

HARVARD

School of Dental Medicine

OFFICE OF RESEARCH

Researchers Explore Immune Checkpoint Therapy to Treat Aggressive Form of Oral Precancerous Disease

In one of the first clinical trials to explore treatment of an aggressive form of oral precancer with immune checkpoint therapy (ICT), researchers from the Harvard School of Dental Medicine (HSDM), Dana-Farber Cancer Institute, and other collaborators found promising results for treating a high-risk oral precancerous disease with ICT.

Their study, "Nivolumab for Patients With High-Risk Oral Leukoplakia" published in *JAMA Oncology*, followed the treatment of 33 patients with high-risk oral proliferative verrucous leukoplakia (PVL), an uncommon but aggressive oral precancerous disease characterized by its tendency to progress to invasive oral squamous cell carcinoma in at least 60% of patients.

PVL first appears as white patches usually on the gums, but may occur anywhere in the mouth, spreading over time. The condition is particularly difficult to control because by the time it is finally diagnosed, the patches are very large and have often spread to multiple areas of the mouth. To date, there have been no therapies shown to affect the progression of the disease.

“This is the first study of its kind that treated this condition which is highly associated with cancer development, using systemic immunotherapy rather than surgery or laser,” said Dr. Sook Bin Woo, co-author of the article and associate professor of Oral Medicine, Infection, and Immunity at HSDM and program director of Oral and Maxillofacial Pathology based at Brigham and Women’s Hospital.

After treating leukoplakia lesions with Nivolumab, a targeted therapy drug that acts as an immune checkpoint inhibitor, findings showed a positive clinical response. Twelve patients (36%) demonstrated the best overall response in the change in their clinical-pathologic composite score, with 3 (9%) demonstrating a greater than 80% reduction in composite score. Two patients had complete resolution of at least one target lesion.

Although few patients had complete lesion regression, Woo says this encouraging trial lays the groundwork for greater study by demonstrating potential clinical activity and acceptable safety with the use of ICT in a population with high-risk precancer.

As cohort Principal Investigator for the InAdvance study 22-200, Woo is leading a biobanking effort launched to evaluate state-of-the-art early detection and precision prevention strategies for people at higher risk of developing cancer and to foster collaboration between researchers. She is building a cohort of oral leukoplakia patients, collecting patient-reported data, medical record data, family history, and biospecimen samples. The InAdvance Study is part of the Centers for Early Detection and Interception of Cancer (CEDI) within the Dana Farber Cancer Institute and will be a unique resource to better understand oral precancerous lesions, progression, and treatment.



Dr. Sook Bin Woo is a cohort Principal Investigator for the InAdvance study 22-200.

GET TO KNOW A RESEARCHER



Dr. Sudipta Baroi is a research fellow in the Department of Oral Medicine, Infection, and Immunity. He works in the Baron-Gori Lab researching skeletal stem cell populations.

Q: What is your educational and research background?

A: I am currently working on skeletal stem cells as a research fellow in Dr. Baron and Dr. Gori's lab at HSDM. I did my PhD in Molecular Medicine in Dr. Beata Lecka-Czernik's lab at the University of Toledo College of

Medicine and Life Sciences. During my PhD, I investigated the role of nuclear receptor PPAR γ in osteocytes in regulation of energy metabolism, bone homeostasis and in cancer metastasis.

I did my B.Pharm and M.Pharm. in Pharmaceutics from University of Dhaka, Bangladesh and was briefly a lecturer for the Department of Pharmacy at Ranada Prasad Shaha University, Bangladesh before joining the PhD program. I studied small molecule targeting of pathways for a breast cancer metastasis model for my Master's program.

Q: Can you share a summary of your current project(s)?

A: In my ongoing project, I am investigating the distinct skeletal stem cell populations residing within our bone structure and studying what role a specific protein of interest plays in these stem populations, particularly, in the context of fracture healing and bone homeostasis.

Furthermore, I am also interested in how we can harness these cellular signaling mechanisms to provide viable solutions to patients with skeletal fragility and fractures.

Q: What is something interesting that you've learned/discovered recently?

