Discovery

Research at Princeton

Can a combination of diet and drugs improve cancer outcomes? **Page 10**

2021-22

PRINCETON UNIVERSITY

An extraordinary year for research

If the past two years have taught us anything, it is that research can provide solutions to global challenges.

Without research, we would not have the benefit of highly effective and safe vaccines against SARS-CoV-2, the virus that causes COVID-19. We would not understand how the virus spreads, and how important masking is as a public health measure. In other words, we would not have the tools that will help us turn the corner on this deadly pandemic.

As we celebrate research that provides direct benefits to our everyday lives, it is important to recognize that many of these discoveries originated as open-ended explorations, questions asked not with personal or corporate gain in mind, but because the asker wanted to know the answer.

Princeton is a place that encourages the pursuit of open-ended questions of the kind that can lead to unexpected places and, in some cases, to great societal rewards. Whether the research is aimed broadly at enriching human knowledge or aimed at a specific challenge, curiosity is often the starting point.

This year's Nobel Prize winners, five of whom have substantial ties to Princeton, remind us of the impact of open-ended, curiosity-driven research. Two faculty members received Nobel Prizes, in chemistry and physics, and three alumni won Nobel Prizes, one for peace and two for economic sciences.

Physics Nobelist Syukuro Manabe, a senior meteorologist who has been at Princeton since 1968, earned the prize for work that laid the foundation for the development of current climate models. Manabe stated of his research, "I was doing it just because of my curiosity. I really enjoyed studying climate change."

PHOTO BY FRANK WOJCIECHOWSKI

David MacMillan, the James S. McDonnell Distinguished University Professor of Chemistry, was awarded the Nobel Prize in chemistry for making catalysts from inexpensive organic materials. Little did he know at the time that the innovation would transform the manufacture of products like pharmaceuticals, clothing and shampoo. "What we care about is trying to invent chemistry that has an impact on society and can do some good," MacMillan said, "and I am thrilled to have a part in that."

These are sentiments that most of our faculty researchers at Princeton can endorse, whether we are conducting open-ended, theoretical work or, as you'll read in these pages, trying to address societal challenges such as preventing pandemics (page 4), treating cancer (page 10), or protecting our environment (page 20).

At Princeton, research and curiosity are integrally woven into the endeavors of our undergraduates and graduate students, postdoctoral researchers, faculty and research staff. I believe these values help explain Princeton's disproportionate share of Nobels this year.

And when the next pandemic strikes — or when we are called upon as a society to address the consequences of our continued reliance on fossil fuels — curiosity will be one of the drivers that spurs our researchers to bold explorations, some producing tangible benefits for humankind, and others enriching our intellect.

Pablo G. Debenedetti
Dean for Research
Class of 1950 Professor in Engineering and Applied Science
Professor of Chemical and Biological Engineering

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Combining therapeutics with dietary changes could prove effective against some forms of cancer. Illustration by Dave Klug

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In the Nation's Service and the Service of Humanity

ARTS AND HUMANITIES

Between living bodies and objects

Dancers navigate sculptures' dangerously sharp elements in the performance installation Two Person Operating System Type 2, a collaboration between Lewis Center for the Arts' Martha Friedman, senior lecturer in visual arts, and Susan Marshall, professor and director of the Program in Dance. Friedman and Marshall worked with industrial objects and materials such as rubber and metal, then choreographed tender, foreboding and meaningful interactions between those materials and the human figures activating them, to probe preconceptions of the material condition of the body and engage viewers to think about the sensory experience of inhabiting a body. The project, which debuted in Princeton's Lewis Center for the Arts Hurley Gallery in June 2021, is supported by the National Endowment for the Arts. ***—Lewis Center for the Arts***

PHOTO BY JONATHAN SWEENEY

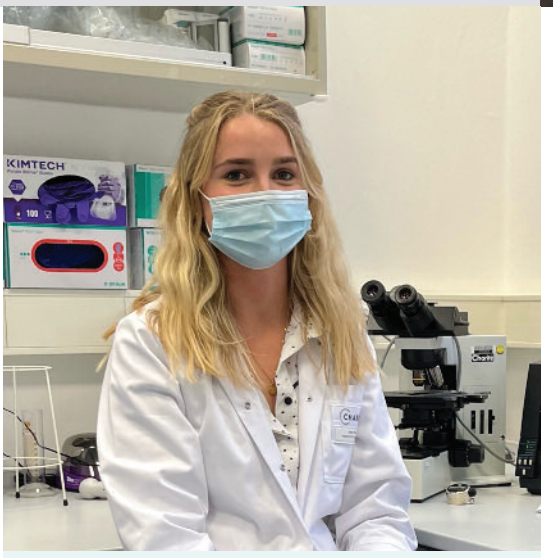


PHOTO COURTESY OF CHRISTABEL MCLAIN

UNDERGRADUATE RESEARCH

Lasting impacts from early-life stress

Christabel Mclain, Class of 2021, explored whether cells in the brain's reward centers that respond to early life stress can be reactivated by stress in adulthood, contributing to depression. She won Princeton's John Brinster, Class of 1943, Neuroscience senior thesis prize and a Fulbright fellowship to study at the Charité-Universitätsmedizin in Berlin. "More than just shadowing or helping senior lab members, Christabel took the reins on her own research project," said Catherine Jensen Peña, assistant professor of neuroscience. "Her senior thesis synthesizes ideas from across fields of neuroscience and uses multiple cutting-edge approaches." ***—Catherine Zandonella***

ENERGY RESEARCH

Reaching for the stars

Fusion is the reaction that drives the sun and stars, generating massive amounts of energy. At the Princeton Plasma Physics Laboratory (PPPL), scientists seek to replicate fusion on Earth with the goal of producing a virtually inexhaustible supply of power. With funding from the U.S. Department of Energy's Advanced Research Projects Agency-Energy, PPPL will design and build permanent magnets that could provide a highly innovative basis for simplifying stellarators — the twisting technology used in experiments for producing fusion energy. "We hope this project will be the start of a program based on permanent magnets," said PPPL physicist David Gates, who leads the team that developed the proposal. ***—John Greenwald***

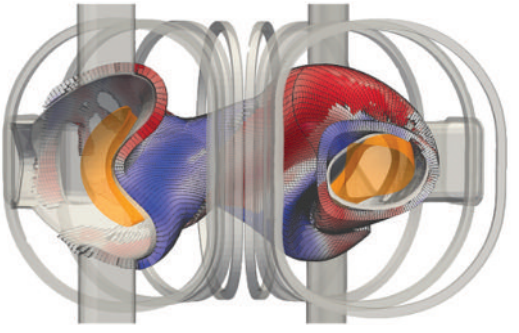


IMAGE COURTESY OF PPPL

A NOBEL YEAR

Princeton scholars and alumni received an unprecedented five Nobel Prizes

NOBEL PRIZE IN CHEMISTRY

‘This idea took off’

David MacMillan, the James S. McDonnell Distinguished University Professor of Chemistry, received the Nobel Prize in chemistry for his role in inventing the field of organocatalysis, which finds revolutionary ways to design and build small organic molecules to drive chemical reactions. Organocatalysts, which are greener than traditional metal catalysts, are used to construct new drugs and materials, and their impact ranges from industrial applications to pharmaceuticals to everyday products like clothing, shampoo, carpet fibers and more.

“All scientists have so many ideas along the way,” MacMillan said. “We have way more ideas than ever succeed — but this one took off, and it took off like gangbusters.”

—Liz Fuller-Wright

PHOTO BY DENISE APPLEWHITE

PHOTO BY DENISE APPLEWHITE

David MacMillan (left).

NOBEL PRIZE IN PHYSICS

‘Following my curiosity’

Princeton University senior meteorologist Syukuro “Suki” Manabe received the Nobel Prize in physics for his climate science research, which laid the foundation for the development of current climate models. Manabe has been on the Princeton faculty since 1968. During a press conference on the day of the announcement, Manabe repeatedly cited the “great fun” to be had in modeling Earth’s climate and urged students to follow their curiosity and their joy, rather than trying to predict what research may prove impactful in future decades. “I never imagined that this thing I was beginning to study [would have] such huge consequences,” he said. “I was doing it just because of my curiosity.”

—Liz Fuller-Wright

NOBEL PRIZES FOR PEACE, ECONOMICS

Safeguarding freedom, insights on the labor market

The 2021 Nobel Peace Prize was awarded to Princeton graduate Maria Ressa of the Class of 1986 for her efforts to “safeguard freedom of expression, which is a precondition for democracy and lasting peace.” Ressa has been a journalist in Asia for more than 30 years, serving as CNN’s bureau chief in Manila and Jakarta and founding the online news site Rappler.com.

Princeton alumni David Card and Joshua Angrist were awarded the 2021 Nobel Memorial Prize in economic sciences for providing new insights about the labor market. Card (Ph.D. ’83) taught at Princeton from 1983-96 and is now at the University of California-Berkeley. Angrist (Ph.D. ’89) is a professor at the Massachusetts Institute of Technology and a research associate at the National Bureau of Economic Research. ***—Denise Valenti***

PHOTOS BY DENISE APPLEWHITE; COURTESY OF THE MIT DEPARTMENT OF ECONOMICS; AND BY JEAN SMITH/UC BERKELEY

From left: Maria Ressa, Joshua Angrist and David Card.

Postdoctoral research associate Karishma Bisht (left) and graduate student Kimberly Sabsay study viruses such as the one that causes COVID-19.

PHOTO BY SAMEER A. KHAN/FOTOBUDDY

Preventing the next pandemic

Humans are vastly outnumbered by viruses with the potential to do us harm.

And yet, pandemics are relatively rare. What makes a particular virus capable of inflicting severe disease? That is a question that A.J. te Velthuis, an assistant professor of molecular biology who arrived at Princeton in early 2021, would very much like to answer.

"Why do these new viruses, when they jump over to us, suddenly become pathogenic, whereas when they were going around in bats or in other species, they seemed almost harmless?" te Velthuis asked.

