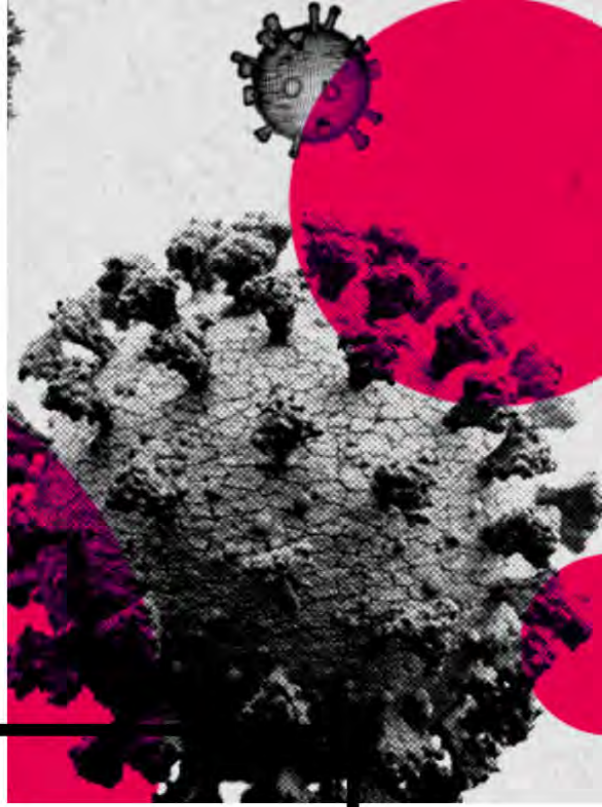
The EXPLORER

JOURNAL OF DENTAL STUDENT AND FACULTY RESEARCH
EDITION XIII | SPRING 2022

10-11 RESEARCHING IN COVID

UCLA School of Dentistry



THE EXPLORER JOURNAL

EDITION XIII

THE EXPLORER TEAM

UCLA School of Dentistry

Joonhee Kim, Editor-In-Chief, Class of 2023

Joonhee Kim followed his dad to the U.S. and grew up in Loma Linda. He is a double Bruin, got a BS at UCLA and now at UCLA SOD. He likes to watch Marvel movies, hang out with friends, and watch the English Premier League. He is passionate about research and improving the oral health of his patients. He is interested in exploring endodontics in the near future.

Menaka Tandon, Editor-In-Chief, Class of 2023

Menaka Tandon is a Bay Area native, Texas educated (go Aggies!), and SoCal loving dental student who enjoys hiking, beach walking, and relaxing with a good book. She is very passionate about mentorship and improving the dental health of the community around her, which she hopes to continue doing as an orthodontist in the future.

Maryam Esmaeili, Contributing Editor, Class of 2022

Maryam Esmaeili was born and raised in Iran. She received her first DDS degree back home and continued her academic path by attending an OMFS residency program; however, she had to decline the offer to move to the states. Maryam graduated with a second DDS degree from UCLA and she is hoping to pursue her education in OMFS in the future. Maryam is a great cook and enjoys hosting dinner parties with her friends.

Lauren Kim, Contributing Editor, Class of 2023

Lauren Kim grew up in Irvine, California and attended college at the University of Pennsylvania. Lauren plays the violin and loves to travel. Her sweet tooth obsessions at Trader Joe's include chocolate covered espresso beans and boba ice cream. Lauren hopes to provide care for underserved populations and empower patients to take charge of their oral health and long-term wellbeing.

Anthony Nguyen, Contributing Editor, Class of 2025

Anthony (Tony) Nguyen was born in Socal and is a triple Bruin! Go Bruins! Tony enjoys climbing and running and has run three marathons. He is excited about learning more about dentistry and serving the people within his community.

Nida-e-Haque Mahmud, Layout Editor, Class of 2023

Nida was born and raised in Pakistan. After graduating dental school back home, she realized she wanted to grow more as a dental professional and started her journey towards gaining a license in the United States, which brought her to UCLA. Nida's favorite part about dentistry is connecting with her patients and understanding their diverse backgrounds. She loves volunteering on the weekends and spending time with the less privileged.

Laura Yoon, Layout Editor, Class of 2024

Laura Yoon immigrated from South Korea and grew up in SoCal. She enjoys watching movies, inviting friends for dinner, and drawing on her iPad. Laura is interested in working with families to encourage heathy oral hygiene habits and to promote oral care in children through fun and creative ways.

Sophia Eliopulos, Layout Editor, Class of 2025

Sophia Eliopulos was born and raised in San Diego and is a double bruin. You can find her hitting the slopes or shredding some waves in her free time. She is passionate about film photography and is an avid dog lover. As a dental student, she enjoys volunteering at OHI events for underserved children. She looks forward to positively impacting her patients in the clinic soon!

Caitlin Neapole, Layout Editor, Class of 2025

Caitlin Neapole is a dual citizen to the UK and Canada. She loves working out with friends and going to the beach. Caitlin is excited to explore all the different fields within dentistry and is passionate about promoting holistic health and wellbeing.

A LETTER FROM THE EDITORS

Dear Readers,

We are proud to present to you the 13th Edition of The Explorer Journal featuring dental students and faculty research. After a 3-year break, we are back with a BANG and are so excited for you to read about all the dental research being done at UCLA! Throughout the pandemic, UCLA School of Dentistry has been a forefront in the research of COVID-19 testing and received funding from the National Institutes of Health (NIH) for various COVID-19 related projects. We are proud to say we have been able to play an important role in stopping the spread and protecting loved ones, all around the world.

