NC STATE

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CMI COMPARATIVE MEDICINE INSTITUTE

FROM THE DIRECTORS

A Year of Change & Future Possibilities

Another exciting year for the CMI! In this issue, we again focus on the many accomplishments of CMI-associated faculty and students and on our new efforts in the area of predictive biology. We also focus on changes to the CMI leadership and future opportunities.

As detailed in this issue, CMI continues to innovate and improve all of its programs, from our entrepreneurial efforts via CATALYZE, focused on encouraging and facilitating faculty and student entrepreneurship, to the Think, Collaborate & Do ideation event, focused on increasing interdisciplinary research collaborations with the goal of improving human and animal health. In addition, we continue our efforts to improve CMI's student mentoring programs, the Young Scholar Program (YSP) and the Summer interdisciplinary Research Initiative (SIRI), and to increase their impact across the university with the expansion of two minors (one for graduate students, and one for undergraduates) focusing on developing future leaders in the biomedical sciences. Our innovative programs continue to impact NC State students and faculty whether it's through the formation of a company, formation of a new interdisciplinary research team, or the mentoring of students in the nuances of participating and leading a multi-disciplinary team. In short, CMI's impact continues to be broad and long-lasting.

But we also want to share changes in our leadership, as well as possible new opportunities for a partnership between CMI and the expanding Integrative Sciences Initiative (ISI). As detailed in this issue, one of us (Joshua Pierce) has accepted the position of Executive Director of the ISI and will be stepping down as co-director of the CMI on September 1, 2023. Discussions are underway to determine who will be the new CMI co-director, and we hope to be able to announce that soon. But this transition also creates new opportunities for CMI and ISI to jointly expand and improve existing programs and work together to develop new ones. We hope to be able to soon announce details of this partnership, but we are confident that the final model will be of great benefit to both CMI and ISI, and all the faculty and students that these units represent.

For now, a massive thank you to all the people that provide us with the resources and support to continue to achieve our vision. Provost Warwick Arden, Senior Vice Provost Rob Dunn, Vice Chancellor and Associate Vice Chancellors of the Office of Research and Innovation Mladen Vouk, Jon Horowitz and Genevieve Garland, and the Deans of the participating colleges (CALS, COE, COS, CVM, and WCOT). We could not do any of this without your support.

Finally, we thank all of our members for your tireless work, your amazing creativity, your unwavering collegiality, and your commitment to the CMI. **You have all made CMI a shining example of what faculty and students working together can achieve!**

Jorge Piedrahita

Randall B. Terry Jr. Distinguished Professor of Translational Medicine &
Alumni Distinguished Professor of Graduate Education
Co-Director, Comparative Medicine Institute
Director, Comparative Molecular Medicine Graduate Training Program
Director, U-TEAM Undergraduate Training program in the Biomedical Sciences

Joshua Pierce

Howard J. Schaeffer Distinguished Professor of Chemistry,
Co-Director, Comparative Medicine Institute,
Executive Director, Integrative Sciences Initiative,
Director, Chemistry of Life Training Program

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LAYOUT, GRAPHIC DESIGN & PHOTOGRAPHY
Sasha Campbell

WRITTEN BY
Kristina Nelson, Nicole Duncan, & Sarah O'Connor

PRODUCED BY
Sarah O'Connor

Many thanks to everyone who took the time to participate in interviews or provide quotes as part of this project:

Rosemary Bayless
Ashley Brown
Yevgeny Brudno
Sue Carson
Suh Hee Cook
Glenn Cruse
Rob Dunn
Hisham El-Shaffey
Matthew Fisher
Jessica Gluck
Grace Hardy
Katelyn Harris
Cristina Lanzas
Santosh Mishra
Nina Moiseiwitsch
Meaghan Nappo
Michael Nolan
Sarah Ozawa
Jorge Piedrahita
Joshua Pierce
Lauren Schnabel
Frank Scholle
Sarah Shelton
Rohan Shirwaiker
Melanie Simpson
Lauren Sylvester
Isaiah Stevens
Thomas Theis
Carolyn Veale
Ian Williamson
Fred Wright
Nicole Zwennes

2022-2023

CMI LEADERSHIP

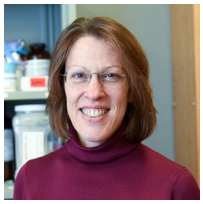
Co-Director
JORGE PIEDRAHITA
japiedra@ncsu.edu

Co-Director
JOSHUA PIERCE
jgpierce@ncsu.edu

Executive Assistant
SARAH O'CONNOR
compmedinst@ncsu.edu

Chemistry of Life

Associate Director
YEVGENY BRUDNO
ybrudno@ncsu.edu



Associate Director
MELANIE SIMPSON
msimpso3@ncsu.edu

Emerging & Infectious Diseases

Associate Director
CRISTINA LANZAS
clanzas@ncsu.edu

Associate Director
FRANK SCHOLLE
fscholl@ncsu.edu

Functional Tissue Engineering

Associate Director
ROHAN SHIRWAIKER
rashirwa@ncsu.edu

Associate Director
LAUREN SCHNABEL
lvschnab@ncsu.edu

Translational Pharmacology & Physiology

Associate Director
SANTOSH MISHRA
skmishra@ncsu.edu

Associate Director
MICHAEL NOLAN
mwnolan@ncsu.edu

Director of Training & Education
ASHLEY BROWN
aecarso2@ncsu.edu

Director of Training & Education
JESSICA GLUCK
jmgluck@ncsu.edu

Director of Entrepreneurship
THOMAS THEIS
ttheis@ncsu.edu

Clinical Research Representative
ELEANOR HAWKINS
echawkin@ncsu.edu

Associate Member Representative
HISHAM EL-SHAFFEY
helshaf@ncsu.edu

Associate Member Representative
JACOB THOMPSON
jdthomp5@ncsu.edu

Training Program Leader
MATTHEW FISHER
mbfisher@ncsu.edu

Training Program Leader
CAROLYN VEALE
cpveale@ncsu.edu

CMI WHO WE ARE

180
Faculty

140
Postdocs & Graduate Students

22
Departments

6
Colleges

5
Universities

RESEARCH PROGRAMS

Chemistry of Life (CLP)

60 Faculty
40 Associate Members

Focus Areas
Molecular Synthesis & Characterization
Molecular Mechanisms of Metabolism & Disease
Molecular Therapeutics & Drug Discovery

Emerging & Infectious Diseases (EID)

71 Faculty
56 Associate Members

Focus Areas
Viral Infections
Diagnostic Biomarkers
Antimicrobial Resistance

Functional Tissue Engineering (FTE)

54 Faculty
64 Associate Members

Focus Areas
Scalable Manufacturing of Novel Therapeutics
Large Animal Models for Regenerative Medicine
Predictive Bioanalytical Systems

Translational Pharmacology & Physiology (TPP)

85 Faculty
55 Associate Members

Focus Areas
Genetic & Physiological Disorders
Novel Treatments for Disease
Large Animal Models of Disease

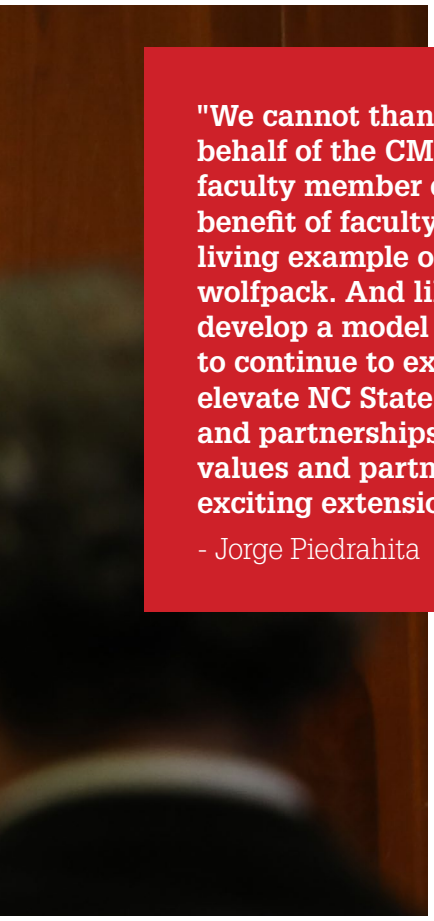
CMI & ISI

A NEW DIRECTION

Dear CMI Colleagues,

I am writing this letter as I prepare to step down as co-director of CMI and assume the role of executive director at the Integrative Sciences Initiative (ISI). This period marks a time of transition – but also one of abundant opportunities. The faculty, staff, and students of CMI form an incredible community, and I will always cherish the personal and professional growth I experienced during my time in this institute — and of course I intend to remain an active member!

My journey at NC State began in January 2012 when I was invited to participate in an event hosted by the Center for Comparative Medicine and Translational Research at the CVM. Sid Thakur, a young leader, engaged me, and over the next couple of years, I became increasingly involved. Together, we worked on developing several large grant proposals focused on novel antibiotics. Although we did not secure those initial grants, the experience of assembling teams of PIs, gaining support from university leaders, and exploring interdisciplinary opportunities on campus was enlightening. During this time, the CCMTR evolved into CMI, and in 2016, I joined the CMI executive committee. Being part of such a dynamic and active leadership group as an assistant professor exposed me to university leadership, and I eagerly sought opportunities to connect CMI's strengths with the College of Sciences. In 2018, I became the co-associate director of the emerging and infectious diseases group, first with Sid Thakur, and later with Ed Breitschwerdt. This period also led to my promotion to associate professor and a heightened focus on programmatic visioning for CMI.



"We cannot thank Josh enough for all of his efforts on behalf of the CMI. He exemplifies how a dedicated faculty member can lead and work with others for the benefit of faculty, students and NC State in general. A living example of the Think and Do mentality of the wolfpack. And like Josh, I am excited to find ways to develop a model where ISI and CMI can work together to continue to expand and improve our programs to elevate NC State faculty and students. Collaboration and partnerships has been at the core of the CMI's values and partnering with ISI is a natural and exciting extension of our values."

- Jorge Piedrahita

As co-associate director, I also emphasized student training and, together with Jorge, served as co-PI on our first T34 NIH training grant for undergraduates. This program originated from the SIRI and YSP programs within CMI, and our success in securing this grant propelled these efforts to the next level. However, I recognized the need for more opportunities for students in the physical and life sciences at large, and thus, the idea of a program in the 'Chemistry of Life' was born. Our vision encompassed research and training efforts in this molecule-focused area. After several meetings with Provost Arden, Dean McGahan, and other key supporters, we launched the Chemistry of Life (CLP) program in December 2020. Importantly, this unit was housed within CMI, ensuring our strengths remained intact while expanding. Along with this expansion, I had the opportunity to step up as co-director of CMI with Jorge and bring new associate directors, Melanie Simpson and Yevgeny Brudno, into the institute for CLP. We quickly achieved success in expanding our graduate and undergraduate training programs in these areas, securing a NIH T32 and Beckman Scholars Program in that same year.

Concurrently, NC State was envisioning a new building dedicated to interdisciplinary chemistry education and research. Being involved with the provost's office regarding the CLP program, I was invited to join the building committee. As the vision for the building took shape, Provost Arden recognized that the original vision aligned perfectly with the CLP vision and saw an opportunity to leverage what we had developed to establish the Integrative Sciences Building. It was envisioned that the building become a campus hub for molecular sciences, and the broader community could unite around this core through the ISI. In 2022, I assumed the position of director of the ISI while continuing as co-director of CMI due to the remarkable synergy between these units. While CMI maintains its biomedical focus, ISI is more broadly dedicated to finding molecular solutions to grand challenges.

Now, we find ourselves at a point where ISI is flourishing, preparing to build a $180 million building and extend its reach across the campus. Simultaneously, CMI requires focused and visionary leadership with a sustainable structure. To this end, we are excited that CMI will retain its current independence and structure but will now exist under the Integrative Sciences umbrella. This will allow for a more formal connection with the growing Office of University Interdisciplinary Programs (OUIP) within the provost's office while maintaining existing reporting to the Office of Research and Innovation (ORI). I am thrilled to continue the work we started at CMI and expand and apply those models more broadly across our campus.

I look forward to supporting the future success of CMI and its integral role in translating discoveries from ISI and beyond. NC State is a special place, and CMI stands as a shining example of leadership development, research excellence, and innovative training. I extend my gratitude to everyone who has contributed to this journey and, especially, to Jorge for granting me the opportunity to lead at an early stage of my career—I will be forever grateful.

Sincerely,
Josh

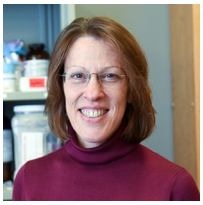
Research Division Highlights

CHEMISTRY OF LIFE

IN APRIL OF THIS YEAR, the NIH-supported Chemistry of Life Training Program hosted its second annual symposium. The symposium, organized by trainees, brought together trainees and faculty for a half-day event of science and hosted panels focused on grant writing, industry and entrepreneurship, and the art of writing accessible and compelling research summaries. Rounding out the program were two keynote speakers, Michael Jewett of Stanford and our very own Tom Makris. Student research was displayed prominently throughout the symposium program, which also featured poster presentations from CLP research groups (see picture). Laney Kimble (undergraduate Beckman Scholar) won first place. Catherine Odhambo and Micah Mallory (graduate students in chemistry and biomedical engineering, respectively) shared second place in the poster session.

This year has also brought a number of recognitions to the faculty and students within the CLP. Nathan Crook received the NSF Career Award. Three faculty members, Arion Kennedy, Yevgeny Brudno, and Caroline Proulx, received the Goodnight Early Career Innovator Awards. In addition, three faculty, Santosh Mishra, Yevgeny Brudno and Manuel Kleiner, were named University Faculty Scholars. Ashley Brown was inducted into the AIMBE. Rudolphe Barrangou was inducted into the National Inventors Hall of Fame. Yang Zhang was awarded an NSF Chemistry division award for collaborative research. Catherine Odhaimbo, Hailey Young, and Carolyn Davern received poster awards at conferences. Catherine Odhaimbo received an award for outstanding senior graduate research. Benjamin Callahan received the ASM Microbiome Data Prize. Ana Sheridan received an NSF Graduate Research Fellowship.

YEVGENY BRUDNO



MELANIE SIMPSON

Research Division Highlights

EMERGING & INFECTIOUS DISEASES

EID had a successful year and saw many accomplishments from senior and associate members. Among our members' achievements, we'd like to highlight the following exciting updates:

CMI-EID awarded a record number of scholarships for associate members

Graduate students and postdoctoral research fellows are important pillars of the CMI. Collaborations across laboratories and innovation are often fostered by our associate members. For the last few years, EID has acknowledged this important role by awarding scholarships to our associate members. These scholarships can be used for a variety of purposes, depending on the research and professional development needs of the associate member. This year we received a record number of 18 applications from the departments of Biology, Chemistry, Chemical Engineering, Clinical Sciences, Entomology, Molecular Biomedical Sciences, Population Health and Pathobiology, and Poultry Science. We were pleased we were able to award scholarships of $750 to each of the applicants. Our associate members requested funds to attend conferences, submit samples to core facilities, attend online conferences, and obtain software licenses.

PhotoCide Protection Inc. receives Dept. of Defense STTR award

PhotoCide Protection Inc., an NC State startup company that develops broad spectrum antimicrobial coatings and NC State received a Phase I STTR award from the U.S. Army to develop novel antimicrobial wound dressings.

Bacterial infections are particularly significant for military personnel in situations where there may be a long delay between the injury and treatment at a hospital or clinic. The requirement is for a technology that is readily available in far-forward situations and effective against the ESKAPE pathogens (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species). Of these, Multi-Drug-Resistant Acinetobacter baumannii (MDRAB) has been reported among veterans and soldiers who served in Iraq and Afghanistan and has been referred to as "Iraqibacter." These organisms are the leading cause of nosocomial infections throughout the world. PhotoCide combined their proprietary light-activated coatings with integrated light and power sources for this project to prevent the contamination of wounds by pathogens. During the six-month effort a proprietary coating formulation compatible with commercially available wound dressings was developed that achieved greater than 5 logs of MDRAB inactivation and greater than 6 logs of Methicillin-Resistant-Staph aureus (MRSA) inactivation.

PhotoCide's technology is based on photoactive compounds that convert molecular oxygen to singlet oxygen upon exposure to visible light. Singlet oxygen causes non-specific damage to proteins, lipids and nucleid acids, inactivating a wide range of pathogens. Advantages of this mechanism of action are: environmentally friendly as singlet oxygen decays back to breathable oxygen within milliseconds, broad spectrum activity against viruses, bacteria and fungi, no development of resistance due to the non-specific damage pathogens sustain.

PhotoCide submitted an application for a phase II award in June 2023. Mr. Robert Sheehan, PhotoCide's Chief Commercialization Officer served as PI on the award and Dr. Reza Ghiladi as the PI on the NCSU subaward. Dr. Frank Scholle, the President of PhotoCide Protection, served as scientific consultant and general grant administrator. Both Drs. Ghiladi and Scholle are members of the Center for Advanced Virus Experimentation (CAVE) and the CMI.