His team has examined this question by comparing the seasonal flu virus H1N1 to two other viruses, the pandemic 1918 virus and the avian influenza virus H5N1. While seasonal flu usually causes mostly mild symptoms, the pandemic and avian flu viruses can trigger a severe reaction in which the lungs become filled with fluid. In 2018, te Velthuis and his team traced this immune system reaction to small bits of viral genetic material called mini viral RNAs.

When the COVID-19 pandemic hit, the question of how emerging viruses cause severe immune responses took on a special urgency. To study the SARS-CoV-2 virus without posing risk to human health, te Velthuis and his team, while still at Cambridge University, developed a version that cannot infect new cells. This weakened virus is useful for testing antivirals or studying new mutations.

The team is now working to discover how SARS-CoV-2 triggers the overreaction of the immune system that makes pandemic viruses so deadly. Finding the mechanism could inform the design of medicines that inactivate this process, transforming a severe health threat into a minor inconvenience.

"If we can have a tool, a drug for instance, that we can use when a pathogenic virus comes around, we can immediately turn it into a more manageable seasonal virus, and we wouldn't see as much pressure on hospitals and other health-care institutes," te Velthuis said. "That's the bigger dream, the bigger goal." ***—Catherine Zandonella with reporting by Liz Fuller-Wright***

Marshall Brown, director of the Princeton Urban Imagination Center, questions the future of traffic signs, parking lots and garbage trucks.

PHOTO BY LAWRENCE AGYEI

When cars no longer rule

How autonomous vehicles could reshape our cities

A city is not a problem to be solved.

So says Marshall Brown, architect, urbanist, associate professor in Princeton's School of Architecture and the director of the Princeton Urban Imagination Center.

In Brown's view, a city is a reflection of our social, political and cultural values. New technologies are not so much solutions as opportunities.

"People ask how will new technologies change our cities, but that is backwards," Brown said. "The question is, how do we want our cities to change, and then how do we leverage the technologies to get there?"

The technology that has been on Brown's mind lately is the autonomous vehicle, and not just the driverless car.

"There will be stuff moving around all the time," said Brown. "Instead of the garbage truck coming to your house, the bin will just roll away when it is full."

Brown has been asking questions about how technology will change urban mobility since 2015, when he was on the faculty at the Illinois Institute of Technology in Chicago. Questions like: How will we turn 20th century streets, roads and parking lots into 21st century infrastructure? And how do we do it in ways that maintain or enhance the livability of cities?

Signs are for humans

Although today's automakers are investing vast resources into self-driving cars, they've given far less thought to the design of the physical urban infrastructure to support them, Brown notes. Take road signs. They were made to tell human drivers what to do. But driverless cars don't need signs — they can get instructions from the road itself. Autonomous vehicles can navigate via cues embedded in roads, by recognizing patterns, textures or materials.

To explore this idea, researchers in the Princeton Urban Imagination Center's Vehicle to Terrain project — which includes faculty collaborators in architecture and Princeton's School of Engineering and Applied Science — are designing and testing ways that cars can communicate via innovations in machine learning, robotics and new materials.

The team, which included architecture graduate students Kaitlin Faherty and Yidian Liu, who earned their master's degrees in 2021, milled wood blocks and used lasers to etch patterns into the blocks embedded in the road. "We store information in the pavement, and this is environmentally sound, and is more beautiful, which is something that we care about in architecture," Brown said.

Parking — not

Another question is how autonomous vehicles will change the nature of pavement, the ubiquitous and vast impermeable cap over the urban landscape. Pavement causes numerous challenges. The impervious surface enables flash flooding and prevents groundwater aquifers from refilling. Heated asphalt contributes to the "heat island effect," in which urban areas experience higher temperatures than outlying regions. The pavement steals spaces that could be covered in green spaces.

Will autonomous vehicles allow us to shrink the pavement footprint in the urban environment by altering roads and parking lots? Parking by definition is stationary, but with driverless cars, the future of parking could be mobile.

Personal automobiles mostly sit unused while their owners are at work or at a play or concert in the urban environment. When cars can drive themselves, they can navigate to lots far from urban centers, although Brown cautions that it is important to guard against low-income areas becoming the parking lots of the future.

Self-driving vehicles can enhance equitable mobility. Although public transportation can help alleviate traffic and pollution, it presents challenges for the very young, the disabled, the elderly and others who may have trouble with stairs, escalators and crowds. "Urbanists might glorify the bus or the train, but public transportation is not the best option for everyone," he said.

Changing the nature of space and time

We think of space and time as fixed. A minute is a minute. A mile is a mile. But, Brown points out, technology has the potential to alter space and time. What was once a 12-hour horse-and-buggy ride has become a 30-minute hop by automobile. Schools, stores and workplaces that once were a day's walk are now an hour's drive.

With autonomous driving, what transformations will occur?

One change is that mobility will no longer be limited to people with driver's licenses. People who cannot drive — or children who want to go to a friend's house — can just summon driverless vehicles that will take them to their destinations.

"Once you start thinking even a little bit about the impact of these technologies," Brown said, "it explodes into thinking about everything at once." ***—Catherine Zandonella***

"The question is, how do we want our cities to change, and then how do we leverage the technologies to get there?" Brown said.

Mystery on the moon

Erin Flowers explores evidence for liquid (and life) on Titan

Even on Titan, the largest moon of Saturn, it's the little things that count. Hydrogen is the smallest molecule in the universe, and in Titan's atmosphere, it's doing something strange — collecting in surprising quantities where scientists least expect it, like near the moon's surface.

"Hydrogen is very light, and it should just kind of float away out of the atmosphere," said Erin Flowers, a graduate student in the Department of Astrophysical Sciences who is studying the chemistry and physics of Titan's atmosphere. "It shouldn't really collect or pool." In an effort to understand this anomaly, Flowers is tracing the source of the mysterious accumulation.

Her search has taken her to another of the solar system's more diminutive players: micrometeoroids. These little chunks of matter range in size from a centimeter across, roughly the size of a chickpea, all the way down to a single micron, just one-sixtieth the size of a grain of table salt. Most micrometeoroids around Titan are icy particles generated by collisions in the comet-strewn Kuiper belt, beyond the orbit of Neptune. When these particles enter Titan's atmosphere, they introduce new material, like hydrogen, to the mix.

"There are no other bodies in the solar system that have standing liquid on their surfaces."

Flowers is using atmospheric data — collected on and around Titan itself during NASA and the European Space Agency's Cassini-Huygens mission — combined with computer modeling to understand how micrometeoroids affect the chemical composition of Titan's atmosphere. "I'm looking at how those particles move, are destroyed, release their chemical components, and mix in the atmosphere," Flowers said.

A grand scale

Titan is *big*, bigger than the planet Mercury, and half again as large as Earth's moon. But it's not size that makes Titan loom large in the study of our solar system.

Of all the bodies in the solar system, Titan's atmosphere is the most similar to ours. On Earth, water exists in all three states of matter: liquid, solid and gas. Titan also has a three-state atmosphere, but instead of water, it has methane, a simple molecule of carbon and hydrogen that we use on Earth for fuel. Titan's landscape includes lakes and even seas of liquid methane. "This is incredible," Flowers said. "There are no other bodies in the solar system that have standing liquid on their surfaces."

Titan's similarities to Earth make Titan a fascinating target for research, said Chris Chyba, professor of astrophysical sciences and international affairs, and Flowers' adviser. At its most speculative, research on Titan could reveal a previously unknown type of life, one based on methane instead of water. Less speculatively, it could help unravel the riddle of life here on Earth. "The kind of chemistry happening in Titan's atmosphere is just the kind of chemistry that, at least in one popular model for the origin of life on Earth, must have happened on Earth 4 billion years ago," Chyba said.

Grounding roots

Flowers can't remember when she was first bitten by the space bug. She spent much of her childhood coveting telescopes and asking permission to stay up late to look at stars and watch meteor showers. And in high school, it took only one lab period in her physics class for her general liking for science and math to click together into something more. "I was able to describe the motion of something with math, and it played out in real life," Flowers said. "I just thought that was the coolest thing."

PHOTO BY SAMEER A. KHAN/FOTOBUDDY

Graduate student Erin Flowers investigates similarities between Earth and Titan, Saturn's largest moon.

Add that to her starstruck childhood, and it's no surprise Flowers chose to become an astrophysicist. "I've honestly always wanted to do astrophysics," Flowers said. "Once I had a word for it, I was like, that's what I want to do."

Flowers combines an in-depth understanding of physics (to characterize the movements of meteoroids) with chemistry (to model atmospheric interactions), while juggling data from multiple spacecraft missions. Her work is currently undergoing peer review, and Flowers and Chyba think the findings are illuminating. "It looks as though the micrometeoroids might be an important part of explaining these peculiarities of Titan's atmosphere," Chyba said.

Reaching skyward

Flowers credits a supportive community — including her fellow graduate students, her adviser Chyba, and a far-flung network of family and friends — as a critical element of her success. And she makes time to pass that support forward through community outreach, including as a math and science teacher at Princeton's Prison Teaching Initiative, through which inmates can pursue an associate's degree. Flowers also recently received a University-wide teaching award for exceptional contributions to undergraduate instruction. "She is terrific at making connections," Chyba said.

Moving forward, Flowers plans to look at the surface of Titan to investigate how methane, once released from Titan's lakes and oceans, interacts with other elements of the atmosphere to result in pockets of hydrogen. Said Flowers, "There's still a lot of space for new discovery in this field."

—Alice McBride

Cancer Connection

Researchers collaborate on the roles of diet, metabolism and medicines in the fight against cancer

Reported by Alice McBride,
written by Catherine Zandonella

ILLUSTRATIONS BY DAVE KLUG

Some say that the origins of the keto diet can be traced to celebrated bodybuilder and publishing entrepreneur Bernarr Macfadden, who in 1905 purchased a 2,000-acre tract of farmland about 15 miles east of Princeton to set up Physical Culture City, a place where men and women could escape the dissipation of modern life and enjoy, according to one of his books, "the vitality of a young lion."

