



The Challenge of COVID

Penn State's
interdisciplinary response

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MEETING THE CHALLENGE

We are living through unprecedented times. The COVID-19 pandemic continues to touch every corner of our lives and our University, including Penn State's vast research enterprise. Like many others, we have had to adapt and find new ways of conducting research and working together to continue our mission of discovery and invention and creating knowledge to benefit all.

Our immediate challenge has been finding ways to harness our strengths to respond effectively to a global pandemic in real-time, by identifying and developing ways to combat, contain, and control this complex disease. I have been tremendously impressed and proud of how our researchers have risen to the call.

Beginning back in February 2020, before the virus had made its way into prevalent public consciousness, our disease experts were discussing what-ifs with colleagues at the World Health Organization and the Centers for Disease Control and Prevention. By March, our interdisciplinary research units were seeding research grants to kick-start projects addressing all aspects of the pandemic, from the need for vaccines to curtailing supply chain upheavals and understanding short- and long-term psychological and social impacts. By April, we had 48 research projects underway.

At the same time, MASC (Manufacturing and Sterilization for COVID-19), a grass-roots effort to harness our 3D printing capabilities to manufacture critically needed supplies, quickly grew to include more than 300 volunteers.

In all, hundreds of researchers across multiple campuses, spanning 10 colleges and more than 25 departments, rapidly transitioned their research programs to address the immediate challenges. Some of their stories are told in the pages that follow.

The keys to this rapid mobilization and all-out effort are the very characteristics that set us apart as a research university: an unmatched breadth and depth of expertise and an ingrained interdisciplinary culture, one that fosters genuine partnerships and a commitment to bringing our combined strengths to bear on the most complex challenges of our time.

This issue not only highlights our dedication and commitment to tackling a worldwide crisis, but it also marks the 40th anniversary of *Research/Penn State* magazine. During these four decades, this magazine has borne witness to a period of remarkable growth for the University's research enterprise, during which Penn State laid the groundwork for and emerged as the interdisciplinary research powerhouse it is today.

I thank everyone for your unyielding dedication and devotion to research excellence, knowledge discovery, and using your talents to help make a difference in our world.

LORA G. WEISS
Senior Vice President for Research



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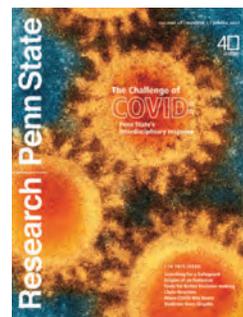
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ON THE COVER:

A colored visualization of an electron microscopy photo of the COVID-19 coronavirus. Penn State's research response to the pandemic has been a model of interdisciplinary collaboration. This special issue highlights that response, beginning on page 9.

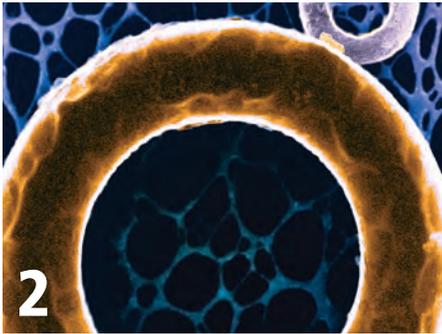
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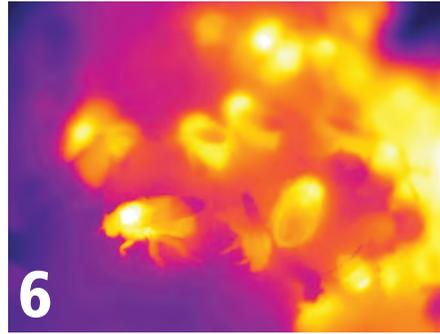




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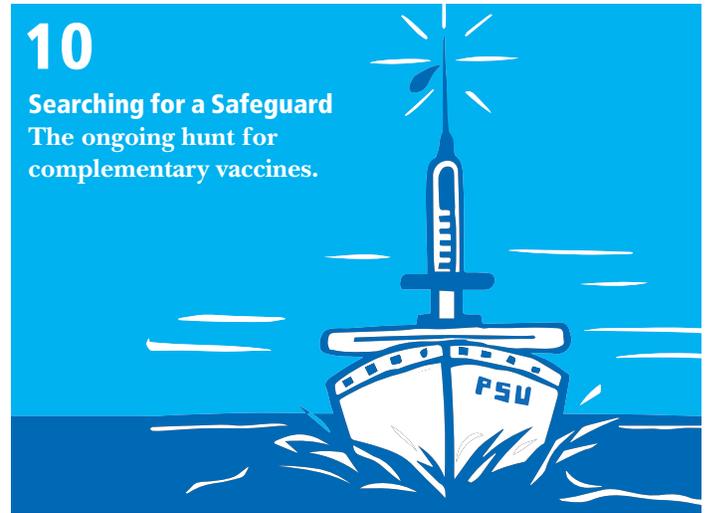
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›› Birds Gotta Fly

A gene newly associated with the migratory patterns of golden-winged and blue-winged warblers could lend insight into the longstanding question of how birds migrate across such long distances.

A new study led by researchers at Penn State and the Cornell Lab of Ornithology is the first to combine whole genome sequencing and migration tracking technology to pinpoint a single gene associated with the complex suite of traits that determine migratory behavior.

Researchers have known for a few decades that there is a genetic component to migration. Recent studies have identified large regions of the bird genome associated with migration, but it has been more difficult to pinpoint the specific roles of any single gene.

“In this study, we found only one gene associated with the final wintering destination of golden-winged and blue-winged warblers,” says David Toews, assistant professor of biology at Penn State.

The researchers studied migration patterns in golden-winged warblers and blue-winged warblers, genetically similar species that breed in the Midwest and northeastern United States. Some birds of each species migrate to wintering grounds in Central America, from Panama to Guatemala, while others travel farther to South America, primarily Venezuela. Birds will usually return to similar breeding grounds and wintering sites each year.

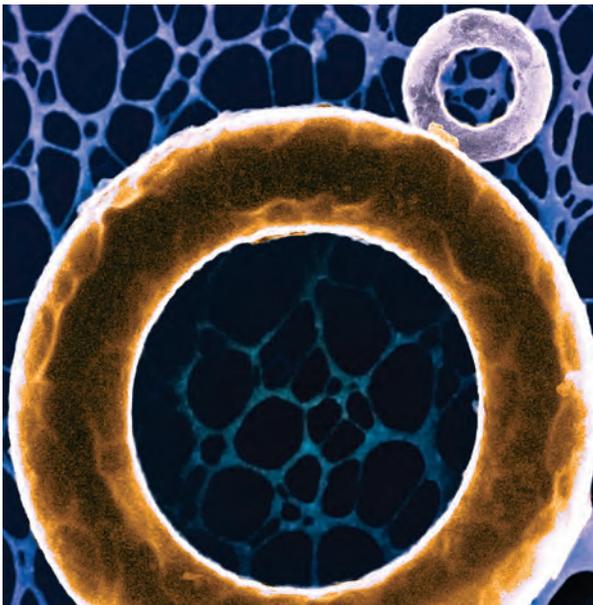
Looking at genetic samples from migrating birds, the group found genetic differences between birds that winter in Central America and those that winter in South America. The majority of these differences occurred in a small region on the bird’s Z chromosome where only one gene, called VPS13A, was present.

—GAIL MCCORMICK



Using whole genome sequencing and migration tracking technology, researchers identified a gene associated with migration in golden-winged (left) and blue-winged (right) warblers. The team compared genetic differences among birds that winter in Central America and those that winter in South America.





Colorized micrograph of two glazed Janus tori (or donuts) with different faces showing. The polymer appears yellow and the platinum thin film appears purple. In this secondary transmission electron microscope image produced by study collaborators at the University of Toronto, the background is a lacey carbon grid.

Tiny Swimming Donuts

Bacteria and other swimming microorganisms evolved to thrive in challenging environments. For researchers eager to mimic their unique abilities for biomedical technologies, fabrication challenges can create a manufacturing bottleneck. Now, microscopic, 3D-printed tori, or donuts, coated with nickel and platinum may bridge the gap between biological and synthetic swimmers, according to an international team of researchers.

These micro swimmers mimic biological behavior and might one day deliver targeted drugs or stir samples in labs-on-a-chip, miniature devices that mimic a full laboratory on a microchip.

“These donuts may eventually have medical applications as active materials,” says Igor Aronson, Huck Chair Professor of Biomedical Engineering, Chemistry and Mathematics. Active materials are those that move on their own.

The researchers have been able to manufacture donuts of 3, 7 and 14 micrometers, with printed features of up to 200 nanometers, using precise laser technology and specially designed photoresists. Spider silk, by comparison, is 3 to 10 micrometers in diameter.

“We create two different designs, horizontal and vertical,” says Remmi Danae Baker, doctoral candidate in materials science and engineering.

For their experiment, the researchers placed the microtori in a hydrogen peroxide solution, which acted as a fuel. Platinum decomposes hydrogen peroxide and powers propulsion of the donuts.

“Originally, it was thought that a horizontal torus would just rise off the substrate and hover, but that doesn’t happen,” says Aronson. “Rather than rise straight up, they begin to tip, reach a 15 degree angle and then they swim like a jet skier.”

—ANDREA ELYSE MESSER

SLIP-SLIDIN’ AWAY

Every day, more than 141 billion liters of water are used to flush toilets. With millions of global citizens experiencing water scarcity, what if that amount could be reduced by 50%? The possibility may exist through research conducted at Penn State.

“Our team has developed a robust bio-inspired, liquid, sludge- and bacteria-repellent coating that can essentially make a toilet self-cleaning,” says Tak-Sing Wong, Wormley Early Career Professor of Engineering.

Co-developed by Jing Wang, a doctoral graduate from Wong’s lab, the liquid-entrenched smooth surface (LESS) coating is a two-step spray that, among other applications, can be applied to a ceramic toilet bowl. The first spray, created from molecularly grafted polymers, creates an extremely smooth and liquid-repellent

foundation. “When it dries, the first spray grows molecules that look like little hairs, with a diameter about a million times thinner than a human’s,” Wang says. A second spray then infuses a thin layer of lubricant around those nanoscopic “hairs” to create a super-slippery surface.

With this novel surface, toilets can effectively clean residue from inside the bowl and dispose of the waste with only a fraction of the water previously needed. The researchers predict the coating could last for 500 flushes before a reapplication is needed.

The technology could also improve waterless toilets, which are used extensively around the world. With the LESS coating, the team predicts these types of fixtures would be more appealing and safer for widespread use.

—ERIN CASSIDY HENDRICK



Getty Images/ByoungJoo

On average, U.S. households waste nearly one-third of their food.

— EDWARD JAENICKE and YANG YU

Agriculture



» Can't Sleep? Think Pink

On average, Americans sleep an hour less each night than they did in the 1940s. This lack of sleep can have harmful consequences on the human body, including weight gain, heart disease, susceptibility to illness, higher blood pressure, and other negative impacts.

Penn State researchers Margeaux Schade, assistant research professor in biobehavioral health; graduate student Gina Marie Mathew; and Orfeu Buxton, professor of biobehavioral health, are collaborating with researchers at the company SleepSpace to develop ways to improve the quality of a night's sleep. Specifically, the researchers are exploring the effects of sleeping with "pink noise."

Many people are familiar with white noise: noise that covers the full range of human hearing at equal intensity, like static from a radio or analogue television set. Pink noise, by contrast, is more intense at lower frequencies, resulting in a deeper sound, like steady rain. Prior research suggests that pink noise might increase the brain waves associated with deep sleep, the type that has been linked to numerous health benefits for the body and mind.

In the current study, by exposing study participants to pink noise during deep sleep cycles, the researchers were able to increase the percentage of time that participants spent in deep sleep.

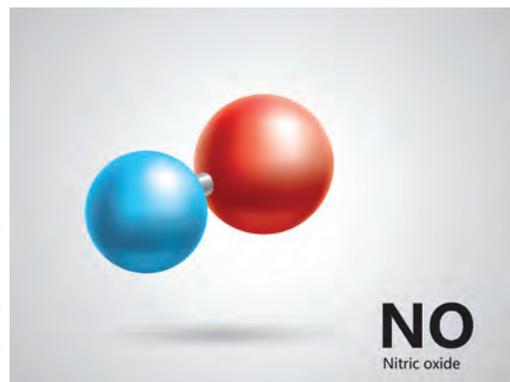
"Our results show how the sleeping brain responds in the moment to sounds," Buxton says. "This suggests we might be able to further develop acoustic methods to improve sleep for everyone."

