UNIVERSITY OF PITTSBURGH

SCHOOL OF DENTAL MEDICINE

23 RESEARCH SYMPOSIUM

SEPTEMBER 11, 2023

University of Pittsburgh | School of Dental Medicine

LEARN HOW PITT DENTAL MEDICINE RESEARCHERS ARE TRANSFORMING PATIENT CARE ACROSS THE COUNTRY AND AROUND THE WORLD

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RESEARCH SYMPOSIUM HISTORY

In 2000, Dr. Mary Marazita became the Associate Dean for Research and recognized that the research taking place at the School of Dental Medicine was not necessarily reflective of a school of this prominence. She quickly drafted a vision to encourage research efforts through the first School of Dental Medicine Research Symposium.

After 23 years, our symposium has become the longest-running research symposium at Pitt—and with good reason.

Including significant speakers from outside of Pitt greatly expanded this inspiring tradition and the event continued to grow in attendance and significance. Concurrently, NIH funding to the school continues to positively impact our discoveries—evidence that Pitt Dental Medicine has become a significant force in dental medicine research.

Since 2013, Dr. Charles Sfeir, Associate Dean for Research, carries on this effort by improving and invigorating the annual symposium. This year, to better integrate our clinician's concerns into our presentations, we refocus and restart the symposium by presenting topics of highest relevance to our students and clinical faculty. Our keynote speakers are high-caliber clinician scientists who are influencing the power of translational research around the world and now here at Pitt. And Pitt Dental Medicine continues to influence research worldwide.

Pitt Dental Medicine recognizes the power of presenting sensible clinical information in an educational format to bring relevance and practicality to research. Innovation intensifies the power and influence of the Research Symposium, enabling it to thrive and successfully become the most dynamic and progressive dental research symposium in the region.

Dear Pitt Dental Medicine friends,

I am honored to welcome you to our Annual School of Dental Medicine Research Symposium after a short hiatus due to the pandemic. This year, we come back together to highlight many successes we have realized in both our clinics and research areas. To share these exciting advancements, Research Symposium 2023 will present to you exciting clinical and basic research as a way to showcase the research impacting patient care the most—and the research we do best.

We not only have much to celebrate this year, but a great opportunity to learn about how the dental field is rapidly advancing toward a bright future.

Research is unquestionably a priority at Pitt Dental Medicine, as demonstrated by our consistent commitment to training the next generation of researchers. This is evidenced and endorsed through the Pittsburgh Craniofacial Sciences Training Program (PCSTP), our first ever National Institute of Dental and Craniofacial Research (NIDCR) funded training grant. Please see page 14 for more about this important program.

MESSAGE FROM THE ASSOCIATE DEAN FOR RESEARCH

"Our Symposium today is designed to celebrate the achievements of our investigators, introduce to clinicians the latest advances, and support our students as they make their way into the exciting worlds of both patient care and research."

Our prominence as a research institution advances the field and, most importantly, improves the lives of our patients.

Our research program is one of our school's biggest assets. Together, we realize this through the collaborative and innovative approaches undertaken by our faculty. Our collaborative research spans basic sciences to translational research—evidenced by the many funded research projects at Pitt Dental Medicine.

Allow me to highlight a couple of these programs:

- An international inter-University collaboration that focuses on genetic variants influencing facial features and their development, led by the Center for Craniofacial and Dental Genetics, which also continues its studies of oral health in Appalachia and cleft and lip palate; and
- Michigan-Pittsburgh-Wyss Resource Center: Supporting Regenerative Medicine in Dental, Oral and Craniofacial Technologies, led at Pitt by our Center for Craniofacial Regeneration, which is now supporting promising projects from the clinical, academic and private sectors, bringing new technologies one step closer to patients.

Our research programs expand and build upon the research strengths at Pitt. Being part of a research-intensive institution and sharing in our collaborative spirit is a privilege for me and the research faculty, clinicians and students who are passionate about discoveries we make each day. Our aim is not only to share knowledge, but enhance the bonds between us as scientists, clinicians and dentists.

Our symposium today is designed to celebrate the achievements of our investigators, introduce to clinicians the latest advances, and support our students as they make their way into the exciting worlds of both patient care and research.

It is a great pleasure to welcome our keynote speakers, Drs. Anibal Diogenes and Imad About, whose innovative approaches in clinical research are an inspiration to many and we all may learn from these experts in our field.

Together, we keep our sights focused on a vision of innovation and excellence encompassing our school's teaching, service and research, to better understand the inner workings of dental genetics, pioneer new technologies and improve our clinical practice as a point of pride for us all.

