CONTENTS | WINTER 2021

ADVANCES

9 The “right diet”
New enzyme could lead to bespoke diets and therapeutics

11 Life’s Frankenstein beginnings
Earth’s first bits of life may have been messier than previously thought

12 The right fold
Kinks in protein folding could lead to new drugs and even fight COVID-19

13 Up close and personal with neuronal networks
Nanoelectrodes record thousands of connected mammalian neurons

14 ADVANCES IN ACTION
A new gold-standard test for COVID-19 antibodies

16 Getting the brain’s attention
The mind can ignore or act on information—how?

17 Molecular cell-killing mechanism
A compound turned cancer-killer could offer new ways to treat drug-resistant tumors

COMMUNITY

6 CCB Voices
Musings on why we research and frank talk about mental health

68 Everyday science
Helping quarantined kids eat up the chemistry of yogurt, cereal, and more

70 Ten Questions
Suyang Xu answers

PROFILES

50 ALUM Jill of all trades
Alum Jill Becker went from selling kid’s shoes to launching successful start-ups

54 UNDERGRAD Not your classical chemist
Orvin Pierre marries science and history to solve the ultimate puzzle

58 GRAD Jete into an ionic bond
Frederick Moss choreographs a life in science and art

62 GRAD A captain for our planet
Christina Chang’s lifelong quest to build a sustainable world

66 STAFF Breaking isolation
Barbara Anderson reaches out to victims of human trafficking

FEATURES

22 Chromosome close-ups
High-resolution, 3D images of human chromosomes in single cells reveal how chromatin structure might influence its function

26 The Crispr chronicles
Base editing gets closer to curing a rapid-aging disease, correcting genetic deafness, manipulating mitochondrial DNA, and more

34 The forest for the trees
Trees, from pre-industrial to modern forests, can impact pollution and climate change—but are they friend or foe?

38 Let the light shine in
This fall, undergraduate students in PS10 couldn’t go to the lab, so they made one at home

42 Microbes might manage our cholesterol
Researchers discover a mysterious bacteria that breaks down cholesterol in the gut

ABOVE: In March 2020, during the first wave of the COVID-19 pandemic, CCB’s lab members and facilities staff gathered all the department’s personal protective equipment (PPE) to donate to local hospitals, help bolster their supplies, and save lives. (Photo courtesy of Mike Paterno, Senior Facilities Manager)
The past year, both pandemics—the coronavirus and deeply rooted racism—brought pain and disruption to many. However, our year was not all bad. The past year afforded us the opportunity to reflect on our culture and community: to question whether all members feel accepted, included, and supported, and to enact new, concrete practices to cultivate bonds that enable us to grow and learn from one another.

That is one reason why the third edition of our CCB Magazine includes a broader spectrum of voices—more profiles on our extraordinary people, and a new section where members of our community can share their unique perspectives. This edition is, like most else these days, virtual. But we hope these stories of our community members inspire you and help all our scattered members re-forged bonds. You might empathize with the quest for the scientific unicorn or share a newfound disbelief for the word “unprecedented.” Or maybe you are just excited to see chromosomes up close or to build your own cardboard spectrometer at home. I hope you enjoy it.

Q & A WITH CCB’S NEW EXECUTIVE DIRECTOR

Q: What attracted you to join CCB originally? While working in the Division of Science, I had an opportunity to get to know many people from all ten of the academic science departments. It gave me a small flavor for the culture and community within each, and I was always intrigued by the number of long-service employees in CCB. I knew that if so many people had stayed in the department for such a long time, they must be doing something right. And that was a community I wanted to be part of.

Q: What have you prided most about working here? Definitely the relationships we’ve crafted while supporting some really exciting and cutting-edge science. Being a small part of the team—that the machine—that enables faculty to do remarkable science. Being able to provide the administrative framework that paves the way for faculty to have the resources they need. Seeing graduate students publish and defend and then become world-class alumni doing incredible things across the globe. Those are truly the things that make me cherish my time in CCB.

Q: What are your priorities for the coming year? It’s important to remember that during the continuing global pandemic, the safety and well-being of our community members is paramount. We are also doing important, critical, introspective work on what makes CCB a place where people want to be, focusing on making this a community that is diverse and inclusive and creating a culture that fosters individuals towards success. That’s where my work will be focused this year.

We also have big goals around extending fellowships for graduate students, which is a fundamental fundraising effort that needs to be undertaken. We’ll partner on that front as well.

Q: Tell us about your background—what led you to the position of Executive Director? I’ve had a somewhat non-traditional path to academia. I earned a bachelor’s degree in political science and a master’s with a concentration in journalism. I had my sights set on becoming a political commentator for CNN but I’ve been re-energized in thinking about science. I’ve been really excited about the ways we can make our department a more welcoming and diverse place to do science. We’ve had to refocus and re-commit to our mission of excellence in teaching and research and despite it all there has still been progress. This is an incredibly resilient department, and I’m really excited about continuing to face these challenges and opportunities together.

Q: What else would you like the department to navigate towards success. Joining the Dean’s office allowed me to do that at the Divisional level, often operating behind the scenes and navigating towards success. Joining the CCB role, my job is to support our remarkable faculty, students, postdocs and staff. Being a part of the scientific enterprise is exciting, challenging and rewarding and exactly where I want to be.

Q: You’re entering this job at an extraordinary time for the department and the University. As Interim Executive Director, you helped manage the transition to remote work, de-densified labs, and, after the anti-racism movement of summer 2020, started to strategize how to create a more inclusive and welcoming environment. What has that process been like?

I remember the challenges in the days ahead, but I’ve been re-energized in thinking about the ways we can make our department a more welcoming and diverse place to do science. I’ve also had to miss out on some cherished experiences: graduation celebrations, retirements, handshakes when meeting new people, and hugs in celebrating outstanding achievements.

We still have big goals. But I’ve been re-energized in thinking about the ways we can make our department a more welcoming and diverse place to do science. We’ve had to refocus and re-commit to our mission of excellence in teaching and research and despite it all there has still been progress. This is an incredibly resilient department, and I’m really excited about continuing to face these challenges and opportunities together.

Q: What else would you like the department to know about you? I’m here. I welcome any and all feedback, ideas, suggestions and conversation, always.

Almost one year ago, on March 15, 2020, CCB shifted from our comfortable routines in labs and offices to an uncertain and unpredictable remote space. These extraordinary times called for measures that may have seemed ordinary—staying home, staying covered, staying healthy and safe—but were in reality extraordinary challenges for our community. By June, our labs reopened at a safe, limited capacity, but much of our work remains virtual—virtual work spaces and lab meetings, virtual classes, virtual town halls on anti-racism and mental health, and virtual recruiting booths at virtual conferences. We are connected in new ways and yet all too disconnected from those we care about. Still, the coronavirus pandemic has taught us that while much of science relies on physical spaces, it can also transcend vast divisions—country lines, demographics, and politics—to solve an extraordinary problem:

Q: What attracted you to join CCB originally? While working in the Division of Science, I had an opportunity to get to know many people from all ten of the academic science departments. It gave me a small flavor for the culture and community within each, and I was always intrigued by the number of long-service employees in CCB. I knew that if so many people had stayed in the department for such a long time, they must be doing something right. And that was a community I wanted to be part of.

Q: What have you prided most about working here? Definitely the relationships we’ve crafted while supporting some really exciting and playing small roles in progress. In this ED role, my job is to support our remarkable faculty, students, postdocs and staff. Being a part of the scientific enterprise is exciting, challenging and rewarding and exactly where I want to be.

Q: You’re entering this job at an extraordinary time for the department and the University. As Interim Executive Director, you helped manage the transition to remote work, de-densified labs, and, after the anti-racism movement of summer 2020, started to strategize how to create a more inclusive and welcoming environment. What has that process been like?

I remember the challenges in the days ahead, but I’ve been re-energized in thinking about the ways we can make our department a more welcoming and diverse place to do science. We’ve had to refocus and re-commit to our mission of excellence in teaching and research and despite it all there has still been progress. This is an incredibly resilient department, and I’m really excited about continuing to face these challenges and opportunities together.

Q: What else would you like the department to know about you? I’m here. I welcome any and all feedback, ideas, suggestions and conversation, always.
UNICORN VS. PURPLE HORSE

You know research is hard. There are times when you devise a great idea you consider field-changing (a unicorn) just to find that someone else did it a few years ago or it is not viable (a donkey). Most of the time, you work hard enough to find something interesting (a purple horse). It is easy to get discouraged, but it usually feels like this one: 

You are at home trying to do something interesting and complicated with your laptop. At one point, you realize, “Oh, I need more battery power.”

You plug the computer into the wall and see the screen light up. Nice. Why wouldn’t it work? You keep doing your work and get excited with the feeling of making steady progress. You are so close to your goal. Then things break. 

Your laptop stops charging, and you realize something must be wrong with your charger since you know it is unlikely your computer got damaged.

Common sense tells you to check your charger. Visibly, there is nothing wrong with it, but, sadly, it is the only one you have. So, you tell yourself: “I know how chargers work; I can fix this!”

You grab a screwdriver, open the charger, and see a mini city of electronics parts. This will be more complicated and time-consuming than you initially thought.

You spend hour after hour bent over the mini city, looking for busted components, hooking up testing equipment borrowed from other colleagues, and see a mini city of electronics parts. This will be more complicated and time-consuming than you initially thought.

You go back home and replace the dead capacitor. But the charger still does not work.

You spend hour after hour bent over the mini city, looking for busted components, hooking up testing equipment borrowed from other colleagues, and see a mini city of electronics parts. This will be more complicated and time-consuming than you initially thought.

That is how research feels like. Real research is not the only thing. Sometimes what worked for me is what made me feel like a total fool. Over the days, weeks, and years, you get more experienced and stop making silly mistakes. You develop intuition about what could be wrong. But still, there is always something that makes no sense, fails, or stops working. There is no glamour, unlike in the movies (I’m looking at you, Tony Stark). You are earning your PhD by trial and error; it is not the essential, you can find something nobody in the history of humanity has ever seen before.

That moment, when you are the first human being nature gifts with one of its many secrets, is what keeps you going. The secret might not be a unicorn with huge implications, but it might be something small, silly maybe, but the consequences are still important. And you still have the “what if”

A gigantic stream of ideas fills your mind and won’t let you sleep. But the world is big with lots of brilliant and capable people, who are just as sleepless as you. We are all different, and being smart is a good thing, but it’s not the only thing. Sometimes what worked for somebody else might not work for you, and personal traits also play a role that increases your chance of serendipity. In the end, what is important is the insight you gain about a particular problem or phenomenon. Memorizing equations, numbers, or concepts does not get you too far. The more you focus on the insight, the more you develop “range,” making you able to see the big picture and understand the consequences and possible caveats. You get to the point where you can feel the answer to a question but not necessarily know how to get there. More careful thinking gets you to the “how.”

After all, unicorns are always somewhere in the jungle waiting to be found. Donkeys and purple horses guide our path.

J. DAVID WONG-CAMPOS

is a graduate student in the Cohen lab where he works on ion trap based quantum computers.

Mental health during Covid-19

I would like to begin by stating that I am not a mental health professional, and these are just some of my observations and experiences. While many of you, when I left CCB on March 12, I had no idea that I would not be back in the building anytime soon. There were glitches and challenges with everything that has happened since that day. We are constantly hearing or seeing news stories about Covid-19, whether it is an article or local to my city, from the non-essential, you can find something nobody in the history of humanity has ever seen before. During this time, there is always something that makes no sense, fails, or stops working.

At some point, you realize, “Oh, I need more battery power.” You plug the computer into the wall and see the screen light up. Nice. Why wouldn’t it work? You keep doing your work and get excited with the feeling of making steady progress. You are so close to your goal. Then things break. 

Your laptop stops charging, and you realize something must be wrong with your charger since you know it is unlikely your computer got damaged.

Common sense tells you to check your charger. Visibly, there is nothing wrong with it, but, sadly, it is the only one you have. So, you tell yourself: “I know how chargers work; I can fix this!”

You grab a screwdriver, open the charger, and see a mini city of electronics parts. This will be more complicated and time-consuming than you initially thought.

You spend hour after hour bent over the mini city, looking for busted components, hooking up testing equipment borrowed from other colleagues, and see a mini city of electronics parts. This will be more complicated and time-consuming than you initially thought.

That is how research feels like. Real research is not the only thing. Sometimes what worked for me is what made me feel like a total fool. Over the days, weeks, and years, you get more experienced and stop making silly mistakes. You develop intuition about what could be wrong. But still, there is always something that makes no sense, fails, or stops working. There is no glamour, unlike in the movies (I’m looking at you, Tony Stark). You are earning your PhD by trial and error; it is not the essential, you can find something nobody in the history of humanity has ever seen before.

That moment, when you are the first human being nature gifts with one of its many secrets, is what keeps you going. The secret might not be a unicorn with huge implications, but it might be something small, silly maybe, but the consequences are still important. And you still have the “what if”

A gigantic stream of ideas fills your mind and won’t let you sleep. But the world is big with lots of brilliant and capable people, who are just as sleepless as you. We are all different, and being smart is a good thing, but it’s not the only thing. Sometimes what worked for somebody else might not work for you, and personal traits also play a role that increases your chance of serendipity. In the end, what is important is the insight you gain about a particular problem or phenomenon. Memorizing equations, numbers, or concepts does not get you too far. The more you focus on the insight, the more you develop “range,” making you able to see the big picture and understand the consequences and possible caveats. You get to the point where you can feel the answer to a question but not necessarily know how to get there. More careful thinking gets you to the “how.”

After all, unicorns are always somewhere in the jungle waiting to be found. Donkeys and purple horses guide our path.

J. DAVID WONG-CAMPOS

is a graduate student in the Cohen lab where he works on ion trap based quantum computers.