FRANK SCHOLLE

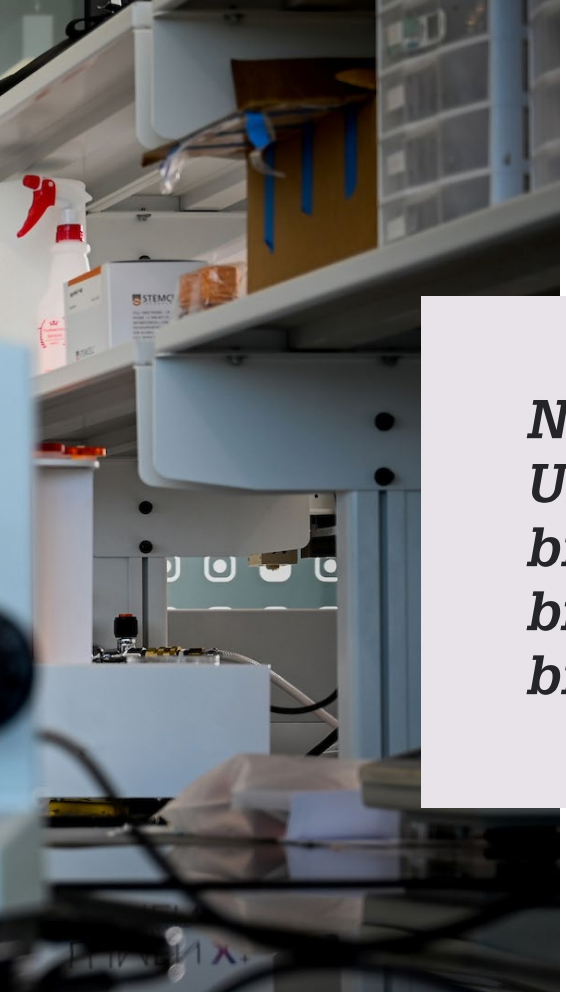
CRISTINA LANZAS

Research Division Highlights

FUNCTIONAL TISSUE ENGINEERING

We acknowledge and thank all FTE senior and associate members for their efforts and accomplishments during an exciting last year! Here are some highlights:

HEARTY CONGRATULATIONS to FTE members that received various recognitions and awards from the University, professional/technical societies, and funding agencies for their illustrious achievements, scientific contributions, and new ideas. While we are highlighting a few awards in particular here, we recognize the outstanding contributions that many other FTE members have made to their field. We congratulate Dr. Ashley Brown for her induction into the 2023 Class of the AIMBE (American Institute for Medical and Biological Engineering) College of Fellows, which is considered one of the greatest honors for medical and biological engineers. Dr. Brown was inducted "for outstanding contributions to the development of biomaterial-based therapies for treating trauma, wounds, and thrombosis." We would also like to congratulate Dr. Jacqueline Cole for receiving the Michael Dickey Outstanding Research Mentor Award at the 2023 NC State Spring Undergraduate Research & Creativity Symposium. This award recognizes NC State Faculty members that have demonstrated excellence in mentoring and supporting undergraduate researchers. From our group of exceptional FTE associate members, we congratulate: Suh Hee Cook of the Gluck Lab for winning 1st place in engineering at the 16th Annual Graduate Student Symposium at NC State; Claudia Alvarado Espino of the Shirwaiker Lab for



NC State will be one of the first US Universities to house this bioprinter that will support a broad range of interdisciplinary biomedicine-oriented projects.

winning the Institute of Industrial and Systems Engineers' (IISE) 2023 Graduate Research Award; Abby Cox Laws of the Traverson Lab for receiving the 2023 Merck Animal Health Veterinary Student Innovation Award; Dr. Adele Moatti of the Greenbaum Lab for receiving a National Institutes of Health NIDCD K99 award; Ana Sheridan of the Brown Lab for being awarded a National Science Foundation Graduate Research Fellowship; and Sandra Stangeland-Molo of the Cole Lab for receiving a National Institutes of Health F31 Kirschstein National Research Service Award. Well done!

We would also like to recognize the substantial research infrastructure that FTE members have put in place at NC State through the CMI Equipment Grant mechanism. In particular, the surgical arthroscopy equipment purchased in 2021 with efforts led by Drs. Schnabel and Fisher, has been utilized in numerous large animal surgical models and has led to NIH and foundation funding. We are also excited about the Poietis NGB-R, the only commercially-available laser-induced forward transfer (LIFT)-enabled bioprinting system in the world, which will be installed in a shared user lab in the Plant Sciences Building in Fall 2023. This acquisition is supported by a National Science Foundation MRI grant led by Drs. Rohan Shirwaiker, Jorge Piedrahita and colleagues, with required cost-share provided by CMI/FTE and others. NC State will be one of the first US Universities to house this bioprinter that will support a broad range of interdisciplinary biomedicine-oriented projects.

Finally, join us in welcoming our newest faculty colleagues, Drs. Rosemary Bayless, Sarah Shelton, and Ian Williamson! We are excited about the new research directions and collaborations that they will establish as members of the Translational Predictive Biology (TPB) cluster. We would also like to thank all FTE senior and associate members that contributed to the conception of the TPB cluster and participated in the search process in Fall 2022 and Spring 2023.

LAUREN SCHNABEL

ROHAN SHIRWAIKER

Research Division Highlights

TRANSLATIONAL PHARMACOLOGY & PHYSIOLOGY

IN 2022/23, Drs. Santosh Mishra (Associate Professor of Neurosciences in the Department of Molecular Biomedical Sciences) and Mike Nolan (Professor of Oncology in the Department of Clinical Sciences) were newly appointed as Associate Directors of the TPP. To gain an understanding of stakeholder needs, they invested time to meet both individually and in groups with each of TPP's full/faculty members. There were 3 major initiatives for this past year. The first was development of a bi-monthly email newsletter to help members get to know each other, and to stay in touch about CMI-TPP activities. There was also establishment of a Seminar Series based on TPP thematic areas to foster networking and collaboration; the first was organized by Dr. Javier Lopez Soto, Assistant Professor of Neurobiology. Dr. Lopez Soto invited Dr. Rajesh Khanna (Director of the NYU Pain Research Center), an internationally known expert in ion channels and pain research to our campus, where on April 20th, he gave an exciting lecture entitled "Dialing down neuropathic pain through allosteric modulation of sodium Nav1.7 channels". Finally, the TPP was able to offer a seed grant opportunity for students and post-graduate trainees. The objective was to fund travel, accommodation, and meals that would enable our trainees to attend host laboratories within the United States to learn scientific techniques to help advance their research and professional development.

Dr. Rajesh Khanna

During his visit to NC State, Dr. Rajesh Khanna gave a lecture illustrating how the Nav1.7 sodium channel was discovered and validated as a therapeutic target for pain relief. He also met with faculty and trainees.

SANTOSH MISHRA

MICHAEL NOLAN

Four awards were made:

Madelyn VanBlunk

MADELYN VANBLUNK OF THE BRUDNO LAB traveled to the Jackson Laboratory in Bar Harbor, Maine to complete a workshop on stereotaxic surgery in laboratory mice. She learned how to use stereotaxic instruments for intracranial injections, brain dissections, brain cannulations, bi-lateral brain cannulations, and cerebral spinal fluid collection. Her research focuses on using biomaterials to manufacture CAR T cells in vivo for treating glioblastoma, an aggressive brain cancer. Attending the workshop was crucial for developing skills needed to perform brain surgeries associated with injecting CAR T cells and implanting biomaterials intracranially. She is now able to teach members of the Brudno Lab (and other NCSU labs!) how to properly use stereotaxic instruments, benefiting many in the CMI.

Ankita Gupta

ANKITA GUPTA OF THE LASCELLES/MISHRA LABS traveled to the Vaika Foundation at Cornell University in Ithaca, New York to collect orthopedic exam data and biological samples from retired sled dogs. Like humans, canine athletes have an increased risk of orthopedic injuries, which may lead to the development of osteoarthritis (OA) and pain, but no studies have investigated objective methods for detecting OA pain in sled dogs or if sled dogs can be used as a model for human athletes with OA/OA pain. She will be the first to build expertise in naturally occurring models for human athletes with OA/OA pain, and hope this study will provide OA pain-related targets.

Ian McConnell

IAN MCCONNELL OF THE MISHRA LAB traveled to Bethesda, Maryland and spent time with the Hoon Lab at the NIH. They provided one-on-one training in rodent stereotaxic surgeries, including cerebral and spinal injections for neuromodulatory experiments that are essential for today's high-powered neuroscience research investigations. Equipped with this new training, Ian has now been able to make possible a new array of investigations and validations of depression and anxiety comorbidities in mouse models of chronic disease. Additionally, this learning opportunity has enabled him to teach these stereotaxic techniques to research colleagues in the Mishra lab, and the greater CMI community.

Adele Moatti

ADELE MOATTI OF THE GREENBAUM LAB traveled to Stanford University to explore the laboratory of Dr. Alan Cheng, whose expertise lies in hearing loss research—a field of great recent interest to the Greenbaum lab. During her visit to the Cheng lab, she had an opportunity to acquire knowledge about the specialized techniques employed particularly in the domain of in-vivo local drug delivery for therapeutic interventions in the inner ear. Notably, these techniques involve targeted injections into the posterior semicircular canal of the inner ear, applicable to both neonate and adult mice. Considering the techniques she learned, it is evident that delivering therapeutics to the porcine inner ear is the next step towards human clinical trials.

CMI IMPACT

OUR **PROGRAMS**

Pilot Project Funding

Student Training

Leadership & Entrepreneurship

RESEARCH

$357,867 in research seed funding distributed to faculty, graduate students and postdocs.

"Think, Collaborate & DO" Ideation event gathers researchers from across campus. Over **$250,000** distributed to **12 projects**.

TRAINING

2 active NIH T32 Ph.D. training programs
1 active NIH T34 for underrepresented undergraduate students

Teamwork in Interdisciplinary Biomedical Research graduate & undergraduate minors approved. **22 students** enrolled for Fall 2023.

ENTREPRENEURSHIP

CATALYZE Commercialization Conference creates a forum and resource for students interested in industry careers and gives faculty and students a place to start with the commercialization of their research. Three awards given for best start-up project pitches.

$7500 in entrepreneurial supplements to support commercialization process for Think, Collaborate and Do proposal.

CMI 2022-2023

MEMBER NEWS & AWARDS

CMI Member Awards:

Tal Ben-Horin. NC State 2022 Outstanding Extension Award

Anthony Blislager. 2023 NC State Alumni Association Outstanding Research Award and was inducted into the NC State Research Leadership Academy

Ashley Brown inducted as AIMBE Fellow and elected as Secretary/Treasurer for the National Society for Biomaterials

Jacqueline Cole, 2023 Michael Dickey Outstanding Research Mentor Award.

Bethanie Cooper, Grayson Jockey Club Research Foundation "Elaine and Bertram Klein Career Development Award"

Glenn Cruse, appointed Associate Editor of the journal Frontiers in Immunology

Alon Greenbaum, Goodnight Early Career Innovators award

Jingjie Hu, Ralph E. Power Junior Faculty Enhancement Award from Oak Ridge Associated Universities (ORAU)

Duncan Lascelles, 2023 NC State Alumni Association Distinguished Graduate Professor Award

Mary Ann Lila, 2023 Senior Outstanding Global Engagement Award

Kurt Marsden was named a University Faculty Scholar

Lauren Schnabel, Veterinary Scholars Program Distinguished Clinician-Scientist Speaker & Daugherty Endowment Challenge 2nd Place award

Casey Theriot, Zoetis Award for Veterinary Research Excellence

Deyu Xie, AAAS Fellow

CONGRATULATIONS!

Associate Members Awards:

Kyla Bosh received the Joint Dept. of Biomedical Engineering Graduate Student Service Award & an American Society of Biomechanics Diversity Travel Award

Suh Hee Cook won 1st place in the NC State Graduate Research Symposium, and 2nd place & People's Choice for her Three Minute Thesis at the Society for Biomaterials Annual Conference

Abby Cox Laws received the Merck Animal Health Veterinary Student Innovation Award

Zachary Davis was a Ph.D. Paper competition finalist at the Summer Biomechanics, Bioengineering & Biotransport Conference

Drew Koch was selected as a finalist in the AVMA/AVMF Early Stage Investigator Award Competition & received the Dept. of Clinical Sciences Graduate Student of the Year

Nasif Mahmood received a STAR Award honorable mention at the Society for Biomaterials Annual Conference

Ranee Miller won 1st Place in the Abstract Presentation Award at the American Academy of Veterinary Pharmacology and Therapeutics (AAVPT) 22nd Biennial Symposium

Adele Moatti received the Postdoctoral Research Achievements Award from the Joint Dept. of Biomedical Engineering

Elizabeth Rose received a Litwack Research Day Honorable Mention for her oral abstract.

Grant Scull was elected as Student President for National Society for Biomaterials

Alejandro Valdes Pena was awarded the Cambrex Award for Excellence in Molecular Research

Associate Members Fellowships:

George Elane received the CMTRP T32 Fellowship

Sara Erwin received an NIH T35 Research Fellowship

Emily Hellstrom received an AAEP Foundation of the Horse EQUUS Foundation Research Fellowship & Morris Animal Foundation Fellowship Training Grant

Drew Koch received The Foundation for The Horse Student/Fellow/Resident Research Grant

Adele Moatti received an NIH/NIDCD K99/R00 award

Nina Moiseiwitsch received an NIH F30 award

Elizabeth Rose received the CMTRP T32 Fellowship

Ana Sheridan received an NSF Graduate Research Fellowship

Alejandro Valdes Pena received the NIH-NC State Molecular Biotechnology Training Program Fellowship.

COLLABORATION LEADS TO NOVEL NEBULIZER PROTOTYPE

By Kristina Nelson

ASTHMA AFFECTS AROUND 300 MILLION PEOPLE WORLDWIDE. In fact, you probably know someone with asthma. The Cruse lab here at NC State is interested in asthma and allergic diseases, and the role that mast cells play in these diseases. Mast cells are immune cells within the body that typically only activate in certain situations, like when an allergen enters the body, causing difficulty breathing and other symptoms. However, in people with asthma, these cells are always 'on', leading to chronic inflammation and airway constriction. Targeting these mast cells could be an effective asthma treatment, with fewer side effects than current remedies. Nebulizers are currently used to treat asthma – they deliver small molecules of medication to targeted areas of the lungs in humans. Intrapulmonary delivery, or delivery into the lungs, is more effective than oral, intravenous, or subcutaneous delivery. It has a faster absorption rate, does not require systemic metabolization, and enables faster pharmacokinetic profiles at lower doses. However, conventional jet nebulizers are slow and require large volumes for effective delivery, making them inefficient. Nebulization efficiency depends on a number of factors, including sample volume, droplet size, and nebulization time. Research is needed to increase nebulization efficiency, so that next generation novel therapeutics may be used in asthma and allergic disease treatments in humans.

Mice are routinely used as model organisms for numerous human-relevant diseases. Because they are obligate nasal breathers like humans, they are useful for studies on asthma and lung inflammation. Dr. Cruse and his research team recognized that novel therapeutics for these conditions in humans could be tested with mouse models. However, there are relatively few options available for administering drugs to the airways of mice. No tunable device for mice had yet been created for the targeted delivery of modern therapeutics, which are temperature-sensitive large molecules.. Scientists have tried to use traditional jet nebulizers but encountered multiple problems. First, these are only built for the delivery of small molecules, not large molecules. Second, they are inefficient, as large quantities of the therapeutic (drug) are needed, but most of it never makes it to the lungs of the mice. So, Dr. Cruse and the team set out to develop a more efficient nebulizer that could deliver small amounts of drug into the lungs of mice while minimizing waste, and without generating high temperatures that could damage these drugs. The researchers developed and characterized a tunable nebulization system, which is composed of a vibrating perforated mesh (VPM) nebulizer with a 3D printed platform that contains a silicone restrictor plate for controlling the nebulization rate.

To create the device, the team went through a multi-step process. They began by identifying the elements of the nebulizer design that influence the most critical

Their studies showed that the VMP nebulizer had a 10x higher delivery efficiency than jet nebulizer systems, with a significantly higher amount of dye in the deep portions of mouse lungs.

factors of targeted drug delivery. Computer simulated models were used to determine the optimal droplet size for delivery to the deepest parts of the lungs – the target area for the drug. They 3D-printed a nebulization platform which was fitted with a piezoelectric transducer and equipped with directed airflow and temperature control. The nebulizer also contained a 1mm silicone restrictor plate membrane on the transducer, allowing the scientists to adjust the nebulization rate to match the mouse breathing rate. To characterize their device, they evaluated the characteristics of other nebulizers. They also evaluated the intrapulmonary delivery capability of their nebulizer by administering dye to mouse models as a proxy for drug delivery. They conducted two different experiments using their VPM nebulizer design to trace the intrapulmonary delivery of the dye. The first was a study designed to detect the respirable fraction of the dye and determine the amount of dye reaching the alveoli and alveolar ducts, the deepest parts of the mouse lungs. The second experiment used the dye to compare their nebulizer to the industry standard jet nebulizer, showing the amount and distribution of dye delivered to different portions of the lung.