We would like to thank our very wonderful team of writers, editors, and designers for their hard work throughout every step of this process. We simply couldn't have done it without you! Along with their hard work, we would like to extend our gratitude to Dean Paul Krebsbach and Dr. Wong, our faculty advisor, for their continued support of The Explorer and their determination to further the field of dental research.

Lastly, with the start of a new school year coming up soon, we would like to wish everyone the best of luck. To fellow students, you inspire us to be a better version of ourselves every day!

Sincerely,

Menaka Tandon
Joonhee Kim
The Explorer Editors-in-Chief

A LETTER FROM DEAN KREBSBACH

Dear Readers,

I would like to introduce the first issue of The Explorer to be published since the pandemic began. I was invited to comment on how COVID-19 has impacted our School from several different angles.

I remember when COVID-19 first began to make headway here in the US, and it was crucial to develop an immediate plan for remote learning. A large group of faculty got together to determine how we could continue our education for students while complying with the LA County Department of Public Health requirements. There were a lot of behind-the-scenes activities, including several tests in the clinics and preclinical labs to determine the air quality and measuring the spaces to determine capacity. Staff and faculty worked diligently to design a way to stay physically distant (6ft) while continuing education in the preclinical lab. We redesigned our preclinical areas with Plexiglass guards and an enhanced PPE plan. Through our tireless efforts, we earned approval from the University to open the School and continue the education of our students. As you may know, many other dental schools were still holding classes remotely at this point, however, I fully believe it is essential to have our students attend the preclinical lab so that they can arrive at the clinic well-prepared.

The guidelines for research at the School were driven by UCLA Vice Chancellor for Research, Roger Wakimoto. His team set the parameters for the University. During the pandemic, our research labs were unable to accept volunteers and undergraduate students and therefore focused on supporting postdoctoral, graduate, and dental students. Researchers had to work unusual hours and follow a rotation system according to the social distancing rules. Although the pandemic did slow the work down, it gave our researchers and students the time to think, read, and write. I am proud to say that our School actually produced more publications and submitted more grants during this time. It was difficult for scientists to work within the COVID restrictions, but when one door closes, another door usually opens. This is especially true because new areas of study were opened to us during this time. A few of our investigators received COVID-specific grants which were not available before. After two years of following the strict COVID-19 protocols, the School is currently resuming normal research activities.

I am pleased that all members of the UCLA Dentistry community showed great persistence and resiliency during the pandemic, and I look forward to another fantastic year with new discoveries in our laboratories, outstanding learning in our classrooms, and excellent patient care in our clinics.

Sincerely,

Paul H. Krebsbach

Paul H. Krebsbach, DDS, PhD
Dean and Professor

AN INTERVIEW WITH DR. DAVID WONG

Dear Readers,

I am so excited to announce the release of *The Explorer* again! It is exciting that two versions will be released in a year for the first time under the leadership of our Editor-in-chiefs Menaka and Joonhee. They have decided that the focus of this first version will be the impact of pandemic on our research.

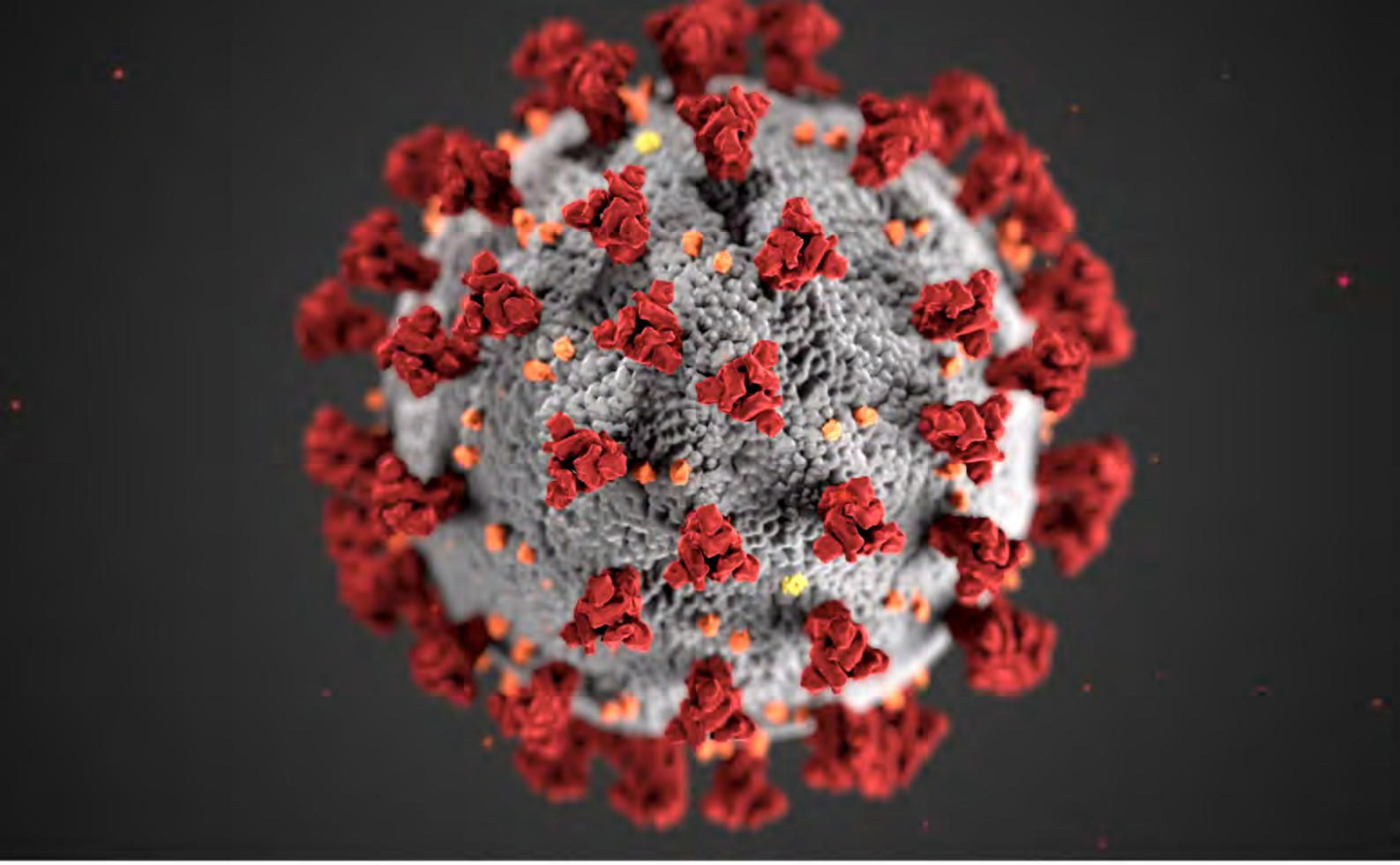
The UCLA School of Dentistry has a stellar record of grant submission each year. During the pandemic, the grant submission by our faculty escalated by 15%, which is a significant increase. When we look back at the nature and content of the grant proposals, several faculties chose the research topics to COVID-19. It is important to realize that our dental school received COVID-related awards as well. The School of Dentistry received NIH COVID-19 RADx grants by working on novel technology to detect viral pathogens. Publications too saw an increased during the pandemic, researchers appeared to have more time working on manuscript and grant submission. It was a difficult time during the pandemic with only essential experiments were carried out, social distancing in place and with mandatory facial masking regulation. Despite these difficulties, UCLA researchers worked diligently in a remote environment and had great success with grant submissions. We took this as a personal challenge and handled the pandemic by working on what they can address. Not only our community sustained enthusiasm for research, we overcame challenges and pivoted to a new direction of research with COVID-19.

