


NIDCR Strategic Plan | 2021–2026

SCIENCE: ADVANCING ORAL HEALTH FOR ALL





“The coming years are certain to pose new challenges for human health and offer new opportunities for scientific exploration. NIH will address this rapidly changing landscape by pursuing, with greater vigor than ever, our mission of seeking fundamental knowledge about the nature and behavior of living systems and applying that knowledge to enhance health, lengthen life, and reduce illness and disability.”

Francis S. Collins, M.D., Ph.D.
Former Director, National Institutes of Health

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Strategic Plan Process

NIDCR conducted long- and short-term program planning to identify Institute priorities. This process considered input from: NIH, the U.S. Department of Health and Human Services, Congress and the Administration, peer reviewers, the extramural scientific community, patient advocacy and professional organizations, the National Advisory Dental and Craniofacial Research Council (NADCRC), the Board of Scientific Counselors, NIH Institutes and Centers, federal agencies, industry, and ad hoc advisory groups. The process was also informed by input from participants at conferences and workshops, who reviewed emerging scientific opportunities, identified public health concerns, and provided state-of-the-science assessments.

In 2019, initiated under the direction of Dr. Martha Somerman, NIDCR began development of a new strategic plan, intended to mark the new decade. Input from hundreds of stakeholders gathered in a similar process to what is outlined above, enabled creation of a set of priorities and objectives. NIDCR staff working groups expanded drafted goals and objectives for each priority area. Then feedback was incorporated from a range of stakeholders – from academia, patient advocacy, non-profits, government and industry – into the priority areas.

Under the leadership of Dr. Rena D'Souza, who assumed the NIDCR directorship in October 2020, NIDCR used the information gathered to update the Institute's mission and create a new overarching vision for the future, four guiding principles, and five strategic priority areas. The Strategic Plan was also influenced by unprecedented advances and lessons learned during the pandemic, which included an analysis of the organization's strengths and limitations in facing the crisis. Updated concepts were published as a Request for Information (RFI) notice number NOT-DE-21-007, from July 15 to August 27, 2021, to solicit broad public input. Further revisions were then made based on feedback received. These insights proved invaluable in making some bold predictions, detailed in this report, about the future of the Institute. The final draft underwent review by internal and external stakeholders, and was approved by NADCRC. The NIDCR Strategic Planning Steering Committee contributed extensively, and provided direction for the development of the plan. NIDCR is indebted to all who provided comments and suggestions through these efforts which were vital to the development of a dynamic and responsive 2021–2026 NIDCR Strategic Plan.

This strategic plan was initially launched on January 7, 2022, and is being implemented through 2026. The plan was reviewed and updated in May 2025 to ensure that it aligns with the Administration's priorities and complies with executive orders.

NIDCR's Statutory Authority and Brief History



Through the signing of legislation into law, President Harry Truman created the National Institute of Dental Research (NIDR), on June 24, 1948, to address a significant public health issue that had been revealed during World War II. Oral health in America was so poor that close to 20 percent of eligible armed forces recruits were rejected because they could not meet Selective Service dental requirements.

The NIDR's mission was to "conduct and support research, training, health information dissemination, and other programs with respect to the cause, prevention, and methods of diagnosis and treatment of dental and oral

diseases and conditions." NIDR moved into its dedicated research facility, Building 30, on the NIH campus in the spring of 1961. On October 21, 1998, President Bill Clinton signed a law adding "Craniofacial" to NIDR's name, to more accurately reflect the Institute's scope of research.

Almost 75 years later, NIDCR can point to significant advances and accomplishments to improve the oral health of the nation. NIDCR funding helped establish community water fluoridation as a safe, effective, and economical intervention for the control of dental caries. In 1971, NIDCR launched the National Caries Program using funds specifically earmarked to accelerate development of preventive methods to reduce tooth decay. The results of that initiative established the safety and efficacy of several caries preventive measures, which were implemented across the country in school demonstration projects through the National Caries Program. NIDCR has also funded research to better understand chronic pain conditions, founding the first multidisciplinary pain clinic in 1983. In 1999, NIDCR was already acknowledging and targeting oral health disparities in its *Strategic Plan to Reduce Racial and Ethnic Health Disparities*, which supported research to address these issues and opportunities to strengthen the scientific workforce.

For 73 years, the Institute has catalyzed scientific advances that have increased our understanding of the basic biological mechanisms of diseases and disorders and the application of such knowledge to the practice of dentistry and health care. NIDCR stands ready to celebrate its diamond jubilee in 2023 and to advance research that improves oral health and public health in a way that enhances the quality of life for all.

NIDCR Directors

	Name	In Office from	To
	H. Trendley Dean	September 1948	March 1953
	Francis A. Arnold, Jr.	April 1953	February 1966
	Seymour J. Kreshover	February 1966	June 1975
	David B. Scott	January 1976	December 1981
	Harald Löe	January 1983	June 1994
	Harold C. Slavkin	July 1995	July 2000
	Lawrence A. Tabak	September 2000	August 2010
	Martha J. Somerman	August 2011	December 2019
	Rena D'Souza	October 2020	January 2025

COVID-19 and NIDCR:

Lessons Learned

Late Friday afternoon on March 13, 2020, NIH staff received an email from Director Francis S. Collins ordering all telework ready employees to come to campus on Monday to gather

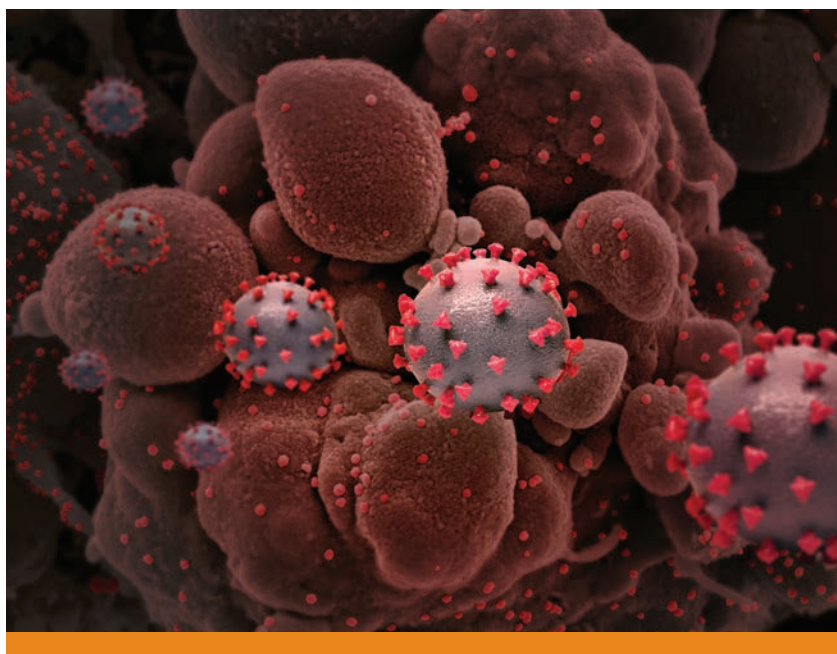


what they needed to do their work off-site—at least until April 3. Two days later, on Sunday, March 15, an email from Lawrence A. Tabak, then the acting director of NIDCR, told staff that the first COVID-19 case had been identified at NIH and more were likely to follow.

As we now know, the impact of the COVID-19 pandemic extended far beyond April 2020 and became business as usual for the next year and a half. In spite of workplace disruption and a great deal of uncertainty, NIDCR's work did not stop. As the U.S. federal government's lead agency for research on dental, oral, and craniofacial health, NIDCR used the strengths of its intramural and extramural programs, carving out funds from our annual appropriation, to quickly create research initiatives that could help us understand the disease that was upending the lives of all Americans.

