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Rising Stars of Regenerative Engineering: The Dynamic of Students and Research Mentors

A Webinar Series from The Cato T. Laurencin Institute for Regenerative Engineering at the University of Connecticut

The Cato T. Laurencin Institute for Regenerative Engineering in partnership with the Advanced Regenerative Manufacturing Institute (ARMI) is producing this webinar series. The webinars will inform participants and the audience on the perspective of young scientists in training conducting research in regenerative engineering supplemented by the interaction with their research mentors. Presenters are selected from the Institute's signature T32 Doctoral and Young Innovative Investigator Programs.

Four Webinars will be held on **4, 11, 18, 25 April** (at 12 noon Eastern) 2023, to cover *(1)* cartilage repair, *(2)* stem cell advancements, *(3)* muscle regeneration, and *(4)* bioprinting engineering. The format will deliver a description of the research by the trainee followed by a dialogue with the mentor.

Beyond the science, the webinars will address the personal dimensions of research training. What is the ideal environment to train young scientists? What are the barriers? How does the young scholar mesh into the fabric of the organization? In all, attendees to the webinars will appreciate contemporary science in regeneration and the dynamics of transferring that science to the next generation in the enterprise.

T32 Doctoral Training. The Program *Regenerative Engineering of Musculoskeletal Tissues: A Convergence Doctoral Training Program* has been funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases NIAMS *(T32 AR079114)* for 5 years (2021-2026). The T32 Program goals are to educate, support and enhance the training of individuals dedicated to careers as independent clinical translational and basic scientists in regenerative engineering. The program offers inter-disciplinary research training at the University of Connecticut (UConn) combining the fields of biomedical science and engineering. Dr. Cato Laurencin is the Principal Investigator.

Young Innovative Investigator Program (YIIP). The Cato T. Laurencin Institute for Regenerative Engineering manages and directs all aspects of YIIP, which offers a Master's Degree in Biomedical Science. Created and founded by the Institute, YIIP has diversified the next generation of biomedical scientists by recruiting and training recent college graduates from underrepresented groups who are interested in pursuing graduate education. Scholars pursue a Master's of Science in Biomedical Science. The research experiences, intense mentorship and professional networking program provides the expertise necessary to advance in biomedical science and gain acceptance to doctoral programs.

Regenerative Engineering is defined as the convergence of advanced materials science, stem cell science, physics, developmental biology, and clinical translation for the regeneration of complex tissues and organ systems. Musculoskeletal regeneration is a field ripe for an inventive approach based on convergence to address challenging issues, advance technology and further fundamental knowledge for therapeutic applications. At the center of the convergence approach is the understanding that new solutions in regeneration will take place through an *'un-siloed'* approach.

FORMAT: Webinar presentation for 40 minutes by the trainee, followed by a 20-minute dialogue with the mentor, and concluding with 15 additional minutes for Q&A via chat from the audience. The events will be hosted and moderated by Dr. Gualberto Ruaño, Director of Special Projects at the Cato T.

Laurencin Institute for Regenerative Engineering, University of Connecticut. *(Mentor and Trainee biographies are included after the Webinar schedule.)*

SCHEDULE

Webinar #1

DATE and TIME: **Tuesday, April 04, at 12 PM Eastern**

TITLE: *A Growth Factor-Based Approach to Articular Cartilage Repair*

Trainee: **Sandro Cloiseau**

Mentor: **Caroline N. Dealy, Ph.D.**
Associate Professor
Department of Craniofacial Sciences, School of Dental Medicine
Department of Biomedical Engineering, School of Dental Medicine
Department of Orthopedic Surgery, School of Medicine
Department of Cell Biology, School of Medicine
University of Connecticut

Description of content: The articular cartilage of the knee functions to absorb shock, bear weight, and provide a smooth articulating surface for joint motion. Traumatic joint injury such as knee ACL tear or severe ankle sprain can damage the articular cartilage and cause Post-Traumatic Osteoarthritis (PT-OA), an especially aggressive form of OA in which the injured articular cartilage degrades and is lost in as little as 15-20 years. PT-OA is a problem for elite athletes and military because traumatic joint injury is common in these groups. Fortunately, PT-OA onset can be delayed, and patients temporarily return to sport or service with a surgery called Osteochondral Allografting (OCA), in which the damaged articular cartilage is removed and replaced with cartilage from a deceased donor. Regrettably, the OCA procedure is not a cure because the graft fails after 5-10 years. The reason for failure is the lack of seamless integration of the graft into the patient's own articular cartilage. The overall goal of this project is to develop an approach to achieve seamless integrative articular cartilage repair.

