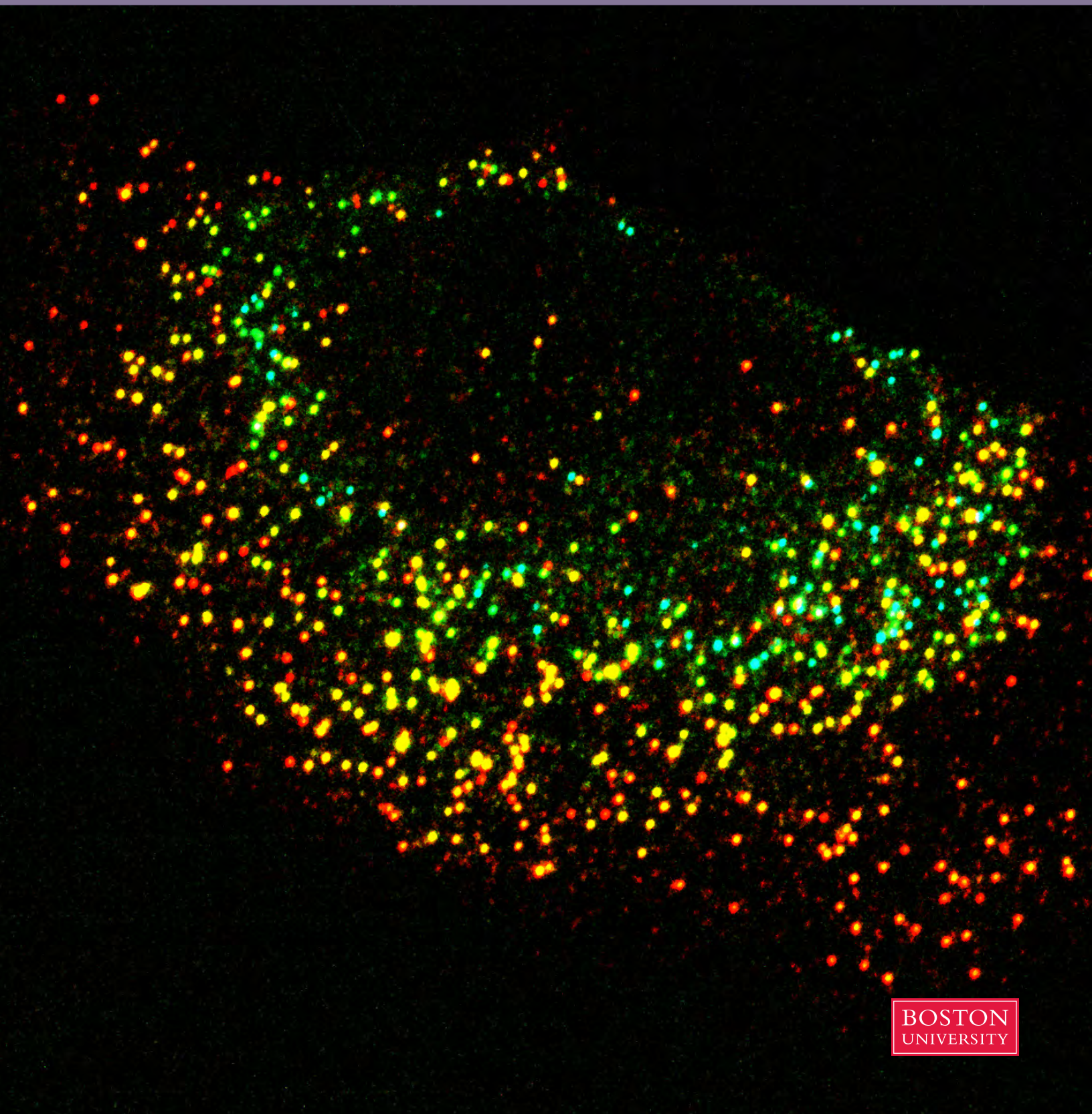
BOSTON UNIVERSITY
BIOLOGICAL DESIGN CENTER

Impact Report | 2025



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Front cover photo: *This image of RNA molecules, color-coded by depth, was obtained through confocal microscopy of fluorescent signal from a protein that was engineered at Boston University to only produce signal when bound to a target RNA. This engineered function reduces background signal, enabling clear display of single RNA molecules. The image was provided by Chris Kuffner, a graduate student working in the lab of Professor John Ngo.*

Spotlights

Professor John Ngo addresses colleagues in the Howard Eichenbaum Colloquium Room.

EXECUTIVE SUMMARY

THE BIOLOGICAL DESIGN CENTER (BDC) brings expertise from multiple disciplines across Boston University – including engineering, biology, physics, and chemistry – to build a vibrant community that conducts ground-breaking research in biological design and sets the standards for education and training in synthetic biology.

Biology has long been a field based on observation, dissection, and classification of the natural world. However, it is now becoming more predictive, easier to design, and broader in scope. To understand the processes that define life and reveal the basic principles behind biological systems, we must learn how different parts come together to form complex structures with a wide range of functions.

By using forward-engineering technologies, like cellular engineering, 3D printing, and synthetic biology to build biological devices and systems from simple components (molecules, cells, extracellular materials, etc.), researchers at the BDC elucidate the design principles important for achieving biological function, thereby complementing and augmenting traditional deconstructionist approaches. Our researchers foster unconventional mixing and matching of disparate research areas to create disruptive ideas and biomedical technologies, drawing scientists from industry and academia alike to tinker, invent, and discover under the center's auspices.

The major goals and associated accomplishments of the BDC are to:

Foster a culture of scientific excellence and deep collaboration between BDC labs. In the past five years, the BDC has been awarded more than $103M in external funding. These awards were for research grants, education and training grants, and predoctoral and postdoctoral fellowships. Our researchers have published more than 80 peer-reviewed articles in the past two years in venues including *Nature, Science, Cell, PNAS, Cell Systems, Nature Methods, Nature Biotechnology, Nature Cell Biology, Molecular Cell, Cell Stem Cell, Cell Systems*, and *Science Advances*. In addition, our faculty members have received numerous awards, including election to the National Academy of Medicine; the Vannevar Bush Faculty Fellowship;the Schmidt Science Polymath Award; the NIH Director's Transformative Research Award; the Presidential Early Career Award for Scientists and Engineers; the NSF CAREER Award; AIMBE Fellowships; an AAAS Fellowship; a Beckman Young Investigator Award; and many others (see page 32).

Expand and mature training programs supporting the BDC mission. We continue to enhance the SB2 Training Program, the Kilachand Multicellular Design Program, and the NSF National Research Training program on Biological Control. We have used the new training paradigms supported in these programs to attract world-class graduate students and postdoctoral fellows, particularly those who work at the intersection of multiple disciplines and who foster collaborations across BDC faculty (see page 22).

Nurture a vibrant community through the development of seminars, courses, and outreach programs for our researchers, industry partners, and other academic colleagues. The BDC has expanded the scope of its seminar series, offering professional development and networking opportunities for trainees while continuing to bridge the gap between academia and industry. We invite the broader BU community (i.e., non-BDC trainees in other departments and colleges) to participate in most of our professional events and all of our internal and external seminars (see page 34).

Elevate BDC science in the local and national scientific community. We have worked diligently toward our goal of growing our network and placing the BDC firmly on the map of leading centers for biological design and biotechnological advancement. To this end, we have undertaken extensive STEM Outreach and Education activities through our STEM Pathways program (see page 28), and our iGEM team returned to Paris to present AgriNOVA, a device that can detect toxic metals in soil, to the judges of the iGEM Grand Jamboree (see page 30). We have also offered BDC Travel Grants for our trainees, so they can share their accomplishments with the broader scientific community; $7,500 was distributed to eight graduate students and postdoctoral fellows this past year.

PhD student Jillian Ness, working in the lab of Professor Zeba Wunderlich, examines fruit fly specimens through a stereoscope.

PhD student Jillian Ness, working in the lab of Professor Zeba Wunderlich, sorts fruit fly specimens.

RESEARCH SPOTLIGHTS

These Plants Aren't for Decoration—They're for Science

BU researchers are testing new genetic engineering techniques to better understand how plants adapt to their environments

SOMETHING UNEXPECTED is hiding behind a tightly sealed door on an upper floor of the ultramodern Boston University Rajen Kilachand Center for Integrated Life Sciences & Engineering: an indoor greenhouse. In a building full of bright white hallways, sparkling floors, and sleek glass office doors, the smell of rain and soil that washes over you when the door opens is a delightfully earthy surprise.

Filled with rows of plants in various stages of their life cycle—from seedlings, to blooming, to producing the next generation—the room is a new addition to the lab of Ahmad "Mo" Khalil, a BU College of Engineering professor of biomedical engineering. Despite feeling like a garden, it's become a place for researchers to study nature's complexity, as they investigate the fundamental genetic makeup of plants and test new genome editing techniques.

"As a lab interested in how genes are expressed in cells, and developing advanced synthetic tools to control that process, it was clear to me that plants would be a really fun and important new frontier for us," Khalil says. That's because plants, with no way to move themselves from one place to another, are very good at adapting to their environments. This has sparked interest in understanding their epigenetics—which is how the outside environment influences what genes are turned on or off during development and throughout life.

"Plants are masters of gene regulation and epigenetics. Because of their unique life cycle, they have evolved and use many different mechanisms to respond to their environment and remember cues," Khalil says. "Our aim is to develop and use synthetic biology and genomics tools to dissect these processes and, in turn, manipulate them to ultimately accelerate and advance crop development."

Ahmad "Mo" Khalil, a BU College of Engineering professor of biomedical engineering, introduced plants to his synthetic biology lab—the first multicellular organisms they're working with.

Khalil is an expert in hacking cells, learning how they work from the inside out to recreate biological processes—like programming immune cells to eliminate cancerous tumors. This is a field known as synthetic biology and Khalil believes it holds boundless potential, from curing diseases to engineering new plants that can withstand climate change. Typically, he and his team use individual cells—like yeast and bacteria—to study and learn how to reengineer them. This is the first time his team has introduced multicellular organisms to their repertoire, and they've already started tinkering with new techniques to manipulate plant genomes and program new behaviors.

One species in the new plant lab is *Nicotiana benthamiana*, a relative of tobacco. The other is *Arabidopsis thaliana*, commonly called thale cress, which is in the mustard

family (and easily spotted outside, sprouting between sidewalk cracks and patches of lawn). It's noticeable that some *Arabidopsis* in the lab have white flowers and some red; that difference is the direct result of gene editing being studied by Will Shaw, a postdoctoral fellow leading the project and the main caretaker of the plants.

"We are coming up with a totally new approach to study gene regulation in plants," Shaw says. He is experimenting with what he's calling a "DNA landing pad." He swaps out a fragment of the plant's DNA for a new, synthetic sequence—the landing pad—that makes it easier to later make precise changes to the genome.