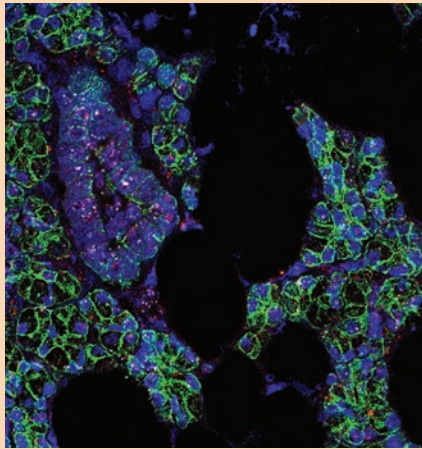
In terms of the practice of dentistry, we knew COVID-19 would impact

access to oral health care and how it was delivered. Because the oral cavity presented a route of transmission, dental practitioners were at high risk of exposure to the virus. Dental offices closed, and before they could reopen, questions had to be answered about how to make sure that oral health care providers and their patients would be safe. Using the already existing National Dental Practice-Based Research Network (PBRN) NIDCR was able to solicit high priority projects to investigate the transmissibility of SARS-CoV-2 in dental settings, develop methods to prevent transmission, and look at the potential for teledentistry to help meet patient needs. Research was also funded to study the physiological involvement of the oral cavity to learn more about viral entry through the oral epithelium, as well as viral infection, replication, and shedding.



In all, NIDCR provided approximately \$4.6 million in supplemental support to current extramural grantees to shift their focus to SARS-CoV-2 research. We also took over the administration of six NIH Rapid Acceleration of Diagnostics Radical (RADx-rad) initiative grants focused on rapidly advancing early testing technologies. Through all of this, NIDCR kept a close and compassionate watch on the wellbeing and productivity of the extramural community—especially early career investigators.

Scientists Discover that Novel Coronavirus Infects the Mouth



People with COVID-19 often have high levels of SARS-CoV-2 in their saliva, and many have reported oral symptoms including taste loss, dry mouth, and blistering. These observations led NIDCR intramural researchers to suspect the virus may infect cells in the mouth.

Working with researchers at the University of North Carolina, the scientists found that cells of the salivary glands and tissue lining the mouth expressed genes encoding the protein receptors the virus uses to get into cells.¹

The team then examined oral tissue from COVID-infected people, including some who had died from the disease.

They found SARS-CoV-2 RNA, and in some cases, evidence of viral replication, in salivary gland cells and in oral cells shed into the saliva. Infected individuals with detectable virus in their saliva were also more likely to report taste loss. Saliva from two volunteers with asymptomatic COVID-19 was shown to infect healthy cells grown in a dish, raising the possibility that even people without symptoms could transmit the virus through saliva.²

The findings reveal a previously unknown role for the oral cavity in SARS-CoV-2 infection and transmission and underscore the importance of prevention, early diagnosis, and development of treatment strategies.

In NIDCR's intramural division, research programs pivoted to move in new and unexpected directions. One area of study took priority, because only COVID-19-related projects were permitted to continue at the beginning of the pandemic. The Salivary Disorders Unit switched from studying Sjögren's syndrome to looking at SARS-CoV-2 in the oral cavity. Working with extramural colleagues, the scientists discovered that the epithelial cells of salivary glands were a major site of SARS-CoV-2 infection.

Another NIDCR intramural group modified an antibody-detecting method created more than a decade ago to detect SARS-CoV-2 antibodies in blood samples. The technique, which has been shown to detect antibodies linked to dozens of disorders, is now spurring further research within the NIH and with the extramural scientific community.

NIDCR has learned a number of lessons from the pandemic and NIH's response to it. Among the most valuable is a clear understanding of the importance of human connection, not just in the dental, oral, and craniofacial (DOC) community, but also in our communities outside of work, where our families, friends, and loved ones live. Our day-to-day lives somehow felt narrowed, but, in many cases, our view of the world widened to encompass the interconnected, global nature of the pandemic.

Battling COVID-19 required ingenuity and a true sense of shared purpose to better understand the role of the oral cavity in the spread of the disease. The relative ease with which the intramural community pivoted to directly address COVID-19-related areas of inquiry reflects how NIH offers investigators the flexibility to make nimble decisions to redirect the trajectory of their research.

The COVID-19 pandemic also laid bare longstanding health disparities. The virus disproportionately affected communities that are underserved by health care providers due to barriers to access or socioeconomic factors. Moving forward, we will need to continue to widen the purview of biomedical research to consider various factors affecting health. Regarding delivery of care, we now know the value of telehealth technologies to increase access to care. This deserves further exploration.

Moving into what is hopefully a post-pandemic America, these lessons will serve us well as we strive to advance better oral health for all.

Key Events

On October 13, 2020, Rena D'Souza, DDS, MS, PhD, was virtually sworn in by Drs. Collins and Tabak as the new director of NIDCR and took on the challenge of leading the Institute during a time of unprecedented challenge. A working group to discuss the creation of a 5-year strategic plan was convened to carefully examine the current goals and challenges in dental and craniofacial research and to plot a course for funding priorities. *Oral Health in America: Advances and Challenges*, which was developed over the course of more than two years, with extensive input from over 400 contributors, was released in the winter of 2021 and examines 20 years of progress in oral health since the first Surgeon General's report in 2000.

Intramural Research Program

NIDCR Division of Intramural Research (DIR) supports basic, translational, and clinical research and training on the NIH campus to advance understanding of biological processes relevant to dental, oral, and craniofacial health. In 2017, the DIR combined all its laboratories and branches to create one entity. This reduced the separation and isolation of different areas of DOC science, promoted interactions, and created a more participatory governance with input from all investigators. All DIR research and operations are overseen by the Office of the Scientific Director and facilitated by the Intramural Administrative Branch.

The NIDCR Division of Intramural Research has five main areas of study:

Craniofacial Developmental, Cell, and Matrix Biology: Tissue morphogenesis, cellular function, differentiation, and cancer to prevent and treat craniofacial disorders. Studies include: neural crest stem cells and derived tissues; regulation of stem cell fate; human craniofacial disorders and anomalies; the interaction of growth factors with the extracellular matrix during craniofacial development and salivary organogenesis; the dynamics of cell migration within extracellular matrix; and the role of glycosylation in developmental and secretory processes, and the relationship to development, disease, and inflammation.

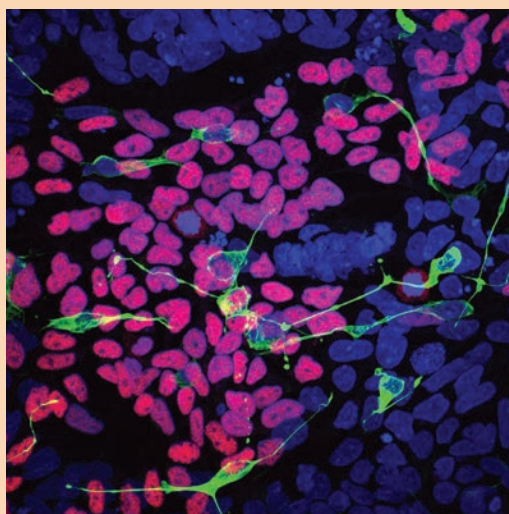
Epithelial and Salivary Gland Biology and Dysfunction: Molecular, and genetic mechanisms underlying development, differentiation, and secretory physiology, with the aim to repair and regenerate function. Studies include: regulation of saliva secretion; epithelial signaling and transport; vector development for gene therapy; and mechanisms of autoimmunity, such as in Sjögren's syndrome and other salivary disorders.