—AARON WAGNER

DISSOLVING SENSORS

Sensors that monitor a patient's condition during and after medical procedures can be expensive, uncomfortable and even dangerous. Now, an international team of researchers has designed a highly sensitive flexible gas sensor that can be implanted — and, after it's no longer needed, safely biodegrade into materials that are absorbed by the body. The flexible, implantable sensor can monitor various forms of nitric oxide and nitrogen dioxide gas in the body, according to Huanyu "Larry" Cheng, Dorothy Quigg Career Development Professor in the Department of Engineering Science and Mechanics.

Nitric oxide, which is produced naturally in the human body, plays an important role in health by relaxing or widening blood vessels to enhance blood flow, allowing oxygen and nutrients to circulate through the body. On the other hand, exposure to nitrogen dioxide from the environment is linked

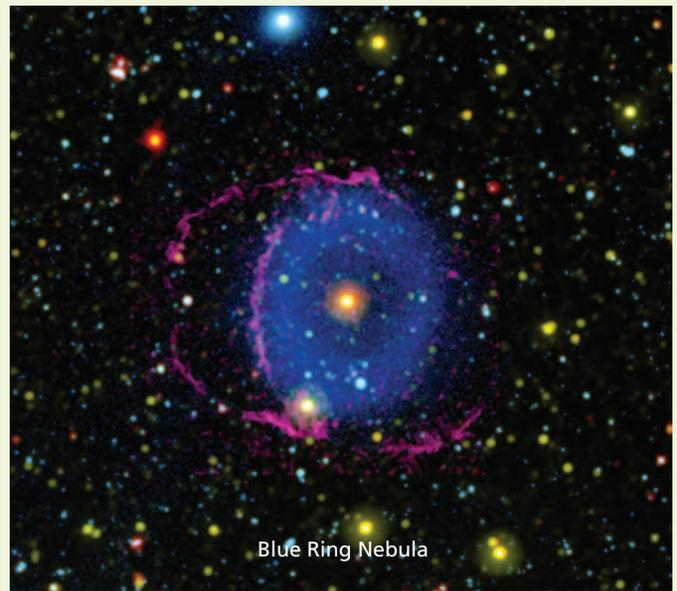


to progression of conditions such as chronic obstructive pulmonary disease.

Current external monitors used to measure these and other

gases are bulky and potentially not as accurate as implantable devices, Cheng says. Implantable devices, however, need to be removed after recovery, which can mean additional surgery. So the researchers investigated a design that is biodegradable: Its components, made of magnesium and silicon, dissolve gradually in water or in bodily fluids, and are safely absorbed when no longer needed. The researchers say future work could look at designing integrated systems that could monitor other bodily functions for healthy aging and various disease applications.

—MATT SWAYNE



Blue Ring Nebula

NASA/JPL-Caltech/M. Seibert (Carnegie Institution for Science)/K. Hoadley (Caltech)/GALEX Team

Mystery Solved

Astronomers may have finally cracked the case of the Blue Ring Nebula, an unusual cloud of gas that has mystified researchers for more than 16 years. An international team including Penn State scientists, after applying cutting-edge theoretical models to the smattering of data available, posits the nebula is likely composed of debris from two stars that collided and merged into a single star.

The nebula was first spotted in 2004 by scientists with NASA's Galaxy Evolution Explorer (GALEX) and was unlike any they'd seen in our Milky Way galaxy: a large, faint blob of gas with a star at its center. Over the next 16 years, astronomers studied the object with Earth- and space-based telescopes, but the more they learned about it, the more mysterious it seemed.

"In 2018 we observed the Blue Ring Nebula with the Habitable Zone Planet Finder (HPF) on the 10m Hobby-Eberly Telescope," says Andrew Monson, associate research professor of astronomy and astrophysics at Penn State. "The spectroscopic data from HPF played a key role in helping us understand this exciting and unusual object."

While merged star systems most likely aren't uncommon, they are nearly impossible to study immediately after they form because they're obscured by debris kicked up by the collision that takes hundreds of thousands of years to clear. In this case, astronomers appear to be seeing the star system only a few thousand years post-merger, the youngest known example of two stars merged into one.

—GAIL MCCORMICK



Tiny device turns waste heat from pipes, electronics, and cars into electricity.

— SHASHANK PRIYA, AMIN NOZARIASBMARZ and BED POUDEL
Materials Science and Engineering



Toxin made by saltwater algal blooms may lead to ALS.

— ELIZABETH PROCTOR and NIKOLAY DOKHOLYAN
College of Medicine



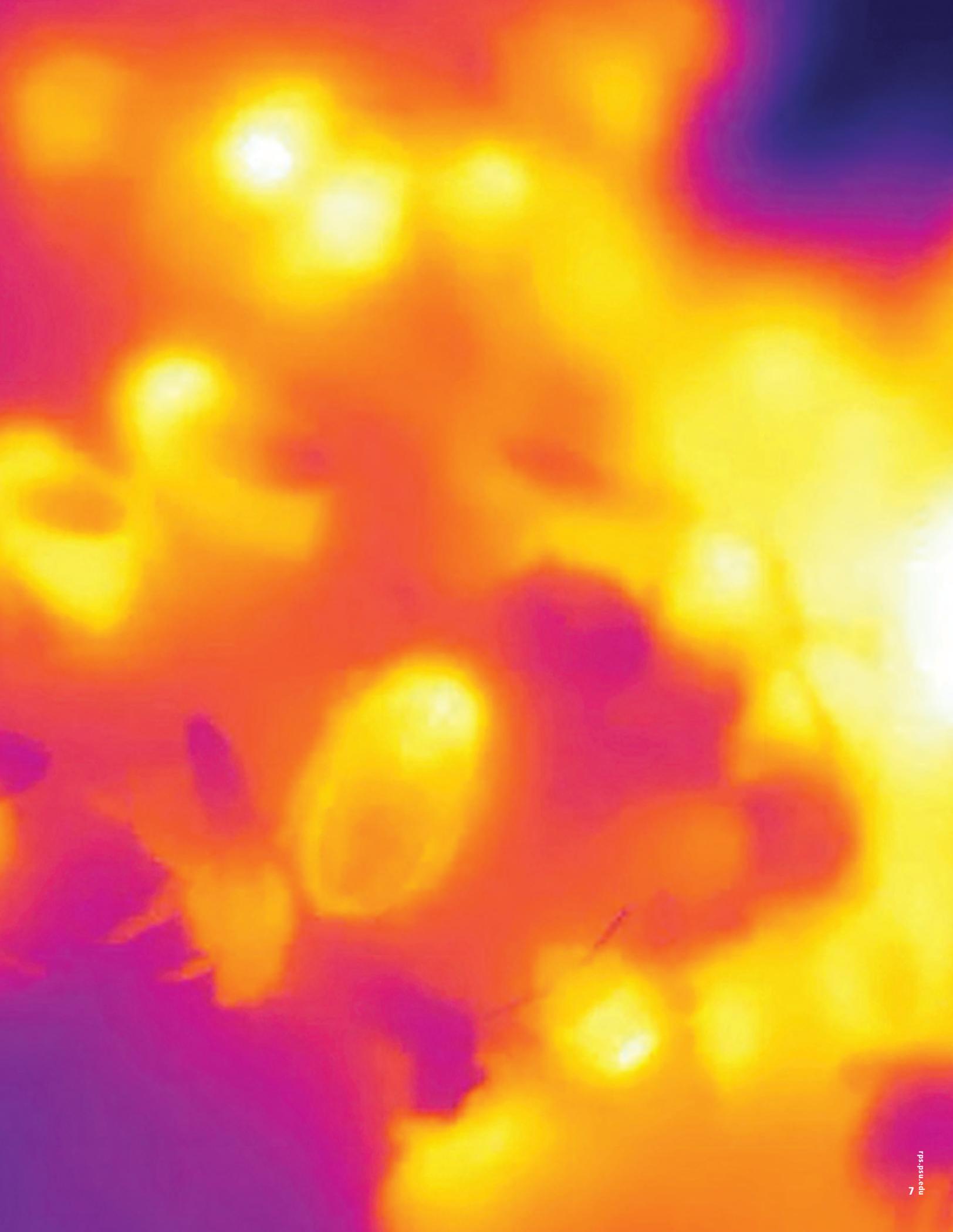
Sorry Einstein: In science, hard workers make better role models than geniuses.

— DANFEI HU
Psychology

WHAT'S THE BUZZ? ‹‹

In a cold room at University Park, a thermal camera reveals that healthy bumble bees incubating larvae in a nest box are several degrees warmer than their surroundings, and their thoraxes are warmest of all. The bees simultaneously contract two sets of muscles to generate enough thoracic heat to support their developing larvae or to take off in flight. In this photo, the brightly-imaged thorax of the bee at lower left is at about 32°C (90°F). Graduate student Hannah Stewart captured the image during her research with Ruud Schilder, assistant professor of entomology and biology. They have found that bees whose immune systems are compromised by infection struggle to maintain the temperatures needed for flight and for brood development.

Photo by Hannah Stewart



MASC

THE POWER OF TEAMWORK

BY DAVID PACCHIOLI

In early March 2020, as COVID-19 cases in the U.S. jumped into the tens of thousands, an interdisciplinary team of Penn State researchers mobilized to address critical shortages of masks, ventilators, and other personal protective equipment (PPE) available to healthcare workers.

The initiative—called Manufacturing and Sterilization for COVID-19, or MASC—began in Tim Simpson’s 3D printing class. Simpson, Paul Morrow Professor Engineering Design and Manufacturing, was looking for a way to give his students a meaningful experience in spite of the campus lockdown.

“It was going to be tough to run a hands-on lab when students weren’t allowed in the labs, so I started looking for ideas about 3D printing COVID-19 PPEs, which students could help design from their homes,” says Simpson, who is also co-director of the Center for Innovative Materials Processing through Direct Digital Deposition. “My students jumped at the opportunity.”

While his students were generating ideas, Simpson was seeing stories from around the world highlighting creative uses of 3D printing to meet the sudden demand. He started sharing these stories with colleagues, and soon a University-wide initiative was born, with volunteers signing on from the College of Engineering, the Applied Research Lab, the Center for Medical Innovation at Penn State’s College of Medicine, and the Smeal College of Business, among other units. Motivated by news headlines, neighbors’ concerns, physicians’ requests, and healthcare workers’ pleas for medical supplies, more than 380 faculty, staff, and students pitched in.

“I think it really helped a lot of us cope with the situation, to feel like there was something we could do,” says Mary Frecker, Riess Chair in Engineering, director of the Penn State Center for Biodevices, and the current co-director of MASC.

Cross-disciplinary teams formed to tackle a growing list of projects. The focus was on design and delivery of rapidly scalable solutions—prototyping and testing done at Penn State followed by transition to an industry partner to scale production and ensure regulatory compliance. Within the first week, MASC researchers created a prototype for a plastic face shield and recruited a local manufacturing company, Universal Protective Packaging, Inc., to mass-produce it. UPPI has since manufactured more than a million of the shields for Hershey Medical Center and others in need.

Meanwhile, another team designed and 3D-printed protective mask prototypes for Hershey physicians to test and provide feedback. Through connections with faculty at Penn State Behrend, the MASC team worked with Plastikos, Inc., in Erie to developing tooling for injection molding to produce the masks in high volume.

As part of the all-out effort, supply chain experts sourced a textile material for use as a mask filter and materials scientists tested it. Architects and engineers collaborated remotely to design and develop an isolation booth to protect nurses and staff working at drive-through testing sites. Costume designers from the School of Theatre patterned and sewed gowns and masks that were then packaged in Penn State’s Meat Lab before being sterilized with gamma rays at the Breazeale Nuclear Reactor.

A sterilization group evaluated techniques such as ultraviolet radiation, vaporized hydrogen peroxide, and plasma methods, and the legal and regulatory team made sure solutions conformed to frequently changing regulations.

Eight months later, with critical shortages relieved, MASC has shifted to longer-term planning.

A “solution catalogue” documents and shares nearly 20 completed projects, with technical specifications, manufacturing instructions, and industry contacts. The MASC team continues to meet weekly, Frecker says, “and part of what we do is talk with the folks at the medical center about what they see coming up that’s going to be needed.”

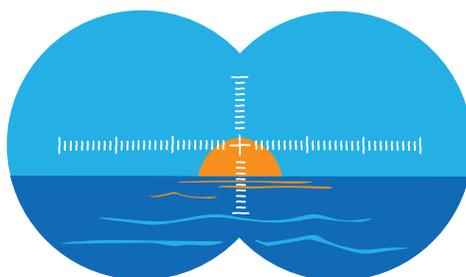
Simpson’s idea for his class bloomed into a total team effort that has had positive impacts all across Pennsylvania. “The story behind it all,” he says, “highlights the power of partnership at Penn State to help support the health and welfare of lives across the commonwealth.”