Thank you,

Charles Sfeir, DDS, PhD
Associate Dean for Research

MESSAGE FROM THE INTERIM DEAN

Dear colleagues and friends,

I am honored to welcome you to the 2023 Pitt Dental Medicine Research Symposium. This is a day to not only share and celebrate our accomplishments, but is an occasion to look ahead to the unique and exciting opportunities that the future holds for us. Research is an essential part of our success as a school. It is a privilege to be part of this exciting event and learn more about our amazing collaborative work in translational and clinical research.

Today, we turn our attention to the achievements of our traditional researchers and to the important role that our students and clinicians play in contributing to our collective discovery. The intersection of research, academics, and patient care is a crucial one, as all three feed and support the success of the other. Our sessions today will showcase that unity through outstanding presentations that will heighten our knowledge, spark our curiosity, and offer us the opportunity to give voice to innovative ideas of our own.

Our profession selflessly accepts the obligation to improve the health and quality of life for our community. It is this aim that ultimately drives our research endeavors—at its heart, our research is about striving to better the lives of as many as we can. It is this obligation to improve the foundations of our profession that drives us toward this meaningful work. This is the secret to our success as researchers, scholars, teachers, and clinicians. It is evident in the passion with which we at Pitt Dental Medicine provide care and pursue innovative discoveries.

I am proud to be a part of this celebration of our remarkable and collaborative work.

Marnie Oakley, DDS
Interim Dean

"I encourage everyone to see this day as a chance not only to learn about our latest advances, but to consider how research and innovation relates to you and enriches the lives of others."

CENTER FOR CRANIOFACIAL AND DENTAL GENETICS

UNCOVERING GENETICS OF HUMAN HEAD AND FACE APPEARANCE

Since 2009, **Seth Weinberg, PhD**, has collaborated with investigators in the United States and Europe to understand how genes contribute to the appearance of the head and face.

"We are conducting large-scale analyses combining genomics, 3D imaging, and morphometrics to discover genetic regions that influence craniofacial features in multiple human populations," he said. "Our findings can shed light on the etiology of common and rare craniofacial conditions, offer insights into human evolution, and serve as a starting point for functional studies designed to reveal the molecular mechanisms that connect genotype to craniofacial phenotype."

This year, the group completed the first comprehensive genetic analysis of human cranial vault shape. The vault is the section of the head that surrounds the brain—"essentially, what is covered when you wear a baseball cap," he explained. The analysis identified 30 associated genetic regions in more than 5,000 children. They also discovered that some of those associated genetic regions are related to craniosynostosis, a birth defect that occurs when the joints in a baby's cranial vault join together too early.

Next steps include a large multi-ancestry genetic analysis of 3D face shape in additional populations. "At some point, we may be able to use a patient's genetic profile to inform clinical care. For example, we may be able to better predict aspects of a patient's facial growth from their genome. The primary applications are in orthodontics and oral and maxillofacial surgery," Dr. Weinberg said.

The work is funded by the National Institute of Dental and Craniofacial Research (NIDCR).

FINDING SHARED MECHANISMS IN ORAL AND SYSTEMIC DISEASE

For 12 years, **Ariadne Letra, DDS, MS, PhD**, and collaborators have been collecting saliva samples from dental patients from multiple sites worldwide. Next-generation sequencing allows the researchers to identify genes and mutations that may be contributing to congenitally missing teeth.

"Our work revolves around the genetics of craniofacial and dental anomalies, heavily focused on the genes that cause congenitally missing teeth," she said. "It is a rather underexplored condition that has extensive clinical significance, with social, functional, and financial impact for patients and families. In addition, clinical management is challenging because you can't provide implants until adulthood, and patients need appliances to replace those missing teeth."

Recently, the team uncovered the first evidence that there may be a polygenic effect in the same individual. They are continuing to recruit patients and model the genetic variants to better understand their biological effects. The team from Pitt, Vanderbilt, and University of Texas is funded by the NIDCR.

Dr. Letra also is applying genetic analyses to explore bidirectional relationships between oral health and systemic health conditions. Her recent research established an epidemiologic and genetic association between endodontic infection and cardiovascular disease. Now, in her recently funded project by the NIH, she is mining demographic, clinical, and genomic data from the All of Us Program database to explore the associations between dental and medical disease concepts to identify biological links potentially explaining interconnectedness between oral health and overall health.

"This research was previously limited because of a lack of integrated medical, dental, and genomic data," Dr. Letra says. "The All of Us Program database houses these data in the same platform for more than 250,000 participants currently. We hope to use those data to glean information that may explain biological mechanisms. This could be instrumental research as the basis for improved diagnostic and therapeutic strategies that will move the field forward."

RECENT FINDINGS ON FACIAL BIRTH DEFECTS AND ORAL HEALTH IN APPALACHIA

Since the late 1980s, **Mary L. Marazita, PhD,** has been conducting pivotal studies into the etiology of facial birth defects, such as cleft lip and palate, utilizing genomic tools made possible by the Human Genome Project.

