

## **Biomaterials**

The Committee is pleased that NIDCR is exploring approaches to prevent dental caries with probiotic therapy, and in the development of biomaterials. The Committee encourages NIDCR to increase its investment in the development of new and improved biomaterials for use in clinical settings to enhance the prevention and treatment of caries.

### Action taken or to be taken:

The National Institute of Dental and Craniofacial Research (NIDCR) supports research to increase the longevity and durability of dental materials for use in clinical settings to enhance the prevention and treatment of caries. Standard treatment for caries involves the application of dental restoratives to replace damaged tooth tissue (a filling) or using a tooth-shaped “cap” to cover the damaged tooth (a crown). However, exposure to the stresses of the mouth, such as chewing and oral bacteria, can lead to damage of the restoration or recurrent dental decay. As a result, fillings or crowns often need to be replaced within 8-10 years. NIDCR-funded research includes a broad range of studies designed to improve restorative materials and dental crowns, enhance the adhesives used to attach them to the tooth, and uncover novel approaches for strengthening and regenerating damaged teeth.

NIDCR-supported investigators are designing potent antibacterial resins with re-mineralizing properties for use in dental composites and adhesives. Researchers are also creating a new form of high-strength ceramics – strong, yet translucent, these dental materials are designed to preserve tooth appearance and structure while extending service life. To reduce the incidence of dental crowns cracking, another group of researchers has developed a computational modeling tool that enables scientists to speed up the discovery process and streamline the development of novel dental materials.

At the center of each tooth lies the dental pulp – a living tissue that contains nerves and blood vessels, as well as stem cells that can form new tooth tissue. Normally dental pulp is covered by a hard layer of enamel. If dental pulp becomes exposed, the result is painful inflammation of the tooth. NIDCR-supported researchers have identified a compound called phenamil that activates dental pulp stem cells to produce new tooth tissue. In the future, researchers hope to integrate phenamil into the protective materials used to cover exposed dental pulp – to stimulate natural tooth repair and help avoid the need for a root canal. Looking to the future, NIDCR is supporting research to ensure new and improved biomaterials are durable and suitable for clinical use to improve the prevention and treatment of caries.

### **Temporomandibular Disorder Trans-NIH**

The Committee recognizes NIDCR's leadership in TMD pain research, which has led to establishing TMD as a multisystem disorder with overlapping pain and non-pain conditions. The Committee encourages NIDCR to continue its leadership as a critical member of the Trans-NIH Working Group on Chronic Overlapping Pain Conditions by promoting and advancing integrated research on these conditions. In addition, as the oral disability associated with TMD affects a patient's nutritional health status, the Committee encourages NIDCR to improve research on orofacial function relevant to the nutritional implications of TMD. Finally, the Committee is aware of the scientific meetings on an integrated systems approach of precision medicine related to cellular-molecular-genetic-epigenetic mechanisms related to diagnosis and treatment of TMD and its comorbid conditions. In 2013, several Institutes co-sponsored a workshop on the topic of the temporomandibular joint. The Committee requests an update on initiatives that resulted from the recommendations that came forth from these meetings in the fiscal year 2019 CJ.

#### Action taken or to be taken:

NIDCR maintains a leadership role on the NIH Pain Consortium and the Trans-NIH Working Group on Chronic Overlapping Pain Conditions, promoting and advancing integrated research on TMD, orofacial pain, and overlapping chronic pain conditions. Over a decade ago, NIDCR launched the Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA) study to accelerate research to improve TMD and orofacial pain treatments. OPPERA is the first-ever large, prospective clinical study to identify risk factors that contribute to someone developing TMD. In FY 2016 NIDCR began partnering with NIDDK to add investigations of chronic overlapping pain conditions (COPCs) to existing pain cohorts, like OPPERA. As a result, OPPERA has received additional funding to expand the research scope beyond TMD and to develop an easy-to-use online research tool to help identify individuals with COPCs and understand common risk factors across COPCs.

NIDCR also supports research to develop patient-centered non-pharmacological strategies to prevent and treat chronic TMD. Scientists are testing a web-based tool designed to improve diet, sleep, and oral health behaviors, tailored for each individual. This program will help develop the evidence base to empower patients to optimally manage their own health.

As a result of the 2013 trans-NIH Temporomandibular Joint in Health and Disease Roundtable, NIDCR is funding a project that is providing longer-lasting TMD pain relief using a state-of-the-art technology called high-definition transcranial direct current stimulation. This non-invasive procedure stimulates the brain to release naturally occurring opioid-like molecules, a part of the body's pain relief system. The researchers are testing the stimulation method to turn on a receptor protein – called the  $\mu$ -opioid receptor – that receives a signal from endorphins or opioids to relieve pain. Additional studies in this area could lead to new non-opioid pain management therapies to treat TMD and other pain conditions.

## **Temporomandibular Disorders (TMD)**

The Committee understands that NIH-funded research has demonstrated that temporomandibular disorders [TMD] are primarily a multisystem disorder with overlapping conditions influenced by multiple biological and environmental factors rather than solely an orofacial pain condition.

However, diagnosis and care of patients have not changed to reflect this major paradigm shift, with many patients continuing to receive treatments solely focused on teeth and jaws. Moreover, the medical community lacks education regarding the complexity and systemic aspects of TMD as well as its many comorbid medical conditions. Patients are treated by a multitude of practitioners across numerous disciplines with treatments that have the potential to cause harm. To address these issues, the Committee requests that NIH provide an update on the state of TMD research, activities related to TMD education, and clinical studies of TMD in the fiscal year 2019 CJ.

### Action taken or to be taken:

To provide the evidence base needed to improve Temporomandibular Disorders (TMD) diagnosis and patient care, the National Institute of Dental and Craniofacial Research (NIDCR) funds a diverse research portfolio focused on the development, structure, function, regeneration, and replacement of the temporomandibular joint (TMJ), as well as studies on chronic orofacial pain and comorbid conditions associated with TMD. NIDCR also supports Centers of Excellence in Pain Education (CoEPEs), key hubs for developing and distributing pain management curriculum resources to enhance and improve how health care professionals are taught about pain and its treatment. Through CoEPEs, a number of online training modules have been developed for comorbid conditions associated with TMD, including a tutorial on Burning Mouth Syndrome and related orofacial pain.<sup>443</sup>

NIDCR supports basic research to understand TMJ biology and function to improve long-term health. Scientists are investigating how the TMJ develops, including formation of the disc and joint cavities, maturation of joint lubricant-producing cells, and the long-term maintenance and renewal of TMJ cells and structures that are essential for joint health. Foundational knowledge on TMJ biology is critical for the advancement of joint repair and regeneration.

Another NIDCR-funded project is developing tools to measure the structural changes to temporomandibular bones to improve the ability to evaluate clinical changes in TMD diagnosis, assessment, and treatment. Clinicians, computer scientists, and engineers are collaborating to investigate the use of imaging markers to analyze bones, making much of their data and tools freely available to the scientific community to accelerate TMD research and the development of new therapies.

NIDCR's Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA) clinical research study is generating the evidence base to inform the development of novel approaches to treat TMD, orofacial pain, and other overlapping pain conditions. The researchers investigated the role of genetics in pain sensation, and have demonstrated an important function for a signaling protein called epiregulin and its corresponding receptor, epidermal growth factor receptor (EGFR). When the epiregulin-EGFR pathway is activated in mice, the perception of pain was increased, while using drugs that inhibit the EGFR pathway reduced the pain sensation.

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<sup>443</sup> <http://painmeded.com/>

Additional research on these therapeutic drugs may open new avenues to treat TMD and other pain conditions.