I like to comment on the salivary diagnostics as well. My lab has worked with saliva for early detection of cancer and we developed few projects through NIH grants. It is exciting to see that salivary diagnostics has its utility with the coronavirus during the pandemic. Scientists in computational medicine perform the campus-wide tests with our salivary samples for early detection of COVID-19. While molecular tests using nasal swab provide information about our genomic RNA to pathogens and antigen, our salivary tests can provide more information and are in the final stage of NIH approval. These tests detect viral RNA, antigen, antibody, and recently neutralizing antibody to the virus. They cover the entire spectrum and address whether the pathogen is shedding or whether antibody is neutralizing the pathogen. Do we have protection? Can we block the virus from entering our body? These are important questions people want to know. We need to decide whether to stay home and quarantine or aboard the plane. With one drop of saliva, the entire spectrum of COVID19 is known and the test offers comprehensive information about the pathogen. It is astounding that saliva can provide this much information. I can say this is a proud moment in dentistry.

Research is always from the heart. The school as a whole has always anchored itself on scholarship from the dean, division chairs, and faculty. They are clinician scientists that are federally funded and they have a reputation of leaders in their field. Our dental students and residents are taught and educated by instructors and professors who are leaders in the field. This makes a true difference. They not only learn good clinical skills, but also are educated by leaders in various disciplines in dentistry, which is truly inspirational. Researchers work like these are answering a call and carry out research that are impactful. Our school has the culture, intellectual fabric that makes UCLA dentistry for what it is.

Sincerely,

David T.W. Wong
Professor
Associate Dean for Research



The Virology of SARS-CoV-2

Menaka Tandon
Class of '23

Severe acute respiratory syndrome coronavirus 2, also known as SARS-CoV-2, is the virus that caused coronavirus disease in 2019 (COVID-19). Coronaviruses belong to the "Coronaviridae family", which causes various diseases such as the common cold, Severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS). According to the World Health Organization (WHO), the main transmission routes for SARS-CoV-2 are droplets and direct contact, airborne transmission, and fecal and oral transmission. The main effect of SARS-CoV-2 is in human respiratory system cells but, new studies have revealed the possibility of impact on cells of the gastrointestinal tract, kidney system, liver, pancreas, eyes, and brain. So far, no definitive curative treatment has been discovered for COVID-19 but there has been a breakthrough with vaccines aiming to reduce complications/symptoms of disease.

Early investigation of the virus's origin led to the idea that SARS-CoV-2 had been transferred to humans by bats, however this has not been confirmed. Usually, coronavirus transmission from animal to human does not lead to disease or additional transmission but on rare occasions, can evolve and replicate in humans and cause disease. It is more likely for the virus to have evolved through some type of immediate host where it underwent a few

rounds of replication and acquired mutations that allowed the virus to efficiently infect and replicate in humans. This most likely happened in areas with high density of people and frequent interactions among animals and public health officials predict this trend will likely continue to happen. This virus has truly caused a global crisis and impacted every living individual in one way or another making it important that we understand the virology of SARS-CoV-2 and reflect on past events so that we can better prepare for the future.

