BIOMEDICAL ENGINEERING AT UVA

presents the third annual

EMERGING LEADERS IN BIOMEDICAL ENGINEERING SYMPOSIUM

The field's brightest early career scientists discuss their work and future directions

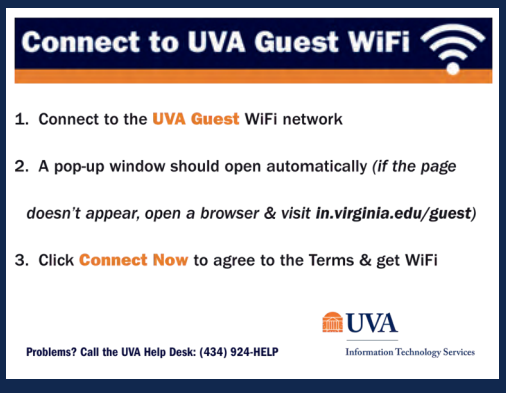
keynote speaker

Erika Moore, Ph.D. Asst. Professor, University of Maryland

SEPT. 6, 2024 9AM - 5PM

Pinn Hall Conference Center,
University of Virginia School of Medicine

Sponsored by the Anderson Symposium Committee, the Department of Biomedical Engineering and the Graduate BME Society at the University of Virginia



UNIVERSITY of VIRGINIA

AGENDA

09.06.24

9:00 - 9:15 am Opening Remarks

Jennifer West, Ph.D., Dean of the School of Engineering and Applied Science and Professor of Biomedical Engineering

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9:15 - 10:15 am Keynote Address

Erika Moore, Ph.D., Assistant Professor, Fischell Department of Bioengineering, University of Maryland, College Park

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10:15 - 10:55 am

Fang-Yi "Ida" Su, Ph.D., Postdoctoral Fellow, Georgia Tech/Emory University

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COFFEE BREAK 10:55 - 11:10 AM

11:10 - 11:50 am

Sarah Libring, Ph.D., Postdoctoral Fellow, Rice University

11:50 - 12:30 pm

Nzinga Mack, Ph.D., Postdoctoral Fellow, Johns Hopkins University

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LUNCH 12:30 - 1:45 PM

1:45 - 2:25 pm

Emma Lessieur Contreras, Ph.D., Postdoctoral Fellow, Univ. of California Irvine

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2:25 - 3:05 pm

Claudia Varela, Ph.D., Postdoctoral Fellow, Boston University

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3:05 - 3:45 PM

Cameron Griffiths, Ph.D., Postdoctoral Fellow, University of Virginia

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COFFEE BREAK 3:45 - 4:00 PM

4:00 - 4:55 PM

Meet the Speakers and Career Panel

4:55 PM Concluding Remarks

Shayn Peirce-Cottler, Ph.D., Professor and Chair of Biomedical Engineering

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HAPPY HOUR IN MR5-6 COURTYARD 5:00 - 6:30 PM

KEYNOTE SPEAKER

Erika Moore, Ph.D.

Assistant Professor, Fischell Department of Bioengineering, University of Maryland, College Park

MACROPHAGE MARVELS: EMBARKING ON NEW PATHS IN TISSUE REGENERATION AND INFLAMMATION

Friday, September 6th

9:15 - 10:15 am

PHCC Auditorium

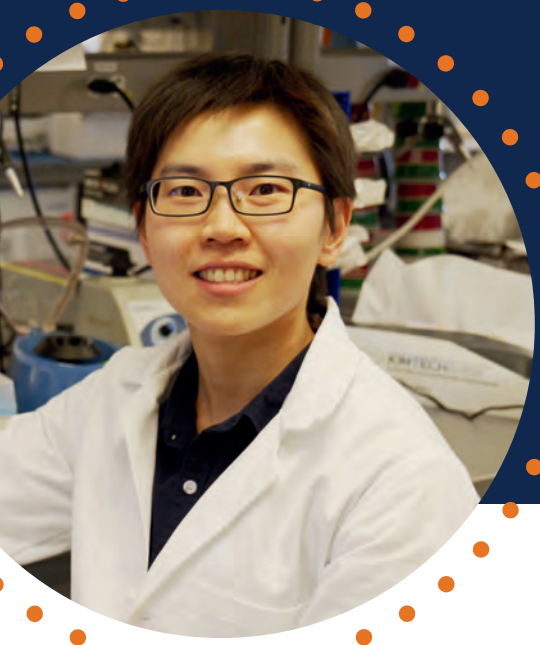
Dr. Erika Moore is an Assistant Professor within the Fischell Department of Bioengineering at the University of Maryland, College Park. Her academic journey began with a Bachelor's degree in Biomedical Engineering from Johns Hopkins University in 2013, followed by a Ph.D. in Biomedical Engineering from Duke University in 2018.