A self-educated fitness guru, Macfadden believed in the power of fasting to cure disease, a practice also espoused in ancient Greece. And although Macfadden's legacy is little remembered — his Physical Culture City lasted only a few years, a casualty of legal battles — his impact on diet remains with us today through the work of one of his protégés, a physician named Hugh Conklin.

Conklin observed that fasting reduces epileptic seizures in children, a finding that was something of a medical miracle at a time when few drugs were available. Other researchers traced the mechanism to the body's response to starvation. Deprived of fuel, the liver converts fat to ketone bodies, which serve as an alternate energy source for the brain and body. This state of ketosis, physician Russell Wilder at the Mayo Clinic found in 1921, could be achieved without starvation by eating a diet high in fat and low in carbohydrates. And a few years later, the ketogenic — or keto for short — diet was born.

One hundred years later, the keto diet has attained widespread popularity for weight loss, although it is still used to treat epilepsy. Now scientists at Princeton and other universities are hoping that the keto diet can treat another disease: cancer. In combination with traditional chemotherapies, this diet might boost the success rate and lead to longer remission for one of the most intractable forms of the disease, pancreatic cancer.

The teaming of chemotherapy and diet is an example of a growing strategy in the fight against cancer: exploiting cancer's links to metabolism. Princeton's Joshua Rabinowitz is one of the leaders in the field. Rabinowitz's interest in cancer treatment grew out of a deeper fascination with how the body processes, or metabolizes, nutrients. A more comprehensive understanding of metabolism, Rabinowitz believes, could help treat a number of diseases. In spring 2021, Rabinowitz teamed with Eileen White of nearby Rutgers University and Princeton colleague Yibin Kang to lead a major new cancer initiative, a new Branch of the Ludwig Institute for Cancer Research, to be located at Princeton and dedicated wholly to the study of cancer metabolism and the translation of its findings into cancer prevention and treatment.

"We're entering a time where people recognize that diet can be used in a much more targeted way to tackle diseases," said Rabinowitz, director of the Ludwig Princeton Branch and a professor of chemistry and the Lewis-Sigler Institute for Integrative Genomics. "Diet is a primary biochemical input to our beings, and there is a relationship that connects our genes, diets and disease states. Unlocking this code — this is one of the greatest opportunities to improve medical care."

Keto comes to the clinic

The approach will be put to the test as part of a randomized clinical trial that will examine whether the keto diet paired with chemotherapy can extend the life of pancreatic cancer patients. Previous trials have already determined that the keto diet alone cannot cure cancer, but Rabinowitz's collaborators hope that forcing the body into starvation mode, combined with cancer-killing drugs, can slow the progress of the disease. "If we can give multiple years of survival — good quality-of-life survival — to people in that disease state, that would be a wonderful achievement," Rabinowitz said.

One of the first inklings that the keto diet could make inroads against cancer came from Lewis Cantley, a professor of cancer biology at the Weill Cornell Medical College in New York. In 2018, Cantley and colleagues found that mice treated with a targeted cancer therapy

PHOTO BY KIM SOKOLOFF

Princeton professor Joshua Rabinowitz is leading efforts to study cancer metabolism and its role in prevention and treatment as the director of a new Branch of the Ludwig Institute for Cancer Research.

that tamps down an enzyme called PI3K lived longer if they were fed a keto diet instead of a normal diet.

Exactly how the keto-treatment combination helps fight cancer is still unclear. The most popular theory has to do with insulin, the hormone that promotes glucose uptake into the cells. Insulin can fuel cancer growth, and it can cancel out the effects of drugs that aim at PI3K. With carbohydrate-rich and sugary foods on the forbidden list, the body takes in less sugar, so the body makes less insulin.

Rabinowitz and his team are also exploring other possibilities. For example, ketone bodies may induce a state of metabolic imbalance in which tumor cells become overloaded with high-energy electrons, leading to a state called redox stress. Another possible explanation is that the low-sugar content of the keto diet starves tumors of the energy molecules needed for growth.

He cautions that there may also be types of cancer for which the ketogenic diet may be ill-advised, such as certain types of lung cancer. "The world of cancer is complicated, and no one should think of this as a cure-all," he said. "It's also premature to think of this as guidance that if you want to avoid cancer, you should eat a ketogenic diet."

His team is exploring the intersection of nutrition and disease with tools that track nutrients as they travel through the body. In his lab at Princeton on the second floor of Frick Chemistry Lab stand some of the most sensitive devices on the planet for measuring the players in metabolism — sugars, proteins, fats and other molecules — in minute amounts.

These are high-powered versions of the machines that a lab technician would use to determine the levels of certain components in a standard blood test. Each one is essentially an elaborate postal scale — but instead of weighing packages, it weighs molecules. By finding the weight of a molecule and knowing its electric charge, researchers can identify a molecule's signature ratio of mass to charge. Although the basic technique has been around for a long time, in the past decade researchers in the Rabinowitz lab have pushed it to a new level of accuracy.

Tapping regional expertise

Rabinowitz's interest in cancer metabolism blossomed in 2009 when he joined a collaboration aimed at developing therapies that cut the fuel supply to pancreatic cancer. The team included researchers at the University of Pennsylvania and Memorial Sloan Kettering Cancer Center in New York City. He also began collaborating with Professor Eileen White, associate director of the Ludwig Princeton Branch and deputy director and chief scientific officer of the Rutgers Cancer Institute of New Jersey, a National Cancer Institute-designated comprehensive cancer center, which Princeton joined in 2011.

Princeton is a global leader in genomics, biology and the computational and physical sciences. The strong collaboration between Rabinowitz and White was one of the factors that led the Ludwig Institute for Cancer to select Princeton as the site of a new Branch, enabling Princeton to rapidly grow its portfolio in cancer research.

"Cancer is a metabolic disease," White said. "For one cancer cell to make more cancer cells requires a massive change in the metabolic activity of the cell."

> Unlocking the connection between genes, diet and disease is one of the greatest opportunities to improve medical care.

The cancer cell needs to transform from a passive existence into full-blown replication mode, White said. Most normal tissues — in the heart, the brain, the muscles or the organs — don't go through this transformation. Cancer cells stand out for their voracious need for nutrients to fuel growth and their eventual, deadly spread to other places in the body.

As these cells take up more nutrients, they also need to activate specific pathways for channeling those nutrients into growth. White wondered, might these metabolic supply chains be attacked — thus weakening the enemy?

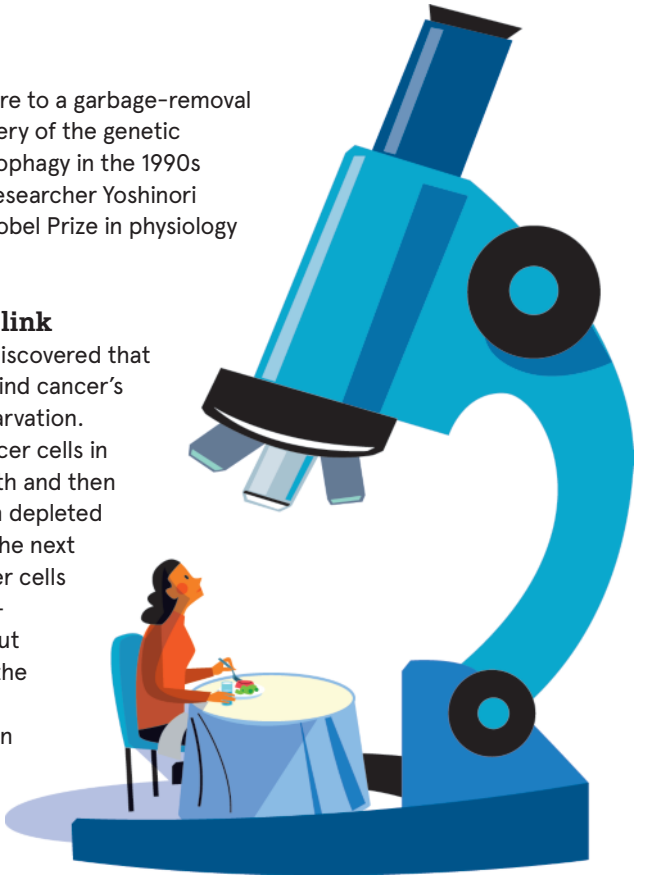
Her team quickly found that this was easier said than done. Cancer cells, it turns out, are very difficult to starve to death. "We had some cancer cells in a plastic dish," White said, "and normally if you take all the nutrients away from a cell, that would be a lethal event. But in many cancer cells, it was not."

Through a series of experiments, White's team discovered the reason why: Cancer cells can cannibalize their own innards to survive a spell of starvation. The cells break down their internal organelles into basic nutrients and use them as energy sources.

This process, known as autophagy, Latin for "self-eating," had been known for decades but was likened more to a garbage-removal service. The discovery of the genetic mechanism for autophagy in the 1990s earned Japanese researcher Yoshinori Ohsumi the 2016 Nobel Prize in physiology or medicine.

Professor Eileen White, deputy director and chief scientific officer of the Rutgers Cancer Institute of New Jersey, is collaborating with Princeton researchers on the study of cancer as a metabolic disease.

PHOTO BY JOHN O'BOYLE



Cancer's weak link

White's team discovered that autophagy was behind cancer's ability to survive starvation. The team grew cancer cells in a nutrient-rich broth and then switched to a broth depleted of nutrients. Over the next few days, the cancer cells shriveled in place — apparently dying. But after several days, the researchers added back the food-laden liquid, and watched via time-lapse video as the cells came back to life. "We called that the cancer horror movie," White said. "The cells just sat there until the food came back, and then they sprung back to life."

To show that autophagy was responsible, the researchers grew identical cancer cells in which an essential gene that enables autophagy had been deleted. When starved, those cells simply shriveled away and died.

