

**National Institute of Dental and
Craniofacial Research**

Strategic Plan

2014-2019

FROM THE DIRECTOR

The oral health of Americans has improved dramatically in the past half-century. These gains have been due in large part to research and research training supported by the National Institute of Dental and Craniofacial Research (NIDCR). Today, the fruits of this research investment enable us to understand human biology like never before. Our challenge is to ensure that new knowledge and technologies are used strategically and quickly to yield evidence-based, individualized oral health care. Our approach must be comprehensive and connected.

NIDCR maintains a varied and productive research portfolio of basic investigations in molecules and cells; animal, tissue, and computer models that interrogate human disease; and clinical studies with individuals, communities, and populations. In charting the Institute's course for the next six years through strategic planning, we have engaged in a process of introspective analyses and consultation with our stakeholders. As an Institute with an expansive agenda, we seek innovative solutions to a broad array of health problems and probe the mysteries of biomedicine as they relate to the NIDCR mission.

The NIDCR Strategic Plan for 2014-2019 embraces the multidisciplinary essence of dental, oral, and craniofacial health and the research that informs its evidence base. The plan centers on four key goals:

Let Science Drive. Our first strategic goal affirms the basic tenet that rigor and reproducibility of experimental design and results are essential elements of scientific investigation. We will support the best basic, translational, clinical, and community-based research to build a strong evidence base in dental, oral, and craniofacial health. Doing so will help bridge the gaps among research, health care practice, and improved human health.

Enable Precise and Personalized Oral Health. As trusted providers of health care, dentists and physicians have long recognized variations among patients and have provided personalized care based on the many biological and behavioral components that shape health. NIDCR-supported research can help enhance personalized health care in two ways. We will encourage enhanced integration between health-related researchers and health practitioners, and we will work to identify influences on oral health at the molecular level through biomarker discovery and the development of risk-assessment tools.

Address Oral Health Disparities. NIDCR's involvement in oral health disparities research is a long-term, deliberate investment. It focuses on building a foundation of knowledge that has had, and will continue to have, a measurable impact on clinical practice and public policy for some of the nation's most vulnerable populations. Although our commitment to eliminating oral health disparities is steadfast, it will continue to take time to reach fruition. This strategic goal signifies the importance of sustained effort that requires collaboration with many partners in government and industry, as well as with a range of organizations and individuals in communities.

Engage a Diverse Oral Health Workforce. Our fourth strategic goal applies to all areas of this strategic plan. It articulates the notion that people — scientists and practitioners, individuals and communities — are the lifeblood of biomedical research. Demographic and scientific diversity is a key contributor to research excellence. Promoting education and scholarship at all levels — from dental students to

laboratory investigators to practitioners — ensures that evidence-based care reaches patients and communities. Novel and collaborative strategies will guide us through the highly dynamic landscape of 21st century biomedicine.

There has never been a better time to take advantage of the remarkable opportunities in science and technology waiting at our doorstep. Seizing this moment brings us closer to preventing and treating dental, oral, and craniofacial conditions as well as other diseases that share risk factors and therapeutic strategies.

I welcome your continued input as we strive to incite a revolution in improving oral health through research!

Martha J. Somerman, D.D.S., Ph.D.

Director, NIDCR

DRAFT

NIDCR STRATEGIC PLAN 2014-2019

This strategic document articulates four goals: supporting excellent science, embracing the value of precise and personalized oral health, reducing oral health disparities, and ensuring a strong workforce. These goals and their supporting objectives will guide NIDCR's decision-making for the next six years toward achieving a balanced research portfolio that improves the nation's dental, oral, and craniofacial health.

GOAL I: Support the best science to improve dental, oral, and craniofacial health.

Biomedical and behavioral research provides knowledge to support the ever-evolving practice of health care. This scientific base requires a broad array of research strategies to understand the fundamental causes of diseases and to transform that knowledge into a lifetime of better health for people everywhere. Most dental, oral, and craniofacial conditions arise from complex interactions of biological, behavioral, environmental, and higher, system-level factors.

Thus, NIDCR-supported research must involve a breadth of approaches including biological mechanistic and interventional studies, behavioral science and public health research, population-health studies, clinical trials, and community-based studies.

Objective 1: Enable basic research to advance knowledge of dental, oral, and craniofacial health.

The diverse and interactive group of cells and tissues that make up the dental, oral, and craniofacial complex provide a powerful system for discovery research. Recent advances in technology offer exciting opportunities to examine these cells and tissues, *in vitro* and *in vivo*, and to develop precise clinical tools for risk assessment, prevention, diagnosis, and treatment of various oral diseases. Several areas of research poised for rapid growth are mentioned below. However, NIDCR remains committed to supporting all areas of science relevant to its broad mission through its intramural and extramural research investments.

The complexity of the oral and craniofacial regions presents special opportunities to investigate basic mechanisms of cell biology, such as growth and development, differentiation, stem-cell function, and regeneration. NIDCR investments will focus on defining the molecules and pathways that contribute to development, maintenance, and remodeling of dental, oral, and craniofacial tissues with the goal of developing predictable materials, factors, and delivery systems to sustain and restore tissues and organs of the dental, oral, and craniofacial complex.

NIDCR will continue to support fundamental oropharyngeal cancer research that will enable pre-emption and early identification of this disease that currently takes a life every hour in the United

NIDCR invests in rigorously designed biomedical and behavioral research studies that drive science forward. NIDCR will serve a leadership role by promoting the use of common quality standards such that basic, translational, and clinical investigators achieve sufficient sample sizes and use consistent measures and data sets. Resonant with comparable trans-NIH efforts, the Institute will collaborate further with the scientific community and other stakeholders on efforts to ensure scientific rigor and the reproducibility of research results.

States.^{1,2} In addition to basic studies of oral cancer biology and tumor immunology, NIDCR will encourage research building on its support of the Oral Cancer Genome Project with the goal of guiding the shift toward precise diagnosis and individualized disease management. One area of special focus will be human papillomavirus (HPV)-associated oropharyngeal cancer, the incidence of which is on the rise.

NIDCR will support novel basic and translational research projects on the many infectious conditions affecting the oral cavity, ranging from caries to HIV/AIDS and HPV. The Institute will continue research on oral mucosal and innate immunity toward the development of a prophylactic HIV vaccine delivered through the oral mucosa. Other areas of research interest related to HIV/AIDS include the role and formation of viral reservoirs in oral cells and tissues, improved animal or cellular models to study host-virus interactions in the oral cavity, and identification of targets for point-of-care diagnostics and new therapies to treat HIV/AIDS and associated oral opportunistic infections.

The Institute's continued investment in salivary gland research will extend general understanding of secretory organs as well as health problems such as dry mouth and its oral manifestations, and salivary gland cancers. Knowledge gained through this research will be used to prevent and treat salivary gland dysfunction resulting from Sjögren's syndrome or irradiation-induced salivary gland damage from head and neck cancer treatment. Encouraging research toward the identification of predictive biomarkers for a variety of oral and systemic diseases will beneficially transform disease screening and monitoring since, as a diagnostic fluid, saliva has many advantages over blood.^{3,4}

NIDCR will be a leader in supporting the development of specialized tools for advancing knowledge about dental, oral, and craniofacial health, including, but not limited to, single-cell methods, stem-cell systems, multiscale imaging modalities, and disease models that accurately represent human biology. Examples of current technologies resulting from NIDCR investment include lab-on-a-chip devices, point-of-care oral health applications, and intravital microscopy.^{5,6} The Institute will continue to fund the Federal Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Programs⁷ to support research on products and devices ready for clinical testing and commercialization (see Goal II, Objective 2).

Objective 2: Promote development and use of comprehensive databases and informatics resources to advance detection and treatment of dental, oral, and craniofacial diseases.

¹ <http://oralcancerfoundation.org/>

² <http://seer.cancer.gov/>

³ Malamud D. Saliva as a diagnostic fluid. *BMJ* 1992;305:207-208.

⁴ Miller CS, Foley JD, Bailey AL, Campell CL, et al. [Current developments in salivary diagnostics](#). *Biomark Med* 2010;4:171-189.

⁵ Weigum SE, Floriano PN, Redding SW, Yeh CK, et al. [Nano-bio-chip sensor platform for examination of oral exfoliative cytology](#). *Cancer Prev Res*. 2010;3:518-28.