As the Principal Investigator of the Moore lab, Dr. Moore is dedicated to engineering biomaterial models that harness the regenerative potential of macrophage immune cells in tissue repair and regeneration. Her research focuses on health inequities, spanning age-associated macrophage dysfunction, macrophage-endothelial inflammation mediation in lupus, and macrophage integrin ligand interactions within the extracellular matrix, and the role of macrophages in propagating uterine fibroids.

Beyond her scientific endeavors, Dr. Moore is a fervent advocate for professional development and financial literacy, especially for underrepresented minorities in STEM. She co-founded #BlackInBME, a support group for Black trainees and faculty in biomedical engineering. Dr. Moore also established Moore Wealth Inc., a non-profit organization aimed at empowering students with financial literacy skills.

Recognized as a 2020 Forbes 30 Under 30 awardee in Healthcare and a 2024 TED Fellow, Dr. Moore's contributions have also been acknowledged through prestigious grants and awards, including the NIH R35 Maximizing Investigators Research Award, Lupus Research Alliance Career Development Award, BMES Rita Schaffer Award, 3M Non-Tenured Faculty Award, and NSF CAREER Award.

INVITED SPEAKER



Fang-Yi “Ida” Su, Ph.D.

Postdoctoral Fellow, Georgia Tech/Emory University

ENGINEERING ANTIGEN-SPECIFIC T CELLS IN VIVO FOR CANCER IMMUNOTHERAPY

Abstract: T cells are key players in our immune system to mount antigen-specific immune responses and therefore are common targets for immunotherapy. Programming the effector functions of T cells directly in the body have shown promises for adoptive cell therapies (e.g., chimeric antigen receptors T cells, CAR T cells) in both preclinic and clinical settings. However, it remains challenging to selectively modulate the T cell subsets that are relevant to a particular disease setting, while leaving the majority of T cells untouched. The ability to selectively engineer antigen-specific T cells is critical for improving the potency of antigen-specific T cells to kill cancer or infected cells and to eliminate autoreactive T cells in T cell–mediated autoimmune diseases. I have recently developed antigen-presenting nanoparticles (APNs) for mRNA delivery to antigen-specific T cells using peptide major histocompatibility complex (pMHC) molecules and lipid nanoparticles. APNs achieved functional mRNA delivery to antigen-specific T cells across three different T cell receptor transgenic mouse models (P14, OT-1, and Pmel) and a mouse mode model of human influenza infection. Moreover, APNs programmed human flu-specific T cells with anti-human BCMA CAR in vivo and achieved tumor regression in mice bearing human multiple myeloma cancer cells. My data to date demonstrates the antigen-specific mRNA delivery to T cell subsets in vivo and the promise of APNs for immune cell therapy.

Friday, September 6th

10:15 - 10:55 am

PHCC Auditorium

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Biography: Dr. Fang-Yi “Ida” Su is a postdoctoral fellow in the laboratory of Dr. Gabe Kwong at Georgia Tech and Emory School of Medicine. Prior to her postdoctoral training, she received her Ph.D. in bioengineering from the University of Washington with Dr. Patrick Stayton. Her research interests lie at the interface between bioengineering and medicine, using tools from immunoengineering, drug/gene delivery, and genome editing. Dr. Su has published 22 papers in top peer-reviewed journals, including Science Advances and Nature BME, and holds five issued or pending patents. In recognition of her work, Dr. Su has been honored with notable awards including NIH NCI K99/R00 award, a postdoctoral fellowship jointly provided by Georgia Tech and Peking University (China), and the HHMI International Student Research Fellowship. Her career goals are to lead a translational research lab and address unmet clinical needs in cancer, infectious diseases, and autoimmunity.

2024 BME EMERGING LEADERS

Sarah Libring, Ph.D.