AFTER THE CLOSE

I asked the department about arranging vir- tual fitness classes, which I had found very helpful. Once I started doing those, I looked more into virtual classes that I could do out- side of working hours. I have found that Tube TV has awesome fitness classes, many of which can be done with no equipment at all. That has been great, especially since it has been so hard to find any type of fit- ness equipment anywhere! A friend also told me about the Peloton app (EF have talked to you about fitness classes recently; I have told you about the Peloton app). You don’t need any of the Peloton equipment, and there are thousands of classes available (they are still offering a free 30-day free trial, so check them out if you are interested).

Something else that I have done which I haven’t done in many, many years has been jigsaw puzzles. I didn’t even realize how much I enjoyed working on these until I was a few hours into one, and I was de- termined to get it done! Once I completed my first jigsaw puzzle, I googled their ben- efits: one of them was stress relief. Again, I am no expert, but I can say that working on a puzzle felt calming and relaxing, es- pecially with everything that is currently going on around us. The only time I was not relaxed was when I borrowed one from my neighbor. After spending hours on it, there was ONE piece missing. I thought I was over it, but I guess not since I just brought it up.

If anybody has questions about anything that I wrote or if you want to share something that you have found helpful, feel free to reach out to me and let’s chat!

FELIX NEGRON

NEGRON is CCB’s Manager of Junior Faculty Support. Here, he poses with his favorite running buddy, Ella the chihuahua, after a 15 kilometer race.

PHOTO COURTESY OF FELIX NEGRON
Everyone seems to have an opinion about which foods to eat or avoid, how to lose weight (and keep it off!), and which superfood to horde. But there’s a better place to search for health secrets than in a tropical berry: the human gut.

Each person’s gut microbiome — the trillions of bacteria living inside the human gastrointestinal tract — is different. And individual strains of bacteria interact with food, drugs, vitamins, and toxins in their own way, which means no single diet, or drug, is right for everyone.

Microbial chemist Emily Balskus recently discovered that certain bacteria eat the common Parkinson’s drug L-dopa and convert it to dopamine, which can dampen the effects of the treatment and cause painful or even life-threatening side-effects. In a new study published in eLife, she and her team took this discovery further, identifying how and why gut microbes metabolize dopamine. In the process, they discovered an entirely new class of enzymes (the tools bacteria use to perform complex chemistry) that degrade chemicals essential for neurological health, like dopamine, but also help digest foods like nuts, berries, and tea, releasing nutrients that may impact human health. Knowing how foods interact with microbial enzymes could, one day, help researchers identify the best diet for each human and their personal microbiome.

There’s more: In animals, plants, and soil, the team discovered similar enzymes with powerful capabilities. Some produce cancer-fighting molecules, while others break down chemicals left over from industrial waste.

“It ended up being a much larger journey,” said Vayu Maini Rekdal, first author on the paper and a Ph.D. candidate in the Molecules, Cells and Organisms program in the Graduate School of Arts and Sciences. “What we study in the human gut is very important for human health and disease and for understanding the
interplay between microbes and the human body, but it can also highlight these broader themes that are relevant across ecosystems and across different microbial communities."

The study’s sweeping results came from one question: Why does a human gut microbe eat dopamine? After months analyzing how the bacteria F. prausnitzii interacts with the neurotransmitter, Balskus and her team discovered the simple answer: Eating dopamine helps them grow. By modifying a molecule’s catalytic group—an organic compound that occurs naturally in, for example, fruits, vegetables and dopamine—the microbe gets a Darwinian boost. But the team learned something surprising, too: The microbial enzyme that consumes dopamine specializes in processing that chemical over all others present in the gut.

“That’s a really cool finding, because it suggests that this enzyme has evolved for the purpose of metabolizing dopamine,” a chemical typically associated with the brain, Maini Rekdal said. Intrigued, he and his lab mates decided to track down similar enzymes that also modify catechol groups. One group, he found, gives humans a health benefit, breaking down foods like pomegranate, chocolate, berries, and coffee to release polyphenols, which may protect against certain diseases and prolong life. These enzymes specialize, too. “Maybe one day I drink coffee, and the microbe recognizes a catechol from coffee, turns on the right enzyme and metabolizes it,” Rekdal said. But what if a coffee drinker, the bacteria might swap a coffee enzyme for a chocolate one. Enzyme upkeep would allow them to grow on different things depending on what’s available. Still, that means without the right enzyme, some people can’t benefit from those health-promoting polyphenols.

Last summer, Maini Rekdal planted dopamine and chemicals from coffee, tea, and chocolate in a variety of mammalian fecal samples to determine whether they share similar enzymes. They do. He found traces of the same chemistry in foxes, dogs, rats, all-paca, guinea pigs, pigs, and wolves. “Humans and wolves have very different lifestyles,” he said. “That this enzyme is found across species indicates its widespread value for microbial life.

The team even found analogous enzymes in soil microbes, where they play a role in cleaning up the Earth’s chemical melting pot, Szostak said. “For entirely different purposes. One produces a molecule that serves as a potent anti-cancer treatment. Maini Rekdal speculates bacteria may have made this molecule for chemical warfare — attacking enemy microbes. Another uses a similar enzyme to break down chemicals and clean up the surrounding soil, a tool that could be appropriated to rid land of toxic pollutants.

The team identified many more related enzymes — in soil and the human gut — that fall under this new classification. But they don’t yet know what valuable or damaging purpose they serve. “Our study now sets the stage for further investigations of the chemical mechanisms and biological consequences of catechol dehydroxylation in the human body and beyond,” Balskus said.
The future of computation is bright — literally.

Researchers from the Harvard John A. Paulson School of Engineering and Applied Sciences (SEAS), in collaboration with researchers at McMaster University and University of Pittsburgh, have developed a new platform for all-optical computing, meaning computations done solely with beams of light.

“Most computation right now uses hard materials such as metal wires, semiconductors, and photodiodes to couple photons to light,” said Amos Meeks, a graduate student at SEAS and co-first author of the research. “The idea behind all-optical computing is to remove those rigid components and control light with light. Imagine, for example, an entirely soft, circuitry-free robot driven by light from the sun.”

These platforms rely on so-called non-linear materials that change their refractive index in response to the intensity of light. When light is shone through these materials, the refractive index in the path of the beam increases, generating its own, light-modeled guide and manipulate light, said co-author Derek Morim, a graduate student in Saravanamuttu’s lab.

“Materials science is changing,” said Joanna Aizenberg, the Amy Smith Berylson Professor of Materials Science at SEAS and co-senior author of the study. “Self-regulated, adaptive materials capable of optimizing their own properties in response to environment replace static, energy-intensive materials such as metal wires. Our reversibly responsive material that controls light at exceptionally small intensities is yet another demonstration of this promising technological revolution.”

Biophysics • Protein Folding

THE RIGHT FOLD

How kinks in protein folding could help researchers design new drugs and even fight COVID-19

By Jordan Wilkerson (Anderson Lab)

Right now, your body is making trillions of proteins essential for even basic tasks. You can read this article, for example, thanks to the proteins that make your eye lenses transparent.

Understanding how proteins fold is crucial since the build-up of these misfolded molecules can cause serious health issues in aging human bodies. Misfolded proteins in the eyes, for instance, clump together to keep them from refolding to the correct shape — this can result in vision issues.

“The protein misfolding process goes wrong as we age. Just as drugs can help researchers design new drugs and even fight COVID-19, the long strings of amino acids could be captured by a computer model: “There’s no reason to believe things can’t be captured by a computer model. “There’s no reason to believe things can’t be captured by a computer model. We’re not making predictions, we’re just looking at data.”

A new generation of researchers is using this technique to help bring true all-optical computing to reality. “There are new materials being created all the time, and we can design new materials to interact with light,” said Meeks.

The future of computing is bright — literally.

Researchers from the Harvard John A. Paulson School of Engineering and Applied Sciences (SEAS), in collaboration with researchers at McMaster University and University of Pittsburgh, have developed a new platform for all-optical computing, meaning computations done solely with beams of light.

“Most computation right now uses hard materials such as metal wires, semiconductors, and photodiodes to couple photons to light,” said Amos Meeks, a graduate student at SEAS and co-first author of the research. “The idea behind all-optical computing is to remove those rigid components and control light with light. Imagine, for example, an entirely soft, circuitry-free robot driven by light from the sun.”

These platforms rely on so-called non-linear materials that change their refractive index in response to the intensity of light. When light is shone through these materials, the refractive index in the path of the beam increases, generating its own, light-modeled guide and manipulate light, said co-author Derek Morim, a graduate student in Saravanamuttu’s lab.

“Materials science is changing,” said Joanna Aizenberg, the Amy Smith Berylson Professor of Materials Science at SEAS and co-senior author of the study. “Self-regulated, adaptive materials capable of optimizing their own properties in response to environment replace static, energy-intensive materials such as metal wires. Our reversibly responsive material that controls light at exceptionally small intensities is yet another demonstration of this promising technological revolution.”
In the early days of the COVID-19 pandemic, most of Eric Fischer's researchers were home in self-quarantine. But those permitted to work shared space at the Dana-Farber Cancer Institute with doctors, nurses, and patients, who were potentially COVID-19 positive. So, Fischer thought, why not test the Institute's employees for antibodies?

But he ran into a problem: Current serological tests that detect COVID-19 antibodies are almost all based on a technology called ELISA, an expensive and time-consuming test with multiple complex steps. “I realized that ELISA is a pretty ridiculous, complicated assay format,” Fischer said.

In March 2020, Fischer, an associate professor at the Harvard Medical School, independent investigator and co-director of the Center for Protein Degradation at Dana-Farber Cancer Institute, teamed up with Ralph Mazitschek, an assistant professor at the Harvard Medical School and Massachusetts General Hospital. With the Fischer lab’s expertise in small molecules and the Mazitschek group’s knowledge of infectious diseases and testing technology, the team set out to design a simpler, cheaper, and scalable test.

A few months later, they did just that: One of their tests, the duo estimated, would cost just one dollar to perform. And, Mazitschek said, they already have enough to test every single person once in the U.S. The cost and simplicity of their test could make it possible for labs across the globe, even those with few resources, to perform population-wide screening for COVID-19 antibodies. And, when vaccines start to emerge, they could help monitor their effectiveness.

“This has a real chance of becoming a standard way of testing for COVID antibodies,” said Mazitschek.

The team reported their results in a preprint last September; the work is now undergoing peer review.

For their test, the team chose to side-step ELISA technology and improve a different assay called a TR-FRET (Time-Resolved Förster Resonance Energy Transfer). TR-FRET technology is not new. But, until now, the required components were either too expensive and complicated to make or were not suitable to detect antibodies.

“If you were to buy a milligram of the reagents performing best for these assays, it would cost you around half a million dollars,” said Connor Payne, a Ph.D. candidate in chemistry in the Graduate School of Arts and Sciences and a member of the Mazitschek lab. In the last year, he whittled down the 25-step process (which Mazitschek said only the most experienced chemists could perform) to about 11 and developed new, easy-to-access TR-FRET reporter molecules that outperform the commercial versions.

“We pretty much eliminated the cost-prohibitive nature of these reagents while still maintaining their integrity and performance,” said Payne. Now, he can make grams at a time. Sold for market value, those viials are worth a hundred million dollars. Of course, their faster, simpler process will bring that price way down.

Radoslaw Nowak — worked to incorporate it into a “shake-and-bake” style COVID-19 antibody test.

Two months after Payne perfected the solution, two Fischer lab members — postdoctoral scholar Hong Yue and senior scientist Padmawati Srivastava — worked to incorporate it into a “shake-and-bake” style COVID-19 antibody test.

Instead of the ELISAs many steps, which slow the process and introduce opportunities for user error, the team’s new test needs just a finger prick worth of diluted patient serum mixed into their solution, incubated for about an hour, and read out in a few seconds. “It really is as simple as that,” Payne said.

Because the ELISA works by increasing the read-out signal, the test is also prone to false positives. Rather than amplifying the signal, the Fischer and Mazitschek team extended the life of their signal by almost a million, eliminating the risk of reading false positives. Without signal amplification, said Fischer, the test could produce false negatives, but they’ve yet to see that happen.

With the new test, an operator could analyze 400 patient samples in one hour (compared to the ELISA’s 100 samples in one day). To speed the process further, Fischer said, they need a faster way to collect patient samples. “That becomes the bottleneck. It’s no longer the assay.” Next, he hopes to design a method for patients to collect their own samples at home to send in to a lab.

And, as COVID-19 vaccines become available to the general public, the team’s assay could track their effectiveness, measuring post-vaccination antibody levels. Though, Mazitschek said, their current version might need some tweaks to identify different types of antibodies, which, he said, would be as easy as changing the adapter on a garden hose.

The Mazitschek lab can also easily adapt their technology to search for a vast range of pathogens — like malaria, their original target — beyond the COVID-19 virus. But for now, the pandemic is their top priority. “We want this to be implemented,” said Payne. “We understand the potential power behind this technology.”

By Caitlin McDermott-Murphy

Illustration by Russell Tate/United Nations

Advances in action

A NEW GOLD STANDARD TEST FOR COVID-19 ANTIBODIES
In the whisker-flick experiment, the stimulus caused the expected result: a neuron spike. But when the team artificially excited the same neuron using a laser, and then added a whisker flick, the neuron went quiet. Why? The team discovered that neurons in layer one maintain a careful balance between excitation and inhibition. If too many neurons are firing at once, they suppress others from firing. “The circuit acts like a novelty detector,” Cohen said. Sudden inputs can spark most neurons to fire, but with long-lasting inputs, most of the neurons inhibit each other and cause the circuit to turn almost completely off. The air puff—a wake-up call for the mouse—added more evidence to this theory. In response to the puff, the few neurons that fired the fastest ended up suppressing their neighbors. If the stimulus is forceful enough, the neurons all spike, competing for dominance, before the winners force the others to quiet down.