⁶ Amornphimoltham P, Masedunskas A, Weigert R. [Intravital microscopy as a tool to study drug delivery in preclinical studies](#). *Adv Drug Deliv Rev*. 2011;63:119-28.

⁷ <http://grants.nih.gov/grants/funding/sbir.htm>

Modern biomedicine is, to a large extent, an information science. Rapid advances in both computing and communications have enabled the capability to collect, store, and retrieve massive amounts of biomedical data and knowledge. In turn, large-scale analyses of interactions among genes, proteins, and many other biomolecules, often referred to as ‘omics approaches, have become not only feasible, but commonplace. Further development of data management and integration tools and enhanced access to and use of comprehensive databases and resources will facilitate future biomedical research as well as improve clinical practice and health-science education. NIDCR is committed to contributing to and exploiting the depth and breadth of 21st-century ‘omics investigations as well as to effectively and efficiently mining rich datasets, often termed Big Data, that these methods produce.

The NIH Common Fund⁸ was established as an incubator for catalyzing transformative research relevant to all NIH components but specific to none. NIDCR will take advantage of the resources and opportunities available through the NIH Common Fund’s *Big Data to Knowledge* initiative.⁹ This important initiative involves all NIH Institutes and Centers and aims to make Big Data and data science more prominent components of all biomedical research. To build on the success of another Common Fund ‘omics initiative, the trans-NIH Human Microbiome Project,¹⁰ NIDCR will build on the knowledge resulting from the Human Oral Microbiome Database that is allowing scientists to better understand the interplay among host, microorganisms, health, and disease (see “The Unexplored Microbial Universe in Our Mouths,” page 26).¹¹ The Institute will encourage research that defines both overlapping and unique roles of the oral microbiota, not only in oral-related illnesses such as dental caries and periodontal diseases, but also as mechanistic contributors to immune function and other disorders.

By funding genome-wide association studies, or GWAS, NIDCR underscores the utility of systems approaches for interrogating oral health biology. Findings from previous GWAS dental caries studies, for example, have identified genome sequences associated with risk suggesting interplay between genes, home fluoride exposure levels, and in some cases, taste.¹² Other results from NIDCR-funded GWAS have identified genetic risk factors for cleft lip with and without cleft palate and established the association of specific genetic variants in cleft lip and/or palate among different ethnic groups — pointing to new research and treatment avenues (see “Oral Health Research Across the Globe,” page 25).^{13,14} The Institute encourages GWAS research that will enrich these findings as well as identify shared risk factors for dental, oral, and craniofacial disorders and other complex disorders such as Sjögren’s syndrome, chronic pain, diabetes, cardiovascular disease, and others.

⁸ <http://commonfund.nih.gov/>

⁹ <http://bd2k.nih.gov>

¹⁰ <http://commonfund.nih.gov/hmp/index>

¹¹ <http://www.homd.org/>

¹² Wendell S, Wang X, Brown M, Cooper ME, et al. [Taste genes associated with dental caries](#). *J Dent Res*. 2010;89:1198-202.

¹³ Ludwig KU, Mangold E, Herms S, Nowak S, et al. [Genome-wide meta-analyses of nonsyndromic cleft lip with or without cleft palate identify six new risk loci](#). *Nat Genet*. 2012;44:968-71.

¹⁴ Beaty TH, Murray JC, Marazita ML, Munger RG, et al. [A genome-wide association study of cleft lip with and without cleft palate identifies risk variants near MAFB and ABCA4](#). *Nat Genet*. 2010;42:525-9.

NIDCR will sustain the national FaceBase Consortium¹⁵ that is designed to untangle the complex web of environmental influences and genetic instructions that construct the middle region of the human face. NIDCR promotes the scientific community's collaboration across geographic and disciplinary lines in this national network that collects, integrates, and disseminates data on craniofacial development and disorders. NIDCR will broaden and deepen its support of the FaceBase resource by generating and disseminating datasets not covered in the launch phase of the consortium. These include data describing additional areas of the developing face or skull; novel informatics methods for integrating, visualizing, and analyzing FaceBase data; and face-related research tools arising from studies in model organisms.

Objective 3: Conduct clinical investigations to improve dental, oral, and craniofacial health.

NIDCR will maintain its support of clinical research that advances knowledge and leads to better patient care outcomes. In partnership with the scientific, clinical, and patient advocacy communities, NIDCR will continue to develop and refine the Institute's clinical research agenda that focuses on the most pressing public health needs that would benefit from innovative treatment approaches (see "NIDCR-Funded Clinical Studies," page 24, for current examples of NIDCR-funded clinical research).

NIDCR will support an array of methods to resolve clinical questions, including, but not limited to, randomized controlled trials, qualitative research, community-based participatory research, cohort analyses, and comparative effectiveness research. The Institute will encourage research on technologies for clinical risk assessment and diagnosis. It will also partner with other Federal agencies and public and private organizations to adopt comprehensive electronic health-record, history, and treatment information models as clinical research tools.

NIDCR will leverage its use of existing cohorts with other clinical research infrastructures. One important resource is the NIH Clinical and Translational Science Award (CTSA) program, which aims to accelerate translation of laboratory discoveries into treatments for patients, to engage communities in clinical research studies, and to train a new generation of clinical and translational researchers.¹⁶ Expanding current CTSA collaborations with the oral health research community will enrich this national health research program. Academic health centers, where CTSA are housed, offer many resources that can augment the training of dental researchers and those from fields such as nursing, behavioral sciences, biostatistics, and epidemiology — moving toward a more translational research orientation and facilitating multi- and interdisciplinary research interactions. The NIH Clinical Center has also extended the availability of clinical research resources to NIH-funded extramural grantees.¹⁷

Objective 4: Maintain the role of NIDCR as a trusted source of information and evidence related to dental, oral, and craniofacial health.

¹⁵ <https://www.facebase.org/>

¹⁶ <https://www.ctsacentral.org/>

¹⁷ Opportunities for Collaborative Research at the NIH Clinical Center (U01):
<http://grants.nih.gov/grants/guide/pa-files/PAR-13-358.html>

An essential companion effort to supporting the highest-quality dental, oral, and craniofacial basic, translational, and clinical research is maintaining and sharing the knowledge this research builds. The oral health evidence base constructed through NIDCR's biomedical and behavioral research provides important information for the nation's practice community. Working with professional organizations and societies, especially dental groups, NIDCR will increase efforts to raise awareness of the importance of evidence-based decision-making in clinical dental practice. This will be accomplished in part through the National Dental Practice-Based Research Network¹⁸ (see Goal IV, Objective 2, page 14), as well as through dynamic modes of communication including social media.

Enhancing oral health surveillance capability in the United States is a cornerstone of enabling evidence-based decision-making in clinical practice. In partnership with organizations including NIH Institutes and Centers, the Centers for Disease Control and Prevention (CDC), and other Federal agencies, NIDCR will continue to collect, analyze, and disseminate oral health data to be used for surveillance and population-based research, as well as to inform public health practice and the development of public policy.

The Institute will encourage self-reported and real-time data collection and development and validation of new methods to measure and document oral diseases, disorders, and conditions. Working with stakeholders including public and private sector organizations, NIDCR will systematically examine practice patterns, professional trends, and other factors that can stimulate research aimed at improving oral health care quality, access, and delivery.

Although national surveys are good sources of population health data, they do not always reflect the diversity of the U.S. population.¹⁹ NIDCR has partnered with NIH's National Heart, Lung, and Blood Institute and six other NIH components to sponsor a multicenter epidemiologic study in Hispanic/Latino populations. The Hispanic Community Health Study/Study of Latinos,²⁰ the largest study of Hispanics ever undertaken by NIH²¹, will determine the prevalence of specific chronic conditions, protective or harmful factors, and the role of acculturation on Hispanic/Latino health. Importantly, the study includes Hispanics of different origins, providing the first opportunity since the 1980s to comprehensively examine the oral health of Latino sub-groups. NIDCR will continue to develop opportunities to support the collection of oral health data within large epidemiologic studies of groups whose health needs and epidemiologic profiles are not well captured in nationally representative data.

GOAL II: Enable precise and personalized oral health care through research.