Their studies showed that the VMP nebulizer had a 10x higher delivery efficiency than jet nebulizer systems, with a significantly higher amount of dye in the deep portions of mouse lungs. This means their novel nebulizer system was significantly more efficient than traditional jet nebulizer systems. These results show the capability of the VPM nebulizer for use in preclinical mouse trials of human pulmonary issues. The ability to match the nebulization rate to the mouse breathing rate allowed the scientists to maximize the dye delivery efficiency, thereby preventing the waste of expensive biologics in these experiments. The researchers hope that their proposed tunable nebulizer design can help to pave the way for future research using novel therapeutic compounds, "not only [with] the compounds we are currently developing, but potential future compounds too," says Dr. Cruse.

This study was the result of collaboration by many individuals across departments – a true interdisciplinary effort. The team of researchers consisted of many

faculty members: Dr. Glenn Cruse, Dr. Rohan Shirwaiker, Dr. Danny Freytes, and Dr. Ke Cheng. Several current and former graduate students - Kristen Popowski, Karl Schuchard, Ana Gracioso Martins, and Doug Snider - and undergraduate student Matias Tenorio were also involved in the project. Dr. Cruse stressed the importance of collaboration on this project, stating, "We had a problem that we knew we could not address without collaborating with researchers in other disciplines. We work in the Biomedical Partnership Center building …we have outstanding investigators across the hall that have very different expertise to

> **"This collaborative project really exemplifies what CMI tries to achieve. [It] started as a collaboration between associate members of CMI who were tasked with coming up with a solution to a real problem we encountered."**
>
> **- Dr. Cruse**

us and provide great opportunities for collaborations to answer big problems… it really fosters this type of collaboration, where we can come together to solve larger problems. Something that the CMI heavily promotes."

All of the researchers involved in this study were also involved with the CMI at some point, and Dr. Cruse believes this connection to the CMI was incredibly valuable. "This collaborative project really exemplifies what CMI tries to achieve. [It] started as a collaboration between associate members of CMI who were tasked with coming up with a solution to a real problem we encountered." The problem "required different expertise, and being a member of the CMI catalyzed the interactions required to realize the vision of how we could address the problem posed." The team discussed the project at CMI summits and events. CMI also assisted in funding the pilot studies of the project through the YSP and SIRI programs. "Participating in the CMI and this project, which is a real multidisciplinary team science project makes you realize that in order to answer some of the major questions and address real problems in science, we all need to think about building teams with diverse expertise. I think the challenges of the last few years have helped to reinforce the importance of collaboration," Dr. Cruse said. "It has made me realize how much we should value getting together and talking with other CMI members to find out what work they are doing and brainstorm ideas."

Think. Collaborate and Do

2024 Ideation Awards

The CMI would like to thank the Kenan Institute for Engineering, Technology & Science, the College of Veterinary Medicine, and the Genetics and Genomics Academy for their generous support of this year's Ideation Awards.

Student Awards

- *Nanotechnology-mediated Detection of Steroid Hormones in Serum to Study Female Reproductive Health.*

  PIs: Hannah Dewey (WCOT) & Jacob Thompson (COE)

  Funded by CMI & KIETS

- *Mathematical understanding of the underlying physical phenomena in viral cellular transduction.*

  PIs: Micah Mallory (COE) & Vishal Srikanth (COE)

  Funded by CMI & KIETS

- *Biodegradable composite scaffolds for high-efficiency cellular transduction and CAR T cell synthesis.*

  PIs: Christopher Moody (COE) & Mengnan Dennis (WCOT)

  Funded by CMI & KIETS, with a CMI supplement for entrepreneurship

- *Cultivation of equine bone marrow-derived mesenchymal stem cells with fibrin-based nanoparticle scaffolds.*

  PIs: Shannon Connard (CVM) & Sanika Pandit (COE)

  Funded by CMI & KIETS

Faculty Awards

- *Development of zebrafish mast cell reporter lines to enhance the in vivo studies of mast cells in neurobiology, infection, and immunity.*

  PIs: Natalia Duque-Wilkens (COS), Kurt Marsden (COS), & Jeffrey Yoder (CVM)

  Funded by CMI, KIETS, & GGA

- *TRAP-dexamethazone as a treatment of equine asthma.*

  PIs: Katie Sheats (CVM) & Katarzyna Dembek (CVM)

  Funded by CMI & KIETS

- *Using metalloenzymes to enable targeted C-C and C-N bond formation for valuable molecules preparation.*

  PIs: Wei-Chen Chang (COS) & Thomas Makris (CALS)

  Funded by CMI & KIETS

- *In vitro analysis of a novel extracorporeal device for cytokine removal in equine sepsis and effects on immune function.*

  PIs: Kallie Hobbs (CVM), Katie Sheats (CVM), & Yu Ueda (CVM)

  Funded by CMI & KIETS

- *Curbing Pathogen Transmission: Unleashing the Potential of a Biodegradable Photosensitizing Polymer.*

  PIs: Tova Williams (WCOT), Chris Gorman (COS), & Reza Ghiladi (COS)

  Funded by CMI & KIETS

- *Strain Effects on Proteolysis of Extracellular Matrix in Biological Tissues.*

  PIs: Shadow Huang (COE) & Aaron Bell (COE)

  Funded by CMI & KIETS

- *LGR5+ progenitor cells in cardiac development and regeneration.*

  PIs: Jessica Gluck (WCOT), Ke Huang (CVM), & Jorge Piedrahita (CVM

  Funded by CMI & KIETS

ABOVE & BEYOND:

In Recognition of an Exceptional Associate Member

By Kristina Nelson

HISHAM EL-SHAFFEY'S journey with CMI has been almost as long as his graduate career here at North Carolina State University. He started as a Ph.D. student in Dr. Joshua Pierce's chemistry lab in 2020. His PI Dr. Pierce sent him an invitation to apply for the Chemistry of Life Training Program, but Hisham was not yet aware of the link to CMI. Hisham had what he called his first 'official' interaction with CMI the following summer, where he gave a symposium presentation on his graduate research. Unfortunately, his worst fears were realized when technological issues occurred during the presentation. He was disappointed and worried it had been hard to follow. But to Hisham's surprise, several people congratulated him on a successful and interesting presentation. Some even asked him follow up questions, demonstrating that they were able to follow the presentation despite the technical difficulties. When Hisham recalls this bump in the road, what he remembers most is the support he received from his peers at CMI during a challenging moment.

Fast-forward to his second year at NC State, when he was offered the Chemistry of Life fellowship. This fellowship requires co-mentorship and collaborative research as part of one's degree. Fellows also get to be involved in planning the Chemistry of Life Training Program (CLPTP) Symposium, a student-driven event whose focus is on encouraging interdisciplinary science and communication among the fellows and with the broader scientific community. Hisham was also part of the CMI's Young Scholars Program (YSP), where students come together to develop a project, and then advertise the project to undergraduate students through the Summer Interdisciplinary Research Initiative (SIRI). YSP students mentor their selected SIRI students throughout the project. Hisham recalls, "I can't think of any other experience in a Ph.D. program where you get to mentor on that scale – where, as graduate students, you and your peers design a project and guide an undergraduate student through completion of that project." It was an incredibly rewarding experience for him, and he deeply enjoyed the opportunity to take on a mentor role.

"I can't think of any other experience in a Ph.D. program where you get to mentor on that scale..."

- Hisham El-Shaffey

That same year, Hisham became an Associate Member of the CMI, and, not long after, he began attending the Associate Member Executive Committee meetings as an Associate Member Representative, one of two leaders of the Associate Members who sit on the CMI's Executive Committee. The Associate Member Representatives are incredibly important, because their contributions and ideas have the power to create lasting change within the CMI. As one of the Associate Members, Hisham helped to organize numerous events and workshops. He chaired the Chemistry of Life Training Program Symposium planning committee in 2022, leading to a very successful symposium this past spring. He also helped to organize the first-ever CATALYZE Commercialization Conference

> **"I just really love CMI…I feel very honored, and very humbled. It feels a little surreal; like I should be the one thanking them for giving me these opportunities."**
>
> - Hisham El-Shaffey

that same year. Hisham once again played a key role in the CATALYZE Conference this year, organizing the student-led aspects of the event. Through all of these accomplishments, Hisham wanted to emphasize the support he has received from others, saying, "I could not have been successful without the help that everyone else put in."

Hisham has become an incredibly important member of CMI during these last few years, immersing himself in countless events, workshops, and programs. The CMI executive committee is delighted to present him with the Exceptional Supporter Award to commemorate his dedication and hard work. This is the first time the award will be given to an Associate Member. In seeing what CMI colleagues have to say about Hisham, this honor is clearly deserved:
"He's always been eager to take full advantage of his time here and of the resources CMI provides. Working with Hisham has been fantastic. He is enthusiastic and interested in all facets of CMI and made my job so much easier… he will be very much missed!" – Sarah O'Connor, CMI Executive Assistant

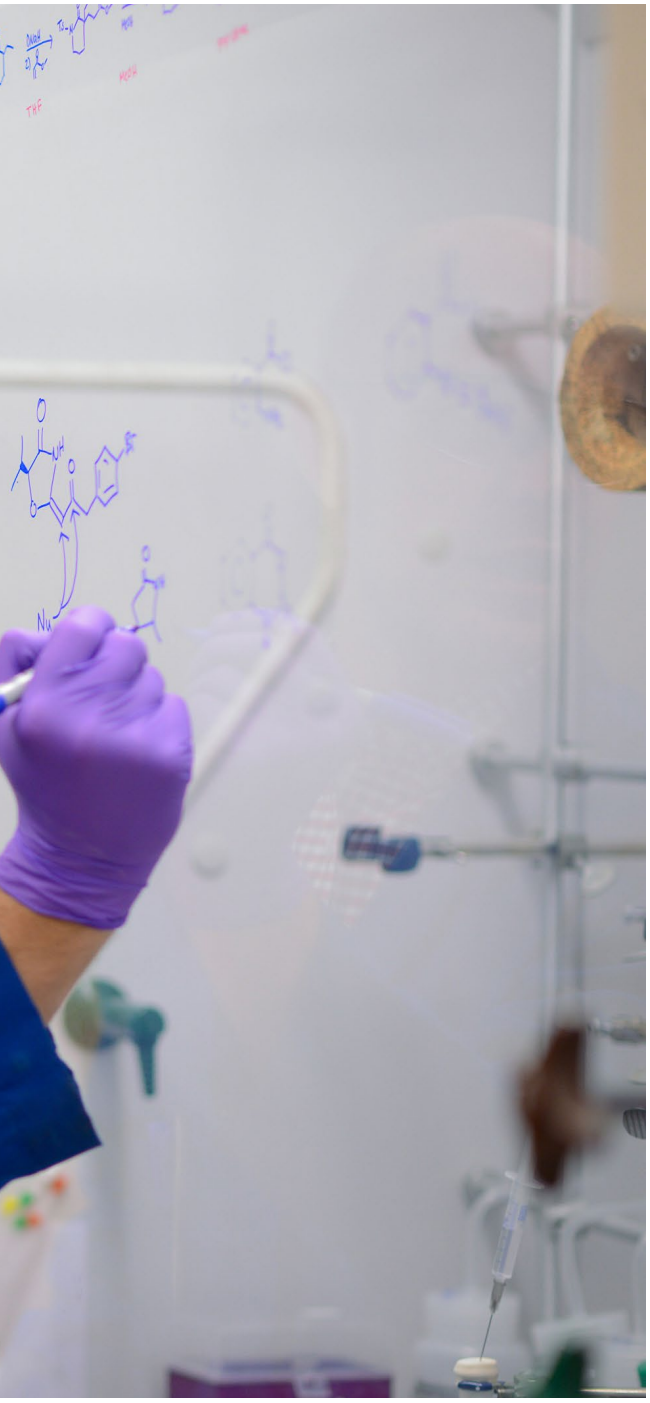
From the moment he joined the CMI he started to look for opportunities to contribute …and the rest as they say is history. Hisham is an exceptional supporter of the CMI, and we thank him, and all AMs, for all they do for the CMI…Hisham is highly deserving of the CMI Exceptional Supporter Award because of his fantastic leadership among the CMI associate members… Hisham stands out as a passionate and curious and kind individual: a true role model." – Jorge Piedrahita, CMI Co-Director
"The breadth of his contributions cannot be overstated, and he is always willing to go the extra mile… CMI is lucky to have him part of our community! Hisham has sacrificed his time to make CMI and NC State a better place and we are thrilled to reward him for these efforts." – Dr. Joshua Pierce, CMI Co-Director

Hisham has had a significant impact on CMI, just as CMI has had a significant impact on him. "I just really love CMI…I feel very honored, and very humbled. It feels a little surreal; like I should be the one thanking them for giving me these opportunities." He will be truly missed as he moves on to his next chapter, but we have no doubt that he has great things ahead.

Thank you Hisham, and congratulations!

"The CMI has provided me with career-changing opportunities and I will be forever grateful. From early leadership opportunities to new research collaborations, CMI enabled me to thrive at NC State. I am most proud of the training grants we have secured and the extension of the CMI into chemistry and the broader basic sciences. I can't wait to see what is next as we launch the ISI. The future is very bright for interdisciplinary programs at NC State."

- Josh Pierce



In Recognition of

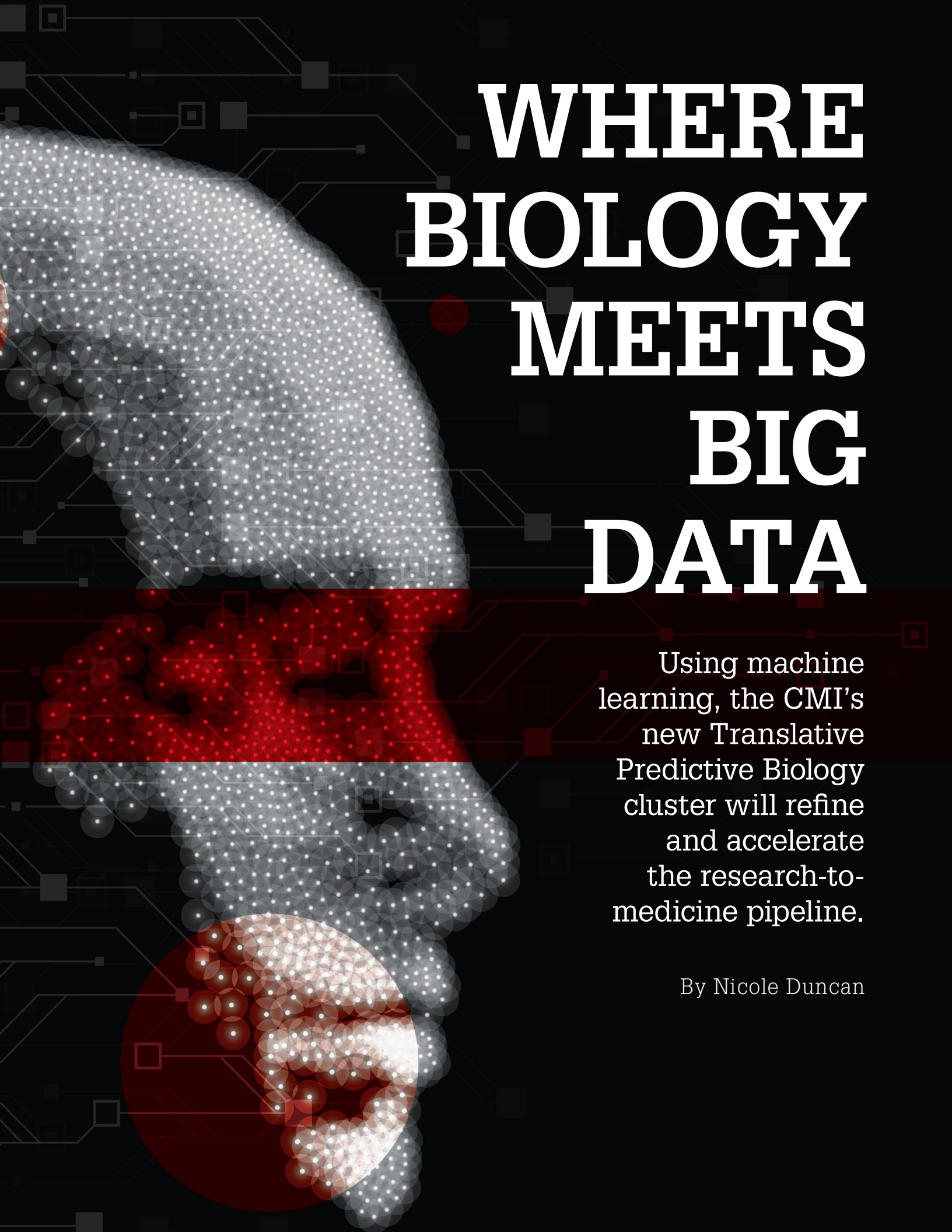
EXCEPTIONAL LEADERSHIP & SUPPORT

AS MANY OF YOU KNOW, CMI gives the exceptional supporter awards only to those individuals that have gone above and beyond to make the CMI the amazing community it is. This year, for the first time since the inception of the CMI, we are recognizing TWO exceptional individuals: Josh Pierce and Hisham El-Shaffey (24).