Immunology and Inflammation: Mucosal immunology, oral inflammatory diseases, and immune tolerance and autoimmunity. Studies include: immune-microbiome dysbiosis in periodontal disease; the effects of proteases and cellular and matrix forces on inflammation and the immune system, the effects of TGF beta signaling on immunity and craniofacial development; oral manifestations of chronic graft-versus-host disease; the development of key immune cell types, such as T-regulatory and dendritic cells; glycosylation of oral microbes; and bioinformatic analysis of the microbiome to understand inflammation and identify treatment targets.

Sensory Biology: Mechanisms of sensation, including taste, somatosensation, and pain, while developing novel pain control strategies. Studies include: the neuroscience of taste and smell; itch and peripheral somatosensation; orofacial pain; and neuronal circuits that influence somatosensation and pain.

Skeletal Biology: Development and maintenance of skeletal tissues—teeth, bone, cartilage, and their associated tissues—with an emphasis on their associated cells, genes, matrix-associated macromolecules, and proteases. Studies include: skeletal stem cells in disease and regeneration; the function of extracellular matrix in skeletal tissues and in genetic craniofacial skeletal defects; bone marrow stromal cells and their immune functions; and bone and mineral metabolism with the aim to improve the lives of individuals with calcium and phosphate metabolic disorders.

Scientists Identify Genetic Disorder of the Brain, Craniofacial Skeleton



An NIH-wide team led by NIDCR intramural scientists recently identified a new genetic disorder named linkage-specific-deubiquitylation-deficiency-induced embryonic defects (LINKED) syndrome, which causes developmental delays and malformations of the brain, heart, and facial skeleton.

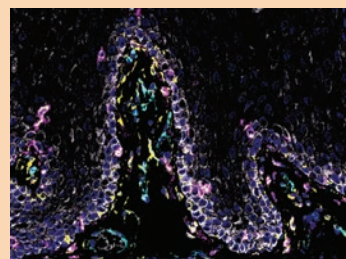
The project began when an NIH clinical scientist examined eight male children who shared a constellation of birth conditions including malformations of the craniofacial skeleton. All the children had mutations in the gene that encodes OTUD5, an enzyme involved in embryo development.

To find out how the mutated gene gave rise to the children's condition, the clinical scientist sought the help of NIDCR researchers who study enzymes like OTUD5. Working with developmental biologists at NIH, the scientists found that the mutated version of the enzyme interferes with key molecular steps in the development of neural crest cells, which give rise to tissues of the craniofacial skeleton, and of neural precursors, cells that eventually give rise to the brain and spinal cord.³

The findings reveal a new molecular pathway essential for human development. Disruptions to the pathway cause LINKED syndrome and may also underlie other birth conditions. The information will help scientists better understand such diseases—both common and rare—and improve patient care.

A Census Inside Your Mouth

To better understand how the mouth's tissues become vulnerable to disease, NIDCR intramural scientists conducted a census of cells from mucosal tissue lining the gums and cheeks of people with and without severe periodontitis.⁴ Cell-by-cell gene expression data revealed a previously unknown role for connective tissue cells called fibroblasts in orchestrating oral mucosal immune responses. In healthy volunteers, fibroblasts seemed wired to recruit neutrophils, immune cells that play a protective role against periodontitis. However, fibroblasts appeared to become overactivated in people with periodontitis, resulting in an exaggerated immune response that could contribute to disease progression.



This data is now publicly available to the scientific community through the Human Cell Atlas, an initiative led by scientists at the Broad Institute in Cambridge, Massachusetts, and the Wellcome Sanger Institute in Cambridge, UK, to create comprehensive reference maps of all human cells. Scientists can now use the oral mucosa data to answer key questions about oral health and disease.

Office of the Clinical Director

The Office of the Clinical Director (OCD) works with the DIR Office of the Scientific Director to provide a collaborative, multidisciplinary environment that promotes the translation of basic research discoveries into clinical practices. OCD supports all NIDCR intramural clinical research activities by overseeing three distinct but integrated functions:

- Support for and monitoring of clinical research protocols through the Dental Clinical Research Core
- Operation of the Dental Clinic
- Training of dentist-scientists



The OCD's **Dental Clinical Research Fellowship Program** offers fellowships to dentists interested in an academic career, which includes an independent clinical research project with relevance to human disease or health.

Office of Training and Education

The Office of Training and Education supports the needs of intramural scientists, trainees, and students at all levels, as related to their training and career development.

Extramural Research Program

The Division of Extramural Research (DER) provides research funds to support basic, translational, and clinical research in dental, oral, and craniofacial health and disease through grants, cooperative agreements, and contracts that support scientists working in institutions throughout the United States. The DER plans, develops, and manages scientific priorities through portfolio analyses and consultation with stakeholders, encouraging the most promising discoveries and emerging technologies for rapid translation to clinical applications.

The Division of Extramural Research is comprised of three branches and one center:

The ***Integrative Biology and Infectious Diseases Branch*** supports basic and translational research programs on oral microbiology; salivary biology and immunology; oral and salivary gland cancers; neuroscience of orofacial pain and temporomandibular disorders; mineralized tissue physiology; dental biomaterials; and tissue engineering and regenerative medicine. The branch aims to accelerate progress in basic and translational research in these areas, and further stimulate the discovery pipeline based on clinical needs.

The ***Translational Genomics Research Branch*** supports basic and translational research in genetics, genomics, developmental biology, and data science toward the goal of improving dental, oral, and craniofacial health. The focus is on deciphering the genetic, molecular, and cellular mechanisms underlying dental, oral, and craniofacial development and anomalies.

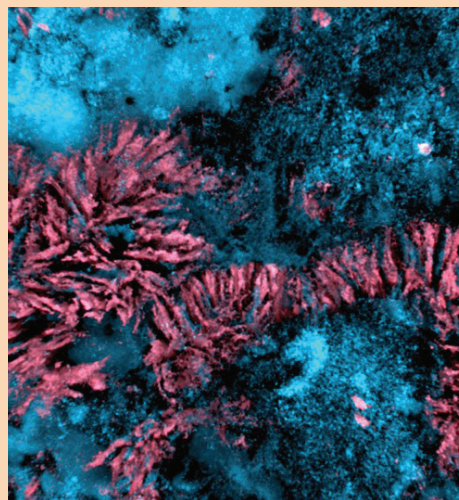
The ***Behavioral and Social Sciences Research Branch*** supports basic and applied research to promote oral health, to prevent oral diseases and related disabilities, and to improve management of craniofacial conditions, disorders, and injury. The program prioritizes mechanistic research that contributes to a cumulative science of behavior change, to maximize the rigor, relevance, and dissemination of efficacious behavior change interventions.

The ***Center for Clinical Research*** supports patient-oriented, population, and community-based research aimed at improving the dental, oral, and craniofacial health of the nation. The Center focuses on a variety of diseases and conditions through clinical trials, epidemiologic studies, practice-based research, the HIV/AIDS and oral health program, and studies of oral health disparities in all areas of programmatic interest to NIDCR. The program encourages investigations that have the potential to translate findings into evidence-based clinical applications.

Biofilm-Busting Nanoparticles Could Clean up Dental Plaque

Bacteria often congregate on surfaces, forming sticky deposits called biofilms. Dental plaque is a type of biofilm that builds up on teeth and can lead to tooth decay if left untreated. Microbes in biofilms are embedded in a protective matrix that makes it hard for antimicrobial agents to penetrate.