The virus, SARS-CoV-2, is coated by an envelope with spiked glycoproteins and membrane proteins. When viewed under an electron microscope, this envelope gives the virus a crown like appearance and this is how this virus received the name corona, which is the Latin term for crown. Inside the viral envelope is a nucleocapsid complex formed between the viral RNA genome and nucleic capsid protein. The coronavirus genome itself consists of single, positive stranded RNA viruses. Positive stranded RNA viruses are viruses with a viral genome that can be directly used for translation. The SARS-CoV-2 virus is composed of 4 main structures: nucleocapsid, spike(s), membrane, and an envelope. Of these, the spike protein is the most well-studied as it mediates binding and fusion of the viral and host cell membrane to deliver the viral RNA genome into the cytoplasm (1).

Each spike is made up of an S glycoprotein (composed of S1 and S2 sub-unit). The S1 subunit binds to the receptor through its receptor binding domain (RBD) and the S2 sub-unit mediates the viral cell membrane fusion between the viral envelope and the target cell membrane. S-Spike proteins bind to angiotensin-converting enzyme 2 (ACE2), are cleaved via proteolysis by Cathepsin, and then fuse with the host's cell membrane. After penetration of the cell membrane, viral RNA genetic material is released into the host cell and the transcription process begins. The virus uses the cell's resources and continues to multiply until the host cell is infected and destroyed (3).

This is a much more simplified explanation of the virology of SARS-CoV-2 whereas viral replication involves many more complicated mechanisms. For this reason, it makes sense that there is a higher chance for mutation to occur in a virus. However, coronavirus has evolved and is able to use its unique proofreading mechanism (differing from most viruses) to keep viruses from accumulating mutations, keeping mutation rates low (8-10 nucleotide differences) and remaining relatively stable. Another unique ability that these viruses have is they can recombine. This means that if two viruses happen to infect the same cell, coronavirus creates a "new single RNA strand" from these parental strands, and this results in a

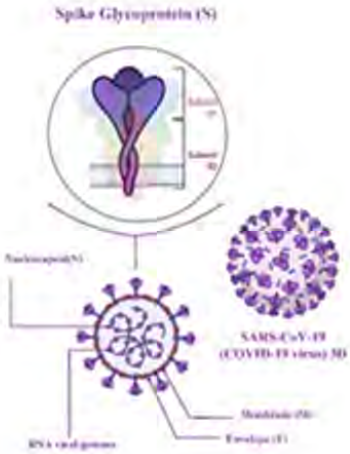


Figure 1. Detailed Coronavirus Diagram with spike glycoproteins (3).

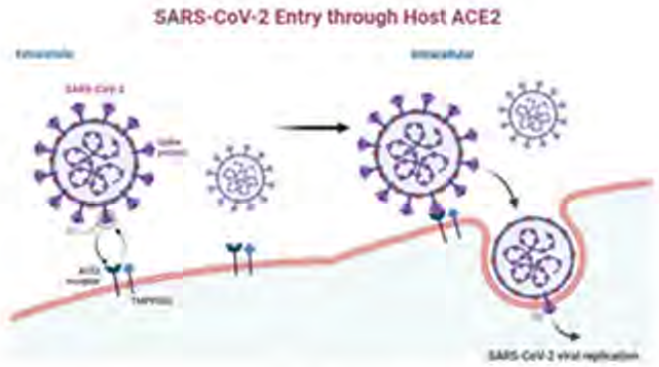


Figure 2. Mechanism of Virus Entry (3).

new virus and a continuation of the transmission cycle (2). This is one of the reasons SARS-CoV-2 has been so difficult to contain.

It is shocking to think that it has been over two years since the start of the SARS-CoV-2 global pandemic because so much has changed in the face of research. Further investigation of coronavirus has allowed us to understand the virology of SARS-CoV-2 and help gear treatment, prevention, and vaccination towards successfully eradicating the disease. Although we have come a far way, we have an even longer way to go as no treatment has been found, and the virus continues to replicate and produce new variants.

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AN INTERVIEW WITH DR. TING-TING WU

Ting Ting Wu, Ph.D.
Associate Professor-in-Residence, Molecular and Medical Pharmacology, UCLA
Associate Professor-in-Residency, Medicine, UCLA

Of the many distinguished professors at UCLA, we had the pleasure of interviewing Dr.Ting-Ting Wu, an Associate Professor in Molecular and Medical Pharmacology at UCLA. Dr. Wu received her undergraduate degree from National Taiwan University and her Ph.D in Cell and Molecular Biology from the University of Pennsylvania. Subsequently, she became a post-doctoral fellow in the lab of Dr. Ren Sun at UCLA. Dr. Wu is an expert in the field of virology and had a hand in creating COVID-19 education modules to provide us students with the most up to date information and specific patient care protocols related to the pandemic.

What are your opinions on the way we are approaching new variants, and what do you think we should do differently?

I think that vaccines are doing a great job to protect infected individuals against hospitalizations. We have multiple options for treatments depending on the stages of the infection to reduce the disease severity in high risk individuals. There are a lot of activities on the development of new generations of vaccines that will provide broad protection, less sensitive to the emergency of new variants.newMasks are still a good strategy for us to keep high risk individuals safe. We need to continue emphasizing the benefits of vaccines and also be educated to know the options for treatments and recognize risk factors for severe diseases. And we should continue supporting the research on vaccines and antivirals.

Do you predict there will be a treatment for SARS-CoV-2? What barriers do you see us facing to get to this point?