Josh has described his many seminal contributions to the CMI (6), but we would like to take the opportunity to expand on just how much a difference he has made from the day he joined the CMI.

From when he first joined the CMI as a new faculty member, then moving to the executive committee, conceptualizing and making the Chemistry of Life program a reality, working to retain CLP within the CMI for the benefit of both, and eventually becoming co-director of the CMI. It is hard to describe just how influential Josh has been. He has positively impacted every aspect of the CMI, always finding ways to improve our mentoring programs, always coming up with novel ideas, and always willing to do the hard work to bring them into the real world. He will be sorely missed, but he leaves behind a huge legacy that will continue to benefit the CMI. We look forward to continuing to work with Josh in his new role as Executive Director of the ISI and continue the tradition of working together to make NC State a better place for all.

On behalf of all of the CMI THANK YOU JOSH FOR ALL YOU HAVE DONE!!



WHERE BIOLOGY MEETS BIG DATA

Using machine learning, the CMI's new Translative Predictive Biology cluster will refine and accelerate the research-to-medicine pipeline.

By Nicole Duncan

AS MACHINE LEARNING ACCELERATES the pace of innovation, it also reveals new opportunities to translate biological research into real-world medical applications. And the Comparative Medicine Institute (CMI) at NC State is ready to lead the charge in exploring these new synergies.

Last year, the CMI, in collaboration with the College of Veterinary Medicine, the College of Engineering and the Chancellor's Excellence faculty Program, announced a new hiring initiative that would bring together researchers from different disciplines to advance the fledgling field of Translative Predictive Biology (TPB). These scientists will share their expertise and data with one another to create a more holistic picture of the impact of new medicines within human physiology. And thanks to ongoing advances in artificial intelligence, the TPB initiative's collective research will be collated and analyzed at multivariable levels that would have been impossible just a decade earlier.

"Scientists are unbelievable at figuring out how to merge all these datasets and get information out of them. But you can imagine the amount of computational power and the amount of programming that's required to figure out how to merge all these pieces of information so that it becomes informative," says Jorge Piedrahita, Co-Director of the CMI. "That's where machine learning comes in. A human being cannot process that [amount of data], but a computer can teach itself how to figure it out."

The new Translative Predictive Biology initiative is positioned to do just that. Through machine learning, scientists can pool their respective research to illuminate new connections among seemingly disparate data points. This deeper understanding of complex biological systems, in turn, paves the way for more precise medical treatments that can be developed and tested at a fraction of the time and cost. And that is the ultimate vision of the TPB cluster: to revolutionize how biology and AI work together so that new medicines can be synthesized faster and also tailored to fit the individual.

"I think the most advanced part of predictive biology is what we call personalized medicine. And that is really looking at the maximum amounts of clinical data and drug responses in populations to try to figure out which drug [an individual] would best respond to," Piedrahita says. "We have data from small models, data from medium-size models, and data from large models. And the goal of the field is, can we collect enough information from those earlier stages to predict the failures in the later stages? So instead of trying 10 drugs and nine failing, we can test one drug and that one drug succeeds."

The CMI is uniquely positioned to house this new initiative. While the spirit of collaboration links many different departments, schools, and centers within the greater NC State system, the CMI has proven itself especially nimble in forging interdisciplinary relationships and delivering tangible results.

"The CMI has shown it's consistently able to bring people together in ways that yield grants and discoveries. Having this effort connected to the CMI leverages that expertise, which I think is quite rare," says Rob Dunn, Senior Vice Provost of Interdisciplinary Programs. "Our advantage in this space at NC State is to be able to build on a decade of investment in our Chancellor's Faculty Excellence program hires and then the expansion of those areas of interdisciplinarity through these strategic clusters."

"The CMI has shown it's consistently able to bring people together in ways that yield grants and discoveries. Having this effort connected to the CMI leverages that expertise, which I think is quite rare,"

- Rob Dunn

The potential of predictive biology

Already the CMI comprises four core units: Chemistry of Life, Emerging and Infectious Diseases, Functional Tissue Engineering, and Translational Pharmacology and Physiology. Translational Predictive Biology is a natural extension of these existing concentrations, with the new TPB clusters drawing from existing disciplines within the CMI.

TPB also fits nicely with the institute's mission to convert scientific advances into real-world, clinical applications. Predictive biology offers a way to not only refine potential treatments and develop new drugs but to also shorten the pathway from the earliest stages to human clinical trials.

"We all respond differently to different drugs, so clinical trials have to study a very large number of individuals to get the average response," Piedrahita says. "What we're trying to do is really a step-up and much more ambitious. Our goal is to be able to use the simplest in vitro systems to predict the behavior in a large animal model, and eventually in humans. But that is difficult to do because we are massively complex biological systems."

To achieve this goal, the TPB initiative is structured in such a way that one cluster position, namely Data Science/Machine Learning, serves as a sort of connective tissue binding the rest. The other four disciplines, namely Organoid Biology, Organ-on-a-Chip Microfluidics, Large Animal Physiology, and Biotherapeutic Drug Delivery, have no shortage of data; however, scientists lack the necessary tools to analyze increasingly complex models.

"Our goal is to be able to use the simplest in vitro systems to predict the behavior in a large animal model, and eventually in humans. But that is difficult to do because we are massively complex biological systems."

Jorge Piedrahita

"The organoid biology, organ-on-chip, large animal, and drug delivery positions can be more experimental in nature and more biology-oriented. They are really studying mechanisms, and, I would say, are more on the side of data generation and data collection," says Rohan Shirwaiker, Professor in the Department of Industrial and Systems Engineering at NC State and Associate Director of the Functional Tissue Engineering Program at the CMI. "But once you have a lot of multimodal information—because you're collecting data of various natures—how do you analyze it? How do you connect it to draw pertinent and unique inferences?"

The use of artificial intelligence within life sciences is still in an embryonic state. Some researchers, often in commercial pharmacology, have worked to organize data and generate predictive models that test toxicity in drugs. But these models are crude at best and have yet to change the pathway from in vitro experiments to in vivo clinical trials.

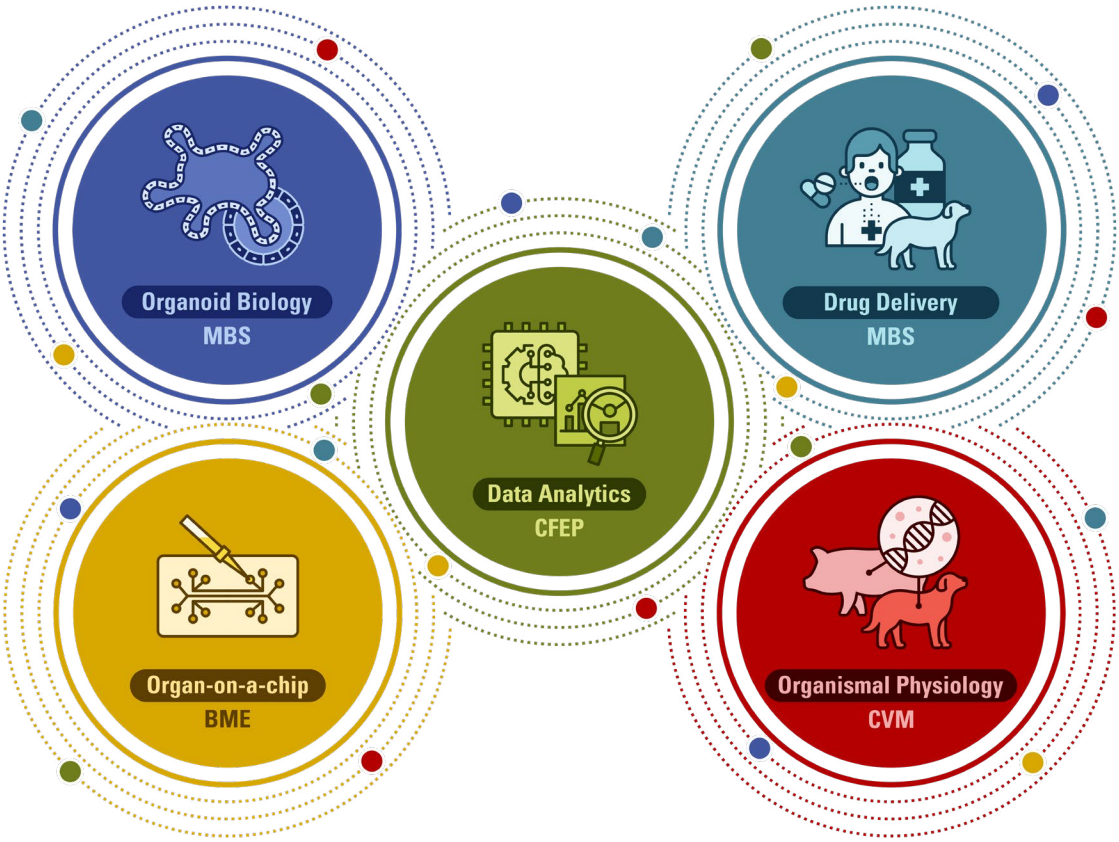
"As new technologies come online, we're able to interrogate what's going on inside the cell at a really deep molecular level. We can see what's going on within DNA. We can see what's going on with the other processes that are started by DNA. And this is true across a vast array of human and model system biology," says Fred Wright, Director of the Bioinformatics Research Center and Goodnight Innovation Professor of Statistics and Biological Sciences at NC State. "But as we gather more data, the ability to analyze it lags behind."

Indeed, in its current state, the process of testing new drugs is both time- and resource-intensive. The promise of TPB is a faster, more accurate, and more cost-effective pipeline.

The drug development pipeline

Synthesizing a new drug or treatment begins with a monolayer cellular culture before progressing to an organoid model. Although both use stem cells, the latter is three-dimensional and functions as a miniature version of its parent organ. Organoids provide a more nuanced picture, but such models have historically relied on treating all cells as uniform, when in fact an organoid, like a real organ, comprises multiple cell types with myriad functions.

The next step in the pipeline delves into microfluidics, specifically organ-on-a-chip technology. These models are not grown from stem cells but rather manufactured and bioengineered to mimic the structural and functional features of organic tissue. Since bioengineers can



control the microenvironment, organs on a chip bring a new dimension to testing, but these models are still not precise enough to bypass the animal testing phase.

Once studies reach the in vivo testing phase, they often begin with murine or other small mammal subjects. Large animal species, however, offer a stronger approximation of human physiology; mammals like pigs, horses, dogs, and primates are often the preferred models.

"In the past, we've proven that small animal models like mice are really important for initial screening, but they don't replicate what happens in people," says Lauren Schnabel, Associate Professor of Equine Orthopedic Surgery at NC State and Associate Director of the Functional Tissue Engineering program at the CMI. "[But] large animals suffer from a lot of the naturally occurring diseases that people do. And then there are some induced models that they're excellent for. Here at the veterinary school, we're concerned with animal health but also with how it translates to human health. So it's a win-win situation."

Other nearby universities, like UNC and Duke, may have teaching hospitals, but NC State is unique in its world-class College of Veterinary Medicine (CVM). Many departments, schools, and institutes, including the CMI, can take their research to the next level thanks to collaborations with the CVM.

"I think the ability to leverage those large animal models is something that not a lot of institutions have," says Yevgeny Brudno, Associate Professor in the UNC-NC State Joint Department of Biomedical Engineering and Associate Director of the Chemistry of Life program at the CMI. "That's really a strong core strength and something that I think will create a lot of value for these scientists and for science."

Another critical component of in vivo testing is drug delivery. Researchers take a comprehensive view by analyzing not only what substance is being delivered but also how it's being delivered and where its final destination lies. For example, a novel drug may show great potential during in vitro testing but then reveal an unintended side effect within an animal or human subject. Or, the drug carrier may prove too flimsy to transport its medicine to the intended target. Any number of complications can arise when a hypothetical treatment is put into real-life practice. Precision is paramount.

"For a lot of diseases, we want the drug to be in just one place. So, let's say in the context of cancer, how do we get drugs to

the tumor—only the tumor and nothing but the tumor?" Brudno says.

All these steps along the discovery pipeline—organoid biology, organ on a chip, large animal physiology, and drug delivery—bring a fresh angle and an abundance of data to the table. The trouble rests in merging those datasets into something cohesive. After all, each specialty field analyzes different cells, functions, reactions, and more, so it can be a matter of comparing apples to oranges.

Because of these limitations, scientists have long followed the slow, step-by-step route. But what if an algorithm allowed researchers to leapfrog from an organoid model to in vivo trials? What if machine learning could build such a sophisticated model that a simple, two-dimensional cellular test of a new drug could calculate its medical efficacy on a human? What if the wheel of translational medicine had a central core connecting its spokes?

These scenarios represent the pinnacle of success for translational predictive biology. "I think if you do translational science well, there's a circle of connections and no one's at the beginning or end, or above or below," Brudno says. "Everyone is connected with everyone else."

Smarter medicine

How quickly a new drug can be accelerated along the pipeline depends on the IQ of the artificial intelligence. As a baseline, IQ 1 denotes the traditional step-by-step process, wherein a treatment progresses from monolayer to three-dimensional organoid to organ on a chip to animals and,

finally, humans. An IQ 2 algorithm jumps over a step, whether it's going from a two-dimensional model on a glass slide to an organ on a chip or from an organoid to a large animal. In the ideal IQ 3 model, scientists would be able to make one-step predictions, starting with the most rudimentary monolayer model and shooting straight to in vivo treatment.

Jonathan Horowitz, Associate Vice Chancellor for Research Infrastructure and Development at NC State, perhaps explains the potential of predictive biology best when he compares it to meteorology a century ago. Although weather stations dotted the country, they didn't have the means to communicate with each other. So if a storm system was rolling in from Tennessee or even western North Carolina, the Raleigh station wouldn't know until it was detected within its radar range.

"We now have gigantic datasets that cover everything you can possibly imagine, and the data is pouring in faster than we can analyze it. What this cluster aims to do is to take advantage of all this data and use it to make predictions about biology and the translation of biological discoveries—much like the National Weather Service now makes predictions about what's going to happen next week or where a hurricane is going to go," Horowitz says. "Models that predict the path of a hurricane have confidence intervals around its predicted path, and depending on which model you use, you may or may not accurately predict who will be affected."

And just like weather models, these TPB predictions won't be 100 percent accurate all the time. But, as Horowitz points out, they will help scientists hone their assays from the very start rather than sifting through mountains of data in the hopes of alighting on relevant clues. And even when AI-generated predictions fall short, those results still offer researchers valuable intel in parsing out underlying cell mechanisms and interactions with different compounds.

Horowitz says that while the meteorology analogy is a useful shorthand in understanding TPB, "biology is really complicated," and becomes infinitely more complex when scaled to human physiology. Machine learning that can analyze reams of data and make informed predictions must begin with machine teaching.

For example, when Fred Wright and his team run cardiological experiments, they'll use known cardiotoxic compounds as positive controls and nontoxic chemicals as negative controls. Using these parameters, an algorithm should be able to discern, with some level of certainty, whether a novel substance is toxic.

Computational toxicology has utilized this approach for years, Wright says, and in a way, it's analogous to what the TPB cluster will do.

"But what's new now is there are other kinds of molecular information that are not from the chemical or the drug or the agent itself, but are from the reaction of a cell being exposed to an agent. So if you have, for example, a cluster of cells that are all trained to think they're liver cells, and you expose them to some sort of drug or agent, then you can get a readout of the molecular response of the cells," Wright says. "Instead of looking at toxicity, one might look at some kind of measured efficacy. Does this drug do a good job in activating a known receptor that we think would potentially be a drug target?"

Rethinking AI

The possibility of a shorter, more precise pipeline has garnered a swell of enthusiasm on both the academic and commercial fronts. AI-integrated biology would not only quicken the research timeline but also open the door to deeper,

"I think if you do translational science well, there's a circle of connections and no one's at the beginning or end, or above or below...Everyone is connected with everyone else."

- Yevgeny Brudno

more complex investigations. In terms of pharmacology, it would also slash the cost of bringing new medicines to market.