Revolutionary changes in health care are on the horizon, driven by advances in technology and a remarkable convergence of knowledge spanning diverse fields of science. The oral health community

¹⁸ <http://www.nationaldentalpbrn.org/>

¹⁹ [2012 National Healthcare Quality Report](#)

²⁰ <http://www.csc.unc.edu/hchs/about.php>

²¹ Daviglus ML, Talavera GA, Avilés-Santa ML, Allison M, et al. [Prevalence of major cardiovascular risk factors and cardiovascular diseases among Hispanic/Latino individuals of diverse backgrounds in the United States](#). *JAMA*. 2012;308:1775-84.

must embrace personalized, precision health care in the near term, and NIDCR is committed to being at the leading edge of this development.

As our understanding increases about signaling pathways, molecular interactions, and novel biomarkers that underlie health and disease, the dental, oral, and craniofacial complex stands out as a unique gateway to assess risk, diagnose and prevent disease, and guide treatment. Science is converging naturally according to common, underlying biological principles, and NIDCR will adapt by establishing firmer connections that reflect these commonalities between oral and general health care practices.

Objective 1: Support research toward precise classification and treatment of dental, oral, and craniofacial health and disease.

Ongoing analyses of genomic information in many fields of biomedicine are uncovering new approaches for diagnosing and managing disease based on molecular signatures, rather than relying mainly on symptoms and affected organs. NIDCR will continue its support of research toward the development of user-focused, point-of-care technologies that detect dental, oral, and craniofacial health problems in a range of diverse settings, including underserved, low-resource communities nationwide and internationally. This is a first step toward developing effective and personalized disease-management strategies.

NIDCR will support an array of complementary research projects pertaining to physical, functional, and biochemical indicators of disease, including biomarkers — especially those with potential utility for clinical practice. Already in progress is an NIDCR-supported research project that recently yielded a miniaturized, portable nanobiochip that uses nanoliter volumes of saliva to identify biomarkers for diagnostic purposes.²²

Progress toward the development of personalized and precision health care requires intensive, interdisciplinary research collaborations, and NIDCR will vigorously pursue encouraging and establishing these team efforts. In partnership with stakeholders and other NIH units with relevant interest and expertise, the Institute will foster the development of imaging techniques that promise to increase risk-assessment accuracy for treatment of dental, oral, and craniofacial diseases and disorders. In particular, NIDCR will encourage focused research on specialized imaging and other technologies to trace both physiological and pathological pathways and processes, recruiting needed expertise from quantitative disciplines such as engineering, computer science, materials science, and physics.

The oral cavity is a key entry point for both healthful nutrients and pathogens. Its diverse cells and tissues enable development of novel drug delivery systems for the dental, oral, and craniofacial complex, as well as for other areas of the body such as the lungs or intestinal tract. NIDCR will encourage basic and clinical research to determine the specificity and effectiveness of orally

²² Weigum SE, Floriano PN, Redding SW, Yeh CK, et al. [Nano-bio-chip sensor platform for examination of oral exfoliative cytology](#). *Cancer Prev Res*. 2010;3:518-28.

administered substances for manipulating various physiological processes with precisely-controlled release kinetics for both time and space.

Objective 2: Engage primary care providers and health specialists toward individualized, evidenced-based health assessment and disease treatments.

Personalized oral health must encompass interactions between individuals and their health care providers as well as interactions with their families and communities. NIDCR will increase efforts to integrate oral health into the broader body of health research initiatives and facilities, as well as within overall clinical care infrastructures. NIDCR will encourage multidisciplinary interactions among providers within Federally Qualified Health Centers²³ and other community-based clinics, as well as in non-traditional patient-care settings (see “White House Recognizes Oral Health Researchers,” page 28).

Poor oral health often co-occurs with other health conditions such as obesity, mental illness, substance abuse, and injury/trauma.^{24,25} NIDCR will support multidisciplinary research to determine contributions to oral health from common disease risk factors. These include unhealthy diet, poor hygiene, smoking, alcohol use, stress, poverty, and lack of access to health care.

Objective 3: Partner with public and private organizations to improve oral health.

As an NIH component with an expansive mission, NIDCR will pursue opportunities to partner with stakeholders in areas that will help advance the Institute’s goals. In particular, these areas will include i) expanding communication among research, practice, educational, advocacy, and public health communities, ii) developing and commercializing products, and iii) addressing global health challenges.

NIDCR will participate in all trans-NIH opportunities that influence advancement of oral health research and research training. The NIH Common Fund will enable NIDCR to extend its reach into efforts related to workforce growth and diversity, basic behavioral and social sciences, ‘omics science, computational biology/informatics, and other areas. As a member of the NIH Pain Consortium,²⁶ NIDCR will promote its pain research agenda via collaboration among researchers across the many NIH Institutes and Centers that have programs and activities addressing pain (see “NIDCR Research Addresses the Many Faces of Pain,” page 29).

Public transparency in NIDCR’s research activities is mutually beneficial for the Institute and its stakeholders, adding diverse perspectives and building both understanding and trust. NIDCR will continue to enhance its digital media capabilities to foster relationships with the public, grantees, and funding/policy collaborators. In November 2013, NIDCR teamed with the Delta Dental Plans Association

²³ <https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/downloads/fqhcfactsheet.pdf>

²⁴ Sheiham A, Watt RG. [The common risk factor approach: a rational basis for promoting oral health](#). *Community Dent Oral Epidemiol*. 2000;28:399-406.

²⁵ Fisher-Owens SA, Gansky SA, Platt LJ, Weintraub JA, et al. [Influences on children's oral health: a conceptual model](#). *Pediatrics*. 2007;120:e510-20.

²⁶ <http://painconsortium.nih.gov/>

and the Institute for Oral Health by hosting the symposium “Science and Dentistry in Action: Leading the Way Towards Better Health.” The meeting launched an effort to bring research and clinical practice communities together for interactive learning and discussion of current areas of science and practice. NIDCR will conduct similar activities that encourage learning and relationship-building on an ongoing basis.

A key aspect of the NIDCR mission is fostering the timely transfer of health-related knowledge gained from research to members of the public, health professionals, researchers, and policy-makers. The Institute achieves this goal through its varied interactions with industry and other health-related Federal agencies. The Federal Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Programs offer special opportunities to match emerging technologies with NIDCR mission needs.

One case in point is an NIDCR-funded SBIR grant to a small company that brought specialized, point-of-care computed tomography (CT) scanners from laboratory to market in three years with no other financial support. Cone-beam CT has become particularly popular in oral and maxillofacial surgery, endodontics, implant dentistry, and orthodontics, because the images provide three-dimensional information and higher resolution than the two-dimensional data provided by a conventional X-ray image. In addition to installing dental scanners worldwide, the company has also produced a compact CT scanner for high-resolution bone imaging of the sinuses, temporal bones, and skull base and continues to develop new products.

Another example is an NIDCR-funded STTR grant that enabled the development of a new disinfecting system for polyurethane tubing used in dental water lines. The project involves attaching selenium to the inside of the tubing, which blocks bacterial attachment. Currently, the investigator is developing a selenium-coating process that can be used commercially and will then test the product in dental-practice settings. If successful, the system could be used to address problematic waterline contamination. This STTR investment also has led to a new line of products with antimicrobial properties.

NIDCR will sustain its longstanding relationships with global partners, including several organizations, international health offices within the U.S. government, and non-governmental entities. These ventures align with NIDCR’s research-based mission that advances dental, oral, and craniofacial research for the benefit of health. They enable the Institute to be a partner in improving oral health, and oral health research, on a global scale, as well as contribute to the integration of oral and general health.

GOAL III: Apply rigorous, multidisciplinary research approaches to overcome disparities in dental, oral, and craniofacial health.

NIDCR-supported research has led to many strategies for promoting oral health and preventing oral disease, but they do not always reach the people and communities who need them most. As we discover and adopt newer and better methods to preempt, prevent, and treat disease, we must improve our ability to translate and disseminate new knowledge effectively for oral health care providers,

communities, and to people in communities that remain underserved and are at greatest risk for poor health.

Tackling the problem of oral health disparities requires an extremely collaborative, multilevel approach that combines mechanistic, implementation, and dissemination research with community engagement and policymaking. NIDCR's role in this complex arena is to lead the effort to serve communities by funding the best research toward building a strong evidence base for cost-effective implementation. The Institute has already developed a knowledge base pertaining to cultural, political, economic, and social factors that impede implementation progress. NIDCR will continue to work with the NIH community, other Federal agencies, professional societies, and community organizations in a determined effort to diminish and eventually eliminate persistent oral health disparities.

Objective 1: Support multidisciplinary, multilevel research and research training to overcome oral health disparities.