To address this problem, NIDCR-funded researchers created tiny iron oxide particles, called nanoparticles, and coated them with small enzyme molecules.⁵ These hybrid creations, known as nanozymes, break down the biofilm matrix and kill microbes. A nanozyme treatment given to rats strongly suppressed dental caries without disrupting healthy bacterial communities in the mouth and gut. The nanozymes could eventually be used in mouthwashes to prevent caries in humans.



In a separate study, the team used the iron oxide nanoparticles to create magnetically controlled microscopic robots that can be moved along precise paths to break up biofilms.⁶ The robotic system was able to scrub biofilm from the insides of a tube, as well as from narrow channels within an extracted tooth. The technology could one day aid in biofilm removal from teeth and medical devices.

Key Initiatives Supported by the Division of Extramural Research

● National Dental Practice-Based Research Network (PBRN)

The main goals of the PBRN are to streamline the implementation of national oral health research studies in dental practices on topics of importance to practitioners and their patients, to provide evidence useful in daily patient care, and to facilitate the translation of research findings into clinical practice. The PBRN has been instrumental in addressing critical knowledge gaps related to the delivery of dental care during the Coronavirus pandemic. A future direction will be to support patient-oriented clinical research experiences and skills development for clinical faculty and dental/postgraduate students/residents by providing opportunities to conduct practice-based research in dental school clinics.



- **Dental, Oral and Craniofacial Tissue Regeneration Consortium (DOCTRC)**

The program is directed toward generating multi-disciplinary team science efforts that lead to novel FDA-approved therapies for the regeneration of DOC tissues lost to disease or trauma.

- **FaceBase**

The overall goal of FaceBase is to support effort that gathers and curates a large variety of high-density datasets and unique resources related to craniofacial development and malformation and makes them publicly accessible to the scientific community. This wealth of information creates a knowledge base that facilitates new opportunities for data mining to understand disease mechanisms and to identify new disease markers and therapeutic candidates.

NIDCR actively contributes to a number of **NIH-wide programs and initiatives**. We co-lead three Common Fund Programs in Glycoscience, Science of Behavior Change, and the Gabriella Miller Kids First Pediatric Research Program. In addition, we participate in other major programs including Helping to End Addiction Long-term Initiative (HEAL), NIH Pain Consortium, NIH Blueprint for Neuroscience Research, All of Us Research Program, Cancer MoonshotSM, The Pediatric HIV/AIDS Cohort Study (PHACS), The Centers for AIDS Research (CFAR) Program, and Rare Diseases Clinical Research Network (RDCRN). Moving forward, we will continue working with NIH Institutes, Centers, and Offices, as well as other federal agencies. On the horizon, NIDCR contributes to new activities coordinated through the Foundation for the NIH (FNIH), including Accelerating Medicines Partnership[®] Program: Autoimmune and Immune-Mediated Diseases (AMP[®] AIM) and Bespoke Gene Therapy Consortium (BGTC). We are developing a roadmap to lead and advance new research in the prevention, early diagnosis, and precision management of temporomandibular disorders (TMD), with NIH-wide engagement. This roadmap addresses recommendations from the National Academy of Sciences Report on Temporomandibular Disorders: Priorities for Research and Care.

Research Resources to Advance Science

NIDCR supports multiple data repositories and cohort studies that collect and store clinical and biospecimen data prospectively and in a standard way. Information gathered from these studies has led to new insights into disease risk factors, clinical interventions, and basic science.

For example, the NIDCR-supported Human Oral Microbiome Database provides the scientific community with curated information on the hundreds of bacterial species present in the human upper digestive and respiratory tracts, including the oral cavity and nasal passages. The data has enabled new understanding of the structures of unique microbial communities within the mouth and may provide clues to their roles in oral health and disease.^{7,8}

FaceBase is another NIDCR-supported knowledge base that offers researchers comprehensive datasets related to craniofacial development and disorders in both humans and model organisms.⁹ FaceBase datasets have contributed to dozens of peer-reviewed scientific papers by researchers around the world, including an analysis that linked certain genetic variants with aspects of human face shape. By supporting these resources for data- and biospecimen-sharing, NIDCR aims to enable future discovery by the research community at large.



NIDCR and the Nobel Prize

On October 4, 2021, the Nobel Assembly at Karolinska Institutet awarded David Julius, PhD, and Ardem Patapoutian, PhD, the Nobel Prize in physiology or medicine. Both scientists received NIDCR funding over a 15-year period in support of their winning research for “their discoveries of receptors of temperature and touch.”



David Julius



Ardem Patapoutian

Julius used capsaicin, the powerful component of chili peppers that causes a burning sensation, to recognize a sensor in the skin’s nerve endings that reacts to heat. Patapoutian, who served on NIDCR’s Board of Scientific Counselors in 2010, used pressure-sensitive cells to identify a new class of sensors that respond to mechanical stimuli in internal organs and the skin.

“Their discoveries exemplify why dental, oral, and craniofacial research is so vital to our ever-evolving understanding of the human body,” said Rena D’Souza, former Director, NIDCR. “This research ultimately shed light on how our bodies sense the environment around us.”

The **Division of Extramural Activities** provides leadership and advice in developing, implementing, and coordinating extramural programs and policies. The Division organizes meetings of the National Advisory Dental and Craniofacial Research Council and the Board of Scientific Counselors.

Research Training and Career Development Branch (RTCDB)



The NIDCR RTCDB programs span the career stages of scientists, supporting research training and career development for PhD and dual degree DDS/DMD-PhD students, postdoctoral scholars, and early career, mid-career, and established investigators.

The RTCDB oversees and coordinates the Institute's programs for extramural fellowships, training grants, career development awards, and NIH loan repayment awards. These include:

- Individual awards for U.S. citizens/permanent residents, which include fellowships (F30, F31, F32, F33), career development awards (K01, K02, K08, K23, K25) and career transition awards.
- Institutional T32 and T90 awards to support predoctoral and postdoctoral research training.
- Institutional K12 career development awards to support dentists pursuing an integrated Dental Specialty and PhD program (DSPP).
- AADR Mentoring Network for a Workforce of the Future (AADR Mind the Future) program, supported through RFA-DE-19-007, which provides mentored research career development and grant writing activities for a cohort of 10 postdoctoral/junior faculty participants annually over the course of 5 years.



Stephanie Momeni



Susana Maria Salazar Marocho



Modupe Coker

From Trainee to Tenure Track: Mentoring Program Supports Path to Research Independence

NIDCR supports a mentoring program called MIND the Future to retain a talented pool of early-stage researchers, launched in 2020 by the American Association for Dental Research.

Participants are matched with experienced investigators for a year of one-on-one mentoring. The mentees also attend weekly interactive educational sessions on grant writing, publishing, mentorship, and other career-related skills, and they receive peer support from their fellow mentees.

“Hearing the perspectives of my peers, who in a few years could be the people reviewing my grants, has been really important in informing my own approach to grant writing,” says Stephanie Momeni, PhD, a postdoctoral researcher studying the oral microbiota at Oregon Health & Science University.

Mentees also benefit from the relationships they build with their mentors, who are well-established scientists in the field. “My MIND mentor and I brainstormed my ideas, and his honest feedback—identifying both the strong points and areas that need more work—really helped me recognize the merit of my research,” says Susana Maria Salazar Marocho, PhD, an assistant professor studying dental ceramics at the University of Mississippi Medical Center.

Dentist-epidemiologist Modupe Coker, DDS, PhD, an assistant professor at Rutgers University, says, “My mentor has become my friend, and our relationship will definitely endure,” she says. “Even if it’s not in a formal setting, I’d like to work with everyone from the program for as long as I can.”