Her team has obtained DNA samples on thousands of families, as well as demographics, morphometrics, pregnancy history, and many other variables to help elucidate the factors contributing to the risk of these common congenital anomalies. Her group has published widely on their findings that to date have identified about 50 distinct regions in the genome that contain risk and/or protective variants for facial birth defects. "Most individuals have no clear-cut genetic inheritance pattern within the family that would indicate a single genetic cause. But we are starting to see certain patterns emerging that indicate there are likely multiple genes working together," she said.

In the past year, the group has begun comprehensive gene x environment interaction studies and have also begun to apply CRISPR/Cas9 technology to examine the implicated gene variants in mouse models, with publications planned in the near future.

Dr. Marazita is also continuing her collaboration with West Virginia University and the University of Michigan exploring the causes of the poor oral health seen in the Northern Appalachian region. The project is investigating several possible contributors to caries in children, including genetics, social determinants of health, the microbiome, behavior, and diet.

A recent line of inquiry recruited pregnant women and followed those children until age 5. This important but rare longitudinal approach is very important, Dr. Marazita said, because the research previously started recruiting at age 2, but many of the children already had caries.

"Genetic studies in this cohort had some really interesting results regarding the trajectory: Some never get caries, some have many from a young age, some have zero or no caries but slowly develop them—and there are different genetic patterns associated with each," she said.

Also emerging are findings at the microbiome level. Using metagenetic techniques, Dr. Marazita and colleagues are bacterial signatures in the saliva microbiome are implicated in caries. The team has identified two major groups of oral bacteria—one that's protective against caries and one that's a risk profile for caries in children as young as 6 months. "That is a year or two before S. mutans (a major cariogenic bacteria) even shows up in the mouth. This is important because it could give us a way to predict which children are more likely to develop dental decay by age 5 or sooner," she said.

The team hopes to ultimately combine all of the factors they are studying to assist in the creation of a robust in-clinic screening modality.

Dr. Marazita's projects are funded by the NIH, primarily the NIDCR.

LEARN MORE ABOUT THE CCDG AT DENTAL.PITT.EDU/CCDG

CENTER FOR CRANIOFACIAL REGENERATION

NIH GRANT FUNDS HIGHLY TRANSLATIONAL RESEARCH

Charles Sfeir, DDS, PhD, founded the Center for Craniofacial Regeneration in 2005 with the goal of developing technologies and treatments for wounds and defects of the face and skull that restore function and appearance.

Myriad projects are fulfilling the center's mission, and every investigator is funded—many as part of a large grant funded by the National Institutes of Health (NIH).

The collaborative Michigan-Pittsburgh-Wyss Regenerative Medicine Resource Center will receive $30 million over five years to help move research into clinical practice. Pitt projects selected by the project include the following:

Juan Taboas, PhD, and his team are developing Vital-Dent, a drug-free implant that would regenerate living tissue in teeth treated with root canals to prolong tooth survival.

Andrew Brown, PhD, has created AmpliMag Barrier Membranes and Membrane Fixation Systems. The devices, made of a patented magnesium alloy, aim to improve dental bone grafting procedures. They are stable enough to form a protective tent over healing tissue, biocompatible with soft tissue, and resorbable.

Alex Almarza, PhD, and his team have designed a biodegradable scaffold made from extracellular matrix for reconstruction of the temporomandibular joint (TMJ). The device would replace the meniscus of the TMJ by inducing the formation of new, functional, patient-specific tissue. This work is also supported by the NIH's Helping to End Addiction Long-term (HEAL) Initiative.

SCAFFOLD-FREE TISSUE REGENERATION

Other funded projects within the center include a novel scaffold-less approach to tissue engineering. **Fatima Syed Picard, MSE, PhD**, has created a synthetic matrix on which cells can crawl and build new tissue that more closely mimics natural tissues. The 3D cellular scaffold-free tissue constructs allow cells to organize and generate their own matrix. The research shows promise for regenerative endodontic therapy, treatment for periodontic disease, tooth replacement, and nerve regeneration.

UNDERSTANDING ENAMEL AND DENTIN BIOMINERALIZATION

Another area of focus for the Center for Craniofacial Regeneration is biomineralization. **Elia Beniash, PhD**, is studying enamel to better understand its formation and development.

"Enamel is a very hard tissue and the only tissue in body that is sophisticated but cannot repair or regenerate itself like bones, ligaments, and the liver. It has unique chemical properties, and it lasts for a lifetime without deteriorating much, if not diseased," Dr. Beniash said. "Understanding how this tissue forms is very important to develop biomaterials to repair dental structures or even to develop other materials you want to be that strong."