"When we made our discovery, every student in my lab wanted to work on it," White said. "They thought this concept that cancer cells could eat themselves, and, in this process would keep themselves alive, was fascinating."

In subsequent experiments, in collaboration with Rabinowitz, the researchers unraveled the role of this self-cannibalization at the chemical level in cancer metabolism. White has since co-founded a company to explore autophagy targets for cancer treatment. From this and other researchers' work, several drugs that inhibit the autophagy pathway in different ways have entered clinical trials.

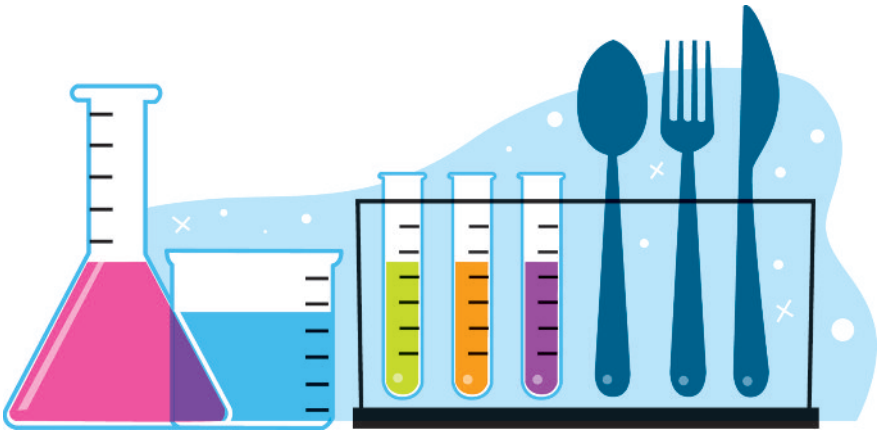
The Ludwig Princeton Branch will focus on three main areas of cancer metabolism: how the body supports tumor growth and spread; how diet can be a strategy for the

prevention and treatment of cancer; and the interplay of human metabolism, the gut microbiome and the anti-cancer immune response.

Branching out

One of the new directions that the Ludwig Princeton team will take is the role of metabolism in metastasis, the spread of cancer cells from the original tumor to other parts of the body. Cancer cells break away from the primary tumor and travel through the bloodstream or lymph system and into other organs such as the liver, the lungs and the brain. One question is what makes the new environment capable of supporting tumor growth.

Yibin Kang, Princeton's Warner-Lambert/Parke-Davis Professor of Molecular Biology, is exploring how cancer cells utilize metabolic pathways to suppress the body's immune system in ways that make the cancer difficult to treat. Over the past two decades, it became apparent that tumors can employ



strategies to suppress the body's immune response. Several new anti-cancer drugs that reactivate the immune system have proved capable of curing cancers that previously were death sentences.

But those cures worked in only a subset of patients, and one of the goals for the Ludwig group is to find out how metabolism may play a role. This is an area that Kang is especially interested in exploring. Much of his work is on breast cancer, which has not responded well to immunotherapy. Also,

PHOTO BY KIM SOKOLOFF

Princeton Professor Yibin Kang is investigating how cancer cells take advantage of metabolic pathways to spread through the body.

studies show that tumors that have already metastasized respond less well to strategies that boost the immune system.

Recently, Kang's team discovered enzymes that tumors use to build an immunosuppressive safe zone in which they can escape immune system attack. Mark Esposito, a former graduate student in Kang's lab, founded a company called KayoThera, supported with funding from the New Jersey Health Foundation, to develop small molecule drugs that block those enzymes. "We make a cold tumor become hot again, so that it becomes recognizable by the immune system," Kang said.

Kang is excited about the influx of energy and support for cancer research via the Princeton Ludwig Branch. The formation of the Ludwig Branch will allow researchers in distinct disciplines — from microbiology and engineering to computer science — to contribute to studies on cancer metabolism and the tumor microenvironment.

Another project that is just taking off focuses on how the body's metabolism of nutrients is affected by the gut microbiome, and how this interaction alters the anti-cancer immune response.

The gut microbiome — the teeming trillions of bacteria that peacefully inhabit our intestines — appear to have an outsized effect on how well nutrients and other ingested items, such as drugs, are able to

pass through the intestinal walls and into the bloodstream. Ludwig Princeton researchers hope to uncover the impact that the microbiome has on cancer metabolism as well.

Like the famed New Jerseyan Bernarr Macfadden from a century ago, researchers based at Princeton and its collaborating institutions think that diet for the treatment of disease has untapped promise. Rabinowitz in particular sees metabolism research as a major area for growth. With about 20% of our genes having some function relating to metabolism, he says it is surprising that scientists don't devote more resources to studying the relationship between what we eat and how we feel.

Certainly our state of health is influenced by many factors. Genetics play a role. Fitness and exercise matter. Love and social support are essential. But when it comes to diet, Rabinowitz admits to a bit of frustration. "Despite all this progress," he said, "if you come to me and say, my back is killing me, or I'm really down with depression, or I have cancer, we still have no reliable guidance on what you should eat to help with your particular disease.

"Diet is one of the foundational pieces of good health," he said, "so it would be really important to be able to tell people, in a more targeted way, what's right for them." ●

The new initiative will focus on how metabolism supports tumor growth and spread, the role of diet in preventing and treating cancer, and the interplay of metabolism, the gut microbiome and the anti-cancer immune response.

Profiling the mutational landscape of human cancers

By Wendy Plump

Metabolism is not the only link to cancer being explored at Princeton. Many researchers across genomics, chemistry, molecular biology, computer science and other departments are looking for ways to understand and kill tumors. Tom Muir, the Van Zandt Williams Jr. Class of 1965 Professor of Chemistry, leads a project to explore cancer-associated mutations in proteins called histones, around which DNA strands coil to form a space-saving structure called chromatin. A study published by his group in *Nature Chemical Biology* in 2021 found that histone mutations may contribute to the development or progression of a wide range of human cancers.


Tom Muir

The research builds on a paper published in collaboration with the team of David Allis of The Rockefeller University in 2020 in *Nature*. "We noticed, based on previous work, that a lot of different mutations in histones were associated with different cancers — and to different degrees," said Michelle Mitchener, one of the study's lead authors and a Princeton postdoctoral research fellow. The previous work, which focused on data mining, provided an overview of where the mutations are located in chromatin, as well as hypotheses about their roles.


Michelle Mitchener


John Bagert

The Muir team "focused on trying to figure out functionally and biochemically what those mutations are actually doing," she said. "If they contribute to cancer, then how? Can we figure out, at a structural and biochemical level, what they're doing?"

With funding from the National Institutes of Health, researchers looked at mutations within the cores of the histones themselves to see if and how they might be impacting disease states.

"We think that mutations that affect chromatin remodeling can contribute to disease and cancers in humans," said John Bagert, the co-lead author on the paper and an associate research scholar. "We've identified the sites and the mutations at those sites that we think are causing problems."

PHOTOS BY C. TODD REICHART

RACE TO THE BOTTOM

How candidates parlay racial animosity into political gain

By Catherine Zandonella

PHOTO BY DENISE APPLEWHITE

Michael Harris wants your vote. In a recent campaign speech, he said he is sick of people blaming the government for problems they created themselves, and he urged "people in the inner city" and Blacks to work harder.

Harris is a fictional character, but he illustrates a real phenomenon: politicians capitalizing on racial stereotypes to curry favor with white voters. You might surmise that Harris is white, but in fact, research by political scientist LaFleur Stephens-Dougan revealed that Black candidates also exploit racial prejudice in pursuit of political gain.

Both white and Black candidates engage in "racial distancing" — the practice of purposefully signaling to white voters that a candidate is not beholden to the interests of racial minorities, Stephens-Dougan found. Through racial distancing, candidates pledge to maintain the nation's unspoken racial hierarchy, in which whites take the top leadership positions throughout politics and business.

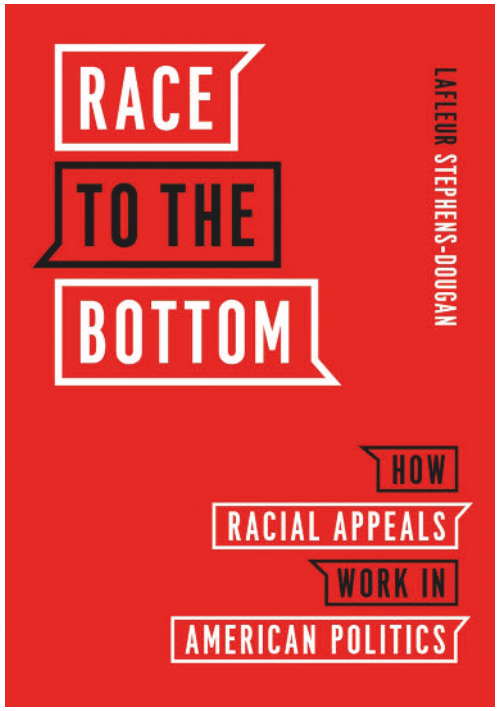
"There is great political utility to Black politicians, and particularly Black Democrats, to signal that they're not beholden to communities of color," said Stephens-Dougan, an assistant professor of politics. "This is especially true in the backdrop of a changing United States that is rapidly diversifying, and in which people are concerned about their economic well-being."

Stephens-Dougan harnessed observations and experiments to explore how white and Black candidates use race when courting white voters. She detailed her findings in *Race to the Bottom: How racial appeals work in American politics* (2020, University of Chicago Press).

It is perhaps not surprising that white conservatives play to voters' negative racial attitudes. But Stephens-Dougan found that white liberals and Black candidates also utilize this strategy, and that Black candidates may benefit more than white liberals from campaign messages that enforce negative racial stereotypes, such as that Blacks are not hardworking.