> "Plants are masters of gene regulation and epigenetics. Because of their unique life cycle, they have evolved and use many different mechanisms to respond to their environment and remember cues,"
>
> - Mo Khalil

"The landing pad contains a few new genes," Shaw says. One is called RUBY and makes the flowers turn red, giving a visual indication of the plants containing the DNA landing pad. "Once we've substituted in the landing pad, it is now primed for putting in new sequences," such as one that can strengthen a plant's ability to withstand drought or extreme heat in the future.

Anjali Gajendiran (ENG'28) (from left), Khalil, Will Shaw, and Liz Tchantouridze (ENG'28) are eager to continue unlocking the mysteries of the plant genome.

"This is something that's been very difficult to do historically," Shaw says. It may seem surprising, since genetically modified plants—corn, soybeans, and potatoes being some of the most common—can be found in just about every grocery store. But precisely reengineering plants using current technologies is very challenging.

One standard technique, for example, involves sending genes into plants using a bacteria, called *Agrobacterium*, that drops a new gene—perhaps to make a plant pest resistant—at a random location in the genome. This isn't ideal, Shaw says, because "this randomness leads to a lot of variability and changes the sequence surrounding the gene, which we know plays an important role in regulation."

Their new approach using the landing pad is an attempt to get around those challenges, and learn the fundamentals of how plants adapt to their environments.

Even though science is the priority, the plants still need their basic needs tended to: bright light, well-draining soil, the right level of humidity, and regular watering. Shaw took time to learn everything he needed to know about plant biology from Massachusetts Institute of Technology biologist Mary Gehring, who coadvises him along with Khalil. The plant lab is still in its early stages, but Shaw has been joined by two graduate students, Liz Tchantouridze (ENG'28) and Anjali Gajendiran (ENG'28), to expand its scope.

"To address the challenges of climate change, it's essential to have a deep understanding of how these genetic processes work to the point where we can predictably engineer new behaviors, such as improved adaptation to rising temperatures. This knowledge is crucial for advancing crop development and ensuring food security for a growing global population," Shaw says.

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This excerpted article, authored by Jessica Colarossi originally appeared in *The Brink* on October 17, 2024.

To read the full article visit: https://tinyurl.com/5bf7smjm

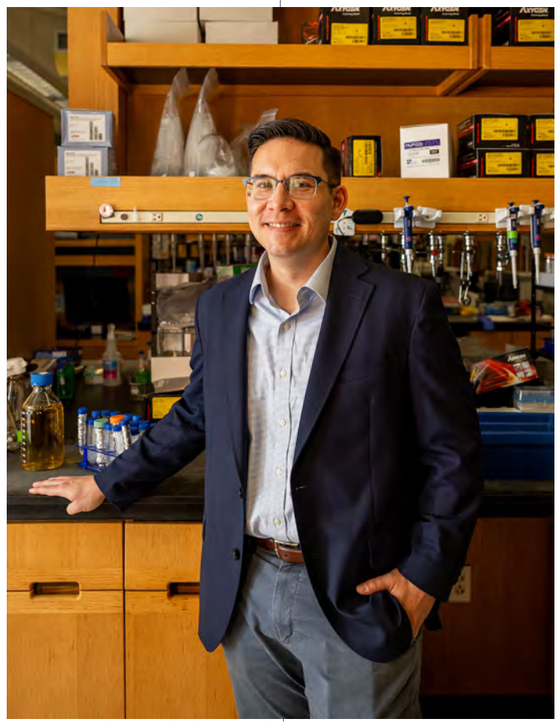
BU Biomedical Engineer Wins a 2024 National Institutes of Health Director's Transformative Research Award

Honor for Alexander A. Green will support high-risk project that could lead to improved cancer treatments and other therapies

BEFORE A NEW CAR ROLLS ONTO THE ROAD, engineers measure how it reacts to different forces, from passengers plonking into the seats to jarring collisions. Understanding the impact of these forces provides essential insights into the durability and effectiveness of the vehicle and its components—an approach taken for just about every new product, from cell phones to simple bottle flip tops.

Now, Boston University engineer Alexander A. Green wants to do the same kind of force measurement for biological cells, with the goal of one day improving cancer therapies.

He hopes that by tracking the forces involved when cells interact with one another, like in cell-based cancer therapies, he can better control their behavior and pave the way for more potent disease treatments. It's an out-there, novel idea—and it could fizzle or it could change lives. But Green's chances of success have just been given a major boost.



Alexander A. Green, a BU College of Engineering associate professor of biomedical engineering, says the NIH award will enable research that is "pushing the frontiers."

A BU College of Engineering associate professor of biomedical engineering, Green has been named a 2024 National Institutes of Health Director's Transformative Research Award winner. Founded in 2009, the award is supported by the NIH Common Fund's High-Risk, High-Reward Research program and is given to researchers "proposing transformative projects that are inherently risky and untested but have the potential to create or overturn fundamental paradigms and may require very large budgets."

Green is sharing the award's $7.2 million funding with two researchers from Yale University, Julien Berro and Xiaolei Su, and he says their proposed cell forces project would typically be a tough one to win backing for—all promise with, so far, little proof that it'll work.

"It's a really important funding mechanism," Green says of the award. "This kind of blue-sky research is super important—we're pushing the frontiers."

Green is just the third BU researcher to be given the honor, behind Bela Suki, an ENG professor of biomedical engineering, and Steve Ramirez (CAS'10), a College of Arts & Sciences associate professor of psychological and brain sciences.

"This NIH award is a terrific acknowledgement of Alex's thought leadership in engineering biology," says Elise Morgan, ENG dean ad interim and Maysarah K. Sukkar Professor of Engineering Design and Innovation. "His work in synthetic biology and synthetic mechanobiology has the potential to produce groundbreaking advances in the treatment of cancer. Alex's efforts represent the best of what engineers can do to serve society, especially when working in conjunction with experts in diverse disciplines."

Green is the team's ribonucleic acid (RNA) expert, bringing his knowledge of the molecules that help regulate cells and translate genetic instructions. He aims to make RNA-based sensors that monitor whether a force-detecting protein—designed by Yale's Berro—is firing.

"The other aspect of the project is to not only detect forces, but to have the cell carry out some kind of response," says

Green, who's also a member of the BU Biological Design Center. "So, we're acting on that information to control cell behavior."

In CAR T-Cell cancer therapy, for example, a patient's immune cells, although reengineered to fight the disease, will often run out of steam: the forces involved in the struggle exhaust them, says Green. But, by influencing the cell's behavior, they could push back its point of burnout and prolong the therapy's effectivenes.

> "Alex's efforts represent the best of what engineers can do to serve society, especially when working in conjunction with experts in diverse disciplines."
>
> **- Elise Morgan**

That innovative approach to improving healthcare technologies and therapies fits with Green's broader research. He studies what's happening in the depths of cells to build organic sensors, known as biomolecular control systems; create antimicrobial coatings; and make better and cheaper diagnostic tests for viruses and diseases—and even to predict the potential performance of athletes and soldiers.

"A lot of the stuff we're working on is tool development," says Green. "I'm an engineer—I like tinkering with things and solving problems."

The cell forces team initially connected through the Research Corporation for Science Advancement's Scialog program, which also backed them with seed funding, allowing them to lay a foundation for the project and generate some preliminary data. Green says the graduate students in his lab—particularly McKayla Vlasity (ENG'26)—played an important role in those initial steps and will continue to be involved as the project progresses.

"They helped build up some of the data we needed for this project and they work so hard in the lab all the time," says Green, who hopes his win inspires his students to "seek out interesting areas of research and find out where the gaps are." Even if, perhaps, that occasionally means ignoring the advice of established researchers like him.

"A lot of times in research you have to not listen to people—you have to go your own way," he says. "Eventually, that's the only way you'll do anything really new. You've got to do things that other people didn't think would work; those are ultimately going to be the most impactful contributions."

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This excerpted article, authored by Andrew Thurston originally appeared in *The Brink* on October 8, 2024.

To read the full article visit: https://tinyurl.com/4m9tezrn

Alexander A. Green (second from right) stands in the lobby of the Kilachand Center with his lab members. Photo courtesy of Green Laboratory

A New Type of RNA Could Revolutionize Vaccines and Cancer Treatments

An accidental discovery turned into an unexpected success when a team of interdisciplinary BU researchers created a new and improved COVID vaccine and improved COVID vaccine

IT ALL STARTED IN THE LAB. Two Boston University doctoral students, Joshua McGee (ENG'26) and Jack Kirsch (ENG'23), were creating and testing different types of RNA—strands of ribonucleic acid, built from chains of chemical compounds called nucleotides, that help carry out genetic instructions in cells. They were determined to see if RNA sequences crafted with small changes to their nucleotides can still work. After running dozens of experiments, they hit a dead end.

"At first, it was a failure," McGee says.

Decades of research have uncovered the mysteries of RNA in living cells. Without it, our cells couldn't perform fundamental tasks, like constructing other cells, carrying amino acids from one part of the cell to the other, or mounting immune responses to viruses.

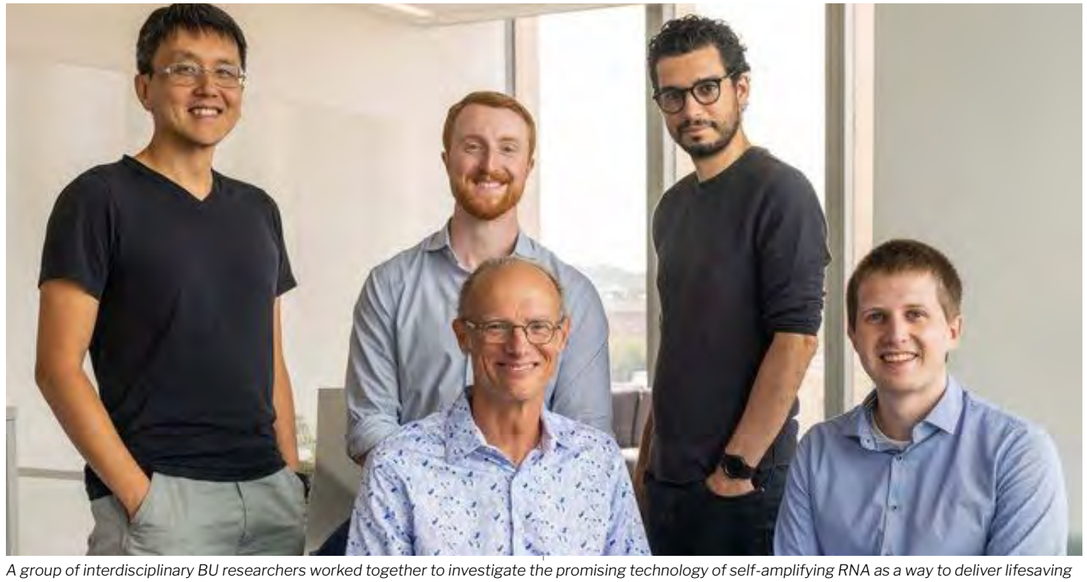
But, more recently, scientists have figured out how to harness RNA to make treatments aimed at fighting genetic diseases and cancer. They've also learned how to use messenger RNA (mRNA) to make COVID-19 vaccines. The experiments that McGee and Kirsch perform are aimed at using RNA to deliver lifesaving drugs and create more effective vaccines than we have today.