There are several available treatments for the active SARS-CoV2 replication phase, such as antibody cocktails, remdesivir, and paxlovid. These are good options for infected individuals that have high risks to develop severe diseases. Steroids are an option for hospitalized patients who progress beyond the phase of active viral replication and need supplemental oxygen. We need to raise awareness of these available treatments for high risk individuals and understand how each of those treatments is used and make it easier for the people who need treatments to get them. Treatments for SARS-CoV2 are also an evolving and active research area. There will be continuous new types of treatments developed in the future.

How do you suggest we protect ourselves from getting the virus and transmitting it to others?

I think that the point is not about protecting us from getting infected. It is pretty clear now that the current mRNA vaccines protect us from severe diseases so we will not jam hospitals and prevent them from treating other diseases. Vaccine-mediated protection against infections or symptoms is moderate. However, we need to understand that providing sterilizing immunity to complete block infection has not been the primary purpose of vaccines. The current vaccines have done an amazing job at keeping infected individuals from hospitalization. And the public needs to understand this. Just imagine the world without the current SARS-CoV2 vaccines. This is not to say that we are going to stop working on vaccines. Scientific community is continuously making efforts to develop more effective vaccines. This goes without saying that if you feel sick or infected, wear masks to reduce transmission of viruses. There are three additional suggestions I have regarding protecting ourselves and others: get vaccinated, understand the risk factors for severe diseases, and be aware of treatment options.

Researching in COVID

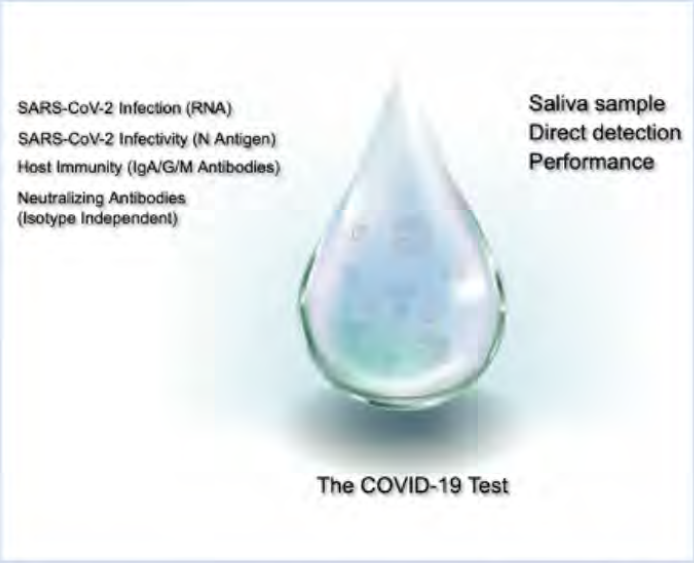
Anthony Nguyen
Class of '25

In March 2020, the World Health Organization (WHO) declared a pandemic for the highly infectious COVID-19. In response, the City of Los Angeles ordered all residents to stay home to limit the spread of the virus. However, educational institutions like UCLA are considered essential businesses. At one point, UCLA implemented the "ramping down" protocol for on-campus research activities, meaning that all on-campus projects and personnel not approved to continue research activities were required to cease operations. The shutdown of UCLA meant different things for the School of Dentistry, whether it was the movement to online school or social distancing within research labs, we have interviewed a few affiliates within the school of dentistry to share their stories.

Anna Kim, a first-year dental student, was pursuing a Master's in Oral Biology under the mentorship of Dr. Ki-Hyuk Shin when COVID erupted. Initially, many concerns came to Anna: are her family and friends healthy? Is she safe? How would research continue? Anna experienced what many other students experienced: a shift to online learning. Zoom University would become the norm for her for a whole year. Her lab came to an indefinite stop as quarantine and isolation were implemented. Members of the lab would have to leave as UCLA would be closed and they would have to return home. However, as time passed, a safety protocol was implemented which included scheduled shifts and social distancing. Anna eventually returned to the lab, but felt uneasy because COVID-19 rates were still soaring.

Dr. Alexandra Polasko, a postdoctoral researcher at UCLA, had a common experience with other graduating students looking for a job. Graduating with her PhD from UCLA in Civil and Environmental Engineering and wanting to stay in Los Angeles, Dr. Polasko applied for every position she could, but faced many hurdles as COVID-19 halted the hiring process for many positions. As time passed, she found an open position in the Ton-That Laboratory. Dr. Polasko entered her new lab with mixed feelings as the dental school was slowly allowing researchers to implement in-person protocols. With the COVID-19 booster not available at the time to her, she was nervous about being exposed to the virus along with the adjustment of in-person work. However, the Ton-That lab surpassed her expectations, as the lab provided masks and had very conservative protocols. Being in person was strange for Dr. Polasko, but she felt safe knowing how serious the lab was taking the situation. Given the obstacles, Dr. Polasko would go on to receive first place at the School of Dentistry Research Day 2022 in her category!

Many research labs were slowed down to a halt. The science community may never gain the time it lost, but major discoveries were made. Dr. David Wong's lab became as busy as ever. When the pandemic struck, it was clear that testing was the key to determining which individuals had the virus in order to limit the spread. People needed to know who was infected, and the Wong lab was very cognizant and proactive with this. The lab wanted to create the best test for detecting the SARS-COV 2 virus. At the time, nasal swab tests were the test of choice but could be very uncomfortable.