NIDCR will continue its substantial investment in oral health disparities research. This portfolio, now over 20 years old, has proven to be a productive and valuable resource for multidisciplinary teams to investigate oral health disparities in innovative ways. Beginning with the establishment of regional centers in the 1990s to the most recent funding of centers in 2008, the program has provided a team-science atmosphere toward advancing knowledge and its implementation, and it has created future capacity through ongoing research training and career development.

NIDCR will continue its support of research to understand how behavioral and social factors contribute to oral health disparities and will apply clinical research strategies to develop effective interventions for oral disease. NIDCR pursues basic and clinical research on determinants of behavior change, and also emphasizes training and mentoring opportunities for investigators to acquire the knowledge and skills to conduct rigorous research in this area through the use of appropriate behavioral mechanisms, theory, and methods.²⁷ NIDCR will encourage research that identifies new outcome measures tightly linked to proposed behavioral mechanisms of action — going beyond current proxy measures such as self-reporting. Selected areas of focus include preventing childhood dental disease, supporting families in establishing life-long healthy habits, optimizing tobacco cessation strategies for use by dental health care providers, promoting recovery after oral and pharyngeal cancer treatment, managing chronic orofacial pain, and enhancing the oral health of vulnerable individuals, including the elderly.

Enhanced support for training in dental public health is an effective strategy for expanding oral health disparities research, and NIDCR will continue to sponsor a 12-month Residency Program in Dental Public Health.²⁸ This program also provides experience in other areas of dental public health, such as public health administration and management, and the organization and financing of dental care programs.

²⁷ <http://www.nidcr.nih.gov/NewsAndFeatures/Announcements/NIDCRSupplement.htm>

²⁸ <http://www.nidcr.nih.gov/CareersAndTraining/Fellowships/DentistsandPhysicians/ResidencyDentalPublicHealth/>

This initiative is designed to develop the next cadre of oral public health experts steeped in the value of research-based methodologies to fill a growing need for such expertise.

Objective 2: Use the tools of implementation and dissemination research to enhance the quality and effectiveness of community health interventions.

Bringing the fruits of research discovery to underserved people and communities is one of the most difficult phases of the biomedical and behavioral research continuum. NIDCR is committed to redressing this intransigent problem using the most recent research models that incorporate a broad range of social, genetic, and environmental risk factors to assess susceptibility to disease as well as health resilience. The Institute seeks to identify effective structures and programs that may be emulated and/or enhanced and that can be embraced fully by individuals in underserved communities. NIDCR also encourages research that tests methods of health-services delivery through a wide range of potential mechanisms.

NIDCR will continue to support community-based participatory research to address health disparities questions and to implement findings as rapidly as possible. In this context, the Institute will partner with patient advocates and community organizations to identify factors, both positive and negative, that influence the acceptance of pertinent research-based approaches that promise improved health outcomes community-wide.

Objective 3: Provide science-based information about oral health and disease to health care providers, patients and caregivers, policy makers, and the general public.

An important facet of the NIDCR mission is disseminating knowledge gained through research, and its implications for health, to all segments of the American public. This task is particularly relevant for members of underserved populations who have uneven access to understandable information about maintaining health.

The Institute supports an in-house program that serves as a resource for science-based information about dental, oral, and craniofacial health. Its Office of Communications and Health Education will continue to produce and disseminate informational materials in expanded ways to take advantage of various new-media formats on a wide variety of topics. These include children's oral health, oral cancer, periodontal disease, and oral health care for Americans with disabilities. NIDCR also provides materials in print and online to the media, health care professionals, educators and students, patient support organizations, caregivers for individuals with special-needs patients, and the research community.

GOAL IV: Ensure that a strong research workforce is dedicated to improving dental, oral, and craniofacial health.

With remarkable advances in science and technology come increased responsibilities to ensure an ample and diverse pipeline of highly competent investigators for years to come. NIDCR believes that a variety of flexible and innovative research training and career development programs is needed to recruit and retain oral health experts with the appropriate skills to conduct research in an increasingly

complex environment. The challenges in doing so include i) improving the recruitment and retention of underrepresented minorities in research, ii) cultivating and sustaining future leaders in clinical and translational research, and iii) developing researchers with multidisciplinary skills to address multi-pronged issues in oral health. Many of these disciplines are just emerging, yet it is critical that they be woven into ongoing and new research projects.

Objective 1: Collaborate with academic institutions, especially schools of dentistry, to create research pathways for faculty and trainees.

NIDCR-sponsored individual and institutional research training and career development programs encompass all career stages in the research continuum.²⁹ NIDCR's primary focus in this continuum is its strong support of a research emphasis in academic dentistry. NIDCR will continue to offer funding opportunities for established researchers, postdoctoral researchers, and undergraduates in various disciplines. The Institute will also adapt funding strategies, using flexibility in design and duration, to attract and mentor qualified individuals to successful careers in oral health research. In keeping with a recommendation from the NIH Advisory Committee to the Director's Working Group on the Biomedical Workforce,³⁰ NIDCR will collaborate with academic institutions to evaluate outcomes of NIDCR-supported programs and approaches that support training and make adjustments over time to further enhance the value of these programs.

NIDCR's emphasis on support of individual research training and career development awards will continue. Such programs have a track record in attracting and retaining oral health researchers. These defined programs include training opportunities for combined dual-degree D.D.S./D.M.D.-Ph.D. students, pre-doctoral Ph.D. students, individuals with dental degrees earning Ph.D. or equivalent research degrees, individuals with a D.D.S./D.M.D. or other clinical degrees seeking protected time for mentored research training and career development, and individuals with a D.D.S./D.M.D., Ph.D., or other doctoral degree pursuing postdoctoral training. The Institute is committed to supporting and nurturing early-stage investigators as well as those new to oral health through various means including, but not limited to, the NIH Pathway to Independence Award program³¹ and the NIH Director's Early Independence Award.³²

In addition to supporting research training and career development for clinical researchers using several individual funding mechanisms, NIDCR encourages oral health scientists and trainees to take advantage of clinical research opportunities within nationwide infrastructures such as the NIH CTSA program. The Institute also encourages the oral health research community to develop and maintain clinical research partnerships with the practicing community, and with other sites that support multidisciplinary research teams, including the NIDCR intramural program and the NIH Clinical Center.

²⁹ <http://www.nidcr.nih.gov/careersandtraining/>

³⁰ <http://acd.od.nih.gov/bwf.htm>

³¹ http://grants.nih.gov/grants/guide/contacts/parent_K99_R00.html

³² <http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-11-007.html>

Objective 2: Sustain career-enhancement opportunities in research.

NIDCR will continue supporting practice-based research. This program has proven to be a highly effective and innovative method for generating and codifying clinical situations that can challenge and strengthen the oral health evidence base. Since launching the Practice-Based Research Network in 2005, NIDCR had supported three regional networks across the country. Each had its own affiliated practitioners, clinical studies, and administrative tasks independent of the others. The second phase of this initiative, launched in 2012, is the National Dental Practice-Based Research Network, or NDPBRN, that consists of one national administrative hub that leads and oversees regional research nodes anchored in six U.S. cities.³³ The expanded network will increase significantly the number of participating practitioners, with the goal of producing data that can be better generalized to the highly diverse U.S. population.

The NDPBRN has, in addition, had extraordinary value in growing the oral health workforce to include clinician-scientists conducting research with people in everyday practice settings (see “Postcards from the Field,” page 30). NDPBRN studies in development, active, or in the data-analysis phase include HPV screening, examining potential benefits of devices for detecting dental decay, improving diagnosis and treatment of cracked teeth, identifying factors that predict successful dental crowns, and testing a dentist-delivered quit-smoking program. An important benefit of the NDPBRN initiative has been the increased value of evidence-based practice in the eyes of the practicing community as well as an increased likelihood that these individuals pursue research.

NIDCR will consider avenues to encourage bidirectional research, an iterative knowledge exchange between basic scientists and clinicians. Scientific insights into biological mechanisms and disease processes inform and spur new clinical interventions. Conversely, clinical observation about the nature and progression of disease stimulates new basic investigations. NIDCR will consider using new digital tools and technologies to crowdsource research questions and encourage ongoing dialogue on clinical issues. Enhanced communication with the practice community will facilitate sharing of research resources, such as biobanks for clinical biospecimens, data-collection tools, and knowledge emanating from new evidence.

