.28), and for allele distribution and TSC1 rs1050700, ($p=0.04$, OR=1.59; 95% C.I. 1.00-2.53).

Conclusions Our studies show that both mTOR pathway and ER stress phenomenon are associated with conditions affecting bone and teeth. The results support that different levels of bone resorption/formation are associated with those genes, suggesting that periodontal disease and periapical lesions share similar underlying genetic etiological factors, which allows us to hypothesize that instead of individually, they should be studied in conjunction in human populations.

Molecular Profiling of Rare Odontogenic Tumors

E.A. Bilodeau, S. Chiosea, A. Berg, S. Muller, B. Purgina, R. Seethala

Background Ameloblastomas are now known to demonstrate frequent BRAF V600E or other MAPK (mitogen-activated protein kinase) pathway mutations (usually mandibular) as well as SMO mutations (usually maxillary). However, the mutational profile for atypical ameloblastomas, ameloblastic carcinomas as well as other rare odontogenic neoplasms is less characterized.

Design 19 odontogenic tumors (11 ameloblastic carcinomas (AC) from 9 patients including 1 metastasis, 4 atypical ameloblastomas (AA) from 4 patients, 2 calcifying epithelial odontogenic carcinomas (CEOT) from 2 patients, 1 odontoameloblastoma (OA), and 1 ghost cell odontogenic carcinoma (GCOC) were successfully

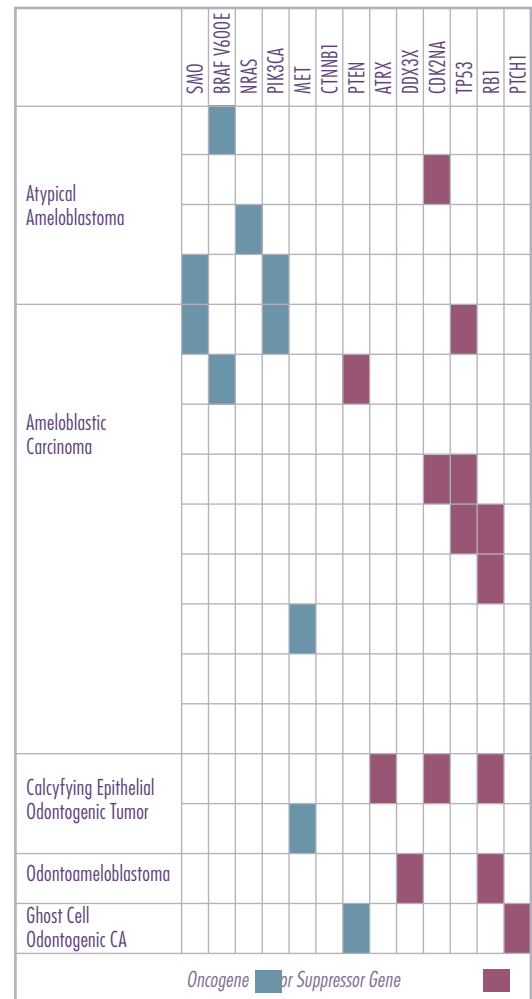


Figure 1.

tested by next generation sequencing (DNA for point mutations in 30 tumor-related genes (>1360 hot spots), copy number alterations in 24 genes, PMID: 26681766). Anatomic site was indexed and clinical follow-up was obtained. CDK2NA and RB1 abnormalities were corroborated with fluorescent in-situ hybridization (FISH) and immunohistochemistry (IHC). TP53, CTTNB1, and ATRX abnormalities were corroborated with IHC.

Results Only a small percentage of AA and AC had BRAF (p.V600E) mutations (2/13 patients, 15.4%; 1/4 AA, 1/9 AC), and 1/4 AA had a NRAS mutation (p.Q61R). SMO mutations (p.L412F, p.VV535L) were seen in 2 patients (1/9 AC and 1/4 AA) in conjunction with a PIK3CA mutation (p.C420R, p.E545K) in both cases. CDK2NA mutation (p.R144C) was present in 1/4 AA with loss in 1/9 AC and 1/2 CEOT confirmed with FISH. TP53 mutation (p.R273C n=2, p.G245C, p.P85Lfs*38) was present in 4 ACs from 3 patients. MET mutation (p.E168D, p.M35L) was present in 1 AC and 1 CEOT. RB1 loss was present in 5 cases in 4 patients (3 AC in 2 patients, 1 CEOT, 1 OA) and was confirmed with FISH and IHC. A DDX3X mutation (p.V271I) was detected in an additional 1/1 OA. 1/2 CEOT exhibited an ATRX mutation (p.I360fs) with loss confirmed via IHC. The GCOC exhibited a CTTNB1 mutation (p.S33C) with nuclear beta-catenin on IHC and a PTCH1 mutation (p.V1413P).

Conclusion The data suggests a pathogenesis for AA/AC distinct from ameloblastoma with alterations more commonly noted in PIK3CA, TP53, CDKN2A, and RB1 and a lower rate of MAPK pathway mutations. As expected GCOC demonstrates CTTNB1 mutation. Novel mutations noted include DDX3X mutation in OA. The presence of ATRX mutation in CEOT implies a role for the alternative telomerase lengthening pathway in its pathogenesis.

Degradable Magnesium Devices for Improved Dental Bone Grafting

A. Brown, P. Amin, A. Chon, K. Williams, C. Sfeir

Objectives

1. Manufacture degradable magnesium dental bone grafting devices

2. Implant devices in a canine vertical ridge augmentation model

3. Assess device degradation and bone regeneration using microCT

4. Assess biocompatibility using histological analysis

Methods Magnesium bone grafting devices were manufactured using laser cutting and CNC methods. Eight dogs were subjected to bilateral extraction of the second through fourth premolars and first molars and allowed an eight week healing period. Standardized alveolar bone defects were then created using a surgical saw and the magnesium bone grafting devices were implanted and compared to collagen and Ti/PTFE barrier membrane control devices. Following either eight or sixteen weeks, hemi-mandibles were explanted and subjected to microCT and histological assessments.

Results TBD

Conclusion TBD

Multilocular Radiolucency of the Anterior Mandible

T. Buraczewski, A. Potluri, B.J. Costello, E.A. Bilodeau

Objectives A 10-year-old boy with a large swelling in the anterior mandible and multiple loose teeth presented. A panoramic radiograph demonstrated a large well-defined, multilocular radiolucency with thin corticated borders in the anterior mandible extending between the premolars bilaterally. Fine, wispy septations were noted within the lesion, giving it a multilocular appearance. The lesion expanded the inferior border of the mandible.