In fact, Black candidates from both sides of the aisle employ such stereotypes, argued Stephens-Dougan. Democratic former President Barack Obama is widely thought to have run a race-neutral campaign. But Stephens-Dougan's analysis showed that his national 2008 presidential campaign played on racial stereotypes.

For example, the campaign ad "Country I Love" emphasized that Obama believed in "working hard without making excuses," a phrase that alludes to stereotypes about Black work ethic. In addition, the 60-second ad lacked any discernable African American faces. In campaign appearances in 2008, Obama exhorted Black men to "get up off the couch" and take responsibility for their lives. By reinforcing negative stereotypes, Stephens-Dougan wrote, Black politicians miss the opportunity to call attention to structural factors such as lack of education and jobs.



Both white and Black candidates engage in "racial distancing" — the practice of purposefully signaling to white voters that a candidate is not beholden to the interests of racial minorities, LaFleur Stephens-Dougan, assistant professor of politics, details in her recent book.

Racial distancing is especially effective when a Black candidate is running in a region with a large white electorate. Blacks make up about 12.5% of the U.S. electorate, so appealing to white voters in presidential elections is essential. White voters may be receptive to racially charged language for a number of reasons. While some may hold views about white racial superiority, others

may be concerned that policies favorable to Blacks could cause them to slip down the economic ladder.

To test the theory that Black candidates can use racial distancing to curry favor among white voters, Stephens-Dougan conducted several experiments using fictitious scenarios, including one in 2018 involving the fictional Harris. For the study, she worked with a survey firm that recruited white volunteers and divided them into groups.

Each group received an article about Harris' campaign speech. The speech was identical except for the headline and one passage that invoked race explicitly, implicitly, or not at all. In the explicit version, Harris said, "I'm tired of Black people blaming the government for problems that they created. Black people need to learn the value of hard work. Work harder!"

In the implicit version, Harris' quote was identical except that "Black people" was replaced by "people in the inner-city," a surrogate term for people who are poor and Black. In the neutral version, Harris exhorted all people to learn the value of hard work. Stephens-Dougan noted that the study did not test the scenario where the candidate urges white people to work harder because that stereotype is largely absent in society.

To explore differences in how white voters perceive the three messages in relation to the race of the candidate, Stephens-Dougan created four versions of the candidate: Black Democrat, Black Republican, white Democrat and white Republican. The researchers randomized the volunteers into groups and asked them to read one of the 12 possible permutations of the article (four versions of the candidate, each with three versions of the article about the speech).

The main question Stephens-Dougan wanted to answer was whether the Black candidate would garner more white votes with the message aimed at Black stereotypes versus the neutral message exhorting all people to work harder. Indeed, she found that white voters were more likely to vote for a Black candidate Harris when he exhorted Black people to work harder, versus exhorting inner-city or all people to work harder. This result was especially strong when the voters were Republicans. Black politicians were especially rewarded by Republican voters for explicitly exhorting other Blacks to work hard.

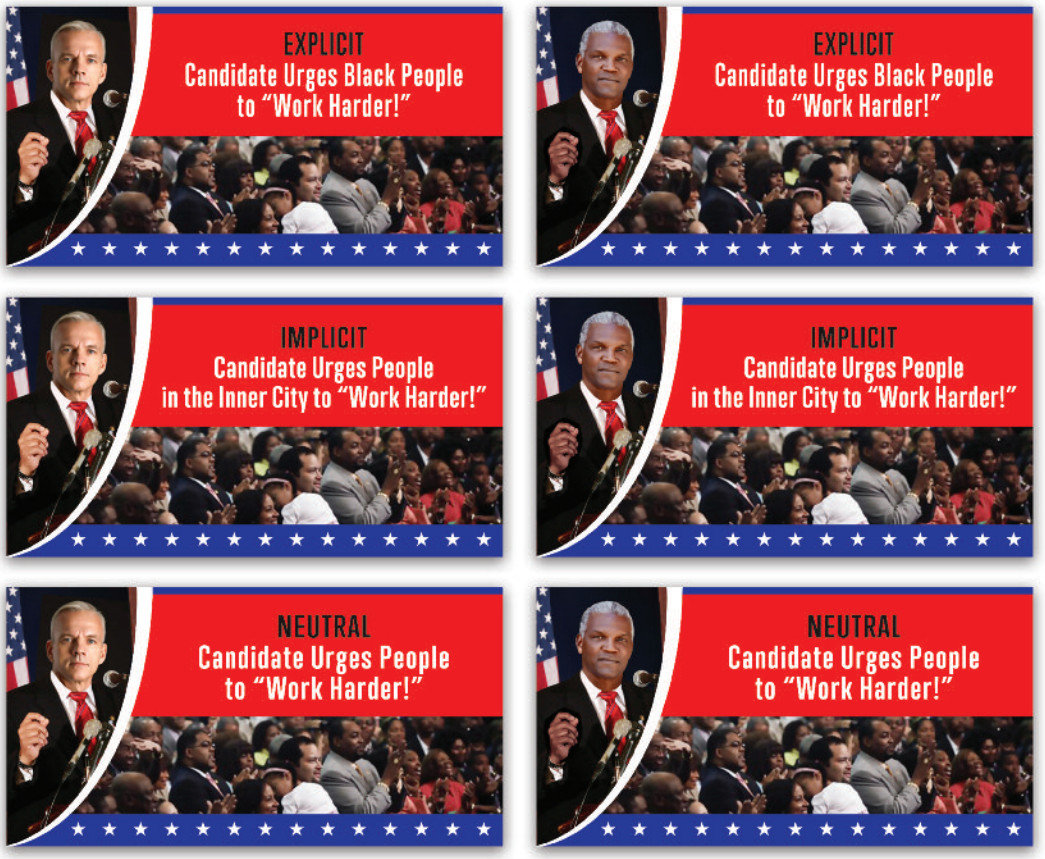
The white version of Harris lost white Democratic voters by goading Blacks to work harder. This finding agrees with research by other scholars indicating that blatant racist appeals fall flat among white voters. However, previous studies looked mainly at racist appeals from white candidates, not those who are Black.

In some cases, statements about race don't have to be negative. Simply featuring Black supporters in campaign ads is enough to turn off white voters who hold racial stereotypes and are concerned about disrupting the racial hierarchy.

This was the finding of an earlier study where Stephens-Dougan surveyed white voters' perceptions of campaign mailers that featured a candidate named Greg Davis. The research team varied the race of the candidate and his supporters, who were well-dressed professionals and students. In one mailer, the supporters were all white, in another they were all Black, and in a third they were a mix of white and Black.

For this study, the team surveyed the white voters to ascertain their level of racial resentment. Racial resentment is determined

"There is an element that taps into people's insecurities, real or imagined, in terms of whether another group is doing better," Stephens-Dougan said. "And politicians know this."



For illustrative purposes only. These are not the actual treatments from the experiment.

To test the theory that by playing on racial stereotypes, Black candidates can curry white votes, researchers recruited white volunteers and provided them with three versions of a news article covering a campaign speech by a fictional candidate named Michael Harris, who was either white or Black. The three articles were identical except that the speech invoked race either explicitly, implicitly, or not at all. Stephens-Dougan found that white voters were more likely to vote for the Black candidate with the explicit racial message. The result was especially strong among conservative white voters.

by asking the volunteers to agree or disagree with statements such as, "It's really a matter of some people not trying hard enough; if Blacks would only try harder they could be just as well off as whites."

The study found that Black candidates having a campaign mailer with all white supporters was not enough to overcome the stereotype among racially resentful voters that the Black candidates would favor Blacks over whites. However, the white Republican candidate was not penalized for the association or inclusion of Black supporters. Stephens-Dougan argues that white Republicans are not penalized for an association with Black people because the stereotype that white Republicans will maintain the racial hierarchy is very strong.

"There is an element that taps into people's insecurities, real or imagined, in terms of whether another group is doing better, what does this mean for me, what does it mean for my kids, and for my position in the hierarchy," Stephens-Dougan said. "And politicians know this."

That politicians would invoke race to ensure that candidates are electable among white voters is troubling for our democracy, Stephens-Dougan concluded. Politicians should be broadening their appeal to all voters rather than chasing racially conservative white voters, she said.

"As Stephens-Dougan demonstrates, both parties employ these strategies and they do it because voters respond to it," said Vincent Hutchings, the Hanes Walton Jr. Collegiate Professor of Political Science and Afroamerican and African Studies and the Diversity and Social Transformation Professor at the University of Michigan, as well as Stephens-Dougan's former Ph.D. adviser. "If we are serious about wanting it to stop, we have to bring the same moral outrage to politicians of either party. Until then, politicians are going to keep doing this as long as it keeps working."

Climate in Crisis

What it will take to step back from the brink

By Alice McBride

Record-setting heat waves, droughts and wildfires across the Western United States and Canada, deadly flooding in Germany, torrential rains in India, and other extreme events have ravaged communities around the globe. Greenhouse gases from human activities, like burning fossil fuels to power cars and factories, are raising temperatures and disrupting the world's climate in an unprecedented way.

But although we've pushed the planet to the brink, it is not too late to pull it back. By prioritizing the cutting of carbon dioxide (CO_2) and other greenhouse gas emissions, drastically and as soon as possible, we may yet reverse the course of climate change.

"We need to do a lot of work in a lot of different sectors, from the water sector, to iron and steel, to cement, to chemicals manufacturing, to everything else," said Eric Larson, senior research engineer at the Andlinger Center for Energy and the Environment, which houses many researchers focused on securing our energy and environmental future. "Pick your favorite topic, and you'll be able to make a contribution."

Larson is a lead author on a report first issued in December 2020 that maps out what it would take to reach a "Net-Zero America," where the amount of greenhouse gases the nation emits is offset by an equal amount removed. The report, the final version of which appeared in October 2021, lays out five pathways to decarbonizing the U.S. economy and reaching net-zero emissions by 2050.