Your brain has to ignore all that stuff and only pay attention to the very few things that are actually relevant.” Now, in a paper published in Cell, Cohen and colleagues report new evidence that could help researchers understand how the brain ignores or acts on different information, knowledge that could offer crucial data on how neuronal circuits function and, one day, help researchers understand and treat neurological disease. Cohen didn’t set out to investigate attention. Recently, his lab invented technology that makes electrical impalements flowing through neurons in a live animal brain observable for the brain’s attention. Since the optical tool uses light to record neuronal activity, Cohen and his team will continue to explore how the layer one circuit works to regulate attention, hoping more data can provide critical information on how neuronal circuits work. “If we can understand how the whisker response works,” Cohen said, “we’ll then be in a much better position to understand much more complicated things like vision or hearing.”

Today, the internet is a sensory free-for-all. Pop-up ads burst into articles every few paragraphs, stealing the screen with lollipop colors and music, and shouting product information from unseen corners. The human body is not so different. Every fingernail, elbow, nostril, and eyebrow is constantly vying for the brain’s attention. The human brain has to ignore all that stuff and only pay attention to the very few things that are actually relevant.”

By Caitlin McDermott-Murphy

Getting the Brain’s Attention

New technology helps dissect how the mind ignores or acts on information

Physical Chemistry · Neuroscience · Optogenetics

By Caitlin McDermott-Murphy

In the whisker-flick experiment, the stimulus caused the expected result: a neuron spike. But when the team artificially excited the same neuron using a laser, and then added a whisker flick, the neuron went quiet. Why? The team discovered that neurons in layer one maintain a careful balance between excitation and inhibition. If too many neurons are firing at once, they suppress others from firing. “The circuit acts like a novelty detector,” Cohen said. Sudden inputs can spark most neurons to fire, but with long-lasting inputs, most of the neurons inhibit each other and cause the circuit to turn almost completely off. The air puff—a wake-up call for the mouse—added more evidence to this theory. In response to the puff, the few neurons that fired the fastest ended up suppressing their neighbors. If the stimulus is forceful enough, the neurons all spike, competing for dominance, before the winners force the others to quiet down.

Your brain has to ignore all that stuff and only pay attention to the very few things that are actually relevant.” Now, in a paper published in Cell, Cohen and colleagues report new evidence that could help researchers understand how the brain ignores or acts on different information, knowledge that could offer crucial data on how neuronal circuits function and, one day, help researchers understand and treat neurological disease. Cohen didn’t set out to investigate attention. Recently, his lab invented technology that makes electrical impalements flowing through neurons in a live animal brain observable for the brain’s attention. Since the optical tool uses light to record neuronal activity, Cohen and his team will continue to explore how the layer one circuit works to regulate attention, hoping more data can provide critical information on how neuronal circuits work. “If we can understand how the whisker response works,” Cohen said, “we’ll then be in a much better position to understand much more complicated things like vision or hearing.”

“Right now, your little toe is sending signals up to your brain, as is every square inch of your body,” said Adam Cohen, a professor of chemistry and chemical biology, and of physics, “but most of it is not interesting to your brain. It ignores all of that stuff and only pays attention to the very few things that are actually relevant.”

Now, in a paper published in Cell, Cohen and colleagues report new evidence that could help researchers understand how the brain ignores or acts on different information, knowledge that could offer crucial data on how neuronal circuits function and, one day, help researchers understand and treat neurological disease. Cohen didn’t set out to investigate attention. Recently, his lab invented technology that makes electrical impalements flowing through neurons in a live animal brain observable for the brain’s attention. Since the optical tool uses light to record neuronal activity, Cohen and his team will continue to explore how the layer one circuit works to regulate attention, hoping more data can provide critical information on how neuronal circuits work. “If we can understand how the whisker response works,” Cohen said, “we’ll then be in a much better position to understand much more complicated things like vision or hearing.”

Today, the internet is a sensory free-for-all. Pop-up ads burst into articles every few paragraphs, stealing the screen with lollipop colors and music, and shouting product information from unseen corners. The human body is not so different. Every fingernail, elbow, nostril, and eyebrow is constantly vying for the brain’s attention. The human brain has to ignore all that stuff and only pay attention to the very few things that are actually relevant.”

By Caitlin McDermott-Murphy

In the whisker-flick experiment, the stimulus caused the expected result: a neuron spike. But when the team artificially excited the same neuron using a laser, and then added a whisker flick, the neuron went quiet. Why? The team discovered that neurons in layer one maintain a careful balance between excitation and inhibition. If too many neurons are firing at once, they suppress others from firing. “The circuit acts like a novelty detector,” Cohen said. Sudden inputs can spark most neurons to fire, but with long-lasting inputs, most of the neurons inhibit each other and cause the circuit to turn almost completely off. The air puff—a wake-up call for the mouse—added more evidence to this theory. In response to the puff, the few neurons that fired the fastest ended up suppressing their neighbors. If the stimulus is forceful enough, the neurons all spike, competing for dominance, before the winners force the others to quiet down.

Your brain has to ignore all that stuff and only pay attention to the very few things that are actually relevant.” Now, in a paper published in Cell, Cohen and colleagues report new evidence that could help researchers understand how the brain ignores or acts on different information, knowledge that could offer crucial data on how neuronal circuits function and, one day, help researchers understand and treat neurological disease. Cohen didn’t set out to investigate attention. Recently, his lab invented technology that makes electrical impalements flowing through neurons in a live animal brain observable for the brain’s attention. Since the optical tool uses light to record neuronal activity, Cohen and his team will continue to explore how the layer one circuit works to regulate attention, hoping more data can provide critical information on how neuronal circuits work. “If we can understand how the whisker response works,” Cohen said, “we’ll then be in a much better position to understand much more complicated things like vision or hearing.”
scientists at Bayer, have solved this chemical conundrum. In a study in Nature Chemical Biology, they show that ML210 transforms within the cell into a new molecule, which transforms into a third molecule that then covalently binds GPX4. The mechanism they revealed is extremely unusual and demonstrates an unappreciated way that “pro-drugs” like ML210 can be converted into molecules capable of covalently binding target proteins within cells.

In the work, the scientists describe a new set of compounds that scientists can use to learn more about how cells undergo ferroptosis, a process discovered only a decade ago. In addition, the molecules are starting points for development candidates that can inhibit GPX4 and kill drug-resistant cancer cells not just in a dish, but potentially also in animal models and even patients.

“I remember saying, ‘I fear I’m going to have to start our own.’” One of the great things about this particular industry-academic collaboration is that, "I think we’ve faced in this research," said Eaton. “I don’t think we would have overcome those challenges on our own.”

The assays confirmed that ML210 was, in fact, inhibiting GPX4 through covalent binding, and that it did so much more precisely than the two chloroacetamides.

This hint led Eaton to further chemical detective work, which revealed that ML210 undergoes a couple of unusual, chemical transformations in the cell to gain the ability to bind and inhibit GPX4. ML210 is first transformed into a compound the team dubbed JKE-1674. The cell converts this compound into another unusual molecule called JKE-1777, which is capable of covalently binding GPX4.

Although JKE-1777 is unstable outside of the cell, JKE-1674 and related compounds that the team synthesized are stable and selective for GPX4, and are more suitable than ML210 for use in animal models or perhaps even patients.

In a related paper in the Journal of the American Chemical Society, the researchers describe another set of compounds known as diafluororans that also inhibit GPX4 covalently. While those compounds aren’t as selective as ML210 or JKE-1674 and are unlikely to be used therapeutically, the company’s study helped the scientists make sense of the novel observations made in the ML210 study.

“These compounds are molecular machines that are unprecedented in the history of chemical biology for the unusual multi-layered chemical features that underlie their specificity,” said co-senior author Vasanthi Viswanathan, a postdoctoral associate in the Schreiber lab.

More work remains to determine what cellular processes guide the transformation of ML210 into its active form, and whether any of the molecules can be used in animal models or even in humans as therapeutic compounds. If the molecules or variants of them prove promising as new therapeutics, they might give rise to a new class of drugs that could one day help fight drug-resistant tumors.
EMILY BALSKU S WINS $1M WATERMAN AWARD

The young scientist is recognized once again for harnessing chemistry to transform the study of microbial communities.

Two plush microbes stare up at everyone who visits Emily Balskus’ office. One, a buttercup yellow, mimics the fuzzy hotdog-shaped E. coli. Another, her yeast or Saccharomyces cerevisiae, is just a white sphere with eyes. Far larger than living microorganisms (and far cuter), these cuddly counterparts reveal not just Balskus’ research area, but also her passions today and her subjects. Most people fear the trillions of bacteria that live in and on the human body. But for Balskus, these microbes provide potential solutions to vast problems in human health and medicine ranging from drug metabolism to cholesterol management and even cancer.

“Emily Balskus has opened up novel ways to explore and exploit the chemistry and biology of microbes that live in our bodies and how they are linked to our health,” said Sethuraman Panchanathan, director of the National Science Foundation (NSF). “And we’re already seeing the potential impact.”

In August 2020, Panchanathan announced that Balskus is one of two recipients of the Alan T. Waterman Award, the NSF’s most prestigious prize for scientists under 40 in the United States. Balskus is only the sixth Harvard scientist to win the award. 

“I hope that through receiving this award I can represent in science as well as gain a platform to highlight the challenges we currently face,” said Balskus. “I understand what it’s like to be the new person in a room. What it’s like to not fit in,” said Christina Woo, who traveled from town to town and school to school as a child. Now, she sees that outsider status as a gift, one that gives her an affinity for reaching a broader range of students. This year, she earned national recognition for her uncanny ability to mentor students, with the title Camille-Dreyfus Teacher-Scholar, an honor given to young chemists who excel in the lab and classroom.

In 2020, Brian Liu was one of three faculty members across the University to earn a Star Family Prize for Excellence in Advising. “I remember how much of an impact my college professors had on me when I was a student, which convinced me to pursue a PhD in chemistry,” Liu said. “To see my efforts, to replicate their dedication to education and advising, make a difference to my own students 15 years later is, of the same time, very touching, rewarding, and motivating.”

Xiaowei Zhong was elected into the National Academy of Medicine (NAM) for “pioneering super-resolution imaging and imaging-based single-cell genomics, and for using these methods to uncover novel structures in cells, novel spatial and functional organization of cells in tissues, and examples of how misregulation may cause diseases.” Zhong also earned an award from the Starr-Friedman Challenge for Promising Scientific Research.

David Liu, who received a Star Family Prize for Excellence in Advising in 2020, was elected into two prestigious scientific organizations: The National Academy of Medicine (NAM) and the American Association for the Advancement of Science (AAAS). “Well deserved,” Stuart Schreiber wrote on Twitter after Liu’s induction into the NAM, “not only for transformative science but also mentorship, leadership, and guidance for the nation through the pandemic.”

To study microbes, Balskus shifted into the biological realm, but her work is still fundamentally chemical. Bacteria perform mysterious chemistry, sometimes forging or dismantling molecules using reactions that he beyond the skills of today’s best chemists. So, Balskus hunts for microbial genes that produce enzymes, protein-based catalysts that perform chemical reactions, to understand how and why microbes do what they do.

“Despite the important roles these organisms play in all habitats, we know very little about how they influence surrounding environments and organisms,” Balskus said. “We don’t understand the chemistry they perform. For example, 85 percent of genes in the human gut microbiome can’t confidently be linked to a microbial activity.”

But in her latest work, Balskus and her team linked genes in the human microbiome to microbial activity, mapping, in a way, how some members of the human gut might influence their host. For example, her lab recently discovered how certain microbes break down cholesterol in the human gut. Only some people host those cholesterol-busting bacteria and those who do tend to experience lower levels of blood cholesterol. This finding could lead to new types of treatment to manage high cholesterol levels.

Balskus also discovered that some gut microbes can interfere with drug metabolism, gubbling up 6-afos, for example, before the Parkinosis treatment can reach the brain and help assuage symptoms of the disease. And, her lab played an important role in discovering how E. coli produce a harmful toxin that damages the digestive system and potentially leads to increased risk of colon cancer.

“Much of our work has focused on elucidating how microbes in this environment are performing chemistry — what are the specific catalysts, or enzymes, that they use to perform chemical transformations that are linked to health or disease,” Balskus said. “With this knowledge, we can more accurately predict the chemistry performed by microbial communities, can begin to study its biological consequences, and can even think about developing tools to control it.”

The Waterman Award, Balskus said, will allow her research team to take on higher-risk projects with potentially greater rewards and pursue creative directions that would have been impossible without NSF support.

But Balskus has more than just scientific ambitions. “I hope that by receiving this award,” she said, “I can inspire women and other individuals who are under-represented in science as well as gain a platform to highlight the challenges we currently face.” Growing up, all her science teachers were women, because of that, she didn’t hesitate to pursue a career in science.

“The future of human health, of medicine, needs Emily’s research,” said Catherine Drennan, a professor of biology and chemistry at MIT. “I’m a fan of Emily. I’m just really inspired by her. And I want my 11-year-old daughter to look at her and say, ‘yes, women can do anything.’”
High-resolution, 3D images of human chromosomes in single cells reveal how chromatin structure might influence its function.

FEATURES

CHROMOSOME CLOSE-UPS
Remember those wonky Xs that textbooks teach are chromosomes? Those cartoons were science’s best guess at what chromosomes look like.

Now, Xiaowei Zhuang, the David B. Arnold, Jr. Professor of Science, and four Ph.D. candidates in the Department of Chemistry and Chemical Biology, Department of Physics, Department of Molecular and Molecular Biology and Biophysics Program in the Graduate School of Arts and Sciences—Bogdan Bintu, Seon Kiont, Jun-Han Su, and Pu Zheng—captured high-resolution 3D images of human chromosomes, the intricately organized houses for a human’s entire instruction manual—"their DNA."