Webinar #2

DATE and TIME: **Tuesday, April 11, at 12 noon Eastern**

TITLE: Synthetic Artificial Stem Cells – A Platform for Precision Medicine in Regenerative Engineering

Trainee: **Rachel Marchini**

Mentor: **Lakshmi S. Nair, M.Phil., Ph.D., FBAO, FAIMBE, FNAI**
Professor
Department of Orthopedic Surgery, UConn Musculoskeletal Institute
Department of Material Science and Engineering
Department of Biomedical Engineering
Associate Director, The Cato T. Laurencin Institute for Regenerative Engineering
University of Connecticut

Description of content: Synthetic artificial stem cells (SASC) have been engineered to reproduce the paracrine effect of the stem cell secretome and provide control of its composition for targeted tissue regeneration. During this presentation, various applications of SASC to osteoarthritis (OA) will be described, choosing growth factors important to chondrogenesis and encapsulating respective recombinant proteins in poly (lactic-coglycolic acid) 85:15 (PLGA). SASC demonstrates the feasibility of precision manufacturing a completely synthetic, tailorable secretome for regenerative engineering.

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Webinar #3

DATE and TIME: **Tuesday, April 18, at 12 noon Eastern**

TITLE: *Aches, Age, and Influenza: Regenerative Insights from a Pathway to Muscle Loss and Disability*

Trainee: **Andreia Cadar**

Mentor: **Jenna M. Bartley, Ph.D.**
Assistant Professor
Center on Aging and Department of Immunology
University of Connecticut

Description of content: Older adults have diminished immune responses that increase susceptibility to infectious diseases, such as influenza (flu). In older adults, flu infection can lead to hospitalization, catastrophic disability, and mortality. We previously demonstrated severe and prolonged muscle degradation and atrophy in aged mice during flu infection. Here, we utilized an unbiased transcriptomic analysis to elucidate mechanisms of flu-induced muscular declines in a mouse model. Our results showed age-related gene expression differences including downregulation of genes associated with muscle regeneration and organization and upregulation of genes associated with pro-inflammatory cytokines and migratory immune pathways in aged mice when compared to young. Pathway analysis revealed significant enrichment of leukocyte migration and T cell activation pathways in the aged muscle during infection. Intramuscular CD4 T cells increased in both young and aged mice during infection, while intramuscular CD8 T cells increased exclusively in aged muscle. CD4 T cells in young muscle were regulatory T cells (Treg), while those in aged were T follicular helper (Tfh) and Th2 cells. Correspondingly, IL-33, an important cytokine for Treg accumulation within tissue, increased only in young flu infected muscle. Conversely, CXCL10 (IP-10) increased only in aged muscle suggesting a continued recruitment of CD8 T cells into the aged muscle during flu infection. Overall, our findings elucidate a link between flu-induced disability and dysregulated intracellular T cell recruitment into flu injured muscle with aging. Furthermore, we uncovered potential pathways involved that can be targeted to develop preventative and therapeutic interventions to avert disability, encourage muscle regeneration and maintain independence following infection.

Webinar #4

DATE and TIME: **Tuesday, April 25, at 12 noon Eastern**

TITLE: *Bioengineering lung tissue using advanced 3D bioprinting technology*

Trainee: **Heather Wanczyk**

Mentor: **Christine Finck, M.D., FACS ,** Surgeon-in-Chief
Chief, Division of Pediatric General and Thoracic Surgery
Connecticut Children's Medical Center
The Peter J. Deckers Endowed Chair in Pediatric Surgery
University of Connecticut

Description of content: Lung transplantation remains the only viable option for individuals suffering from end-stage lung failure, but current limitations exist including a continuing shortage of suitable donor lungs and immune rejection following transplantation. To address these concerns, engineering a decellularized biocompatible lung scaffold from cadavers reseeded with autologous lung cells to promote tissue regeneration has been explored. Proof-of-concept transplantation of these bioengineered lungs into animal models has been accomplished. However, failure to fully regenerate and repopulate lung scaffolds with all of the distinct cell populations necessary for proper function remains a significant hurdle. Therefore, bioengineering lung tissue using advanced 3D bioprinting technology in combination with lung-derived stem cells is currently being explored as an alternative approach and may help to address not only donor shortages but provide a means to create patient-specific therapies for both pediatric and adult populations suffering from respiratory illnesses. The following talk will provide an update on cells currently used for lung tissue engineering as well as recent progress in the development of a 3D bio printed pediatric-sized airway for future transplantation.

MENTOR BIOGRAPHIES

Jenna M. Bartley, Ph.D. received her B.S., M.S. and Ph.D. in Kinesiology from the University of Connecticut. Her graduate research focused on interrelated aspects of human health, metabolism, and muscle function focusing on human subject research. She completed a postdoctoral fellowship focused on immunology and aging utilizing murine models of aging and infection. She became an Assistant Professor in 2019 in the Dept of Immunology and Center on Aging at UConn Health. Her independent research focuses on combining her unique education and training background in both murine and human subject research to focus on translational aging research. Her multidisciplinary research uses geroscience approaches to bridge the bench and the bedside to uncover common pathways among the aging process and to develop potential interventions to prevent age-related declines in immune responses, physical function, and overall healthspan.

Caroline N. Dealy, Ph.D. is pursuing the broad research goal to inform and develop clinically-relevant approaches to address debilitating human conditions affecting the joints and limbs. Her research philosophy is to understand the cellular and molecular mechanisms that cause disease and impair healing and growth. By integrating studies in molecular, skeletal, and developmental biology, Dr. Dealy's laboratory is providing knowledge that can be used to develop clinical therapies that augment the body's own natural defenses and regenerative responses. Her current research areas include: Osteoarthritis, Rheumatoid Arthritis, and Limb Regeneration.