Objective 3: Support research, training, and career development programs that value team science, transformative approaches, and diversity at all levels.

NIDCR remains committed to increasing diversity in the biomedical and behavioral research workforce. In 2013, the Institute established a workforce committee to improve efforts to recruit, train, and nurture individuals from diverse backgrounds underrepresented in biomedical research. Investigative activities will include new networking and mentoring opportunities that dovetail with ongoing efforts at NIH to increase diversity in the biomedical workforce. NIDCR will consider rigorous outreach programs to enlist professional societies, government agencies, academic institutions, industry, and community

³³ <http://www.nidcr.nih.gov/Research/DER/ClinicalResearch/DentalPracticeBasedResearchNetwork/default.htm>

organizations to develop new approaches to attract a more diverse population to the workforce confronting research problems in dental, oral, and craniofacial health.

Dental, oral, and craniofacial research investigations often draw from the measures and methods of multiple scientific disciplines. NIDCR will continue to recruit researchers trained in complementary areas of biomedical and behavioral research to oral health research. The NIDCR K18 program, launched in 2013, solicits applications for short-term mentored career enhancement awards in dental, oral, and craniofacial research, with a focus on behavioral and social sciences or genetic/genomic research — two areas of science poised for rapid growth.³⁴ This program's intent is to provide mid-career or senior investigators with short-term training in the theories, tools, methods or approaches in behavioral and social sciences or genetic/genomic research to either i) enrich an investigator's existing dental, oral, and craniofacial research program; or ii) facilitate the introduction of dental, oral, and craniofacial research into other investigators' existing research area.

The Institute pursues a balanced research portfolio that appropriately embraces the concept of high-risk, high-reward research. NIDCR will continue to participate in NIH Common Fund initiatives that enable such research. These include the NIH Director's New Innovator Award,³⁵ the NIH Director's Pioneer Award,³⁶ and the NIH Director's Transformative Research Award.³⁷ NIDCR will also participate in the NIH Common Fund Broadening Experiences in Scientific Training (BEST) program,³⁸ which aims to enhance biomedical and behavioral research training experiences so graduates are better prepared to enter the modern scientific workforce that extends well beyond academic research.

³⁴ Short-term Mentored Career Enhancement Award in Dental, Oral and Craniofacial Research for Mid-Career and Senior Investigators (K18): <http://grants.nih.gov/grants/guide/pa-files/PAR-14-039.html>

³⁵ <https://commonfund.nih.gov/newinnovator/index>

³⁶ <http://commonfund.nih.gov/pioneer/index>

³⁷ <http://commonfund.nih.gov/TRA>

³⁸ <http://www.nih.gov/news/health/sep2013/od-23.htm>

About This Plan

In consultation with NIH leadership, NIDCR conducts long- and short-term program planning to identify Institute priorities. These efforts develop and use information from several sources and consult a broad range of key stakeholders including the extramural scientific community, patient advocacy and professional organizations, the National Advisory Dental and Craniofacial Research Council and Board of Scientific Counselors, other NIH Institutes and Centers, other Federal agencies, industry, and *ad hoc* advisory groups. The Institute also obtains input through a range of conferences and workshops that review emerging scientific opportunities, identify public health concerns, and provide state-of-the-science assessments. NIDCR conducts its planning and priority setting within a larger context that considers input from NIH, the Department of Health and Human Services, Congress and the Administration, and external peer review.

The 2014-2019 NIDCR strategic planning process gathered public and stakeholder input about prospective activities, areas of research emphasis, future research approaches, needs, and opportunities. NIDCR obtained this input in several ways, through:

- A series of individual and group meetings with NIDCR staff to obtain input on NIDCR goals, opportunities, and priorities;
- Presentations and discussions during National Advisory Dental and Craniofacial Research Council meetings;
- An open-forum conference with NIDCR patient advocate organization representatives (April 2013);
- A presentation and discussion by the NIDCR Director at the American Association of Dental Research Boston chapter meeting (December 2012);
- A presentation and discussion on “National Oral Health Surveillance: Gaps, Priorities and Future Strategies” at the EpiForum held during the International Association for Dental Research meeting in Seattle, Washington (March 2013);
- A presentation and discussion on “Training the Next Generation of Oral, Dental and Craniofacial Researchers” at the International Association for Dental Research meeting in Seattle, Washington (March 2013);
- An open-forum strategic plan listening session — augmented by informal conversations — at the International Association for Dental Research meeting in Seattle, Washington (March 2013);
- A meeting with leaders of the American Association of Public Health Dentistry, the Association of State and Territorial Dental Directors, and the American Board of Dental Public Health at the National Oral Health Conference in Huntsville, Alabama (April 2013);
- 491 online responses from 108 individuals and organizations to six strategic planning questions posted on the NIDCR website between August and September 2013;
- A day-long NIDCR Bidirectional Research Roundtable Meeting in Bethesda, Maryland (June 2013);
- A day-long NIDCR Oral Health Disparities Roundtable Meeting in Bethesda, Maryland (June 2013); and
- Public comments obtained through online posting of the draft Strategic Plan (January 2014).

STAND-ALONE FEATURES

NIDCR MISSION

The mission of the National Institute of Dental and Craniofacial Research (NIDCR) is to improve dental, oral, and craniofacial health through research, research training, and the dissemination of health information. We accomplish our mission by:

- Performing and supporting basic, translational, and clinical research;
- Conducting and funding research training and career development programs to ensure an adequate number of talented, well-prepared, and diverse investigators;
- Coordinating and assisting relevant research and research-related activities among all sectors of the research community; and
- Promoting the timely transfer of knowledge gained from research and its implications for health to the public, health professionals, researchers, and policy-makers.

“The National Institute of Dental and Craniofacial Research will be recognized as a catalyst for transforming how oral health care is delivered. This includes a more comprehensive integration of basic, clinical, and population science to devise new tools and approaches to improve oral health.”

Dr. Martha Somerman, NIDCR Director

Discover – Enable the best science to solve problems in dental, oral, and craniofacial health.

Integrate – Promote the convergence of science, health care, and the research workforce toward ensuring that oral health is integral to overall health.

Collaborate – Partner with individuals and organizations within and outside dentistry, government, and academia, to improve the nation’s dental, oral, and craniofacial health.

Salivary Gland Tumor BioRepository

Salivary gland cancers are rare, with only a few thousand new cases in the United States each year.³⁹ They also are often fatal. Research progress has been slowed by the fact that the rarity of this cancer type means that there are few tumor samples available for researchers to study. To address this need, and to open salivary gland cancer investigation to more scientists from other disciplines, NIDCR collaborated with the MD Anderson Cancer Center to create a centralized salivary gland tumor biorepository in 2009.⁴⁰ Achieving this goal got a significant push from a series of workshops co-sponsored by NIDCR and the Adenoid Cystic Carcinoma Research Foundation, which highlighted the need for centralized and accessible biological samples.

This project has relied on expertise and materials from many sources, in particular the input of patient advocates helping to advance research. Leading the biorepository effort today is MD Anderson's Adel El-Naggar, M.D., a nationally and internationally recognized expert in salivary gland tumor biology and among the most prominent head-and-neck pathologists in the world. Other contributing centers include Johns Hopkins Medical Institution, Rhode Island Hospital, the University of Virginia, the University of Pittsburgh Medical Center, and the University of Mississippi Medical Center.

In addition to facilitating resource sharing, the effort has another important goal: data standardization. By carefully monitoring and controlling collection of tumor samples and related clinical information, the biorepository can minimize variability among research groups. The resource serves the needs of clinical researchers as well as basic scientists, by generating cell lines from primary tumor tissues and cataloging and storing cells, biofluids, and tissues in a centralized facility. A robust database will be a central feature of the biorepository. It will track collection, storage, distribution, and usage of biospecimens and cell lines. Also, a secure online portal will be developed and posted on the NIH website as well as on the biorepository's own website.

³⁹ American Cancer Society: <http://www.cancer.org/cancer/salivaryglandcancer/detailedguide/salivary-gland-cancer-what-is-key-statistics>

⁴⁰ https://research.mdacc.tmc.edu/Salivary_DB/

Body: Heal Thyself

What if a damaged tooth or diseased gum — or a broken jaw — could heal itself quickly and effectively with a natural repair kit delivered promptly to the injured or diseased site? This science fiction could someday soon become reality as a result of impressive progress in NIDCR-supported research that aims to understand how to use natural physiological processes as therapies. Two examples are immune-system modulation that redirects potentially harmful inflammation and the use of stem cells in regenerative medicine approaches.