Dr. Neerav Goyal, a physician at Hershey Medical Center, tests a 3D-printed filtration mask prototype.

Penn State Health/Jason Plotkin (2)





Searching for a Safeguard

Penn State researchers are applying decades of expertise toward the development of COVID-19 vaccine candidates.

by Sara LaJeunesse

From almost the beginning of the COVID-19 outbreak in early 2020, the world has waited anxiously for a vaccine, the safeguard that would enable a return to normal life. Researchers around the world have eagerly picked up the challenge.

Penn State scientists have been active among them from the earliest days. Drawing on the knowledge, skills, and technologies they have developed over their careers, and taking advantage of infrastructure built for the purpose, teams of experts around the university moved rapidly to face the crisis.

“As a university, we’ve put a lot of care and effort into positioning ourselves to be able to

respond to pressing global needs,” says Leslie Parent, vice dean for research and graduate studies at the College of Medicine, and a leader of one of those teams. “So, when it became apparent that a COVID-19 vaccine was urgently needed, we already had the people and facilities in place to act very quickly.”

By year’s end, thankfully, the all-out global effort had begun to bear fruit, as two major pharmaceutical companies, Pfizer and Moderna, began to roll out their purportedly highly effective vaccines. But the race for a cure is far from over.

“When it became apparent that a COVID-19 vaccine was urgently needed, we already had the people and facilities in place to act very quickly.”

— Leslie Parent



Penn State Health

Leslie Parent

“It’s hard to imagine that the first thing that comes along will be perfect right out of the gate,” explains Andrew Read, Evan Pugh Professor of Biology and Entomology and director of the Huck Institutes of the Life Sciences. “No matter how good the Pfizer and Moderna vaccines turn out to be, additional options will likely be needed to achieve the highest possible immunity levels for the greatest number of people across the globe.”

Accordingly, Penn State researchers are still hard at work. Using a variety of approaches, they are pursuing COVID-19 vaccine candidates that aim to complement the first-generation solutions. The hope is to develop options that may be even more efficacious, and better able to reach different segments of the population, such as the young and elderly, in rich and poor countries alike. New mechanisms of action and modes of delivery may also be useful for fighting future coronaviruses and other pathogens.

Penn State’s scientists, Read notes, are particularly well situated to conduct the innovative, cross-disciplinary research that yields novel materials and procedures with the potential to advance vaccines to more sophisticated levels. “Very few universities have the strength we do in bringing people in engineering together with people in life sciences and clinical research to address a complex problem like this,” he says.

FROM HIV TO COVID-19

With previous experience creating a vaccine candidate for HIV, Nikolay Dokholyan, the G. Thomas Passananti Professor in the College of Medicine, used that knowledge, along with novel technologies he developed, to pursue a COVID-19 vaccine.

Dokholyan explains that one of the reasons HIV has been so hard to defeat is because it has such a high mutation rate. “This has made it difficult to target with a vaccine,” he says. “If you create a vaccine for one strain of the virus, it won’t work against other, mutated strains.” But not all parts of the virus mutate, he adds. Some of HIV’s genetic material is conserved, meaning it remains constant from generation to generation.

“These conserved areas are vulnerable spots on the virus that can be targeted with a vaccine,” he says.

As it turns out, these conserved areas, called epitopes, also occur on SARS-CoV-2, the virus that causes COVID-19. To build a vaccine for COVID-19, Dokholyan and his team adapted software it had previously created, using it to identify the SARS-CoV-2 epitopes.

Next, the team performed what they call molecular transplantology. “We used molecular scissors to cut the epitopes out of SARS-CoV-2 and transplant them all over small protein scaffolds,” explains Dokholyan. “This increases the chances that antibodies will find the epitopes and launch an immune response.”

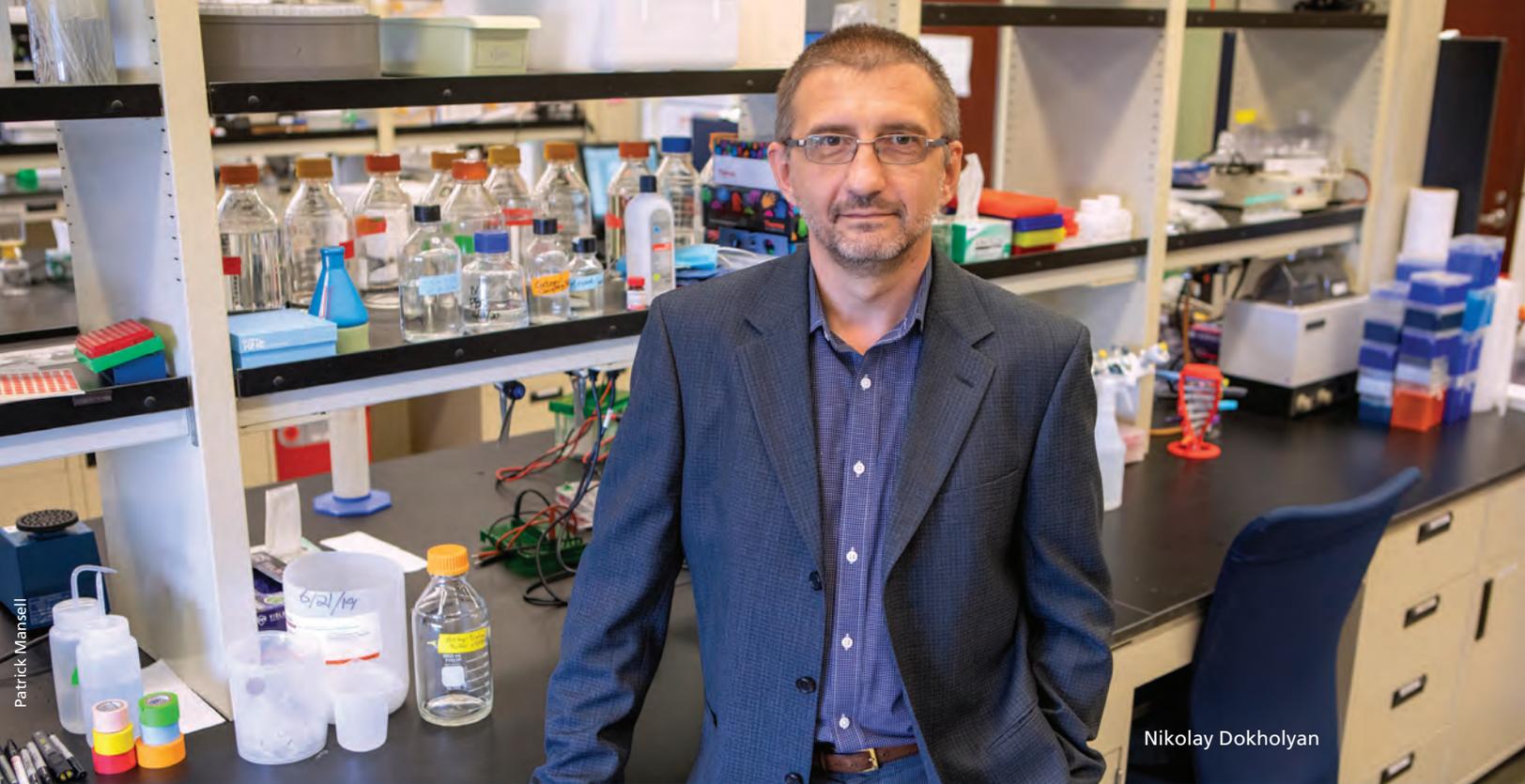
In collaboration with Neil Christensen, professor of pathology and microbiology and immunology, the team is currently testing its vaccine candidate in mice and rabbits. Already, the team has found that the transplanted epitopes produce a significant immune response in these animals. The researchers have also seen similar responses in antibodies collected from patients who had COVID and developed an immune reaction. If the lab work continues to prove successful, the next step, says Dokholyan, will be to run human clinical trials.

PROTECTION AT THE SITE OF INFECTION

With prior experience studying intranasal influenza vaccines, Troy Sutton, assistant professor of veterinary and biomedical sciences, recognized the benefit of an intranasal vaccine that targeted the primary site of COVID-19 infections—the nose.

“Other COVID-19 vaccines in development are designed to be delivered intramuscularly,” Sutton explains. “These vaccines can protect the lungs and that may be good enough to keep people out of the intensive care unit, but if you really want a vaccine that both protects you from getting sick and prevents transmission you need to target the site of the infection.”

Sutton teamed up with Scott Lindner, associate professor of biochemistry and molecular biology, who, along with Susan Hafenstein, professor of biochemistry and



Nikolay Dokholyan

Patrick Mansell

“If you really want a vaccine that both protects you from getting sick and prevents transmission you need to target the site of the infection.”

— Troy Sutton



Troy Sutton



Scott Lindner

Patrick Mansell (2)

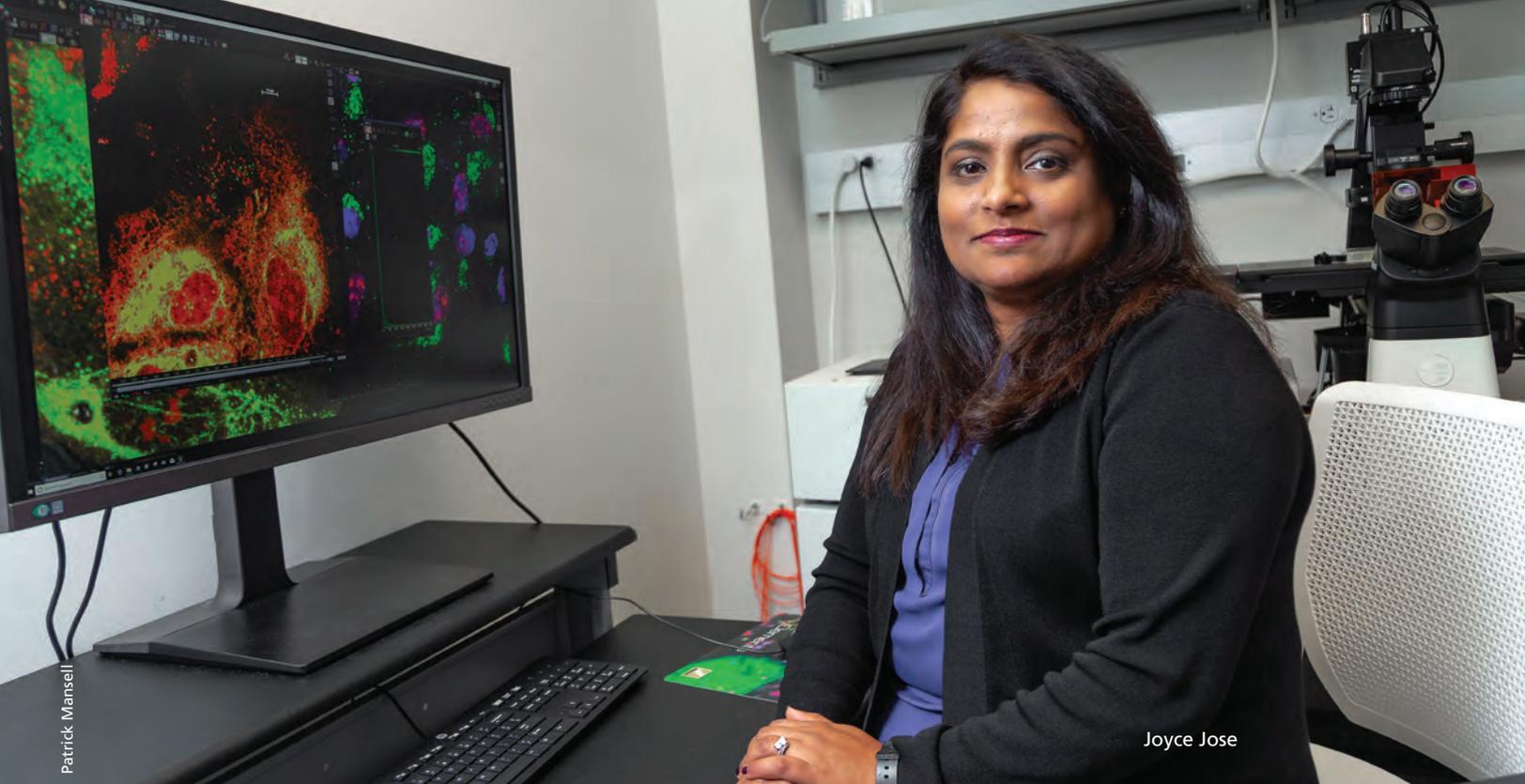
molecular biology, had previously engineered and patented a self-assembling soccer-ball-shaped scaffold made of proteins that could display up to 60 additional proteins on its surface.