Enamel is 95% mineral and 1% protein, and the rest is water, Dr. Beniash said. Using chemical experiments in vitro, then a mouse model, he and **Henry Margolis, PhD**, have discovered that a single phosphate is essential to the protein in enamel formation. When the phosphate is not present, enamel's structure is compromised.

The work, which is funded by the National Institute of Dental and Craniofacial Research (NIDCR), will continue through 2025. Next steps are to focus on cellular implications, likely in a cell culture model. The research could have implications for dental conditions such as amelogenesis imperfecta, an inherited enamel disorder.

STUDYING SKELETAL SUPERGLUE IN SPACE

One of the Center's research projects has moved far beyond the lab—into space.

This past year, a team led by **Giuseppe Intini, PhD**, sent a mouse model on a NASA mission. Pitt and RevBio collaborated with the SpaceX-26 RR25 mission to study the effects of lack of gravity on skeletal stem cells. The flight tested the ability of a novel bone adhesive to induce bone regeneration.

LEARN MORE ABOUT THE CCR AT DENTAL.PITT.EDU/CCR

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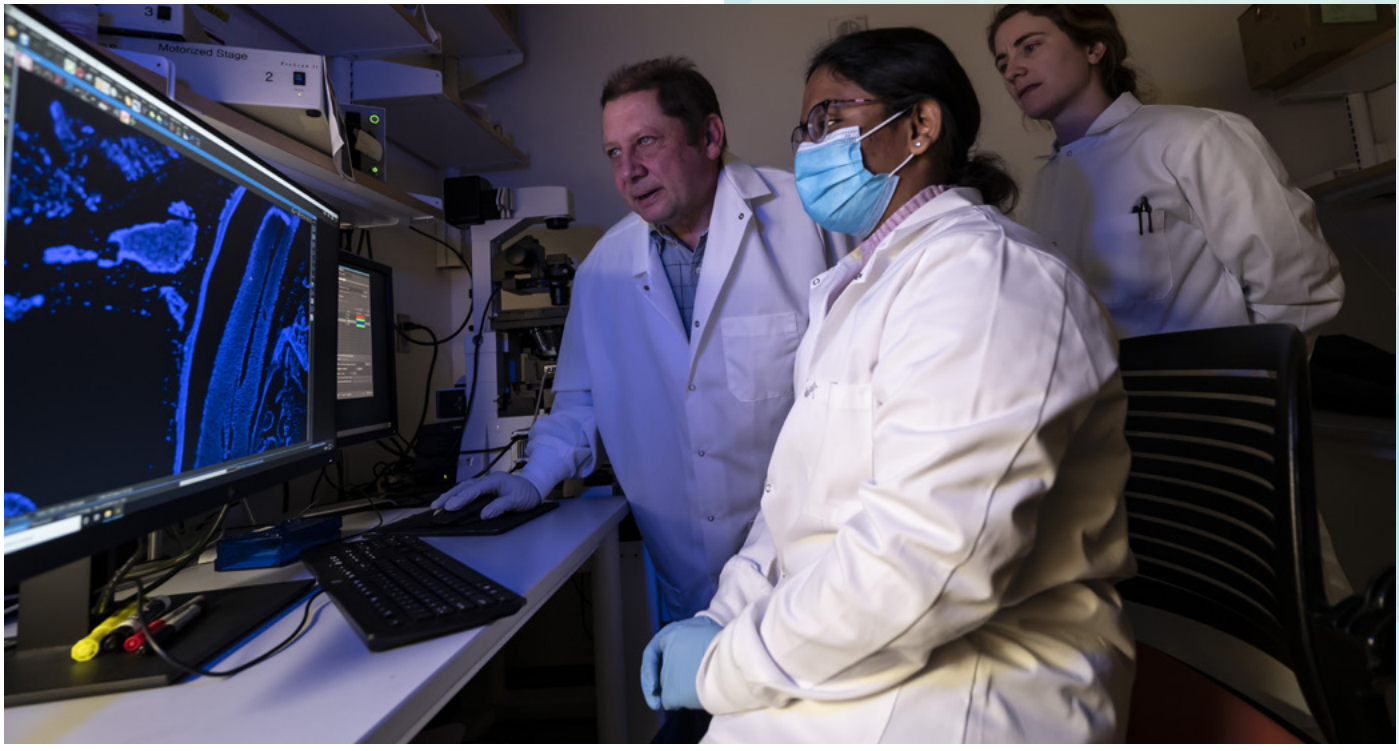

ESTABLISHING STANDARDS OF CARE FOR ACUTE DENTAL PAIN

Studies have indicated that about 40% of the population have experienced dental pain in the past year. The federal government has identified it as a significant health problem, impacting productivity and increasing healthcare costs. However, pain management is complicated and fraught with risks related to opioid use. The University of Pittsburgh School of Dental Medicine Department of Dental Public Health has been working on a $1.5 million award from the U.S. Food and Drug Administration to address the complex problem.