Working alongside Mark Grinstaff, BU's William Fairfield Warren Distinguished Professor of biomedical engineering and chemistry, and Wilson Wong, a College of Engineering associate professor of biomedical engineering, they started talking about what to do next—and what to do with the chemical components left over from the initial experiments. They decided to focus on modifying the chemical structure of a lesser-known type of RNA, called self-amplifying RNA (saRNA), which is manufactured in the lab and replicates itself multiple times in a cell to produce a higher number of the proteins it's programmed to make.

The new method worked: their modified saRNA was replicating itself in a petri dish.

"Our reaction to that was a lot of excitement, but also the normal scientist thinking, 'Did we do this right?'" McGee says. "We went back to do it again and again. And we got the same results."

The results kicked off a yearlong research project that moved from Grinstaff's chemistry lab to Wong's genetics engineering lab to BU's National Emerging Infectious Diseases Laboratories (NEIDL), where they tested their modified saRNA as a vaccine against the COVID-19 virus. They found that a lower dose of their new vaccine in mice



A group of interdisciplinary BU researchers worked together to investigate the promising technology of self-amplifying RNA as a way to deliver lifesaving drugs and create more effective vaccines. Clockwise, from back left: Wilson Wong, Jack Kirsch, Florian Douam, Joshua McGee, and Mark Grinstaff.

protected them from the disease just as well as current mRNA vaccines. Their findings are published in *Nature Biotechnology*.

It'll be years of further testing before this vaccine can be approved for humans. Even though there is one type of saRNA vaccine—approved last year for use in Japan—the researchers hope their modified version will make the technology more appealing to drug manufacturers, as well as overcome the challenges of using saRNA as a vaccine. "The challenge with regular self-amplifying RNA is that there are two competing processes—the RNA is trying to make more and more protein, and at the same time the immune system is degrading it," says Grinstaff. Standard mRNA COVID vaccines tell cells to produce a spike protein that mimics the real virus. That, in turn, causes the immune system to kick in and fight the virus. But an saRNA vaccine goes one step further by repeating those instructions to the cell over and over, making more of the machinery to create the spike proteins. More proteins means you don't need as high a dose and the immune system remembers how to fight the virus over a longer period of time.

"So the idea is that this could give you a long duration of protein expression, even when using a lower dose," Grinstaff says.

Another challenge is that saRNA could create a much-too-strong reaction that can lead to uncomfortable side effects—worse than those of current COVID vaccines, which typically cause some people to develop a mild fever or aches.

Grinstaff, Wong, and the team collaborated closely with Florian Douam, a BU Chobanian & Avedisian School of Medicine assistant professor of virology, immunology, and microbiology and a core faculty member at NEIDL. He and his team performed a study—called a "viral challenge"—to evaluate if a COVID-19 vaccine built with the modified saRNA technology could protect mice more effectively against severe COVID-19 disease than earlier saRNA and mRNA vaccines.

"The viral challenge aspect was particularly important," Douam says. "It exposed how a very low dose of this novel saRNA technology is able to protect mice against lethal disease much more effectively than traditional saRNA and mRNA COVID-19 vaccines at a similar dose." Douam says that the new vaccine, which incorporates modified nucleotides called m5C (5-methylcytidine), also triggered very low levels of inflammation upon vaccination comparable to mRNA vaccines.

"There is still plenty of work to be done to unveil all of the advantages of this technology over other existing RNA vaccine approaches," Douam says. But this was a promising start.

The next question is whether their modified saRNA can provide longer-lasting protection against virus infection compared to existing RNA-based vaccines at a similar dosage.

More Promising Treatments

Besides COVID vaccines, the team's well-tolerated saRNA could open the door for other types of treatments and gene therapy.

"At the end of the day, this is a protein-producing system," Wong says. "A gene-delivery system."

For a genetic disorder, saRNA could be programmed to produce a missing gene or replace a defective one, Wong says. For treating lung, breast, and other cancers, "we can have it produce an anticancer drug for disease that requires a high dose and a lot of protein being made."

"That's why we're really excited about our self-amplifying RNA technology—because we think we can lower the dose that's needed to enable some of these therapeutic applications," Wong says. "That's how we envision it."

> "That's why we're really excited about our self-amplifying RNA technology—because we think we can lower the dose that's needed to enable some of these therapeutic applications. That's how we envision it.
>
> – Wilson Wong

Grinstaff recently received an inaugural Trailblazer Engineering Impact Award from the National Science Foundation, which comes with a $3 million grant, to continue exploring saRNA technology—something that can "fundamentally alter the genetic engineering paradigm," according to the NSF.

"There's so much work that we're doing now to further understand what we have discovered," says McGee, who is coadvised by Wong and Grinstaff. "There are a lot of publications out there that suggested research on saRNA would also fail. This made me realize that it's okay to try things that other people think might fail, because, who knows, they could be wrong."

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This article, authored by Jessica Colarossi, originally appeared in *The Brink* on September 9, 2024.

To read the original article visit: https://tinyurl.com/3jary55h

ECE CHIPs In

Miniscule Hardware, Maximum Impact

IN A FEW SHORT YEARS, Professor Rabia Yazicigil has made a name for herself in microelectronics research as a collaborative, flexible innovator motivated to cross disciplinary lines in pursuit of cutting-edge technical advances with broad applications to the betterment of society. In many ways, she is the very image of the kind of scientist and engineer called for by the CHIPS Act: productive, inventive, application-focused, collaborative- and service-minded, and an active mentor cultivating similar values and capabilities in a younger generation of innovators.

Professor Yazicigil specializes in low-power, custom micro-scale integrated circuit design, purpose-built for a growing variety of applications from communications to synthetic biology. She has been instrumental in bringing the revolutionary, code-agnostic decoder algorithm GRAND–often termed "the universal decoder"–to hardware realization, working closely with local and overseas collaborators to develop a series of custom chips utilizing and improving GRAND's method of "intelligent noise guessing" to streamline, speed up, and secure future wireless communications.

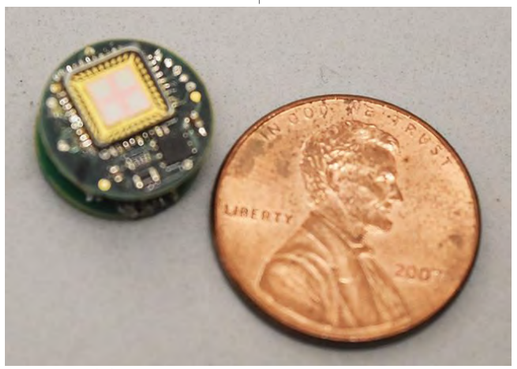
Rabia Yazicigil, an assistant professor at BU's College of Engineering, is driving innovative research that pushes boundaries in microelectronics and interdisciplinary applications.

Expanding the focus on efficient wireless communications beyond the looming concern of capacity crunch, Professor Yazicigil has been particularly noted for her increasing body of collaborative work in interdisciplinary, biomedical-centric projects. Her miniscule, resource-light designs are ideal for medical applications, as exemplified by her ongoing collaboration with researchers from MIT on the development of a tiny ingestible capsule or "smart pill" for monitoring the human gastrointestinal tract in real time. Their prototypical device, which uses her customized, energy-efficient sensor readout circuit, could have a positive impact on the lives of millions of patients suffering from gut ailments around the world.

Professor Yazicigil's evident facility with forming productive, interdisciplinary collaborative relationships is not limited to colleagues at other institutions, of course. She has partnered several times with members of BU's Biomedical Engineering department and with fellow BU ECE Professor Douglas Densmore on projects such as an ambitious effort to advance biomanufacturing, enabling the conversion of food waste and manure into useful products which are currently derived from fossil fuels. Adapting her highly miniaturized, low-power sensor technology for integrated use in bioreactors is a key component of the BioMADE consortium's approach. The duo have also recently been awarded a $315K grant from the Semiconductor Research Corporation (SRC) to develop hybrid microfluidic-CMOS biosensors specifically to monitor wastewater for harmful byproducts of the semiconductor industry itself.

The community-oriented approach Professor Yazicigil brings to her work encompasses her students as well as her peers. Since she joined BU ECE in 2018, student researchers in her WISE-Circuits Lab have taken an active and vital role in her projects, often first-authoring key journal and conference articles and performing initial demonstrations of key advances. Some of her Ph.D. advisees have won awards as a result, such as Arslan Riaz's Best Demo Award and Best Research Demo Award at COMSNETS 2023 and 2022, respectively, for custom GRAND algorithm chip demonstrations, and Qijun (Mandy) Liu's 2023 IEEE Solid-State Circuits Society Predoctoral Achievement Award.

Liu, who is poised to become the lab's first graduate after defending her dissertation in December, has recently been selected for an IEEE ISSCC 2023 Student Research Preview Best Poster Award, to be presented at ISSCC 2024 in February.



A device prototype.

With all this vital research already in progress, Processor Yazicigil shows no signs of slowing down, serving as Boston University's institutional lead in the Northeast Microelectronics Coalition (NEMC) Hub's 5G/6G project under the co-leadership of longtime collaborator and GRAND algorithm co-creator Professor Muriel Médard of MIT and other top-tier researchers. The NEMC is one of eight Microelectronics Commons Regional Innovation Hubs established by the DoD with a $238M CHIPS Act award, its largest to date, and with $2B in anticipated funding over the next four fiscal years. Professor Yazicigil's group is interested in continuing to push the boundaries with the GRAND family of algorithms, as realized in innovative chip designs that can improve on all key metrics. Professor Yazicigil has also received a recent $270K award from the SRC and the Texas Analog Center of Excellence (TxACE) to work on physical-layer security measures for wireless communications.

In addition to her outstanding research and mentorship, Professor Rabia Yazicigil has a stellar track record when it comes to serving her scholarly community; an IEEE Senior Member, she was elected to the IEEE Solid-State Circuits Society AdCom as a 2024 Member-at-Large, in addition to serving as its representative on the IEEE Council on RFID (CRFID) since 2022. She is the recipient of the 2021 BU ECE Outstanding Faculty Service Award, and has recently contributed to the "Hardware-Limited Task-Based Quantization in Systems" chapter in Women in Telecommunications, part of Springer Nature's Women in Engineering and Science book series, in addition to invited talks and event organization at conferences such as ISSCC 2023.

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This article, authored by A.J. Kleber, originally appeared on BU College of Engineering's website on January 18, 2024.

To read the original article visit: https://tinyurl.com/2fes8skj

The Biological Design Center occupies several floors of the Rajen Kilachand Center for Integrated Life Sciences and Engineering, located on the Charles River Campus at Boston University.

This microscopic image of bacteria undergoing changes in membrane potential was captured by PhD student Maya Kostman who works in the lab of Professor Joseph Larkin.

This image of a single dermal fibroblast cell stained for nuclei (blue) and actin cytoskeleton (red) was captured by PhD student Emily Davis in the lab of Professor Christopher Chen.

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Outside the BDC staff offices

PhD student Chris Kuffner pipetting in the lab of John Ngo.