These pathways can be achieved with today's technologies — electric vehicles, heat pumps, wind and solar power, nuclear energy, and fossil fuels and biomass with carbon capture and storage. To transform our energy landscape in ways that enable people to live to their full potential across the planet, however, we'll need new approaches and technologies, such as those being developed in Princeton's School of Engineering and Applied Sciences. Advances in reclaiming carbon from wastewater, lithium-ion-battery recycling, innovative building materials and new approaches to urban infrastructures are active areas of research at Princeton.

Eric Larson is a lead author of Net-Zero America, which charts ways to reduce greenhouse gas emissions by 2050.

PHOTO BY SAMEER A. KHAN/FOTOBUDDY

PHOTO BY SAMEER A. KHAN/FOTOBUDDY

Z. Jason Ren explores ways to reduce carbon emissions associated with water purification.

Wasted carbon no more

Think of carbon dioxide, and you might envision smokestacks and car tailpipes. But carbon is in solid waste and wastewater as well.

"Carbon dioxide, wastewater, all the food and garbage we throw away — these all contain wasted carbon, just in different forms," said Zhiyong Jason Ren, professor of civil and environmental engineering and the Andlinger Center for Energy and the Environment.

And these are not small quantities of carbon. A study by the U.S. Department of Energy found that the amount of chemical energy stored in the liquid waste stream is about equal to 11 billion gallons of gasoline per year, which is about 8% to 10% of the U.S. gasoline demand. In other words, if we could somehow capture the carbon and reuse it, we could dramatically reduce the amount of new carbon that we dig out of the ground.

Ren works on water infrastructure, looking at ways to reduce the carbon emissions associated with water purification and wastewater treatment, while recovering carbon to make new fuels and chemicals. He cites New York City as an example where remedying wastewater treatment could yield significant benefits. The city's infrastructure and populace rely heavily on fossil fuel-based energy and emit large amounts of greenhouse gases, and the city also spends over $1 billion per year maintaining the water and wastewater infrastructure.

By installing systems that capture carbon from wastewater and convert it to fuels, chemicals and plastics, the city could turn a money-losing waste treatment center into a revenue center, Ren said. According to Ren's calculations, this approach could generate millions of dollars in income for the city.

"When you clean up wastewater, at the same time you can generate renewable fuels, chemicals and bioplastics, and this is just one of the ways in which infrastructure and decarbonization are connected," Ren said. "All these sectors are linked."

To put wastewater to work, Ren and his team rely on microbes that digest carbon and generate free electrons. Under normal conditions, the microbes breathe and grow by consuming oxygen from the surrounding environment, then transferring electrons to the oxygen molecules. With Ren's microbial electrochemistry platform, researchers sidetrack the flow of electrons, collect them and put them to work.

"We basically steal electrons from bacteria," Ren said. "The bacteria transfer their electrons not to oxygen but to our electrode."

The electrons can be transformed into electrical current, used in the production of fuels or even used to split water to release hydrogen for fuel cells.

This source of electrons could also drive salt removal — turning seawater into drinking water — or facilitate ocean mining for critical minerals like lithium. Typically, desalinization plants filter water via reverse osmosis, in which massive amounts of water are pushed through a filter to recover a relatively small amount of drinking water. By taking advantage of the electrical potential generated between electrodes, these charged ions, salts and minerals will be extracted and recovered, resulting in separate outputs of clean water and concentrated mineral solutions.

Ren recently received a prestigious award from the Water Research Foundation to map greenhouse gas emissions in the water sector and help the industry decarbonize. "Water, energy and climate are intrinsically connected," Ren said, "so it is imperative to understand how they are related and to develop cross-disciplinary solutions to tackle these challenges."

Battery recycling

With the increasing popularity of electric vehicles and the role they play in getting to a net-zero economy, lithium-ion-battery recycling is a growing area of research. A group of researchers at Princeton have developed a new process for recycling lithium-ion batteries using clouds of charged particles called plasmas to recover valuable metals such as cobalt and other battery materials, while avoiding the harsh chemical washes and high temperatures that are used in existing recycling methods.

The four-person team — which includes Bruce Koel, professor of chemical and biological engineering; Yiguang Ju, the Robert Porter Patterson Professor of Mechanical and Aerospace Engineering; Chao Yan, a postdoctoral researcher; and Xiaofang Yang, formerly a postdoctoral researcher at Princeton — founded a startup called Princeton NuEnergy to develop the technology.

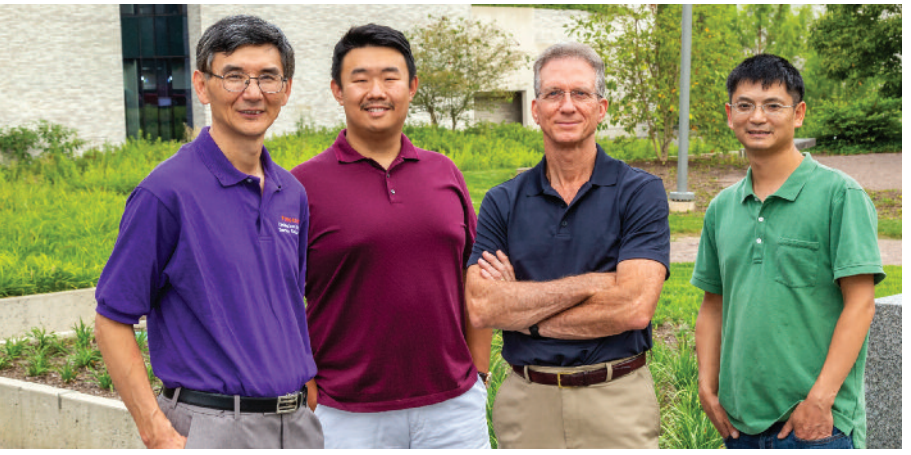


PHOTO BY DAVID KELLY CROW

From left: Yiguang Ju, Chao Yan, Bruce Koel and Xiaofang Yang co-founded the startup Princeton NuEnergy to develop a more environmentally friendly lithium-ion-battery recycling technology.

Existing recycling strategies can recover materials like lithium, nickel and cobalt from spent batteries, but the processes are inefficient, environmentally harmful and costly. First, batteries are shredded to expose their various internal components, which are then separated. The electrode materials are then either smelted or dissolved in acid. Next, there are multiple rounds of chemical separation to obtain the target metals, which finally must be remade into a functional form that can be used again as battery electrode materials. "Going through all these steps generates a tremendous amount of liquid waste, and consumes a lot of resources in the process," Koel said.

Instead, the team uses several innovations for the component separation steps, then applies an electrically charged gas or plasma to remove contaminants and other impurities from the electrodes. The charged ions of the plasma react chemically with the impurities, cleaning them away without destroying the structure and composition of the still-usable material underneath.

The process can reclaim roughly 95% of a battery's original lithium and other metals — which is comparable to the performance of existing recycling methods but cuts both energy use and CO_2 emissions by more than half, while consuming far less water.

The researchers are now tailoring the process for each of the most commonly used varieties of lithium-ion battery, while also laying the groundwork to deploy the method at a large scale. "Transferring from the lab scale to the industrial scale is always challenging," Yan said. "But as we become increasingly reliant on lithium-ion batteries, the prospect of being able to efficiently regenerate them is worth the effort."

Better blocks

The net-zero future will also require changes to how we build things. When it comes to construction, concrete is essential. This mixture of sand, rocks, water and cement powder is one of the most-used materials on the planet, second only to water in its service to global society. But the critical ingredient, cement powder, is responsible for vast amounts of CO_2 emissions.

Claire White, an associate professor in the Department of Civil and Environmental Engineering and the Andlinger Center, is an expert on concrete. White is developing low-emissions alternatives to the traditional Portland cement powder, an industry staple since it was invented in the 1800s.

"Around 7% to 8% of all CO_2 emissions come from cement manufacturing," White said. "Per ton of Portland cement powder you produce, you get about 900 kilograms of CO_2 being emitted."

Many of those emissions occur during the manufacturing process, when crushed limestone and clay are baked at 2600 degrees Fahrenheit. As the limestone heats up, it releases CO_2.

One tactic to shrink the environmental impact is to use less Portland cement powder in the concrete mixture — replacing some of it with other materials, such as byproducts like fly ash from the coal industry. But White and her group are going one step further: They're aiming for concrete mixtures that don't need any Portland cement powder.

White's current focus is on materials called alkali-activated calcined clays. These are mineral-rich clays that have been exposed briefly to intense heat, then mixed with an alkaline solution such as sodium silicate. The alkali causes the calcined clays to dissolve and form the binding cement "gel" that holds concrete together.

To determine the strength and durability of the resulting alternative concretes, White uses computer modeling and techniques like X-ray scattering to understand how the atoms interact. "We do a lot of this fundamental characterization to understand what's going on at the nanoscale," White said.

Some of the mixtures have the potential to outperform traditional concrete under harsh conditions. With support from the National Science Foundation and the Department of Energy, White's group is developing fire-resistant concretes that can help minimize damage from wildfires, as well as concretes that stand up to the strongly acidic environment found in sewage systems.

But there are hurdles to overcome before these novel cements can be deployed on a large scale. "All of our construction codes are based on Portland-cement concrete," White said.

Another impediment is the cost. Cement alternatives are expensive, and alternative concretes can cost twice as much as traditional concrete. These materials are currently manufactured for industries that require higher levels of purity than what is needed for making cement — clays are used in making paper, for example, while certain alkali activators are used in food production. To make these materials affordable for use in construction, manufacturing methods will have to evolve.

Addressing these challenges will take time, but White believes that more sustainable cements will eventually transform the concrete industry.

PHOTO BY SAMEER A. KHAN/FOTOBUDDY

Claire White aims to cut CO_2 emissions by developing alternatives to the ingredients in concrete.

Urban transformation

Lowering emissions to reach net-zero targets must be done in ways that meet the needs of society and individuals. Environmental engineer Anu Ramaswami thinks a lot about this challenge. "Cities are a really important action arena," Ramaswami said. "They contribute to more than 70% of global greenhouse gas emissions."