Strategic Plan:

Mission, Vision, and Guiding Principles

This Strategic Plan lays out NIDCR's strategic direction—organized around four Guiding Principles and five Strategic Priorities—to fulfill its public health mission and to make sure it is a good steward of the nation's investment in its research. Above all, it puts people at the center of the biomedical research endeavor.

VISION

We aspire to transform human lives through scientific discoveries and innovations that advance dental, oral, and craniofacial health and overall wellbeing for all.

MISSION

We advance fundamental knowledge about dental, oral, and craniofacial health and disease and translate these findings into prevention, early detection, and treatment strategies that improve overall health for all individuals and communities across the lifespan.

GUIDING PRINCIPLES

Core values ground our thinking and guide our decisions across all aspects of the NIDCR research endeavor.

Scientific Excellence

We are dedicated to excellence and integrity in DOC research and apply core principles of research, rigor, and reproducibility to all funded studies. We ensure that all research is conducted ethically, and that data collected is well-described for replication or applications in other settings.

We accelerate innovative and translational research with strategic investments in areas that are ripe for rapid advancement.

Workforce Development

We are committed to developing a research workforce across all disciplines of dental, oral, and craniofacial health and disease. Through its workforce development funding opportunities, NIDCR constantly strives to increase the pool of dentist-scientists.

Stewardship

We are responsible stewards of our resources and continually develop the next generation of researchers and those that support the research enterprise through the strengthening and building of our research capacity. We strive for transparency in our decision-making processes and hold ourselves accountable to all our stakeholders by managing our resources to achieve results that improve DOC health and reduce or eliminate DOC diseases for all people.

Embracing and Managing Change

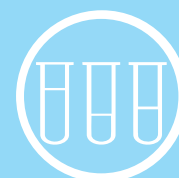
We understand that change is inevitable within our world, our field of science, and our workforce. We are committed to being proactive and nimble in our responses to challenges, emergencies, and crises. We encourage a learning culture that continually evaluates our processes and our accomplishments. Guided by our experiences and the lessons learned, we strive to find ways to apply these insights across our research endeavor.

Strategic Priorities

Although not meant to be fully comprehensive, these Strategic Priorities provide a snapshot of areas of focus that NIDCR considers to be valuable in supporting the Institute's mission and vision. Below each priority are associated objectives, or goals, followed by specific tactics that the Institute plans to implement in coming years. The numbering of priorities is not rank-ordered and is intended for ease of reference.

Strategic Priority #1 ***Integrate Oral and General Health***

Advance discoveries across the translational research spectrum and drive innovations that improve the early diagnosis, prevention, and treatment of DOC diseases across the lifespan.



Objectives and Tactics:

- Elucidate the genetic, epigenetic, molecular, cellular, and externally-driven mechanisms that drive the normal development of DOC tissues and characterize how disturbances in these mechanisms cause disorders and diseases of the DOC complex.
 - ◇ Key mechanisms that regulate the formation of the craniofacial complex – mineralized tissues (bones, tooth structures), soft tissues (muscles, lip, palate, tongue, salivary glands), and interfacing structures (cranial sutures, periodontal ligament, TMJ disc).
 - ◇ Gene-based technologies, including adenoviral-associated vector platform delivery, gene-editing and targeted replacement therapies to correct single-gene or complex developmental anomalies.
 - ◇ Basic, translational, and clinical studies on sex-based differences as a biological variable.
 - ◇ Deep phenotyping and genotype-phenotype correlations; external and social factors that influence health and disease in individuals, within families, and in communities.
 - ◇ Biomineralization of tooth and bone matrices to develop treatments and therapies for inherited and acquired mineralized tissue defects.
 - ◇ Characterization of rare diseases of the DOC complex and underlying disease mechanisms that lead to the development of targeted therapies.
 - ◇ Mechanisms driving salivary gland morphogenesis and function to inform the development of effective saliva substitutes, as well as treatment and therapies for salivary gland dysfunction, including Sjögrens syndrome.
 - ◇ Integration of DOC conditions with systemic diseases using *All of Us* data.

- Unravel the complexities and connections of the human oral microbiome in healthy dental and oral tissues and explore the functional and metabolic alterations associated with diseased states.
 - ◇ Microbial biomarker/molecular signatures for the development of probiotics, targeted therapies, and pharmaceuticals that can combat dental caries and periodontal disease.
 - ◇ Complications and secondary effects of therapies that alter the homeostatic balance of DOC function (radiation-, medication-, chemotherapy-induced conditions that cause osteoradionecrosis, osteonecrosis, mucositis, and sicca complex).
 - ◇ Interactions of microbial communities within dental and oral biofilms in healthy and diseased states, including underlying molecular and cellular immunology.
 - ◇ Unique and shared taxonomies among the oral cavity, gut, and brain, in health and disease; the potential mechanisms of pathogenic transmission that modulate the development, progression, and response to the treatment of human systemic diseases.
 - ◇ Natural progression and biology of healthy aging DOC tissues versus other mechanisms that result in chronic and immunologic conditions and diseases in older people.
 - ◇ Bidirectional consequences of oral inflammation to systemic illness at distant sites.
 - ◇ Mucosal immunologic responses to vaccines.
- Advance prevention, early detection, and treatments for benign and malignant head and neck cancers.
 - ◇ Molecular mechanisms that regulate aggressive phenotypes, including growth, invasion, and metastasis of cancers of the oral cavity and oropharynx.
 - ◇ Identification of environmental and polygenic risk factors that create susceptibility to disease progression.
 - ◇ Characterization of HPV+ oropharyngeal cancers, salivary gland tumor onset and progression to develop treatments in small early-stage clinical trials.
 - ◇ Oral microbiome involvement in the development and progression of oral cancer and its potential to enhance the response of oral cancer to treatment.
 - ◇ Immunomodulation of the tumor microenvironment to control tumor progression.
 - ◇ Molecular and phenotypic signatures that could predict response to treatment and could optimize treatment selection.
 - ◇ Mechanisms of treatment resistance that could be used to develop sensitizers to treatment.

- Stimulate and sustain collaborative efforts across the research spectrum to prevent, modulate, and treat dental pain and orofacial neuropathies.

- ◆ Holistic approaches to discern pain phenotypes and the environmental, behavioral, and social factors that impact and modulate DOC-related pain.
- ◆ Precision medicine approaches including pharmacogenomics and biopsychosocial factors to manage dental and facial pain and predict responses to treatment.
- ◆ Mechanisms of endogenous resolution of acute pain, protective factors, and resiliency to prevent the transition of acute to chronic DOC pain.
- ◆ Safe, effective, and optimal medication regimens for non-opioid analgesic management of acute pain.
- ◆ Effective clinical decision support systems to redirect dental professional opioid prescriptions for pain management toward evidence-based non-opioid treatments.
- ◆ NIH-wide, patient-focused research to advance TMJ basic and clinical research, research training, and translation to evidence-based treatments and improved clinical care.

- Transform material and biomaterial products through innovations in engineering, chemistry, and biophysics.

- ◆ Building interdisciplinary expertise in nanotechnology, microfluidics, multiscale imaging, and computational biology.
- ◆ Design and development of smart and high-performing biomaterials, implantable/wearable systems, biosensors, additive manufacturing, biofabrication, and associated surgical planning and navigation systems for DOC applications.
- ◆ Computational modeling and predictive algorithms to forge connections between basic, translational research, and long-term clinical performance of biomaterials along with tools to measure interactions with tissue microenvironments.
- ◆ Development and functional integration of biocompatible and biomimetic materials for regenerative therapies for the DOC complex.
- ◆ Tissue-material interfaces for proper healing, integration, and mechanical integrity.