Methods To determine the extent of the lesion, we prescribed a computed tomographic (CT) examination. A sagittal view (Figure 2) of the area demonstrated a multilocular lesion causing buccolingual expansion of the anterior mandible

with thinning of the buccal and lingual plates, and root resorption. Axial bone window sections (Figure 3) showed the extent of the lesion in a buccolingual direction, as well as the extent of the lesion from the left mandible to the right, crossing the midline and extending into the bilateral molar areas, which was not clearly visible on a standard panoramic radiograph. The lesion was more extensive on the right side and extended to the right buccal vestibule and posteriorly to the molar area. The lesion was 4.6 × 2.7 × 2.3 centimeters. A soft-tissue window with contrast showed the lesion had areas of density compared with the nearby soft tissues within the septations and also scattered calcifications. It also showed the extent of the expansion, thinning of the cortices, and preservation of the cortices.

Results Central giant cell granulomas (CGCGs) are benign entities of the jaw with an unknown cause. They are considered nonneoplastic; however, they can exhibit aggressive clinical behavior. The lesions are twice as common in the mandible as in the maxilla and have a predilection for the anterior mandible. Commonly, the lesion crosses the midline. It is seen more commonly in female than in male patients, with variable ratios cited in the literature, but generally, a 2:1 ratio of female to male is accepted. Historically, these have been called giant cell reparative granulomas, but there is little evidence to support the theory of a reparative cause. The lesion commonly is seen in patients between the ages of 10 and 25 years but can be seen at any age. Commonly asymptomatic when they manifest, CGCG lesions often are detected on routine radiographs. If CGCG lesions cause symptoms, they may cause pain and paresthesia. They can cause displacement of teeth, which may lead to malocclusion. If the cortical plate is perforated, they can manifest as a swelling or an ulceration. The lesions may be separated clinically into 2 categories: nonaggressive and aggressive. Most cases are nonaggressive lesions, which manifest as slow-growing, asymptomatic lesions without root resorption of teeth. Aggressive lesions are painful and rapidly enlarging, with root resorption and cortical plate perforation. Typically, aggressive lesions are larger than nonaggressive lesions and usually are seen in younger patients. Distinguishing between nonaggressive and aggressive lesions typically is based on clinical symptoms and radiographic features.

Conclusion All of the lesions listed may have similar radiographic features, with widely different recurrence rates and treatment options. We recommend incisional biopsy (especially in the case of large lesions) for an accurate diagnosis and proper treatment planning. All of the diagnoses require long-term follow-up. In the case we reported, we used corticosteroid injections to attempt to shrink the lesion, but it continued to enlarge. The second line of adjuvant therapy was interferon. Because of its adverse effect profile, interferon should be used only in select cases. The lesion in the case we presented was responsive to interferon therapy, diminishing in size, and permitting surgery to be less invasive.

Molecular and Cellular Mechanisms Underlying Cleft Palate in *Trps1*^{-/-} Mice

K.Y.A Cho, D. Monier, D. Napierala

Objectives TRPS1 gene codes for the transcriptional repressor TRPS1, which works by binding GATA sequences. Heterozygous TRPS1 mutations lead to an autosomal dominant disorder named trichorhinophalangeal syndrome (TRPS). Key features of TRPS involve hair, skeletal, dental and craniofacial abnormalities, including some cases of cleft palate. Mice with heterozygous *Trps1* mutation (*Trps1*^{+/-} mice) demonstrate hair, skeletal and high-arched palate phenotype similar to TRPS patients. Interestingly, homozygous mutant mice (*Trps1*^{-/-} mice) exhibit cleft palate. Our objectives were to delineate the role of *Trps1* during palatogenesis and identify the mechanism of cleft palate in *Trps1*^{-/-} mice.

Methods To determine the ability of *Trps1*^{-/-} palatal shelves to fuse, 24h ex vivo culture of palatal shelves from wildtype (WT) and *Trps1*^{-/-} E13.5 mice embryos was performed. Immunohistochemistry was used to delineate expression of *Trps1* in WT mice at E12.5, E13.5 and E14.5. Chondroitin sulfate proteoglycan (CSPG), Tgfb3, Twist1, and β-catenin, all of which play significant roles in palatal fusion, were analyzed by immunohistochemistry in E14.5 WT and *Trps1*^{-/-} mice.

Results The initiation of the palatal shelf fusion was observed in all cultured WT palates (n=11)

but in none of the *Trps1*^{-/-} palates (n=11). At earlier embryonic stages (E12.5 and E13.5), *Trps1* was expressed in palatal shelf epithelium and maxillary mesenchyme. *Trps1* expression was greater in posterior palatal epithelium than in anterior palate. At E14.5, *Trps1* was expressed within the palatal shelves epithelium, specifically the medial edge epithelium (MEE), and maxillary mesenchyme. CSPG, Tgfβ3, β-catenin and *Twist1* were detected at E14.5 WT MEE as well, but the expression of each protein was lost in *Trps1*^{-/-} palatal shelves.

Conclusions Our findings indicate that *Trps1* is necessary for palatal fusion and expression of other proteins important for this process. The presence of *Trps1* in maxillary mesenchyme also suggests that *Trps1* plays additional roles in palatal development in addition to fusion.

Early Diagnosis of Periodontal Disease Needs Less Treatment and Prevent Tooth Loss

P. Famili, N. Shah, N. Anzur

Objectives The aim of this study was to measure the number of teeth lost among a random sample of individuals receiving periodontal treatment and maintained for long-term follow-up at a university faculty practice.

Methods One-hundred subjects who had received periodontal treatment and had been on recall for three or six months for at least five years, up to twenty years, participated in this study. Subjects had at least twenty teeth. The same periodontist treated all patients. Treatment was scaling and root-planing for mild periodontitis, or scaling and root-planing plus surgery for moderate to advanced periodontitis; then all patients were on recall every three months or six months

Results 22 men (38.60%) had tooth loss, compared to 37 women (40.22%) who lost their teeth. This was not significant (p=0.84). The difference between patients who had scaling and root-planing versus scaling and root-planing with surgery was significant (p=0.025), but the recall interval was not significant (p=0.139). After adjusting for age, gender and recall, treatment was still statistically significant.

Conclusion This study showed early diagnosis of periodontal disease could be treated by mere scaling and root-planing, with patients losing fewer teeth than treating patients with moderate to advanced periodontal disease by required surgery. Early diagnosis of periodontal treatment needs less treatment and prevents surgery, is less painful, and saves many expenses.

Third Molar Agenesis and Craniofacial Morphology

E. Kello, Y. Zhou, A. Vieira

Objectives Previously, the relationship between 3rd molar agenesis and particular craniofacial morphology parameters has been widely studied with conflicting results. Furthermore, 3rd molar agenesis has been associated with reduced tooth size and morphology. In this study, we aim to test the null hypotheses: (1) a smaller ANB angle is not associated 3rd molar agenesis. (2) shorter palatal length is not associated with 3rd molar agenesis. Furthermore, second molar crown formation and first molar root formation complete around the time when third molar development starts, thus to investigate the potential local influence of these events on third molar initiation, we test the association between 3rd molar agenesis and average crown width of second molars, as well as length of first molar roots.