The idea behind the scaffold is to hold proteins that are too tiny and unstable to be seen—even with Penn State’s FEI Titan Krios cryo-electron microscope, a one-of-a-kind instrument that is the gold standard for visualizing small biological molecules. The scaffold makes it possible to study these molecules for the first time. Its size and shape, in this instance, also make it perfect for an intranasal vaccine.

As Lindner explains, “The scaffold is roughly the size of a coronavirus and with coronavirus proteins attached to it, it looks a lot like SARS-CoV-2. Yet it cannot replicate, so you don’t have the safety concerns that come with a live attenuated virus.”

A VIRUS-LIKE PARTICLE THAT MIMICS SARS-COV-2

A virologist who studies Zika, dengue, and other flaviviruses, Joyce Jose is investigating another way to trick the immune system into eliciting a response. Her vaccine, developed in collaboration with Hafenstein, is a virus-like particle (VLP), a non-infectious particle that resembles a virus.



Patrick Mansell

Joyce Jose

“ We’re trying to make our VLP look like a real virus by incorporating all of the virus’s surface proteins. ”

— Joyce Jose

VLPs are typically designed to hold a single virus protein, but her team is doing something different. “We’re trying to make our VLP look like a real virus by incorporating all of the virus’s surface proteins,” says Jose. These include the spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins.

Jose, an assistant professor of biochemistry and molecular biology, explains that a VLP that expresses four viral proteins could trigger a more robust immune response than a vaccine that employs just one. One difficulty, however, is packaging the four proteins together into the same delivery container.

“This is the novelty in our work,” says Jose. “We are stitching together the proteins using molecular biology techniques. So, in solution, when the proteins see each other, they come together, assemble into one RNA, and emerge as VLPs.”

At the College of Medicine, a team led by Nick Buchkovich, associate professor of microbiology and immunology, and Leslie Parent is also developing a VLP that expresses the SARS-CoV-2 surface proteins. Buchkovich, a virologist who studies human cytomegalovirus, a type of herpes virus that causes congenital birth defects, says the team hopes its vaccine will provide longer-term immune protection than many others in development.

A problem with some of the current vaccines being developed, he explains, is that they use the actual SARS-CoV-2 virus in either a weakened or inactivated state to elicit an immune response.

“After the immune system sees those vaccines a couple of times, it might develop antibodies against the vaccines themselves,” he says. VLPs tend to avoid this problem. “Previous research in influenza vaccines suggests that resistance to the vaccine is less likely to develop with the use of VLPs and that they therefore provide longer-lasting immunity.”

The researchers are currently working to optimize and scale-up the production of their VLPs and are starting to test them in mice.

“In mice, we know we get a robust antibody response, which is good, but we’re still working on analyzing the T-cell and B-cell responses, which we know will be critical for getting longer-term protection,” says Parent, an expert on retroviruses. “If we get good data in animals, we will begin to look for industry partners to help us take the vaccine to clinical trial.”

“Using a non-human adenovirus as a vector for delivering the vaccine is important because it means that the human population will have no preexisting immunity to it.”

— Suresh Kuchipudi



Patrick Mansell

Suresh Kuchipudi

AN “AEROGEL” TO DELIVER NUCLEIC-ACID-BASED VACCINES

Of the various vaccine types in clinical use, vaccines based on nucleic acid, including DNA and RNA, are among the easiest to develop and produce, and they induce a wide range of immune response types, thereby providing robust protection.

“Unfortunately,” says Scott Medina, assistant professor of biomedical engineering, “nucleic-acid-based vaccines have, until recently, not been widely adopted because they are rapidly degraded by enzymes in the body and they are not readily taken up by host cells.”

Medina, whose pre-COVID research focuses on developing a universal flu vaccine, has found a way around these obstacles by developing a gel-like nanoparticle aerosol, or “aerogel”, that protects the vaccine from degradation and promotes its uptake into cells. His vaccine is intended to be delivered to the lungs through inhalation.

“We’ve designed the aerogel to mimic human lung tissue,” Medina explains. “Immune cells in the lungs are really sensitive to these types of materials because they look like pieces of lung tissue that have been degraded or destroyed by a bacterial or viral infection. These immune cells in the lungs [called macrophages] basically eat and digest them to remove them.”

He explains that the aerogel encapsulates DNA that encodes for a protein on the surface of SARS-CoV-2. “When macrophages clean up what they detect as pieces of damaged lung tissue, they internalize the DNA and express a viral protein, which stimulates an immune response to the virus.”

The team is currently testing its vaccine in hamsters in collaboration with Girish Kirimanjeswara, associate professor of veterinary and biomedical sciences.

A VACCINE BUILT FROM A NON-HUMAN ADENOVIRUS

Adenoviruses are responsible for human illnesses including the common cold and pink eye and, in

principle, because they are so good at infecting humans, adenoviruses make good candidates for vaccine vectors. With a \$3.8 million grant from the National Institutes of Health, Suresh Kuchipudi, clinical professor of veterinary and biomedical sciences, and his colleagues are developing a novel vaccine that uses an adenovirus as a delivery vehicle.

“Unfortunately, because many of us have already been exposed to these adenoviruses, our bodies could be immune to an adenovirus-based SARS-CoV-2 vaccine,” he says. To get around that and make the vaccine more effective, the group is using a harmless form of a common cold-like adenovirus found in cattle as a vaccine platform. “Using a non-human adenovirus as a vector for delivering the vaccine is important because it means that the human population will have no preexisting immunity to it,” says Kuchipudi.

Working in mice, the team is assessing the quality and durability of the immune response that their vaccine creates. So far, Kuchipudi says, the work suggests that their novel adenovirus vector system could serve as an excellent delivery vehicle, both for the development of recombinant vaccines against SARS-CoV-2, and for future emerging pathogens.

“An effective vaccine is the best hope to finally end this pandemic,” Kuchipudi adds. “But it will take more than just one vaccine to solve the problem. We will likely need to deploy multiple vaccines with different mechanisms of action. A key focus of our technology is to develop a COVID-19 vaccine that is also effective in older people with weakened immune systems who are at a higher risk of developing severe disease. We will also need effective therapeutics to treat the virus after infection and to treat the symptoms of the virus.”

“Finally, and it can’t be said enough, if we all strictly follow recommendations for social distancing, mask wearing, and handwashing, we can go a long way toward protecting ourselves and each other from this virus.”



ORIGINS OF AN OUTBREAK

TRACKING THE
COVID-19 VIRUS
TO ITS SOURCE

BY DAVID PACCHIOLI



Getty Images/Ilya Lukichev

It was late January 2020 when Maciej Boni realized that the COVID-19 pandemic was about to take over his life.

Boni, associate professor of biology, is an epidemiologist with extensive expertise in viral evolution, including a recent focus on human and avian flu. When COVID hit, he tapped into a network of colleagues around the world, quickly joining an international team intent on tracking the outbreak to its origins.

“CORONAVIRUSES ARE HIGHLY RECOMBINANT, EACH A GENETIC MASH-UP OF BITS AND PIECES PICKED UP AND DISCARDED THROUGH GENERATIONS OF EVOLUTION.” —MACIEJ BONI



Maciej Boni

Patrick Mansell



◀ The evolutionary tree that Boni and colleagues created shows that SARS-CoV-2 has been circulating in bats for decades.

“THERE ARE PROBABLY DOZENS OR HUNDREDS OF OTHER VIRUSES ON THIS VIRAL LINEAGE, SOME OF WHICH ARE READY TO JUMP TO HUMANS WHENEVER THERE’S AN OPPORTUNITY.” —MACIEJ BONI

Coronaviruses like SARS-CoV-2, Boni knew, are highly recombinant, each a genetic mash-up of bits and pieces picked up and discarded through generations of evolution. As a graduate student, he had created the recombination detection algorithm 3SEQ, the most accurate method yet devised for identifying recombinant viruses, and his research group in Penn State’s Center for Infectious Disease Dynamics continues to maintain this important tool. “So I thought, Why not see how highly recombinant SARS-CoV-2 is?” he says.

The first reason for wanting to know the viral origins of an outbreak is to stop it. “Identify the point source and close a poultry market, close a wet market, isolate a single district before it’s gotten to thousands of people,” as Boni says. In the case of SARS-CoV-2, however, the outbreak had already spread too far for that kind of intervention. If he and other experts could determine where the virus had come from, they would have a better chance at predicting where it was going. Understanding the evolutionary history, moreover, would be critical for preventing future outbreaks.

To untangle the details of the SARS-CoV-2 genome, Boni and his colleagues used bioinformatics to pull out the recombinant segments. “That left us with two or three major segments that, as far as we can tell, have not been broken up and pasted back together,” he says. Using these fixed elements as a kind of evolutionary backbone, they created a family tree of all the coronaviruses they could identify in what was left. Within that panoply, they calculated that SARS-CoV-2 and its closest relative, a bat virus called RaTG13, diverged from a common ancestor between 40 and 70 years ago.

That means SARS-CoV-2 has been circulating in bats for decades, Boni says. What’s more, one of the older traits that SARS-CoV-2 shares with RaTG13 and other close relatives is its receptor-binding site, the genetic mechanism that enables the virus to recognize and bind to receptors inside the human lung.

“The receptor binding site was not acquired by recombination from another virus,” he explains. “That’s something that just exists in bats—and in pangolins, it turns out. It’s just a trait of these specific bat coronaviruses that they can also infect humans.”

The scary part? “There are probably dozens or hundreds of other viruses on this viral lineage, some of which are ready to jump to humans whenever there’s an opportunity,” Boni says. The key to preventing the next outbreak, then, is preventing those opportunities, along with improved screening so that where crossover does occur, any further spreading can be quickly minimized.

By late February, however, the present outbreak was commanding Boni’s full attention, as the full scope of the threat became clear. “I quickly wrapped up all the evolutionary work and started shifting to epidemiology,” he says.

For this work, he has teamed up with Ephraim Hanks, associate professor of statistics, and Justin Pritchard, assistant professor of bioengineering, to assist and advise the state departments of health for Pennsylvania, Massachusetts, and Rhode Island. Using data provided by each state, he explains, the three are conducting statistical analyses to help hospitals forecast future needs.

Long-term forecasting, he stresses, is next to impossible, because there is too large an unknown variable: human behavior. But what they can do with existing data is provide more accurate estimates that can help health officials get a better handle on the present state of the epidemic.

By feeding thousands of data points into their mathematical model, they get estimates of factors such as the percentage of 40-49-year-olds infected with the virus who become hospitalized, the percentage of hospitalized patients that are moved into the intensive care unit (ICU), and the average length of stay in the ICU or length of time on a ventilator.

With enough data from reported cases and a finely tuned model, they can then begin to get a better handle on the number of people who were infected, but did not report that they were.

“The most valuable thing we can do,” Boni says, “is to provide states with a more accurate estimate of the total number of people who have been infected so far.”



Getty Images/reklamilar

Tools for Better Decision-making

Researchers across disciplines harness the power of predictive modeling.

By studying the mechanisms by which the COVID-19 virus spreads, as well as the effects of coordinated response, researchers can help predict future patterns and develop strategies and recommendations for public health interventions.

Infectious disease experts from Penn State's Center for Infectious Disease Dynamics have been involved in predictive modeling efforts from the pandemic's earliest days, working in concert with the World Health Organization, the Centers for Disease Control and Prevention, and various state health agencies. They have been joined by researchers from across the University, bringing new approaches to develop tools for better decision-making. Here are a few examples.

FROM PHYSICS TO FORECASTING

Mike Norton came to COVID modeling from a physics lab. "My background is in dynamical systems," he says. "Before this I was modeling fluid dynamics."

Since the outbreak, statisticians and others have turned increasingly to dynamical systems to model the spread of disease. Norton, research assistant professor of neural engineering, and an international team of colleagues examined one popular approach, the Susceptible Infected Recovered, or SIR, model, with the idea of using it to track and predict the spread of the COVID-19 virus across the African continent. They found that SIR has significant limitations.



Michael Norton

Although it can coarsely capture the probability of spread through a population, Norton explains, an SIR model assumes an idealized version of how disease progresses that, especially in the first stages of an epidemic, is difficult to fit accurately to real-world data. "That's why the early predictions were all over the place," he says.

