

Grant Spurs Next Stage Testing of Tissue-Engineered Material for TMJ Disc Complex

A \$6 million award from [The California Institute of Regenerative Medicine \(CIRM\)](#) has been awarded to the [University of California, Irvine \(UCI\)](#) researchers for their late-stage preclinical project, “Treatment of the TMJ Disc Complex.” Leading the effort will be Kyriacos Athanasiou, PhD, PE, and his team at Driving Engineering & Life-science Translational Advances at Irvine (DELTAi) in collaboration with Cartilage Inc. Joining him on this project are Jerry Hu, PhD, Ryan Donahue, PhD, Wendy Brown, PhD, MRSc, and Kiley Athanasiou, MBA.



Caption: From left to right, Ryan Donahue, Kiley Athanasiou, Kyriacos Athanasiou, Wendy Brown, Jerry Hu, the UCI-Cartilage Inc. team charged with advancing Hyaleon® through the CIRM CLIN1 grant.

“The aim of this grant is to bring Hyaleon®, our tissue-engineered implant, to regulatory authorization to start human clinical trials,” said Dr. Athanasiou. “We have shown very promising results thus far. With this grant, we will perform additional, key preclinical studies that will enable a Hyaleon’s® Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA).”

The grant will enable manufacturing process development, preclinical studies, shipping and stability testing, regulatory submission, and clinical trial start-up plans, Dr. Hu said, “These activities are crucial to establish a safe and efficacious Hyaleon® implant for eventual human use. The studies will need to be rigorous and held to a high standard in order to gain regulatory authorization for clinical trials.”

Dr. Brown, who has been leading interactions with the FDA, is excited about the agency’s response. “Our team submitted a pre-IND meeting request and a Hyaleon® briefing package to the FDA in Fall 2022 and the FDA gave us extremely valuable feedback on our study designs and plans. Completing this meeting was a requirement for the funding opportunity, and the work we will be doing for this grant is directly reflective of the FDA’s feedback.”

A portion of the work will be done by Cartilage Inc., a UCI-based start-up company aimed at commercializing Hyaleon®. Cartilage Inc.’s CEO, Ms. Athanasiou, commented that “This funding to DELTAi at UCI is fundamental to advancing translational efforts for Hyaleon®. Upon IND submission, which is the final requirement of the grant, Hyaleon® will be substantially de-risked and move further down the translational pipeline.”

Significantly, the researchers are excited by the hope that the clinical translation of Hyaleon® will benefit TMJ patients who need better therapeutic interventions. “While we are still several years away from Hyaleon® becoming a commercial medical product, this funding from CIRM advances the work to the threshold of being able to treat humans with Hyaleon® in clinical trials. Our hope is that Hyaleon® proves to be safe and efficacious in reducing pain and improving jaw function for those suffering from defects of the TMJ disc complex,” said Dr. Donahue, who is the Project Manager for the grant and also a member of The TMJ Association’s International Scientific Advisory Council.

While a clinical trial is not a part of this grant, CIRM offers a CLIN2 funding mechanism, which provides funds to perform clinical trials. “Pending the success of the initial project, we will consider applying for a CLIN2 to continue the clinical translation of Hyaleon®. Right now, though, our focus is to successfully complete our IND-enabling preclinical studies and to submit Hyaleon’s® IND to the FDA. We are excited about the opportunities that it will bring,” said Dr. Donahue.

This two-and-a-half-year project is slated to start this summer.

An International Effort to Improve Dental Care of TMJ Patients

Last year we reported that The TMJ Association collaborated with researchers at Newcastle University and the International Network for Orofacial Pain and Related Disorders Methodology (INFORM) to create a guide for general dentists, dental hygienists, and other dental care providers on how to best make dental care for those living with Temporomandibular Disorders (TMD) as safe and comfortable as possible, given their symptoms and limitations in jaw function.

In its simplest format, it could be considered a “do” and “don’t do” list with

helpful pointers, such as:

- the need for extra time in appointments
- deferring elective treatment when there is an active flare-up of TMD

The guide was developed in an international partnership with clinicians and patients. We are pleased to report that our article, *How dental teams can help patients with temporomandibular disorders receive general dental care: An International Delphi process*, was published in the March 2023 edition of the *Journal of Oral Rehabilitation*. [To view the publication, click here.](#)

We encourage you to share this paper with dental professionals. We hope it will receive wide dissemination, given the global partnerships involved in its development. It will be a first step towards providing more compassionate care and understanding of TMJ patient issues in the receipt of dental care.

Accept Help from Others!

When you don't feel well, it's OKAY to get help from friends and family. As it happens, I have a TMJ problem related to a group of genetic disorders called [Ehlers Danlos Syndrome. The most common symptoms are loose joints and fragile skin, but some cases also involve weakened blood vessel walls](#) (see article in [TMJ News Bites, Issue 3, 2022](#)). Recently, I have also been struggling with a flare-up of dysautonomia. That's the general term for malfunctions in the autonomic nervous system, which are the nerves used in breathing, blood circulation, digestion, and other essential functions. The past few months have been rough for me, as I have been trying to find someone who could treat it. There were days when I couldn't get off the couch because my heart was beating so rapidly.

