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Lin Han, PhD, receives 2021 Kappa Delta Young Investigator Award for the study of cartilage function, regeneration and disease intervention in osteoarthritis

ROSEMONT, Ill. (February 12, 2021)—The 2021 Kappa Delta Young Investigator Award was presented to Lin Han, PhD, for research on the structure and function of cartilage extracellular matrix (ECM) and its impact on tissue regeneration and disease evolution in osteoarthritis (OA). The Young Investigator Award recognizes outstanding clinical research related to musculoskeletal disease or injury by investigators under 40 years old.

Dr. Han and his colleagues provided a new understanding for how to improve cartilage regeneration and disease intervention. By utilizing nanomechanical tools, which measure molecules at a very minute scale,[i] they found new molecular activities that govern the proper functioning of healthy cartilage ECM (structural support cells that regulate cellular growth[ii]) and the degeneration of ECM that occurs in OA.

OA is the most common degenerative musculoskeletal disease,[iii] affecting more than 32 million Americans, mainly elderly.[iv] There is currently no treatment or drug available to treat it.

"Cartilage is one of the simplest tissues in the human body, yet the more we discover, the more we become aware of the unknowns," said Dr. Han, associate professor, School of Biomedical Engineering, Science and Health Systems, Drexel University, Philadelphia, Pa. "Even after decades of research on cartilage tissue engineering and regeneration, we still cannot find a way to fully restore the function of native cartilage. When cartilage is damaged by injury, overuse or inflammation, patients may go through a period where they cannot continue life as normal."

Understanding Cartilage ECM

Articular cartilage covers the ends of bones and provides functions critical for joint motion, including load bearing, energy dissipation and lubrication; however, it has poor self-healing capabilities. The major trademark of OA is the irreversible breakdown of cartilage ECM. The limited understanding of how ECM works in healthy and disease states has hindered the treatment of OA.

ECM is made of water, collagens, proteoglycans (mainly aggrecan), DNAs and proteins. Aggrecan plays an important role in the proper functioning of articular cartilage[v] and is a key indicator of cartilage health and disease. In healthy cartilage, aggrecan is essential for load bearing and energy dissipation. When a patient has OA, aggrecan fragmentation is one of the earliest molecular events.

Dr. Han and colleagues used atomic force microscopy (AFM)-based tools to evaluate the nanomechanics of aggrecan under various loading modalities, such as compression, which

allowed the researchers to understand the biometric assembly of aggrecan. AFM tools allow scientists to scan surfaces at a very small scale. The outcomes showed new methods of molecular interactions that strengthen the assembly of aggrecan networks may exist. This work was the first to study the dynamic mechanical behaviors of cartilage on such a minute level, setting the path for several follow-up studies.

Collagens and Other Proteins in the ECM

The cartilage ECM is a porous collagen network that contributes to tissue strength and serves as a scaffold that entraps aggrecan. Dr. Han and his research colleagues studied the interactions between aggrecan and the collagen II fibrillar network. Collagen II is a protein that is one of the primary connective tissues of the body.[vi] The researchers found that aggrecan and collagen undergo molecular adhesion when compressed, contributing to a number of biophysical factors that help aggrecan and collagen II evolve. These results demonstrated that the interactions between aggrecan and collagen II could play an important role in the reliability of ECM.

Further studies discovered that decorin plays an essential role in regulating the integrity of cartilage ECM. Decorin is a component of the cartilage's ECM, which is like a house for the cell. The research found that decorin functions as a "physical linker" to strengthen the integration of the aggrecan network in ECM and delays the loss of fragmented aggrecan from degenerative cartilage. In mouse models with decorin deficiency, loss of decorin showed impaired load bearing and energy dissipation capabilities of native cartilage. Following induced knee injury in mice, absence of decorin accelerates the loss of aggrecan and the fibrillation of cartilage. Thus, these mice develop more severe OA.

"We found that this protein has a very important role in mediating the integrity of cartilage tissue, especially aggrecan," said Dr. Han. "This is important because aggrecan is the molecule that determines the shock absorption and the load bearing function. Knowing this, we can potentially design new strategies that use decorin to promote the regeneration of articular cartilage and could lead to new treatment strategies."

ECM in Post-Traumatic Osteoarthritis

Post-traumatic osteoarthritis (PTOA) is the most widespread form of OA in young adults, resulting in a decreased quality of life over the long term. Early diagnosis and effective intervention are difficult due to the limited understanding of the initiation of PTOA.

Utilizing mice injury studies, Dr. Han found that cartilage modulus (the measure of the ability to withstand changes) begins to weaken as early as one week after surgery and continues until 12 weeks, preceding historical signs of cartilage damage at four to eight weeks. However, administering a small molecule inhibitor can reduce the modulus reduction.

For the first time, the researchers were able to quantify the biomechanical changes of cartilage in the initiation of PTOA, demonstrating how highly sensitive cartilage is when OA begins. Further studies showed that the impairment of cartilage matrix, as a result of aggrecan degrading, is a leading event in PTOA initiation.

Ongoing studies are testing the potential of improving cartilage regeneration or OA intervention by regulating the activities of particular molecules through the use of collagen II and native decorin.

“The findings will eventually help guide surgeons in designing more specific strategies for patients,” said Dr. Han. “For example, hypothetically, there may be a type of mechanical load that would be more advantageous for us to stimulate cartilage cells and, in turn, strengthen the articular cartilage tissue. Physical therapists and surgeons can then understand what exercises are going to benefit particular patients.”

About the Kappa Delta Awards
In 1947, at its golden anniversary, the Kappa Delta Sorority established the Kappa Delta Research Fellowship in Orthopaedics, the first award ever created to honor achievements in the field of orthopaedic research. The first annual award, a single stipend of $1,000, was made available to the Academy in 1949 and presented at the AAOS meeting in 1950. The Kappa Delta Awards have been presented by the Academy to persons who have performed research in orthopaedic surgery that is of high significance and impact.

The sorority has since added two more awards and increased the award amounts to $20,000 each. Two awards are named for the sorority national past presidents who were instrumental in the creation of the awards: Elizabeth Winston Lanier, and Ann Doner Vaughn. The third is known as the Young Investigator Award. For more information about the manuscript submission process, please visit aaos.org/kappadelta.

Kappa Delta Foundation
Kappa Delta Sorority is a national organization for women with nearly 260,000 members, more than 500 chartered alumnae chapters and 169 active collegiate chapters. Established in 1981, the Kappa Delta Foundation is a 501(c)3 organization whose mission is to secure funds for the educational, leadership and charitable purposes of Kappa Delta Sorority. The foundation is supported by member donations and bequests that fund programs and initiatives such as scholarships, internships, grants and more. Kappa Delta National Headquarters is in Memphis, Tennessee. For more information, visit www.kappadelta.org/foundation/.

About the AAOS
With more than 39,000 members, the American Academy of Orthopaedic Surgeons is the world’s largest medical association of musculoskeletal specialists. The AAOS is the trusted leader in advancing musculoskeletal health. It provides the highest quality, most comprehensive education to help orthopaedic surgeons and allied health professionals at every career level best treat patients in their daily practices. The AAOS is the source for information on bone and joint conditions, treatments and related musculoskeletal health care issues and it leads the health care discussion on advancing quality.

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Disclosure

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