The COVID-19 Test

An alternative choice, saliva testing was met with skepticism, but when it became clear that the virus was detectable in the saliva, the lab was energized. Many labs were working on a saliva test, but with the collaboration of Dr. Gil Omenn from the University of Michigan, they knew the immunoglobulins in blood and saliva were very linear. The similarities meant that, "If you can find it in the blood you can find it in the saliva." Dr. Wong knew that a test searching for the antigen, antibody, and viral RNA could be developed; the lab just needed time. Dr. Samantha Chiang D.D.S. Ph.D, a postdoc of the Wong lab, came masked up with a face shield day after day and single-handedly developed the first saliva SARS-CoV-2 antibody test. "Am I infected?" "Am I shedding the virus?" These are questions we ask ourselves, and hopefully soon we will have the answers. The Wong lab finds themselves embraced by the scientific community and are currently working with the National Institution of Health to commercialize their test on May 8th.

The emergence of COVID-19 came with lost opportunities among researchers. For others, COVID-19 was a time of rest and self-reflection that people used to restructure for the betterment of their lives. We as researchers have persevered through this hard time and will continuously persevere in order to make new progress.

It's hard to put in words but I'm glad we can contribute to the science world. I have so much pride in what we do. We're going to put ourselves in front of COVID-19 testing.
-Dr. David Wong

DR. KIM AND THE ART OF "REPULPALIZING THE PULP"

Lauren Kim
Class of '23

Dr. Reuben Kim, DDS, PhD is Professor and Chair of the Section of Restorative Dentistry in the Division of Preventive and Restorative Sciences at the UCLA School of Dentistry. Dr. Kim received both his DDS and PhD from UCLA in 2003 and 2008, respectively. He is one of the few faculty members who is heavily involved in both teaching and research in our school and has conducted several influential studies on osteomucosal healing in osteonecrosis of the jaw and pulpal regeneration with reparative dentin formation. In addition to teaching both didactic and clinical courses for the predoctoral and postdoctoral students as well as conducting groundbreaking research, Dr. Kim provides quality dental care for patients at the Faculty Group Dental Practice. Dr. Kim continues to make leading advancements for our school and mentor students to become some of the brightest leaders and caretakers of the community.

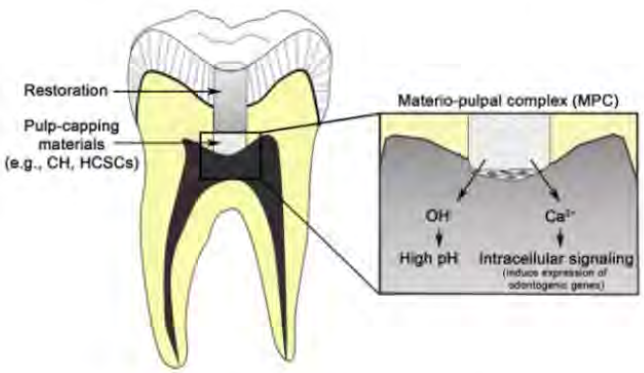
As students drill a Class II prep, one of their greatest fears is an iatrogenic pulpal exposure. Restorative dentists are often apprehensive of managing a pulpal exposure while treating a deep carious lesion, conventionally resorting to root canal therapy (RCT) or referring the case to an endodontist. Indeed, for infected pulp, dentists have long been trained to remove the entirety of pulpal tissues instead of saving them. Unlike other medical specialties that focus on saving the respective organ system, why is it that we don't try to "repulpalize" the diseased pulp?

For the past years, Dr. Kim has conducted extensive research on toxicity of dental materials and pulp regeneration in restorative dentistry. The pulp is a multipotent organ with great resilience and ability to differentiate. Dr. Kim has investigated the cytotoxicity of dental materials (Kim et al., 2013; Williams et al., 2013) and potential of healing the pulp with procedures such as direct pulp capping (DPC), reformulating the way we approach caries control and pulpal management in restorative dentistry.

DPC is a procedure performed upon pulpal exposure to induce reparative dentin, which serves as a "biological seal" to protect and maintain pulpal vitality. Calcium hydroxide (CH), known to be the gold standard DPC material for centuries in dentistry, generates hydroxyl anions that alkalize the local environment and promote remineralization via the activity of alkaline phosphatase. However, CH has several major drawbacks such as inflammation and necrosis, tunnel defects from its high solubility, and potential for microleakage and degradation. Another increasingly popular material for DPC is hydraulic calcium silicate cements (HCSCs), which are derivatives of mineral trioxide aggregate (MTA). MTA's biocompatibility, osteoconductivity, and partial odontoinductivity make it advantageous for DPC (Song et al. 2017). However, MTA is not without limitations: it has a long setting time, risk of discoloration, cost, and challenges of manipulation. The regenerative mechanism of these two materials, CH and HCSCs,

Reuben Kim, D.D.S., Ph.D.
Professor and Chair of the Section of Restorative Dentistry

revolves around forming a dentinal bridge with released calcium that triggers intracellular calcium signaling cascades and promotes tissue mineralization such as reparative dentin – the driving mechanism of healing with bone grafting materials (Yuan et al., 2010). The ORAI1 calcium-channel protein is one of the regulators of the intracellular calcium signaling pathway and promotes differentiation and mineralization of dental pulp stem cells (Sohn et al. 2015; Lee et al., 2016).



