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Kappa Delta Ann Doner Vaughn Award Presented to Cato T. Laurencin, MD, PhD, FAAOS for pioneering research in bone regenerative engineering

ROSEMONT, Ill. (February 12, 2021)—Cato T. Laurencin, MD, PhD, was named the 2021 Kappa Delta Ann Doner Vaughn Award recipient for his 30 years of scientific research in musculoskeletal regenerative engineering, the field which he founded and brought to the forefront of translational medicine. Dr. Laurencin's work has led to the development and advancement of biodegradable polymeric materials in bone repair and tissue regeneration. The Kappa Delta Awards recognize research in musculoskeletal disease and injury. Dr. Laurencin's work has had great impact in advancing patient care.

"When I first started my laboratory at the Massachusetts Institute of Technology in 1988, bone was a primary target to study and develop as scientists had just learned how to actually grow human bone cells outside the body," said Dr. Laurencin, the Albert and Wilda Van Dusen Distinguished Endowed Professor of Orthopaedic Surgery and chief executive officer, Connecticut Convergence Institute for Translation in Regenerative Engineering, University of Connecticut. "We essentially started a new field—regenerative engineering—and have continued to progress the field with a journal and a society, which brings together individuals from broad areas and viewpoints for the purposes of studying regeneration."

Dr. Laurencin is the pioneer of the field, with an expertise in biomaterials science, stem cell science, biophysics and developmental biology. His work in regenerative engineering has led to singular honors. He is the first to receive the oldest/highest award of the National Academy of Medicine (the Walsh McDermott Medal) and the oldest/highest award of the National Academy of Engineering (the Simon Ramo Founders Award). In 2016, he received the National Medal of Technology and Innovation, America's highest honor for technological achievement from President Barack Obama in ceremonies at the White House.

Bone Regeneration Discovery

Each year, more than two million bone graft procedures worldwide are performed.[i] Autografts, where a patient's own tissue is used, are the standard of care, but have constraints such as requiring a second surgery for graft harvesting. Allografts, which use donor tissue, run the risk of infection, have limited availability and may cause immune hypersensitivity. Therefore, there was a need to find an alternative, synthetic solution.

"Autografts are the gold standard for use in bone regeneration, but they have limitations in terms of donor site morbidity for harvesting and supply," said Dr. Laurencin. "There has been great interest in examining ways to create engineered materials for bone regeneration in a variety of different areas and for different uses. Some of our work focused on the fact that we could create engineered materials that are actually inductive, that is, they can foster bone regeneration by themselves without the addition of morphogenetic factors."

To discover an alternative, synthetic solution, Dr. Laurencin and his colleagues began to engineer musculoskeletal tissues, applying biological, chemical and engineering principles to repair, restore or regenerate living tissue using biomaterials, cells and additional factors alone and in combination. Over the past 30 years, he has explored the use of biodegradable polymeric and ceramic materials for use in bone repair, focusing on poly(ester), poly(anhydride) and poly(phosphazene) biomaterials alone or in combination with hydroxyapatite, a naturally occurring mineral, and other ceramics to form two- and three-dimensional (2D, 3D) matrices.

The research showed that the use of a matrix system could facilitate bone regeneration, providing a framework which osteoblasts (cells that form new bone) may bind its extracellular matrix (ECM) and bridge bone defects. The ECM is a structural support for cells that directs cell adhesion and migration as well as regulates cellular growth.[ii] The matrices are biodegradable and designed so that, over time, the osteoblasts secrete ECM, allowing the biomaterial to be completely absorbed and only regenerated bone remains.

Evaluating Bone Regeneration
Dr. Laurencin set out to study the behavior of osteoblasts on new materials, starting with 2D matrices, which supported the attachment, growth and osteoblast traits by osteoblast-like cells. He was able to design and produce novel materials that provided alternatives to currently available materials and has continued to develop additional novel polymers, making innovative blends with other degradable polymers. Polymers are materials made of long, repeating chains of molecules and are often used in plastics.[iii] Studies demonstrated that unique polymer systems, which have superior lab and animal studies performance, excellent physicochemical properties and unique erosion mechanisms, representing a major paradigm shift in biomaterials design for regenerative engineering.