Extended in a straight line, the DNA inside a single cell can reach the length of an average bicycle—about six feet. But the 23 pairs of chromosomes inside each cell nucleus are like obsessive-compulsive packrats. They wind genetic material in tight, complex structures. For a human—or any organism—to grow and function properly, cells must constantly divide to replace old, worn-out cells with new ones. A hitch in the chromosome structure could be the death knell of that cell.

Still, for a 3D image of the genome, they needed more—thousands—so they turned to a "multiplexed" approach, which can’t make a comprehensive picture. By connecting the dots—a lot of dots—they could form a fairly comprehensive picture.

But there was a drawback. Previously, the number of loci one could simultaneously image and identify was traditionally limited to the number of color channels that could be discerned in a fluorescence microscope, which is no more than a handful. If there are only a few different hues, only a few loci can be captured in one image, which can’t make a comprehensive picture.

So, Zhuang and her team came up with a multiplexed approach: Image a few different loci, query the signal, and then image a few more in rapid succession. With that technique, each locus gets two identifying marks: color and image round. With that approach, they could image, localize, and identify several tens to hundreds of loci in a few gets a barcode starting with “10.” With ten-bit barcodes, the team could differentiate more than 1,000 loci in just ten rounds of single-color imaging or five rounds of two-color imaging. They also built error-detection into their barcodes, which increased the number of imaging rounds needed but achieved high detection accuracy. Even so, with just a few tens of rounds, they imaged and localized the thousands of loci needed for a comprehensive picture.

“In this combinatorial way, we can increase the number of loci imaged and identified much more rapidly,” said Zhuang. She and her lab developed this approach, called MERFISH (multiplexed error robust fluorescence in situ hybridization), to image the transcriptome, the full suite of messenger RNA.

Now, the team trained MERFISH to capture the 3D genome, imaging about 2,000 chromatin loci per cell, or enough to form a high-resolution image of what the structure looks like in its native habitat. But they didn’t stop there: They also imaged transcriptivity (when RNA replicates genetic material from DNA) of more than 1,000 genes and nuclear structures, including nuclear speckles and nucleoli. With their 3D Google Maps of the genome, they can start to analyze how structure regulates genome function.

Researchers already know chromatin has different compartments and, within those, different domains, but what these terrains look like from cell to cell and how they function has been largely unknown. With their high-resolution images, the team determined that compartments of active chromatin (gene-rich chromatin prone to transcription) tend to flock to other active chromatin compartments. The same is true for inactive chromatin compartments, though active chromatin compartments hunt for each other over greater distances. They also found that the local chromatin environment impacts transcription activity. Genomic loci residing in an environment enriched with active chromatin tend to have higher transcription activity. Structure does influence function.

The team also discovered high variability between domains even in cells that are, otherwise, functionally similar. Even in their cell cultures—which were full of identical cells—no two chromosomes looked the same. Since these differences increase in the huge variety of cells that make up the human body, far more work needs to be done to build a Google Maps for all cell types.

“Trying to be possible to be possible to build just on our work,” Zhuang said. “We need to build on many, many labs’ work in order to have a comprehensive understanding.” That’s why Zhuang not only shares instructions for other labs to replicate their experiments, she also offers trainings. There are too many biological mysteries for one group to solve.

What about the mystery of those oblong Xs in biology textbooks? Do chromosomes really look like that? Only in a small fraction of the time. Most of the time, they twist into other shapes suitable to their function. Now, the Zhuang lab has the pictures to prove it.
In 2020, the Crispr gene editing technology known as base editing (or rather the restless scientists behind the technology) got busy solving unreachable genetic problems like the rapid-aging disease, progeria, with greater precision and new abilities.
Promise to restore hearing

In a first, researchers use base editing to correct recessive genetic deafness and restore partial hearing

BY Caitlin McDermott-Murphy

When Wei-Hsi (Ariel) Yeh was a young undergraduate student, one of her close friends went from normal hearing to complete deafness in the span of one month. He was 29 years old. Doctors didn’t know why then and they still don’t. Frustrated and fearful for her friend, Yeh, who graduated last month with a Ph.D. from the Graduate School of Arts and Sciences, dedicated her research in chemistry to solving some of the vast genetic mysteries behind hearing loss.

In the United States, one in eight people aged 12 years or older has hearing loss in both ears. While technologies like hearing aids and cochlear implants can amplify sound, they can’t correct the problem. But gene editing could — genetic anomalies contribute to half of all cases.

About two years ago, Yeh and David R. Liu, Thomas Dudley Cabot Professor of the Natural Sciences and a member of the Broad Institute and the Howard Hughes Medical Institute (HHMI), repaired a dominant mutation and prevented hearing loss in a mouse model for the first time. But, Liu said, “Most genetic diseases are not caused by dominant mutations, they’re caused by recessive ones, including most genetic hearing losses.”

Now, in a new study, Liu, Yeh and researchers at Harvard University, the Broad Institute, and the Howard Hughes Medical Institute achieved another first: They restored partial hearing to mice with a recessive mutation in the gene TMC1 that causes genetic deafness and restore partial hearing in mice at just 4 weeks of age.

Jeffrey Holt, Professor of Otolaryngology and Neurology at the Harvard Medical School and an author on the paper, successfully treated TMC1-related deafness with gene therapy by siting cells with healthy versions of the gene in among the unhealthy to counteract the disease-causing mutation. But Volha (Olgia) Shubina-Alrnik, a postdoctoral fellow in the Holt lab, said gene augmentation therapy may have a limited duration. “That is why we need more advanced techniques such as gene editing, which may last a lifetime.”

Yeh spent designing a base editor that could find and erase the disease-causing mutation and replace it with the correct DNA code. But even after she demonstrated good results in vitro, there was a problem: Base editors are too large to edit the genome of an early stage embryo, adeno-associated virus or AAV. To solve this problem, the team, led by Liu lab member Jonathan Levy, split the base editor in half, sending each piece in with its own viral rescue. “But for recessive diseases,” Liu said, “you can’t do that. By definition, the recessive allele means that you have two bad copies. So, you can’t just destroy the bad copy.” You have to fix one or both.

To hear, animals rely on hair cells in the inner ear, which ripple under the pressure of sound waves and send electrical impulses to the brain. The recessive mutation to TMC1 that Liu and Yeh hoped to correct caused rapid deterioration of those hair cells, leading to profound deafness in mice at just 4 weeks of age.

The team, led by Liu lab member Aleinik, a postdoctoral fellow in the Holt lab, said gene augmentation therapy may have a limited duration. “That is why we need more advanced techniques such as gene editing, which may last a lifetime.”

After the treatment, Yeh and team performed an informal test. They clapped their hands. Mice that had previously lost all hearing ability, jumped and turned to look. Formal tests revealed the base editor worked, at least in part: Treated mice had partially restored hearing and could respond to loud and even some medium sounds, Yeh said.

Of course, more work needs to be done before the treatment can be used in humans. Unedited cells continued to die, causing deafness to return even after the base editor restored function to others.

But the study also proved that the clancet-dentinc AAV delivery method works. Already, Liu is using AAV to tackle other genetic diseases, including progeria (premature aging), sickle cell anemia, and degenerative motor diseases. “We’re actually going after quite a few genetic diseases now, including some prominent ones that have caused a lot of suffering and energized pretty passionate communities of patients and patient families to do anything to find a treatment,” Liu said. “For progeria, there’s no cure. The best treatments extend a child’s average lifespan to about 14 to 14.5 years.”

For Yeh, whose friend is still living with hearing loss, genetic deafness remains her primary target. “There’s still a lot to explore,” she said. “There’s so much unknown.”

Where the BEs are

BE-Hive, a new machine learning model, predicts which base editor performs best to repair thousands of disease-causing mutations

BY Caitlin McDermott-Murphy

Gene editing technology is getting better and growing faster than ever before. New and improved base editors — an especially efficient and precise kind of genetic corrector — inch the tech closer to treating genetic diseases in humans. But, the base editor boom comes with a new challenge: Like a massive key ring with no guide, scientists can sink huge amounts of time into searching for the best tool to solve genetic malfunctions like those that cause sickle cell anemia or progeria (a rapid aging disease). For patients, time is too important to waste.

“New base editors come out seemingly every week,” said David Liu, Thomas Dudley Cabot Professor of the Natural Sciences and a core institute member of the Broad Institute and the Howard Hughes Medical Institute (HHMI). “The progress is terrific, but it leaves researchers with a bewildering array of choices for what base editor to use.”

Liu invented base editors. Fittingly, he and his research team have now invented a way to identify which is most likely to achieve desired edits, as reported in Cell. Using experimental data from editing more than 34,000 target sites in human and mouse cells with 11 of the most popular base editors (BEs), they created a machine-learning model that accurately predicts base editing outcomes, Liu said. The library, called BE-Hive, is available for public use. But the effort produced more than a neat catalog of BEs; the machine-learning model discovered new editor properties and capabilities that humans failed to notice.

“If you set out to use base editing to correct a single disease-causing mutation,” said Mandana Arbab, a postdoctoral fellow in the Liu lab and co-first author on the study, “you’re left with a mass of possible ways to do it and it is difficult to know which ones are most likely to work.”

Base editors may be more precise than other forms of gene editing, but they can still cause unwanted, often unpredictable, edits

“Most genetic diseases are not caused by dominant mutations, they’re caused by recessive ones, including most genetic hearing losses.”
The genome in mitochondria — the cell’s energy-producing organelles — is involved in disease and key biological functions, and the ability to precisely alter this DNA would allow scientists to learn more about the effects of these genes and mutations. But the precision editing technologies that have revolutionized DNA editing in the cell nucleus have been unable to reach the mitochondrial genome. Now, a team at the Broad Institute of MIT and Harvard, and the University of Washington School of Medicine has broken this barrier with a new type of molecular editor that can make precise DNA changes in mitochondrial DNA. The editor, engineered from a bacterial toxin, enables modeling of disease-associated mitochondrial DNA mutations, opening the door to a better understanding of genetic changes associated with cancer, aging, and more.

New molecular tool edits mitochondrial DNA precisely

An engineered bacterial toxin is a key part of a gene editor that can make single-base changes in human mitochondria

The genome in mitochondria — the cell’s energy-producing organelles — is involved in disease and key biological functions, and the ability to precisely alter this DNA would allow scientists to learn more about the effects of these genes and mutations. But the precision editing technologies that have revolutionized DNA editing in the cell nucleus have been unable to reach the mitochondrial genome. Now, a team at the Broad Institute of MIT and Harvard, and the University of Washington School of Medicine has broken this barrier with a new type of molecular editor that can make precise DNA changes in mitochondrial DNA. The editor, engineered from a bacterial toxin, enables modeling of disease-associated mitochondrial DNA mutations, opening the door to a better understanding of genetic changes associated with cancer, aging, and more.

The work is described in Nature, with co-first authors Beverly Mok, a graduate student at the Broad, and Marcos de Moraes, a postdoctoral fellow at the University of Washington (UW).

The work was jointly supervised by Joseph Mougous, professor of microbiology and an investigator at the Howard Hughes Medical Institute (HHMI), and David Liu, the Richard Merkin Professor and director of the Merkin Institute of Translational Genomics and Medicine. Liu is also the Richard Merkin Professor of chemistry and chemical biology at Harvard University, and HHMI investigator.

“The team has developed a new way of manipulating DNA and used it to precisely edit the human mitochondrial genome for the first time, to our knowledge — providing a solution to a long-standing challenge in molecular biology,” said Liu. “The work is a testament to collaboration in basic and applied research, and may have further applications beyond mitochondrial biology.”

Most current approaches to studying specific mutations or normal DNA involve using patient-derived cells, or a small number of animal models, in which mutations have occurred by chance. “But these methods pose major limitations, and creating new, defined models has been impossible,” said co-author Vamsi Mootha, institute member and co-director of the Metabolism Program at Broad. Mootha is also an HHMI investigator and professor of medicine at Massachusetts General Hospital.

While CRISPR-based technologies can rapidly and precisely edit DNA in the cell nucleus, greatly facilitating model creation for many diseases, these tools haven’t been able to edit mitochondrial DNA because they rely on a guide RNA to target a location in the genome. The mitochondrial membrane allows proteins to enter the organelle, but is not known to have accessible pathways for transporting RNA.

One piece of a potential solution arose when the Mougous lab identified a toxic protein made by the pathogenic Burkholderia cenocepacia. This protein can kill other bacteria directly changing cytosine (C) to uracil (U) in double-stranded DNA.

“What’s special about this protein, and what suggested to us that it might have unique editing applications, is its ability to target double-stranded DNA. All previously described deaminases that target DNA work only on the single-stranded form, which limits how they can be applied to mitochondria,” said Mougous. His team determined the structure and biochemical characteristics of the toxin, called DdA.

“We realized that the properties of this bacterial warfare agent could allow it to be paired with a non-CRISPR-based DNA-targeting system, raising the possibility of making base editors that do not rely on CRISPR or on guide RNAs,” explained Liu. “It could enable us to finally precisely model genome editing in one of the last corners of biology that has remained untouched by such technology — mitochondrial DNA.”

The team’s first major challenge was to eliminate the toxicity of the bacterial agent — what Liu described to Mougous as “taming the beast” — so that it could edit DNA without damaging the cell. The researchers divided the protein into two inactive halves that could edit DNA only when they combined. The two halves can recognize each other, the complex reassembles into its active form, and converts C to U at that location — ultimately resulting in a C-to-U mismatch base editor, called DdA-derived cytosine base editor (DdA-CBE). The team tested DdA-CBE on five genes in the mitochondrial genome in human cells and found that DdA-CBE installed precise base edits in up to 50 percent of the mitochondrial DNA. They focused on the gene ND4, which encodes a subunit of the mitochondrial enzyme complex I, for further characterization. Mootha’s lab analyzed the mitochondrial physiology and chemistry of the edited cells and showed that the edited mitochondria functioned normally.