Deborah Polk, PhD, assistant professor of dental public health, and her team have developed clinical practice guidelines for the management of acute dental pain. Their project also involves disseminating the guidance and providing dental professionals with ways to implement the strategies. Finally, the researchers will evaluate whether the guidance has changed prescribing behaviors. The goals are to establish a standard of care to guide the field and provide safe and effective pain relief to patients.

Dr. Polk is collaborating with the American Dental Association (ADA) Science and Research Institute and Alonso Carrasco-Labra, DDS, MSc, PhD, formerly of the ADA and now a faculty member at the University of Pennsylvania. The team has conducted and published several systematic reviews this year, available for open access:

> "Acute Postoperative Pain Due to Dental Extraction in the Adult Population: A Systematic Review and Network Meta-Analysis"
>
> "Patient Values and Preferences for Managing Acute Dental Pain Elicited through Online Deliberation"
>
> "Injectable and Topical Local Anesthetics for Acute Dental Pain: 2 Systematic Reviews"
>
> "Corticosteroids for Managing Acute Pain Subsequent to Surgical Extraction of Mandibular Third Molars"
>
> Analgesics for the management of acute dental pain in the pediatric population. A systematic review and meta-analysis

Based on those reviews and several others accepted for publication, the team is now developing and releasing guidelines: one for the management of acute dental pain in pediatric patients, expected to be released in August 2023, and a second for the management of acute dental pain in adolescents and adults. In addition, ADA is offering a free continuing education (CE) course based on the research, and that has been accessed by more than 2,900 dental professionals already.

Future plans involve analyzing information from a national prescription database and conducting a survey to see whether the guidelines and CE course affect prescribing behaviors. "We would expect that if they've read the guideline and taken the course, then we will see a change in behaviors and guideline concordance."

ASSESSING PROVIDER ADHERENCE TO SEALANT GUIDELINES

ADA has an evidence-based clinical practice guideline regarding the use of pit-and-fissure dental sealants. The guideline has two parts: one involving the use of sealants to prevent a cavity from forming

and one regarding the use of sealants to stop decay that has just started.

Dr. Polk is assessing adoption of the guideline's non-cavitated caries component among 16 clinics with 140 dentists. The project used a "deliberative loop" approach, whereby stakeholders received background information, participated in a facilitated discussion, and shared their experiences and opinions. The goal was to understand what could increase clinics' adherence to the guideline. The hypothesis was that the deliberative loop intervention would increase sealant placement on eligible patients.

"Despite the fact that this guideline has been out since 2008 and was updated in 2016, that part of the guideline has not been well adopted by dentists," Dr. Polk said. Before the deliberative loop intervention, 2.3% of eligible patients received the treatment, and the number changed to only 2.6% after the intervention. "That's really no change. We brought together the providers and staff in each clinic, and we had them talk about what their clinics could do to help them adhere to the guideline more closely." Dr. Polk is currently analyzing those discussions and working toward publishing her findings.

ASSESSING EMERGENCY PERSONNEL'S KNOWLEDGE OF DRY SOCKET

The Department of Dental Public Health is fostering research by its students. **Archana Ramesh** a rising D4, is launching a project to explore what emergency medicine providers know about oral pain after dental surgery.

"She had an experience with a patient who had dry socket, a painful condition after dental surgery that often sends people to the emergency department," Dr. Polk said. "She wanted to get a better understanding of emergency medicine providers' knowledge about dry socket—how to recognize it and how to manage it."

After a literature review, Ms. Ramesh designed a survey, obtained approval from the Institutional Review Board, and recently distributed the survey to more than 150 UPMC emergency medicine providers. Responses are coming in, and Ms. Ramesh plans to analyze the data and write an article on her findings.

PITTSBURGH CRANIOFACIAL SCIENCES TRAINING PROGRAM

Pittsburgh Craniofacial Sciences Training Program (PCSTP) was established in 2022 with a goal to train and mentor a new generation of leading scientists in dental, oral, and craniofacial sciences (DOC). This NIH-funded program is one of 23 NIH-funded projects at Pitt Dental Medicine—and that number continues to grow. Pitt Dental Medicine research proposal submissions saw a 45% increase from FY20-21. Our strength in translational and pre-clinical research will be the focus of this T90/R90 training grant.

Through this program we aim to train the next generation of craniofacial and dental scientists through the following:

- multi- and inter-disciplinary research training in areas of applicable DOC diseases, conditions, and disorders:
- supply flexible paths of research training for candidates at both pre and post-doctoral levels:
- encourage student interest in career paths that include DOC research: and
- develop new and diverse group of DOC investigators to make novel discoveries.