Furthermore, there's a regulatory incentive—and a sense of urgency—to invest in translative predictive biology. Back in 2019, the EPA announced it would cease conducting and funding studies that use mammal subjects by 2035. Then, late last year, Congress passed the bipartisan FDA Modernization Act 2.0. Under this new law, the FDA will no longer require animal tests for a drug to begin human clinical trials. Some speculate a ban on animal testing could follow in the future. "That is one of the arguments we made when we proposed the TPB cluster. The government is requiring us to go in this direction, and whoever builds these clusters first is going to have the opportunity to make a big impact," Piedrahita says.

But for all the excitement and possibility around predictive biology, some feelings of unease have also emerged. AI has faced an uptick in public scrutiny following the advent of chatbots (like the infamous ChatGPT), fully autonomous warehouse robots, and AIs that can do everything from content creation to complex coding.

AI in the context of translative predictive biology is a world apart from the aforementioned applications. As Piedrahita and his colleagues point out, predictive biology models do things that are impossible for a human to do. In this case, AI is not supplanting a job or mimicking a person; it is taking science—and medicine—to new heights.

Still, many researchers agree there should be discussions within the scientific community and with the general public to address these concerns rather than automatically dismissing them.

"With every new technology, there are questions about risk. Policies have to be developed to provide some guidance as to what should and should not be done," Horowitz says. "There will be some people who are alarmed by the use of AI in human biomedicine."

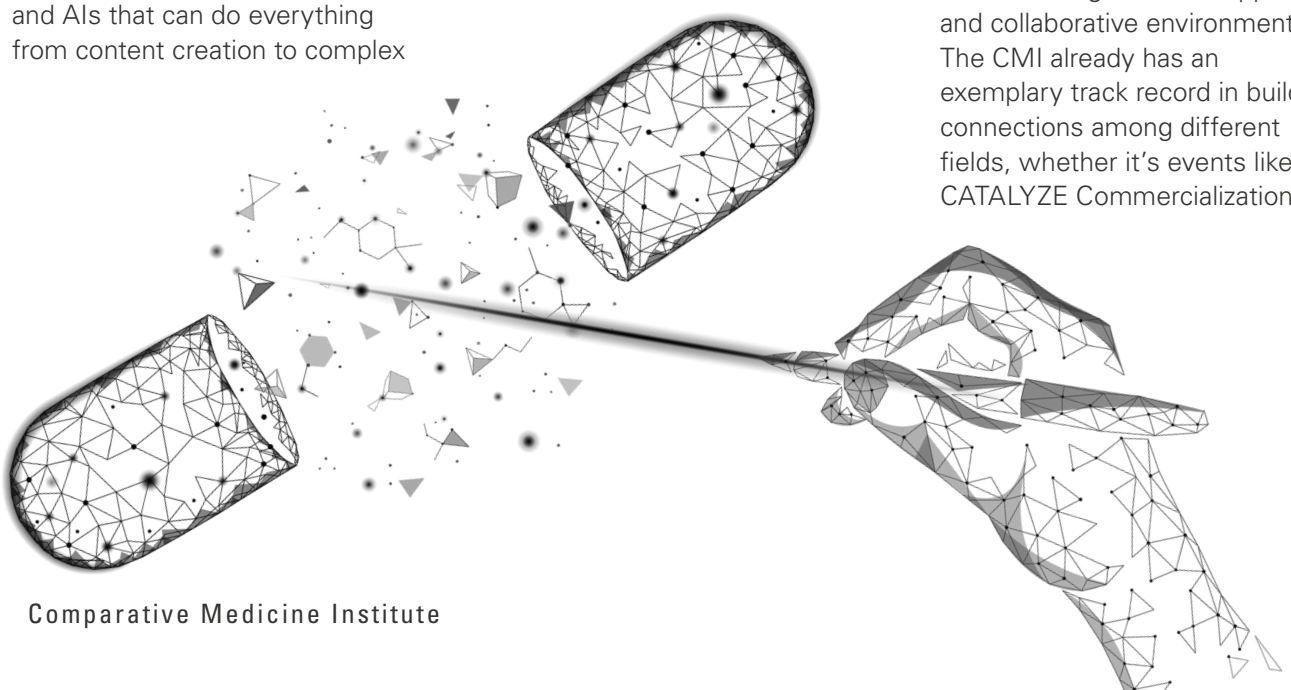
He offers CRISPR as an example. In the face of its misuse—most notably, the birth of genetically edited twins five years ago—it's natural for the public to have questions about the utility of such technology, as well as the ethical implications. Horowitz thinks these concerns are valid and it's yet another reason NC State is the ideal institution for the TPB cluster. The university boasts the Genetic Engineering and Society Center (GES), which tackles the thorny questions surrounding policy and ethics. And like many other interdisciplinary programs at NC State, the TPB initiative will interface with the center.

"This cluster is going to break down some of the technical silos that separate scientists. We do the same thing at the university level to try to bring people together, to make sure that relevant expertise is brought together to drive synergies that wouldn't happen otherwise," Horowitz adds. "I really look forward to the continuing discussion between GES and the people in the TPB cluster."

Bringing it all together

For now, the discussion is just getting started within the TPB initiative.

Drilling down to such granular levels will require not just cutting-edge AI, but also a dynamic team working within a supportive and collaborative environment. The CMI already has an exemplary track record in building connections among different fields, whether it's events like the CATALYZE Commercialization



Conference, student programs like the Comparative Molecular Medicine Training Program, or joint research projects comprising multiple schools and departments.

"We are designed to develop interdisciplinary groups. That is the whole point of the CMI: to encourage interaction with individuals," Piedrahita says. "We're also really good at identifying future leaders among the incoming faculty. You can put the best scientists in the world in a room, but if they don't know how to work together, you did nothing."

Piedrahita and his colleagues are especially excited about the TPB hires who are not only exceptional scholars, but also curious scientists (Read more about the new faculty members on page TK.) Although their research interests and specialties vary, the trio are united in their multi-discipline backgrounds, as well as their eagerness to learn from one another.

And that's where the magic happens. Or, if you ask Rob Dunn, that's where the jamming begins.

"For me, it's like music. It's like improvisation and jazz and bluegrass where you've got these different instruments. They can play on their own, but the music you get from a bunch of banjos is insufficient," Dunn says. "The beauty is bringing people together with the subtlety and power of each of the individual instruments of their scholarship in a way that they can jam by relying on those different bits of disciplinary knowledge. And I think when we're doing it at our best, that's the most exciting thing in the world."

THE SYNERGY CONTINUES WITH ISI

THE NEW TRANSLATIONAL PREDICTIVE BIOLOGY (TPB) CLUSTER comes at an especially fortuitous time. In May, the NIH awarded a seven-year, $70 million grant to NC State, the University of North Carolina at Chapel Hill, and North Carolina A&T to continue their joint research in clinical and translational science. Then in July, the UNC Research Opportunities Initiative awarded funding to a group at NC State that's building a self-driving lab, which combines artificial intelligence and robotics to study lesser-known metallic nanomaterials.

But perhaps the most significant intersection is the one with the new Integrative Sciences Initiative (ISI). Like the Comparative Medicine Institute, this initiative seeks to cultivate greater synergy within STEM. Its focus will be broader than the CMI, encompassing chemistry, biochemistry, biology, physics, engineering, and more. In a way, it's a natural evolution of the CMI's Chemistry of Life cluster, and as such, Joshua Pierce, who started the cluster and serves as the CMI co-director, is now leading the ISI as its director.

"I think it's an extension of a lot of the things we've done in the CMI. We're excited to continue building those bridges between all the units within the CMI and ultimately, the Innovative Sciences program," Pierce says. "Both are part of the growing interdisciplinary landscape at NC State." Construction recently began on the Integrative Sciences Building, which is slated to open in 2026. The five-story, 53,000-square-foot building will feature a mix of teaching and meeting spaces, as well as state-of-the-art labs.

"The predictive biology cluster is a great example where there can be a lot of synergy between us. We're going to be developing new, potential solutions to human and animal health that ultimately need to be tested and validated and verified in models," Pierce says. "The CMI is going to be a valued partner in developing the technologies within Integrative Sciences."

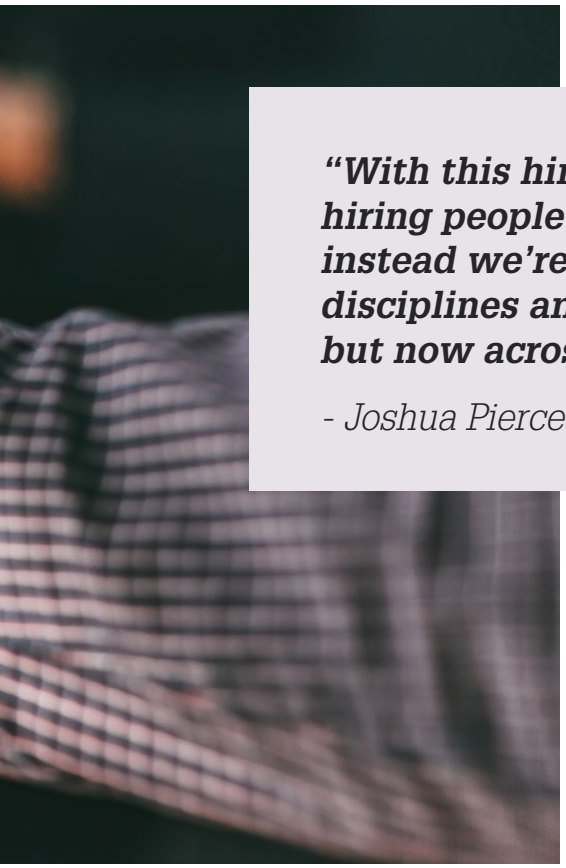
THE ANATOMY OF A NEW CLUSTER

Three new faculty members bring a diverse set of expertise to the Translative Predictive Biology initiative, with an additional two forthcoming hires tying them all together.

By Nicole Duncan

AT ITS MOST ESSENTIAL level**,** the new Translative Predictive Biology (TPB) cluster is as much about the people driving the research forward as it is the research itself. Making meaningful progress that yields real-world applications requires a fully integrated team, with each member bringing their own areas of expertise as well as a deep-seated desire to learn and work together.

"You cannot have a computational biologist sitting in a corner somewhere and then somebody that knows about drugs in another place. You have to build a team where they sit down and jointly design the experiment, where every person is playing a key role in that experiment," says Jorge Piedrahita, Co-Director of the Comparative Medicine Institute (CMI). "There has to be discussion throughout the project conception



> ***"With this hiring strategy, we're not just thinking about hiring people for departments and for teaching needs; instead we're building these research teams across disciplines and not only bridging programs within the CMI but now across integrative sciences and other units as well."***
>
> *- Joshua Pierce*

to come up with a pipeline that is feasible for everybody and can still achieve something. That, for us, is where the magic happens—when the whole team has the same goal in mind."

The new hires are Ian Williamson for Organoid Biology, Sarah Shelton for Organ on a Chip, and Rosemary Bayless for Large Animal Physiology. In addition, the search is continuing for candidates in Drug Delivery and Data Science/ Machine Learning specialties.

From the beginning, the highly interdisciplinary search committee (multiple colleges and areas of study) knew these five positions were not the standard faculty jobs and as such, the people who came into them had to be exceptional in their own right. Williamson, Shelton, and Bayless vary in their areas of expertise, but all possess a multi-disciplinary background, which will be crucial in these roles. The new faculty members will have to venture outside their specialty niches to learn from one another—but this approach to collaboration has hardly been the norm in STEM.

"When you train somebody for 10 years to do one thing really well only to say, 'OK, now go into this awkward meeting where you're going to feel uncomfortable, where you're not going to know quite enough about the other [specialties], where you're going to have to explain things you take for granted,' you're going to fumble a little bit so that you can work together. It's not easy; it's not how we're trained," says Rob Dunn, Senior Vice Provost of Interdisciplinary Programs.

Nevertheless, Piedrahita has observed a different mindset among younger faculty members who are more accustomed to working with one another. The CMI has been a leader in its interdisciplinary approach, and it's inspiring other centers, like the new Integrative Sciences Initiative (ISI) to follow suit.

Already the new hires are eager to pick each others' brains regarding their individual research as well as the joint project they'll start as a team. What's more, all three are driven by the promise of converting their research into medical applications that can improve both human and animal health.

"We don't have a medical school, but our vet school allows there to be really innovative models that can be used to drive things forward. And so I think it's the reality of the uniqueness that NC State brings to the table; the CMI is simply aligning those resources toward these goals," says Joshua Pierce, Director of the ISI and Co-Director of the CMI. "With this hiring strategy, we're not just thinking about hiring people for departments and for teaching needs; instead we're building these research teams across disciplines and not only bridging programs within the CMI but now across integrative sciences and other units as well."

With Williamson, Shelton, and Bayless settling into their new roles, the TPB initiative is already underway. But once the remaining two cluster positions are filled, their work will launch into hyperdrive.

Organoid Biology
MBS

Organoid Biology

Ian Williamson

IAN WILLIAMSON JOINS the TPB team from Duke University, where he was a Postdoctoral Associate at the School of Medicine. In Rodger Liddle's lab, his research explored the gastrointestinal system's involvement within neurodegenerative diseases. He previously earned his undergraduate degree and Ph.D. in Biomedical Engineering at UNC-Chapel Hill.

Now, Williamson is zeroing in on an essential class of amino acids that can't be synthesized by the body and must be delivered through diet or potentially gut microbes. His NIH-funded lab stands to uncover a link between the metabolism of these amino acids and the onset and progression of obesity, as well as type 2 diabetes.

"The overall goal is to better our understanding of nutrient handling by the intestine and how it governs the import of material that you ingest into the body and how the initial handling of those materials can augment health or disease in a more tangible way," he says. So far, his clinical research has been limited to mice, but at the CMI, Williamson can study these metabolic processes within larger mammals.

"Working with mice is a useful and necessary tool. [But now] I'll be able to diversify my model set to look at animals that have different dietary patterns and also are more similar to us in handling and circulating nutrient pools," he says.

As such, he's especially excited that the TPB group includes a large animal physiology expert. Rohan Shirwaiker, Associate Director of the Functional Tissue Engineering program at the CMI and a member of the TPB search committee, says this a prime example of how the new cluster reaches beyond a single shared project.

"I talk about synergy between the candidates, but it's also about synergy between the candidate as an independent researcher and the broader cluster or the CMI as a whole," Shirwaiker says. "While we certainly benefit from having these great scientists working together on some unique problems from their own perspective, I think by being hired into a cluster, they will be able to do and explore some things that they wouldn't otherwise in a more typical faculty position."

Shirwaiker and the other search committee members were especially impressed by Williamson's training in both biology and biomedical engineering. Throughout his graduate and postdoctoral research, he's consistently worked with organoid systems. His focus on the gastrointestinal tract is another bonus since NC State is a home to a number of GI

researchers.
Williamson also has experience in the artificial intelligence field. At Duke, he was involved with the Woo Center for Big Data and Precision Health. Although this center used machine learning to analyze massive datasets on behalf of various labs, it didn't actively link those groups or foster connections between them.

"It's difficult to have a connected vision of how you're building your tools and how they're going to be implemented on campus, so you find yourself kind of working in multiple avenues of research rather than researching all of them simultaneously," he says. "It will be exciting to see the cluster start off in such a connected way."

Williamson considers himself a highly collaborative scientist who relishes the opportunity to work with others, and he's looking forward to returning to a university that boasts a larger undergraduate population. Shirwaiker says this a boon for NC State and the CMI given Williamson's accomplishments and his friendly nature.

"And in Ian's case, we really saw a strong emphasis on mentoring—not just doing his own research but also being able to train students. He's had leadership roles in societies like Black Men in Medicine, and I think those are all really great elements that we would like to see in our faculty," Shirwaiker says. "Also, he's an underrepresented minority in a STEM field. He has the ability to serve as a role model early in his career—he's already accomplished so much. And I think having role models helps our undergrads and graduates as a whole."

Organ-on-a-chip

Sarah Shelton

THROUGHOUT HER CAREER, Sarah Shelton has studied cancer, but the lenses through which she views the disease have evolved over the years. In her master's program at UNC-Chapel Hill, Shelton did mathematical modeling of nutrient transport to tumors. In her Ph.D. program in the UNC-NC State Joint Department of Biomedical Engineering, she moved into diagnostic ultrasound imaging to examine the geometric changes in blood vessels as a tumor grows.

But Shelton still sought a more comprehensive vantage point, and thus began her interest in microfluidics.

"After my Ph.D. years where I was looking at tumors and imaging for vascular systems, I wanted to understand it on a smaller scale and have models that I could build and manipulate rather than being on the other side where you're watching what's happening and assessing what's changing," Shelton says. "I like bridging the

gap between manipulating the model and then observing what happens."