Postdoctoral Fellow, Rice University

CANCER-ASSOCIATED FIBROBLASTS IN ALTERING THE EXTRACELLULAR MATRIX AND DEVELOPING A PREMETASTATIC NICHE FOR BREAST CANCER CELLS

Friday, September 6th

11:10 - 11:50 am

PHCC Auditorium

Abstract: Metastatic breast cancer (BC) has a 5-year survival rate of 27%. Recent research has highlighted a complex dynamic between cancer cells and the tumor microenvironment as essential for the formation of macrometastases. Within this field, tissue stiffening through matrix accumulation and altered matrix organization at the primary tumor site were recently linked with sustained proliferation and increased migration of tumor cells. Separately, elevated levels of the glycoprotein, fibronectin, were correlated to poor BC patient survival and were linked to enhanced seeding of disseminated tumor cells at metastatic sites. Through my graduate work, we identified several mechanisms through which accumulated fibronectin impacts the metastatic potential of BC cells. First, we identified a transient increase in extracellular fibronectin in the lungs, which peaked before overt metastasis, coupled with a non-transient increase in total lung volume. To better recapitulate physiological conditions, we then developed a magnetically-actuating device with the ability to apply tensile strain on cells at various amplitudes and frequencies in a multi-well culture plate using suspended fibrillar fibronectin for 3D cell culture that is not reliant on a synthetic substrate. Using this as a biomimetic lung model, we found that cyclic mechanical force acted as a suppressor of cancer cell growth, implicating the accumulation and reorganization of extracellular matrix as an attempt by the cancer cells to alter the mechanical properties of the lung tissue and resist entering dormancy. However, our results showed that BC cells could not organize extracellular fibronectin independently. Instead, BC cells altered the accumulation and architecture of fibronectin by conditioning fibroblasts through soluble factors and extracellular vesicles. We observed that the fibronectin produced by conditioned fibroblasts varied as an effect of both the method of conditioning and the phenotype of the BC cell as the conditioning source.

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Through my postdoctoral work, we are now using a metastatic progression series to study how BC cells of varying metastatic potential transform normal fibroblasts into cancer-associated fibroblasts (CAF) in the premetastatic lung niche and to subsequently characterize the unique CAF subtypes formed. We have also helped identify other cancer cell-CAF interactions that boost metastatic progression. Specifically, breast cancer cells and fibroblasts formed tunneling nanotubes through which CAF mitochondria was unidirectionally transferred, resulting in increased cell migration and total ATP production in the recipient cancer cells. Taken together, these results have increased our knowledge of the relationships between breast cancer cells, fibroblasts, and fibronectin architecture at the primary tumor and in the early metastatic lung niche that may allow for further investigation on targeting disseminated BC cells during early disease intervention to inhibit later overt metastatic outgrowth.

Biography: Sarah Libring is a postdoc in Bioengineering under Cynthia Reinhart-King at Rice University. Her body of research is focused mainly on metastatic triple negative breast cancer. Sarah received a B.S. in Biomedical Engineering from Rutgers University in 2017 and a Ph.D. in the same field under the supervision of Dr. Luis Solorio at Purdue University in 2022. Her graduate work focused on how cancer cells of different phenotypes express and secrete varied levels of fibronectin and other extracellular matrix-related proteins, such as transglutaminase-2, during metastatic progression. Her work then led into the field of cancer-associated fibroblasts (CAF), where she is now investigating the transformation of normal fibroblasts into CAFs in premetastatic niches, as well as studying broader breast cancer cell-CAF dynamics during the metastatic cascade. She started her postdoctoral work at Vanderbilt University and transferred with Dr. Reinhart-King to Rice University in 2024. Sarah has extensive training in tissue engineering, having developed tools to aid in phenotypically-relevant cell culture, and is a part of three patents. She was also able to research abroad through an NSF-funded award in early 2020, using fibronectin-coated scaffolds to grow breast cancer patient pleural effusion samples at the Netherlands Cancer Institute. Her goal is to become a professor at an R1 university to continue to study the interaction of various cells with the stroma and with stroma-producing cells.

INVITED SPEAKER

Nzinga Mack, Ph.D.

Postdoctoral Fellow, Johns Hopkins University

MECHANISTIC COMPUTATIONAL MODELING OF IL-2 IMMUNOCYTOKINES TO ADVANCE IMMUNOTHERAPY

Friday, September 6th

11:50 am - 12:30 pm

PHCC Auditorium

Abstract: Interleukin-2 (IL-2) stimulates the survival, activation, and expansion of T lymphocytes. Due to its critical role in immune function, the IL-2 cytokine has been FDA-approved for the treatment of certain metastatic cancers. However, the off-target effects of IL-2 and its vanishingly short half-life have hampered clinical progress. To circumvent the therapeutic shortcomings of the natural cytokine, our lab tethered IL-2 to anti-IL-2 antibodies to form immunocytokines, which enhance target specificity and significantly prolong the serum persistence of IL-2. To advance therapeutic translation, we are building a computational pharmacological model that mechanistically characterizes the activity of IL-2 and IL-2-based immunocytokines.