Once Dr. Laurencin and his team established that these biomaterials could be used as bone regeneration platforms, they were the first to develop porous, biodegradable 3D-poly (organophosphazenes) [P(PHOS)] matrices for tissue regeneration. Studies demonstrated that the use of a 3D matrix increased the amount of cell growth on the matrix because of the significant increase in surface area over 2D structures. The matrices interconnecting, porous network enabled organized cell growth, ECM formation and mineralization (when the bone matrix becomes filled with calcium phosphate nanocrystals), showing that these materials could be used for bone engineering applications.

The researchers next developed a novel sintered microsphere matrix, a 3D matrix with a complete interconnected pore structure, resembling the structure of trabecular bone, which is found at the end of long bones such as the femur. This design allowed the newly forming bone to actually occupy the pore structure while the matrix degraded. After the matrix completely degraded, only the pore structure of the newly formed trabecular bone remained.

***In Vivo* Studies**
The 3D matrix was then studied in animals (*in vivo*) and showed significant bone formation throughout the implant site by week eight when combined with growth factors demonstrating that the 3D matrix could be an effective bone graft.

Further *in vivo* research examined the potential of the 3D matrices as a composite without growth factors, utilizing matrices with human-derived mesenchymal stem cells, which are found in bone marrow. Composite materials, which are composed of two or more materials, were studied because these materials can offer numerous advantages such as strength. The results suggested that the composite designed with low crystalline ceramics had inherent osteoinductive properties, meaning new bone is formed by the transformation of stem cells into bone. The studies showed the flexibility of the matrices for bone engineering and the versatility for these matrices to deliver results through stem cells, bone cells, transfected cells (cells that have been introduced to foreign DNA) or directly from the scaffold. The composite matrix demonstrated that it could remineralize and remodel the defect site within eight weeks of injury without growth factors.

“Our work involving matrix- and material-based regeneration found that as we moved from smaller animals to larger animals, the materials tended to have an ability to become more functional and bioactive,” said Dr. Laurencin. “In a number of our regeneration studies for bone as well as soft tissue, we found that as we move to larger animals, we’ve been able to demonstrate more bioactivity and inductivity in terms of polymer ceramic materials.”

The Next Frontier: Limb Regeneration
Building on his work in bone and soft tissue regeneration, Dr. Laurencin has begun to apply regenerative engineering principals as an approach to regenerating complex tissues with the goal of limb regeneration. In 2016, the University of Connecticut announced a revolutionary project overseen by Dr. Laurencin—the Hartford Engineering a Limb (HEAL) Project, which aims to regenerate a human limb by 2030. Laurencin’s ambitious work has been recognized by the American Association for the Advancement of Science in awarding him the Philip Hauge Abelson Prize for “signal contributions to the advancement of science in the United States.”

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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- Dr. Laurencin has received royalties from Globus Medical Company for some of the technologies based on this work.
- Dr. Laurencin is the founder of Healing Orthopaedic Technologies Company, Healing Orthopaedic Technologies-Bone Company, and a member of the board of directors of MiMedx Corporation.
- Dr. Laurencin is the recipient of the NIH Director's Pioneer Grant Award for his research involving limb regeneration.

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[i] Campana V, Milano G, Pagano E, et al. Bone substitutes in orthopaedic surgery: from basic science to clinical practice. *J Mater Sci Mater Med*. 2014;25(10): 2445–2461.
[ii] ScienceDirect. Extracellular Matrix. https://www.sciencedirect.com/topics/neuroscience/extracellular-matrix. Accessed 1/11/2021.
[iii] Live Science. What is a Polymer? https://www.livescience.com/60682-polymers.html. Updated 11/14/2017. Accessed 1/18/2021.