Most recently, Shelton was a Postdoctoral Fellow at the Massachusetts Institute of Technology (MIT), where her research utilized organ-on-a-chip technology to better understand resistance to some immunotherapy treatments in melanoma. She has also worked with the Dana-Farber Cancer Institute and incorporated patient samples into her models. "I try to strike a balance between engineered and natural tumors from real patients," she says.

This multi-disciplined approach to science inquiry exemplifies the type of environment the CMI hopes to cultivate in its TPB cluster. Matt Fisher, Associate Professor in the UNC-NC State Joint Department of Biomedical Engineering and a member of the TPB search committee, expects the field of microfluidics to become increasingly complex over the next decade—to the point it can fully mimic human physiology.

"I think the field as a whole would like organ-on-a-chip systems to advance to the degree that they are truly predictive of the in vivo environment, and one can go from an organ-on-a-chip system directly into human clinical trials without the need for animal models," Fisher says. "It's just a matter of getting the systems to the point that we could show that they are truly predicted."

He adds that Shelton's research is already advancing in that direction. Her past models have incorporated multiple cell types, which is closer to how the human body works. By increasing the multicellular capacity of organs on a chip, the models can yield more complex physiological responses instead of mere cellular responses.

For her individual research, Shelton hopes to develop organ-on-chip models that are patient-specific and represent cells from a single person, rather than a group. "A lot of immunology work is difficult when you're trying to make cells from different people—and there are differences between animals and humans," she says. "Having a single-patient tumor on a chip will be really exciting for immunology studies."

"It's really great that we've got this team-science approach of bringing people together from different disciplines so we can look at different scales, different fields, and different ideas."

- Sarah Shelton

In terms of her new TPB cohort, Shelton is looking forward to uncovering natural synergies between organ-on-a-chip systems and organoid biology. Together, they'll be able to produce even more data that can then be incorporated into machine learning.

Shelton also enjoys being situated midway along the TPB discovery pipeline; on one side is organoid biology and on the other, large animal physiology. Being in the center, microfluidics has the potential to incorporate organoid data and then scale up to animal and human models within a self-contained microenvironment.

In addition to Shelton's professional achievements, Fisher says her team-oriented mindset and experience make her an ideal fit for the TPB initiative. At MIT, she was mentored by principal investigators in both engineering and oncology.

"The fact she was able to negotiate being mentored by two people during her postdoc speaks well to her ability to work within a team science perspective," Fisher says. "And that's what we're asking these cluster hires to do. And we may also ask them to co-mentor students."

For Shelton, part of the appeal in joining the TPB initiative is the translational element. She wants her contributions to science to extend beyond the lab.

"I think discovery and pure science is exciting. But I think what feels more meaningful and purposeful is doing work that can have impact and be translational," Shelton says. "It's really great that we've got this team-science approach of bringing people together from different disciplines so we can look at different scales, different fields, and different ideas. I think all together that builds a clearer picture of what's happening and will ultimately lead to more impactful outcomes."

Organismal Physiology
CVM

Large Animal Physiology

Rosemary Bayless

ROSEMARY BAYLESS HAS already started making her mark on NC State, where she's worked as an Assistant Research Fellow in the Department of Clinical Sciences at the College of Veterinary Medicine. Prior to earning a Ph.D. in Comparative Biomedical Science at NC State, she obtained her Doctorate of Veterinary Medicine at Kansas State University. She honed her expertise in large animal physiology through a combined residency/master's program at Colorado State University.

For Bayless, the driving force in her academic and research pursuits has always been unmet clinical needs in veterinary and human populations. Combining the expertise of a clinician and a biomedical scientist, she has a keen perspective on how to convert laboratory findings into therapeutic treatments.

"I'm really passionate about leveraging those similarities as a way to benefit both species, but also as a way to communicate the value of our large-animal, spontaneously occurring models," Bayless says. "I'm interested in both the mechanistic side—the nitty-gritty of how it works and why it works—and then my medical background brings it into the clinical applications."

Lauren Schnabel, Associate Professor of Equine Orthopedic Surgery at the School of Veterinary Medicine and Associate Director of the CMI's Functional Tissue Engineering program, met Bayless through an NIH-funded program for veterinarians pursuing their Ph.D.

"I got to know Rosemary very well through running that program, and she was fantastic in all regards. Although I'm an orthopedic surgeon in sports medicine, [our department] interacts closely with internal medicine, so now I get to work with her in the hospital, too," Schnabel says. "She stood out as an applicant because of her specialty training in internal medicine, which involves a tremendous amount of physiology, but also procedural skills, etc. So she was really unique as a specialty-trained veterinarian."

In her current research, Bayless is studying the therapeutic potential of the plant-derived compound withaferin A. Inflammatory diseases like rheumatoid arthritis, diabetes, and even some cancers have been linked to a dysregulation of neutrophils—the most common type of white blood cell in humans and many veterinary species—but withaferin A could inhibit those dysfunctional cells without collateral damage to other systems.

"It's a really promising anti-cancer drug," Bayless says. "My goal is to understand how this molecule is working, which will allow us to

preemptively identify and predict any off-target effects it might have."

And this is one avenue where the CMI and the new AI-driven cluster could help Bayless accelerate her work.

"I think there's a large space for me to not only continue my in vivo work but also explore the computational side of things, so using computers to understand the mechanism of this molecule and what it binds to and how it works," she says. "We can use computational biology to run it through AI first and say, 'OK, based on the structure of this compound, what is it likely to be interacting with?' And that way, we can really hone our experimental setup so we can maximize the bang for our buck when we're actually doing the experiments."

As the FDA moves away from mandatory animal testing, there's a heightened incentive to incorporate machine learning into large animal physiology research. Bayless says she imagines veterinarians and researchers will still test new treatments on animals, but they will be naturally occurring diseases rather than induced ones. That's why new technology farther up the discovery pipeline—say, in organoid or microfluidic models—could have a major impact on large animal research.

But such advances can only be achieved if the various disciplines work in concert with one another. Thankfully, Bayless, like her fellow hires, is coming in with a team-oriented mindset and experience working with other researchers. "Her personality was such a great fit for this position. She already has a lot of collaborations—plus her openness and warm personality and willingness to collaborate with everybody. And she's super-enthusiastic about hearing other people's ideas and working with them," Schnabel says.

Indeed, Bayless is ready to learn more about her colleagues' individual research and begin planning their collective project, with each person sharing their insights.

"I think there's valuable information to be gained all along the way," she says. "Just bringing together people from a lot of different backgrounds and different expertise—that's what really excites me about this cluster."

Drug Delivery

THE FOURTH CLUSTER WITHIN the TPB initiative expands into the realm of pharmacology. A novel medicine may appear effective under controlled environments but delivering it to the intended cells of a complex living organism is an altogether different matter.

"We need to understand the biology, we need to have deep, basic science insights into disease areas and physiology. But then as you develop those, you have to ask, what are you going to do with that? How are you going to take advantage of the insights created by the predictive biology cluster?" says Yevgeny Brudno, Associate Professor in the UNC-NC State Joint Department of Biomedical Engineering and Associate Director of the Chemistry of Life program in the CMI.

This is where the drug delivery position comes into play. A researcher with experience in drug bioavailability, large biological therapeutics, such as proteins and nucleic acids, and biomedical engineering could use the findings of the other clusters to implement the drug in question. Ideally this hire would be familiar with microphysiological models, animal physiology, and predictive models for drug delivery so they could more deftly collaborate with others in the TPB initiative.

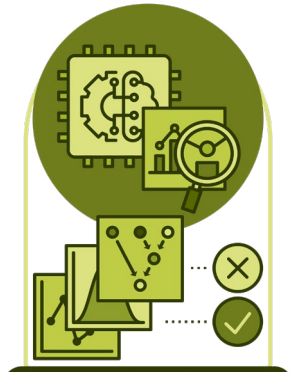
That shouldn't be a problem, Brudno says. By nature, drug delivery is a highly interdisciplinary field because it requires an understanding of the disease, the afflicted organism, and the medical agent. He compares scientists in this field to mail

couriers, who know the map of the neighborhood, what letters need delivering, and who can also interact with the letter-writers.

"I think interdisciplinarity comes with the territory with the drug delivery space—and the ability to talk to the people who know the map," Brudno says. "The kind of candidates we see with drug delivery searches are very often experts in material science who also understand cancer or an expert in nanoparticulates who also understands wound healing."

With three of the five positions filled, the committee can hone its search based on the expertise and research interests of the existing TPB team members. Like the other four specialties, an appetite for collaboration is paramount.

"We're really looking for someone who's going to be both developing new methods for bringing therapies to where they are most needed within the body, but, at the same time, someone who is able to connect with others in the cluster and take advantage of their insights," Brudno says.



Data Science & Machine Learning

THE FIFTH AND FINAL SPECIALTY within the TPB initiative differs from the rest. Historically, biology and pharmacology haven't been associated with artificial intelligence the way other fields like mathematics and engineering have. But that's changing—as the very existence of this new cluster demonstrates.

"We're really trying to find novel ways of predicting drug responses by using new and exciting computational methods. And that can only be achieved by very complex computational methods," Piedrahita says. "This is a more ambitious application of personalized medicine, which is taking it to the next step—not in the drug responses per se, but rather the drug development component."

The computational power of AI will bring terabytes of seemingly disparate data points together in a way previously thought impossible. And through those analyses, scientists can better glimpse the interweavings along each step of the pipeline, from monolayer to organoid to organ on a chip to animal models.

In addition to connecting these specialties, Joshua Pierce believes both the drug delivery and the data science position will deepen the ties between the CMI and newly minted ISI, of which he is the director (read more on page TK).

"I think leveraging integrative sciences to hire faculty that would bridge the ISI and CMI would be a fruitful way to further connect the two units and allow there to be a continuum between basic science discovery and the predictive biology, translational research component," Pierce says. "So I envision these cluster positions as the glue that would help hold those units together."

As with the drug delivery position, the search committee will zero in on candidates whose backgrounds and interests are best aligned with the existing hires. The data science hire would skew toward more of a computational background, but interest in medicine and life sciences—and maybe even some past experience—is crucial.

"We're looking for somebody who has a very strong mathematical or systems modeling and data science background, but also a person who has an understanding and appreciation for the biological and cellular data that will be generated during the cluster's collaborative research," Shirwaiker says. "This is a very niche position, but if we are able to hire the right candidate, I think it could take the CMI and NC State as a whole to the next level—and not just in terms of research that's done in the lab, but also research that impacts actual animal and human patients."

CMI 2022-2023

Training Programs & Opportunities

1. *Young Scholars Program (YSP)*
2. *Summer Interdisciplinary Scholars Initiative (SIRI)*
3. *Campbell University School of Osteopathic Medicine Research Experience*
4. *Beckman Scholar Awards in the Chemistry of Life*
5. *NIH-Funded Undergraduate Training Grant*
6. *NIH-Funded Graduate Training Grant in Comparative Molecular Medicine*
7. *NIH-Funded Graduate Training Grant in Chemistry of Life*

More info on training grants

cmi.research.ncsu.edu/education-training/

This award allows Associate Members (graduate students and postdoctoral researchers) to take the lead on a project of their own design, and experience life as a principal investigator, while learning leadership and mentoring skills with an undergraduate research assistant.

Each summer, the CMI offers undergraduate students the chance to conduct their own research and become part of a successful research team, providing strong connections and valuable insight. Students are selected by YSP awardees to participate in a mentored research project.

This program invites students at CUSOM who want lab experience to join one of the existing mentorship teams and receive the same training and opportunities as the YSP & SIRI students, while working on a parallel research project of their own.

The Beckman Scholars Program is a 15-month research experience that matches exceptional undergraduate students in chemistry and biological science with CMI faculty-lead mentorship teams.

This NIH training grant funds underrepresented undergraduate juniors and seniors for two years and one summer of research, emphasizing interdisciplinary, hands-on training in preparation for Ph.D. programs in biomedical sciences or MD/Ph.D. programs.

Graduate NIH training grant in Comparative Molecular Medicine with a minor in Team Leadership and Communication in the Biomedical Sciences. This 2-year fellowship includes a stipend with benefits and tuition.

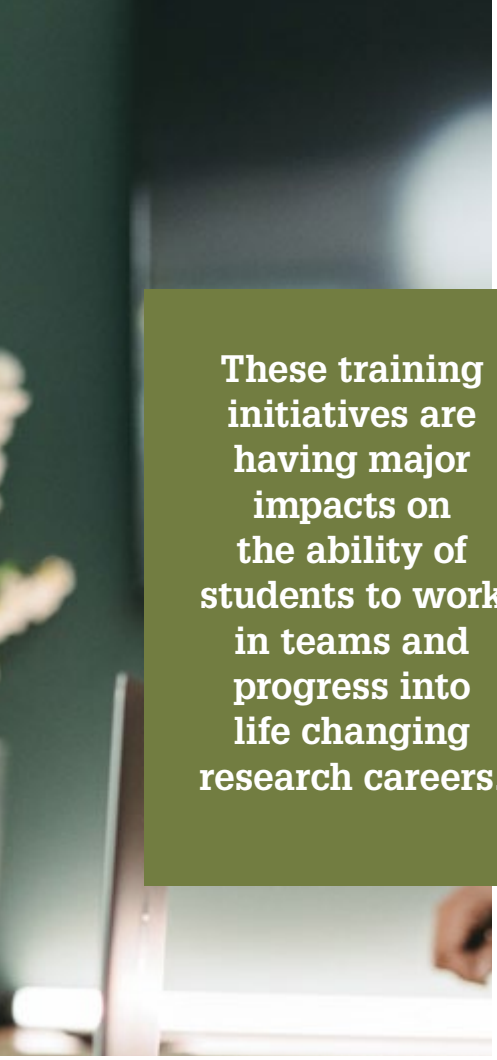
Graduate NIH training grant in Chemistry and Life Sciences, with certificate in Team Science. This 2-year fellowship includes a stipend with benefits and tuition.

GROWTH IN ALL DIRECTIONS

A YSP/SIRI Team Shares How Their Project Helped Them Transition into the Next Phase of Their Careers

By Kristina Nelson

CMI IS HOME TO A VARIETY of student training programs & other opportunities for students to gain hands-on research experience. The Young Scholars Program (YSP) gives graduate students and postdocs (CMI's Associate Members) the opportunity to come together at an annual event where they can network and form teams to create a research grant proposal for the Young Scholar Awards. Teams consist of at least two graduate students or postdocs from different disciplines. Those who are selected receive a $10,000 total prize. These awards go toward funding an undergraduate student as a full-time research assistant for the following summer, as well as toward research supplies and professional development funds. The selected Young Scholars' projects are then posted on the CURiOuS (Connecting Undergraduates to Research Opportunities in the Sciences) website where undergraduate students can apply to them, just



These training initiatives are having major impacts on the ability of students to work in teams and progress into life changing research careers.

like they would any other job. The YSP graduate students interview the undergraduate applicants for their project and select the student who is the best fit. This is what we call the Summer Interdisciplinary Research Initiative (SIRI) program. The YSP graduate students then become the principal investigators (PIs) for the project, training and mentoring the SIRI student for the duration of the summer. In most cases, the team stays together after the completion of the YSP/SIRI program, usually until the undergraduate student graduates.

The U-TEAM T34 program, a component of the SIRI program, is an NIH-funded undergraduate training fellowship, and a collaborative effort between CMI and the University Honors Program (UHP). U-TEAM program manager Carolyn Veale says the primary goal of the program is to, "attract high-achieving underrepresented minority students to the biomedical research field and give [them] the unique opportunity to participate in team science by providing them with a research placement and team mentoring. The program is intended to help these students develop a true science identity in which they can go on and become competitive Ph.D. candidates that will go on to engage in cutting-edge biomedical research." These students receive a stipend, tuition coverage, and funds to support summer research and professional development. T34 students are required to participate in SIRI-format summer research projects.

In addition to giving students the opportunity to get hands-on research experience, these programs are also meant to help students foster collaborations and make connections that will benefit them throughout their career. These connections often last far beyond the duration of the program. This is true for graduate students Nina Moiseiwitsch and Suh Hee Cook, and undergraduate Nicole Zwennes. This group of students came together through the YSP and T34 programs in 2021, and continue to work together to this day. Dr. Ashley Brown, Nina's faculty PI, calls them a "dream team." Dr. Jessica Gluck, Suh Hee Cook's PI was equally impressed with their work. This student team had some insights to share about their research and experience within CMI's programs, and where they hope those experiences will lead them.

Ashley Brown

Jessica Gluck

Nina came to the University of North Carolina-Chapel Hill as an M.D.-Ph.D. candidate in 2018. She began her Ph.D. in Dr. Ashley Brown's lab in the UNC-NC State Joint Department of Biomedical Engineering in 2020. According to Dr. Brown, her lab specializes in "development of novel fibrin and colloidal-based biomaterials for regenerative medicine applications. We are particularly interested in developing novel materials to stop bleeding, treat chronic wounds, address thrombosis, fight infection, and treat cardiovascular disease." Nina's Ph.D. work focuses on "developing a novel surgical sealant to treat vascular anastomosis." A vascular anastomosis is a surgical connection made between two blood vessels, such as in coronary bypass surgery. This sealant is like a gel that is applied over the stitches where these two blood vessels are joined. According to Nina, the motivation for the work, "came from the fact that the more porous structure of these gels and the drug loading capacity of the particles could be used to improve tissue healing. I chose to focus on the clinical application of vascular surgery because that is my clinical area of interest."