- Develop safe and effective cellular and acellular regenerative strategies through rigorous pre-clinical testing and clinical trials for human use.
 - ◇ Cell sources, matrices, drugs, biologics, biomaterials, and scaffold delivery systems for clinical applications.
 - ◇ Quality control standards, predictive biomarkers, and well-defined procedures to ensure that functional DOC cells, tissues, and scaffolds meet rigor and reproducibility standards for clinical applications.
 - ◇ Autotherapies that take advantage of the body's innate ability to repair and regenerate damaged or diseased tissues.
 - ◇ Targeted manipulation of stem cell niches to promote local self-healing.
 - ◇ Novel methodologies that direct cells locally in the body — within a pro-regenerative environment — to replace damaged or missing tissues.
 - ◇ Pre-clinical activities such as animal pharmacology and toxicology studies; safety, potency, and efficacy studies; and scale-up tactics that help scientists meet regulatory requirements for initiating first-in-human studies.

Strategic Priority #2

Precision Dental Medicine

Develop more precise and individualized treatments for the management and prevention of DOC diseases.



Objectives and Tactics:

- Characterize individual variability in genetic makeup, environmental exposures, and lifestyle choices to derive personalized strategies.
 - ◇ Precise multi-omic, molecular, cellular, and physiological elements and mechanisms that contribute to DOC health and disease.
 - ◇ Biological factors underlying health disparities in early caries, gum diseases, and tooth loss.
 - ◇ Genomic, molecular, cellular, and imaging technologies to identify risks for diseases and conditions at early, more treatable stages.
 - ◇ Identify potential sex differences in DOC diseases, especially those that contribute to susceptibility and disparate treatment outcomes for women.

- Expand data ecosystems that use computational tools and mobile technologies to improve health outcomes in individuals and specific populations.
 - ◇ Rapid and less costly point-of-care technologies with high resolution data capture that improve patient health outcomes and facilitate remote or virtual teledentistry.
 - ◇ Reliable patient-reported and compliance outcomes, provider-reported assessments, and objective evidence-based outcomes of surgical and non-surgical interventions for clinicians and researchers.
 - ◇ High resolution and portable imaging (3D stereophotogrammetry, cone-beam computed tomography) for DOC structures that guide, predict, or lead to accurate diagnosis, improve treatment planning, and quantify outcome parameters or progression of disease.
 - ◇ Translation and implementation of efficacious precision oral health tools, techniques, and practices into the clinic.
 - ◇ Optimization of the delivery and implementation of strategies to reduce barriers so that precision oral health is available to all individuals and communities.

Strategic Priority #3

Translate and Implement

Accelerate the translation of research and the implementation of new discoveries into oral and general healthcare practices that reduce health disparities and improve oral health outcomes for all individuals and communities.



Objectives and Tactics:

- Advance the scientific study of methods that promote evidence-based practices for oral health and their integration into healthcare and educational systems.
 - ◇ Study designs that accelerate progress by overcoming barriers that impede translation of discoveries into clinical care.
 - ◇ Preventive, diagnostic, and treatment practices proven to improve oral health outcomes for individuals and communities.
- Leverage resources in new and existing NIDCR-funded networks and consortia to expand the capacity for research innovation.
 - ◇ Intervention-based trials that can be tested in real world settings.
 - ◇ Novel platforms and advanced technologies that gather medical, dental health, personal, and other health systems data (VA and CMS) into electronic health records that have been consented for research — including data-sorting algorithms that help identify potential participants in clinical trials research.

- ◇ Research protocol development, data collection, analysis, and sharing practices, and the standardization of methods through practice-based networks.
 - ◇ Cross-disciplinary research that uses a community-based model for the implementation of oral health care prevention and treatment and engages researchers, clinicians, practitioners, public health officers, social workers, teachers, and other service providers.
- Employ “Learning Health System” approaches to evaluate and incorporate new research findings into evidence-based practices that improve their effectiveness and application to individuals.
 - ◇ Addition of dental records into healthcare data ecosystems and infrastructure — such as NIH’s *All of Us* — to firmly establish the interconnectedness of oral health with overall health.
 - ◇ Health informatics and data science research to generate the knowledgebase needed to drive better-informed and more personalized treatment decisions for individuals and communities.
 - ◇ Standardized DOC disease-related ontologies.
 - ◇ Innovative methodologies to ascertain study populations and evaluate population variance and phenotyping.
- Identify successful interventions that reduce or eliminate health disparities, and scale-up study methods to sustain them in clinical and community settings.
 - ◇ Biological, behavioral, social, environmental, and commercial factors of health that contribute to how oral health care is delivered in various settings.
 - ◇ Scientific methods, metrics, measures, and tools that quantify health disparities in DOC health and disease and that measure effectiveness and efficiencies of evidence-based interventions.
 - ◇ Artificial Intelligence/Machine Learning (AI/ML) approaches to leverage electronic health record (EHR) and other types of data that are consented for research (e.g., genomics, imaging) to redress health disparities and advance health.
 - ◇ Public-private agreements and small business initiatives that develop innovative and data-driven technologies and products to improve DOC health for all.
 - ◇ Novel approaches in teledentistry and integrated mobile delivery systems that provide preventive, diagnostic, and treatment services to individuals with disabilities and remote-access communities.

- Accelerate research on best practices of health wellness and promotion, cost-effective disease prevention, and health literacy that overcome obstacles and improve practices.
 - ◊ Factors that impact patients' and healthcare professionals' clinical decision making and organizational structures within clinical and population settings to strengthen positive adaptive behaviors and practices and to decrease barriers.
 - ◊ Studies that eliminate interventional or invasive practices that have little or no clinical benefit to individuals and communities.
- Pursue oral health research to reduce the burden of oral health disparities and to improve overall health outcomes for all.



- ◊ Advancement of science on the prevention of non- communicable diseases affecting DOC tissues and the identification of risk factors shared with other complex conditions that pose public health challenges.
- ◊ International research consortia and analytic frameworks for the reporting of human, intellectual, and technological resources and the planning and implementation of research into oral health practices.
- ◊ Participation in a health DOC research network to enable a rigorous assessment of evidence for prevention, management, and cost-effective delivery.

Strategic Priority #4

Robust Research Pipeline

Nurture future generations of DOC researchers and oral health professional scholars who can address public health needs within a continually evolving landscape of science and technology advances.



Objectives and Tactics:

- Develop new programs that enrich pipelines of trainees to strengthen the oral health sciences workforce.
 - ◊ Participation in NIH-wide trainee recruitment initiatives by engaging key stakeholders.
 - ◊ Role modeling and mentorship practices that encourage interdisciplinary work and a continuum of learning.
 - ◊ Strategies that increase the recruitment and retention of students in DOC research, as well as the development and testing of best practices to identify programs that support students as they move through their careers.



- Improve the training, development, and retention of skilled clinician scientists who can transfer knowledge across the translational research spectrum into practice.
- ◆ Transformation of dual-degree training programs for clinician scientists to enhance their retention and success in the health research workforce.
- ◆ Expansion of clinical trials research workforce through skills development and experiential learning.

- ◆ Optimization of clinical specialty and research training to retain clinician-scientists among dental specialists.
- ◆ Creation of multiple pathways for clinicians to enter or re-enter research careers and be sustained through transitions across all career stages.
- Establish interdisciplinary programs that provide financial support and business expertise to interdisciplinary teams to promote commercialization of promising treatments and technologies.
- Target areas of health research in which workforce training can be tailored to meet emergent opportunities and challenges driven by unmet clinical needs.
- ◆ Create new training and career development programs that harness the power of data science applications.