Methods We examined if the previously studied ANB angle correlated with third molar agenesis. Panoramic and profile radiographs were obtained from 40 total orthodontic patients from the University of Pittsburgh Dental Registry and DNA Repository. These were divided into two groups: (1) patients that have agenesis of at least one 3rd molar and (2) patients that do not have agenesis of any 3rd molar. Information on third molar extraction was not available so patients selected are between 10 and 17 years of age where third molars can be expected to be in the process of developing and therefore visible on radiographs. Mesiodistal crown dimensions were recorded by measuring all erupted permanent second molars. The length of the mesial-buccal root on the mandibular and maxillary first molars was measured from the root tip to the cervical line. The ANB angle is the cephalometric standard for measuring degree of prognathism. This

was calculated using the formula $SNA-SNB=ANB$. Palatal length was measured between the anterior nasal spine (ANS) and posterior nasal spine (PNS). A two-tailed t-test was used to compare each variable to 3rd molar agenesis one at a time. A linear regression model was used to quantify the relationship between both maxillary and mandibular 3rd molar agenesis and crown length, root length, palatal length and ANB angle. Results will be summarized in this presentation.

Understanding Phosphate Signaling Cascade in Mineralization

S. Khalid, D.E. Monier, D. Napierala

Abstract Phosphate (Pi) is the second most abundant mineral in human body and is an important structural and functional regulator of bone mineralization process. Hyper- and hypophosphatemia represent an increase or decrease in normal serum phosphate levels, respectively. Both conditions have been shown to effect bone mineralization and have severe clinical manifestations. However, the molecular mechanism(s) involved in Pi-induced pathologies are not well understood. Previous studies have demonstrated sodium phosphate transporter as an essential component for Pi transportation into the cells and role of ERK1/2 (member of mitogen activated protein kinases) in regulation of Pi induced osteogenic gene expression and mineralization. In this study, we have investigated the molecular cascade involved in Pi induced ERK activity and mineralization by targeting the potential bone regulatory genes that are scoped out in our global gene analysis. Using 171A11 odontoblast cells as a bone mineralization model, we have studied the possible involvement of these genes in Pi induced ERK activity and mineralization. We employed shRNA mediated loss and over-expression vectors mediated gain of gene expression to study the role of our genes of interest in Pi-induced mineralization. ERK activity was analyzed by western blotting and regulation of classical Pi responsive osteogenic genes were examined by quantitative RT-PCR. We further validated our findings using other osteogenic cell lines like MLO-A5 and MOVAS. Our results demonstrated the potential signaling pathway that is involved in Pi signaling in odontoblast.

Hand vs Rotary File Glide Path Creation in Calcified Canals: A Microcomputed Tomography Pilot Study

M. Korch, H. Sahib, H.L. Ray, A. Sadkin, K.J. Shields, R. Chong, O.A. Peters, P.S. Salmon, K. Verdelis

Objectives To compare the preservation of original canal anatomy when stainless steel hand and Ni-Ti rotary glide path files are used to create a glide path in calcified root canals

Methods 10 roots of anterior decoronated teeth with calcified canals, selected after preliminary digital radiography and microCT scans from a pool of 150 to have matching canal anatomy and calcification pattern, were microCT imaged (10 micron voxel resolution, 60 Kvp, set A). A glide path was created in the canals using either hand files (sizes 15-20 n=5) or Path files (Dentsply, sizes 1-3, n=5) after an initial preparation with 08-10 size hand files and roots were imaged again (set B). Set A and B volumes for every root were digitally registered and transportation of the canal at 1, 5 and 9mm from the apex was measured.

Results Transportation was not significantly different for any of the locations examined between the hand and Path file group, respectively. The transportation on an average was higher in the hand file vs. the Path file group (49 ± 55 vs. 0 ± 0 microns, 65 ± 29 vs. 13 ± 33 microns and 194 ± 109 vs. 48 ± 33 microns, for 1, 5, and 9mm, respectively).

Conclusion Non-destructive 3D analysis of canal transportation during glide path creation by stainless steel hand and Ni-Ti rotary glide path files can describe the canal transportation involved in calcified canal cases in a quantitative manner. No significant differences in canal transportation were detected between the glide path creation methods examined and the number of specimens used in the study.

The effect of endodontic access on the compressive strength at fracture of extracted maxillary molars

M. Lentz, S. Khaliq, M. Madoori, I. No, A. Maslia, S. Jabir, A. Almarza, H. Ray

Objectives The purpose of this study was to compare the fracture resistance of extracted maxillary molars without access preparation, or with conservative access size, traditional access size, or traditional access size with simulated loss of marginal ridge integrity. The null hypothesis was that there is no statistically significant difference in the fracture resistance of endodontically accessed teeth based on size of access.

Methods Forty extracted maxillary molars were used in this study. The teeth were divided into four groups based on access size: group 1 (control, no access), group 2 (conservative access), group 3 (traditional access), and group 4 (traditional access with mesio-occlusal preparation to simulate previous restoration or caries resulting in loss of marginal ridge). The teeth were then fractured using an Instron machine, and compressive strength and load force at fracture were recorded. Data were analyzed with one-way analysis of variance with significance level set at $p = 0.05$.

Results No statistically significant differences were observed among the groups regarding load force ($p = 0.45$) and compressive strength at fracture ($p = 0.57$).

Conclusion Based on the results of this study, access size did not have a significant effect on load force and compressive strength to fracture endodontically accessed teeth.

Orofacial Pain Assessment of Rats with Bite-Raising Splints

W. Li, X. Liu, J.P. Farias, M. Gold, A. Almarza

Objectives To investigate whether a sudden change in occlusion is associated with the emergence of hypersensitivity in the TMJ area in adult male rats.

Methods Perioral hypersensitivity was assessed before and after splint placement with the orofacial pain assay. Rats were trained to access a 5%

sucrose solution via a window in the side of the cage. Cumulative contact time (CT) with the sucrose sipper tube was determined for each 10 min training and subsequent testing session. For testing, 18-pin wire arrays were placed in the window to provide bi-lateral mechanical stimulation of the face when the sucrose solution was accessed. Baseline data were collected 4 days before, 1 day after, and then once per week after splint placement. Splints consisted of dental resin poured to about 1 mm in thickness, which were applied unilaterally to the right maxillary molars.

Results Increase in CT was observed during training, which plateaued by day three. CT was significantly decreased when mechanical stimulation was added (by $80\% \pm 11\%$, $p < 0.05$). CT was decreased further still following splint placement (by $58\% \pm 16\%$, $p < 0.05$).

Conclusions Our results are consistent with an increased sensitivity to noxious mechanical stimuli following altered TMJ loading. The orofacial pain assay appears to be a sensitive way to quantify changes in peri-orbital mechanical sensitivity. Additional experiments will be needed to confirm that the changes in behavior reflect an increase in nociception.