“This is the first time in my career that we’ve been able to engineer a precise edit in mitochondrial DNA,” said Mootha. “It’s a quantum leap forward — if we can make targeted mutations, we can develop models to study disease-associated variants, determine what role they actually play in disease, and screen the effects of drugs on the pathways involved.”

One goal for the field now will be to develop editors that can precisely make other types of genetic changes in mitochondrial DNA.

“A mitochondrial genome editor has the long-term potential to be developed into a therapeutic to treat mitochondrial-derived diseases, and it has more immediate value as a tool that scientists can use to better model mitochondrial diseases and explore fundamental questions pertaining to mitochondrial biology and genetics,” said Mougous.

The team added that some features of DdA-CBE, such as its lack of RNA, may also be attractive for other gene-editing applications beyond the mitochondria.
Luke Koblan sat at his desk, staring at some data. Excited but baffled, the grad student thought, there's no way those numbers could be right. He shared the results with his boss, Professor David Liu, and now four years later, that data spurred a team of scientists from the Broad Institute of MIT and Harvard (including Koblan and Liu), the National Institutes of Health, and Vanderbilt University Medical Center, to achieve an almost unbelievable leap for the CRISPR gene-editing tool known as base editing, moving the technology a critical step closer to being a treatment for progeria, a deadly premature aging disease.

Several hundred children worldwide live with the malady. In most cases, just one small error involving one of the four main bases, or building blocks, of DNA — a thymine (T) in place of a cytosine (C) at one position in just one copy of the lamin A gene that causes the body to produce a toxic protein (meaning, the gene editor did not cause any detected unwanted edits, an important sign for the safety of a potential new treatment).

Though very promising, the team still needed to verify the treatment would work in live animals. Using the same progeria mouse model (in which mice carry two copies of the human lamin A gene variant that causes the disease), they delivered the treatment either three or 14 days after birth (roughly analogous in maturation level to one and five years of age in a human). When mice with progeria reach six months old, the disease has already caused rapid deterioration of blood vessels. Healthy cells die off, scar tissue builds up. But mice treated with the team's base editor saw almost 100 percent restoration of these especially vulnerable cells. "The aorta cross-sections were statistically indistinguishable from a wild-type mouse," said Koblan. Untreated mice lived an average of 215 days (just over seven months); treated mice lived a median of 510 (just under a year and a half) — a 137 percent extension of their lifespan.

In about half of all known disease-causing mutations are single-letter errors (like progeria), other scientists could use this study as a guide to hone base editors to cure far more genetic disorders in humans. "But mice certainly aren't humans," said Collins in an NIH Director's Blog post about the study's results. While he's hopeful the technique could lead to a cure for progeria, more work needs to be done to ensure the treatment is safe for humans.

While the team observed no significant off-target edits, some of the longest-living mice developed liver tumors, a known complication when using adenovirus-associated viruses (AAV) to deliver genes into mice that are allowed to live into old age. The side effect has yet to be observed in humans, said Koblan, but to be safe, they hope to eliminate the complication in mice prior to human use. Also, some base editors discovered after the study's launch have higher editing efficiencies and could be effective with lower doses of the virus. Ongoing and future studies will search for the most ideal base editor, treatment timing, and viral delivery method while monitoring where the editor goes and how it performs once injected.

Still, some scientists are eager to start clinical trials soon. "We will find a way to get this done for these kids," said Leslie Gordon, a Brown University physician whose son Sam died from progeria, in an article in Science. Gordon co-founded the Progeria Research Foundation, which provided the skin cells for the study. Koblan, who met Gordon mid-project, said her work is an important reminder to other scientists that the patient is central. "Once you see the consequences of what you work on, you get a better perspective on what you're doing and why you're doing it," he said. "It's no longer just an intellectual challenge, it's "I have to get this right, and if I don't, there are consequences."
Everyone knows that telltale pine forest smell. Candies and deodorants try to duplicate the scent. The most iconic air fresheners are even shaped like little pine trees. But that perfume may not be so innocent.

“The plants don’t do this because we find it pleasurable to walk around in a pine forest,” said Frank Keutsch, Professor of Chemistry and Chemical Biology at Harvard. Although scientists have demystified much of plant chemistry, some questions — like why pine forests smell so darn good — still don’t have a clear answer.

For Keutsch, an atmospheric chemist, this question is intriguing for reasons far more important than fragrance. Pine scent comes from a collection of molecules known as volatile organic compounds (VOCs). When trees emit these chemicals, they can react with oxidants to form other pollutants like particulate matter and ozone, both of which can impact climate change and also respiratory diseases, potentially even COVID-19.

To figure out exactly how forests impact air quality and human health, experts like Keutsch first need to understand the chemical chaos of the outdoor environment. So, once the Joshes collect enough data in a controlled space, they can backtrace the amount of VOC that was originally emitted. “That could help scientists understand how particulate matter and ozone are produced from VOC oxidation.”

In the summer of 2016, Shutter visited a Michigan forest that has returned to near-pre-industrial conditions and took HCHO measurements. His data showed something unusual: There was far more HCHO floating around than atmospheric models predicted. Keutsch came up with a hypothesis: maybe HCHO is not just a byproduct; maybe trees emit it from their leaves.

Back in the lab, the Joshes tested the theory. In a basement room the size of a garage, they grew red oak saplings, a common species in that Michigan forest. They placed the leaves in a softball-sized glass enclosure with precisely controlled temperature, humidity, carbon dioxide, and lighting and introduced the tiniest amount of HCHO, 100,000 times less than the concentration of carbon dioxide in outdoor air.

The Keutsch lab’s laser-based instrument is precise enough to pick up even these trace concentrations. Contrary to Keutsch’s hypothesis, the Joshes discovered their leaves did not emit HCHO under ambient conditions in the forest — rather, they absorbed it. That meant the models accounted for even less of the high levels of HCHO Shutter measured in Michigan. “Something in our understanding is wrong,” Keutsch said. “What can possibly account for this level of HCHO in pristine forests?”

He doesn’t have an answer, but he does have a new hypothesis. Trees may absorb HCHO, but other gases perform more complex interactions with trees. Some, like organic peroxides, react with leaves and return to the atmosphere as different, sometimes more harmful, molecules, Keutsch said. Maybe, he said, the most abundant of these peroxides — isoprene hydroperoxide, or ISOPOOH — acts with leaves to form HCHO.

If not for the campus shutdown due to COVID-19, the Joshes would be testing this hypothesis. Since the Keutsch lab and NASA demonstrated that ISOPOOH is converted to HCHO on metal surfaces, leaf surfaces could potentially do the same.

Still, plants perform chemical reactions — like those responsible for that rich pine aroma — that scientists don’t yet understand. And a lab, of course, cannot replicate the chemical chaos of the outdoor environment. So, once the Joshes collect enough data in a controlled space, they will take their experiment outside, partnering with plant scientists to investigate how different species react to pre-industrial versus modern atmospheric chemicals.

Our main goal, Cox said, is to collect precise data on atmosphere and plant interactions from pre-industrial to modern conditions. “It’s really about trying to understand all these fundamental processes,” Cox said, “so that we know what chemistry is going on that drives air pollution and climate.”
Let the light shine in

This fall, PS10 students couldn’t go to lab, so they made one at home.
Jeremy Rasmussen
Benjamin LaFond

their spectrometer, they could analyze exactly how acid forces vinegar—their solution morphed into a fluorescent purple. With blue butterfly pea flower tea. When they added acid—lemon or

to analyze a very complex concept: the quantum na

trometer “kit.” He cut cardboard with a razor blade, tinkered with the circuitry, and designed code. He built dozens of prototypes, which, Hsu said, are “starting to take up way too much room in my tiny apartment.”

In October, when PS10 students constructed Hsu’s final spec

trometer to detect infrared light, which

over Zoom, PS10 students held up their homemade spectrometers, which

Over, the summer, when an in-person semester seemed less likely, Hsu scrambled to invent a build-it-yourself spectrometer “kit.” He cut cardboard with a razor blade, tinkered with the circuitry, and designed code. He built dozens of prototypes, which, Hsu said, are “starting to take up way too much room in my tiny apartment.”

In October, when PS10 students constructed Hsu’s final spectrometer design, their toaster-sized instruments fit easily on a desk or counter. After guiding students through the build (and adding office hours to handle snags in the circuity or code), the teaching crew led them through a series of hands-on labs to analyze how colored lights interact with colored water. With just water, food coloring, light, and their new spectrometer, they could see, touch, and analyze a very complex concept: the quantum nature of light.

In one lab, for example, Jeremy Rasmussen, a fresh-
man who plans to major in chemistry with a minor in politics, chose to upgrade his spectrometer to detect infrared light, which can sense the radiation emanating from warm objects and measure their temperature. Rasmussen is pleased he gets to keep the device after the course ends, so he can tinker with more upgrades at home. Other students plan to use their spectrometers to measure the temperature of the sun by analyzing its spectrum of light. Another will tap a seltzer bottle to measure how carbon dioxide gas absorbs infrared light, an experiment that mimics the greenhouse effect in the Earth’s atmosphere.

For example, Jeremy Rasmussen, a fresh-
man who plans to major in chemistry with a minor in politics, chose to upgrade his spectrometer to detect infrared light, which can sense the radiation emanating from warm objects and measure their temperature. Rasmussen is pleased he gets to keep the device after the course ends, so he can tinker with more upgrades at home. Other students plan to use their spectrometers to measure the temperature of the sun by analyzing its spectrum of light. Another will tap a seltzer bottle to measure how carbon dioxide gas absorbs infrared light, an experiment that mimics the greenhouse effect in the Earth’s atmosphere.

But Brayant Garcia, a sophomore concentrating in physics and chemistry, plans to stay in the theoretical realm to study the precarious balance necessary for efficient (and non-explosive) nuclear fission reactions. At the same time, during the January break, he plans to volunteer with local middle schools to help even younger students build their own do-it-yourself launcher—the same hands-on experiment that attracted him to study science.

Garcia said he learned just as much in a virtual PS10 than he did in previous on-campus courses. But one component—wet labs with volatile chemicals—was still too dangerous to replicate at home. (The students did perform one wet lab, which required a lab safety component. Each student, said Rasmussen, had to “submit a selfie of yourself in full lab gear: long sleeve shirt, long pants, closed-toe shoes, gloves, goggles” before they could dissolve their copper nitrate into salt water).

So, Garcia is eager to return to campus and use a real spectrometer.

“When they use a real one,” said Cohen, “they’ll actually know what’s going on under the hood.”

40 CCB MAG • WINTER 2021

41 WINTER 2021 • @HarvardCCB

Michelle Lu
Aaron Chin
Sarah Girma
Joshua Ng
Michael Bender
Preceptor Lu Wang and Teaching Fellow Alvin Hsu (in pink) offered extra virtual office hours to troubleshoot crossed wires (literal and figurative).

PHOTOS courtesy of Lu Wang and the fall 2020 PS10 cohort

Over Zoom, PS10 students held up their homemade spectrometers, which they used for at-home experiments. In one, they analyzed how a chameleon tea changed from a sapphire blue to a fluorescent purple.

Jeremy Rasmussen
Joshua Ng
Ariel Wang ('23), a freshman who plans to concentrate in mechanical engineering, said of all her courses, PS10 changed the most to accommodate for remote learning. She was surprised and delighted at how hands-on the curriculum ended up. “I guess it satisfies the engineering interest in me,” she said. She most enjoyed creating a build-it-yourself spectrometer. Hsu and colleagues, too: “What we’re doing now is far more interesting and engaging for the students than what we had ever done in the past,” he said, “because it’s not served on a silver platter and it’s much more of an adventure.”

Ariel Wang (‘23), a freshman who plans to concentrate in mechanical engineering, said of all her courses, PS10 changed the most to accommodate for remote learning. She was surprised and delighted at how hands-on the curriculum ended up. “I guess it satisfies the engineering interest in me,” she said. She most enjoyed constructing her spectrometer, which she said was “surprisingly accurate.”

In an ironic shift, PS10 teaching staff also changed the course’s final project. In previous years, when students could access the lab, most took a theoretical approach to a topic like solar cells, steam engines, or batteries. This year, they could choose an experimental approach instead.

This fall, undergraduate students in Physical Sciences 10 (PS10) got a big package in the mail. Some opened it in a dorm room, others tore into the cardboard in kitchens and bedrooms across the world (one package flew across the pond to a European kitchen). They pulled out: more cardboard—laser cut into a puzzle of rectangles—wires, and multicolored LED light bulbs in the shape of tiny mushroom caps.

“Don’t worry about breaking the cardboard,” said Alvin Hsu, a Ph.D. candidate in the Graduate School of Arts and Sciences and head teaching fellow for PS10. In an instructional video for students, Hsu showed Lu Wang, a preceptor in chemistry, how to punch one of those LEDs through a cardboard slab. She pushed harder, and the light popped through.

For centuries, chemicals could stroll down to their local pharmacy (“the chemist”) to pick up all they needed to perform experiments at home. For safety, most chemistry is now confined to sterile labs. There’s another reason: Modern equipment, like thousands of dollars per meter, is expensive. In previous years, PS10 labs with volatile chemicals—was still too dangerous to replicate at home. (The students did perform one wet lab, which required a lab safety component. Each student, said Rasmussen, had to “submit a selfie of yourself in full lab gear: long sleeve shirt, long pants, closed-toe shoes, gloves, goggles” before they could dissolve their copper nitrate into salt water).

So, Garcia is eager to return to campus and use a real spectrometer.

“When they use a real one,” said Cohen, “they’ll actually know what’s going on under the hood.”