When it came time to create a practical tool, Norton and his colleagues, a team including epidemiologists, statisticians, geographers, and meteorologists, decided on a different approach. They swapped out their SIR model for a data-driven one that doesn't try to estimate underlying mechanisms, but instead predicts reported cases purely as a function of previously reported ones.

The resulting surveillance model can't make predictions about things like transmission rates, Norton says, "but it does have the potential to do short-term forecasting—up to a week, say—in the face of messy data."

Using this approach, the team reports, they have identified a number of contributing factors that have influenced the spread of the virus in Africa, including a country's testing capacity, social policy, landlocked status, temperature, and humidity.

They have also produced an open-source version for public health professionals. "We hope it will enable them to get a rough forecast not of what's going to happen, but, given the previous data, of what is reasonable to expect," Norton says. "Then, if you start seeing cases that really diverge from your prediction, that's your indication that something significant has changed."

—DAVID PACCHIOLI

MOVEMENT OF THE PEOPLE

Nita Bharti uses new technologies to track population movement and its relationship to human health. In response to the pandemic, she and Anthony Robinson are studying how monitoring the movement of people might be used to predict COVID-19 transmission and guide health policy decisions for early intervention.

“We usually see about a two-week lag between when cases of COVID-19 are reported and when those cases were actually transmitted,” says Bharti, Lloyd Huck Early Career Professor and assistant professor of biology. “Transmission pretty closely tracks with contact between people, which is reduced when people stay home during lockdowns and increases when people start moving around again.”

Using passive satellite surveillance data, she says, she and Robinson, associate professor of geography, can observe changes in nighttime lights and air pollution associated with this movement, and compare levels of movement during various levels of lockdown. By looking at specific areas in China, Italy, and South Korea where there were rapid responses, for example, they might see changes in movement linked to subsequent waves of cases.



Nita Bharti

Locally, the team is monitoring movement captured by traffic cameras across Centre County through different phases of restrictions, investigating whether traffic volume—used as a measure of how much people are moving around—is correlated to weekly fluctuations in numbers of COVID-19 cases reported.

“We see traffic levels responding to restriction phases,” she says. “This indicates measurable compliance with those regulations, which has been a hard thing to estimate. We then see a two-week lagged correlation between traffic and reported cases, and we are still working to estimate the statistical strength of that relationship.”

If it proves robust, she says, “These interactions can tell us how much of an impact we might expect behavioral interventions to have on transmission in Centre County and similar areas. This would be informative for outbreak management of COVID-19 as well as other directly transmitted pathogens.”

—SAM SHOLTIS

CLUES TO CLEANER AIR

The massive behavioral changes associated with a worldwide pandemic have far-reaching impacts. Among these, stay-at-home measures instituted across the U.S. in April to help curb the spread of COVID-19 provided atmospheric scientists with some clues for improving future air quality.

Guido Cervone, professor of geography and meteorology and atmospheric science at Penn State, and Cristina Archer, a colleague at the University of Delaware, have examined the pandemic’s effects on two key pollutants—nitrogen dioxide and fine particulate matter.



Guido Cervone

“One of the big uncertainties with trying to forecast future air quality is how the atmosphere will respond to lower emissions of certain pollutants,” says Cervone. “COVID-19 gave us some insights into the effects of lower emission rates on the environment. We had this unique situation that showed us what happens if people stop driving.”

Fewer passenger vehicles on the road resulted

in an average 13 percent drop in nitrogen oxide levels across the U.S., they found. Levels of fine particulate matter remained mostly unchanged, with increases in some places due to higher-than-usual diesel-fueled truck traffic and more home heating and electricity use.

These findings provide a better idea of how the atmosphere reacts to reduced emissions from vehicular traffic, which can help to improve air quality models, the researchers say.

“If we can validate the effect of reduced emissions on air quality, we can better parameterize our models and have less uncertainty as to what will happen 10 or 20 years down the road under different emissions scenarios,” Cervone says.

Properly simulating the responses observed in the study, Archer adds, will allow researchers to test how future interventions, such as traffic restrictions in certain areas or incentives to switch to electric vehicles or heat pumps for home heating, will affect air quality.

“These model improvements will give people better air quality and ultimately better health,” she says.

—FRANCISCO TUTELLA

As COVID-19 unsettles our food supply chains, agricultural researchers aim to head off future disruptions



OUR CHAIN REACTION

by Sara LaJeunesse



IT WAS FRIDAY, THE 13TH OF MARCH. CARISSA ITLE-WESTRICK AND HER FAMILY HAD PLANNED TO DO THEIR USUAL END-OF-WEEK WORK, WHICH INCLUDED MIXING UP CHOCOLATE MILK FOR THE 25 LOCAL SCHOOLS THEY WOULD SERVICE ON MONDAY. BUT THEY HELD OFF.

“We’d heard a rumor that the schools might close for the pandemic,” says Itle-Westrick, owner of Vale Wood Farms, a 200-cow, family-owned dairy farm in Cambria County, Pennsylvania. “Once milk gets turned into chocolate milk and poured into containers, it’s too late to do anything else with it. Chocolate skim milk is a product we only make for schools, and we didn’t have any other customers we could transition that product to.”

Itle-Westrick’s concerns were shared by thousands of other dairy farmers in the United States. By mid-April, the Dairy Farmers of America estimated that the loss of school, hotel, and restaurant customers led to farmers having to dump nearly four million gallons of milk each day.

Fortunately, Itle-Westrick was able to find an outlet for her white milk.

“We posted an invitation on our Facebook page for customers to come to our dairy store to purchase the cases of half pints that had been destined for the schools; we sold out of them in a day,” she says.

In addition to concessions, Vale Wood Farms also saw an increase in home delivery sales. Itle-Westrick credits her farm’s ability to remain in the green during the COVID-19 pandemic to the personal relationships that her family has nurtured with customers over generations.

“Supply chains are built on relationships,” she says. “Our close relationship with our customers was our saving grace.”



Right, Vale Wood Farms in Cambria County, like many dairy producers, has seen pandemic-related changes in milk sales. Facing page, left: Vale Wood Farms dairy cows; right: David Ablar.



Michel Garrett

Dairy isn't the only agricultural industry that has been affected by the pandemic. Meat processing facilities have been suffering as their workers have fallen ill with COVID-19, and fruit and vegetable producers have been struggling to find workers as travel from countries like Mexico has been disrupted.

Meanwhile, consumers are paying higher prices for meat and have at times been unable to secure staples such as pasta, flour, and frozen goods.

"These disruptions have exposed weak links and a lack of resilience in some U.S. food supply chains," says David Ablar, professor and associate head of agricultural economics, sociology, and education. "It is apparent that food and agricultural policy initiatives to increase the resilience of the system are needed."

Ablar is one of several researchers in the College of Agricultural Sciences who is investigating the impacts of COVID-19 on food systems with a goal, not only of informing decision making now, but also to better prepare for other types of disruptions in the future.

MODELING RESILIENCE

Despite the importance of resilience in food supply chains, little research had been done on the topic, according to Ablar. "Conceptual models exist to investigate different aspects of supply chains, but the complexity of real-life systems has yet to be explored," he says.

For example, he adds, existing supply chain models do not consider the spatial relationships among components. "If gasoline prices were to go through the roof, large urban areas that depend on produce being trucked in from distant agricultural areas may see a drop in availability, whereas small towns that are adjacent to agricultural areas may be less affected."

Existing models also tend to focus on single supply chains in isolation. For example, a farmer produces raw milk and sells it to a company that processes and packages the milk. That company then sells the finished products to retail outlets, which in turn, sell the products to customers.

"This is too simplistic," says Ablar. "Real-world supply chains interact with each other through competition for products and services. A fungal infestation on the feed source for a large dairy operation could cause milk production to decline, and that may lead to milk processors purchasing milk from other farms that are farther away."

Current models also tend to focus on disruptions that occur individually, whereas real-world supply chains may simultaneously face multiple disruptions that interact with and reinforce each other—for example, disease and drought.

With support from a COVID-19 seed grant from the college's Institute for Sustainable Agricultural, Food, and Environmental Science, Ablar and his colleagues—James Shortle, Distinguished Professor of Agricultural and Environmental Economics; Alfonso Mejia, associate professor of civil and environmental engineering; and Caitlin Grady, assistant professor of civil and environmental engineering—are developing a more realistic model of food supply chains in the United States. The team has already built a prototype and generated preliminary results, which they used to apply for a grant from the U.S. Department of Agriculture to further refine their model.

The model includes layered geographical and political boundaries to assess how climate, market, and other forces affect food systems. It can estimate the impact of changes in labor availability, multiple simultaneous shocks, changes in inventory, and other conditions on vegetable and dairy production.

"We know that food supply chains have been disrupted by COVID-19, but we need more information about which regions in the U.S. and which parts of the supply chains have been affected, as well as how disruptions in non-food supply chains have spilled over into supply chain disruptions for food," Ablar says. "Our model can help provide that kind of information. It can highlight weak links, tipping points, and bottlenecks in supply chains and reveal how disruptions to one supply chain in one part of the United States can propagate to other supply chains or products in the same or different parts of the country."



“Conceptual models exist to investigate different aspects of supply chains, but the complexity of real-life systems has yet to be explored.” —DAVID ABLER



Michel Garrett



Michel Garrett

PA STRONG

One weak link that has been revealed by the coronavirus pandemic is the vulnerability of workers. By early June 2020, more than 20,000 infections across 216 facilities located in 33 states were reported among employees of meatpacking plants in 216 facilities in across 33 states. Dozens of plants temporarily closed. The result was a jump in meat prices.

Fruit and vegetable packing plants have suffered similarly, as immigrant fieldworkers were prevented from entering the country. Such temporary foreign visa workers, especially those from Mexico, account for 20 percent of the country’s farm workers, according to the American Farm Bureau Federation.

Yet, according to Armen Kemanian, associate professor of production systems and modeling in the Department of Plant Science, Pennsylvania has a strong family farm community and is, therefore, less reliant on hired labor than some other states.

Kemanian and his colleagues have been closely following the ways in which COVID-19 is impacting agriculture in Pennsylvania. The team has observed that despite taking a hit during the early part of the pandemic when restaurants and schools closed, the industry has managed to stay afloat due, in part, to the relatively small sizes of its farms.

“The majority of Pennsylvania’s small farms are members of co-operatives, meaning that milk is pooled and brought to a central location for pasteurization, or for processing into other dairy items,” he says. “This gave them an advantage when the school and restaurant customers disappeared, as the losses from dumped milk were spread among members of the co-ops. As a result, no farms went out of business during this crunch.” About \$15 million dollars available through the CARES Act (Dairy Indemnity Program) helped buffer some of the damage.

But with the renewed surge in COVID-19 cases in the fall and winter of 2020, especially with outbreaks widespread and not localized in big cities, farms and processing plants could suffer another setback.

“We stated in the summer that the prospects of dairy farmers are highly dependent on whether the U.S. experiences a second wave of infection, and of what magnitude,” says Kemanian. “Though prices may not plummet as before, it is unlikely that many farmers will be able to survive sustained low prices.”

A spike in disease cases in the fall and winter could also have environmental consequences. “Fall is when cover crops are planted,” says Kemanian, referring to the practice of growing crops that improve the soil, prevent soil erosion, and reduce runoff after the market crops are harvested.



“Pennsylvania is a pioneer in cover cropping. A sudden contraction in cover cropping area because of a decline in the availability of farmworkers could have effects on our water quality.” —ARMEN KEMANIAN



“Pennsylvania is a pioneer in cover cropping. A sudden contraction in cover cropping area because of a decline in the availability of farmworkers could have effects on our water quality.” Low corn yields due to a dry summer have left many soils with excess mineral nitrogen prone to winter runoff, he adds, which increases pollution risks.

With seed grants from the College of Agricultural Science’s Institute for Sustainable Agricultural, Food, and Environmental Science and the Penn State Huck Institutes of the Life Sciences, Kemanian and his colleagues are building a set of diagnostic tools for assessing risks in the food system, not only from COVID-19, but from other potential disruptions as well. The tools will provide quantitative assessments of emerging risks and plausible interventions.

The researchers are using Sugar Valley, an 18-mile-long valley located in Clinton County, Pennsylvania, as an initial case study. “We chose Sugar Valley because it is enclosed by mountains and a well-defined waterway outlet, which makes for a convenient case study,” says Kemanian.