Materials and Methods. We built and validated a computational mechanistic model that can simulate the dynamics of both IL-2 and IL-2 immunocytokines. The model incorporates ligand-receptor binding, trafficking dynamics, and signaling in two cell types (effector T cells and regulatory T cells). The model includes 12 molecules, 59 parameters, and 24 rate terms representing different mechanistic processes for the system, which were used to write 15 ordinary differential equations. The model was parameterized using experimental data when available, and physiological estimates when necessary. The level of IL-2 signaling induction (represented in the model as ligand-receptor binding) was used as a predictor of downstream intracellular signaling. The model was validated against experimental measurements of signaling (specifically, phosphorylation of signal transducer and activator of transcription 5 [STAT5]) induced by IL-2 and the IL-2-based immunocytokines

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Results/Discussion/Conclusions. Based on initial model simulations, the relative difference in signal activation between the two T cell types following stimulation by IL-2 could be explained by the differences in receptor expression between those cell types; however, IL-2 signaling in the simulation based on ligand-receptor binding alone required IL-2 doses well above that needed to induce phosphorylation of STAT5 in the comparable experiments. We first hypothesized that binding rate constants might be faster than previously measured, and using parameter optimization, we were able to identify binding parameters that could reproduce the experimental data. However, this method was not parsimonious. Instead, we introduced an intermediate signaling step in the model between the ligand-receptor activation and the signaling readout, using a Hill function to permit amplification of the receptor activation. This transformation allowed for the previously measured binding affinities to reproduce the observed cell-type-specific responses to IL-2 using a consistent set of parameters. We used the same model to characterize how IL-2 differs from IL-2 immunocytokines in their activation of receptors and downstream signaling pathways. We particularly focused on bias of these IL-2-based molecules towards activation of various T cell subsets. We are now translating the mechanistic model to a computational pharmacological model to simulate IL-2 and the IL-2-based immunocytokine as therapeutics in the body, to help accelerate therapeutic regimen development. Further iteration between experimentation and modeling will make the computational mechanistic model more robust and predictive. Better mechanistic understanding of immunocytokines presents a new paradigm for the translation of safe and effective cytokine-based therapeutics, which has the potential to accelerate progress on the treatment of immune diseases.

Biography:
Undergrad: B.S., Biology, Howard University | PhD: Pharmacology, Florida A & M University. At FAMU her research focused on disrupting metabolism in triple negative breast cancer and colon cancers, and she was named a National Rising Graduate Scholar. Nzinga also helped develop and teach GRE and MCAT preparation programs at FAMU that were free to undergraduate students.
Postdoc: Johns Hopkins University ASPIRE scholar; with Drs. Jamie Spangler and Feilim Mac Gabhann. Nzinga's work focuses on building a computational mechanistic model of Interleukin-2 (IL-2), IL-2 immunocytokines and IL-2 receptor activation. Nzinga continues to teach and mentor historically excluded students.
Other: Nzinga is a nature lover who was born and raised in Harlem, NY. Her mission is to attack health disparities by focusing on under-researched disorders, and training upcoming scientists. When Nzinga is not working, she can be found gardening, making jewelry and enjoying nature.

INVITED SPEAKER

Emma Lessieur Contreras, Ph.D.

Postdoctoral Fellow, University of California Irvine

EXTRACELLULAR VESICLES IN DIABETIC RETINOPATHY: THEIR POTENTIAL ROLE IN PATHOGENESIS AND THERAPY

Abstract: Diabetic retinopathy is the most common complication of long-term diabetes, and the leading cause of blindness around the world. Defined for long time as a purely vascular disease of the retina, it is in recent years that an increasing number of studies suggests that neural cells in the retina play a previously unappreciated role in the development of the disease, however the mechanism by which this occurs is not clear.

Extracellular vesicles (EVs) are cell-derived membranous structures harboring a variety of biomolecules. Recently, increased levels of EVs in plasma have been associated with the development of diabetic retinopathy, but from where those plasma EVs originated from, and whether they affect the progression and severity of the disease is yet to be defined.