Ramaswami is director of the Sustainable Healthy Cities Network, a National Science Foundation-funded network based at Princeton in which researchers from major universities

> By prioritizing the cutting of carbon dioxide and other greenhouse gas emissions, drastically and as soon as possible, we may yet reverse the course of climate change.

work with industry and policy partners to make cities simultaneously more livable and better for the planet. She sees urban infrastructure as a set of seven interconnected systems — water, energy, food, shelter, transportation, waste management and public spaces.

"I study the city as a sort of the ultimate engineered system," said Ramaswami, who is a chemical engineer by training and holds joint appointments in the Department of Civil and

Anu Ramaswami pioneers methods for making cities more livable and more environmentally sustainable.

PHOTO BY DAVID KELLY CROW

Environmental Engineering, Princeton's High Meadows Environmental Institute, and the Princeton Institute of International and Regional Studies. "I ask how we can think of redesigning and innovating cities in ways that advance human and planetary outcomes."

The seven systems are highly interdependent and work across geographic scales that extend beyond city limits, Ramaswami and her team showed in an influential paper published in 2016 in *Science*. For example, greenhouse gas emissions associated with cities can come from far outside the city's boundaries, from power plants and trucking routes that supply the city. "I pioneered methodologies for cities to account for their emissions all along the supply chain," she said.

For Ramaswami, there are four factors that tell whether a city's infrastructure is doing its job: environment, health, well-being and equity. This last one is especially important.

Infrastructure is at the heart of urban inequality. For example, transportation is the gateway for access to jobs, health care and many other human needs. Access to energy — such as electricity to power your laptop — is essential for finding a job and connecting with services and with one another. "These physical infrastructure systems are really foundational," Ramaswami said. "Without them, all other things become that much more difficult."

But measuring outcomes such as equity can quickly become subjective. Ramaswami and her team wanted to find a reliable way to measure social equity across cities. They partnered with electric utilities to look at energy usage patterns in two cities, Tallahassee, Florida, and St. Paul, Minnesota, looking for patterns of inequality. They found that the amount and intensity of energy usage varies by income but also by race independent of income, yielding important metrics of inequality. The study was published in the *Proceedings of the National Academy of Sciences* in June 2021.

"Now we have a methodology to actually measure infrastructure inequality, unpacking income and race effects," she said.

Ramaswami is working on a scenario-planning tool that enables cities to bring all the sectors together to identify how changes to various sectors will return benefits to the environment, as well as health, well-being and equity. The tool will allow users to make policy choices — such as land-use planning and incentives for electric vehicles — with the goal of informing pathways toward a net-zero future.

She is also developing partnerships with entities and governments in India. Using machine learning and other technologies, her team has developed an energy-usage database for all 600-plus districts in India. "That's sort of a new frontier," said Ramaswami, who is Princeton's Sanjay Swani '87 Professor of India Studies and director of the M.S. Chadha Center for Global India, which is focused on interactions between India and the world on issues such as water, climate, health and the arts. "How do you go from working with a few cities, to providing data and models to all cities? That is the challenge, as well as a huge opportunity to inform beneficial infrastructure transformations across large numbers of cities."

Shaping the future

As countries around the world consider ways to decarbonize the global economy, designing and deploying new infrastructure provides an opportunity to make deliberate choices about the shape of our societies.

Reaching a Net-Zero America

The Net-Zero America project aims to inform and ground political, business, and societal conversations regarding what it would take for the U.S. to achieve an economy-wide target of net-zero emissions of greenhouse gases by 2050. The study provides granular guidance on what getting to net-zero really requires and on the actions needed to translate pledges into tangible progress.

The two-year research effort was funded primarily by the High Meadows Environmental Institute's Carbon Mitigation Initiative, a research program focused on studying and addressing climate change that is funded by BP, and ExxonMobil through the Andlinger Center's Princeton E-ffiliates Partnership.

PHOTO COURTESY OF ERIN MAYFIELD

Erin Mayfield asks what if infrastructure decisions optimized multiple outcomes rather than just prioritizing costs.

Traditionally, planning new or expanded infrastructure has been based around a single goal: cost-effectiveness. "Federal and state agendas are informed by computational energy system models that optimize for costs," said Erin Mayfield, a former postdoctoral scholar at Princeton's High Meadows Environmental Institute, Andlinger Center and Carbon Mitigation Initiative, who recently became Dartmouth's Hodgson Family Assistant Professor of Engineering. "Basically, they're trying to select least-cost technology options to reach some type of emissions target."

But the real world is far more multidimensional. A change in infrastructure — like closing down a natural-gas facility or building a new wind farm — could mean an increase or decrease in levels of employment, property values and local air quality. It's a delicate balance that links environmental policy and planning to questions of social equity.

Mayfield builds computational models that optimize multiple objectives rather than just prioritizing low cost, giving policymakers tools to incorporate the goals of different stakeholders when making decisions. These goals could be minimizing air pollution-related mortality in vulnerable communities or job creation across regions. And these policy changes, Mayfield said, "might not translate to much more cost, or might not mean more cost at all."

Toward 2050

One of the conclusions in the Net-Zero America report is that the annual cost of implementing the pathway to carbon neutrality by 2050 is about the same as what the country already spends on energy, or about 4% to 6% of gross domestic product (GDP).

"Net-zero pathways for the U.S. require spending a similar fraction of GDP that we spend on energy today, but we have to immediately shift investments toward new clean infrastructure instead of existing systems," said Jesse Jenkins, an assistant professor of mechanical and aerospace engineering and the Andlinger Center for Energy and the Environment. Jenkins was a lead author of the Net-Zero America report with Larson and Chris Greig, the Theodora D. '78 & William H. Walton III '74 Senior Research Scientist at the Andlinger Center.

If the U.S. can realize such a shift, there is hope that other countries might be able to as well.

By 2050, will the planet still be experiencing unprecedented flash floods, town-consuming fires and crippling droughts? That's an unanswerable question today, but through the research being conducted at Princeton and other institutions, combined with policy decisions and new innovations, our planet may stand a chance. ●

Jesse Jenkins, a Net-Zero America co-author, says carbon-neutral pathways can be achieved without increasing energy spending as a fraction of GDP.

PHOTO BY FRANK WOJCIECHOWSKI

Age of Intolerance?

Exploring the medieval origins of modern racism

By Catherine Zandonella

Walking through a marketplace in Rome in about 580 C.E., a priest named Gregory came upon a group of slaves whose skin was "shining white." Upon learning that they came from the British Isles and were pagan Angles (today, English), Gregory is said to have remarked that the name fit because they looked like angels in heaven. Years later, when the priest became Pope Gregory the Great, he sent missionaries to the British Isles to convert the Angles to Christianity.

This tale, written down by a historian known as the Venerable Bede in 731, was widely recognized through the ages as the story of how Christianity came to England. More recently, however, the story has taken on additional significance as a window into how skin color and race were viewed during the Middle Ages, the formative years of modern European culture.

While some scholars trace today's racial attitudes to the medieval period, others caution against ascribing modern viewpoints to the peoples of the past.

For decades, the accepted view among historians and scholars was that race during the medieval period — which ranged from about 400 to 1500 C.E. — was not a relevant concept. Religion, geography, ethnicity and class, far more than skin color, determined one's status in society. Many scholars consider the concept of race to have been invented more recently — during the colonial period — to justify the exploitation of human labor.

Over the past few decades, however, across university departments of history, literature and art, through books, blogs and social media, discussions about the relevance of race in the medieval period have bubbled to the surface. The display of medieval symbols by white supremacists, such as those who marched in Charlottesville, Virginia, in 2017, further galvanized scholars to examine connections between racialized attitudes and the Middle Ages.

Yet the connection between racism and the Middle Ages is not without controversy. While some scholars trace today's racial attitudes to the medieval period or earlier, others caution against ascribing modern viewpoints to the peoples of the past. Scholars must rely on surviving records, literature, art and artifacts, which may have multiple interpretations.

To explore medieval perceptions of race and how these perceptions may have influenced the modern era, a group of scholars from universities on both sides of the Atlantic convened a series of online meetings at Princeton during 2020-21. The group, supported by the Princeton Humanities Council, includes scholars from Princeton University, the nearby Institute for Advanced Study, the Austrian Academy of Sciences, and the academic professional association known as the Medievalists of Color.

"By exploring race in a comparative setting across the U.S. and Europe from different disciplines and different historical contexts, we hope to gain a greater understanding of how modern concepts of race came to be," said Helmut Reimitz, professor of history and director of the Program in Medieval Studies at Princeton

SOURCE: CREATIVE COMMONS LICENSE, YELKROKOYADE

The literature and art of the medieval period depict the lives of people from Africa and beyond. Egyptian soldier St. Maurice (right), depicted in this painting by Matthias Grünewald in the 16th century, was patron saint of the Holy Roman Empire.

and convener of the series, *Race, Race-Thinking and Identity in the Middle Ages and Medieval Studies*. "And by doing so we also hope to learn more about how this history shapes the way that people think about race today."

The medieval period was a time of trade and travel, with Muslims migrating west along the Mediterranean to occupy northern Africa and most of what is now Spain and Portugal by the 700s, Christian crusaders traveling east during the 1000s to 1300s and Jews circulating throughout the region. Non-European people dot the literature and art of the period. For example, the fictional Sir Moriaen, a knight who fought alongside Lancelot in a King Arthur legend dated to the 13th century, was dark-skinned and of African descent.

Slavery was commonplace, but it didn't consistently target a single racial or ethnic group, said Pamela Patton, director of the Index of Medieval Art in Princeton's Department of Art and Archaeology. Being conquered, falling on hard times, or being of the wrong religion could also lead to enslavement. "The common denominator was 'if you're not like us, then we may enslave you,'" Patton said.

What was more, a slave often could be set free by converting to Christianity. The Church was dedicated to converting as many people as possible, regardless of their skin color or place of origin.