The team is building a virtual model using baseline data on biogeochemistry, water balance, crop production, livestock numbers, soils, weather, and more. “We can use that data as a reference to ask questions about how changes to one part

of the system might affect other parts,” says Kemanian. “For example, we could ask what would happen if we needed to delay planting dates because laborers are out sick. We could then predict that we will have to dump milk or that we will see a signature of the pollution in the water coming out of the valley.”

Kemanian explains that the smaller-scale model will provide a realistic assessment of what it will take to scale up the model to county, state, or even national levels. “We have played catch up with the cascading effects of COVID-19. A state-level model of agriculture would let us explore potential scenarios and interventions ahead of time, giving state agencies and stakeholders information that helps mitigate problems.”

Meanwhile, Abler’s team is gathering data from news reports and other online sources to develop several real-world case studies to further test and validate their supply chain network model.

“COVID-19 has dramatically altered food supply chains in the United States, with disruptions to food production, processing, transport, and retail,” says Abler. “We are addressing it by gathering data in near real-time and using it to inform our model and generate results that are highly policy relevant.”

LESSONS FROM A CRISIS

When the COVID-19 crisis hit in early March, faculty of Penn State's Center for Supply Chain Research® and its top-ranked department of Supply Chain and Information Systems sprang into action. Steve Tracey, executive director of the center, along with colleagues Sue Purdum, Brent Moritz, Kusumal Ruamsook, Terry Harrison, Jason Acimovic, and Kevin Linderman, shared expertise at many levels, from aiding a grassroots effort to solve the shortage of personal protective equipment (see story page 9) to writing white papers for the COVID-19 Healthcare Coalition, a national initiative started by The Mitre Corporation and the Mayo Clinic.

In addition, Tracey has served as a consultant to the Penn State Health System on supply chain matters and as co-chair (with Kevin Black, dean of the College of Medicine) of the Health Resources Task Force, charged with designing the University's testing and contact tracing systems.

In its early stages, the pandemic caused unprecedented supply chain disruptions in the U.S. healthcare system. "We have learned a tremendous amount since then, both about the virus and about how to manage resources," Tracey says.

In the case of PPE, for example, one factor that exacerbated shortages was an overreliance on single-use disposables, he says. This reflects a decades-long shift away from reusable equipment in all facets of hospital operation, driven mostly by cost concerns. In ordinary circumstances, he says, disposables had become the cheaper option, but when the pandemic hit, and demand skyrocketed, production could not keep up, and existing stockpiles were not enough to meet the need.

Facing page, left: Empty grocery store shelves were a common sight early in the pandemic; right, Armen Kemanian. This page: An overreliance on disposable masks may have contributed to early shortages.

The answer was not simply to have more PPE on hand, Tracey says. "It was learning how to manage existing PPE better. Recycling and re-using disposables. Re-establishing sterilization procedures. It turns out the optimal solution is a mix of reusables and disposables, not all one or the other."

That kind of balance, Tracey says, has been missing from the larger healthcare supply system.

"The model we have migrated toward is efficient, but not resilient," he says. Among other things, a skewed emphasis on cost savings led to a situation where 70 percent of the world's PPE supply was being produced in a single country.

As a result of the pandemic, "Smarter companies are realizing that there has to be a balance between low cost and low capital investment on the one hand and resiliency and risk avoidance on the other," he says. Government has a role in striking that balance. But it's not simply a matter of buying and storing more inventory in case of an emergency.

"It's thinking differently about inventory, about capacity. It's having a plan in place for quickly increasing production. It's a combination of things. You have to think about comprehensive solutions, as opposed to single-point solutions," Tracey says. "Single point solutions are single points of failure."



Michel Garrett



WHEN COVID HITS H♥HOME

Understanding the
fight with fear

by Katie Bohn

When the first U.S. case of COVID-19 due to community spread was diagnosed in late February 2020, it set off a rapid series of events. As cases surged, many states issued stay-at-home orders, and schools and childcare centers shut down. With such rapid, widespread disruption, it's no wonder that many people found themselves struggling with fear and anxiety.

Unfortunately, these emotions may trigger adverse effects on the body and mind. Previous studies have linked fear with depressed immune system functioning, cardiovascular problems, and long-term mental health issues like post-traumatic stress disorder. And in a pandemic, these repercussions could be even more harmful than usual.

James Dillard, Distinguished Professor of Communication Arts and Sciences, says people use a variety of strategies to cope with their fear in situations like this. While he is not currently studying fear during the coronavirus pandemic, he did research on how pregnant women dealt with fear during the 2015 Zika epidemic, which posed an extra threat to babies in utero.

One strategy Dillard and his team investigated was "avoidance," where people try to manage fear by avoiding a topic altogether, such as turning off the TV and not talking about it. This did not reduce fear for the participants in the study. A second strategy was called "contesting," which means denying the problem exists or saying it is blown out of proportion. This also was ultimately ineffective.

"One of the most surprising things we found was in regard to the suppression of emotions," Dillard says. "There's this idea that you can say, 'I know I'm feeling this, but I'm going to push it down and ignore it,' but people who do that actually experience more fear. It's very counterproductive and something to avoid."

While media coverage can be overwhelming or frightening, Dillard says it is still important to stay up to date with the latest recommendations from public health officials and other experts. To stay informed while minimizing fear, he recommends creating a plan for how much and what kind of media you consume.

"If you feel consistently uncomfortable or are unable to sleep, it may be best to back off the media," Dillard says. "It's also important to choose media sources carefully. There are some outlets that actively try to increase your fear, but fortunately, they're not that hard to avoid."

EXPECTING DURING THE PANDEMIC

Other researchers across the university are exploring how fear, uncertainty, and other psychological stresses due to the COVID-19 pandemic are affecting individuals and families.

In a project funded by a seed grant from the Huck Institutes of the Life Sciences, Aleksandra Zgierska, family medicine and addiction medicine physician at Penn State College of Medicine, is leading research to discover how the coronavirus pandemic is affecting pregnant and postpartum women in central Pennsylvania.

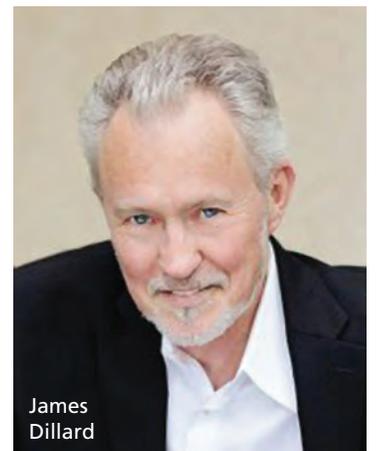
"The pandemic could be affecting these women in a couple different ways," says Jessica Wright, project manager for the team. "It could be the risk from the COVID-19 infection itself, or it could be social distancing requirements and other restrictions that may lead to job and food insecurity or contribute to domestic abuse. And of course, heightened anxiety about the child's health due to COVID-19 exposure may also impact the women's well-being and mental health."

Asking women themselves about their experiences can help better understand the pandemic's impact, the researchers say. Interestingly, experiences may be both positive and negative.

"My husband has been working from home the majority of the past six months so that has been a huge blessing," reported one participant. "He's been able to help with my transition back to full time work. At the same time, I mourn the loss of the experiences I thought I would have during my maternity leave, not being able to spend time with friends and family and not being able to share the joys of the first months of my son's life with anyone else."

The research team is using a survey and screening tool to identify pregnant women who are experiencing risk factors such as depression, substance misuse, or anxiety, that could lead to adverse outcomes such as premature birth or potential difficulties due to loss of income, isolation from support systems, and other stressors. These women will then be provided with a personalized list of resources or a link to a Penn State Health clinic where they can then schedule an online or in-person appointment with a clinician.

As a pregnant woman herself, Wright knows firsthand how difficult it can be expecting a child during a pandemic. She says that while it's always important to make healthy choices during pregnancy, making those choices is more stressful now than ever. "Each decision I make is weighed against the potential impact of becoming COVID positive on my older children and the baby, too," she says.



James Dillard

Penn State

“Each decision I make is weighed against the potential impact of becoming **COVID positive** on my older children and the baby, too.”

—JESSICA WRIGHT



Penn State Health



Aleksandra Zgierska

Penn State Health



Above, Jessica Wright and son. Wright is project manager for a study led by Penn State Hershey family physician Aleksandra Zgierska that seeks to understand how the coronavirus pandemic is affecting pregnant and postpartum women in central Pennsylvania.



“Pregnancy and child birth can bring joy but also add complexity and stress to our lives,” adds Zgierska. “The pandemic has heightened that stress among expectant mothers and families who now worry about impacts on pregnancy, mother and child health, and family well-being. We need to actively support pregnant women, new mothers, and their families so that families and children can thrive.”

TOO MUCH OF A GOOD THING?

Another Huck seed grant focuses on how the pandemic might influence family dynamics. From stay-at-home orders that were issued in the early spring to the recognition that their children will be educated at least partially through remote learning, many families have been spending an unprecedented amount of time with each other. While this has some benefits, it can also aggravate existing strains and create new ones.

Mark Feinberg, research professor of health and human development at Penn State, says families may face a range of stressors during the pandemic. When lockdown orders went into effect across the country, many people were suddenly unemployed or on furlough, without a steady income in an already tumultuous time. Feinberg says it is hard to overestimate the stress this can bring to an individual, let alone a family.

“There’s a lot of research that shows financial stress translates into more family conflict and aggression, harsh parenting, and even child abuse,” he says. “This stress affects how calm, patient, and supportive a parent can be. Research from previous times of widespread economic stress shows how detrimental it can be for families, parenting, and ultimately for kids’ well-being.”

The parent-child relationship is not the only one within many households. There are also relationships between siblings. While sibling roughhousing and teasing are sometimes written off as harmless, Feinberg says these relationships can sometimes become high-conflict and even abusive, with effects lasting into adulthood.

He added that sibling relations can have almost as much of an influence on children’s lifelong well-being, mental health, social competence, and quality of romantic relationships as parenting.

“There’s a lot of jealousy, rivalry, physical aggression, and other dimensions of conflict that go on in some sibling relationships,” Feinberg says. “And while some researchers are working in the field of sibling relations, there’s still not a lot of understanding about how to deal with the more violent aspects.”

Feinberg says that while he and other researchers can use their previous work to predict how the pandemic is affecting

families, there is still a lot they do not know. He recently received COVID-19 seed grant funding to study the effects of the pandemic on two groups of families that the researchers have been studying for several years.

“We’re hoping to survey these families several times during the pandemic and over the next few years to examine how lockdowns and other changes to daily life initially disrupted their lives and how they’re adjusting over time,” Feinberg says.

One of the groups being studied is part of a randomized trial of Family Foundations, a program developed by Feinberg that helps expecting couples build a strong, supportive parenting team with a series of brief sessions both prior to and after the birth of their child.

According to Feinberg, the program is based on the idea that a solid coparenting relationship—one that is built on teamwork and mutual support—is one of the fundamental bases of family well-being. So far, the study has found that parents who have gone through the program tend to be less stressed, less depressed, and less anxious than parents who have not, and as a result, are more patient and less harsh with their children.

And, Feinberg says, they may be weathering the COVID-19 pandemic better.

“Our initial results suggest that during the pandemic, those Family Foundations families are also doing better, relative to other families,” he says. “This family support and prevention approach appears to have long-term benefits, even in this unexpected and acutely stressful situation.”