The PCSTP provides a highly collaborative, vibrant and multidisciplinary environment where trainees from different backgrounds, such as oral and craniofacial sciences, bioengineering, immunology and human genetics, work side-by-side to develop therapies.

The PCSTP provides courses, research experiences, seminar series, journal clubs, an annual symposium, and an annual retreat. Trainees have full access to all University resources, such as artificial intelligence, responsible conduct of research, and grant writing among others. They benefit from a wealth of seminars, conferences, intramural funding opportunities, and specialized training and experiences available through hundreds of laboratories and clinics across the six schools of the health sciences, Swanson School of Engineering and the Pitt Clinical and Translational Sciences Institute.

LEARN MORE ABOUT THE PCSTP AT DENTAL.PITT.EDU/PCSTP.

Alejandro Almarza

Dr. Almarza is an associate professor in Oral and Craniofacial Sciences 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 focused on tissue engineering and regeneration of the of soft and hard musculoskeletal tissues with natural and synthetic scaffolds. And in a departure from tissue engineering efforts, Dr. Almarza is now exploring research in pain and joint damage. Dr. Almarza first embarked on focused on the use of extracellular matrix (ECM) scaffolds for regeneration of soft tissues, like the TMJ disc. The regeneration observed was remarkable, and Dr. Almarza been working on commercial translation of the technology, which has involved various discussions with FDA, and the coordination of good laboratory practices (GLP) large animal studies for safety and efficacy of the ECM scaffold manufactured under good manufacturing practices (GMP). Nevertheless, there is still a lot that we do not understand in terms of the basic science for the site appropriate remodeling observed. In the pain field, Dr. Almarza has worked on the rat model with a bite block, which deviates the jaw and causes abnormal loading. This in turns leads to mandibular condyle damage and oralfacial hypersensitivity. In the future, Dr. Almarza plans to use different therapeutic agents during both these stages based on basic science understanding of inflammation and osteoarthritis (OA). One example is the use current gene editing technologies, such as CRISPR/CAS9, to develop rat lines to understand OA.

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 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.

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 Assistant Director for Commercial Translation Programs at sciVelo, a translational research acceleration program at the University of Pittsburgh.

Mariana Bezamat Chappel

Dr. Bezamat is interested in the field of phenomics, specifically how oral health and disease respond to environmental changes considering genetic variation, as well as their impact on systemic health, particularly in cancers and atherosclerotic cardiovascular diseases.

Daniel Clark

Dr. Clark's research is focused on osteoimmunology and uses models of periodontal disease and bone regeneration. He is also interested in how aging affects the immune response in disease and during tissue regeneration.

Rebecca Michelle Green

Dr. Green's research focuses on understanding how genetics and environment interact to lead to craniofacial birth defects. Many of these birth defects result in mis-patterning or morphology changes in cranial bones. The goal is to understand the developmental origins of these changes by understanding cell biological changes during the patterning and development of these bones. Her work uses the mouse as a model system to explore how genetic changes are passed through developmental processes to lead to altered facial growth. Her work focuses on a systems based prospective, integrating genetic and epigenetic analysis with 3D morphological analysis (micro CT and microscopy based).

Current projects in her lab focus on the roles on how various genetic and epigenetic mechanisms control variation in the development of the face. She is part of an international team working to understand the links between normal and disease variation in facial development and another team working on modeling human disease polymorphisms in mouse models.

Giuseppe Intini

Dr. Intini's research interests include basic and translational science topics. His basic science research focuses on skeletal stem cells and their roles in bone homeostasis and bone diseases (such as osteosarcoma). His clinical and translational research focuses on the identification of novel therapeutic approaches for bone mass augmentation and for bone regeneration.

Ariadne Letra

Dr. Letra's research focuses on understanding the cellular and molecular mechanisms underlying complex craniofacial and oral traits and conditions. Her work utilizes human genetics coupled with functional genomic characterization in in vitro and in vivo model systems to identify and characterize the effects of genetic variation contributing to cleft lip/palate, tooth agenesis and apical periodontitis. Another aspect of Dr. Letra's work focuses on identifying shared genetic variants potentially contributing to oral health-systemic health connections.

Samantha Lee Manna

Dr. Manna's primary research is the joint application of molecular and computational approaches to assess the effects of genetic variation on complex traits and diseases. At the present, Dr. Manna's work focuses on characterizing the function of the gene CREBRF in cellular metabolism and on gene expression and investigating the role of CREBRF in osteosarcoma. Additionally, she is working to identify the mechanism(s) by which variation in this gene is associated with anthropometric phenotypes, such as height and body mass index (BMI). She also studies the genetic associations of cardiometabolic traits in the Samoan population as a member of the Obesity, Lifestyle, and Genetic Adaptations (OLaGA, "life" in Samoan) study group and is interested in oral health of the Samoan population. Dr. Manna has a secondary appointment in the Pitt School of Public Health Department of Human Genetics.