Nicole Zwennes joined Dr. Brown's lab in the Fall of 2021 as a T34 U-TEAM student when she was a rising junior. Nicole was one of the first two T34 students to complete the Teamwork in Interdisciplinary Biomedical Research minor program (which was born out of the T34 grant), when she graduated this past May.

The goal of her research with Nina and Dr. Brown was to develop a dual-loaded drug delivery system which would allow for delivery of two drugs at separate time scales. This is very clinically useful, as drugs used in early and late stages of healing are typically different. Fibrin-based nanoparticles (FBNs) would allow for rapid release of a drug to promote healing, while polycaprolactone (PCL)-gelatin blend scaffolds with delayed release of an antihyperplastic would prevent neointimal hyperplasia. This is when the interior of the vessel heals incorrectly, causing it to go from "a garden hose to a straw," as Nina put it.

As the sealant project grew, the team began a collaborative effort with Dr. Jessica Gluck and her graduate student, Suh Hee Cook. Dr. Gluck recalls, "We collaborated to see if there was a way to use some of our fibrous biomaterials (electrospun nanofibrous scaffolds) for their new approach." Dr. Gluck's lab focuses on stem cell differentiation and function, specifically in the cardiovascular system and cornea. They make fibrous biomaterials with tunable properties, and seed stem cells in efforts to drive differentiation to a specific tissue.

Suh Hee Cook was the first graduate student to join Dr. Gluck's lab shortly after it opened in 2019, and the PI is tremendously grateful for the effort Suh Hee has put into the lab since her arrival. Suh Hee's Ph.D. research focuses on using electrospun scaffolds to stimulate stem cell-derived cardiomyocytes – the cells that cause the heart to contract – to electrically couple to native tissue. She is an active associate member of the CMI, and has also received a CMI's Functional Tissue Engineering Associate Member scholarship. She has collaborated on several other YSP projects since becoming involved in the CMI. The first was 'exploring ultrasound-mediated piezoelectric stimulation of induced pluripotent stem cell derived-cardiomyocytes,' the second is this project with Nina and Nicole. Dr. Gluck has also had several projects funded through the CMI, so the CMI has further contributed to Suh Hee's research by supporting her PI.

"Their passion for their respective areas of research is commendable and infectious. It was very rewarding to witness the evolution of the project and how each of them became experts in this area of research."

- Dr. Gluck

Nicole joined Dr. Gluck and Dr. Brown's labs as the SIRI student on Nina and Suh Hee's project. Suh Hee trained Nicole on how to electrospin samples; something she does quite frequently in her own Ph.D. research. "It was nice to use electrospinning in a completely different context with this project focused more on drug delivery." Nina taught Nicole how to run biomedical tests to evaluate the material strength, and how to conduct drug release testing. She also instructed Nicole on nanoparticle synthesis and cell work.

The preliminary research that came out of this project helped to support an NIH F30 program application for Nina. The F30 program is a fellowship program designed to fund research for predoctoral M.D.-Ph.D. students. Nina's proposal received a perfect score of 10, meaning the committee unanimously agreed on the significance of the proposed research. Nina was a bit shocked when she heard the news; "It was a huge honor. Honestly, I thought it was a typo when I first got my score back. It was definitely validating to know that someone apart from just me thinks that my project is worthwhile. I think the score is largely a testament to how lucky I have been to have such great mentors and people to reach out to throughout the grant writing process. Hopefully in a few years I can help future students through their first grant writing experiences."

For now, Nina is continuing her Ph.D. work in the Brown lab, which she aims to complete next year. After that, she hopes to continue with her journey to medical school. Suh Hee Cook also plans to graduate next year and will be pursuing postdoctoral opportunities. Nicole graduated from NC State in Spring 2023, with a Bachelor of Science in Biological Sciences, Human Biology concentration. Though she has earned her degree and finished her programs, she is still working with Dr. Brown and Nina to finish data analysis and complete studies for their manuscript. The team hopes to submit their research for publication this fall.

Nicole, Nina, and Suh Hee greatly enjoyed their experience in their CMI programs and learned a tremendous amount as well. When asked to reflect on their experiences, this is what they shared:

Nicole Zwennes

"I really enjoyed being part of the SIRI and U-Team programs because they gave me the opportunity to be exposed to high quality research, even as an undergraduate student. I was able to collaborate with researchers of different backgrounds and levels of education. I was truly made to feel like a 'real' scientific researcher, and I really appreciated this, especially as an undergraduate student. Through my experience in both the SIRI and U-TEAM T34 programs, I have learned so many foundational qualities that it takes to make a great researcher. Being able to develop these skills early in my career has created a strong foundation for my research skills that I will continue to build upon for my future. It reaffirmed and strengthened my interest in medicine and biomedical research."

"I would tell other students who are interested in participating in CMI programs to explore the plethora of opportunities that are made available to them through the CMI. The emphasis on interdisciplinary research ensures that there is an area of interest for any aspiring researcher, and the members of the institute are eager to collaborate and create innovation."

Nina Moiseiwitsch

"Working with Nicole has been one of the highlights of my graduate work. Getting to watch her grow as a scientist has been really meaningful and fun. I have felt for a long time that teaching and mentorship are important aspects that I want to preserve in my future career, and this experience has reinforced just how meaningful these parts of the scientific process can be. I have definitely learned how to be a more effective mentor and teacher, and how to adjust my teaching/mentoring style to best fit a student's needs. I've learned a lot about team-based science and organizing across a larger group to harness everyone's individual skills while still remaining relatively efficient."

"There is such a wide variety of expertise within the CMI, so whatever you are interested in, there's someone who would love to be your mentor! Working across disciplines and research groups, as in the YSP/SIRI program, is a great way to learn about how scientific collaboration works and jump into some exciting work!"

Suh Hee Cook

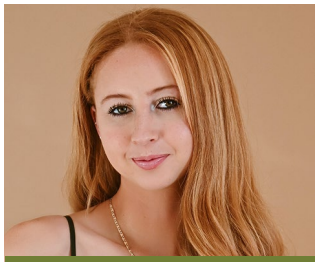
"Working with Nina and Nicole was great! The primary takeaway has been the importance of collaborative science, across not only lab groups but across disciplines. I've also been shown over and over again that we learn just as much from our mentees as they learn from us. Participation in the Young Scholars Program and CMI has confirmed my desire to stay in academia and research." When asked what she would tell students that are interested in participating in these training programs and other opportunities at CMI, she said, "Definitely do it! It's a wonderful experience and enriched my Ph.D. experience… it was instrumental in guiding my path to where I am today."

WELCOME TO THE U-TEAM

Newest Undergraduate Scholars Discuss the Surprising Things They Learned this Summer

EVERY YEAR, THE NIH-FUNDED U-TEAM T34 training program selects four highly talented rising juniors to receive a two-year fellowship that covers their tuition, health insurance, and a monthly stipend. Selected students also receive individual mentoring and professional development opportunities, as well as research experience in their chosen field of interest. This year, Grace Hardy, Katelyn Harris, Isaiah Stevens, and Lauren Sylvester were selected to receive the fellowship. After a meet and greet barbecue this past spring, they began their lab training and then went on to participate in full-time research over the summer. We sat down with them to discuss their experiences in the program, as well as their present and future goals.

Grace Hardy



Katelyn Harris

Isaiah Stevens

Lauren Sylvester

How did you become interested in biomedical research?

Grace: I was able to take some hands-on classes about biomedical engineering and biotechnology in high school and fell in love with it!

Katelyn: I took a Biomedical class in 9th grade, which taught me so much about the career field and its importance.

Isaiah: I've always been interested in medicine, and biomedical research came with my initial pre-medical school track.

Lauren: Through courses I have taken during undergrad.

What is your summer research project on?

Grace: The project I'm working on this summer is to develop novel neonatal and adult fibrin-based gels for enhanced cellular response.

Katelyn: The presence and viability of Bartonella in fetal and placental tissues of two invasive animal species

Isaiah: Modeling Chronic Thromboembolic Hypertension (CTEPH) Using 1D fluid dynamics.

Lauren: The total synthesis of Leopolic acid A and analogs to eradicate MRSA biofilms.

Did you learn anything surprising or unexpected this summer?

Grace: During our research bootcamp we learned about the importance of good record keeping in research, and working in the lab I was able to see firsthand why it matters. Record keeping was something I knew was important but working in a lab firsthand, I was surprised by the amount of detail sometimes required and some of the cases where it can save an experiment or sample.

Katelyn: I am conducting research on Bartonella spp. and I am so surprised at how many species of Bartonella exist. There are so many strains of these bacteria, each with their own hosts which they primarily infect. I never knew that there were so many intricate procedures that needed to take place to sequence DNA, and for testing tissues/blood. Learning how important each of these small steps are for a positive outcome was something I did not expect.

Isaiah: Even when other scholars conduct research in a similar field, interest is hard to keep if your hooks are not strong.

Lauren: I learned a lot more about myself and what I truly enjoy learning about, and what I want to focus on for the rest of my career.

What will you take away from the summer research experience?

Grace: My mentor told me a piece of advice that I will take away from this summer and remember as I apply to graduate school. It was that a good lab environment is one of the most important things to consider when choosing a Ph.D. program.

Katelyn: I will take away a greater knowledge on how to conduct lab research in the most efficient way. I have learned how to communicate effectively with a team and how to give academic presentations in a way that keeps the team engaged. I will take away a new perspective on how important biomedical lab work is for the health of society, and why each project is crucial to the future.

Isaiah: Research is quite difficult, and significantly differs from academic work. It requires you to dedicate yourself to your final goal and overarching benefit of your project. In addition to this, working hard and collaboratively with your peers is key to a project's success.

Isaiah: Research is quite difficult, and significantly differs from academia. It requires you to dedicate yourself to your final goal and overarching benefit of your project. In addition to this, working hard and collaboratively with your peers is key to a project's success.

Lauren: I will continue to utilize the many skills I have learned from both labs, and apply those skills to further research

What is your ultimate career goal?

Grace: I hope to get a Ph.D. in biomedical engineering before transitioning to a position in industry researching pharmaceuticals or regenerative medicine.

Katelyn: My ultimate career goal is to continue my education post-undergrad and to either go to veterinary school, or continue research in the infectious disease unit at NC State's Research Lab.

Isaiah: I would like to work as an epidemiological mathematician in the field of public health. After this, I would like to be a professor at a major university.

Lauren: To be a physician-scientist that specializes in pain management therapeutics.

How do you expect the U-TEAM program will impact your future career plans?

Grace: The U-TEAM program has allowed me to do research in undergrad and opened up doors for me to pursue a Ph.D. I also have access to a lot of mentors and advice about my future plans that I wouldn't have otherwise.

Katelyn: The U-TEAM program will allow me to gain a greater understanding of the importance of research for our society. It will help me to acquire experience working in the infectious disease research field with animals, so I can gain knowledge on how pathogens infect an animal host. The U-TEAM program will help to prepare me for post-graduate programs, in which I will need to use my knowledge on animal sciences.

Isaiah: It will develop my research skills, presentation skills, medical knowledge, and professional portfolio.

Lauren: The U-TEAM program will provide me with great opportunities to learn an interdisciplinary approach to solving ongoing challenges the healthcare system faces. It will also provide me a lot of hands-on research experience that I can apply post graduation.

Mentorship Team & Projects

Anna Castillo

Evaluation of TRAP-dexamethasone as a novel treatment for equine post-traumatic osteoarthritis in vitro

Mentors: ***Shannon Connard & Micah Mallory***

Faculty PI: ***Lauren Schnabel (CVM)***

Nabil Chedid

Origami-inspired 3D-printed Soft Electromagnetic Robotics for Assisting Treatment of Ventricular Heart Failure

Mentors: ***Kevin Li & Sen Zhang***

Faculty PI: ***Xiaomeng Fang (WCOT)***

Evie Dallmann

Impact of Flame Retardant Mixture Exposure on Hypothalamic Neuropeptide System Assessed by Light Sheet Microscopy

Mentors: ***Andrew Newell, Mani Rai & Rene Cai***

Faculty PI: ***Heather Patisaul (COS)***

Novietta De Britto

Developing surgical techniques for local inner ear drug delivery in pigs

Mentors: ***Adele Moatti & Shannon Connard***

Faculty PI: ***Alon Greenbaum (COE)***

Hannah Haynes

Novel "TRAPs" delivery system allows local presentation of corticosteroids for treatment of equine asthma

Mentors: ***Rukesh Chinthapatla & Bethanie Cooper***

Faculty PI: ***Yevgeny Brudno (COE)***

Emma Norris

Exosomal viral vector delivery to the inner ear

Mentors: ***Haven Roberts & Adele Moatti***

Faculty PI: ***Alon Greenbaum (COE)***

YSP&SIRI 2023

Lauren Sylvester

Optimization of Leopolic Acid A and its Effects on Bacterial Pathogens

Mentors: ***Andrew Ratchford & Jamie Breunig***

Faculty PI: ***Joshua Pierce (COS)***

Tanya Upadhyay

Recapitulating the microenvironment of stem cell-derived cardiomyocytes with the help of 3D bioprinting

Mentors: ***Kiran Ali & Tavila Sharmin***

Faculty PI: ***Jessica Gluck (WCOT)***

Peiqi Zhang

Develop Enzyme-Hydrogel Fibers to Improve Gas Acquisition in Bioreactor for Enhanced Productivity of the Biopharmaceutical Process

Mentors: ***Sen Zhang & Lydia Jordache***

Faculty PI: ***Xiaomeng Fang (WCOT)***

Team Science

TEAM-BUILDING IN THE WILD

March 3, 2023
U-TEAM Spring BBQ Social

April 14, 2023
Chemistry of Life Training Program Symposium

May 25, 2023
Summer Training Program Kickoff


NC STATE

Before Vetletics, there were no dynamic pneumatic compression devices available for use on horses. However, thanks to Drs. Schnabel, Perdew, and Breen, horses are finally able to have long-term relief with the EQ Press.

Vetletics, Inc:

PAVING THE WAY FOR HORSE HEALTH

By Kristina Nelson

DR. LAUREN SCHNABEL IS A WOMAN who wears many hats. She is a professor of equine orthopedic surgery here at NC State, an NC State Faculty Scholar, PI of the Schnabel Equine Sports Medicine Laboratory, Associate Director of the Comparative Medicine and Translational Research Training Program, and an Associate Director of CMI. She has a DVM and PhD from Cornell University and is board certified by both the American College of Veterinary Surgeons and the American College of Veterinary Sports Medicine and Rehabilitation. In the midst of all this, she still had time to co-found a startup company, Vetletics, Inc. in 2020, along with NC State colleagues Dr. Irina Perdew and Dr. Matthew Breen, where she serves as Chief Medical Officer and Company Secretary.

Vetletics' flagship product is the EQ Press, a device created to help treat horses with lymphatic issues and to improve athletic recovery. Unfortunately, lymphatic problems are common in horses. The lymphatic system is part of the immune system and this network of organs, tissues, glands, and vessels plays several key roles in the body including maintaining fluid levels, protecting against infection, and removing waste products. Lymph, the fluid that runs through the lymphatic system, collects excess fluid and proteins as it moves through the body. Regular circulation of the fluid helps to prevent swelling and waste buildup. Once in the lymph nodes, the white blood cells there fight any harmful bacteria, viruses, and parasites that may be present in the lymph. In horses, their lack of musculature often causes lymph fluid to accumulate in the legs. It does not drain the way it should, leading to swelling in the limbs. In some cases, this can be temporary – like during athletic recovery. But in others, the lymph buildup can lead to more serious complications, like lymphedema, infections, or sepsis. Humans can also suffer from this buildup of lymph fluid and are treated using pneumatic compression devices. These devices force lymph fluid out of the limbs and through the lymphatic system. The condition is the same in both humans and horses, and human treatment devices are well understood, but designs for human devices cannot be used for horses. Human devices are designed for the patient to lay down during use and go over the abdomen. Before Vetletics, there were no dynamic pneumatic compression devices available for use on horses. Horse owners only had access to temporary treatments such as ice or wraps for their animals. However, thanks to Drs. Schnabel, Perdew, and Breen, horses are finally able to have long-term relief with the EQ Press.