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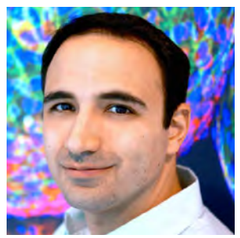

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Professor Ahmad "Mo" Khalil gives Boston University President Melissa Gilliam a tour of the BDC labs.

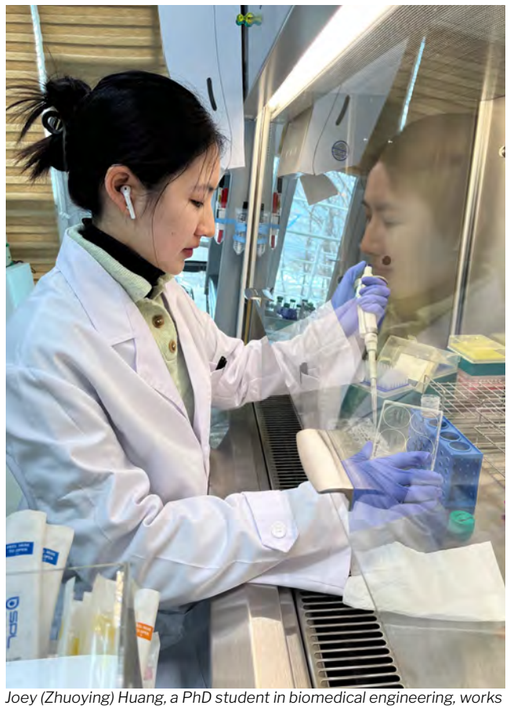
TRAINING SPOTLIGHT

SB2 Provides Trainees with Supportive Community and Industry Exposure

A chat with PhD student Joey Huang

Joey Huang, a Fourth-Year PhD Student in a flagship training program at the Biological Design Center (BDC) is the NIH T32 PhD Training Program on Synthetic Biology and Biotechnology, a.k.a. the "SB2 Training Program." The goals of this program are to provide a unique, field-defining, and interdisciplinary training environment in synthetic biology; broaden participation of underrepresented groups; develop new training opportunities that emphasize professional skills; and increase exposure to the biotech industry.

Joey (Zhuoying) Huang, a fourth-year PhD student in biomedical engineering who works in the lab of Professor Wilson Wong, discussed her personal experience in the SB2 Training Program, including her internship with a Boston-area biotech company.



Joey (Zhuoying) Huang, a PhD student in biomedical engineering, works in the lab of BDC researcher Professor Wilson Wong and participated in BDC's SB2 Training Program. Image provided by Joey Huang.

For background, can you first describe your research in the Wong Lab?

When I first joined the Wong Lab, I worked on an existing project developing chimeric antigen receptor (CAR) T cell therapy for autoimmune diseases. Eventually, I proposed a new study on "T-cell exhaustion," a phenomenon we're increasingly observing in solid tumor treatments using CAR T therapy. CAR T therapy works by engineering T cells with receptors designed to target specific markers on disease-causing cells. When these receptors latch onto a target, they activate the T cell to destroy the target cell.

Over time, however, the CAR T cells lose their effector function, exhibiting reduced proliferation, impaired cytotoxicity, and sustained expression of inhibitory receptors. In the "exhausted" state, even when CARs bind to their target antigen, the downstream signaling fails to elicit an effective immune response, resulting in suboptimal tumor clearance. Our research will help us better understand this phenomenon and how to mitigate it in order to improve CAR T-cell therapies.

What is the SB2 training program?

The SB2 program is a grant initiative designed for synthetic biology, but it's more than just funding—it's a comprehensive training and networking platform that helps participants understand the broader synthetic biology landscape and explore diverse career opportunities.

One key function of the program is that it creates a supportive community of synthetic biologists, and mentorship is an important component of that support. Each trainee has two faculty mentors. The primary mentor (in my case Wilson Wong) is the trainee's traditional Ph.D. supervisor, and the secondary mentor (in my case John Ngo) supports the trainee by acting as an additional advisor – for example, they might help the trainee with research questions, but they may also offer professional advice or connect trainees with contacts in their professional network. BDC Executive Director Joshua Finkelstein also provides mentorship to all trainees and is intimately involved in their search for the program's required industry internship.

Another key program feature is the exposure it provides. There are monthly seminars featuring industry experts from various sectors, including public policy, biotech start-ups, big pharma, and venture capital, etc. These sessions broaden our understanding of synthetic biology in the real world. Personally, I found this invaluable, as it expanded my perspective on career possibilities. Before the program, I assumed a scientist's role was limited to R&D in a biotech or big pharma company, but the seminars introduced me to many additional avenues, such as consulting, venture capital, and even intellectual property law. The community is so valuable that many SB2 "alumni" (i.e., students who have completed the training) continue attending the monthly SB2 meetings and the seminars—myself included.

> "One key function of the SB2 training program is that it creates a supportive community of synthetic biologists, and mentorship is an important component of that support."
>
> – Joey Huang

How did the SB2 program help you find an industry internship?

I had a specific company in mind that I considered my dream internship. I was particularly interested in B-cell engineering, which is research not really being done at BU. I tried leveraging my connections to gain a foothold into this company, but unfortunately they were not hiring that year. Josh Finkelstein encouraged me to broaden my search, as the job market was tough at the time. He shared a long list of start-ups for me to consider. He also suggested looking into big pharma.

Broadening my focus, I reached out to various companies. At this point, it was a full-on job hunt, and I was eager to get my foot in the door anywhere. It certainly wasn't a straightforward process. I cold messaged perhaps 20 to 30 companies and sometimes messaged several people at the same company, hoping to increase the chances that I was directing my inquiry to the most appropriate person.

Eventually, Josh leveraged his own network, connecting with someone at Novartis who circulated my resume around the company, and I received a response quickly. This led to a conversation with a director at Novartis—it didn't even feel like an interview, just a pleasant, informal discussion with a fellow expert in the field. Soon after that 90-minute conversation, Novartis offered me the internship.

By that time, I came to appreciate what a hustle it was to land a professional opportunity, especially in a competitive field.

What was your internship experience at Novartis like?

Initially, my day-to-day at Novartis was similar to my lab work. I spent most of my time in the tissue culture room or running experiments at the flow cytometry core. It was a nine-to-five routine focused on experiments. I was encouraged to network, but at first I was pretty reserved and didn't reach out to many people. Toward the end of my internship, however, I started making time in my day to converse with people from different departments. I'd schedule coffee dates to ask them about their work, career paths, and the decisions that led them to Novartis.

These conversations were enriching. Many of those I spoke to had fascinating backgrounds—some were doctors who switched fields, others had experience in academia or other companies. I shared my own story, my PhD journey, including the uncertainty I feel about my future, and opened up about wanting guidance and advice on how to navigate the path ahead. People were very open to talking and offering advice. Often, they'd refer me to more colleagues to talk to, which helped me build an even larger network of connections. Everyone was incredibly kind and welcoming, and I'm so grateful for that.

Why did Novartis turn out to be the right fit for your internship?

Initially, I never thought I wanted to go into big pharma. I wanted to do something outside my field and learn new skills, so Novartis felt contrary to what I wanted in an internship. What changed my perspective was a conversation with the person who became my manager. We talked about technologies in the field and my research at the Wong Lab. He shared his insights, including some downstream applications I hadn't considered, and that intrigued me. That conversation made me realize just how much I still had to learn in my current field, and it just clicked.

At my Novartis internship, I was able to contribute the expertise I'd already developed as well as learn new skills, and I engaged in meaningful conversations with people across the company, which not only deepened my understanding of the field but also lent me a great deal of emotional support and strength.

What advice would you give to prospective SB2 trainees?

Don't limit your options by assuming you should explore something entirely new. Consider also how you can unlock the full potential of what you're currently working on. In my case, my initial knowledge on what I could do with CAR T was confined to academia and the bubble of my lab, and I believed, very arrogantly, that my Ph.D. was enough to fully understand the field's potential. Thankfully, the SB2 program led me to an experience that challenged my perception, allowing me to gain insight into the start-to-finish of a cell therapy product, and to witness the extended R&D efforts surrounding a drug. My internship pushed me out of my comfort zone even within my current field and exposed me to opportunities I hadn't considered.

The experience also taught me how to manage expectations when seeking professional opportunities. I initially thought I could find a job purely to learn new skills, but the reality is that companies hire you to do specific work based on the experience they see on your resume. I came to realize that it was unrealistic to expect being hired based primarily on my interest in learning something new. This understanding will shape my approach to future job searches and resume crafting. Overall, the hustle to find and secure an opportunity was intense, but the search was possibly as valuable of a learning experience as the internship itself. In hindsight, both persistence and flexibility were key in finding the right opportunity.

One more thing the experience taught me is that job hunting is a connections game, so don't hesitate to use your network. Initially, I felt bad about asking Wilson and Josh to leverage their connections on my behalf. I didn't want to trouble them, but they—and most people I reached out to in the industry—were more than willing to help. I also worried that if I got the position through professional connections, whether I "deserved" the job. I came to realize that, while professional connections and recommendations might open doors, actually earning the offer comes down to what you personally bring to the table. It's about your abilities, your work, and your presentation. Trust yourself—you're there because you've earned it.

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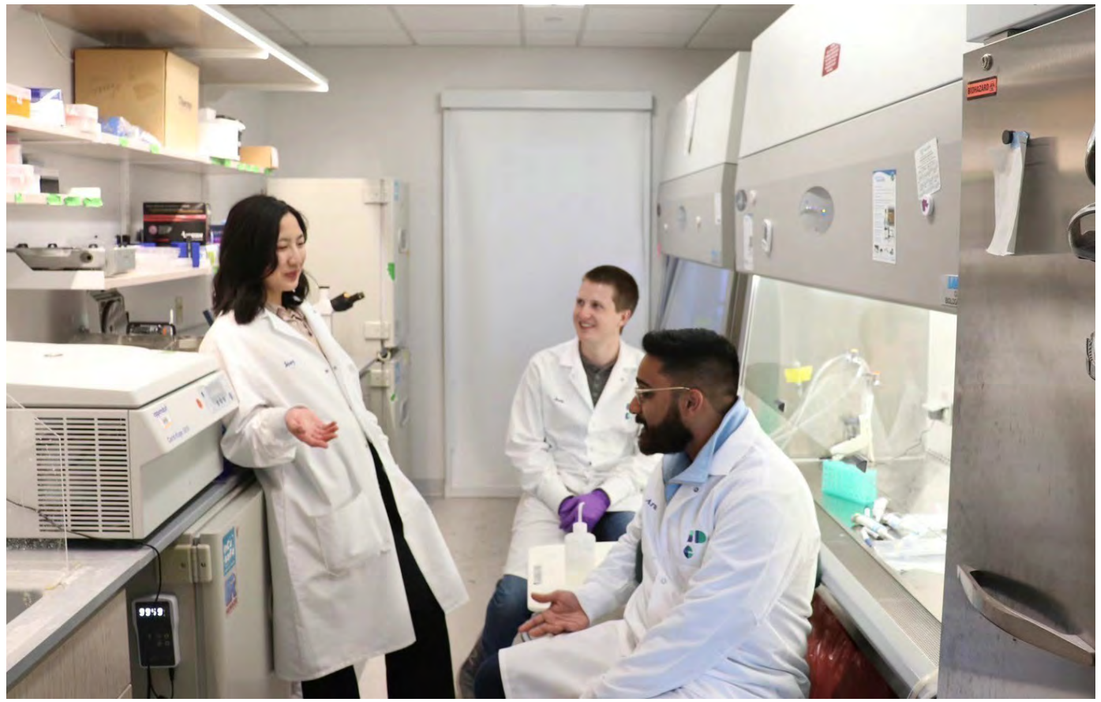
This interview was conducted by Jim Cooney, and edited by Jim Cooney and Tanvi Agrawal.