Biography: Emma was raised in El Mante Tamaulipas, a small town in the rural countryside northeast of Mexico City. She obtained her medical degree from the Universidad Autónoma de Tamaulipas in Mexico and earned her Ph.D. in molecular medicine from the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University in Ohio.

Friday, September 6th

1:45 - 2:25 pm

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Currently, Dr. Lessieur Contreras is an advanced postdoctoral scholar at the University of California Irvine under the supervision of Dr. Timothy Kern. Her current research focuses on the immune system's role in diabetic retinopathy. Dr. Lessieur Contreras research has been continuously supported by different mechanism from the NEI that include a recently awarded K99. She is also an NIH-MOSAIC Fellow.

Emma is committed to leadership, mentorship, and outreach activities to enhance diversity in the biomedical sciences. She is the chair of the Chican@/Latin@ Staff Association mentorship program, which aims to inspire, guide, and support the next generation of UCI undergraduate Latinx students to pursue further training. She is also an active member of the Committee of Women in Vision Research in UCI, seeking to empower women of all backgrounds to achieve full potential in their careers as researchers, clinicians, and leaders.

INVITED SPEAKER

Claudia Varela, Ph.D.

Postdoctoral Fellow, Boston University

IMPLANTABLE DEVICES AND HUMAN-ENGINEERED CULTURE MODELS TO BIOMECHANICALLY PROBE THE INFARCTED HEART

Abstract: After a heart attack or myocardial infarction (MI), the infarcted heart muscle ceases to contract and transitions to be stretched by adjacent, unaffected muscle, impairing cardiac function. If blood flow to the region is not promptly restored, the heart muscle cells die and are replaced by a collagenous scar, exacerbating cardiac function decline and maladaptive remodeling, which can lead to heart failure. Strategies to mitigate this progression involve modifying the biological and/or mechanical environment of the infarcted heart early after MI to improve cardiac function and reduce adverse remodeling. Two notable approaches include: 1) injecting biological agents into the infarct border zone to induce in situ regeneration, and 2) coupling mechanically reinforcing materials to the infarct region to prevent dilation and reduce abnormal biomechanics.

Despite promising preclinical results, the optimal dosing and treatment regimens for these interventions, both early and late in the remodeling process, remain unclear. Additionally, the origin, evolution, and role of the unique biomechanical environment of the infarct border zone in post-MI remodeling, with or without these treatments, is not well understood. To enable systematic and mechanistic studies, tunable device platforms for precise spatiotemporal administration of multiple treatments in vivo and in vitro systems that mimic the biomechanical features of the infarct and border zone regions are required.

Friday, September 6th

2:25 - 3:05 pm

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This talk will describe the development of implantable device platforms suitable for evaluating the preclinical impact of 1) multidose biological agent regimens without necessitating repeated injections, and 2) varying degrees of mechanical reinforcement without confounding biological variables from material chemistry alterations typically required for mechanical tunability. Additionally, I will discuss preliminary efforts in developing an in vitro model that recapitulates the biomechanical environment of the infarct border zone. These technologies enable iterative and systematic explorations that elucidate the impact of distinct biomechanical interventions and the infarct border zone on adverse remodeling. These implantable devices and culture models also hold significant promise for identifying and optimizing therapeutic strategies, accelerating their advancement towards clinical impact.

Biography: Dr. Claudia Elena Varela is a scientist, professional dancer, and STEM diversity advocate from Reynosa, Mexico. She graduated Cum Laude from UC San Diego with a Bioengineering B.S. and a Dance B.A., conducting research with Dr. Francisco Villarreal. She earned her Ph.D. in Medical Engineering and Medical Physics at the Harvard-MIT Program in Health Sciences and Technology under Dr. Ellen Roche's mentorship with support from the NSF's GRFP and Ford Foundation Predoctoral fellowship. Currently, Dr. Varela is pursuing her postdoctoral training with Dr. Christopher Chen at Boston University, supported by a Ford Foundation Postdoctoral Fellowship.

INVITED SPEAKER

Cameron Griffiths, Ph.D.

Postdoctoral Fellow, University of Virginia

UNDERSTANDING HOST RESPONSES TO VIRAL INFECTION USING SYSTEMS BIOLOGY

Abstract: Viral infections cause a wide array of illnesses, which largely depend on the type of infecting virus. However, there is substantial heterogeneity in host responses to even a single viral species. A deep understanding of the different ways humans respond to a viral infection is critical to stratifying those at risk for severe infection and designing treatments.