Mary L. Marazita

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

Dr. Marazita is involved in 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 NIDCR FaceBase Consortium (**www.FaceBase.org**), the NIH Director's Office All of Us Precisian Medicine Research Program (All of Us, **https://allofus.nih.gov/**) and other national and international research initiatives.

Henry C. Margolis

Dr. Margolis' research interests center on fundamental aspects of biomineralization, focusing on protein-mediated mineralization and the mechanism of dental enamel formation. Prior studies in Dr. Margolis' laboratory utilized in vitro approaches to elucidate the structure and mechanism of formation of higher-order assemblies of key enamel matrix proteins and their influence on mineralization and crystal organization. In vitro approaches were also used to provide new understanding of how protein self-assembly, protein phosphorylation, and proteolytic processing of matrix proteins influence dental enamel formation. Protein molecular assembly has been assessed using dynamic light scattering, small-angle x-ray scattering, TEM, and other quantitative and semi-quantitative approaches. Notably, we have extended our NIH-supported work to investigate critical aspects of hypotheses developed based on our in vitro findings using mouse models, including a novel knock-in mouse that is phosphorylation defective. Such studies have now shown that amelogenin phosphorylation in essential for proper enamel formation and ameloblast integrity, in part, by enhancing the capacity of amelogenin to stabilize an amorphous calcium phosphate precursor phase during the secretory stage of amelogenesis. Long term, such information should also provide new insights for the development of bio-inspired materials and novel approaches for hard tissue repair.

Dobrawa Napierala

The focus of Dr. Napierala's research is on the development and homeostasis of skeletal and dental tissues, and regulation of the mineralization process. Dr. Napierala studies molecular networks in the cellular and animal models of human dental and skeletal diseases with the goal to understanding of the molecular pathologies underlying human diseases to improve the preventive and therapeutic approaches. Dr. Napierala's research interest includes the elucidation of the molecular mechanisms involved in the cellular response to phosphate, phosphate homeostasis disorders, molecular networks of the Trps1 transcription factor in mineralizing tissues.

Fatima N. 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 as advanced microscopy and microfluidic devices.

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 areas of research focus are:

1. Modulation of the immune system to develop therapies for periodontal disease: 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.
2. Biodegradable metals, developing load bearing bone fixation devices: 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.
3. Bone and Dentin Tissue Engineering, utilizing biomaterials and cellular strategies to regenerate mineralized tissues: Biomimetic scaffolds development for bone/dentin tissue engineering using biomineralization principles. Biomaterials development such as calcium phosphates or polymeric materials to regenerate bone and dentin
4. Biomineralization, Post-translational modifications of non-collagenous proteins in bone and dentin: Role of protein kinases in bone and dentin formation; Role of phosphorylation in biomineralization
5. Pulp tissue regeneration, develop strategies to achieve better endodontic therapies using biomaterials versus cellular approaches

Juan Taboas

Dr. Taboas' research interests are regeneration of mineralized tissue and soft tissues that interface with bone and dentin, such as mandibular condylar cartilage and tooth pulp. They study pathogenesis of skeletal diseases with engineered tissue models to develop interventions, and hold several patents for culture systems, scaffold fabrication, and regenerative devices.

Konstantinos Verdelis

Dr. Verdelis' research has focused on the use of microcomputed tomography for analysis of bones and teeth morphometry and densitometry, as well as analysis of biomaterials and soft tissues

after preparation. Present research interests also include optimization of cone beam CT parameters for endodontics-related imaging and assessment of simulated clinical procedures in endodontics outcome through high resolution imaging. His interests have in the past included mineral and matrix changes in the dentin and enamel of developing teeth using Fourier Transform Infrared and Raman imaging coupled with microcomputed tomography and histology. At present he pursues analysis of similar changes in developing enamel via high resolution vibrational spectroscopy imaging. He currently serves as the director for the microcomputed tomography core at the School of Dental Medicine.

Alexandre R. Vieira

Dr. Vieira's research interests include the reasons why individuals born with clefts and/or dental anomalies are more susceptible to cancer later in life; epigenetics influence on cleft lip and palate; and the impact of genetics on painful responses and resistance to certain drug treatments.

Seth M. 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 normal-range craniofacial traits (e.g., the size and shape of facial features) and congenital anomalies that affect the head and face (e.g., cleft palate).