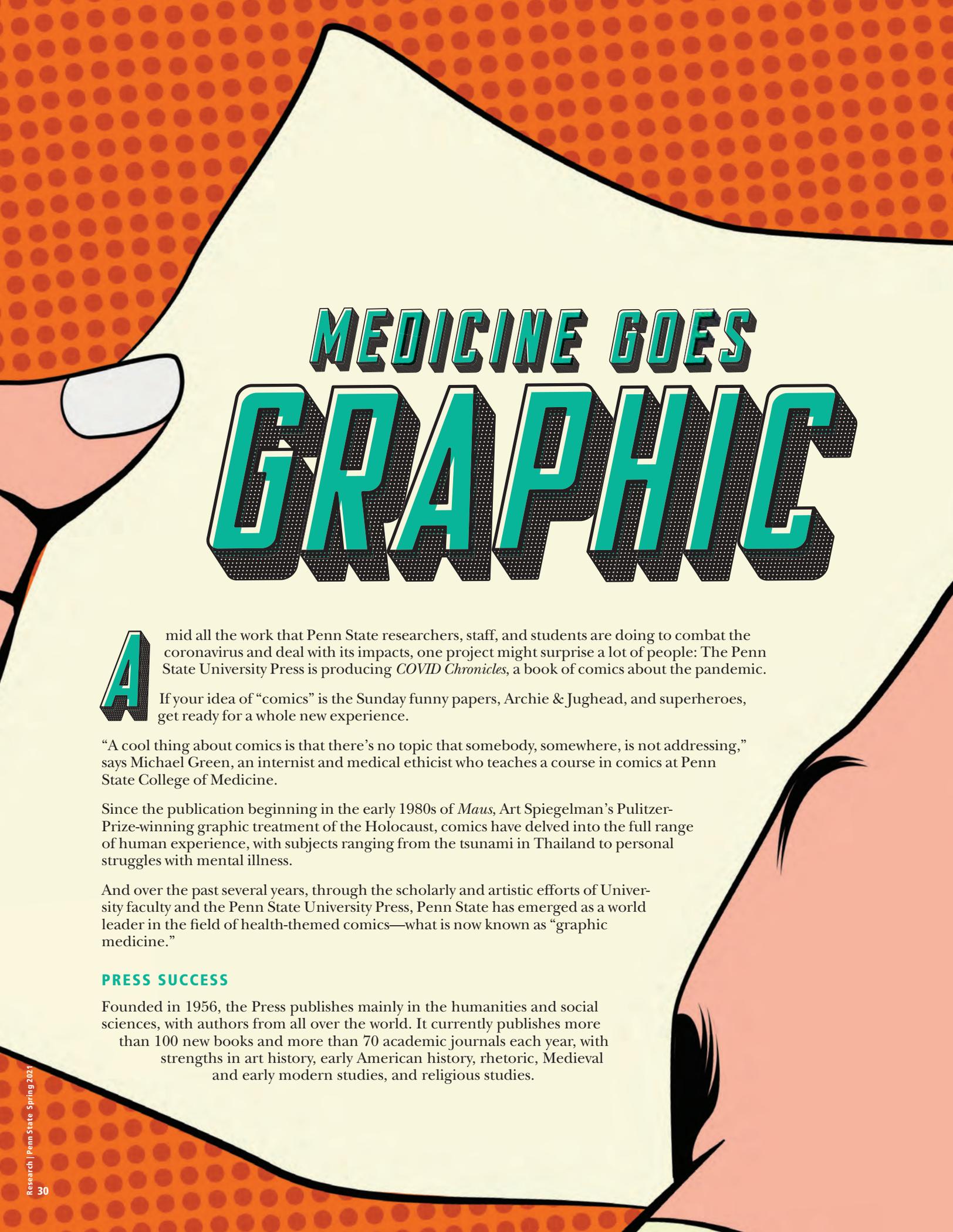
While the pandemic has put unprecedented stress on nearly everyone, Feinberg says it is still possible to find a silver lining in what is an incredibly tough situation. In normal times, many families are operating under busy schedules, and the pandemic may have given them an unexpected gift—time.

“Despite the stress and hardships, I hope that families can also enjoy their time together,” Feinberg says. “If families are finding themselves spending more time together, I hope they can have fewer distractions and more opportunities to play games, enjoy each other, and do things together that they normally wouldn’t.”



Mark Feinberg

Penn State



MEDICINE GOES GRAPHIC

Amid all the work that Penn State researchers, staff, and students are doing to combat the coronavirus and deal with its impacts, one project might surprise a lot of people: The Penn State University Press is producing *COVID Chronicles*, a book of comics about the pandemic. If your idea of “comics” is the Sunday funny papers, Archie & Jughead, and superheroes, get ready for a whole new experience.

“A cool thing about comics is that there’s no topic that somebody, somewhere, is not addressing,” says Michael Green, an internist and medical ethicist who teaches a course in comics at Penn State College of Medicine.

Since the publication beginning in the early 1980s of *Maus*, Art Spiegelman’s Pulitzer-Prize-winning graphic treatment of the Holocaust, comics have delved into the full range of human experience, with subjects ranging from the tsunami in Thailand to personal struggles with mental illness.

And over the past several years, through the scholarly and artistic efforts of University faculty and the Penn State University Press, Penn State has emerged as a world leader in the field of health-themed comics—what is now known as “graphic medicine.”

PRESS SUCCESS

Founded in 1956, the Press publishes mainly in the humanities and social sciences, with authors from all over the world. It currently publishes more than 100 new books and more than 70 academic journals each year, with strengths in art history, early American history, rhetoric, Medieval and early modern studies, and religious studies.

**COVERING SUBJECTS FROM
PARKINSON'S TO GENOCIDE
TO COVID-19, COMICS AREN'T
JUST FOR KIDS ANY MORE.**

BY CHERIE WINNER



Patrick Mansell

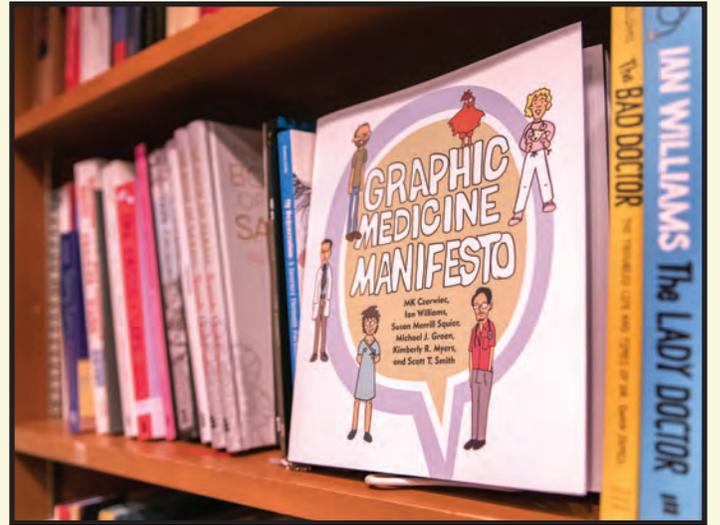
➤ Susan Squier, Brill Professor Emeritus, works on the comics journal she keeps as a way to experience firsthand the power of comics to describe events and express ideas.

In other words, the Penn State University Press offers books of serious scholarship about serious subjects. Graphic narratives—comics—seemed like a radical departure in 2012, when Brill Professor of English Susan Squier urged editor-in-chief Kendra Boileau to publish graphic medicine books.

Squier, an eminent scholar of Virginia Woolf, got interested in comics in the 1990s, when she began exploring ethical issues of in vitro fertilization. “I was using cartoons to talk about debates about human embryo research and organ transplantation,” she says. “I found that when I gave talks on my work, if I started with a cartoon, the audience would engage. A comic helped bring people out.”

But at the Press, it was a tough sell. Comics as a subject for serious scholarship did not fit expectations. Graphic novels were also a stretch for Boileau personally. Unlike Squier, who had been studying and writing about graphic medicine for several years, Boileau was a novice in the field.

Once she committed, Boileau’s first steps into graphic medicine were not timid. In 2015, the Press brought out two volumes. *The Graphic Medicine Manifesto* laid out the case for comics as a medium to explore issues of health and illness. Squier and Green each wrote a chapter, as did fellow Penn State faculty Kimberly Myers, professor of humanities and medicine in the College of Medicine, and Scott T. Smith, associate professor of English and comparative literature. The other book was *My Degeneration: A Journey Through Parkinson’s*, a first-person account by newspaper cartoonist Peter Dunlap-Shohl.



Patrick Mansell

Left, Kendra Boileau, editor-in-chief of the Penn State University Press, has overseen the publication of 18 graphic novels and anthologies and four scholarly books on graphic medicine since 2015. Right, the *Graphic Medicine Manifesto*, the first of these volumes, laid out the case for comics as a medium to explore issues of health and illness.

Since then, the Press has published 18 graphic novels and anthologies and four scholarly books on graphic medicine. Boileau says she expected that most of the books in the graphic medicine series would be scholarship *about* graphic medicine, and that books *of* graphic medicine would be more like an occasional treat. As it turns out, it's the graphic narratives that have really taken off. Boileau says she gets more submissions and proposals for comics than she can keep up with—and those books have been selling very well.

They have been so successful that the Press had planned to launch a new imprint in the fall of 2020. Graphic Mundi (“graphic worlds”), as they named it, would publish graphic medicine novels, broadly conceived. The initial lineup of six titles would include a memoir of growing up with a mother who is bipolar, a humorous look at the biology of sex in animals, and an account of environmental and social devastation in the Amazonian oil fields. Then came COVID-19.

THE COVID CHRONICLES

When it became apparent how severely the pandemic would interrupt business-as-usual, the Press pushed the debut of Graphic Mundi to the spring of 2021. They also considered adding a book of short stories on COVID-19 to the initial group.

“I was actually resisting it, because it seemed opportunistic,” says Boileau. After much discussion, she and her colleagues came up with a way to defuse that concern. They asked the artists to contribute their work for no fee, thereby reducing the cost of production, and will donate all profits from sales of the book to organizations that support small bookstores, bookstore employees, and comics artists, many of whom are suffering economic hardship during the pandemic.

In mid-April, 2020, the Press posted a call for short comics dealing with COVID-related stories ranging from personal tales of isolation, grief, or economic fallout of the pandemic, to the experience of having or treating the disease, to political aspects of how communities and nations are dealing with it. Within days, Boileau’s inbox was flooded with proposals. Delivery is planned for February 2021.

REACHING READERS

The list of topics in *COVID Chronicles* confirms that “graphic medicine” often encompasses more than straightforward accounts of disease.

“Narrowly defined, it has to deal with an illness and has to be explicitly about a patient,” says Green. “But many of us are thinking much more broadly than that.”

Squier agrees. “Sure, it’s what’s in the hospital, in the clinic, but it’s also health care, it’s public health, it’s big issues like the impacts of war, the health impacts of climate change, environmental pollution, social disparities, class, race.”

Green believes “graphic novels,” as both fiction and nonfiction books of comics are commonly called, are excellent vehicles for subjects many of us might find difficult to approach in more traditional ways. They are usually quick to read, yet they are emotionally powerful and able to evoke empathy for people and situations the reader might never have encountered before. “Something about the combination of words and images delivers more information than you would get from just the sum of its parts,” he says. “When you put them together, there’s an almost magical third thing that happens.”

Squier thinks the “third thing” is a visceral response to the pictures. “The image draws you in,” she says. “It makes you pause and connect to it with your emotions, with your *body*.” The images can be looked at again and again, as the reader identifies with each one and tries to understand it. Boileau thumbs through *Vanni*, a tale of a family’s struggles during the Sri Lankan conflict that the Press published in 2019, and finds a wordless panel that shows a man in a small fishing boat at night. The scene is peaceful, yet the man is despondent, almost in shock. “Just the expression on his face...” she says. The image can be taken in quickly, but it invites a closer look, a deeper read. Reading a graphic narrative “is more a digging down than following a thread across,” she says.

A panel from *Vanni*, published in 2019, by Benjamin Dix and Lindsay Pollock



Boileau has found that comics reach a wide variety of audiences, from those who can’t or won’t read long text pieces to highly-educated professionals, and are especially helpful in getting information to people who might have trouble reading it in text form.

Comics are even being used in legal documents. A hospital in Berlin, Germany, developed a graphic version of its informed-consent form for cardiac stent surgery and assessed how effective the 10-page comic was compared to its standard 40-page text version. “The comic version did better at reducing pre-op anxiety, it had better post-op outcomes, it was better right across the board,” says Squier. “People who got the long form would say, ‘You gave me all that, I was just too anxious to read it.’”

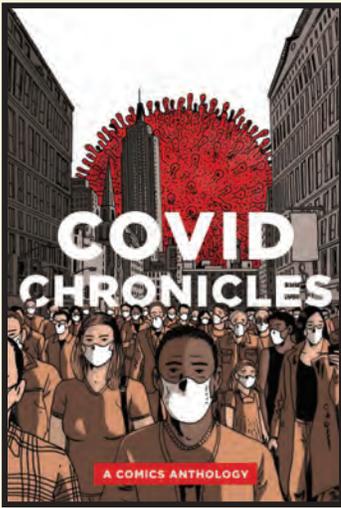
WHOSE STORY COUNTS?

Despite the success of ambitious, medical-themed comics, until recently, graphic novels were viewed by many as being something of a joke, especially when they dealt with serious subjects. “One touchstone moment for me was meeting [a prominent physician/scientist] and saying, ‘I’m working on comics in medicine’ and having him go, ‘I fail to see what’s so funny about medicine,’” says Squier. “He assumes that comics are funny and trivial.”

She traces much of the stigma against comics in the U.S. to “disguised class resentment” against the poor and less well-educated immigrants who were the audience for many early comics in the U.S. “There’s the sort of ‘high culture’ view that if it’s accessible, it must be stupid,” she says.