Yet, I have always found it hard to accept help from friends and family. (Call it pride, or self-reliance.) So, it was a lesson I had to learn. Because when we let others extend a hand to us, it helps them as well. The adage that it's a blessing to give as well as to receive, is true.

- My friend, Christine, decided to cook her authentic Chinese dish for my family. My daughter absolutely loved this dinner and it gave me a chance to rest.
- My friend, Andrey, offered to watch my daughter for me while my husband and I went to a doctor's appointment. When I got home I saw that she had cleaned and organized my entire kitchen for me.



- One night, I was feeling blue and my husband brought home a beautiful bouquet of flowers which lifted my mood. Flowers have always made me smile.
- My daughter's *Younglife* leader at our church came



over and prayed for me a week ago. We were chatting about where we were from, and a couple days ago he texted me that he had free tickets for the three of us to see the Padres play the Red Sox. Being from Boston, I jumped at the chance to see the game.

- Another night, my friend Patti brought me a quilt that her church *Quilt and Prayer Ministry* made. She told me each knot on the quilt was a prayer from a different woman in the ministry. This beautiful quilt and prayers made me feel so special.

I have received cards and many messages from friends and family over the last few months and it has made me feel loved and helped me to keep moving forward.

I encourage you to let people help you in your time of need. After all, science tells us that we humans have survived as a species because we learned to cooperate and collaborate early on. And when you accept help, not only will it comfort you, but it also gratifies the person doing the helping. When you are in a better place, you will find that you want to reach out to someone else who is suffering— and make them feel special, too.



Lisa

The Invisible Podcast

The TMJ Association was contacted a few months ago by Leighann Talbert, a 13-year-old Junior High student from Arkansas. A class project inspired her to create “The Invisible Podcast”, a podcast dedicated to spreading awareness of invisible pain-causing diseases, and helping others with these diseases to feel less alone. Leighann has struggled with two of these diseases herself for almost five years.

The TMJ Association connected Leighann to Christin Veasley, the Co-founder and Executive Director of the [Chronic Pain Research Alliance](#), an initiative of The TMJ Association, and Alexandra Andrea a TMJ patient and advocate, both of whom are featured on her podcast. You can listen to them, and other episodes on [Spotify](#) and [Apple Podcasts](#).

Report TMJ Splint-related Issues to the Food and Drug Administration

The U.S. Food and Drug Administration (FDA) is evaluating safety concerns

with the use of certain dental devices that are **fixed** (non-removable) palatal expanders used on adults to remodel the jaw or to treat conditions.

The devices of concern include:

- Anterior Growth Guidance Appliance (AGGA) and Fixed Anterior Growth Guidance Appliance (FAGGA),
- Anterior Remodeling Appliance (ARA) and Fixed Anterior Remodeling Appliance (FARA),
- Osseo-Restoration Appliance (ORA) and Fixed Osseo-Restoration Appliance (FORA), and
- Any other similar device types.

The FDA is aware of these devices being used to treat conditions such as obstructive sleep apnea (OSA) and temporomandibular joint disorder (TMD) and remodeling the jaw in adults. However, the safety and effectiveness of these devices intended for these uses have not been established, and these devices are not cleared or approved by the FDA.

The FDA is also aware of reports of serious complications with use of these devices. The FDA is asking patients, caregivers, and health care providers to report any complications with these devices to the FDA. Prompt reporting of adverse events can help the FDA identify and better understand the risks associated with medical devices. The FDA is working to evaluate information from all available sources to provide additional information on this issue.

Source: <https://www.fda.gov/medical-devices/safety-communications/evaluation-safety-concerns-certain-dental-devices-used-adults-fda-safety-communication>

CBS investigation which triggered this response:

<https://www.cbsnews.com/news/criminal-investigation-agga-dental-device-and-its-inventor/>



**“Sometimes a TMJ patient needs
inspiration just to
get through each day.”**

- The TMJ Association, Ltd.

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Patients Needed for Studies

Central and Peripheral Factors in Temporomandibular Disorder (TMD)

Researchers at Emory University in Atlanta are in need of TMJ patients to participate in their study. They are investigating people who experience chronic pain in the head and/or face in everyday life. They are using unique tests to find out how the brain processes chronic and acute pain messages and will observe patients to see how pain and sensory processing differs in TMD. [Click here to view the informed consent form for this study](#). Contact Daniel Harper, PhD (Principal Investigator) at 404-727-7789 or daniel.harper@emory.edu with any questions and to participate.