One promising application for the development of such natural repair kits is periodontal disease, which is a group of conditions that affect the periodontium, the collection of specialized tissues that surround and support teeth and connect them to the bones of the face. Periodontal disease is a health issue affecting one-half of American adults.⁴¹ It is characterized by red, swollen, and painful gums, and in severe cases, bone destruction. It is caused by constant exposure to a microbial community called a biofilm, which envelops the teeth and gums. When immune cells attack bacterial invaders in the mouth, an over-exuberant response can result in persistent inflammation that progressively degrades soft tissue and bone.

NIDCR-funded scientists are learning the step-by-step process that immune cells and natural substances use in the periodontium, and they are devising ways to interrupt or deliberately change it to control inflammation that can be problematic when it runs rampant. For example, researchers working with a mouse model of disease developed a system of polymer microspheres that slowly release a substance that attracts T-regulatory immune cells to injured or diseased oral tissue.⁴² These T cells are often absent at diseased sites, and re-introducing them allows them to act like local police toward other immune system components, tamping down inflammation and limiting the breakdown of bone, leading to natural healing.

Other NIDCR-funded research on natural repair involves a group of substances called lipoxins. The body creates these and other similar molecules called resolvins naturally from fatty acids, and their production is enhanced in the presence of aspirin.⁴³ Studies in animal models have shown that lipoxins reduce cellular inflammation better than current non-opioid pain relievers, and resolvins also appear to have bone-preserving properties.⁴⁴ A lipoxin rinse is currently being developed by NIDCR-funded

⁴¹ Eke PI, Dye BA, Wei L, Thornton-Evans GO, et al. [Prevalence of Periodontitis in Adults in the United States: 2009 and 2010](#). *J Dent Res*. 2012;91:914-20.

⁴² Glowacki AJ, Yoshizawa S, Jhunjhunwala S, Vieira AE, et al. [Prevention of inflammation-mediated bone loss in murine and canine periodontal disease via recruitment of regulatory lymphocytes](#). *Proc Natl Acad Sci U S A*. 2013;110:18525-30.

⁴³ Ji RR, Xu ZZ, Strichartz G, Serhan CN. [Emerging roles of resolvins in the resolution of inflammation and pain](#). *Trends Neurosci*. 2011;34:599-609.

⁴⁴ Gao L, Faibish D, Fredman G, Herrera BS, et al. [Resolvin E1 and chemokine-like receptor 1 mediate bone preservation](#). *J Immunol*. 2013;190:689-94.

scientists as treatment for gingivitis, or inflammation of the gums, and human studies are planned through a phase I/II dose-escalation trial.

Harnessing the regenerative properties of stem cells, other NIDCR-funded scientists are testing the ability of mesenchymal stem cells, or MSCs, to re-grow bone damaged by craniofacial disease or injury.⁴⁵ MSCs in oral tissues have the ability to become bone, cartilage, or fat, depending on the body's needs, and new evidence reveals that certain types of these multitalented cells can also be prompted, with the correct molecular signals, to relieve disease caused by inflammation. Researchers are also using MSCs taken from gum and bone tissue to study wound healing and scar formation, as well to investigate the complex interactions between immune cells in the mouth and various oral structures.

DRAFT

⁴⁵ Liu Y, Wang L, Kikuri T, Akiyama K, et al. [Mesenchymal stem cell-based tissue regeneration is governed by recipient T lymphocytes via IFN- \$\gamma\$ and TNF- \$\alpha\$](#) . *Nat Med*. 2011;17:1594-601.

NIDCR Intramural Scientists Explain Taste, Smell, Thermosensation, and Itch

For many years, NIDCR-funded research has made formative contributions to the field of sensory biology, in particular taste and smell. These two chemical senses play a significant role in perceiving the external world, and they are also important control points for feeding behavior that affects a huge array of oral and other health conditions.

As a senior investigator in NIDCR's intramural research program, Nicholas Ryba, Ph.D., has spent more than two decades untangling the fundamental underpinnings of taste and smell. Throughout this period, Ryba has maintained a model collaborative spirit through longstanding scientific relationships with academic partners as well as with other researchers on the NIH campus. In particular, Ryba and Charles Zuker, Ph.D., of Columbia University in New York have worked together to define how the sense of taste detects and distinguishes specific qualities. In wide-ranging studies, they have mapped the pathways responsible for sweet, bitter, salty, sour, and savory taste — from the surface of the tongue to the depths of the brain.⁴⁶ Their work has revealed that “good” and “bad” tastes are largely innate and genetically specified to influence eating and other behaviors.

Our sense of smell is of course intimately linked to taste and plays an even more important role in food-choice than the sense of taste itself. But studying the sense of smell may also help us understand brain disorders. For example, Ryba's group recently generated genetically altered mice with such a heightened ability to perceive specific odors that these smells triggered powerful seizures.⁴⁷ The results add to our knowledge of how smell is sensed as well as provide new avenues for studying epilepsy.

Recent findings from NIDCR-supported intramural scientists also shed new light on itch, thermosensation, and pain. By examining neuropeptides, transmitters that convey information between nerve cells, Mark Hoon, Ph.D., discovered that one of these molecules is required for the sensation of itch and that another molecule is responsible for sensing certain types of pain.⁴⁸ Hoon and his team found that genetically altered mice in which the itch-related molecule had been removed could not sense all of the itch-inducing agents the researchers tested. In another surprise, the scientists found that, unlike previously thought, the itch pathway is independent of other sensations, such as temperature, pain, and touch. Hoon is now looking to see if the human nervous system communicates the perception of itch the same way as mice do. If such similarities exist, they provide a promising target for drugs to provide relief to the millions of people with chronic itch conditions, such as eczema and psoriasis. Studies are also ongoing to understand more about the mechanism by which pain signals are detected.

⁴⁶ Chen X, Gabitto M, Peng Y, Ryba NJ, Zuker CS. [A gustotopic map of taste qualities in the mammalian brain](#). *Science*. 2011;333:1262-6.

⁴⁷ Nguyen MQ, Ryba NJ. [A smell that causes seizure](#). *PLoS One*. 2012;7:e41899.

⁴⁸ Mishra SK, Hoon MA. [The cells and circuitry for itch responses in mice](#). *Science*. 2013;340:968-71.

NIDCR-Funded Clinical Studies

NIDCR funds extramural and intramural clinical research that addresses a range of scientific questions related to the Institute's mission. Selected examples include:

- Assessment of fluoride treatment of dental decay with polarization-sensitive optical coherence tomography
- Biomarkers of periodontal disease progression
- Characterization of suspicious oral lesions using novel lab-on-a-chip ensembles
- Clinical genetics of amelogenesis imperfecta, dentinogenesis imperfecta, or dentin dysplasia
- Fluoride and other factors in childhood and adolescent bone development
- Genetic factors contributing to oral health disparities in Appalachia
- Genetic studies of Temporomandibular joint disorders (TMJD): Genome-wide association and exome-sequencing studies
- Imaging early caries lesions with near-infrared light
- Immune control of Kaposi's sarcoma-associated herpesvirus infection and impact of HIV infection and therapy
- Mechanisms and treatment response of aggressive periodontitis in children
- National Dental Practice-Based Research Network cracked-tooth registry
- Perivascular niche for salivary gland cancer stem cells and resistance to therapy
- Predicting caries risk in underserved toddlers in primary health care settings
- Prevalence of oral HPV infections in the United States population
- Role of human papillomavirus (HPV) in head and neck squamous cell cancer
- Selective ablation of dental caries and the use of composite
- Safety and feasibility of administration of DNA vaccine in HPV-16 associated head and neck cancer patients
- Single-suture craniosynostosis: Candidate gene and pathway discovery
- TMJD: Onset and transition from acute to chronic
- Tissue regeneration with adipose-derived mesenchymal cells
- TMJD intra-articular disorders: Impact on pain, functioning, and disability



Oral Health Research Across the Globe

NIDCR supports research in a number of countries throughout the world, and a significant focus area is clefting — birth defects that occur during early pregnancy when an infant’s lip or mouth does not form properly. The result can be cleft lip, cleft palate, or both, and these malformations create problems for feeding, speech, hearing, and dental development. Children with cleft lip and/or palate often endure multiple corrective surgeries, incurring a high emotional and financial toll on their families.