A: Part of my recent work was published in *PNAS* in November 2023, where we unveiled the crucial role Sfrp4 plays in preserving the functionality of a particular stem cell population staple for fracture repair and healing. The discovery is very interesting as it provides us with an outstanding opportunity to understand

the intricate mechanisms underlying bone regeneration and repair. Additionally, it holds profound implications to advance therapeutic options for treating human diseases of impaired healing, fragility, and fractures. I'm very excited to continue the project forward.

Q: What is your favorite thing about the HSDM/Harvard community?

A: The vast array of resources available for research at HSDM/HMS and in the affiliated hospitals and institutes are truly remarkable and this is definitely my favorite thing about the HSDM/Harvard community. Next in line for favorite things would be the The Harvard Medical Postdoc Association (HMPA), the public health cafeteria, and the table tennis set-up in the HSDM lobby.

Q: Describe your role at HMPA and how you got involved.

A: I currently serve as chair of the HMPA Committee for Professional Development and interim vice-chair of the HMPA. As part of HMPA, we organize seminars, workshops, networking events, etc. to help our fellow postdocs have a better understanding of their career options and find the best fit that matches their skills and interests to have a successful career. We also do postdoc interviews and run surveys to understand the needs and problems faced by postdocs and advocate for postdoc benefits and well-being.

After joining Harvard, I learned about HMPA through a friend of mine and Dr. Emily Moore from Dr. Rosen lab helped me in getting involved with the organization. I started as a member of the HMPA Entrepreneurship Committee and still work closely with them in organizing different events.

Q: What are your future career goals?

A: In the future, I would like to have my independent research lab and study molecular mechanisms and signaling pathways regulating bone and develop novel therapeutic options for human diseases associated with bone fragility and impaired bone healing. I'm also working on developing a start-up of my own. Harvard i-labs has been a great resource. I am excited to see how it unfolds and contributes to changing the world for better.

DEPARTMENT NEWS

Developmental Biology

Rachel Korman, a second year pediatric dentistry resident, will present her research titled "Caries Risk in Children with a Dual-Diagnosis of Down Syndrome and Autism Spectrum Disorder" at the International Conference of the Trisomy 21 Research Society, in Rome, Italy this June. Korman's mentors for the project are Isabelle Chase, assistant professor of Developmental Biology at HSDM, and Nicolas Oreskovic, MPH08, assistant professor of pediatrics at HMS.



Developmental Biology researchers Qian Cong, an instructor and member of the Yang Lab, and Emily Moore, a research fellow in the Rosen Lab, have recently accepted faculty positions and will be starting their independent research laboratories. Cong starts her assistant professorship at Texas A&M School of Dentistry in July. Her lab will be in the Department of Biomedical Sciences and will work to understand how abnormal regulation of cell signaling leads to various bone diseases. She is

particularly interested in studying injury-induced immune responses and cell fate determination in tendons and muscles. Moore will start her tenure-track research faculty position in the Department of Biology at Northeastern University in January 2025. Her lab will focus on studying the role of mechanical loading and associated cell signaling pathways to protect or regenerate bone and dental tissues with age.

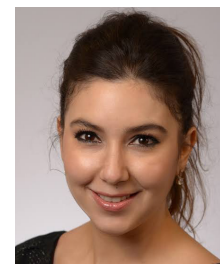
Oral and Maxillofacial Surgery



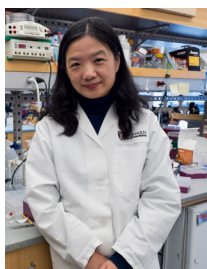
Fernando Guastaldi, an assistant professor of Oral and Maxillofacial Surgery, was elected to serve as vice president for the Boston Section in the 2023 American Association for Dental, Oral, and Craniofacial Research (AADOCR) general election. Guastaldi's term officially began following the the conclusion of the 2024 IADR/AADOCR/CADR General Session & Exhibition in March. As a Section officer, Guastaldi assists in the governing the of the Boston Section, managing Section activities and helping ensure the growth and engagement of the region. Specifically, the vice president is responsible for gathering nominations for other elected officers and overseeing the Section's budget. The Boston Section has a long history with AADOCR, and was the second city Section to be founded on December 17, 1920, the same month the AADOCR was established. Today, there are 44 Sections across the country.