Impact of Daily Physical Activity and Chronic Musculoskeletal Pain Survey

A research team from the Faculty of Rehabilitation Sciences of Hasselt University in Belgium is investigating the relationship between the intensity of daily physical activity and chronic musculoskeletal pain. They will be looking at fibromyalgia, chronic temporomandibular disorder, osteoarthritis, chronic neck pain, chronic shoulder pain, and chronic low back pain. The study involves an online survey which will take approx. 50 minutes to complete. More details and a link to the study is available at:

https://uhasselt.qualtrics.com/jfe/form/SV_etl78e58y2YeUDQ

Understanding and Restoring Whole Joint in Pain Management: An NIH HEAL Initiative (Virtual) Workshop

Date: July 25 & July 26, 2023, 10:00 a.m. - 5:00 p.m. ET

The purpose of this Helping to End Addiction Long-term[®] Initiative, or NIH HEAL Initiative[®], workshop is to examine the current literature on joint pain research and identify critical knowledge gaps in order to gain a comprehensive understanding of the whole joint, including the contributions of various articular and periarticular tissue pathologies that lead to pain in different types of joints. In addition, the workshop will explore manipulations and interventions that may help to restore whole joint health. Of particular interest, workshop participants will examine the relationships and interactions among the different tissue components of joints, including myofascial tissues, and their contributions to and impact on reducing pain by preserving and restoring joint health and function.

*"Research on joint health has also been fragmented and siloed in other ways. Much has been learned about joint tissues at both the macro and micro levels, but, for example, investigators who study biomechanics don't necessarily interact with those who study genetics and biochemistry. And, researchers who specialize in one type of joint, like the knee or hip, haven't spent much time with those who study other joints, like the facet joints of the spine or the **temporomandibular joint**."*

Five scientific sessions and a final discussion session will cover structural changes in joints, mechanisms of whole joint pathology, differences among joint types and joint pain populations, interventions to address joint pain and disease, and emerging technologies that can be leveraged to advance scientific understanding of joints as complex "organs." **The intended audience is interested scientists, clinicians, as well as patients, advocates, and other interested stakeholders.**

More details at: <https://www.nccih.nih.gov/about/offices/od/director/past-messages/join-us-for-an-nih-heal-initiative-workshop-on-whole-joint-health?nav=govd>

NIH Grant Opportunity for Researchers

HEAL Initiative: Toward Developing Quantitative Imaging and Other Relevant Biomarkers of Myofascial Tissues for Clinical Pain Management (R61/R33, Clinical Trial Required)

The National Institutes of Health (NIH) intends to support the development of innovative quantitative measures involving myofascial tissues for pain management involving research participants using a two-phase grant funding mechanism. This study is part of the NIH's Helping to End Addiction Long-term (HEAL) initiative to speed scientific solutions to the national opioid public health crisis. The NIH HEAL Initiative bolsters research across NIH to (1) improve treatment for opioid misuse and addiction and (2) enhance pain management.

More information about the HEAL Initiative is available at: <https://heal.nih.gov/> This notice of a funding opportunity (NOFO) seeks research applications that will develop quantitative measures to facilitate the development of future biomarkers of myofascial tissues and assess their abilities to detect changes in myofascial tissues across a variety of pain management interventions, manipulations, or therapies. Promising quantitative measures may be based on minimally invasive imaging technologies, electrophysiological recordings, integration of multiparametric imaging and electrophysiology approaches, or their integration with other markers (e.g. immune factors, genomic markers, physiological factors) through multiscale modeling or machine learning analysis. The first phase, funded by the R61, will provide funding for up to 3 years to develop quantitative measures that can differentiate abnormal myofascial tissue from healthy tissues, using cross-sectional correlations with clinical signs/symptoms. In addition, the R61 phase should include planning activities for the R33 phase. The second phase, funded under the R33, will support studies to assess the ability of the quantitative measures developed in the R61 phase to detect changes to myofascial tissues across a variety of pain interventions in rigorous, longitudinal clinical studies. The combined R61/R33 cannot exceed 5 years. Transition from the R61 to the R33 phase of the award will be administratively reviewed and will be determined based on successful completion of "Transition Milestones" that need to be clearly specified in the R61 phase application.

More details at: https://grants.nih.gov/grants/guide/rfa-files/RFA-AT-24-003.html?utm_medium=email&utm_source=govdelivery

Changing the Face of TMJ

We cannot change the face of TMJ without YOU!

When you donate, you are making the following happen:

- Advancing TMJ Scientific Research
- Advocating for TMJ Patients
- Supporting and Guiding Patients
- Educating Health Care Professionals
- Providing Trusted Information

The TMJ Association is the *ONLY* patient advocacy organization fighting for the best science that will lead to a greater understanding of Temporomandibular and related disorders and treatments that will help and not harm patients.

We cannot change the face of TMJ without YOU. [Make a tax-deductible contribution today!](#) Your contribution is more than a donation. It is how we will ensure that TMJ patients have a voice — through education, patient support and advocacy.

We cannot do this important work without you! Thank you for your generosity.

About The TMJ Association...*Changing the Face of TMJ*

The TMJ Association, Ltd. is a nonprofit, patient advocacy organization whose mission is to improve the quality of health care and lives of everyone affected by Temporomandibular Disorders (TMJ). For over 30 years, we have shared reliable information on TMJ with people like you. We invite you to visit our website, www.tmj.org.



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