1009x1005
In the darkest parts of the world where light fails to block out the unfathomable bounty of the stars, look up. There are still fewer specks illuminating the universe than there are bacteria in the world, hidden from sight, a whole universe inside just one human gut. Many species are known, like E. coli, but many more, sometimes referred to as "microbial dark matter," remain elusive. "We know it's there," said Doug Kenny, a Ph.D. candidate in the Graduate School of Arts and Sciences, "because of how it affects things around it." Kenny is co-first author on a new study in Cell Host and Microbe that illuminates a bit of that microbial dark matter: a species of gut bacteria that can affect cholesterol levels in humans.

"The metabolism of cholesterol by these microbes may play an important role in reducing both intestinal and blood serum cholesterol concentrations, directly impacting human health," said Emily Balskus, professor of chemistry and chemical biology at Harvard University and co-senior author with Ramnik Xavier, core...
member at the Broad, co-director of the Center for informatics and therapeutics at MIT and investigator at Massachusetts General Hospital. The newly discovered bacteria could one day help people manage their cholesterol levels through diet, probiotics, or novel treatments based on individual microbiomes.

According to the Centers for Disease Control and Prevention (CDC), in 2016, over 12 percent of adults in the United States age 20 and older had high cholesterol levels, a risk factor for the country’s number one cause of death: heart disease. Only half of that group take medications like statins to manage their cholesterol levels; while such drugs are a valuable tool, they don’t work for all patients and, though rare, can have concerning side effects.

“We’re not looking for the silver bullet to solve cardiovascular disease,” Kenny said, “but there’s this other organ, the microbiome, another system at play that could be regulating cholesterol levels that we haven’t thought about yet.”

Since the late 1800s, scientists knew that something was happening to cholesterol in the gut. Over decades, work inched closer to an answer. One study even found evidence of cholesterol-consuming bacteria living in a hog sewage lagoon. But those microbes preferred to live in hogs, not humans. Prior studies are like a case file of clues (one 1977 lab even isolated the telltale microbe but the samples were lost). One huge clue is coprostanol, the byproduct of cholesterol metabolism in the gut. “Because the hog sewage lagoon microbe also formed coprostanol,” said Balskus, “we decided to identify the genes responsible for this activity, hoping we might find similar genes in the human gut.”

Meanwhile, Damian Plichta, a computational scientist at the Broad Institute and co-first author with Kenny, searched for clues in human data sets. Hundreds of species of bacteria, viruses and fungi that live in the human gut have yet to be isolated and described, he said. But so-called metagenomics can help researchers bypass a step: Instead of locating a species of bacteria first and then figuring out what it can do, they can analyze the wealth of genetic material found in human microbiomes to determine what capabilities those genes encode.

Plichta cross-referenced massive microbiome genome data with human stool samples to find which genes corresponded with high levels of coprostanol. “From this massive amount of correlations,” he said, “we zoomed in on a few potentially interesting genes that we could then follow up on.” Meanwhile, after Balskus and Kenny sequenced the entire genome of the cholesterol-consuming hog bacterium, they mined the data and discovered similar genes: A signal that they were getting closer.

Then Kenny narrowed their search further. In the lab, he inserted each potential gene into bacteria and tested which made enzymes to break down cholesterol into coprostanol. Eventually, he found the best candidate, which the team named the Intestinal Steroid Metabolism A (IsmA) gene.

“We could now correlate the presence or absence of potential bacteria that have these enzymes with blood cholesterol levels collected from the same individuals,” said Xavier. Using human microbiome data sets from China, Netherlands and the United States, they discovered that people who carry the IsmA gene in their microbiome had 55 to 75 percent less cholesterol in their stool than those without.

Those who have this enzyme activity basically have lower cholesterol,” Xavier said. The discovery, Xavier said, could lead to new therapeutics—like a “biotic cocktail” or direct enzyme delivery to the gut—to help people manage their blood cholesterol levels. But there’s a lot of work to do first: The team may have identified the crucial enzyme, but they still need to isolate the microbe responsible. They need to prove not just correlation but causation—that the microbe and its enzyme are directly responsible for lowering cholesterol in humans. And, they need to analyze what effect coprostanol, the reaction byproduct, has on human health.

“It doesn’t mean that we’re going to have answers tomorrow, but we have an outline of how to go about it,” Xavier said.

“Those who have this enzyme activity basically have lower cholesterol”
CROSSING THE SCIENCE/COMMUNITY DIVIDE

Heidi Vollmer-Snarr teaches chemistry students to see how small reactions can help solve global problems like COVID-19

BY Caitlin McDermott-Murphy

COVID-19 is illuminating disparities too often overlooked—from access to computers and reliable internet, to economic stability, and, most importantly, healthcare. These issues may seem too big, too tangled for a handful of chemistry undergraduates to solve. But Heidi Vollmer-Snarr, the director of advanced undergraduate laboratories and a senior preceptor in chemistry and chemical biology, doesn’t think so. In her classes, students learn to design solutions for global problems ranging from pesticide poisoning to COVID-19 antibody testing; they turn backyards and taps into mini-labs and even advocate for science-backed policy changes on Capitol Hill.

“We want them to not just regurgitate what they learned in a lecture,” Vollmer-Snarr said, “but to affect society in some meaningful way.”

Mid-pandemic, on June 1, 2020, Harvard recognized Vollmer-Snarr with a Faculty Curricular Innovation Award from the Mindich Program in Engaged Scholarship (MPES). “By transcending the boundaries of the classroom,” says the program’s website, “the MPES aims to link academic study to real-world questions, problems, and opportunities,” to demonstrate how course content “sign is portable, easy to use, and relatively low cost. But the tool Lee helped design with help from Visiting Scholar and Whitesides lab member Khaled Abdelazim, designed a tool to test pesticide levels in blood serum. “It could help alleviate some health care disparities,” Lee said. Some rural areas lack funding to purchase expensive machines to perform blood tests, and patients may forgo testing if the procedure is too costly. But the tool Lee helped design is portable, easy to use, and relatively cheap ($50 in the field or up to $300 in the lab, compared to standard lab machines that cost anywhere from $500,000 to $1 million). And, she said, it can also test whether certain treatments help decrease pesticide levels in blood.

“There are many applications that can be done with these ion sensors,” said Vollmer-Snarr. For communities beyond the reach of traditional healthcare, such ion sensors could test for other biomarkers like electrolytes or heavy metals.

Of COVID-19 virus and antibodies. Another student, Raymond So, wrote a proposal to use the ion sensor as a detection method for a faster, lower cost, and portable antibody test, again with the help of Abdelazim. “Honestly, they proposed the idea,” said Abdelazim of his students. (This summer, in Harvard Summer School’s “Experimental Chemistry” course, which he teaches with Vollmer-Snarr, Abdelazim and another student, Shria Moturi, began working on fine-tuning the antibody test and a viral test, both also faster, low cost, and portable. Next, they’ll test their new system, though Abdelazim said he hopes it proves effective enough to be a cheap, mass-producible option for cities, institutions, and patients to test for COVID-19 virus and antibodies).

“They started to think outside the box,” Abdelazim said of his students after the pandemic forced everyone to leave campus. “Not limited to the lab, they start to think how can we use this to solve real life problems.”

In another small group, he helped students design a test to see how different patients react to anesthesia. “Some people recover after 10 minutes,” Abdelazim said, “some people recover after 10 hours.” The sensor can determine how a patient metabolizes the drug before administration, helping physicians prevent adverse reactions.

Last semester, Vollmer-Snarr and Abdelazim sent students in CHEM 100R their own ion sensors to perform experiments anywhere. The sensor can deliver data straight to a cell phone, so, with just a smart phone and wireless internet, students can own a portable lab.

Of course, not all students have access to a smart phone. So, this spring, Vollmer-Snarr is adapting her curriculum to focus on one thing everyone has access to: water. The Charles River, which flows through Massachusetts, the Harvard campus, and out into the Boston Harbor, accumulates pollutants that can cause rampant and toxic algae growth. This problem threatens water sources worldwide, but the source of the pollutants is not always clear. In socially-distant, outdoor tests, students in or near Cambridge will analyze which chemicals pollute the Charles and where they originated: They’ll check nearby parking lots and manicured landscapes to match pollutants to their source. Students can explore their remote worlds, too. With the portable ion sensor, they can test local water sources and determine what environmental pollutants might affect water all over the world. Since Harvard will prioritize bringing students without reliable internet access or virtual technology back to campus, Vollmer-Snarr hopes every one of her students will have access to a portable lab.

Beyond the science

At the end of the course, Vollmer-Snarr will have students present their work not just to her or their classmates but to those who can act on their data and push for change. For example, those who analyze the Charles River will virtually present their findings to
the Charles River Watershed Association, a nonprofit that helps clean and protect the health of the river. “A lot of students don’t think about the policy side of things,” said Lee, “because we’re always focused on what’s going on in the lab.” But policies can help turn research into action. And they impact scientific funding and education. That’s why Vollmer-Snarr, an advocate herself, pushes students to practice policy advocacy in real meetings with real legislators.

Perhaps now more than ever, science and community are inextricably linked but not always compatible. “As you’ve seen during this pandemic,” said Vollmer-Snarr, “there’s a large community here in the United States that still closes the door on science.”

“We need more scientists getting involved in this type of work and not just staying in the lab,” Vollmer-Snarr continued. “They can do their lab work but they can also connect with the community and let them know the importance of science.” Last spring, the pandemic forced her to cancel her bi-annual student trip to D.C. to meet face-to-face with representatives. But some students persisted. Raymond So spoke to a member of Elizabeth Warren’s office on the phone, and Ji Hae Lee called her State Representative from Hawaii to advocate for sustainability and environmental protection policies.

“If we teach students to advocate for change at an early age,” Vollmer-Snarr said, “this is a tool that they’ll have for the rest of their career. These are future leaders.”

Lee, who is currently working remotely for Boston Children’s Hospital’s cardiology unit, plans to apply for medical school in two years. She said Vollmer-Snarr taught her to look beyond a chemical reaction — a single challenge — to solve global problems like pesticide poisoning.

When asked if this skill might be useful as a doctor, Lee paused, then laughed. “Yeah!”

FAR LEFT Heidi Vollmer-Snarr presents at a conference.

PHOTOS Courtesy of Khaled Abdelazim and Heidi Vollmer-Snarr, respectively

ABOVE Ji Hae Lee gets ready to pitch policy to her Hawaii state representative during the 2019 fall trip to D.C.

RIGHT TOP In 2019, Vollmer-Snarr (front row, left) planned a trip to D.C. for students to present their policy positions directly to legislators. In spring 2020, she had to cancel the bi-annual trip because of the COVID-19 pandemic. Instead, students called their representatives to push for science policies they care about.
JILL OF ALL TRADES

How alumna Jill Becker ('03) went from selling kid’s shoes to launching successful start-ups

BY CATLIN MCDERMOTT-MURPHY

s a kid, Jill Becker ('03) commanded her brother's chemistry set. She dismantled the phone, the TV, and other household electronics and put them back together again (they still worked, too). She boiled Coca Cola and Diet Coke to isolate their essential ingredients (and decided never to drink either again). She concocted her own soda and sold it to neighbors. At age 16, she paid 1,000 Canadian dollars for a junk yard car, 16 for the manual, and made it run.

These might seem like the archetypal habits of a future inventor. And Becker did aspire to become one. But her path from an amateur tinkerer to a scientist and start-up founder was anything but archetypal. In high school, she worked in a grocery store and a kidde shoe store while earning an Ontario Scholar award for her high grade-point average; she paid for a year of college with modeling gigs and the rest with waitressing; while earning her Ph.D. in the Department of Chemistry and Chemical Biology at Harvard University, she dabbled in real estate, flipping a condo near Tufts University.

"Although I have a Ph.D. in chemistry, I think of myself more as a jack of all trades," Becker said. Now, Becker is a professional dabbler. According to her dad, she picked up a disease called "Entrepreneuring." As of today, she has founded and run three start-ups. Her current company, Kebotix, lifts dabbling to a massive, global stage: The "ultimate IP factory," as Becker calls it, harnesses artificial intelligence to rapidly survey the almost unlimited universe of unexplored molecules. The right combination of atoms could lead to potentially life-saving drugs and almost unlimited universe of unexplored molecules. The right combination of atoms could lead to potentially life-saving drugs and improve electronics. "What we are doing at Kebotix is magic," Becker said. The applications, like the molecules themselves, like Becker's cornucopia of ambitions, are almost limitless.

So how did Becker go from hocking knock-off soda on doorsteps to selling magic on an international scale? Her sweeping experience—from fixing cars to modelling and real estate—may have helped. In his 2019 book "Range," David Epstein argues that generalists (a.k.a. dabblers) are better positioned to excel than specialists. If he's right, the "jack-of-all-trades, master of none" slight is a misnomer. Becker—the "jill-of-all-trades"—may have flit from one job to another, but each experience, whether a success or failure, gave her the tools she needed to launch and run tech companies—in a sense, to create magic.

Born in Germany, and raised in Canada, Becker wanted two things as a kid: to use her mind and "get the heck out of dodge." "All I ever wanted was to be was smart," she said. But Becker found school boring and skipped classes like stones, enough that she came close to failing. Her older brother—a 16-year-old freshman at the University of Toronto—convinced her that a little investment in school would pay for her future. She trusted him; he was, after all, the second highest ranking chess player in the country and her over-the-phone calculus tutor. He encouraged her to take all the math and science classes since, she said, business and arts would always let you in. So, she made side deals with her science teachers: Since she risked detention for arriving late but not for skipping, they agreed not to report her as long as she showed up. She did. When she graduated, her grades put her in the top 20 percent of students in Canada.