The EQ Press was designed to function in a similar fashion to its human counterpart, by forcing lymph fluid out of the legs. Unlike the human device, the EQ Press allows the horse to remain standing. Dr. Perdew was a vet student at NC State when she conceived the EQ Press. She had worked extensively with human pneumatic compression devices, specifically in basketball players. Dr. Perdew approached Dr. Schnabel with the idea to create a similar device for horses. The two then

VETLETICS™

HUMAN TESTED, ANIMAL APPROVED

worked together here at NCSU to design the device, along with Mego Afek A.C. Ltd., the leading manufacturer of human pneumatic compression devices worldwide. They currently have a patent pending for the equine garments and have been selling the EQ Press since 2020 with guidance from the Poole College Andrews Launch Accelerator Program which Dr. Perdew was selected to participate in as leader of Vetletics.

The EQ Press resembles four sleeves attached to a harness, almost akin to a jacket. But the garment does not go over the horse's body. Instead, the sleeves only cover the legs, but go up as high as they can. It uses battery powered pumps in a saddle pad to create compression, pushing lymphatic fluid up the horse's legs. Drs. Schnabel and Perdew knew that the EQ Press had a lot of potential because of the success of human devices but needed to prove the efficacy of moving lymph fluid in horses. "People are always asking; how do you know it works in the horse?" recalls Dr. Schnabel. "And I, as a scientist, obviously can't just say, well, I think it does because of the human literature." While there was significant evidence to support that these types of devices are effective in humans, until this point, there had only been anecdotal data and case studies in horses. So, to answer this question, they carried out a lymphoscintigraphy study here at NC State in 2022 led by CMI associate member Dr. Drew Koch, who was a PhD candidate in Dr. Schnabel's laboratory at the time. This study was funded by a generous donation to NC State from a supporter.

Lymphoscintigraphy is the process of using a radioisotope to track/follow the movement of lymph fluid through the body. Using this technique, scientists can determine how quickly lymphatic clearance occurs. For the study, the tracker was injected just above the coronary band at the level of the horse's foot, to see the movement of lymph fluid up the leg. Horses wearing the EQ Press were compared to control horses that were not wearing the device. The scientists were able to show that horses wearing the EQ Press had dramatically and significantly faster lymphatic clearance than those not wearing the device. According to Dr. Schnabel, lymph fluid in the EQ Press horses "actually reached the lymph node at the top of the leg very fast. The control horses that weren't wearing the EQ Press, never even reached that lymph node. So that was super exciting." The team has presented their work at several conferences and also received the Daugherty Endowment Fund and NC IDEA SEED grant this year to support Vetletics and further research and sales efforts.

Each cofounder of Vetletics brings their own expertise to the partnership. Dr. Schnabel is an equine orthopedic surgeon and sports medicine specialist in the College of Veterinary Medicine. Dr. Breen has both veterinary knowledge and entrepreneurial experience, with several other successful startups. And Dr. Perdew, who was a veterinary student at NC State at the time of founding, has connections with Mego Afek as well as many years of sales experience prior to veterinary school. She also serves as the company's Chief Commercial Officer. "It's a great team," Dr. Schnabel comments, "and NC State has been incredibly supportive all along." But the team has faced some challenges on the path from product design to founding Vetletics to conducting research. One of the biggest challenges for Dr. Schnabel as Company Secretary has been understanding the financial aspects of a startup company. Earlier this year, Vetletics named a new CEO, Sam Drew, who is an experienced startup executive, which Dr. Schnabel is very excited about. For Dr. Schnabel, an additional challenge was adding Vetletics to her already very hectic schedule. Managing all of these things has been "overwhelming at times, but we have excellent support here, for sure." She

also found it somewhat difficult to "work backwards". Vetletics was founded before conducting the pilot study for the EQ Press. Instead, they had this idea for a garment for horses, saw something similar was working in humans, designed and sold the device for horse use. And only then conducted a study to show its effectiveness in horses. Dr. Schnabel is used to new applications going from veterinary research to human medicine, rather than human to equine. So she enjoyed the twist, but it was a different experience for her.

According to Dr. Schnabel, the support from NCSU and the CMI was instrumental in the success of Vetletics. Dr. Schnabel has been a member of CMI since 2013, and as a result has made numerous connections here. Those connections have been invaluable to her as someone who was a scientist first and an entrepreneur second. One of her most valuable connections has been to fellow CMI Member Dr. Breen, who is now a co-founder of Vetletics. "I don't know that I would have interacted with him much otherwise, just in our daily lives and sort of our different research fields." Many CMI members have their own startup companies, including Drs. Schnabel and Breen. They often work together or rely on each other for advice. Dr. Schnabel, Dr. Josh Pierce and Dr. Ashley Brown have also assisted each other with their startup companies. "We've had a lot of general supportive discussions, surrounding our NC State careers, our companies and entrepreneurship, and how to make this all work." Being part of CMI has also allowed access to additional funding opportunities, like the federal Small Business Innovation Research and Small Business Technology Transfer programs.

Due to the CMI's close connections within NC State's College of Veterinary Medicine, the team has access to not only veterinary tools and expertise, patients to test and fit the EQ Press, but has gained entrepreneurial experience from their connections at CMI. They were able to design the EQ Press, use it in clinical settings, and begin selling it before conducting their lymphoscintigraphy study in 2022. The study then allowed them to create even more connections. Dr. Schnabel is also very excited about the new resources that the CMI offers. For instance, the new CATALYZE Conference that began in 2022 with its goal of bridging the gap between scientific research and the market.

Resources for individuals interested in entrepreneurship extend beyond the CMI to other parts of NC State as well. The Office of Research Commercialization is another excellent resource for those looking to bridge the gap between research and industry and offered valuable support to the Vetletics founders. NC State is also helping Vetletics find investors, via the Wolfpack Investors Network. Drs. Schnabel, Perdew, and Breen along with Mr. Drew have been actively working with the group on the next steps of fundraising for the EQ Press. They hope to increase fundraising efforts in the next six to twelve months to continue their work. The team is also currently designing some other garments and accessories to go with the EQ Press. One such product is hygiene garments that can be worn under the EQ Press device. These would be especially useful in hospital settings, where multiple animals would be housed and undergoing treatment.

When asked about any advice she would have for people interested in taking an idea from lab to startup, or founding their own startup company, she stressed taking advantage of all the resources available here at NC State and CMI.

- Dr. Schnabel

When asked about any advice she would have for people interested in taking an idea from lab to startup, or founding their own startup company, she stressed taking advantage of all the resources available here at NC State and CMI. "There's so many resources to get the company formed and started. I think the actual day to day running of it and how to be successful, especially financially, is just something that's hard to teach. The vast majority of us as veterinarians and scientists don't have MBAs; I don't know how to do that. So, to have the support of NCSU and CMI has been incredibly helpful, especially on the business side of things" (Dr. Schnabel). So while it may be overwhelming at first, the resources and support are there. NC State and CMI have allowed Drs. Schnabel, Perdew, and Breen to take their dreams of creating the EQ Press and forming Vetletics a reality. We look forward to seeing what the future will bring to Drs. Schnabel, Perdew, and Breen, and Vetletics.

The competition gives students the opportunity to "reach across the skills divide and see what else is involved in getting a successful product up and going"

- Hisham El-Shaffey

CATALYZING CONNECTIONS:

CATALYZE Conference Returns for 2nd Year

By Kristina Nelson

THE ANNUAL CATALYZE Commercialization Conference returned for its second year this past February, bringing with it some new ideas, minds, and pitches. The conference focuses on bridging the gap between scientific research and entrepreneurship. One of the main goals of the conference is to connect students and faculty at NC State with all the available commercialization resources at the university and beyond. This includes funding opportunities, training, and workshops through the CMI and the Office of Research Commercialization, to name just a few. CATALYZE is a way for individuals interested in research commercialization to get access to hands-on experience. The organizers also hope to connect to those who may not be as familiar with commercialization. A third aim of the conference is to highlight the value of research commercialization, both in the academic sphere and in the economy.

The CATALYZE Conference featured a combination of talks and workshops, rounded out by the student pitch startup contest. Many familiar faces returned to the conference to give talks this year. Dr. Thomas Theis and Hisham El-Shaffey from CMI gave the opening remarks. Lisa Chang, the Director of Technology Entrepreneurship and Commercialization in the Poole College of Management, spoke about the array of entrepreneurship resources available at NC State. Multiple speakers from the Office of Research Commercialization, including Kultaran Chohan, provided insights into the importance of commercialization, available programs, and startup services. Sue Carson and Meagan Nappo informed conference-goers about the Business and Medicine Master of Microbial Technology Program. CATALYZE also featured several newcomers, including keynote speaker Dr. Chris Paddon. Dr. Paddon is currently the Senior Director of Technical Innovation at Amyris, a biotechnology company dedicated to helping other companies create sustainable products. He also serves as the scientific lead for the company's vaccine and pharma projects, including their malaria drug research, the focus of his CATALYZE presentation. The talk was titled "Semi-synthetic Artemisinin: Using Synthetic Biology to Stabilize Production of the World's most important Anti-Malarial Drug." Also new this year was the "Beginners Guide to SBIR/STTR: An introductory workshop to secure funding for your startup." The Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs are federally funded and give small businesses the opportunity to engage in Federal research, innovation, and commercialization.

One of the main events of the conference, and a favorite of Dr. Theis, is the student startup pitch competition. Graduate students form teams to gain first-hand experience in the entire research commercialization process. The teams choose a current biomedical problem to research, design a product meant to address or resolve the problem, and then determine the business strategies needed to put that product on the market. This includes fundraising, production, company partnerships, and distribution. The main goal of the competition is to have students make connections between scientific research and entrepreneurship. The competition gives students the opportunity to "reach across the skills divide and see what else is involved in getting a successful product up and going" (Hisham El-Shaffey). Students that have a stronger scientific background have the opportunity to connect and work with business students, and vice-versa. Teams then present

their product research proposal at CATALYZE. Winning teams are then awarded a cash prize to be used toward bringing their proposal to life in any way they choose.

From the many excellent pitches this year, three teams were selected to receive an award. Team Next-Generation Biosensors for Improved Parkinson's Disease Treatment: (Kartheek Batchu, Kevin Robinson), focused on creating a novel L-DOPA sensor to better detect a person's dopamine levels, which can decrease with Parkinson's. They hope to ultimately use this sensor to construct a closed-loop treatment system for Parkinson's disease. Team Hapi-er Solutions: (Robin Jacob, Kali Boyes, Shane Harrington, Jordan Sweger, Joshua Pecoraro) aimed to prevent pressure injury formation in patients during hospital stays. They created sensors to detect a patient's risk areas and alert nurses. They have completed work on their first prototype and hope to shortly begin work on their second. Team Biosensys: (Jocelyne Akamaliza, Robin Jacob, Vince Ryan, Kalindi Kapadia) focused on helping hospitals find a faster way to detect sepsis. Their proposal involved using a wearable sensor to detect lactate levels in patient sweat, which increases with sepsis. For the team, CATALYZE, "was an opportunity to validate our idea and get confirmation that we are on the right track" (Jocelyne Akamaliza). Participation in the competition also brought them additional success, as they went on to win two outside pitch competitions. According to Jocelyne, the team plans to use the funds to, "pay for the incorporation expenses and get started on a prototype as that will put us ahead to start applying for more funds to bring our idea into reality." Hisham El-Shaffey, who worked closely with the student teams, was very impressed by this year's teams and ideas. Dr. Theis called the competition, "one of the highlights of the conference…The teams really thought through in detail, their ideas and the potential commercialization, and they performed well."

Organizers hope to bring some exciting changes and additions to the conference in 2024. First, they would like to provide more opportunities for networking and connection. They plan to invite local startup companies, giving students the opportunity to meet local startup professionals. Students can not only network but ask questions and learn from these individuals. The startups, in turn, meet students who are interested in commercialization. Organizers hope this addition and others to come stimulate more participation and attract an even wider audience.

Numerous individuals helped to make CATALYZE an even bigger success for its second year. In addition to those already mentioned above, special thanks to students Seth Dilday, Megan Pike, and Shannon Connrad. Bringing so many different people together from both inside and outside CMI allows students to be immersed in the commercialization information and resources available to them at NC State. Hisham El-Shaffey has enjoyed being involved in planning CATALYZE these last two years, and as a graduate student he has seen tremendous benefit; "Having a place where you can meet in person with this singular goal of commercializing your research… having that goal gets all of these people in one place at one time, earmarks the time in your schedule to go think about these ideas. And it gives you all the contacts to meet the people who would help you solve those problems." If you are interested in research commercialization, this is an event you will not want to miss. We look forward to returning in 2024!

NC State's Office of Research Commercialization

is here to help you advance your idea to the marketplace through a robust offering of services and programs designed to help you succeed.

Technology Transfer Services

Technology Evaluation
Protection of Intellectual Property (IP)
Execution of Confidentiality & Material Transfer Agreements (MTA)
Marketing of Research Discoveries
Licensing of IP

Funding Support

Early-stage commercialization funding
Customer discovery & validation training
Business plan competition
Startup grant writing support
Angel investor network

Creative Services

Logo & Branded Materials Creation
Website Development
Pitch Deck Design and Layout
Videography & Photography Support

Startup Company Support

Company Incorporation
Regulatory Consulting
Business Plan & Grant Writing Assistance
Co-Working Space
ORC Advisors Network

NC STATE UNIVERSITY **Office of Research Commercialization**

To learn more contact Kultaran Chohan:
kultaran_chohan@ncsu.edu

Please visit our website:
research.ncsu.edu/commercialization

2023

BUSINESS & MEDICINE TEAMS

The Business & Medicine (BaM) program pairs CMI students with students in the Master of Microbial Biotechnology (MMB) program (CALS). MMB students receive dual training in the science and business of biotechnology and are comfortable evaluating market potential, intellectual property, and the competitive landscape for biotechnology products and companies. BaM partnerships begin when, during the summer, CMI researchers submit a one-paragraph description of their ideas and types of questions that they would like to pursue. The appropriate student teams are established and then in the fall, the MMB students spend five weeks focused on the problem. A detailed final report is delivered to each Principal Investigator (PI) and the groups present highlights in a combined meeting of all the researchers and student teams.

1 From Gene Editing to Diagnostics: ***Using CRISPR to Detect Viruses***

Mentor: Dr. Rodolphe Barrangou
MMB Team Members: Ramya Vijapurapu*, Rachel Brunjes, Sophie Lindem, Logan Miller, Emory New & Miguel Sanchez

2 Canine Clinical Trials: ***Not Just a Walk in the Park***

Mentoring CMI PI: Dr. Yevgeny Brudno
MMB Team Members: Emory New, Erin Cavanaugh, Stephanie Charino, Yahara Touprong, & Haley Woolard

3 Evaluation of the Parahydrogen-based ***Hyperpolarization Market Viability***

Mentoring CMI PI: Dr. Thomas Theis
MMB Team Members: Sophie LIndem, Spencer Harolds, Madison Hellner, Charné Meintjes, Ryan Puckett, & Miguel Sanchez

4 Assessment of Market Opportunity, Competitive Landscape, and Drug Delivery Methods for a Novel Treatment of ***Pluri-microbial Human and Porcine Pneumonia***

Mentoring CMI PI: Dr. Elisa Crisci
MMB Team Members: Connor Steenbock, Michaela Coates, Autumn Rorrer, Cassandra Suedbeck, & Lucas Tonnesen

5 A Shorter Ride to ***Macrolide***

Mentoring CMI PI: Dr. Gavin Williams
MMB Team Members: Gordon Sylvester, Marriane de Bedout, Monica Judd, Joshua Scolz, & Tom Williams

6 ***Treatment of Eosinophilic Esophagitis***–A Market Analysis

Mentoring CMI PI: Dr. David Zaharoff
MMB Team Members: Diego Rendon, Rachel Shreeja Chaaya, Kylie Herst, Kathryn Landry, Mason Neal, & Raazia Zia

*-Team Lead

Keep an eye out for these exciting

UPCOMING EVENTS

Fall (November)
Young Scholar Program

Winter (February)
CATALYZE Conference

Spring (May)
Think, Collaborate and Do Ideation Event

Summer (August)
Annual Summit

NC STATE UNIVERSITY

CMI COMPARATIVE MEDICINE INSTITUTE

SUPPORT THE CMI

The Comparative Medicine Institute fosters innovative student mentoring, and research collaborations and commercialization efforts, all focused on improving animal and human health and training the next generation of wolf pack leaders.

The generosity of alumni and friends helps safeguard the institute's ability to support student training, extend research opportunities to talented students and faculty from basic sciences and clinical disciplines, and facilitate the development of new treatments for human and animal diseases.

CMI ONE MEDICINE FUND

Gifts to the CMI One Medicine Fund gives current students and faculty the opportunity to use their skills and creativity to make game-changing discoveries. These critical resources from the CMI One Medicine Fund support a far-reaching membership base, including students, postdoctoral researchers and faculty. With your help and generosity, we can continue to address urgent clinical needs for both humans and animals, provide a world-class research environment for all our members, and expand our transformational mentoring experiences to impact even more students.

North Carolina State University
Comparative Medicine Institute
Campus Box 8401
Raleigh, NC 27607

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