Malocclusion on the Histology of the TMJ Cartilage of Rats

X. Liu, W. Li, M. Gold, A. Almarza

Objectives We have previously demonstrated that a change in temporomandibular joint (TMJ) loading associated with unilateral splint placement over a maxillary arch is sufficient to drive degeneration of the mandibular condyle in the rabbit. Because of the variety of validated assays of orofacial nociception available in the rat, the objective of the present study was to determine whether it was possible to adapt the splint model of TMJ disorder (TMJD) developed in the rabbit, to the rat.

Methods Resin bite-raising splints (around 1mm) were applied unilaterally to the maxillary molars of 5-month-old male Sprague-Dawley rats ($n=4$). After 4 weeks, all the rats were euthanized and histological analysis of the TMJ was carried out on both splinted and contralateral sides of the jaw with Hematoxylin & Eosin (H&E), safranin O, Masson's trichrome, and Picrosirius red staining.

Results Primary tissue boundaries were detectable on the condyles ipsi- and contri-lateral to the splint placement. These included the fibrous zone, proliferation zone, mature zone, hypertrophic zone and subchondral bone (Figure 2A). However, except for the faint staining around the pericellular area, there was no staining for glycosaminoglycans (GAG) in the cartilage layer (Figure 2B). Collagen was widely stained throughout the condyle (Figure 2C, D).

Conclusions The absence of GAG staining in the condyle is consistent with the presence of joint degeneration. The bilateral nature of the change suggests the impact of a unilateral splint is bi-lateral. In addition to sham controls, it will be important to further characterize to time course of both the onset and recovery of the changes in the joint and determine the extent to which the histological changes correlate with changes in joint sensitivity.

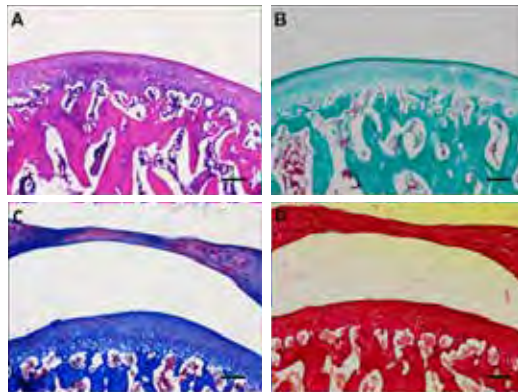


Figure 2. Histology of the TMJ condyles for the splinted side after 4 weeks of splinting. A. H&E staining; B. Safranin O staining; C. Masson's trichrome staining; D. Picrosirius red staining. (scale bar = 100µm)

Analytic Survey of 57 Cases of Oral Metastases

Y. Liu, R.J. Vargo, E.A. Bilodeau

Background Oral lesions have been reported among the first signs of an undiagnosed metastatic disease. Accurate diagnosis of an occult metastasis remains critical in determining the treatment course. Previous studies regarding oral metastatic tumors present varied data regarding the most frequent metastases to the oral cavity. These discrepancies echo the changes in incidence rates for certain malignancies over time and demonstrate the need for periodic updates in oral metastasis studies.

Methods: Using Text Information Extraction System, a de-identified pathology database, we compiled

57 cases over a period of nineteen years using key terms to search for oral metastases.

Results For both males and females, the most common primary sites were lung (21.1%), liver (12.3%), breast (10.5%), kidney (10.5%), and colorectal (8.8%). We found an equal number of lung and breast metastases in females and metastases from the liver to be the most prevalent for males. In most of our cases (54.9%), the patient had no history of the primary malignancy and the oral lesion preceded awareness of the widespread cancer.

Conclusions As a departure from many previous case series, we found lung and breast metastases to be equally numerous in women and liver as the most common oral metastasis in men. Also, we identified a tendency for the patient to present with a previous history in certain malignancies, like breast cancer, whereas in other malignancies, such as renal cell carcinoma, our data demonstrated a propensity to present in the oral cavity without history of a primary tumor.

Kidney Disease, Increased BMI, and Restorations on Anterior Maxillary Teeth

C. Littlejohn, Vieira A.R.

Objectives Since enamel defects are more common in individuals with developmental kidney disorders, we tested if individuals with chronic disease have more restorations in anterior maxillary teeth.

Methods Using the Dental Registry and DNA Repository project's database, statistics on patients' oral conditions were compared based on systemic conditions. This research was carried out in three parts. The initial was to study the relationship between restoration frequency and kidney disease. The second was to explore the relationship between Body Mass Index (BMI) and restoration frequency. The third was to connect the previous two explorations through studying the relationship between BMI and kidney disease.

Results From the initial experiment, it was found that there was a correlation between kidney disease and increased restoration frequencies. In addition, when the second portion was analyzed, there

was a positive relationship between patients' BMI and their restoration frequency. Lastly, there was a correlation between higher BMI and kidney disease.

Conclusions Patients who have kidney disease will more often need anterior composite resin restorations that are possibly surrogates of enamel aesthetic concerns or higher caries experience, as compared to the total population of patients in the study. Patients who have higher BMIs tend to have higher restoration frequencies. We found a correlation between kidney disease and patients' BMI. The identification of individuals with "caries predisposing enamel" not only would allow for personalizing preventive strategies, but also provide support for the popular belief of a correlation between "weak teeth" and having many "cavities."

Does Drinking Fluoridated Water Correlate with Lower Caries Prevalence in Appalachian Children?

J.L. Prasad, N. Shah, R.J. Weyant

Objectives This study aims to determine if drinking fluoridated water correlates with a lower caries prevalence in Appalachian children, given competing sources of fluoride in modern society and accounting for social and economic factors that could influence oral health outcomes. The findings of the study will help guide recommendations for appropriate and effective caries prevention strategies.

Methods The study is based on cross-sectional data from the Center for Oral Health Research in Appalachia (COHRA) etiology study database, and includes information derived from interviews, questionnaires, clinical examinations, and water samples of families in rural Appalachia.

T-tests will be used to determine if drinking fluoridated water correlates with caries prevalence in the primary and permanent dentitions in children 10 years and under. Caries prevalence will be based on age-adjusted dmfs and DMFS scores. Linear regression analysis (or Poisson regression) will be used to determine if other variables also correlate with caries prevalence, including socioeconomic factors (parent education and household income), oral hygiene practices, dental

history, history of breastfeeding, dental insurance, and access to health information.

Results The study hypothesis is that drinking fluoridated water correlates with lower caries in Appalachian children 10 years and younger, regardless of competing sources of fluoride. The results of the study are still pending.

Conclusion Pending results.

Post Removal-Induced Dentinal Crack Formation by Modern Ultrasonic or Mechanical Force Systems: A Microcomputed Tomography Pilot Study

T.H. Reiter, M.B. Jiorle, H.L. Ray, K.J. Shields, A. Tran, R. Chong, O.A. Peters, P.S. Salmon, K. Verdelis

Objectives To compare the incidence of dentinal cracks generated during post removal through modern ultrasonic tip instrumentation and mechanical force systems to reports from an earlier study (Althshul et al, JOE 1997).