Clefting is a major public health problem, affecting one in every 500-1,000 births worldwide.^{49,50} International clefting studies yield new understanding about disease causes and progression, and they can lead to new therapies that U.S.-based studies alone might not achieve. For example, research with populations that have a higher birth prevalence of cleft lip/cleft palate enables researchers to reduce genetic noise in looking for molecular signatures linked to the condition.

Collectively, NIDCR-supported studies on clefting are conducted in Singapore, Taiwan, China, Germany, Denmark, Norway, the Philippines, Brazil, and Africa, as well as within the United States with research participants from specific ethnic groups, such as those of African ancestry, that have been underrepresented in cleft lip/cleft palate research. Multidisciplinary teams participate in this research.

Selected areas currently under investigation include understanding more about:

- Genetic variants for both diagnostic purposes and understanding disease formation
- Environmental contributors, such as maternal behaviors and other factors
- Epigenetics and metabolism in clefting
- The optimal timing of corrective surgery
- Potential associated health issues, such as impaired wound healing and cancers later in life

⁴⁹ Mossey, P.A. and Little, J. (2002) Epidemiology of oral clefts: an international perspective. In *Cleft Lip and Palate: From Origin to Treatment* (Wyszynski, D.F., ed.), pp. 127–144, Oxford University Press

⁵⁰ Study Provides New Leads into Genetics of Cleft Lip and/or Palate (NIDCR web site):

<http://www.nidcr.nih.gov/Research/ResearchResults/NewsReleases/ArchivedNewsReleases/NewsReleases2010/Cleft.htm>

The Unexplored Microbial Universe in Our Mouths

Not unlike early astronomers exploring the heavens, biomedical scientists are increasingly astounded by the vastness and complexity of microbial life in the human body. By the numbers, we are more bacterial than human, and by a long shot — about 10 bacteria to every one human cell — although single-cell microorganisms are much, much smaller than our own. Understanding more about the bacteria that call us “home,” the human microbiota, is a matter of intense interest in the scientific community, since many health conditions have been directly or indirectly linked to specific bacterial types as well as bacterial neighborhoods that vary substantially from person to person, and within the same individual under different conditions and physiological circumstances.

Exploring and characterizing the human oral microbiota is at once a huge opportunity and an immense challenge. We know that host oral tissues and fluids have remarkable protective roles that are also affected by the particular population of resident bacterial species in the host. We also know from NIDCR-supported research that about 600 unique microbial species populate the oral cavity. Less than half of these species can be cultivated using conventional laboratory conditions.⁵¹

The NIDCR-supported open access Human Oral Microbiome Database aims to break open this complexity by promoting distribution of genetic, phenotypic, clinical, and bibliographic data for unnamed and uncultivated members of the oral microbiota.⁵² This resource, along with new methods to study uncultivable oral microbiota, will accelerate translation of basic discoveries to tomorrow’s clinical breakthroughs.

What types of practical applications might benefit the most? Complex infectious oral diseases, such as early childhood caries and destructive periodontal diseases, could serve as models of polymicrobial disease. More broadly, this research will extend the foundation of existing microbiome research to explore and map an exciting new frontier in oral microbiology. The goal of the Human Oral Microbiome Database is to provide the research community with direct access to DNA-sequence information for the hundreds of species of organisms that are present in the human oral microbiota, many of which were previously uncultivable, enabling a deeper understanding of the role of bacteria in immune function. Importantly, NIDCR believes that this research investment will yield novel approaches to study the function of the uncultivable oral microbiota, fostering hypothesis-driven basic research, and supporting the translation of new discoveries to targeted and improved prevention, diagnosis and early treatment of oral polymicrobial diseases.

⁵¹ Dewhirst FE, Chen T, Izard J, Paster BJ, et al. [The human oral microbiome](#). *J Bacteriol.* 2010;192:5002-17.

⁵² <http://www.homd.org/>

New Opportunities to Track Oropharyngeal Cancer

Human papillomavirus (HPV) infects human cells in mucous membranes, and distinct viral strains can cause cervical cancer or oropharyngeal cancer.^{53,54} Most people exposed to HPV never develop cancer at all. However, current reports state that the incidence of HPV-associated oropharyngeal cancer has more than tripled from 1988 to 2004,⁵⁵ calling for continued research to understand why this has occurred and how to stem the rise through population-health approaches. An even higher risk of HPV-associated oropharyngeal cancer has arisen in people affected by HIV/AIDS.⁵⁶

HPV-associated oropharyngeal cancers differ markedly from non-HPV oropharyngeal cancers. Survival rates for the two types are dramatically different: people with HPV-associated oropharyngeal cancer have far better survival rates than people with non-HPV oropharyngeal cancer. Not surprisingly, the two cancers are also different at the molecular level and respond differently to treatments, indicating that they are by most accounts completely separate diseases. But scientists need to learn much more about HPV-associated oropharyngeal cancer, and NIDCR-supported research is actively pursuing questions related to incidence, risk factors, and disease progression. Researchers have identified a perplexing sex-based difference in the prevalence of oropharyngeal HPV infection, with three-fold higher infection rates in men compared to women.⁵⁷ Smoking also has been shown to be an independent risk factor for oropharyngeal HPV infection — potentially due to mutagenic or immunosuppressive effects.

Many questions remain, but the FDA-approved HPV vaccine Gardasil⁵⁸ is effective against the particular strains of HPV implicated in oropharyngeal cancers. Also, a recently published National Cancer Institute-funded clinical trial of 5,840 women demonstrated that another HPV vaccine, Cervarix, was highly effective at preventing oral HPV infection in women with or without HPV cervical infections.⁵⁹ NIDCR remains vigilant to this public health opportunity for cancer prevention and will encourage research to fill gaps in understanding.

⁵³ Ryerson AB, Peters ES, Coughlin SS, Chen VW, et al. [Burden of potentially human papillomavirus-associated cancers of the oropharynx and oral cavity in the US, 1998-2003](#). *Cancer*. 2008;113:2901-9.

⁵⁴ American Cancer Society: <http://www.cancer.org/cancer/news/hpv-vaccine-shown-to-protect-against-oral-form-of-infection>

⁵⁵ Chaturvedi AK, Engels EA, Pfeiffer RM, Hernandez BY, et al. [Human papillomavirus and rising oropharyngeal cancer incidence in the United States](#). *J Clin Oncol*. 2011;29:4294-301.

⁵⁶ Beachler DC, Weber KM, Margolick JB, Strickler HD, et al. [Risk factors for oral HPV infection among a high prevalence population of HIV-positive and at-risk HIV-negative adults](#). *Cancer Epidemiol Biomarkers Prev*. 2012;21:122-33.

⁵⁷ Gillison ML, Broutian T, Pickard RK, Tong ZY, et al. [Prevalence of oral HPV infection in the United States, 2009-2010](#). *JAMA*. 2012;307:693-703.

⁵⁸ <http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM094042>

⁵⁹ Herrero R, Quint W, Hildesheim A, Gonzalez P, et al. [Reduced prevalence of oral human papillomavirus \(HPV\) 4 years after bivalent HPV vaccination in a randomized clinical trial in Costa Rica](#). *PLoS One*. 2013;8:e68329.

White House Recognizes Two NIDCR Grantees Advancing Oral Health in Children

The Presidential Early Career Award for Scientists and Engineers, or PECASE, is the highest honor bestowed by the U.S. government on outstanding scientists and engineers beginning their independent careers. In recent years, two NIDCR-funded scientists won this prestigious honor. Both women are investigating issues related to oral health in children.

Margherita R. Fontana, D.D.S., Ph.D., of the University of Michigan School of Dentistry, received a 2011 PECASE award for her research on the ability to predict caries risk in underserved Hispanic toddlers in primary health care settings. Her work focuses on addressing oral health inequities among preschool-aged children. A key motivator for Fontana's research is the troubling increase in dental caries within children aged two to five years, especially in underserved and minority population groups. She views targeted prevention and care as a promising strategy for improved oral health in this age group.

Candidate risk factors for caries development include specific metrics such as past and present caries in both child and caregiver, but also more general information such as a caregiver's rating of the child's overall health status. Also important, Fontana predicts, are those risks stemming from culturally derived eating and behavior patterns. She believes that an objective, easy-to-implement, and validated risk-assessment tool that can be used widely would be extremely useful. In particular, she sees the need for such a prevention resource in non-dental settings such as schools, clinics, and physicians' offices. Her caries-risk work is part of a larger prospective longitudinal study that will track the natural history of dental caries over a period of four years, in which she will look for other ways to prevent caries in vulnerable populations at the earliest stage possible.