Multiple viruses can infect the human heart and infection causes a range of outcomes from asymptomatic disease to heart failure. Using unmapped RNA-sequencing reads, we identified undiagnosed viral infections in 189 of the 979 publicly available human heart samples examined. The virus-positive samples showed one of three gene expression profiles, which were not determined by the species of the infecting virus. One profile was associated with heart failure, while another showed signs of resolved infection. In parallel, we engineered chronic infection of coxsackievirus B3 (cardio-pathogenic virus) in twelve clonal cardiac cell lines, which each displayed a gene expression profile matching one of the human-derived profiles. Activating/inhibiting underlying cell signaling pathways in the clones highlighted connections between the profiles and suggested that the profiles can switch when perturbed. This work provides a framework for interpreting viral heart infections and may lead to interventions that halt the progression to heart failure.

Friday, September 6th

3:05 - 3:45 pm

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Department of Biomedical Engineering

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Rhinovirus (RV) infections are associated with recurrent wheeze in preschool children and predict the development of asthma. Moreover, RV infection is the most important trigger of asthma exacerbations in school children and young adults. We examined asymptomatic RV infections in children undergoing bronchoscopies that are clinically indicated for recurrent wheeze. RV-positive children showed upregulation of inflammatory gene pathways, genes associated with asthma, and markers for secretory nasal cells. Since longitudinal RV inoculation experiments are not feasible in children, adults with and without asthma were experimentally infected with RV and nasal samples were collected. Asthmatic donors had dampened RV replication and accompanying inflammatory response compared to non-asthmatics. Comparing adults and children, the RV-positive children had gene expression signatures similar to the non-asthmatic adults. Although the children have recurrent wheeze, their similarity to non-asthmatic adults in response to RV may reflect having not yet undergone the airway remodeling seen in adult asthmatics.

Biography: As a first-generation student, I obtained my BSc in Honors Immunology and Infection at the University of Alberta, in Canada. I then pursued a PhD in Virology in the lab of Dr. David Marchant studying respiratory syncytial virus cell entry, at the University of Alberta. In 2020, I moved to the USA and started my postdoctoral work in Kevin Janes' lab, at the University of Virginia. My postdoctoral work focuses on using systems approaches to study viral heart infections. In addition, I have been collaborating with Drs. Gerald Teague and Larry Borish to study rhinovirus infections in young children with wheeze. In the future, I plan to lead a lab of my own, studying why some people get sick and others don't when exposed to respiratory viruses.

IN THE NEWS

Emerging Leaders in Biomedical Engineering at the University of Virginia

Teaching the Immune System How to Regenerate Tissue

Assistant professor of biomedical engineering Daniel Abebayehu is tackling fibrosis by identifying the different types of fibroblasts and determining how they work with immune cells after damage from disease or injury. The NIH is backing Abebayehu's research with a MOSAIC Pathway to Independence Award (K99/R00).

Innovating Pediatric Brain Tumor Treatment

High-risk brain tumors in children often don't respond well to existing treatments, but assistant professor of biomedical engineering Natasha Sheybani and her collaborators at Children's National Hospital hope a fusion of therapies will offer a better option. The research is funded by a $600,000 Idea Award, administered by the U.S. Department of Defense.

Using "Theranostics" To Treat Cancer

New assistant professor of biomedical engineering Kelsey Kubelick brings an interest in theranostics, a research discipline that blends diagnostics with therapies. She has explored the subject in her use of ultrasound, photoacoustic and magnetic resonance imaging to guide and improve design of new therapies.

Finding Answers for Patients and Families Affected by Neurodevelopmental Disorders

New assistant professor of cell biology and biomedical engineering Sameer Bajikar will focus on developing new human neuronal modeling systems to study dosage-sensitive "Goldilocks" genes like MECP2. He will use the models to look for common molecular and biological pathways disrupted across multiple neurodevelopmental disorders.

Blood Cancer Discovery Identifies High-Risk Patients, Could Improve Outcomes

During his postdoc, Bishal Paudel and his team developed a new way to identify patients with acute myeloid leukemia. They found that they could measure specific "bioactive molecules" in cancer cells – molecules that result from microbial activity – and identify patients at risk of poor outcomes. Paudel is now an assistant professor of research in the School of Medicine.

More Information

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