Soon after, she too enrolled at the University of Toronto where she chose to specialize in chemistry—she wanted to not just conceive an idea (which she could do with mathematics) but build it, too. For the first time, she not only showed up to class, she sat in the front row. The dedication paid off. In her first two years, she received a fellowship from the National Science and Engineering Research Council of Canada (the equivalent of the U.S. National Science Foundation) to work at the Xerox research center in Mississauga. There, she studied how to replace heavy metals with organic pigments in toner cartridges to make them recyclable. One day, while trying to pressurize carbon dioxide into a supercritical state, the whole thing blew, showering Becker in red pigment. "At least it was non-toxic," she said. The next summer, they let her put an infrared spectrometer on a wagon. "I don't think they knew what to do with me." One of her greatest memories was a moment of pure scientific magic. In an advanced lab in college, she was instructed to design a polymer that would never burn. So, she created her own superconducting puck that she heated up and up and up, trying to light it on fire. But as her puck cooled down, something strange happened. It started to levitate. She poked the disc with a pencil, and it rotated like a UFO. "I got goosebumps," Becker said. "It made me feel so powerful. Like a wizard."

She felt powerful in another magical moment: When her senior year thesis earned an award from the Ministry of Environment and Energy, she told her friends to look for her on TV. "I'm the only woman here besides the waitress!" After Becker earned her Bachelor's in Science from the University of Toronto, Harvard University (and a few other top tier schools) offered her scholarships. She chose Harvard, and—when she arrived in Cambridge—bought a house with four friends. The quartet later flipped a condo together (Becker re-tiled the place). Even though they barely broke even, Becker said she learned an important lesson...
She was the first of her class to graduate. By the time she earned her Ph.D., she was considered the world's expert in ALD, thanks, she said, to Gordon and her group.

With her graduate degree, Becker had more career options than ever before. And yet, at the time, she considered academia and industry too limiting. Neither could give her the experimental freedom she craved. So, against the advice of almost everyone, she decided to launch a start-up. “I knew who my customer was,” Becker said. “They were just like me. They just wanted a tool to get to their research results faster.”

In her bedroom in a worker's cottage, she built Cambridge NanoTech, Inc., a company that designed and manufactured research equipment for Becker's specialty, ALD. The start-up was so successful, the Harvard Business Review wrote a case study praising Becker's business model. Then, in 2012, Cambridge NanoTech, Inc. was sold and Becker launched her second start-up, 02139 Inc., a consulting company that assisted other companies to transform innovation into commercial success.

Scientists, Becker said, make good entrepreneurs because they expect failure; it's part of the job. But it's easy to live with failure when you also experience success. At its inception, NanoTech Inc. was one of the fastest growing companies, according to the Boston Business Journal. Kebotix, where Becker is currently CEO, is just over two years old and has already been featured in C&EN's Top 10 Chemistry Startups to Watch in 2019 and MIT Technology Review's "10 Breakthrough Technologies of 2020." Last year, it was named the 2020 Technology Pioneer by the World Economic Forum.

"We're built to solve problems," Becker said, reflecting on why she started a company. "I think that's our purpose." Kebotix, which Becker has a hyper, excitable energy. During our interview, she cracked an egg to make ice cream with liquid nitrogen.

"We're built to solve problems. I think that's our purpose."
One sunny day in elementary school, Orvin Pierre ’22 was playing basketball outside on a concrete court with two friends when one, Omari, went up for a lay-up, battled for the hoop, and landed headfirst on the concrete. Pierre, about 10 years old at the time, saw blood creep from Omari’s head and panic: He thought his friend was dying. He ran to get the school nurse, who strolled out to the court as calm as Pierre was frantic. Minutes later, Omari was sitting up, chatty, and holding a bag of ice to his bandaged head.

“I was just fascinated,” Pierre said. The nurse had performed two miracles: fixed Omari’s body and soothed Pierre’s mind. “She helped both of us at the same time.”

In that childhood moment, Pierre decided he wanted to do that, to fix people — make them calm, healed, better. Now, the Dunster House junior is concentrating in chemistry and classics, a pairing that makes perfect sense on his path toward a medical career. Because if there’s one thing Pierre loves, it’s a good puzzle. And, he decided, if he was going to have to piece together what his patients thought and felt with their medical data, a background in both science and humanism would be the best preparation.

After Pierre witnessed the Great Omari Rescue, he scoured YouTube videos of medical explanations and surgical animations. He peppered his mother — a nurse — with questions about her work. Later, he dug up old episodes of the TV show “House” and, even though the surly protagonist was no behavioral role model, Pierre loved how the brilliant diagnostician solved puzzles hidden in patients — not just their bodies, but their behaviors and personalities, too.

Growing up in Bridgewater, Mass., Pierre found more mysteries in books, solving whodunits alongside some of his favorite detectives, like Encyclopedia Brown and Sherlock Holmes. But the real challenge came when he had to decide which kind of puzzle to turn into a concentration and, later, a career. When a fifth-grade teacher demonstrated the elephant toothpaste experiment — where hydrogen peroxide, dish soap, and yeast bloom a massive tube of foam — he thought he would pursue science. But then in high school at St. Sebastian’s in Needham, Latin and the fantastical myths from ancient Rome and Greece attracted him too. When he arrived at Harvard as a freshman, he was torn: Which concentration to choose?

He chose both. “With classics,” Pierre said, “I can understand the why behind everything. Why does a society work the way it does? Why do we follow a certain set of rules? The best way for me to understand why we do something now is to understand why we did something in the past.”

If classics solves the “why,” chemistry explains the “how,” Pierre said. Through chemistry, he could understand how electrons transfer energy and movement, how objects collect kinetic energy to move, and what’s behind a beam of light. “I can get the human portion and then the science background,” Pierre said. Pierre can speak for more than an hour with no more than a few seconds to breathe, a talent he uses in sports broadcasting, too. He attributes his garrulous nature to his father, whom he calls a “very social person.” Both his parents are Haitian immigrants with careers in health care (his father is a sleep technician), who pushed him to become a doctor or lawyer. Pierre wanted to make the decision for himself. Though he considered scientific research, he disliked the idea of standing alone at a benchtop all day with little social interaction. Instead, he imagines the moment when he can solve a patient’s problem face-to-face: “You tell them, ‘You’re going to be OK,’ their face lights up and then their family’s faces light up,” he said.

Pierre has a lot of experience bringing joy. As a Peer Advising Fellow (PAF), he guides a group of first-year students through their transitions into academic and social college life; he also serves as a PAF in the Office of Career Services’ Career Cluster, where he advises students who are considering careers in the life sciences, biotechnology, or pharmaceuticals. And he’s a member of the Crimson underg...
Key Society, a student community service organization; Persephone, an undergraduate classics journal, the Harvard Caribbean Club, and the Harvard Black Men’s Forum (BMF) where, as of this year, Pierre serves as president. “I want to make BMF as best as it can be,” he said. That means extending the same support he received as a freshman to other young Black students, including those in elementary and middle schools, to show them “not only is college something I should pursue but something I can pursue.”

Pierre slips easily into the mentor role but has been an eager mentee, too. As a young chemist, he found a role model in T.J. Hazen, a chemistry concentrator who graduated from Harvard in 2020 and is now enrolled at Harvard Medical School. “That’s exactly where I want to be,” Pierre said. “That kind of pressure might dissuade less determined students, but it’s exactly what attracted 10-year-old Pierre to medicine that day on the basketball court when he thought Omari was straddling life and death. Now, if he has his way, he’ll solve the impossible puzzle: How to save everyone. “My goal is to retire never having failed someone,” he said.

“I know that’s very unreasonable,” he continued with a half-smile. “But this time, the call came from Sweden with some of the best news a scientist can receive: Karplus had won the 2013 Nobel Prize in Chemistry. In his 2020 autobiography, "Spinach on the Ceiling: The Multifaceted Life of a Theoretical Chemist," Karplus shares his journey from refugee to Nobel Laureate, from a young boy who “wanted around bandaging chairlegs” as if they were broken bones to studying under the great Linus Pauling. In the United States, Karplus may have found greater opportunities to pursue research than he would have back in Austria, but it was his grit, quiet confidence, and even serendipity that earned him positions at some of the most prestigious schools in the world, including [we’re proud to say] Harvard University. “What I have written,” Karplus wrote in his preface, “provides at best only a fragmentary picture of my life, even of my scientific life.” Still, he made sure to include the more than 250 graduate students, postdoctoral fellows, and visiting faculty who make up "The Karplusians," the lab’s scientific children, grandchildren and great-grandchildren.

Karplus was no doubt a stellar scientist. Despite naysayers who demeaned his work as a waste of time, he trusted his instincts; his advances ended up forming a central component of both chemistry and biology. He won his Nobel Prize for developing a computer-based method for modeling complex chemical systems. But he also worked as a professional chef, gracing the kitchens of some of the best restaurants in France and Spain, and as a world-hopping photographer. “Try new things,” Karplus said in a "Harvard Magazine" article, “even if you don’t know if they’ll work.”

Today, Karplus still lives his own advice. After combining theoretical chemistry with biology, working on molecular dynamics behind big biological questions like oxygen transport in blood, the chemistry of vision, and how proteins fold, he’s now working on a new problem: the human immune response to HIV. “What if,” he asked in a Harvard Gazette interview, “there were a vaccine someday that conferred a broad-based immunity that keeps ahead of HIV mutations? More generally, for any virus, such as the flu virus, is there a way to confer permanent immunity?” He hopes to, one day, generate antibodies that bind better to the virus, but not so strongly that the antibodies are too specific.

Although Karplus never realized his childhood wish to become a physician (a degree he and the world surely cannot regret), two of his three children, sisters Reba and Tammy, fulfilled this dream on his behalf. And Mischa, the son of Karplus and his wife Marci (who also manages his lab), earned multiple degrees in public policy and law. “Without my family,” Karplus writes, “my life would have been an empty one, even with scientific success.”
JETÉ INTO AN IONIC BOND

How graduate student Frederick Moss choreographs a life in science and art
BY CAITLIN MCDERMOTT-MURPHY

Frederick Moss (right) performs a duet with Boston-based freelance performer Caitlin Canty at the Museum of Fine Arts' annual Hanukkah celebration.
PHOTOS by Rose Lincoln/Harvard Staff Photographer
A chemistry Ph.D. student at the Graduate School of Arts and Sciences, Moss is also a professional dancer, gliding between the seemingly incongruous worlds of science and art. Neither is just a hobby. So when one tries — and fails — to appropriate the other, he cringes. "You don't have either side taking the other seriously," Moss said. "When the two come together, you are often met with underdeveloped inspiration and left with immemorable comedic bits."

"If the art is just something pretty to look at, then it's not really of any value," he said.

Far less experienced than the other dancers in the company, Moss often had to learn technique on the fly. Sometimes literally: In a contemporary piece choreographed by Chun-Jou ("Dream") Tsai, dancers propelled over the shoulders of a standing partner, like acrobatic leapfrogging. Back to back, one partner stood firm while the other held a handstand before launching up and over their partner's shoulders and to a standing position on the floor. When the leap wasn't timed just right, both partners crashed to the floor with dangerous force. But Moss wasn't fazed: "When those hiccups were happening," he said, "it wasn't this freakout moment." Like when an experiment didn't go as planned, he just tweaked his calculations and started again.

"If the art is just something pretty to look at, then it's not really of any value," he said. "Sure, it's a movement of electrons or atoms, but it's still movement on this smaller-than-the-eye level!"

In August 2019, Moss left Urbanity Dance to spend more time in the lab. But he didn't leave dance behind. That fall, he was selected for a two-year fellowship at the Institute of Contemporary Art in Boston, where he leads post-show talks and facilitates seminars with choreographers. He freelances, too. Recently, he danced through the bright balloon structures in Nick Cave's Boston sculpture installation (with Peter DiMuro's Public Displays of Motion) and filmed movement research — experiments with the body's mechanical limits — in the Old North Church (with cinematographer Sue Murad and the Reciprocity Collective).

In December 2019, Moss performed a duet with Caitlin Canty called "The Flared Place," choreographed by Jenna Pollack. The dance, presented to an audience at the Museum of Fine Arts' "Festival of Lights," illustrated the tension and balance of light and dark in Jewish history.

Moss is also working with a group of five other Harvard graduate students, both dancers and musicians, to explore the concept of "responsible partnering." "How much pressure you're putting on another person and how much you're receiving," he explained. As one of the dancers, Moss will wear a sound suit embedded with tiny sensors that blueprint louder under heavier force.

Eventually, Moss wants to build his own "responsible partnership" between his two loves, replacing kitschy attempts to fuse science and art with choreography loyal to technical concepts. "If the art is just something pretty to look at," Moss said, "then it's not really of any value."
How Christina Chang shifted from cold showers to tech development in her quest for a more sustainable world

BY CAITLIN MCDERMOTT-MURPHY

As a captain for our planet

Christina Chang was already a mini-sustainability activist. She recycled and reused. She turned lights off in empty rooms. She screened "Captain Planet and the Planeteers" at her school on Earth Day. And, for two years in high school, she showed sustainability-style: turning the water on just long enough to get wet, then lather up, and rinse off under a quick burst of cold water.

"I was unwarrantedly stoically proud of my extreme shower practices," Chang said, "until I learned about the order of magnitude that is needed to make a real difference."

Most individuals won't climb through two years of sustainability showers. But it doesn't matter. Compared to industrial production, livestock farms, and highways jammed with cars, a cold shower won't foot the climate bill. That power gap might deflate the benefits, "Chang said, "but it's still somewhat expensive for the majority of people."

Her invention could drop the price and speed production, livestock farms, and coal plants, and concrete and plastic industries.

"I realized that my habits as an individual will not make a big enough difference to matter," Chang said, "but maybe my inventions could."

As an undergraduate at Princeton University, she invented a water decontamination process. As a master's student and Marshall Scholar at Cambridge University, she created a new solar-to-hydrogen technology. Then, as a chemistry Ph.D. candidate in the Harvard Graduate School of Arts and Sciences (GSAS) she co-invented a method that could enable the production of cheaper, longer-lasting solar panels that can be mass produced at a rate of a few feet per minute.

"Switching from fossil fuels to renewable energy has many benefits," Chang said, "but it's still somewhat expensive for the majority of people." Her invention could drop the price and speed production.