Christine Finck, M.D., FACS is the Executive VP and Surgeon in Chief at Connecticut Children's Medical Center. Her lifelong passion has been the pursuit of improving the care we deliver to children. The research in the Finck Laboratory focuses on various pediatric and neonatal diseases that originate from congenital defects, preterm birth, accidental injuries and cancer. The focus of her research work began with pediatric lung disease and utilizing stem cells, de-cellularized lung scaffolds, and 3D printing to study and potentially treat pediatric lung diseases. Additionally, her laboratory also focuses on tissue engineering approaches for esophageal defects due to atresia, caustic injuries and cancer. The research is now evaluating the use of synthetic polymers and scaffolding as a potential therapeutic option for these conditions. Finally, her laboratory has a strong interest in obesity as it is a disease that affects many children, and is currently working on identifying cellular changes that occur after bariatric surgery.

Lakshmi S. Nair, Ph.D. is Professor in the Department of Orthopedic Surgery, and Departments of Materials Science Engineering and Biomedical Engineering at the University of Connecticut. She also serves as the Associate Director of the Cato T. Laurencin Institute for Regenerative Engineering. Dr. Nair's research is committed to developing injectable and biomimetic biomaterials, and identifying bioactive molecules that could accelerate tissue regeneration and reduce musculoskeletal pain. She has more than 130 peer-reviewed publications, 25 book chapters, and edited books biomaterials, injectable hydrogels and regenerative engineering. Her research has been supported by federal funding agencies including current NIH R01 as well as private foundations. She is an innovator with several national and international awarded patents and is an elected fellow of the National Academy of Inventors. She currently serves as Secretary of the Regenerative Engineering Society and has served in the national and international program committees for the Society for Biomaterials, USA and the International Union of Societies for Biomaterial Science and Engineering. She was also appointed to the Panel on Materials Science and Engineering at Army Research Laboratory by the National Academy of Sciences. Dr. Nair is currently the Vice President of the UConn chapter of the National Academy of Inventors.

TRAINEE BIOGRAPHIES

Andreia Cadar is a Ph.D. candidate in the UConn Center on Aging and Department of Immunology in the lab of Dr. Jenna Bartley. Andreia's research focuses on developing translationally relevant interventions to improve regenerative capacity of aged muscle after an insult. Her work in the lab focuses on unveiling mechanism related to flu-associated muscle degradation and atrophy using an aged mouse model. Currently, her experiments are focused specifically on characterizing immune cell populations that contribute to muscle degradation and prolonged inflammation in response to flu infection. She also works on a multi-site clinical trial, Starting a Testosterone and Exercise Program after Hip Injury (Step-HI, NCT02938923), to gain clinical perspective on the challenges older adults face in regaining function following a traumatic fall. Overall, her multifaceted research focuses on novel treatments to improve muscle regeneration in older adults and allow them to maintain their independence following any stressor that causes disability, such as flu, falls, or other age-related conditions.

Sandro Cloiseau is a Master's candidate in the field of biomedical science at the University of Connecticut. He graduated from UConn (Storrs, CT) with Honors and as a Ronald E. McNair Scholar in May 2021, majoring in Biological Sciences and minoring in English Literature. While at Storrs, Sandro conducted research under Nichole Broderick, studying the gut microbiome of Drosophila melanogaster (the fruit fly). His thesis project investigated the misuse of the herbicide 'glyphosate' and its effects on the human microbial community. Sandro became very interested in translational research. Currently, Sandro is a second-year scholar in the Young Innovative Investigator Program at UConn, mentored by Dr. Caroline N. Dealy. He is working on approaches to seamlessly heal cartilage in hopes of developing a therapeutic approach for patients with Post-traumatic Osteoarthritis.

Rachel Marchini is a Ph.D. student in chemical and biomolecular engineering at the University of Connecticut. She joined the Cato T. Laurencin Institute for Regenerative Engineering in 2021 after completing her BS in chemical engineering at the Storrs campus. Her research focuses on the regeneration of articular cartilage in treating osteoarthritis and to continue into osteochondral defects with a focus on the regeneration of the bone/cartilage interface. Her work aims to expand the concept behind the synthetic artificial stem cell (SASC) and develop it for use in additional disease models.

Heather Wanczyk is a Ph.D. student in Biomedical Science at the University of Connecticut Health Center-Department of Cell Biology. She has extensive training and experience in developing regenerative therapies to treat congenital defects of the lung, trachea and esophagus. She has a Bachelors degree in Animal Science as well as a Master's degree in Immunology from the University of Connecticut. Her research focuses on using advanced 3D bioprinting technology in combination with stem cells to develop pediatric-sized airways that will help reduce transplant shortages in individuals suffering from chronic respiratory diseases. She is also interested in developing novel biomaterials to repair congenital defects of the esophagus and trachea. Her ultimate goal is to pursue a career in regenerative engineering where she can harness her skills and experience to develop improved therapies and treatments for diseases affecting the musculoskeletal system.