Oral Health Policy and Epidemiology

Steffany Chamut, an instructor in Oral Health Policy and Epidemiology, presented research titled " Global Medical-Dental Integration, Nutrition and Healthy Aging" at the Global Oral Health Forum II this April. Led by the University of Pennsylvania Penn Dental Medicine's Center for Integrative Global Oral Health, the forum included stakeholders from over 20 countries including educators, chief dental officers, government officials, and other leaders responsible for organizing and implementing regional oral health strategies and policies.



GRANTS AND AWARDS



The American Association for the Advancement of Science (AAAS) has elected Yingzi Yang, associate dean for Research and professor of Developmental Biology at HSDM, to the 2023 cohort of AAAS Fellows. The lifetime honor is considered to be one of the most prestigious a U.S. scientist can receive. This year's cohort includes 502 scientists, engineers, and innovators across 24 disciplines. Each year, Fellows are elected by their peers for work that is scientifically or socially distinguished. Yang was selected for her contributions to the understanding of molecular mechanisms underlying Wnt and Hedgehog signaling in skeletal biology and diseases. Through her research, she has made substantial contributions to understanding how cells communicate with each other to ensure proper control of embryonic development and physiological functions of the skeleton and liver. Her work has successfully bridged discoveries of fundamental mechanisms with the characterization and treatment of diseases.

A team of HSDM researchers led by Magda Feres, chair of the Department of Oral Medicine, Infection, and Immunity (OMII), were recently selected for the HMS Dean's Innovation Award. The award supports innovative applications of artificial intelligence (AI) that enhance learning, improve health outcomes, increase productivity, and accelerate biomedical discoveries. The research team includes collaborators Balazs Feher, a research fellow in OMII, Chia-Yu (Jennifer) Chen, director of Predoctoral Periodontology, and Sang Lee, assistant dean for Clinical Affairs.



With the \$100,000 award, Feres and the team will explore simulation-based learning in dental education through generative AI. The project uses deidentified patient data from the Harvard Dental Center's (HDC) electronic dental records to engineer and fine tune a large language model (LLM) to create synthetic patient cases with dental records, clinical parameters, and imaging data that can be used for teaching.

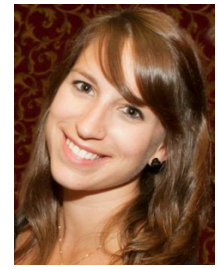


Magda Feres, chair of OMII, Eduardo H. de Souza Oliveira, research associate, and collaborators from the University of São Paulo Bauro School of Dentistry, have been named awardees of the 2024 Lemann Brazil Research Fund. Their project, "Exploring the Effects of CaneStat, a Novel Hybrid Protein, on Oral Proteome Dynamics and Microbiome Composition," evaluates the impact of CaneStat mouthwash on patients' oral proteome/microbiome. Established in 2016, the Lemann Brazil Research Fund supports Brazil-related research in all areas related to education, as well as research in any other disciplinary area undertaken with a Brazilian colleague.

This year's Donald B. Giddon Lecture in Behavioral Medicine and Dentistry featured a keynote presentation from Janice Lee, the clinical director and chief of the Craniofacial Anomalies and Regeneration Section at the National Institute of Dental and Craniofacial Research (NIDCR). Lee's lecture, "A Paradigm Shift – Modular Integration to Predict Facial Development," discussed the current challenges in managing craniofacial anomalies and the role of morphological integration in predicting facial development. She also discussed opportunities at the NIDCR for students interested in furthering their careers in research. The annual lectureship was established through the Dr. Donald B. Giddon Teaching Fund to support HSDM's teaching programs.



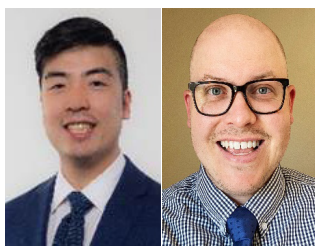
Emily Moore, a research fellow in the Department of Developmental Biology, received the Advances in Mineral Metabolism (AIMM) 2024 Young Investigator Award during the AIMM-ASBMR John Haddad Young Investigator Meeting this April in Colorado. At the meeting, Moore gave an oral presentation of her work titled "Understanding periosteal signaling to harness its osteogenic potential."