Methods Roots from 10 human maxillary central incisors and canines of similar canal diameter and shape were instrumented using the EdgeFile X-3 system, followed by the preparation of the coronal 8mm with a ParaPost drill#5 and were imaged by high resolution microCT (set A: 10micron voxel resolution, 60 kvp). 10mm-long ParaPost posts of the same size were cemented (Fuji 2 luting system) in the prepared spaces. Posts were removed after a week using either an ultrasonic tip under water cooling (n=5) or the Ruddle post removal system (Kerr Dental, n=5). MicroCT imaging of the roots was repeated with same conditions (set B), and the presence, number and location of dentinal defects was recorded. Defects observed in set A or initiated in the dentinal wall periphery were not included in the final results

Results One complete and one incomplete crack (both around the cervical 3mm of post space) were detected on one specimen (Ruddle post removal system group), while all other were crack-free.

Conclusion Post removal using either ultrasonics or based on the original Gonon modern systems

may be a process that incurs a significantly lower risk of crack formation than this reported for similar methods in the past.

Phosphate Alters Protein Composition of Extracellular Vesicles (EV) Released by Odontoblasts

V. Smethurst, S. Khalid, S.S. Chaudhary, J. Mobley, A. Huet, J.F. Conway, D. Napierala

Objectives “Extracellular vesicles” (EV) is a collective term used for a variety of lipid membrane-enclosed particles of sub-micron size, which are released by cells to the extracellular space. Molecular composition of EV is thought to reflect the function of EV. A subset of EV released by osteogenic cells are matrix vesicles and are thought to be sites of mineral nucleation. In our previously published research we observed that phosphate treatment of odontoblasts initiated increased release of EV. The aim of the current study was to determine the molecular composition of the EV released and if phosphate treatment alters their composition.

Methods Mouse preodontoblast-derived 17IIA11 cell line was treated with 10mM of sodium phosphate or water in 10% exome-depleted FBS DMEM medium. EV was collected from medium and extracellular matrix using differential ultracentrifugation, quality was assessed by silver stain and cryo-electron microscopy. Mass spectrometric analysis was performed on 4 groups of vesicles: Control vesicles from either medium or extracellular matrix (ECM) (Ctrl-med, Ctrl-ECM) and Phosphate vesicles from either medium or ECM (Pi-med, Pi-ECM). Gene ontology was used to analyze mass spectrometry results. Western blot analysis and qRT-PCR were used to evaluate protein and RNA, respectively.

Results We found 1164 proteins total from all 4 groups analyzed, with 302 (26% of all proteins) shared between all groups. 30% of total proteins were unique to ECM and 14% were unique to medium groups. Pi-ECM group had the greatest number of unique proteins (22% of proteins detected within this group) and Pi-med had the smallest number (6% of proteins detected within this group). Between medium groups, phosphate significantly altered levels of 75 (16%) proteins, 45

were decreased and 30 were increased. Between ECM groups, phosphate significantly altered levels of 207 (40%) proteins, 107 were decreased and 100 were increased. These changes in vesicle composition were not linked to RNA expression changes. Finally, pathway analysis revealed N and O-glycosylation as being pathways significantly increased by phosphate treatment in ECM.

Conclusions Our results indicate for the first time, EV released into the medium and ECM are separate populations. We have also shown that phosphate significantly alters the composition of EV released.

Retrocuspid Papilla: A Series of Forty-three Cases

T. Stansbury, E. Bilodeau

Objectives We present a case series of retrocuspid papillae (RCP), an entity seen in up to 99% of children, known to regress with age to a prevalence of 19% of older adults. The RCP is thought to be a variant of normal anatomy or a developmental anomaly present at birth; enlarging during childhood and adolescence and involuting during adulthood. Some believe it develops as a mass because of the unique position of the permanent and primary mandibular canine. Clinically, it may mimic pathoses, prompting biopsy. The goal of this research was to determine the frequency of regression, clinical features, and differential diagnoses.

Methods Case information was collected from the University of Pittsburgh Oral Pathology Biopsy Service archives (1998-2016). The clinical and demographic data was reviewed.

Results We present a series of 43 cases of RCP in 42 patients. The mean age was 29.9 years (range: 4-79). No sex predilection was noted (M:F, 1:1). All 43 cases presented in the anterior mandibular lingual gingival area. 52.4% of the patients were older than 20. Bilateral involvement was present in only one case. Clinical descriptions included asymptomatic (43/43, 100%), firm (20/43, 46.5%), and pink (19/43, 44.2%). Clinical impressions included fibroma (23/43, 53.5%) and papilloma (9/43, 20.9%). More than one clinical diagnosis was provided in five cases. The average size was 0.41cm (range 0.15-0.8cm).

Conclusion Only one of 43 cases had a clinical diagnosis of RCP. Thus, clinicians should be made aware of this under-recognized entity in adults. 97.6% of our cases were unilateral, suggesting that only asymmetrical cases are biopsied. The lack of RCP regression could lead to misidentification as pathosis by clinicians, prompting unnecessary biopsy of an anatomic variant.

TNAP is Involved in Odontoblasts Response to Phosphate

B.T. Chae, D. Monier, S. Kahlid, V. Smethurst, D. Napierala

Objectives Mutations in the TRPS1 gene causes Tricho-Rhino-Phalangeal syndrome manifesting with dental and skeletal abnormalities including impaired mineralization. We have shown before Trps1-deficient odontoblasts exhibits impaired mineralization through the down regulation of mineralization genes. One of them is tissue-nonspecific alkaline phosphatase (TNAP). This enzyme hydrolyzes pyrophosphate (PPi), which is a major inhibitor of mineralization, ultimately providing odontoblasts with the necessary phosphate (Pi) for mineralization. Based on the expression pattern and its role in dentin mineralization we hypothesize TNAP deficiency is the major cause for the loss of mineralization potential in Trps-1 deficient odontoblasts.

Methods Previously generated Trps-1 deficient odontoblasts clonal cell lines 17IIA11 were used to restore TNAP expression through transposon-mediated genomic integration of a TNAP-expressing construct. Three TNAP restored clonal cell lines were generated. TNAP expression was analyzed by quantitative reverse transcription PCR (qRT-PCR). Effects of restored TNAP expression on mineralization were evaluated with alizarin red staining. Changes in gene expression critical for dentin mineralization PTHr1, Smpd3, Phospho1, Runx2 and SP7 (Osx) were evaluated with qRT-PCR. Induction of phosphate signaling was evaluated based on the activation of Erk1/2 kinase by western blot analysis. In all assays unmodified 17IIA11 (WT), Trps1 deficient (Trps1-KD) and TNAP-restored 17IIA11 odontoblasts were compared.

Results: Three clonal cell lines expressing same levels of TNAP as unmodified 17IIA11 cells were chosen. TNAP restored cells showed an increase in mineralization, in comparison with Trps1-KD cells. However, Trps1 expression has not changed. Analyses of expression of mineralization related genes revealed that restoring TNAP expression significantly upregulated expression of PTHr1, Smpd3, Phospho1, Runx2 and SP7 (Osx) in comparison with Trps1-KD cells.