Dr. Kim and his team studied the pulpal responses to the DPC materials by iatrogenically exposing the pulp in mice, placing MTA and composite, and tracking the histologic changes over the course of six weeks (Song et al. 2017). They analyzed the dentinal bridge formation versus development of a periapical radiolucency (PARL) across various materials and compared the results with a control group (Song et al. 2017).

The mice in the treatment groups of PROROOT MTA, TheraCal LC, EndoSequence BC RRM, and Endo-Eze MTAFlow exhibited dentinal bridge formation in histological examination, whereas the control and UltraCal XS (DyCal) groups lacked bridge formation. Moreover, the control, DyCal, and TheraCal groups developed PARLs on some teeth, with DyCal having the highest proportion of mice with PARL. [KR1] The results of this study have shown that DPC may have a measurable effect on dentinal reformation, although further supporting studies may be needed.

DPC clinically requires a set of technique-sensitive procedures to ensure a favorable outcome. Optimal isolation with a rubber dam followed by peripheral carious removal with a high-speed large round bur is of paramount importance, followed by switching to low-speed for the pulpal and axial caries. The practitioner then applies 3.5% sodium hypochlorite on the exposed pulp to control bleeding, seals the opening with HCSCs, conditions with 10% polyacrylic acid to remove the smear layer and enhance binding, lines with resin-modified glass ionomer (RMGI) to seal the capping materials, etch-prime-bonds, and finally restores the tooth with composite (Song et al. 2017). Although DPC has a high potential of preserving the pulpal vitality, its success largely depends on factors such as operator technique and host response.

Whereas previously, a sizable exposure (>1mm) of either iatrogenic or infectious origin strongly indicated the necessity of prophylactic or therapeutic RCT, Dr. Kim's research provides strong evidence for a more conservative approach with partial pulpal removal either extending to the chamber or orifices followed by the application of HCSCs, which is already practiced in pediatric dentistry for a tooth with prematurely formed roots.

Restorative dentistry continues to undergo exciting research and new treatment modalities, especially involving regeneration and dentin reformation – for example, novel studies on inducing tertiary dentin formation including mechanisms for reparative or sclerotic dentin by targeting one single gene or its signaling pathway. These findings promote our overall understanding of the aging process in our body not merely limited to the oral cavity. Moreover, Dr. Kim's work reinforces evidence-based methods of keeping dentistry as minimally invasive as possible without compromising treatment efficacy, serving a critical purpose in public health: with these toolboxes, we can improve access to dental care for underserved populations with barriers to compliance with more extensive and complex treatment options.

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[KR1]This study will be submitted for publication soon.

Using the Coresignation Technique in Micro-computed Tomography

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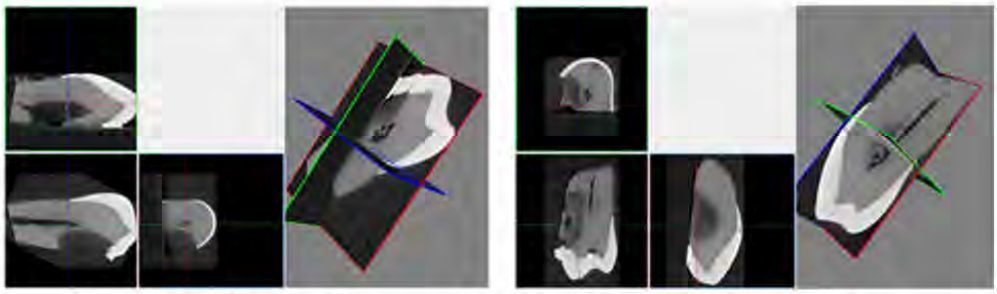
MICRO-COMPUTED TOMOGRAPHY (MICRO-CT) is a non-destructive tool that allows for the visualization and quantification of both the internal and external aspects of a wide variety of materials using x-rays without damaging the original samples. This technique is taken from the medical field and applied into small objects in a laboratory setting. Briefly, a sample is placed within the micro-CT machine and rotated in front of an x-ray source, which produces hundreds or thousands of two dimensional raw images. After that, the raw images are reassembled into three dimensional reconstructed images illustrating the cross-sectional structures of the sample. To analyze the reconstructed images, a range of gray values representing different radiodensities of the sample can be quantified using a segmentation (thresholding) function in the micro-CT software.

Micro-CT has many applications in scientific research, and is currently being applied to dentistry at UCLA by Dr. Jabbour, an Assistant Clinical Professor in the Sections of Restorative Dentistry and Oral Medicine to study Silver Diamine Fluoride (SDF). Dr Jabbour holds DMD and PhD degrees from McGill University in Montreal, Canada. Although Dr. Jabbour is a clinical faculty, he has interest in research and used the

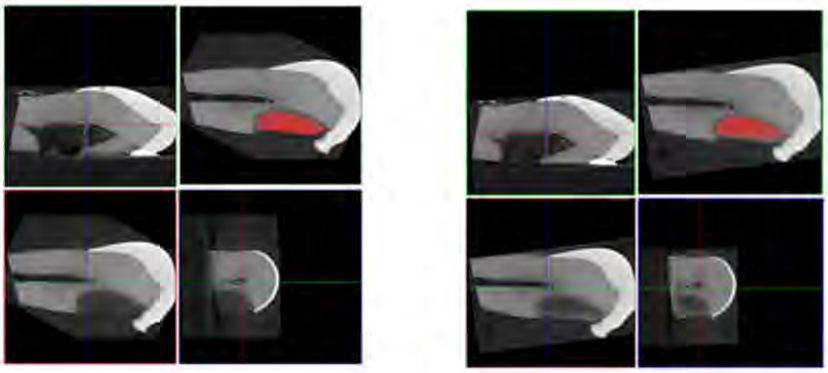
Figure 1



Preoperative micro CT images (reference images)