Jessica Y. Lee, D.D.S., M.P.H., Ph.D., of the University of North Carolina at Chapel Hill, received a 2010 PECASE award for her studies of how factors such as parental oral health literacy and practitioner culture can affect children's oral health. Lee surmised that pediatric dentists might serve as gatekeepers to identify and intervene early for children at high risk for being overweight or obese.

To begin to explore this possibility, she surveyed the practices and attitudes of pediatric dentists on the topic of both weight- and caries-related counseling. Lee discovered that only nine percent of pediatric dentists surveyed offered weight-related counseling compared to 80 percent who offered caries-related counseling to young patients and/or their parents and caregivers.⁶⁰

Her results highlight potential barriers to implementing screening on a wider scale. In particular, Lee found that while many pediatric dentists recognized the value of screening, they also feared offending parents and their children, and they worried about whether their advice would be respected and heeded. Although more research is needed to follow up on Lee's survey results, her findings suggest the

⁶⁰ Lee JY, Caplan DJ, Gizlice Z, Ammerman A, et al. [US pediatric dentists' counseling practices in addressing childhood obesity](#). *Pediatr Dent*. 2012;34:245-50.

need for developing dedicated staff-based training programs and counseling services to screen for weight-related problems in dental settings.

NIDCR Research Addresses the Many Faces of Pain

According to the 2011 Institute of Medicine report “Pain in America,” chronic pain costs the United States up to \$635 billion each year in medical treatment and lost productivity.⁶¹ To anyone who has either experienced chronic pain or knows someone who has, the costs are truly immeasurable. A multitude of conditions cause chronic pain. These include chronic fatigue syndrome, endometriosis, fibromyalgia, interstitial cystitis, irritable bowel syndrome, chronic headache, temporomandibular joint and muscle disorders, or TMJD, and vulvodynia. For reasons that are not thoroughly understood, all of these conditions exact a bigger toll on women than on men. Often an injury or health problem like an infection triggers short-term, or acute, pain, which can then transform into a years- or even decades-long health nightmare. Why do some pain conditions, and not others, turn into longstanding problems? Which treatments work for short- and long-term pain, and can anything be done to mitigate the suffering of millions of Americans?

NIDCR has been a long-time supporter of research on pain, in general, and on specific painful oral conditions such as TMJD, a group of conditions that cause intense jaw and facial pain. Common TMJD symptoms include pain from chewing or in the jaw joint, limited jaw opening, painful clicking, and popping or grating in the jaw joint when opening or closing the mouth. Research has shown that people with TMD also often have other, related chronic painful conditions such as fibromyalgia and irritable bowel syndrome. Scientists suspect that the overlap of chronic pain conditions is not coincidental, and they are looking for common features in the susceptibility, severity, and progression of various chronic pain conditions — with the twin goals of understanding the cause of pain and determining treatments effective for several conditions at once.

NIDCR supports a wide range of basic research investigating how pain begins as well as studies focused on determining novel ways to treat pain, including non-opioid analgesics that control inflammation. NIDCR also collaborates extensively with the NIH community to tackle the problem of chronic pain by co-funding a range of multidisciplinary and interdisciplinary basic and clinical research approaches. The seven-year Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA I) study aimed to identify causes of first-onset TMJD. The results, published in 2013, indicate that a broad range of factors such as sociodemographics, health status, clinical orofacial factors, psychological function, and pain sensitivity influence the course of TMJD.⁶² The follow-up study, OPFERA-II, will identify risk factors that predict whether acute TMD will transition into a chronic condition. OPFERA II will also identify genetic aspects and other risk factors that determine whether acute TMD will develop as a single condition or in

⁶¹ [Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research](#) (Institute of Medicine report, 2011)

⁶² Slade GD, Fillingim RB, Sanders AE, Bair E, et al. [Summary of Findings From the OPFERA Prospective Cohort Study of Incidence of First-Onset Temporomandibular Disorder: Implications and Future Directions](#). *J Pain*. 2013;14(12 Suppl):T116-24.

conjunction with other chronic pain conditions, including headache, low back pain, irritable bowel syndrome, and widespread body pain.⁶³

Postcards from the Field

“Instead of reading about the future of dentistry, I was a part of doing the research and building that future. I’ve met colleagues through the PBRN network who have been some of the best and brightest, and they’ve given me ideas and helped to re-energize me in my practice.”

“There really is no other way to say it. Joining a PBRN is the best thing that I’ve done for my practice, my patients, and actually myself since graduating from dental school.”

Dr. Julie Ann Barna, Lewisburg, PA

D.M.D., University of Pennsylvania (1980)

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“The National Dental PBRN has had a positive influence on me and my practice. It has re-energized my enthusiasm by challenging me to improve my critical thinking. Doing these research studies has gently nudged me to stay current, making me a better clinical scientist and in doing so, has opened a new avenue for my professional development.”

“By connecting me with other network dentists, this experience makes me feel less isolated from my colleagues.”

Dr. Paul Benjamin, Miami, FL

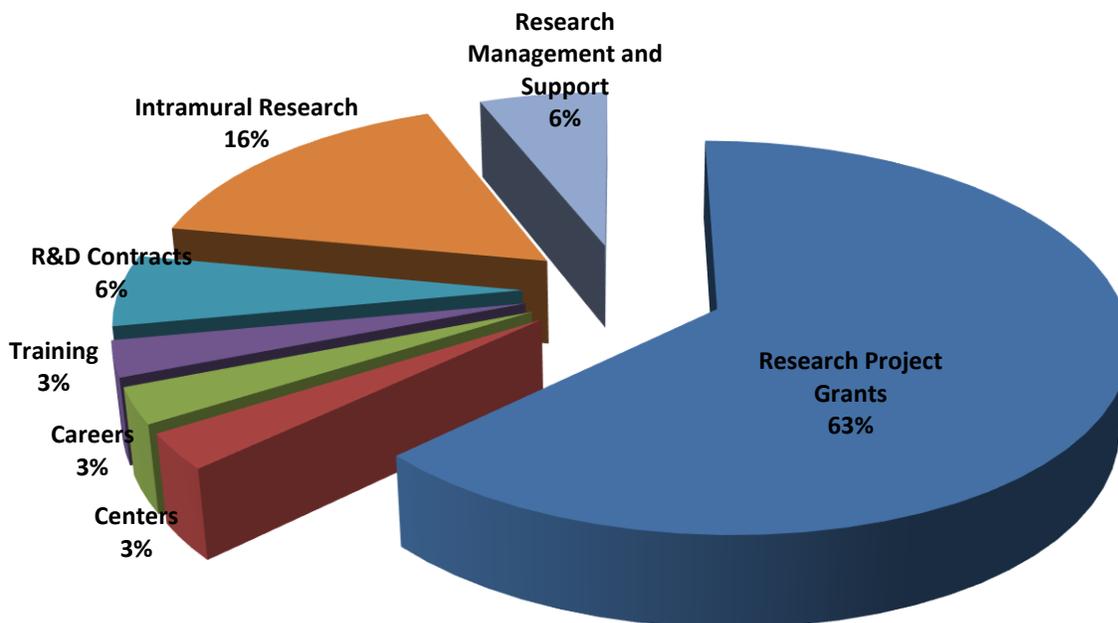
D.M.D., University of Florida College of Dentistry (1976)

⁶³ Dworkin SF. [The OPPERA Study: Act Two](#). *J Pain*. 2013;14(12 Suppl):T1.

NIDCR at a Glance

Part of the National Institutes of Health, NIDCR is the Federal government's lead agency for scientific research on dental, oral, and craniofacial diseases. Scientists supported by NIDCR use modern biomedical and behavioral research tools to conduct research on the full spectrum of topics related to diseases and conditions that fall within the Institute's mission.

In efforts to improve dental, oral, and craniofacial health, NIDCR prioritizes scientific opportunities on the basis of their potential impact to improve health, the readiness of the scientific community to accomplish them, and their alignment with the Institute's mission.



NIDCR FY 2013 Funding Distribution (total of \$387 million)

This figure shows the proportion of NIDCR spending across the various funding mechanisms during Fiscal Year 2013, with the majority of the budget used to fund research project grants (dark blue).