PhD student and SB2 trainee Joey Huang talks with fellow PhD students Joshua McGee (center) and Arun Nambiar, all of whom work in the lab of Professor Wilson Wong. Image provided by Joey Huang.

SB2 TRAINING PROGRAM

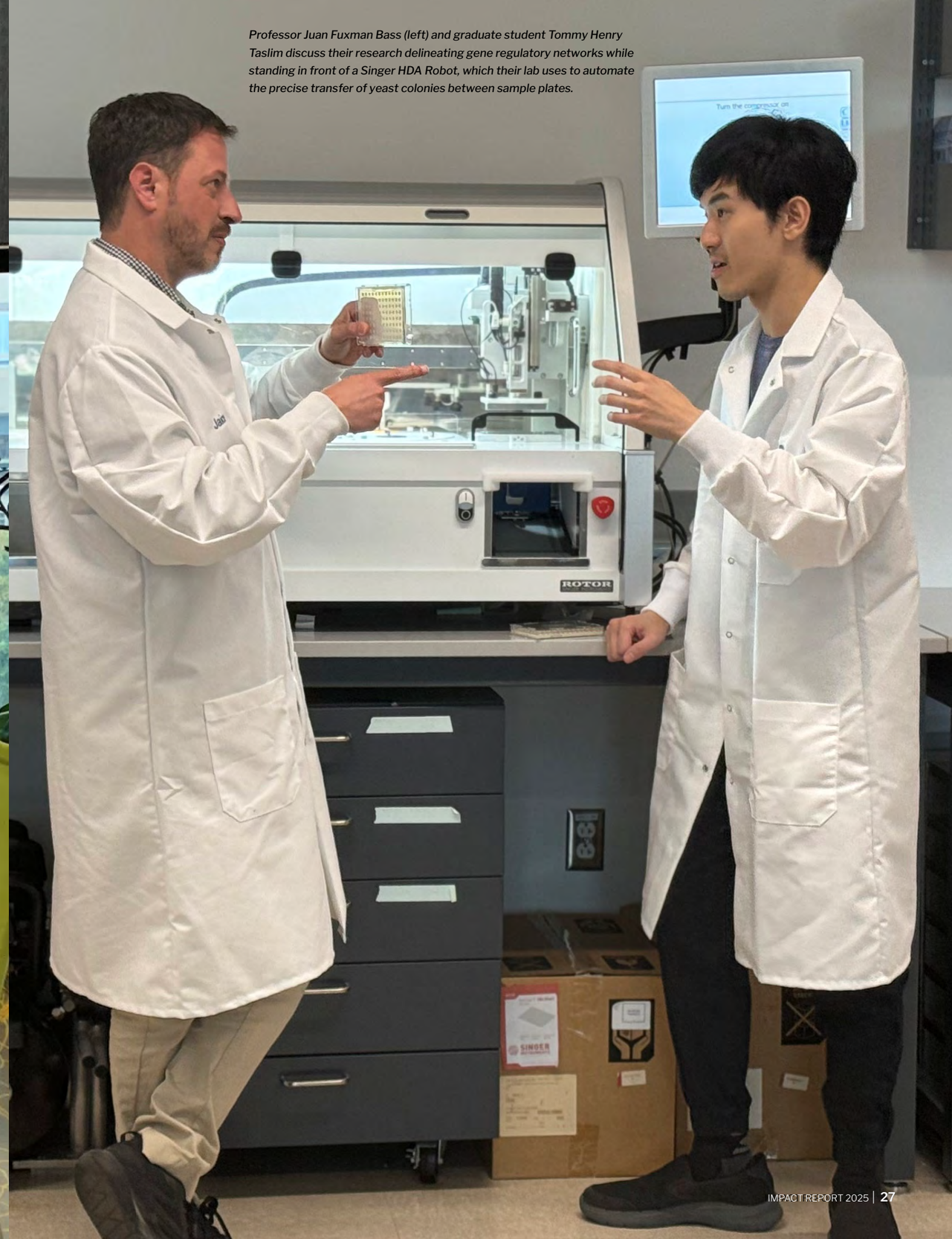
EARLY WORK IN SYNTHETIC BIOLOGY centered on "tinkering" with small genetic circuits in model microorganisms and re-engineering metabolic pathways, mostly for biofuel production. Since then, the field has undergone considerable growth in scope and output. Synthetic biology tools are now being applied to a wider array of systems and organisms: many people regularly consume plant-based meats, and numerous FDA-approved cell and gene therapies have emerged. Accompanying and driving this development are rapid technological advancements, like the capability to sequence, edit, and synthesize genomes. We have reached an exciting and critical juncture for the field. To fully capitalize on these significant developments, we must continue to formalize theory, practices, and standards, as well as revise our training modalities to prepare the next generation of Ph.D. graduates.

The goals of our **NIH T32 PhD Training Program on Synthetic Biology and Biotechnology (SB2)** are to provide a unique, field-defining, and interdisciplinary training environment in synthetic biology in order to broaden participation of underrepresented groups as well as to develop new training opportunities that emphasize professional skills and increase exposure to the biotech industry.

Trainees come from the Boston University's Department of Biomedical Engineering, the Bioinformatics Program, and the Molecular Biology, Cell Biology, & Biochemistry Program. All trainees are mentored by at least two faculty members, and the program provides 24 months of salary support. A key component of this training program is a ≥12-week internship in a Boston-area pharmaceutical and biotechnology company. In the past few years, trainees were placed at Beam Therapeutics, Funga, Joyn Bio, LanzaTech, Pearl Bio, Pfizer, Strand Therapeutics, Takeda Pharmaceuticals, The Engine, The Novartis Institutes for BioMedical Research, Vedanta Biosciences, AstraZeneca, and Concerto Biosciences.

For more information about this training program, please visit https://sites.bu.edu/sb2/. If your company is interested in hosting one of our graduate students as a summer intern, please contact us at bdcinfo@bu.edu.

Professor Zeba Wunderlich shows off a blanket gifted to her by one of her former graduate student trainees.



Professor Juan Fuxman Bass (left) and graduate student Tommy Henry Taslim discuss their research delineating gene regulatory networks while standing in front of a Singer HDA Robot, which their lab uses to automate the precise transfer of yeast colonies between sample plates.

OUTREACH SPOTLIGHTS

Swallowing jitters and marshaling a semester's worth of research, 11 teams of local high schoolers arrived at Boston University on a recent spring day to pitch products to a panel of BU faculty and affiliates playing the part of skeptical investors. It was the second annual Synthetic Biology Shark Tank Competition, which was held at the BU Life Sciences & Engineering Building April 26.

Mentored by undergrad and graduate students from BU's College of Engineering, the 28 seniors from Boston's diverse New Mission High School conceived of, and fleshed out, synthetic biology solutions to real-world problems. Among the products they pitched: crops modified to survive unseasonable cold snaps; marine bacteria engineered to clean up oil spills; and a microorganism that warns mountain climbers of impending altitude sickness.

New Mission High School seniors Darareaksmey Chhim (from left), Mario Fils, and Dorian Planto pitching their plastic-eating bacteria concept at BU's Biological Design Center's Synthetic Biology Shark Tank Competition April 26.

No actual dollars were invested in these on-paper concepts, but the experience taught the students valuable skills and got them thinking like real engineers and biotech developers.

"Eventually, I want to run a lab that does its own research," says Mario Fils, whose team proposed Jurassic Plastic (tagline: "Making Plastic Extinct"), a plastic-eating bacteria that would be deployed in landfills, where at least half of plastic waste ends up. "The deeper I got into it, the more I realized that this is a big, big issue. So I can see myself continuing this research and maybe even releasing the product that we came up with."

"Whether in academia or industry, you have to get your stuff funded," says Sarah Goldberg, the students' biotechnology instructor at New Mission High. "Either to get grants for your research or to get investors to invest in your product, you have to pitch your idea."

And students chose these ideas on their own. "I didn't give them a list of topics," Goldberg says. "I said, 'What matters to you? What interests you?' And that's where we start. Some of them picked plastic degradation or treating heroin addiction or detecting and treating high blood pressure. No matter how far they get into the actual science, they're pushing themselves to learn and create in some form."

Jackelyn Merida wanted to tackle cancer because "it has impacted my family," she says. "At a young age I witnessed my grandmother go through stage 4 breast cancer, and recently my uncle was diagnosed with lymphoma cancer."

Merida suggested focusing on inflammatory breast cancer (IBC), a rare and aggressive type of breast cancer with worse outcomes for people of color, and her teammate Calia Sutton agreed.

"As a woman of color, the fact that we have a higher death rate [from IBC] struck me," Sutton says. "Not only is it a disease that is causing extraordinary pain, and the cost to treat it is atrocious, but my people are suffering and there's not enough being done about it."

That kind of disparity is a big part of why BU's Biological Design Center launched STEM Pathways, the STEM outreach program that sponsored the competition. When technology is developed without diverse perspectives integrated into the process from the outset, the results can be things like pulse oximeters and facial recognition programs that are stymied by brown skin, as well as uneven treatment for some diseases.

"I can't expect them all to go into biotech," Goldberg says of her students, "but before they come into the class, they don't even know it's an option."

Goldberg's class at New Mission slightly predates STEM Pathways, but her students have benefited a great deal from the partnership over the past couple of years, she says. Many of the competitors at the Shark Tank event had attended Saturday STEM workshops at BU, and several worked full-time for five weeks last summer in labs at the BU Biological Design Center. Merida, for example, helped Wilson Wong, an ENG associate biomedical engineering professor, in his efforts to develop cancer-killing T-cells.

Once the high schoolers settled on a product idea, BU student mentors helped guide them as they researched the global challenges they wanted to solve, studied the pros and cons of current solutions (existing or under development), and assembled slideshows and rehearsed presentations.

Trophies were awarded by a panel of judges, among them Liangliang Hao, an ENG assistant professor of biomedical engineering, and Stephen Sweet (ENG'23), an engineer at General Dynamics.

"Having that additional support, the projects have gotten so much better," says Goldberg.

"Whenever we were confused," Fils says, "there was never a time when our mentor wasn't able to help us find articles or help us get everything organized. Honestly, we wouldn't have made it this far in the project without her help."