Conclusion TNAP plays a critical role in Trps1-regulated mineralization by improving cellular response to phosphate and expression of downstream target genes.

Oral Health Status and Dental Utilization Differs by Rurality in Appalachia

Y. Zhou, R. Cuddy, D.W. McNeil, C.D. Wright, D. Polk, R.J. Crout, R.J. Weyant, E. Feingold, K. Neiswanger, M.L. Marazita, J.R. Shaffer

Objectives This study determined how rurality covaried with access to dental care, oral health behaviors, and oral health status among adults living in northern Appalachia.

Methods Participants were Appalachian resident adults aged 18-59 (n=1089) from the Center for Oral Health Research in Appalachia (COHRA). Rural-Urban Continuum (RUC) codes corresponding to the GPS coordinates of participants' residences were used to classify participants as metropolitan or nonmetropolitan (i.e., small town and rural). Logistic and linear regression were used to estimate the association of rurality with measures of oral health status, dental care utilization, oral health related behaviors. Models were adjusted for socio-demographics variables such as age, sex, race, income, and dental insurance.

Results Nonmetropolitan residents exhibited fewer sound teeth ($\beta=-1.71$, $p<0.001$), more white-spot carious lesions ($\beta=0.65$, $p<0.0005$), higher rates of gingival recession (OR=4.0, $p<10^{-12}$), and higher rates of complete edentulism (OR=2.8, $p=0.017$). Likewise, differences in dental care utilization behaviors were observed between nonmetropolitan and metropolitan residents for 8

of 9 utilization measures tested (all $p < 0.0005$). For example, nonmetropolitan residents were less likely to go to dentist for routine checkups (OR=0.4, $p < 0.00001$) and were more prone to seek care only after experiencing a dental problem (OR=2.2, $p < 0.00001$). These differences were not explained by socio-demographic variables. However, nonmetropolitan residents were more likely to report "costs too high" (OR=6.0, $p < 10^{-12}$) as a major reason for not utilizing dental care services. The oral health related behaviors of brushing, flossing, and using mouthwash did not differ significantly by rurality.

Conclusions After adjusting for socio-demographic variables nonmetropolitan resident adults in Northern Appalachia were found to differ significantly from metropolitan resident adults with respect to their oral health status and utilization of dental services. This finding suggests that rurality is associated with risks to oral health that may need to be explicitly addressed through targeted disparity reduction interventions.

Prevention of Inflammatory Bone Loss Via Induction of M2 Macrophages

Z. Zhuang, S. Yoshizawa, M. Shehabeldin, C. Sfeir

Objectives To assess the effect of local induction of M2 macrophages in modulating the immune response and preventing alveolar bone loss in murine periodontitis models.

Methods We first encapsulated the M2 macrophages inducing C-C motif chemokine ligand 2 (CCL2) in poly lactic-co-glycolic acid (PLGA) microparticles (MPs) using double emulsion technique and determined the release profile of CCL2. Next, we assessed the ability of CCL2 to induce the polarization of mouse derived macrophages toward the M2 phenotype and to inhibit the expression of TNF-alpha by RAW 264.7 cells treated with P. gingivalis lipopolysaccharide. Finally, we locally delivered the CCL2 MPs into the gingival tissues of mice where experimental periodontitis was induced and assessed alveolar bone loss, osteoclasts number and the expression of inflammatory and the M1 and M2 macrophages markers.

Results We successfully fabricated recombinant mouse CCL2 releasing PLGA MPs that continued to sustainably release CCL2 for up to 70

days. Moreover, we demonstrated that mouse macrophages treated with CCL2 enhanced their expression of the M2 macrophages surface marker CD206. Additionally, CCL2 was able to reduce TNF-alpha expression in LPS treated RAW cells. Using mouse experimental periodontitis models, we showed that local delivery of CCL2 MPs resulted in significant inhibition of alveolar bone resorption that was positively correlated with a reduction in the number of osteoclasts. Immunostaining for the M1 and M2 macrophages surface markers revealed that CCL2 MPs injection skewed the M1/M2 ratio in the periodontium toward an M2-polarized profile. Finally, our qPCR results showed significant increase in IL1ra mRNA expression and decrease in RANKL mRNA expression in mice maxillae where CCL2 MPs were injected.

Conclusions We conclude that local delivery of CCL2 skewed resident macrophages towards the anti-inflammatory M2 phenotype and inhibited alveolar bone loss in mouse periodontitis models. This approach could serve as a promising immunomodulatory strategy for treatment of periodontitis.

ACT ARCO Students

Madiha Bhatti

Surbhi Chandna

Making it Unique: Fundamentals of Teaching and Learning in Dental Education

Samiya Jabir

An Unlikely Journey into Teaching

Saniya Kamran

Wearing Both Shoes: A Reflection of Experiences in Academic Dentistry as a Student being the Teacher

Ashley Lazar

Teaching to Create Good Students: Exploring Ways to Help Students Get the Most of their Education

Giana Lupinetti

Pursuing a Career Path That Merges Clinical and Academic Dentistry

Katherine Ni

Building Intentional Dental Educators



STUDENT RESEARCH

The role of the Director of Student Research is to facilitate the engagement of students in research and scholarly activities. The director oversees the Dean's Summer Scholarship Program and promotes student participation in AADR meetings. The director also helps students in identifying mentors and mechanisms to improve their involvement in research. Finally, the director oversees the student research competition and encourages participation in the American Dental Association Foundation Annual Dental Students' Conference on Research and the Hinman Student Research Symposium.

Alexandre R. **Vieira**, DDS, MS, PhD
Director of Student Research

The University of Pittsburgh School of Dental Medicine Chapter of the American Association for Dental Research (AADR) National Student Research Group (NSRG) provides opportunities for dental students to pursue both basic science and clinical research. The group helps students find projects and mentors that are related to their chosen research topics ranging from regenerative medicine to dental materials. Students also are given the opportunity to present their findings at national meetings, where they will have many opportunities to meet students and professors from other institutions with similar interests.

For more information on potential projects, please visit our website at dental.pitt.edu/research.

Accolades 2018 Mary J. Hauk, DDS, MPH Memorial Scholarship for Dental Residents

Dr. Kah Yan (Alyssa) Cho, resident in the Orthodontics program

Dr. Cho received this award in recognition of her research on the mechanism of cleft palate using a mouse model of the trichorhinophalangeal syndrome. This research is important for understanding the molecular pathology underlying the characteristic craniofacial phenotype of the trichorhinophalangeal syndrome.

American Association for Dental Research 2018 Student Research Fellowship

ByongSoo (Timothy) Chae, third-year dental student
Mr. Chae is the recipient of the AADR 2018 Student Research Fellowship in support of his research project on understanding the role of tissue-nonspecific alkaline phosphatase in phosphate signaling in dental tissues. This research is important for deciphering the molecular pathology in mineralization disorders caused by phosphate deficiency.