Strategic Priority #5

Partner and Collaborate

Expand existing relationships and create new ones to advance the NIDCR research enterprise and increase its reach and impact.



Objectives and Tactics:

- Expand collaborations with other NIH Institutes, Centers and Offices (ICOs), and other federal agencies.
- ◆ Participation in NIH-wide programs that enhance interdisciplinary clinical research training, knowledge sharing, and the leveraging of innovations.



- ◊ Adoption of centralized NIH initiatives and systems-level assessments and actions by other ICOs to evaluate and manage NIDCR programs.
 - ◊ Increasing campus-wide visibility of NIDCR programs and initiatives, both intramural and extramural, through team efforts.
- Establish federal interagency pipelines of communication for the seamless flow of information and the sharing of knowledge and expertise.
 - ◊ Engagement with federal stakeholders and other agencies on key oral health priorities identified in NIDCR's *2021 Report on the Oral Health of America: Advances and Challenges*.
 - ◊ Building an evidence base for advancing oral health through interagency coordination.
- Expand cross-sector initiatives with professional organizations, industry members, community leaders, oral health practitioners, and patient advocacy groups to advance research that improves oral health for all.
 - ◊ Building an active network of state and local agencies that communicate oral health priorities to their constituencies.
 - ◊ Knowledge-sharing with stakeholder groups through outreach, and identification of gaps in knowledge that relate to public health challenges.
 - ◊ Communicating the impact of DOC research advances and informing evidence-informed solutions that improve oral health practices.
 - ◊ Engagement with NIDCR stakeholders about the need for training and developing future generations of oral health researchers.
- Broaden the research community by engaging employees, administrators, and thought leaders to advance initiatives that expand the health research workforce.
 - ◊ Innovative models that leverage NIH-wide programs and relationships with dental schools.
 - ◊ Support relationships between research-intensive institutions and resource-limited dental schools that aspire to increase their research infrastructure and capacity.

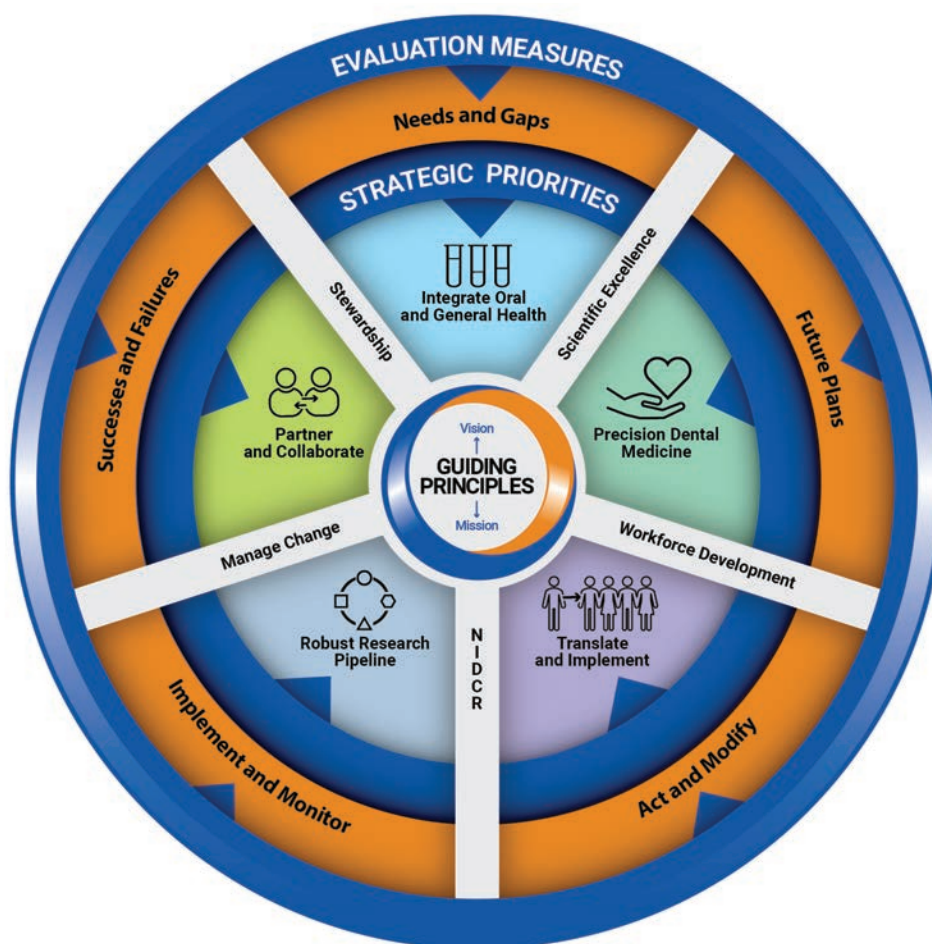
Outcomes Assessment:

How We Measure Success

As a federal agency, NIDCR is accountable for the efficient and effective use of taxpayer funds to support research on dental, oral, and craniofacial diseases and disorders and improving the oral health of all Americans. Accountability—measuring whether we successfully meet our goals—means carefully defining and assessing what constitutes success. This applies not just to the research NIDCR funds, but also to the effectiveness of the overall organization and the impact on relationships with stakeholders.

This Strategic Plan establishes the foundation for scientific discoveries that include transparent and rigorous planning and priority setting, continuous and consistent reviews of progress, and an increasing focus on the development of a highly skilled and nimble workforce that can rapidly respond to scientific breakthroughs and public health challenges.

Quantitative and qualitative approaches will be used to measure the progress and effectiveness of NIDCR programs and priorities, the scientific advances they drive, and their contribution to improvements in oral health and health care practice.



NIDCR will continue to employ all evaluation domains, from needs assessment and strategic planning to implementation and process evaluation, performance measurement, and outcomes and impact analysis. The enhanced federal focus on collecting and using evaluative evidence (*The Foundations for Evidence-Based Policymaking Act of 2018*) affirms an increased commitment to collecting evidence and to learning from that evidence as we proceed with the Strategic Plan. NIDCR will develop rigorous and appropriate evaluation methods for its strategic objectives, expecting successes and challenges and continuing to learn from both.

NIDCR also will be applying these methods to workforce development to widen the pipeline for new researchers, improve their retention, and build a robust infrastructure for research within the communities served.

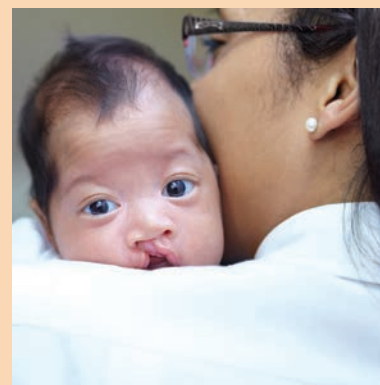
NIDCR will continue to include the valuable input of those who have a stake in the research it funds, depending on the National Advisory Dental and Craniofacial Research Council to represent the voices of the academic, scientific, and advocacy communities that we support. There will also be regular and ongoing outreach to these communities—as well as private industry—through targeted communications, workshops, and online and in-person interactions to identify gaps and opportunities in specific research areas, cross-cutting scientific themes, and possibilities for clinical research.

NIDCR is committed to managing for results.

Orofacial Clefting Research to Improve Clinical Outcomes

Orofacial clefting is a birth condition that occurs during early pregnancy when an infant's lip or mouth does not form properly. The result can be cleft lip, cleft palate, or both, which can lead to impairments in feeding, speech, hearing, and dental development.