Post-operative micro CT images (target images)

Figure 2



Pre-operative 3D images with pre-operative region of interest

Pre-operative region of interest transferred to post-operative images

micro-CT as a tool to visualize the changes in radiopacity of teeth with carious lesions after SDF application. SDF was originally approved by the Food and Drug Administration (FDA) as an anti-sensitivity agent in 2014. However it seems to have a potential beneficial effect in slowing the progression and arresting dental caries, and it could be used as an alternative non-surgical method for the management of decayed teeth. Currently, surgical removal of carious lesions and replacement of tooth structure with biocompatible materials such as dental amalgam, resin or glass ionomer is the most common method for addressing dental caries. Although the mechanism of the action of SDF is not fully understood, the silver component displays antibacterial properties and the fluoride component promotes the remineralization of hydroxyapatite in enamel and dentine.

Since the micro-CT is a non-destructive tool that preserves the original sample, it allows comparison of the change in radiopacity of teeth with carious lesions before and after SDF application. In order to study the same carious regions of interest (ROI), Dr. Jabbour uses a coregistration technique. He uses pre-operative reconstructed images of teeth with carious lesions as reference images which stayed stationary (Figure 1).

Then he repositions the post-operative reconstructed images (target images) of the same teeth after SDF application and registers them in three dimensions over the reference images. From this, he is able to transfer the same ROI from the pre-operative reference images to the post-operative target images (Figure 2).

Analysis of these results suggest that application of SDF leads to a significant increase in the radiopacity of carious lesions. The coregistered images show that SDF penetrates throughout the entire depth of the carious lesions and precipitates at the junction of affected and infected dentin. From the analysis of these images, Dr. Jabbour is hoping to use the results of this coregistration technique to better understand the limitations of SDF and improve its utilization in the clinic as a non-surgical alternative for caries management. Perhaps in future studies, the coregistration technique can also be used to test different dental materials in-vitro before applying them in the clinic.

INVESTIGATING MEDICATION-RELATED OSTEONECROSIS OF THE JAW

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Medication-Related Osteonecrosis of the Jaw (MRONJ) is one of the most well-researched topics in the field of Oral and Maxillofacial Surgery, and we help lead the research here at UCLA. MRONJ is a complication of antiresorptive medication resulting in exposed, necrotic and non-healing bone. Antiresorptive medications, such as bisphosphonate and denosumab, are used to prevent the breakdown of bone and manage and prevent bone fracture due to metastatic malignancy and osteoporosis.

These medications function by inhibiting osteoclast differentiation and causing apoptosis of these cells, which leads to decreased bone resorption and remodeling. A diagnosis of MRONJ is considered when patients present with all three of the following criteria as outlined by the 2022 update of the American Association of Oral and Maxillofacial Surgeons' Position Paper on Medication-Related Osteonecrosis of the Jaws:

1. Current or previous treatment with antiresorptive therapy alone or in combination with immune modulators or antiangiogenic medications.
2. Exposed bone or bone that can be probed through an intraoral or extraoral fistula(e) in the maxillofacial region that has persisted for more than 8 weeks.
3. No history of radiation therapy to the jaws or metastatic disease to the jaws.

These guidelines were created by a special committee appointed by the AAOMS Board of Trustees (4), and includes our very own Dr. Aghaloo. As a student researcher in Dr. Aghaloo's Lab, we carry out research in a wide range of topics including MRONJ and developing/testing new strategies to regenerate bone in small or large defects and inflamed or infected defects (peri-implantitis, osteomyelitis, osteoradionecrosis). One of the projects we are working on currently involves measuring osteoclastic activity of rat bone with periapical disease (an induced defect). Rat subjects are pre-treated with bisphosphonate, induced with periapical disease and undergo a single-tooth molar extraction. After 4 weeks, we discontinue bisphosphonate

treatment. Throughout the experiment, osteoclastic activity is measured at various time points and compared pre- and post-treatment. This experiment serves to replicate a very common situation in the field of Oral and Maxillofacial Surgery: patients taking (or having taken) bisphosphonate medication and requiring an extraction. Often, in fear of causing more harm, clinicians are hesitant to treat these patients, leaving them in poor periodontal health leading to even more dental infection. For this reason, it is important that we understand the basics of the effects of bisphosphonate medication and the goals of treatment delivered to these patients.

There are two modes of administration of bisphosphonates: intravenously (IV) and orally. Patients administering (or having administered) bisphosphonate intravenously are at a greater risk for developing MRONJ because of the greater potency as it is more readily absorbed and therefore more readily bioavailable (1). For these patients, elective procedures should be avoided and root canal treatment is the preferred method of treatment in place of an extraction. These preferred treatments pose issues for patients with non-restorable teeth, remaining root tips, and teeth unable to undergo root canal treatment. For clinical application further research is being conducted through several experiments.

We are in the process of collecting and analyzing data; however past experiments have shown that 4 weeks after tooth extraction, most animals treated with bisphosphonate developed histologic and radiographic signs of osteonecrosis. If we continue to produce same results, this study will provide more information (via more test subjects) about the risks/outcomes for patients with chronic periapical disease taking bisphosphonate medications and undergoing a required extraction, which is a common situation in the field of Oral and Maxillofacial Surgery.

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Edition XIII