"Oh, stop!" Kristen Sheldon, a senior lab technologist at BU's DAMP Lab and a mentor to Fils' team, said with a laugh as the contestants sat at tables awaiting the results of the judges' deliberations. "It gave me an opportunity to apply my skills and knowledge to help them and help shape them as scientists. I think it was important that they got to choose a product [idea] they were passionate about."

That choice was by design, says Hailey Gordon, director of STEM Pathways. "We aimed to make each mentor session mentee-led, so that the high school students had agency within their project development."

At the same time, Gordon adds, the experience was useful for the mentors as well, building skills they'll need if they enter academia and run their own labs.

Some of the product pitches were delivered with confidence, others were peppered with the "likes" and "ums" that are almost to be expected in public presentations given by teenagers (and many adults). But it was obvious that all of the students had done their homework. Their slideshows were clear and well organized, and students like Merida and Sutton shined in the follow-up Q&A. They answered judges' questions about IBC statistics without hesitation and rattled off the risks of both their proposed cure and prevailing treatments.

At the end, awards were given out in categories such as Most Innovative and Highest Potential Impact. Fils and his teammates Darareaksmey Chhim and Dorian Planto won no less than three awards—Most Engaging Pitch, Most Invested, and People's Choice (a poll of their peers)—for Jurassic Plastic.

> "[Mentorship] gave me an opportunity to apply my skills and knowledge to help them and help shape them as scientists."
>
> **– Kristen Sheldon**

Goldberg also handed out medals to all students, recognizing their hard work and perhaps spurring them to keep at it in the biotech game. "I know people [criticize] 'participation awards,'" she said, "but this was a high-level task, and you all did a great job. I'm truly proud of each and every one of you."

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This article, authored by Patrick L. Kennedy, originally appeared in *BU Today* on May 7, 2024.

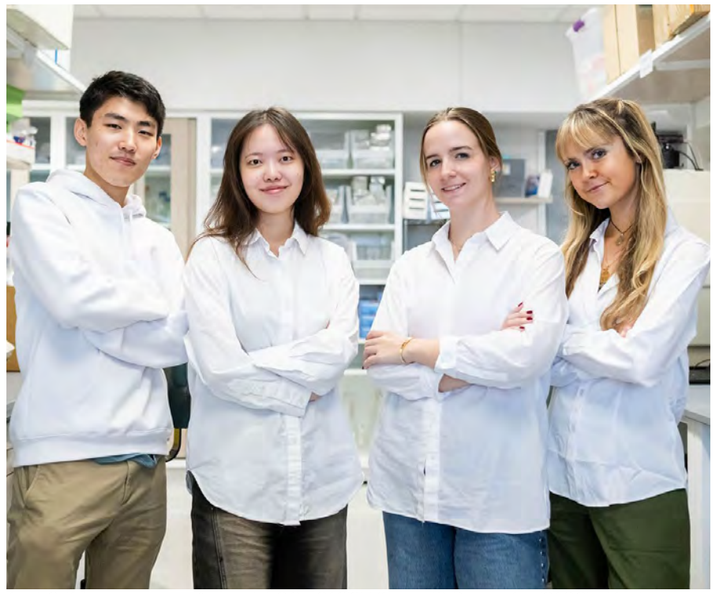
To read the original article visit: https://tinyurl.com/hp45zbps

BU Students Head to Paris to Compete in International Synthetic Biology Competition

Team will present their device, AgriNOVA, that can detect toxic metals in soil

Aiming to keep heavy metals out of the food we eat, a team of Boston University undergrads has traveled to Paris this week to pitch a soil monitor they invented, as part of the annual International Genetically Engineered Machine (iGEM) Grand Jamboree.

Some 427 student teams from around the globe are competing for awards in more than a dozen categories in what one contestant calls "a giant science fair" focused on synthetic biology. And whether or not the Terriers take home a prize, they have crafted a novel solution to a serious public health problem.



AgriNOVA team members Kevin Li (ENG'25, CAS'25) (from left), Brenda Kim (CAS'25), Meritxell Ortodo (ENG'26), Trinity Olander (CAS'26), and Abby Smith (ENG'25) (not pictured) are in Paris, demonstrating their novel biosensor that monitors soil for toxic heavy metals.

Toxic heavy metals from industrial pollution can leach into agricultural soil, eventually winding up in our food. Numerous instances have been reported recently. Earlier this year, Consumer Reports urged the USDA to drop Lunchables from the National School Lunch Program after the nonprofit tested the products and found "concerning levels" of heavy metals, such as lead and cadmium.

Current methods of testing soil for such contaminants involve large chemical analysis machines, and the process—sending samples to a far-off lab and awaiting results—is too expensive and time-consuming for many small farmers in under-resourced regions.

Enter AgriNOVA, the BU student team and their device of the same name. Barely bigger than a toaster oven, the tester contains bacteria that have been genetically engineered to light up when they encounter cadmium or manganese. These light signals are picked up by an optical system embedded in the hardware, and the results are displayed on-screen in a user-friendly format.

The goal is to empower farmers to quickly interpret the data and act upon it. (Soil remediation techniques can include proper waste disposal and a reduction in the use of chemical fertilizers.) Ultimately, the AgriNOVA team envisions a farmer being able to deploy a network of the devices to automatically collect and assess samples from different fields.

"The farmers can use it on-site themselves," says Trinity Olander (ENG'26), who is majoring in molecular biology. "We want to integrate a mapping system so they can track heavy metals across a farm plot and over time."

Moreover, the team would like to add more biosensors, widening the scope of the monitor beyond cadmium and manganese. "Both are heavy metals which are really toxic to the environment and also to people" at high levels, says Minseo (Brenda) Kim (CAS'25), a senior majoring in data science and minoring in biology. "But obviously we're hoping to expand that to other contaminants, such as lead, mercury, and arsenic."

Best of all, the students say, their streamlined device would be affordable, making the technology available to the largest number of people. "The goal is overall accessibility, since toxic metals in agricultural soil is such a big threat," says Kim.

"We were struck by the fact that there were no low-cost alternatives in heavy metal detection," says Meritxell Ortodo (ENG'26), a biomedical engineering major.

That's why the team plans to make detailed plans for AgriNOVA publicly available. "We developed a DIY, step-by-step guide, with files for laser-cutting, 3D-printing, and other ways to build the device," says Ortodo. "So for farmers, or engineers working with farmers, or even high school students, say, who don't have access to the labs we do, here's a low-cost alternative where they can follow the steps to replicate this device exactly."

> "We're making connections and learning about other people's projects. It's building a community."
>
> **–Meritxell Ortodo (ENG'26)**

The team also includes Abby Smith (ENG'25), a biomedical engineering major and Kilachand Honors College Scholar, and Kevin Li (ENG'25, CAS'25), who is double majoring in biochemistry and molecular biology and in computer science. This interdisciplinary mix has been a boon to the creation of a device that combines optics, microfluidics, mechanics, and genetic engineering.

"This was just the perfect opportunity and example of how biology could be integrated with hardware and electronics, which was really cool, and the team being so diverse was very helpful," says Ortodo. "There's a lot of different perspectives that really build on the idea. Everybody is [learning from] and feeding off each other."

Ortodo and teammates designed and built a prototype of their agricultural soil monitor in labs at BU's Biological Design Center.

The team was guided by lead principal investigator Miguel Jimenez, an ENG assistant professor of biomedical engineering, and secondary PI Hailey Gordon, director of STEM Pathways, the STEM outreach program based at BU's Biological Design Center (BDC). STEM Pathways sponsors a BU iGEM team each year.

"They achieved all their goals, working hard, collaboratively," says Gordon, who also points out that the students benefited from the resources in BDC, such as the DAMP Lab for the biology work, and the CIDAR Lab for the hardware. "I don't think we'd be able to do the project without either one of those labs' support," she says.

The undergrads also consulted with grad student mentors and industry professionals from two farm tech companies, Farmblox and Talam Biotech, to better understand the needs of farmers as well as modern approaches to soil management.

In addition to presenting their own work at the Paris event, the BU students will spend some of the week circulating through the expo's 14 halls, or "villages," devoted to different categories, such as diagnostics, space, and biomanufacturing. That's part of the value, and the excitement, of such a large gathering of young synthetic biology researchers, the team says—although iGEM is a competition, it's also about networking and advancing science. "We're making connections and learning about other people's projects," Olander says. "It's building a community."

* * *

This article, written by Patrick L. Kennedy, originally appeared in *BU Today* on October 18, 2024.

To read the original article visit: https://tinyurl.com/zvmxa2xs

ACHIEVEMENTS & AWARDS

CENTER FACULTY celebrated a wide array of achievements and awards over the course of the past fiscal year, including:

Samagya Banskota
- Massachusetts Life Sciences Center Novel Therapeutics Delivery Award

Christopher Chen
- BMES-CMBE Shu Chien Achievement Award
- Member, National Academy of Medicine

Brian Cleary
- Shibulal Family Career Development Assistant Professor

Mary Dunlop
- Vice Chair, Boston University Department of Biomedical Engineering
- Award for Excellence in Mentoring Postdocs, Boston University
- Dorf-Ebner Distinguished Faculty Fellow, College of Engineering, Boston University
- College of Engineering Faculty Service Award, Boston University
- 2024 Kilachand Fund Award, Boston University

Alexander Green
- National Institutes of Health Director's Transformative Research Award
- 2024 Kilachand Fund Award, Boston University

Liang Hao
- Beckman Young Investigator Award
- Innovation Award from the American Lung Association
- 2024 Dean's Research Infrastructure Award, Boston University
- Rainin Foundation Innovator Award, with Miguel Jimenez

Miguel Jimenez
- 2024 Dean's Research Infrastructure Award, Boston University
- Rainin Foundation Innovator Award, with Liang Hao
- Elected to BioMADE Technical Committee

Ahmad (Mo) Khalil
- 2024 Kilachand Fund Award, Boston University
- 2025 Dean's Catalyst Award, Boston University

Joseph Larkin
- 2024 Kilachand Fund Award, Boston University

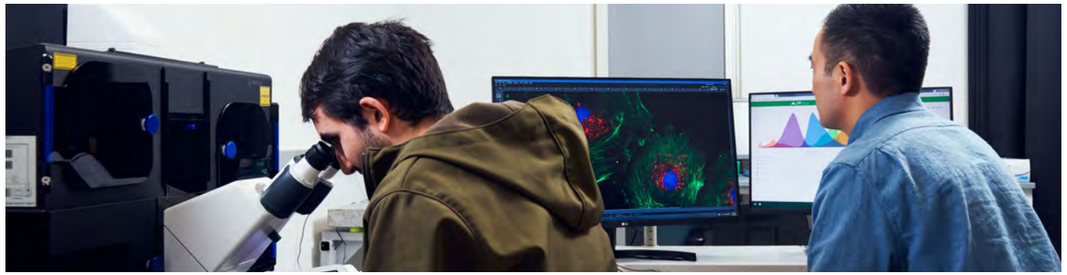
John Ngo
- 2025 BU Ignition Award

Daniel Segrè
- AAAS Fellow

Wilson Wong
- American Institute for Medical and Biological Engineering (AIMBE) Fellow
- 2024 Kilachand Fund Award, Boston University

Zeba Wunderlich
- 2024 Dean's Research Infrastructure Award, Boston University
- 2025 Presidential Early Career Award for Scientists and Engineers (PECASE)

Rabia Yazicigil
- 2024 NSF CAREER Award
- Elected to the 2024 Grainger Foundation Frontiers of Engineering Symposium, National Academy of Engineering
- Early Career Excellence in Research Award for the Boston University College of Engineering



Viewing samples in the lab of John Ngo.