Samer Zaky

Instead of the subjective pain tests used to determine the status of the dental pulp inflammation, Dr. Zaky's interest focuses on finding an objective chairside measurement that can help to tell apart reversible from irreversible pulpitis. Finding such objective measurement is expected to mitigate devitalization (root canal treatment) of many teeth whose inflamed core still maintains reversibility potential. For an objective measurement, Dr. Zaky's research is looking for correlation between neurotransmitters in the gingival crevicular fluid and the inflammatory markers within the dental pulp tissue on the spatial single-cell level.

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KEYNOTE SPEAKER

THE ADDED VALUE OF CALCIUM SILICATES IN VITAL PULP THERAPY

Imad About, Phd
School of Dental Medicine
Aix-Marseille University
Professor of Oral Biology and Director of the research laboratory in the School of Dental Medicine at Aix-Marseille University, France

Imad About, PhD, is professor of oral biology at Aix-Marseille University and responsible of the research Laboratory at the school of dental medicine, Marseille, France.

He is associate editor of Clinical Oral Investigations, president of the Pan European Region and past-president of both the Pulp Biology and Regeneration Group and the Continental European Division of the International Association for Dental Research.

The research group of Dr. About is involved in investigating the pulp tissue regeneration and the effects of pulp capping materials on modulating the balance between pulp inflammation and regeneration.

Dr. Imad About is actively involved in developing new dental materials for tissue regeneration and he is one of the main academic members involved in Biodentine development.

Dr. About is renowned speaker and frequently invited to major international conferences. He is a well-recognized expert in pulp tissue regeneration. He published more than 220 peer reviewed papers, abstracts and book chapters. He also edited a book on Biodentine in 2021.

Dr. About was the winner of the European Society of Endodontology annual research grant in 2012. In recognition of his investigations in pulp biology, he has been awarded the "Distinguished scientist award" of the Pulp Biology and Regeneration Group in 2018. He was also the winner of the Journal of Endodontics Awards in the category of Basic Research: Biology in 2022.

Vital pulp treatment has the potential to significantly extend the life of a tooth. However, preserving pulp vitality following exposures or caries remains as a real challenge where healing is highly dependent on the inflammation degree. The balance between inflammation and regeneration is crucial in determining the overall pulp healing capacity within an inextensible environment.

Tricalcium silicates are now considered as the materials of choice for vital pulp therapy due to their chemical, physical and bioactive properties. In addition to the hermetic seal they provide once applied onto the pulp, newly reported data demonstrated that they have an anti-inflammatory potential which creates the adequate conditions for dentin-pulp regeneration and successful clinical outcome. Moreover, the recently demonstrated pulp capacity to kill infiltrating cariogenic bacteria, contributes to our understanding of how these materials push the limits of vital pulp therapy through their successful use in treating dental trauma with pulp exposure and irreversible pulpitis.

This presentation will demonstrate the pulp regeneration potential and its capacity to kill cariogenic bacteria. It will highlight Calcium silicate bioactive properties, demonstrate their anti-inflammatory effects and how it decreases post-operative pain when used as direct pulp capping material.

Finally, this presentation will explain how the capping material choice affects the balance between pulp inflammation and regeneration and the overall outcome of vital pulp therapy.

KEYNOTE SPEAKER

REGENERATIVE ENDODONTICS: JOINING BASIC AND CLINICAL SCIENCES

Anibal R Diogenes, DDS, MS, PhD
University of Texas Health Science Center at San Antonio
Director, Advanced Program in Endodontics
Diplomate, American Board of Endodontics

Dr. Anibal Diogenes received his DDS from UFPE in Brazil, his MS in molecular biology from the University of Nebraska. He earned his PhD in pharmacology and a certificate in endodontics from the University of Texas Health Science Center at San Antonio.

Dr. Diogenes is a tenured professor and vice-chair in the Department of Endodontics at the University of Texas Health Science Center at San Antonio. His areas of research include, inflammation, pain and regenerative endodontics. He is also a director of the American Board of Endodontics.

Regenerative endodontics represents a paradigm shift in endodontics that has the primary goal of preservation or reestablishment of homeostatic physiological pulp functions. An inflamed dental pulp has been thought to be incapable of healing. This dogma is even reflected in the diagnostic term: "irreversible pulpitis". Also, pulp necrosis has been a condition that required root canal spaces to be filled with inert materials to prevent growth of microorganisms. Unfortunately, obturation also prevents the growth of patients own living tissues that could bring back important physiological functions lost due to partial or total pulp necrosis. Advancements in biological understanding, techniques and materials have made regenerative endodontic procedures (vital pulp therapies and revitalization) alternatives to teeth requiring non-surgical endodontic treatment. In this lecture, the application of regenerative endodontic approaches will be discussed in light of real clinical scenarios, presenting the advantages and disadvantages of these procedures and their possible pitfalls while contrasting with what is well-known in more "traditional" non-surgical endodontic therapies.

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