Several HSDM students received awards at the 2024 American Academy of Oral Medicine (AAOM) Annual Conference this April. Abdulrahman Nakshabandi, DMSc26, an Oral Medicine/Oral Oncology candidate, and Joud Omari, DMSc24, an Oral and Maxillofacial Pathology candidate, were both awarded Case Report Awards for their research. Case Report Awards were given to the five best research trainee submissions, who were then invited to give an oral case presentation at the AAOM meeting and received a monetary prize. Nakshabandi was recognized for his project, "The

Intended and Incidental: A Case of Oral Mucosal Melanoma and Lung Adenocarcinoma." Omari received the award for her research titled, "Sarcoidosis affecting the maxilla: A report of two cases," which she completed with Sook-Bin Woo, a professor of Oral Medicine, Infection, and Immunity.

Malak Al-Hadlaq, DMSc24, an Oral Medicine and Dentistry candidate, was also recognized with the Robert and Kay Schattner Award for having the best oral presentation of an original investigation for her project, "Expression of Specialized Pro-resolving Lipid Mediators and Their Receptors on Oral Neutrophils in Oral Lichen Planus." The presentation shared findings of less specialized pro-resolving lipid mediators (SPMs) and decreased expression of the ERV1 receptor on oral neutrophils in cases of oral lichen planus (OLP) compared to controls. These results suggest a failure of the inflammation resolution pathway in OLP and provide a foundation for future translational studies using SPMs as a treatment option for OLP.



Two second year pediatric dentistry residents at Boston Children's Hospital were chosen as finalists in the Graduate Student Research Award competition for the American Academy of Pediatric Dentistry annual meeting. Albert Chen was selected for his research titled, "Long-term Outcomes of Traumatized Permanent Maxillary Incisors" and Joshua Vert was chosen for his research titled, "Short Bowel Syndrome: An Analysis of the Oral Microbiome." Chen and Vert presented their research at the meeting in Toronto, Canada in May.

A group of nine graduates from the HSDM class of 2024 received Honors in Research for their thesis projects that went above and beyond a typical scholarly endeavor. From the DMSc program, those graduating with Honors in Research are Jessica Latimer, Periodontology; Joad Omari, Oral Pathology; Kedkanya Mesil, Oral Pathology; Nicha Tokavanich, Orthodontics; and Ridhima Seth, Research Academy. The students graduating with Honors in Research from the DMD program are Sapna Nath, Lisbeth Garcia, Abigail McVicar, and Dahee Chung. Congratulations to these students and to the entire class of 2024 for their outstanding achievements!



STUDENT RESEARCH DAY 2024

Basic/Translational Research Awards

Kedkanya Mesil, DMSc24, Oral Pathology

The Role of Bone Morphogenetic Protein and Activin Membrane-Bound Inhibitor (BAMBI) in PTH Signaling in Bone

Ridhima Seth, DMSc24, Research Academy

PTH Signaling in Ctsk+ Lineage Cells is Critical For Skeletal Homeostasis and Tooth Formation and Eruption

Joud Omari, DMSc24, Oral Pathology

Blockade of a Novel T Cell-Mediated Pathway Prevents Oral Carcinogenesis

Natalie Yam, MMSc24, Periodontology

Comparative Analysis of Sharpening Devices for Periodontal Hand Instruments and Their Impact on Root Surface Roughness: An In Vitro Study

Abigail McVicar, DMD24

Investigation of The Age-Related Changes in Immune Function in Age-Associated Periodontal Disease Reveals Fgf2 Treatment as a Potential Therapeutic Approach For Aging-Associated Periodontal Disease

Clinical Research Awards

Grace Huang, MMSc24, Orthodontics

Individualizing Aligner Change Schedule: A Single-Blind, Randomized Controlled Trial

Lindsey Pius, DMD24

Arthroscopic and Histologic Findings Associated with the Temporomandibular Joint Direct Joint Loading Test

Public Health and Dental Education Awards

Precious Ettah, MMSc24, Dental Health Education

Impact of Health Professional Shortage Area Scores on Dental Services at Federally Qualified Health Centers: A Comparison of Urban and Rural Areas

Sheridan Danquah, DMD24

Can Remote Learning and Low Fidelity Simulation Trainers Improve Confidence and Fundamental Skills in TMJ Arthroscopy?



Student Research Day poster presentations



Basic/Translational Research Award recipients



Clinical Research Award recipients



Public Health and Dental Education Award recipient (Precious Ettah not pictured)

PUBLICATIONS

Developmental Biology

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Oral Medicine, Infection, and Immunity

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