Thomas W. Braun Master of Excellence Award

Award recipient will be named at the event

Langkamp-Allison Award

Hira Akbar and **Andrea Montoya**

The Langkamp-Allison Award recognizes a third-year dental student interested in pursuing a career in dental education.

SCADA Award and Dentsply Sirona Student Clinician Program Award

Patrick Donnelly

This award recognizes outstanding clinical or basic science research by a first-, second-, or third-year dental student. The recipient receives a bronze plaque and a trip to the AADR meeting to compete nationally.

Hinman Student Research Symposium Competition

Meer Ahmed

Competitive national research symposium at the University of Tennessee in Memphis for students involved in clinical and basic science dental research

AADR – Local Pittsburgh Chapter Award

Vera Liu

This award recognizes outstanding clinical or basic science research by a predoctoral, dental hygiene, or graduate student. The recipient's name will be engraved on a bronze plaque in the Pitt Dental Medicine Learning Resource Center.

School of Dental Medicine Awards (A.K.A. Dr. O. Jack Penhall Award)

First place **Ariana Kelly**

Second place **Erin Schwoegl**

Third place **Cara Maloney**

This award recognizes outstanding clinical science research by a dental student, and was initiated by Dr. O. Jack Penhall (DMD '73), a Pitt Dental Medicine alumnus who is in private practice in Greensburg, Pa., and is a National ADA Student Research Judge.

ASDA Award

First place **Kaitlyn Frey**

Second place **Timothy Chae**

Third place **Patrick Donnelly**

This award recognizes outstanding clinical or basic science research by a dental student.

Dr. Gerald Orner Award

Tamara Latif

This award recognizes an outstanding fourth-year student researcher who is likely to succeed in postgraduate academic dentistry, and honors Dr. Gerald Orner (DDS '63). It is provided by a Pitt Dental Medicine Alumni.

Quintessence Award for Research Achievement

Sara Barna

This award recognizes an outstanding fourth-year student researcher for their research achievements. The award is provided by the Quintessence Publishing Co., Inc.

AADR Student Research Day Award

Award recipient will be named at the event

Last year's awardee: Jennifer Zhou

This award provides support to participate in the 2018 AADR meeting in Vancouver, British Columbia, Canada (meeting registration cost and help with travel expenses).

Student Research Awards

STUDENT RESEARCH GROUP

The Pitt Dental Medicine Dean's Summer Research Scholar Program provides a unique opportunity for incoming dental students to participate in research prior to starting their first-year curriculum. Thirteen students in the class of 2021 participated in the program in 2017, a record number of participants since the program was established. Student projects spanned the research spectrum for the program, which is supported by Dean Braun and research mentors at the dental school. This program allows incoming dental students with diverse research interests to explore opportunities within the dental school. Participating students are encouraged to continue research throughout their four-year dental program, while building research relationships and developing research skills.

Developing Dental Scholars

For Patrick Donnelly, PhD, under the mentorship of Dr. Juan Taboas, being a summer scholar meant building on his PhD in chemistry and applying his extensive research skills to the field of dentistry. Patrick described, "I spent the summer developing and testing gelatin sponges that were to be used as part of a device for dental pulp regeneration following root canal therapy. The sponges were used in a chorioallantoic membrane model at the end of the summer to simulate cell infiltration as would occur in vivo." This research resulted in his project, A Chorioallantoic Membrane Model for Dental Pulp Regeneration, a clinical application focused in basic science research. "The research helped me to get acquainted with the current research problems in dentistry and the approaches people are taking to solve them," explained Patrick. Like many of his colleagues, Patrick uses online media, such as LinkedIn and Google Scholar to communicate with other researchers about his research findings.

Outside of the basic science wet lab, Andrew

Bertot, mentored by Dr. Seth Weinberg, is investigating prenatal androgen exposure and tooth development. As an integral part of the COHRA studies undertaken at the University of Pittsburgh and West Virginia University, Andrew analyzed the distance between the flexion creases on digits two through five. "The digit ratio is an indication of prenatal androgen levels and may give clinicians a quick insight into the best treatment plan for a patient, simply by looking at their hands," Andrew pointed out. Utilizing current technology, Andrew was able to track patients' development over many years through electronic analysis of hundreds of digit ratio scans.

In the clinics, students addressed current protocols used at Pitt Dental Medicine as they relate to clinical knowledge and patients' rights. Renee Stevens, with the mentorship of Dr. Sarah Grafton and Dr. Katie Ryan, investigated dental treatment planning considerations for patients who use cannabis.

"The prevalence of marijuana use has been on the rise in recent years and it's important for dentists to consider the effects of marijuana use on dental treatment and develop specific, safe protocols for treating these patients. The purpose of this project is to explore those possibilities," explained Renee. Her project holds a potential for changes in clinical protocol regarding patient consent within the dental school clinics.

Similarly, Andrew Herr, mentored by Dr. Anitha Potluri and Dr. Elizabeth Bilodeau, examined the use of evidence-based dentistry (EBD) in the dental clinics as it relates to radiograph selection criteria. Andrew explained, "The objective of this study was to assess whether the dental faculty and students were aware of the FDA guidelines, their adherence to these guidelines, and their understanding of the principles of EBD." To collect data from students, and dental faculty, Andrew relied on Qualtrics, "...a fantastic survey software which is free for Pitt faculty and students." Qualtrics allowed Andrew to collect data quickly from many people throughout the dental school.



Student Research Group Officers

Co-President

Ms. Yaella Landau

Co-President

Mr. Roman Garcia

Secretary/Treasurer

Ms. Katherine Ni



The Dean's Summer Scholars explored a wide range of research topics. The group's diverse interests and previous research experiences resulted in exposure to new opportunities within the field of dentistry. For Cara Maloney, under the mentorship of Dr. Christine Wankiiri-Hale and Dr. Zsuzsa Horvath, her summer project meant considering new career possibilities. "[My project] gave me a lot of insight into how the school works before I even started and also introduced me to academic dentistry as an option in my future career," stated Cara.

Arianna Kelly shares Cara's experience of discovery through her involvement in a research project coordinated with Dr. Alexandre Vieira. She explained, "I have gained more knowledge on the topic of caries, specifically the prevalence of the disease, how they are measured, and novel ways to detect and treat them." The new knowledge discovered here at Pitt Dental Medicine has given the Dean's Scholars a more profound perspective on courses throughout their first year curriculum, such as Professionalism and Cariology.