That view highlights what she and her comics colleagues think is a major strength of graphic novels: They speak for those whose voice is often disregarded in society.





Courtesy PSU Press/ © Joe Decie

“A lot of us who work in health care try to think about whose story counts?” says Green. “Illness is typically presented from the doctor’s point of view, and the patient’s voice gets drowned out. Many of the comics that have been written around medical topics prioritize the voice of the patient in a way that’s really important for doctors to understand. It’s not just what’s happening pathologically when somebody gets ill, but what their *experience* is like. How do they feel when they have this diagnosis, and how does it affect different aspects of their life?”

“Seeing that story unfold from a variety of different points of view can be really illuminating. Using comics is quite helpful for doctors to really see and understand more fully what illness is like.”

HUMANIZING MEDICINE

Green sees his work with comics as following in the strong tradition of humanities at Penn State College of Medicine, the first medical school in the nation with a department of medical humanities. He credits current department chair Bernice Hausman and the college’s leadership with being open to courses that use a variety of ways to explore what it means to be a doctor.

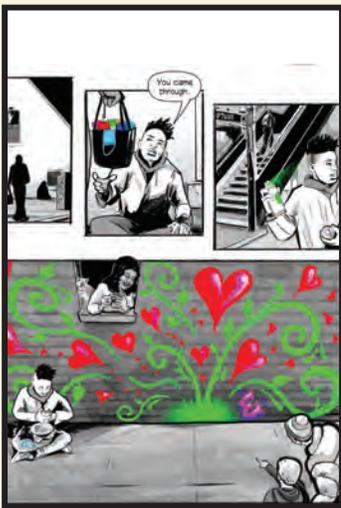
His own interest in comics and drawing goes way back; at a recent high-school reunion, Green’s classmates still recalled him as the class artist. But he didn’t realize the power of comics to deal with serious subjects until the early ‘90s, when he read the groundbreaking *Maus*.

“It just blew me away,” he recalls. “I had read a lot of Holocaust literature. This was as good as or better than anything I’d read, in terms of the impact. So I said, I wonder if there are similar examples that have to do with health and illness. I started looking, and that’s what got me down this road.”

For the past 11 years, he has taught a month-long elective course in which fourth-year students read medical-themed comics and produce their own graphic story about an experience from their time in medical school. Few of them have expertise in drawing, but through conversations with professional artists and workshopping their drafts with classmates, they create vivid graphic stories about events like connecting with a difficult patient, making a mistake, or being chewed out by a supervisor.

“I wasn’t surprised that they were having some dark experiences,” says Green. “I *was* surprised, pleasantly surprised, with their willingness to be open about the negative things that they were experiencing and how powerful their stories are.”

So far, Green has gotten overwhelmingly positive responses to the course from Penn State colleagues and college administrators, but he is sometimes asked why such a

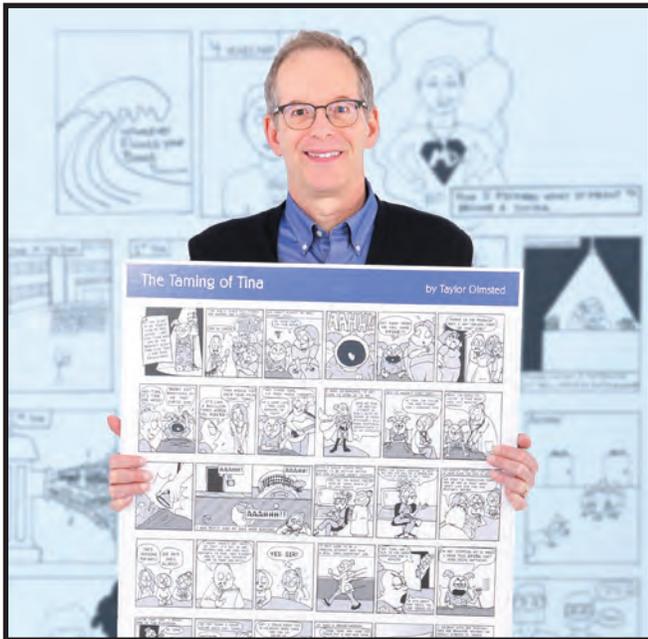


Courtesy PSU Press/ © Emily Steinberg



Courtesy PSU Press/ © Gerry Chow

At top left, the cover of *COVID Chronicles*, a collection of short graphic stories published by the Penn State University Press in early 2021. Following are panels from the collection. The panel directly above is from a comic contributed by Emily Steinberg, lecturer in fine art at Penn State Abington.



course should be taught in a medical school. Beyond the value of giving students a platform to describe aspects of their schooling that are important to them, he says, the course achieves what might be called stealth goals.

“I think there are skills involved in making a comic that are transferrable to the skills of being an effective physician,” he says. “Being able to communicate non-verbally and to understand other people’s non-verbal communication. Being willing to deal with the discomfort of not being good at something and not knowing how to do it. Being able to ask somebody else for help.

“It’s hard to teach these skills, and who says the only way to do it is by explicitly medical means? Sometimes you can achieve these other kinds of goals by doing something that’s entirely different.”

As it turns out, he says, “These are all things that people get better at by reading and drawing comics. To me, that’s the ultimate reason why we should teach graphic medicine in medical school.

“What I want is for the students to become better doctors.”

WHAT’S NEXT

With faculty at three campuses active in producing, studying, or teaching about graphic medicine, Penn State scholars have been instrumental in the field’s growth and in pursuing research on the impact and uses of comics in health care.

Squier and Green helped found the graphic medicine movement and are still major contributors to the field. Squier, now retired from Penn State, continues to explore the linguistic and artistic value of comics and is active in Pathographics, a Berlin-based group that focuses on stories of specific medical conditions and how they affect individuals and communities. She is president and Green is vice

Michael Green, professor of humanities and internal medicine at Penn State College of Medicine, with a poster of a student’s comic about an experience she had as a medical student.

president of the Graphic Medicine International Collective, a nonprofit organization devoted to expanding the use of graphic narratives to tell stories related to human health.

Green and College of Medicine colleague Kimberly Myers are doing research to find out whether medical comics can help caregivers, patients, and patients’ loved ones cope with a serious health threat. In a recent study, they surveyed clinicians at a movement disorder clinic before and after reading *My Degeneration*. The staff already knew a lot about Parkinson’s, so their knowledge of the disease did not go up, says Green, “but their empathy for patients and their understanding of what patients worry about improved greatly.” He and Myers are now conducting a follow-up study of how reading the book affects patients.

Green himself wrote a short comic about a mistake he made as a young resident. It was published in the *Annals of Internal Medicine*, the preeminent journal in the field, whose editorial board liked it so much it decided to develop a graphic medicine section, with Green as its editor.

Emily Steinberg, lecturer in fine art at Penn State Abington, is a graphic novelist whose 2019 story about her experience with hip replacement surgery was published in the Press’ book *Menopause: A Comic Treatment*.

At the Penn State University Press, the new Graphic Mundi imprint is on track to debut early this year with *COVID Chronicles* and the six other titles originally planned. The Press is also tapping into the robust comics scene in other countries, acquiring North American and translation rights to graphic novels from Europe, Asia, and elsewhere.

“Penn State, and the Penn State University Press, Kendra in particular, have really been worldwide leaders in this area,” says Green. “We’re getting to be known as *the* place to go to for these graphic medicine comics.”

Reflecting on the appeal of graphic medicine and the unexpected power of comics to make readers see things in a new way, Squier says, “It requires a kind of open-mindedness to be willing to sit with something that at first may read as trivial. It really pushes us outside of our comfort zone and makes us have to learn how to do something new. That’s just the best. That’s how you keep yourself alive.”

Kendra Boileau is assistant director and editor-in-chief of the Penn State University Press. Michael Green is professor in the departments of humanities and internal medicine and director of the program in bioethics at Penn State College of Medicine. Susan Merrill Squier is Brill Professor Emeritus of English and Women’s, Gender, and Sexuality Studies at Penn State and Einstein Visiting Fellow at the Freie Universität, Berlin. Kimberly Myers is professor of humanities and medicine and Distinguished Educator in the College of Medicine.





BETH McGRAW ON RESPONDING QUICKLY TO A PANDEMIC

Vector biologist Elizabeth McGraw, professor and Huck scholar in entomology, received her Ph.D. at Penn State in 1998. In 2017, she returned to University Park from a faculty position in Australia, and a year later she was appointed director of the Center for Infectious Disease Dynamics (CIDD).

This spring, McGraw chaired the review committee for a seed grant program spearheaded by the Huck Institutes of the Life Sciences that has awarded \$2.4 million in rapid start-up funds to more than 135 faculty members in 48 research teams from across 10 colleges at Penn State to pursue research advances for the COVID-19 pandemic. McGraw also conceived of the “Ask CIDD” video series, an outreach project created both to answer the public’s questions about COVID-19 and to combat scientific misinformation about the pandemic.

WHAT BROUGHT YOU BACK FROM AUSTRALIA?

I was drawn here by the research concentration in vector biology and infectious diseases. CIDD looked like a bit of a dream. There’s nothing like coming to work every day and being surrounded by 50 other incredibly talented research teams that are all studying disease from different perspectives.

WHEN DID CIDD BEGIN TO GET INVOLVED WITH THE PANDEMIC?

Very early on. Initially it was our modelers, who have connections with the World Health Organization and the Centers for Disease Control. Several of our researchers were involved with state health agencies. In early March, we knew we had to act. Our faculty had too much talent to sit idle, so we decided to launch the seed-grant initiative.

None of our faculty were working explicitly on coronaviruses. It’s a very small field, and it had gone quiet since SARS and MERS died down. But we have an outstanding group of world-renowned faculty conducting cutting-edge research on a range of other viruses. With that powerhouse of knowledge and experience, we rapidly shifted to COVID research.

We knew this would be an interdisciplinary effort, since COVID is impacting all aspects of our society and there were so many unknowns, from understanding the disease dynamics, to understanding the molecular structures, to human behavior and how best to communicate with the public. We wanted to harness Penn State’s breadth and depth of expertise—and its exceptional scientific facilities—and have our talent-pool focus on the pandemic. The goal was to quickly get them to a point where they were having an impact on the science, and then to help them get external funding to expand their developments on a larger scale.

AND WHAT WAS THE RESPONSE?

It was huge! We had so much interest, with so many people who knew that science was key to conquering this disease. We developed a rolling process for individuals and teams to submit proposals, where we promised a quick turn-around for the review. It was impressive to see the diversity of solutions our researchers were proposing.

This was a collaborative effort. Five of our university’s interdisciplinary research institutes participated in the call for proposals. The Huck Institutes of Life Sciences, the Social Science Research Institute, the Materials Research Institute, the Institute for Computational and Data Sciences, and the Institutes for Energy and the Environment all came together very unselfishly to put monetary support behind these proposals, and with researchers stepping up to rapidly vet them. This wasn’t limited to just University Park. We also received proposals from the College of Medicine and from the Commonwealth Campuses, many featuring new collaborations.

Many of our seed grants have already been awarded external funds, predominantly from the National Institutes of Health and the National Science Foundation. We’ve also had many publications, sharing results world-wide across the scientific community. So the process worked extremely well. And it’s been exciting to see the connections our researchers have made—between social scientists and biologists, engineers and clinicians. The new partnerships have been inspiring.

HOW DID THE “ASK CIDD” VIDEOS COME ABOUT?

Faculty in CIDD were constantly being asked questions about the virus and the disease by our families, neighbors, friends, and colleagues. We realized there was a more public need for answers. The situation was changing extremely quickly, however. There was an important role to play in staying on top of and disseminating the latest scientific information. We also wanted to correct misinformation whenever we saw it pop up. We’ve made more than 60 videos that have been widely shared via social media. We offered the public a crash course in epidemiology during this pandemic.

WHAT IS CIDD’S ROLE GOING FORWARD?

CIDD was established long before COVID-19 with the goal to tackle the hardest challenges in infectious diseases. It brings together infectious disease biologists across multiple scales of complexity, from the molecular to population levels, and across all host taxonomies. This work is not going to diminish. I think CIDD will continue to play a role in the developments of COVID-19 even after a vaccine has been effectively deployed. Throughout all of this, we continue to take stock in our efforts—to look at what we did well and what we could have done better. Moving forward, CIDD will be even better positioned to play a significant role in combating future pandemics and outbreaks.

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Courtesy PSU Press/ © Julio Anta, Jacoby Salcedo, and Hassan Otsmane-Elhaou

Medicine Goes Graphic

Covering subjects from Parkinson's to genocide to COVID-19, comics aren't just for kids anymore.

SEE STORY, PAGE 30