Postdoctoral fellow Menna Siddiqui, who works in the lab of Professor Wilson Wong, examines a sample of target cancer cells through a stereoscope after a using a transduction procedure to compel the cells to express a particular protein. Eventually, the Wong Lab will deploy T cells that it has engineered to be able to identify and kill these cancer cells.

SELECTED EVENTS

THE CENTER HOSTED A SYMPOSIUM, several seminars, and a number of other events at Boston University featuring both BU speakers and external speakers.

2024

February 10

STEM Pathways held our third mini-Jamboree, which is a free, interactive day of learning and fun that aims to increase awareness of synthetic biology and biotechnology in high school students. This mini-Jamboree focused on teaching high school students electronic, DNA, and RNA biosensor foundations through interactive demonstrations and engaging experiments. With expert-led sessions, students gained a deep understanding of cutting-edge biotechnology, which helped spark their curiosity and inspire the next generation of innovators in the field.

February 28

Seminar: **Vincent Ling** (Senior Director, Center for External Innovation at Takeda Pharmaceuticals), *Drug Delivery Technologies, an Industrial Perspective.*

Boston-area high school students participate in the third STEM Pathways mini-Jamboree.

March 22

Barbara Cheifet (Chief Editor of *Nature Biotechnology*) visited the Biological Design Center.

Miho Kaneko, an associate with Goodwin Procter LLP, discusses patent law basics at the BDC's Business of Biotech Seminar.

April 26

STEM Pathways hosted New Mission High School's Annual Shark Tank Competition, where members of their Biotechnology II class–which had been mentored throughout the spring by BDC graduate students and postdoctoral fellows–pitched biotech concepts that used synthetic biology principles to design a synthetic organism. (see page 28).

April 27

STEM Pathways hosted a Biomedical Imaging Hackathon, where high school students learned how to use the Python Programming language to edit and manipulate biomedical images. They also learned how scientists use imaging tools to classify tumors, how to identify and analyze cellular growth patterns, and how to write neural network models to predict images from a set of given input images.

September 9

Seminar: **Shrikrishnan Sankaran**, (Head of Bioprogrammable Materials at the Leibniz Institute for New Materials), *Living Therapeutic Materials: Bacterial hydrogels for smart drug delivery*

October 21

The BDC Annual Symposium featured talks from BDC faculty members **Mary Dunlop, Alexander Green, Joseph Larkin**, and **Liang Hao**, as well as four of our graduate students, one postdoctoral fellow, and the 2025 iGEM team. The day concluded with the 2024 Charles Cantor Lecture, which was given by **Wendell Lim** (Professor at University of California San Francisco) and entitled *Generative Biology: Learning to Program Cellular Machines and Circuits.*

2025

January 14

Lunch-and-learn with **Portal Bio**, who have developed a new intracellular delivery technology to enable novel cell engineering and intracellular analytics.

March 18

Business of Biotech Seminar: **Miho Kaneko** (Associate, Goodwin Procter LLP), *Patent Law Basics for Scientists and Engineers & Career in Patent Law.*

April 3

BDC Comm Lab Workshop: Guided graphical abstract work session and Adobe Illustrator tips.

April 17

Women's Health Seminar: **Lucy Pérez** (Senior Partner at McKinsey & Company and a Global Leader of the McKinsey Health Institute), *Blueprint to Close the Women's Health Gap.*

May 6

Lunch-and-learn with Dr. **Carla Reimold** (Executive Vice President of Scientific Innovation and Strategic Investments at the Massachusetts Life Sciences Center.)

May 16

STEM Pathways hosted New Mission High School's Annual Shark Tank Competition, where members of their Biotechnology II class–which had been mentored throughout the spring by BDC graduate students and postdoctoral fellows–pitched biotech concepts that used synthetic biology principles to design a synthetic organism (see page 28).

Professor Wendell Lim from the University of California San Francisco delivered the 2024 Charles Cantor Lecture during the BDC Annual Symposium.

June 3

Boston University hosts MassBioEd's 2025 Life Sciences Workforce Conference.

July 16

Science Policy event with **Kei Koizumi** (former Special Assistant to the President and Principal Deputy Director for Science, White House Office of Science and Technology Policy), *From BU to the White House: My Journey to Science Policy for Impact.*

September 23

BDC Comm Lab Fellowship Writing Workshop: Helped students in the BU community with their applications for various graduate fellowships, including the NSF GRFP, DoD NDSEG, and F31 Fellowships.

November 11

Event with Nucleate Boston, and the Inflammation Research Association: *Connecting Discovery and Cure: Industry Leaders Networking and Roundtable.*

November 17

The BDC Annual Symposium featured talks from BDC faculty members **John Ngo, Miguel Jimenez, Daniel Segré**, and **Zeba Wunderlich**, as well as four of our graduate students, one postdoctoral fellow, and the 2025 iGEM team.

November 19

Emma Yee (Editor of *Cell*) visited the Biological Design Center.

December 2

BU Graduate Student Internships Panel Discussion, featuring Ph.D. students who participated in internships at AstraZeneca, Draper, IRIS Kinetics, MatTek, Concerto Biosciences, and Pfizer.

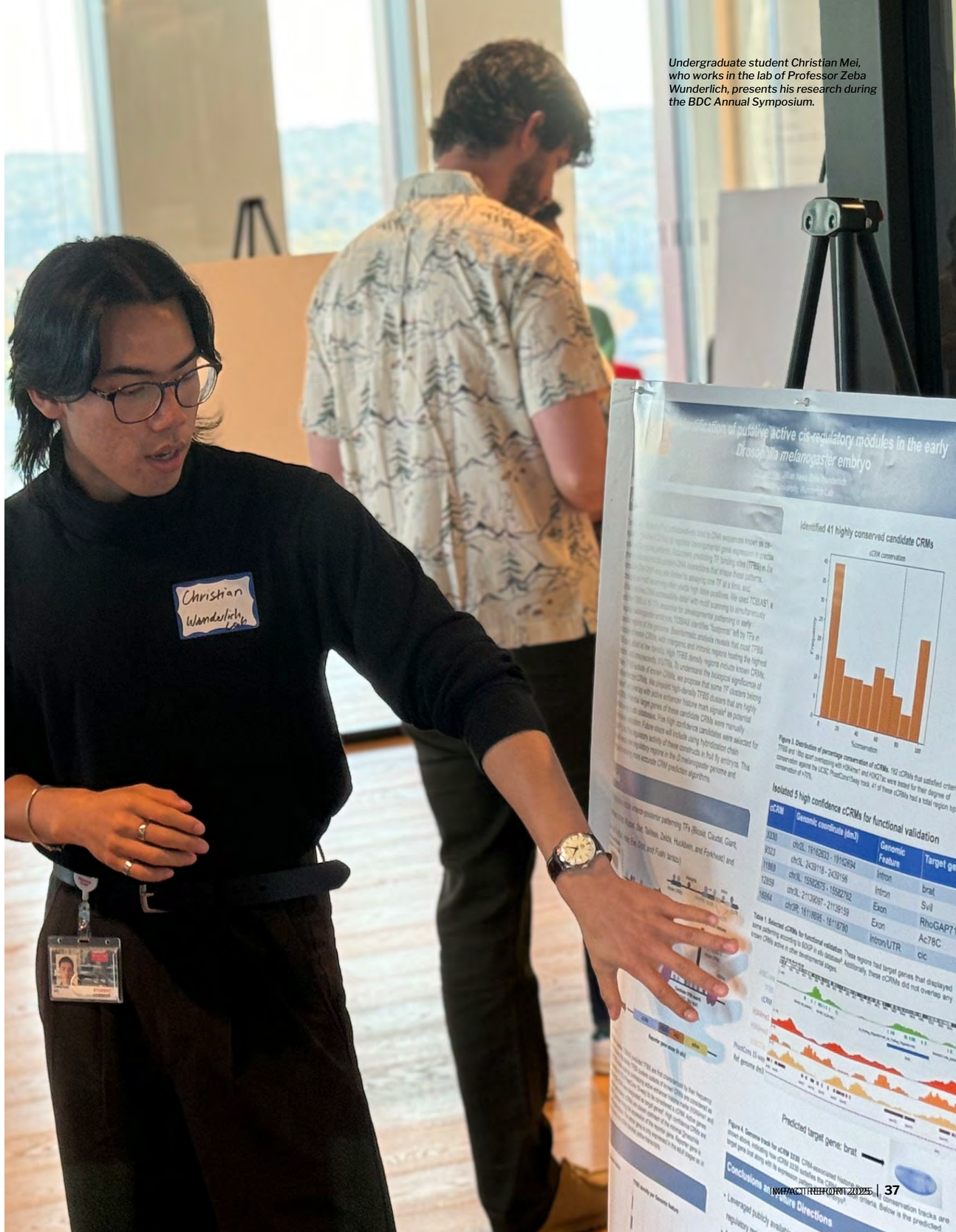
December 5

Annual Symposium for the NIH T32 Training Program in Quantitative Biology & Physiology, the NIH T32 Translational Research in Biomaterials Training Program, the NIH T32 Training Program in Synthetic Biology and Biotechnology, and the NRT (NSF Research Traineeship) in Biological Feedback Control.

December 11

Lunch-and-learn with **Twist Bioscience**, to learn about their products for synthetic biology and next-generation sequencing solutions.

Professor Zeba Wunderlich mentors Jillian Ness, a PhD student, as they examine fruit fly specimens under the microscope in the lab.



Undergraduate student Christian Mei, who works in the lab of Professor Zeba Wunderlich, presents his research during the BDC Annual Symposium.