NIDCR-supported research on orofacial clefting has shed light on the causes, diagnosis, and treatment of these conditions. Basic science studies, as well as genomic analyses, have uncovered genes and molecules that may be involved in orofacial clefting.^{10,11} Clinically, scientists have made advances in determining the optimal timing of surgery to improve speech outcomes, identifying surgical techniques that most effectively improve facial appearance, and evaluating visualization tools to assist in surgical decision-making.¹²⁻¹⁴ One group of scientists developed a computational modeling method to objectively determine the extent of nasal dysfunction in individuals with clefting, which could help inform treatment.¹⁵⁻¹⁷ Researchers have assessed the impact of cleft repair on children's oral health, speech, and academic and social functions.^{18,19} Drawing on recent insights into the genetic architecture of face shape, scientists are also developing and testing artificial intelligence and machine learning-based methods for detecting craniofacial abnormalities.



Bold Predictions

Working within our strategic priorities, these aspirational goals exemplify the Institute's bold visioning and far-reaching optimism. By seizing the opportunities that the rich bounties of biomedical research and population sciences provide, we will extend the boundaries of innovation and translation to the fullest.

- Effective social, commercial, and behavioral interventions that significantly reduce oral health disparities, improve oral health, and prevent disease throughout the lifespan.
- A comprehensive and integrated knowledge base of patient-centered data that predicts biological health and disease profiles as well as prevention and treatment outcomes.
- Use of novel patient-controlled technologies and interventions created in the COVID-19 pandemic, including salivary diagnostics and an expanded outreach effort to help improve oral health.
- Highly accurate facial imaging and artificial intelligence (AI)-based rapid methods for diagnosis of multiple craniofacial diseases and conditions that can enter clinical practice.
- Safe and effective replacement agonist therapies for the reversal of craniofacial disorders of single-gene origin, including the use of adenovirus-associated platforms for gene transfer therapy.
- Novel techniques for restoring the integrity of enamel, dentin, cementum, and bone using advances in material sciences, bioengineering, and tissue regeneration.
- Oral biosensing technologies and FDA-approved point-of-care devices for the detection and diagnosis of a broad range of oral and systemic diseases, including infectious diseases that can be used by those who cannot access health care easily.
- High-resolution imaging, synthetic biosensors, and multiplex biomarkers that are validated and FDA-approved in clinical practice for early detection and diagnosis of HPV-associated and other oropharyngeal cancers.
- Innovations targeted to the prevention and/or treatment of oral malignancies, dental caries, and periodontal disease.
- FDA-approved gene therapy treatments for radiation-induced xerostomia, Sjögrens Disease, and other autoimmune-driven salivary gland disorders.

- New therapies that counteract periodontitis-associated tissue destruction and contributions to local and systemic inflammation, to be tested in FDA-approved clinical trials, and transitioned into clinical practice.
- High-throughput “omic” technologies and studies on the interplay with human behavior that lead to early diagnosis and potential therapies for temporomandibular joint disorders.
- Digital technologies, including blockchain, artificial intelligence, and machine learning, to advance translation of new scientific discoveries in dental biomaterials research to FDA-enabled clinical studies.
- Nanoscale drug delivery technologies for personalized selective targeting and activation of drugs in specific cell compartments, that will enable non-opioid treatments for intractable pain with minimal side effects.
- Reduction in opioid use by practicing oral health professionals through efficacious tools and novel therapies for the stratification and management of acute and chronic pain.
- Miniaturized three-dimensional human tissues, including tissue chips as an acceptable and routine pre-clinical testing platform for reducing animal experimentation and supporting human clinical trial implementation.
- Successful clinical trials of probiotics and/or oral microbiome transplants that replace a dysbiotic oral microbiota with sustained healthy flora.
- Initiatives that support and implement oral health sciences research investments by applying the scientific method to assess outcomes that improve public health outcomes.

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References

1. Huang N, et al. SARS-CoV-2 infection of the oral cavity and saliva. *Nat Med*. 2021;27(5):892-903.
2. Burbelo PD, et al. Detection of nucleocapsid antibody to SARS-CoV-2 is more sensitive than antibody to spike protein in COVID-19 patients. *medRxiv* [Preprint]. 2020;2020.04.20.20071423.
3. Beck DB, et al. Linkage-specific deubiquitylation by OTUD5 defines an embryonic pathway intolerant to genomic variation. *Sci Adv*. 2021;7(4):eabe2116.
4. Williams DW, et al. Human oral mucosa cell atlas reveals a stromal-neutrophil axis regulating tissue immunity. *Cell*. 2021;184(15):4090-4104.e15.
5. Huang Y, et al. Precision targeting of bacterial pathogen via bi-functional nanozyme activated by biofilm microenvironment. *Biomaterials*. 2021;268:120581.
6. Hwang G, et al. Catalytic antimicrobial robots for biofilm eradication. *Sci Robot*. 2019;4(29):eaaw2388.
7. Shrivastava A, et al. Cargo transport shapes the spatial organization of a microbial community. *Proc Natl Acad Sci*. 2018;115(34):8633-8638.
8. Mark Welch JL, et al. Biogeography of the oral microbiome: The site-specialist hypothesis. *Annu Rev Microbiol*. 2019;73:335-358.
9. Shaffer JR, et al. Genome-wide association study reveals multiple loci influencing normal human facial morphology. *PLoS Genet*. 2016;12(8):e1006149.
10. Leslie EJ, et al. A multi-ethnic genome-wide association study identifies novel loci for non-syndromic cleft lip with or without cleft palate on 2p24.2, 17q23 and 19q13. *Hum Mol Genet*. 2016;25(13):2862-2872.
11. Li H, et al. The molecular anatomy of mammalian upper lip and primary palate fusion at single cell resolution. *Development*. 2019;146(12):dev174888. doi: 10.1242/dev.174888.
12. Shaw W, et al. Timing of Primary Surgery for cleft palate (TOPS): Protocol for a randomised trial of palate surgery at 6 months versus 12 months of age. *BMJ Open*. 2019;9(7):e029780.
13. Broder HL, et al. Surgeon's and caregivers' appraisals of primary cleft lip treatment with and without nasoalveolar molding: A prospective multicenter pilot study. *Plast Reconstr Surg*. 2016;137(3):938-945.
14. Trotman C-A, et al. Influence of objective three-dimensional measures and movement images on surgeon treatment planning for lip revision surgery. *Cleft Palate Craniofac J*. 2013;50(6):684-95.

15. Frank-Ito DO, et al. Computational analysis of the mature unilateral cleft lip nasal deformity on nasal patency. *Plast Reconstr Surg Glob Open*. 2019;7(5):e2244.
16. Croquet B, et al. Automated landmarking for palatal shape analysis using geometric deep learning. *Orthod Craniofac Res*. 2021. Online ahead of print.
17. Matthews HS, et al. Large-scale open-source three-dimensional growth curves for clinical facial assessment and objective description of facial dysmorphism. *Sci Rep*. 2021;11(1):12175.
18. Rosenberg J, et al. Parent observations of the health status of infants with clefts of the lip: Results from qualitative interviews. *The Cleft Palate-Craniofacial Journal: Official Publication of the American Cleft Palate-Craniofacial Association*. 2019;56(5):646-657. doi:10.1177/1055665618793062
19. Sischo L, et al. Quality-of-life in children with orofacial clefts and caregiver well-being. *Journal of Dental Research*. 2017;96(13):1474-1481. doi:10.1177/0022034517725707



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