One of her co-inventors was also her graduate school mentor and advisor, Roy Gordon, the Thomas Dudley Cabot professor of chemistry and professor of materials science. Chang joined Gordon's lab not just for the physical and solid-state chemistry or even the focus on sustainable energy technology. "Roy graciously gave me the freedom to direct and develop my own interests," Chang said, "from my solar panel research to my professional interests like teaching and machine shop training. He has been an incredibly generous mentor, and certainly the best boss I'll ever have."

With that freedom, Chang filled her nights and weekends chasing curiosities that extended beyond her Ph.D. work and even beyond her discipline. When she learned how much carbon disoxide the steel industry emits — production generates between 7 and 9 percent of global emissions, according to steel industry figures — she invented a sustainable chemical steel manufacturing process that could decrease those emissions. Her side project won the 2019 President's Innovation Challenge Ingenuity Award for ideas with potential to be world-changing. "The only way [the world] gets better," said Harvard President Larry Bacow in his introductory remarks at the award ceremony, "is if good people like you are willing to make it so."

Chang is willing and more than able. At Harvard, she was president of the chemistry department's Graduate Student and Postdoctoral Council for two years and then president of the Energy Journal Club for another two.

Curious about psychological techniques to promote sustainability, she co-founded a cross-disciplinary conference called "Nudging Toward a Cleaner Future." In March, she received her Ph.D. in chemistry, surprising no one.

Though Chang decided to devote her life to sustainable technology at 19, that wasn't her first unshakable commitment. At age 12, she decided to become fluent in Spanish and, with help from the Spanish-speaking residents in her native Austin, Texas, she did.

At Harvard, to maintain a self-imposed rule to practice Spanish (and French) at least once every week, she co-organized GSAS Spanish and French language tables for fellow linguaphiles. Recently, her Spanish skills faced a high-stakes test.

"Three years ago, she found a new devotion: rock climbing, which she said taught her to plan for risk and prepare back-up systems for inevitable failures."

In January 2020, after defending her dissertation, Chang packed a backpack with clothes, anti-malaria pills, rock-climbing gear, sunblock, her passport, and 12 Clif Bars, and flew to Peru on a one-way ticket. When people asked if she felt safe as a woman traveling alone in Latin America, she said, "I hung off sheer rock faces — this trip is way less scary."

From January to March, Chang backpacked alone through rural Latin America. She climbed volcanic cliffs in Peru and scaled 1,200-foot canyons in Mexico. In Guatemala, she taught chemistry to middle schoolers and installed ventilated "eco-stoves," which
improve respiratory health over traditional open-fire cooking.

In the Peruvian Amazon, she joined Harvard Professor Joost Vlassak as a teaching assistant for his course on sustainability challenges. Together with Professor Carlos Rios from Peru’s University of Engineering and Technology, they took undergraduate students deep into the rainforest to talk to informal miners, who extract gold from the Amazon river’s basin with methods toxic to their soil and health, helping them to find safer methods.

“If we’re going to help invent solutions for folks in the developing world,” Chang said, “we have to understand a little bit about what life is like there and not just assume we know what the problems are.”

In mid-March, the COVID-19 pandemic forced Chang to cut her trip short, and she flew home to shelter in place.

Last summer, she joined the Department of Energy as an ARPA-E Fellow. There, she develops sustainable technologies for industries that collectively account for one-third of global energy use — concrete, steel, aluminum, pulp and paper, plastics and chemicals.

“For example,” Chang said, “if we could develop a technology eliminating the carbon footprint of steelmaking, we would save over 5 percent of global CO2 emissions. If steelmaking were a country, its emissions would rank fourth in the world, just below India and above Russia.

“In spite of my naïve sustainability fanaticism as a kid,” Chang continued, “today I don’t proselytize or chastise or advocate for everyone with the privilege of a career choice to adopt sustainability as their pet cause. My vision for the world is one where we lower our carbon footprint not through ground-up, individual actions, but by creating systems that make sustainability automatic, so that people can go about their lives and do the jobs they are called to do — doctoring, lawyering, homemaking — without needing to add sustainability to their list of worries.”

Unlike Captain Planet, Chang no longer tries to save the world one small act at a time; instead, she’s helping to build a world that no longer needs saving.
BREAKING ISOLATION
How Barbara Anderson reached out to victims of human trafficking during the COVID-19 crisis

BY CAITLIN MCDERMOTT-MURPHY

Every mid-pandemic morning, Barbara Anderson cooks a huge diner-style breakfast: egg burritos and home fries, biscuits cooked with ham bits and topped with a sloppy egg or jam. Her daughter Kerri walks in around 9:30 a.m. after a night shift at the United Postal Service. Her husband, an essential staff member at Harvard, gets his fill before heading out for a half-day shift while her 92-year-old mother settles in for another day at home with more family around than usual.

Anderson, the academic affairs and human resources coordinator for the department of chemistry and chemical biology at Harvard (until she retired in December 2020), is stuck at home but far from isolated. She knows she’s lucky, for others, COVID-19 intensifies a pre-pandemic drift toward isolation and loneliness. Victims of human trafficking are especially vulnerable. According to the United Nations Office on Drugs and Crime, the global health crisis is preventing law enforcement and public services from reaching victims or prosecuting abusers, and increasing poverty is driving people — especially children — to search for work or solicit money on the street where the risk of exploitation is higher.

In 2010, Anderson founded All Hands In, a nonprofit that raises awareness about Boston-area human trafficking and organizes outreach events for survivors. “I realized that human trafficking was not just something that happened overseas in foreign countries,” she said in a promotional video on the organization’s website, “but happened right here in my own back yard, in the United States and the greater Boston area.”

In 2019, the Zonta Club of Malden honored Anderson with their “Women Making a Difference” award. In 2020, she hired her first staff member to ramp up speaking and fundraising events with the ultimate goal of purchasing a house for victims to stay while they recover and build a new life. But the pandemic ramped up first.

“Tis trying to find creative ways to stay connected,” Anderson said. “To stay in touch with survivors, she planned an evening Zoom pajama party, is organizing a virtual concert, and texts daily with one victim. Others reach out by email when they need extra support. “I think a lot of these women are isolated right now,” she said. Next, she will send each a copy of the book “Love Heals” by Becca Stevens, who founded Thistle Farms, a refuge for human trafficking victims in Nashville, Tennessee that originally inspired Anderson to build her own.

Every week, Anderson sends out an e-newsletter to her All Hands In members; during several months in 2020, she also sent a wellness-themed one to the department’s faculty, students and staff. Instead of adding to the deluge of COVID-19 updates, Anderson includes quirky delights like a gif of Storm Troopers dancing on May 4, a photo of a sign claiming “Gardening is cheaper than therapy and you get tomatoes,” and a recipe for pineapple upside down cake on National Pineapple Upside Down Cake Day.

She practices what she preaches, too. At home, Anderson is starting an herb garden with dill, rosemary, thyme and basil. Every day, she cooks family meals — those diner-style breakfasts and dinners with chicken cooked in her backyard smoker and potato salad (her family dubbed every month potato salad season). For dessert, she bakes old school treats like Lunch Lady Brownies, which get slathered with a thick smear of chocolate frosting. Most of her bakes are the kind of decadence that can’t be eaten without big gulps of cold milk.

Anderson hasn’t slowed down one bit, but every once in a while she bumps into COVID-19 blockades: Her mother needs Tylenol to manage her arthritis pain. But when the pandemic hit Massachusetts, the drug disappeared from the shelves. Anderson had to call her brother in Maine, who drove the medicine and down. Going without butter or flour — other goods that flew off the shelves — is nothing compared to going without pain relief.

Though Anderson lives with three others and connects to far more, she still misses those impromptu social interactions that are no longer possible. On her way to work in the Mallinckrodt chemistry complex, she used to stop at Northwest Café to pick up breakfast. The chef, Nelson, would apologize if she was out of a dish she knew she liked; the Café manager, John, would ask her the simple question, “How ya doin today?” “Things like that, those personal interactions,” Anderson said, “is what I miss the most.”
Nina Pappas was waiting in a socially distant line outside Trader Joe’s when she got the idea: It was mid-March, right after schools, labs, and nonessentials shut their doors without knowing when or how they might reopen. All around her in line, families wrangled antsy kids, who faced an uncertain, restricted, and potentially claustrophobic summer cooped up indoors without access to the usual diverting activities: hide-and-seek at the park, swimming at the community pool, or summer camp.

Pappas remembers thinking, “Dang, this really sucks for these kids.” Then, she remembered ooblek. One rainy day when she was a kid, Pappas, now a chemistry Ph.D. candidate in the Graduate School of Arts and Sciences, mixed corn starch and water to form ooblek, mysterious stuff that oozes like a liquid and hardens like a solid when squeezed. Playing with that bizarre substance sparked an intense curiosity: What was this stuff? Why was it so weird? While not necessarily beyond what most kids know, it’s a question that piques curiosity and can inspire more buttoned-up and a little more analogous to what you might see professionals presenting but make it very clear and accessible,” Pappas said.

The posters, which so far include a yogurt-making mission, iron extraction from “magnetic cereal,” and a window sill garden project to sprout beans and green onions, go beyond the basic steps of how to carry out the experiment. Each starts with an overview (yogurt is food for microbes, not just humans; iron keeps skin and hair healthy; and beans are actually seeds!) and includes leading questions to, as Pappas said, encourage kids to explore the chemical oddities behind their experiment. Rather than answer all the questions, the posters give kids space to consider: Would a seed grow better in water that is acidic, basic, or neutral? Would the bacteria in yogurt grow faster in cooler temperatures? Why does crushed cereal react to a magnet if whole cereal doesn’t? Pappas hopes that, like her ooblek experience, those open-ended mysteries encourage kids to chase curiosities.

Still, Pappas is aware that her place in the bubble comes with limitations: She can’t always know what might grab a kid’s attention or, since Pappas is white, what Black and Brown communities might need to feel included and welcome. For Pappas, that means making sure that every community she’s interacting with—her lab mates, kids stuck at home in quarantine, or her family members—have created these posters, modelled off the style scientists use to present their research findings, to encourage budding scientists (and their parents) to practice curiosity at home.

IMAGES courtesy of HWIC

The Harvard Women in Chemistry (HWIC) group launched a new “Science at Home” initiative not long after the COVID-19 pandemic closed kids off from schools and other in-person STEM programs. So far, they have created three posters, modelled off the style scientists use to present their research findings, to encourage budding scientists (and their parents) to practice curiosity at home.

By October, the posters—which HWIC posted on their Twitter page, @HarvardWIC—attached the attention of the Boston Public Library, which invited the group to present a live, interactive program on strawberry DNA extraction for kids age 5 to 12. The event helped HWIC with another goal: to create a space for back-and-forth communication between scientists and their next generation.

“People are way more nuanced than science can be,” she said.

Maybe even as mysterious as ooblek.
Launching a lab at a new University is hard enough; launching a lab through a computer screen is harder still. Just about two months after Suyang Xu joined CCB as an assistant professor on January 1, 2020, the University shut down due to the Covid-19 pandemic. But Xu takes the advice he gives: "Never give up," "time quickly elapses" so "have a sense of urgency." Without tools to study and unravel the beauty of quantum crystals, he wrote papers and threw himself into cooking, a chemical cousin.

Xu, who works to solve fundamental challenges in physics, chemistry and biology to advance new technology for clean energy, low-power electronics, and even quantum computing, earned his undergraduate degree from Peking University in China before joining Zahid Hasan's group at Princeton University as a graduate student. His research with Hasan on Weyl semimetals was named a Top-10 breakthrough of the year by Physics World.

After a postdoctoral fellowship with Nuh Gedik's group at the Massachusetts Institute of Technology (where he and the team performed work that earned the February 2020 cover of Nature), Xu joined CCB where he hopes to tap into his vast, international collaborative network to explore and uncover the stunning beauty of quantum crystals.

**Beyond the Lab**

This year, our graduates scattered not just to start new jobs but to quarantine all over the world (some did both at the same time, to start new jobs but to quarantine all over). This year, our graduates scattered not just to start new jobs but to quarantine all over the world (some did both at the same time, to start new jobs but to quarantine all over). This year, our graduates scattered not just to start new jobs but to quarantine all over the world (some did both at the same time, to start new jobs but to quarantine all over). This year, our graduates scattered not just to start new jobs but to quarantine all over the world (some did both at the same time, to start new jobs but to quarantine all over).

**I L I L L U S T R A T I O N S** by Carrie McDermott-Murphy PHOTO (LEFT) courtesy of Suyang Xu

**ADVICE FOR STUDENTS?**

The first year of my Ph.D. was spent testing a poorly thought-out hypothesis of my advisor's that didn't work. I learned the hard way that I have to think for myself. Once I thought through the hypothesis more carefully and in context of existing work I dug into, I was able to develop a better understanding of why the procedure was failing and develop better hypotheses.

**WHAT PIVOTAL MOMENT CHANGED HOW YOU THINK?**

During the first two weeks in college, I realized that I should actively learn things to prepare for my future career instead of just taking classes. I became very hard-working since then.

**BAD RECOMMENDATIONS YOU HEAR IN YOUR PROFESSION?**

A lot of people told me to do a postdoc/stay in academia, despite being sure that I wanted to go into industry. It's not that it was bad advice—it's more that it showed me how important it is to know yourself and what you want.

**WHAT NEW BELIEF, BEHAVIOR, OR HABIT HAS IMPROVED YOUR LIFE?**

My advice would be: never give up. Always have a sense of urgency. Without a sense of urgency, one will find time quickly elapses.

**WHAT ADVICE WOULD YOU GIVE TO A SMART, DRIVEN COLLEGE STUDENT ABOUT TO ENTER THE "REAL WORLD"?**

When you feel overwhelmed or unfocused, what do you do? I usually walk around and try to reflect.

When has helped you cope during the pandemic? Cooking and writing papers!