SELECTED PUBLICATIONS

Use this table to explore publications by category; connect to full citations/DOIs online.
Because of the interdisciplinary nature of BDC research, publications may span multiple categories

Designing Living Systems	Chen J, Borison A, **Densmore D, Wong WW**.	Cell-free recombinase-integrated Boolean output system	*Cell Syst*
	Kang NR, Im J, Biondo JR, Sharpes CE, Rhea KA,Garden PM, Jaramillo Montezco JJ, Ringaci A, Grinstaff, Grinstaff MW, Phillips DA, Miklos AE, **Green AA**.	A rapid and modular nanobody assay for Plug-and-Play Antigen Detection	*ACS Synth Biol*
	Le Q, **Ngo JT**.	Protease-containing nanobodies for detecting and manipulating intracellular antigens using antiviral drugs	*ACS Chem Biol*
	McGee JE, Kirsch JR, Kenney D, Cerbo F, Chavez EC, Shih TY, Douam F, **Wong WW**, Grinstaff MW.	Complete substitution with modified nucleotides in self-amplifying RNA suppresses the interferon response and increases potency	*Nat Biotechnol*
	McIntyre D, Arguijo D, Kawata K, **Densmore D**.	Component library creation and pixel array generation with micromilled droplet microfluidics	*Microsyst Nanoeng*
	Padmakumar JP, Sun JJ, Cho W, Zhou Y, Krenz C, Han WZ, **Densmore D**, Sontag ED, Voigt CA.	Partitioning of a 2-bit hash function across 66 communicating cells	*Nat Chem Biol*
	Riley AT, Robson JM, Ulanova A, **Green AA**.	Generative and predictive neural networks for the design of functional RNA molecules	*Nat Commun*
	Tous C, Kinstlinger IS, Rice MEL, Deng J, **Wong WW**.	Multiplexing light-inducible recombinases to control cell fate, Boolean logic, and cell patterning in mammalian cells	*Sci Adv*
	Tran JC, Kuffner CJ, Marzilli AM, Miller RE, Silfen ZE, McMahan JB, Sloas DC, **Chen CS, Ngo JT**.	Fluorescein-based SynNotch adaptors for regulating gene expression responses to diverse extracellular and matrix-based cues	*Nat Commun*
	Yan Z, Li Y, Eshed A, Wu K, Ticktin ZM, Murugan V, Lim ES, Hong F, **Green AA**.	Programmable fluorescent aptamer-based RNA switches for rapid identification of point mutations	*Nat Chem*
	Yang X, Rocks JW, Jiang K, Walters AJ, Rai K, Liu J, Nguyen J, Olson SD, **Mehta P**, Collins JJ, Daringer NM, Bashor CJ.	Engineering synthetic phosphorylation signaling networks in human cells	*Science*
	Yazicigil RT, Bali A, Caygara D, **Densmore D**.	Improving engineered biological systems with electronics and microfluidics	*Nat Biotechnol*
	Zhou Y, Voigt CA, **Densmore D**.	Constraint-based sub-graph partitioning for multi-cellular biological networks	*IEEE Trans Comput Biol Bioinform*
Understanding Biological Systems	Descoteaux AE, Radulovic M, Alburi D, **Bradham CA**.	CMTM4 is an adhesion modulator that regulates skeletal patternina and primary mesenchyme cell migratiol in sea urchin embryos	*Dev Biol*
	Feng Z, Blumenthal E, **Mehta P**, Goyal A.	A theory of ecological invasions and its implications for eco-evolutionary dynamic	*Proc Natl Acad Sci USA*
	Gibbs JR, Mei C, **Wunderlich Z**.	Beyond the heat shock pathway: Heat stress responses in *Drosophila* development	*Dev Biol*
	Goyal A, Rocks JW, **Mehta P**.	Universal niche geometry governs the response of ecosystems to environmental perturbations	*PRX Life*
	Lion AT, Bodine SM, McCutcheon KR, Ghogale M, Chandragiri S, Abayawardena D, Shrestha BD, Descoteaux A, Alvarez K, [...], Wong JY, Prakash VN, **Bradham CA**.	PFAS compounds PFOA and Gen X are teratogenic to sea urchin embryos	*Dev Biol*
	Scott H, **Segrè D**.	Metabolic flux modeling in marine ecosystems	*Ann Rev Mar Sci*
	Williams LM, Wang W, Grigoryeva AV, Navarro-Rosado A, Peart JA, Calderon A, Gill CL, Black S, Alsante KM, [...], DiRusso CJ, Cohen LB, **Wunderlich Z**, Grone BP, Gilmore TD.	Comparison of activities of transcription factor NF-kB from two jellyfish models	*Comp Immunol Rep*
	Zhu Y, **Wunderlich Z**, Lander AD.	Epithelial cell competition is promoted by signaling from immune cells	*Nat Commun*

Synthetic circuits, RNA switches, recombinases, & programmable cell behavior

Development, ecology, environmental perturbation, & marine ecosystems

Seeing Biology in New Ways	Binan L, Jiang A, Danquah SA, Valakh V, Simonton B, Bezney J, Manguso RT, Yates KB, Nehme R, **Cleary B**, Farhi SL.	Simultaneous CRISPR screening and spatial transcriptomics reveal intracellular, intercellular, and functional transcriptional circuits	*Cell*
	Ching T, van Steen ACI, Gray-Scherr D, Teo JL, Vasan A, Jeon J, Shah J, Patel A, Stoddard AE, Bays JL, **Eyckmans J, Chen CS**.	TapeTech microfluidic connectors: adhesive tape-enabled solution for organ-on-a-chip system integration	*Lab Chip*
	Ewoldt JK, DePalma SJ, Jewett ME, Karakan MÇ, Lin YM, Mir Hashemian P, Gao X, Lou L, [...], Bifano TG, Ramaswamy S, White AE, Agarwal A, Lejeune E, Baker BM, **Chen CS**.	Induced pluripotent stem cell-derived cardiomyocyte *in vitro* models: benchmarking progress and ongoing challenges	*Nat Methods*
	Huang R, Kratka CE, Pea J, McCann C, Nelson J, Bryan JP, Zhou LT, Russo DD, Zaniker-Gomez EJ, Gandhi AH, Shalek AK, **Cleary B**, Farhi SL, Duncan FE, Goods BA.	Single-cell and spatiotemporal profile of ovulation in the mouse ovary	*PLoS Biol*
	Incandela JT, Hu K, Joshi P, Rosenstein JK, **Larkin JW**.	Non-optical, label-free electrical capacitance imaging of microorganisms	*mBio*
	Kuffner CJ, Marzilli AM, **Ngo JT**.	RNA-stabilized coat proteins for sensitive and simultaneous imaging of distinct single mRNAs in live cells	*Nat Methods*
	Lin H, Seitz S, Tan Y, Lugagne JB, Wang L, Ding G, He H, Rauwolf TJ, **Dunlop MJ**, Connor JH, Porco JA Jr, Tian L, Cheng JX.	Label-free nanoscopy of cell metabolism by ultrasensitive reweighted visible stimulated Raman scattering	*Nat Methods*
	Ribis JW, Nieto C, DiBenedetto NV, Mehra A, Kuhn P, Dong Q, Nagawa I, El Meouche I, Aldridge BB, **Dunlop MJ**, Tamayo R, Singh A, Shen A.	Unique growth and morphology properties of Clade 5 *Clostridioides difficile* strains revealed by single-cell time-lapse microscopy	*PLoS Pathog*
Modeling Life Across Scales	Alnahhas RN, Andreani V, **Dunlop MJ**.	Evaluating the predictive power of combined gene expression dynamics from single cells on antibiotic survival	*mSystems*
	Brooks C, Yao M, McCool JT, Gillman A, Süel GM, Mugler A, **Larkin JW**.	Computational model of fractal interface formation in bacterial biofilms	*Phys Rev E*
	Dukovski I, Golden L, Zhang J, Osborne M, **Segrè D, Korolev KS**.	Biophysical metabolic modeling of complex bacterial colony morphology	*Cell Syst*
	Lambourne L, Mattioli K, Santoso C, Sheynkman G, Inukai S, [...], Salomonis N, Calderwood MA, Hill DE, Sahni N, Vidal M, Bulyk ML, **Fuxman Bass JI**.	Widespread variation in molecular interactions and regulatory properties among transcription factor isoforms	*Mol Cell*
	Li Z, **Fuxman Bass JI**.	ICARus: a pipeline to extract robust gene expression signatures from transcriptome datasets	*Front Bioinform*
	Moyer DC, Reimertz J, **Fuxman Bass JI, Segrè D.**	Flux sampling and context-specific genome-scale metabolic models for biotechnological applications	*Trends Biotechnol*
	Moyer DC, Reimertz J, **Segrè D, Fuxman Bass JI**.	MACAW: a method for semi-automatic detection of errors in genome-scale metabolic models	*Genome Biol*
	Mulder OJ, Peters Kostman M, Almodaimegh A, Edge MD, **Larkin JW**.	An agent-based model of metabolic signaling oscillations in *Bacillus subtilis* biofilms	*PLoS Comput Biol*
	O'Connor OM, **Dunlop MJ**.	Cell-TRACTR: A transformer-based model for end-to-end segmentation and tracking of cells	*PLoS Comput Biol*
	Peng H, Kotelnikov S, Egbert ME, Ofaim S, Stevens GC, Phanse S, Saccon T, Ignatov M, Dutta S, Istace Z, [...], Parkinson J, **Segrè D**, Babu M, Kozakov D, Emili A.	Ligand interaction landscape of transcription factors and essential enzymes in *E. coli*	*Cell*
	Rijal K, **Mehta P. A**.	A differentiable Gillespie algorithm for simulating chemical kinetics, parameter estimation, and designing synthetic biological circuits	*Elife*
Moving Toward Translation	Baka T, Moore J, Qin F, Yurista SR, Zhang A, He H, Chambers JM, Croteau D, Goel RK, Smith H, Wang MC, **Chen CS**, Hobai IA, Rombaldova M, [...], Emili A, Colucci WS, Luptak I.	Empagliflozin enhances metabolic efficiency and improves left ventricular hypertrophy in a hypertrophic ardiomyopathy mouse model	*Eur Heart J*
	Floros KV, Fairchild CK Jr, Li J, Zhang K, Roberts JL, Kurupi R, Paudel D, Xing Y, Hu B, [...], **Siggers T**, Banito A, Dozmorov MG, Jones KB, Radhakrishnan SK, Faber AC.	Targeting SUMOylation promotes BAF complex stabilization and disruption of the SS18::5SX transcriptome in synovial sarcoma	*Nat Commun*
	Li L, Yang J, Perry L, Bays JL, Bhatia SN, **Eyckmans J, Chen CS**.	Engineering a heparin-mimetic biomaterial to promote tissue vascularization	*Commun Biol*
	Lu C, Li Y, Cummings JR, **Banskota S**.	Delivery of genome editors with engineered virus-like particles	*Methods Enzymol*
	Patalano SD, Fuxman Bass P, **Fuxman Bass JI**.	Transcription factors in the development and treatment of immune disorders	*Transcription*
	Vasan A, Kim S, Davis E, Roh DS, **Eyckmans J**.	Advances in designer materials for chronic wound healing	*Adv Wound Care*

Imaging, nanoscopy, & detection platforms

AI, metabolic modeling, cell tracking, & ecosystem-scale prediction

Disease models, genome editor delivery, biomaterials, & therapeutic platforms

Test tube samples from the lab of Zeba Wunderlich.

HOW TO ENGAGE WITH US

The offices of the leadership and administrators for the Biological Design Center are located at 610 Commonwealth Avenue on the fourth, fifth, and sixth floors.

The seminars for the Biological Design Center typically take place in the Eichenbaum Memorial Colloquium Room on the 1st floor of the Rajen Kilachand Center for Integrated Life Sciences & Engineering, 610 Commonwealth Avenue, Boston, MA.

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Back cover photo: *Luminescent E. coli colonies grow in a mold rendered as a QR code in the lab of Miguel Jimenez.* Image provided by PhD student Dev Bhatt.

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