The Future of Student Research

The lasting impact and strength of the Dean's Summer Scholar Program is evident through the recent reestablishment of the AADR Student Research Group (SRG) within the dental school. This group, which has been rather inactive in recent years, serves to enrich participant's dental

education through research. "Through my work in Dr. Heather Szabo-Roger's lab, I recognized the important interplay between research and dental education. To me, the SRG is a way to share my summer experience with my peers and ignite a continued interest in research throughout the dental school," explained SRG President, Casey White, a class of 2021 Dean's Summer Scholar. The newly established SRG has over 40 student members, including pre-doctoral and biology graduate students. Club sponsored events feature a welcome event for the newest Dean's Summer Scholars, as well as a "How to Get Involved in Research" workshop for dental students.

Kailtyn Frey, mentored by Dr. Fatima Syed-Picard, offered a piece of advice to the newest class of Dean's Summer Scholars, "Enjoy the summer and take the time to get the most out of your research experience. The program is a great introduction to both Pitt and all that dentistry has to offer. Embrace the opportunity to learn for fun and explore different aspects of dentistry before classes begin." Whether in academic classrooms, the clinics, or the basic science wet lab, the Dean's Summer Scholars continue to provide meaningful contributions, while exploring and expanding the current state of knowledge within the dental research community.

To learn more about the Student Research Group at Pitt Dental Medicine, please visit their website at dental.pitt.edu/srg.



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PRESENTATIONS

International Congress of Oral Implantologists (ICOI) Winter Implant Symposium

New Orleans, La.
February 16-18, 2017

McGowan Institute for Regenerative Medicine Annual Scientific Retreat

Pittsburgh, Pa.
March 5-7, 2017

95th General Session of the International Association for Dental Research

San Francisco, Calif.
March 22-25, 2017

2017 National Rx Drug Abuse & Heroin Summit

Atlanta, Ga.
April 17-20, 2017

American Association of Endodontists 2017 Annual Meeting (AAE17)

New Orleans, La.
April 26-29, 2017

American Academy of Orofacial Pain (AAOP) 41st Scientific Meeting

Scottsdale, Ariz.
May 4-7, 2017

60th Spring Meeting of The Japanese Society of Periodontology

Fukuoka, Japan
May 12-15, 2017

37th Australian Dental Conference

Melbourne, Australia
May 17-21, 2017

2017 American Academy of CranioMaxilloFacial Surgeons Annual Meeting

Pittsburgh, Pa.
May 19-20, 2017

American Academy of Pediatric Dentistry 70th Annual Session

Washington, D.C.
May 25-28, 2017

The III Brazilian Congress of Orofacial Pain

São Paulo, Brazil
June 3, 2017

Geistlich Biomaterials Symposium—Multidisciplinary Treatment Solutions for Peri-Implantitis

Chicago, Ill.
June 6-9, 2017

2017 ADEA (American Dental Education Association) Annual Session & Exhibition

Baltimore, Md.
June 6-8, 2017

2017 ADEA Commission on Change and Innovation in Dental Education (ADEA CCI) Liaisons Summer Meeting

Baltimore, Md.
June 6-8, 2017

2017 AcademyHealth Annual Research Meeting

New Orleans, La.
June 25-27, 2017

Penn Periodontal Conference 2017

Philadelphia, Pa.
June 25-30, 2017

64th European Organisation for Caries Research (ORCA) Congress

Oslo, Norway
July 5-8, 2017

2017 ADEA Summer Program for Emerging Academic Leaders

Freeport, Maine
July 11-14, 2017

21st American Conference on Crystal Growth and Epitaxy (ACCGE-21)

Santa Fe, N.M.
July 30-August 4, 2017

9th Symposium on Biodegradable Metals – Bertinoro

Bertinoro, Italy
August 27-September 1, 2017

2017 American Society for Clinical Pathology (ASCP) Annual Meeting

Chicago, Ill.
September 6-8, 2017

American Society for Bone and Mineral Research 2017 Annual Meeting

Denver, Colo.
September 8-11, 2017

American Academy of Periodontology (AAP) 103rd Annual Meeting,

Boston, Mass.
September 9-12, 2017

Eastern Society of Teachers of Oral Pathology (ESTOP) 2017 Annual Conference

Burlington, Vt.
September 15-17, 2017

11th IADR World Congress on Preventive Dentistry
New Delhi, India
October 3-6, 2017

2017 ADEA Sections on Business and Financial Administration and Clinic Administration (ADEA BFACA) Meeting
San Diego, Calif.
October 4-7, 2017

AAOMR 2017– American Academy of Oral & Maxillofacial Radiology
St. Louis, Mo.
October 4-7, 2017

99th American Association of Oral and Maxillofacial Surgeons (AAOMS) Annual Meeting, Scientific Sessions and Exhibition
San Francisco, Calif.
October 9-14, 2017

67th Annual Meeting of the American Society of Human Genetics
Orlando, Fla.
October 17-21, 2017

American Dental Association 2017 (ADA)
Atlanta, Ga.
October 18-21, 2017

47th Annual Session of the American College of Prosthodontists
San Francisco, Calif.
November 1-2, 2017

Hinman Student Research Symposium
Memphis, Tenn.
November 3-5, 2017

Helmholtz-Zentrum Geesthacht Centre for Materials and Coastal Research (HZG) “Key Technologies Matter” Scientific Evaluation
Berlin, Germany
November 7-9, 2017

Fourth Annual Mid-Year Symposium on Sleep Medicine & Orofacial Pain
Chicago, Ill.
November 11, 2017

QUEST Symposium
Hood River, Ore.
November 17, 2017

Tissue Engineering and Regenerative Medicine International Society (TERMIS) Americas Annual Conference and Exhibition
Charlotte, N.C.
December 3-6, 2017

2017 American Academy of Oral and Maxillofacial Pathology (AAOMP) Annual Meeting
Newport, R.I.

2018 ADEA Leadership Institute Phase V
Atlanta, Ga.
February 1-4, 2018

2018 National Osteology Symposium, State-of-the-Art Regenerative Therapies: Enhancing Success Around Teeth and Implants
Phoenix, Ariz.
February 9-10, 2018

Gordon Research Conference on Craniofacial Morphogenesis and Tissue Engineering
Lucca, Italy
February 11-16, 2018

2018 Emerging OMS Leadership Workshop
Rosemont, Ill.
March 3-4, 2018

2018 ADEA Annual Session & Exhibition
Orlando, Fla.
March 17-20, 2018

United States & Canadian Academy of Pathology 2018 Annual Meeting
Vancouver, B.C., Canada
March 17-23, 2018

47th Annual AADR Meeting & Exhibition/42th Annual CADR Meeting
Fort Lauderdale, Fla.
March 21-24, 2018

2018 American Academy of Oral Medicine (AAOM) Annual Meeting
San Antonio, Tex.
April 10-14, 2018

American Cleft Palate—Craniofacial Association 75th Annual Meeting
Pittsburgh, Pa.
April 10-14, 2018

American Academy of Orofacial Pain (AAOP) 42nd Scientific Meeting
Chicago, Ill.
April 26-29, 2018

Pennsylvania Society of Oral and Maxillofacial Surgery 2018 Annual Meeting
Hershey, Pa.
April 29-30, 2018