Medieval metaphors

Despite the inclusivity of the Church, precursors of what might be deemed racism can be found in medieval art and literature. For example, one tale from the 14th century recounts how the Sultan of Damascus, whose appearance was "black and loathsome," fell in love with a princess whose skin was "as white as a swan's feather." When the sultan experienced God's grace, he became "fair," or "white," depending on the translation.

In this and other tales from the period, the color of the sultan's skin has a deeper meaning: His black skin is a metaphor for his non-Christian soul, according to Cord Whitaker, associate professor of English at Wellesley College, a member of the Institute for Advanced Study, and one of the founding members of the Princeton collaboration.

Whitaker explored the range of meanings of blackness in his book, *Black Metaphors: How Modern Racism Emerged from Medieval Race-Thinking* (University of Pennsylvania Press, 2019). Blackness could represent a sinful soul, but it could also represent holiness, as in the example of the black St. Maurice, patron saint of the Holy Roman Empire. Whitaker defines race-thinking as the ways in which medieval-era societies viewed differences between peoples. "In medieval race-thinking, identity categories and their consequences are sometimes quite similar to those in modern racial ideology," Whitaker said. "Nevertheless, medieval race-thinking identities are also much more malleable."

Another influential examination of medieval attitudes on race came from scholar Geraldine Heng, a professor of English and comparative literature at the University of Texas-Austin. In her book, *The Invention of Race in the European Middle Ages* (Cambridge University Press, 2018),

Heng explored what she calls "race-making" as the very active process of developing techniques and strategies to exploit and discriminate against others.

Yet not all scholars agree that these examples indicate that racism as we define it today was present in the Middle Ages. William Chester Jordan, Princeton's Dayton-Stockton Professor of History, author of numerous books on medieval history and former president of two of the field's most prestigious academic societies, is skeptical. Jordan admits that there was a great deal of dislike, distrust and exploitation of others based on religion, ethnicity, class, geography, appearance, disability, gender and other factors, but he questions whether these attitudes should be described as racism, especially given that converting to the Christian faith trumped all. "I don't think that race is powerful as an analytical tool to help us understand the world of the Middle Ages," Jordan said.

SOURCE: CREATIVE COMMONS LICENSE, THE BRITISH MUSEUM

The medieval tale of St. Gregory's discovery of English slaves for sale in a Roman marketplace became the basis of colonial-era justifications for domination of brown and Black peoples. This etching based on Sir George Scharf's drawing of St. Gregory with the slaves was published in 1847.

Historical evidence suggests that the people of the Middle Ages were relatively intolerant of strangers, however. It was common to believe that environment determined one's physical appearance and mental and physical abilities, said Suzanne Conklin Akbari, professor of medieval studies at the Institute for Advanced Study. Just as certain types of plants grow in specific geographic regions, the theory went, human attributes developed depending on one's climate.

A person's intelligence and trustworthiness could be determined not just by evaluating one's geographical home, but also by scrutinizing one's physical appearance, according to a widely embraced pseudoscience called physiognomy. Both climate theory and physiognomy influenced attitudes of medieval Christians toward Muslims and Jews, as Akbari chronicled in her book *Idols in the East: European Representations of Islam and the Orient, 1100-1450* (Cornell University Press, 2009).

"These ideas were conducive to theories of racialization that would emerge at the end of the Middle Ages," Akbari said. "Instead of trying to figure out when did people start to think about race, it makes more sense to examine the overall process, which we call racialization, race-thinking or race-making."

The medieval-era tendency to suspect or ostracize a person for their appearance may have gradually metamorphosed into an outright classification of people into races that could then be marginalized. Most scholars agree that race became legitimized as a justification for enslavement around the time of the discovery of the Americas. "You start seeing a convergence of dynamics once the Roman Catholic Church ceases to be the hegemonic power it once was," Whitaker said. "The pseudoscientific theories have left their mark, and the religious umbrella that held those justifications at bay becomes a lot less important."

Co-opting medieval history

By the 1800s in England, the history of the Middle Ages — with its stories of fair-skinned angels — had been solidly co-opted to provide a rationale for supremacy over the Black and brown people in England's colonies, said collaboration member Celia Chazelle, a professor of history at The College of New Jersey, and a member of the Institute for Advanced Study.

"By the 19th century, the country's medieval past had become very directly tied to ideas about the British Empire being the engine of civilization for the rest of the developing world," said Chazelle, who is researching the story of Gregory the Great and the conversion of the English to Christianity. An uptick in literacy rates during the industrial era led to a surge of interest in the Middle Ages among everyday people. The story of the fair-skinned slaves — and how they were singled out for salvation due to their skin color — became a staple of student textbooks.

Another example of how medieval history served race-motivated agendas involves the construction of the German identity, ideas that were later drawn upon by the Nazi party. In his book, *History, Frankish Identity and the Framing*

of Western Ethnicity, 550–850 (Cambridge University Press, 2015), Princeton scholar Reimitz examines the formation of a cohesive identity among Germanic-speaking peoples, known as the Franks, after the decline of the Western Roman Empire in the late 400s.

"The assumption was that an inborn essence in all of these peoples was what made their success and persistence possible," Reimitz wrote. "Because of their great political success, the Franks were even taken as evidence of the triumph of the nation over the supra-national civilization of the Roman Empire. As more recent works have shown, the 'Fall of Rome' was not a melodramatic 'clash of cultures' but rather a long-term process of transformation. The changing meaning of ethnic identity has to be understood as part of this process."

The Nazi focus on racial purity led most post-war German-speaking scholars to eschew the term "race" in favor of the term "ethnicity," Reimitz said. But with the trans-Atlantic dialogue fostered among the group, and the involvement of Walter Pohl, a leading scholar and professor of medieval history at the University of Vienna, researchers are beginning to find common ground.

"One of the main interventions of our collaboration is to try to create more crosstalk, more interaction and more explicit citation between North American scholars working on the pre-modern history of race and European scholars working on matters of ethnicity," Whitaker said.

Beyond Charlottesville

When neo-Nazis marched in Charlottesville wearing medieval insignia, many scholars saw the event as evidence that scholars themselves need to ensure that studying medieval history — which until recently has been done primarily by people of European descent — is welcoming to people of all backgrounds.

One outgrowth was the student reader *Whose Middle Ages?* (Fordham University Press, 2019), to which Patton and Whitaker contributed. "We're trying to develop scholarship that gives us a better sense of the diversity and complexity of the Middle Ages, and we're also trying to change the makeup of the field by bringing in scholars who didn't have a stake before or maybe didn't have a seat at the table," Patton said.

The Medievalists of Color formed in part as a response to a lack of representation in the field, said Whitaker, a founding member of the organization's steering committee. Since its formation in 2017, the group has provided mentorship and professional support, and has worked to increase awareness of insensitivity to the experiences of non-white medievalist scholars.

Attracting scholars of color to medieval studies is worthwhile, Jordan said. He is less sure whether scholars have the ability to control interpretations of their work. He offers as an example his book, *The Apple of His Eye: Converts from Islam in the Reign of Louis IX* (Princeton University Press, 2019). In it, Jordan chronicles how the French King Louis IX brought Muslims who'd suffered losses in the Crusades to France, where he gave them stipends and helped them assimilate into French life. The reception of Jordan's book has been overwhelmingly positive, including among French critics.

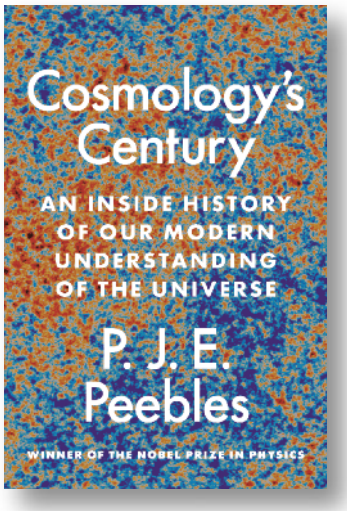
The book has also spurred a range of conclusions about its meaning for today's European immigration situation, Jordan said. Some critics say the book proves that modern France should subsidize immigrants, while others argue that it justifies the view that immigrants should embrace Christianity and French culture.

From this, Jordan concludes that people will always find ways to justify their views. "White supremacists will find justification for their racism in medieval studies," he said, "just as there are multiple ways that my book is being read in France right now."

> "Instead of trying to figure out when did people start to think about race, it makes more sense to examine the overall process, which we call racialization, race-thinking or race-making."

Given the ways that medieval history can be misapplied, Reimitz said, it is important that scholars take an active part in conversations about how the Middle Ages inform societal beliefs and actions today.

"Everything has a history, and so do our concepts of race," he said. "These concepts did not happen by default but were the result of deliberate and conscious choices — in the Middle Ages as well as today." ●



Cosmology's Century: An Inside History of Our Modern Understanding of the Universe

Princeton University Press, 2020

P. James E. Peebles, the Albert Einstein Professor of Science, Emeritus

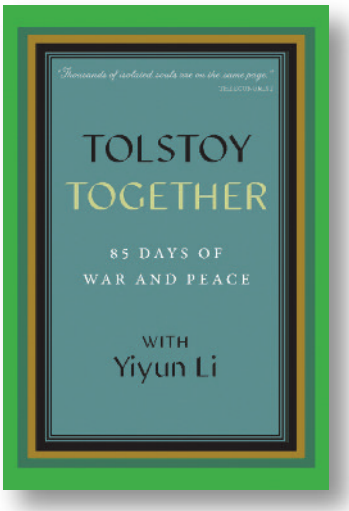
Modern cosmology began a century ago with Albert Einstein's general theory of relativity and his notion of a homogenous, philosophically satisfying cosmos. *Cosmology's Century* is the story of how generations of scientists built on these thoughts and many new measurements to arrive at a well-tested physical theory of the structure and evolution of our expanding universe. In this landmark book, cosmologist P. James E. Peebles, a winner of the Nobel Prize in Physics in 2019, offers an unparalleled personal perspective on how the field developed.

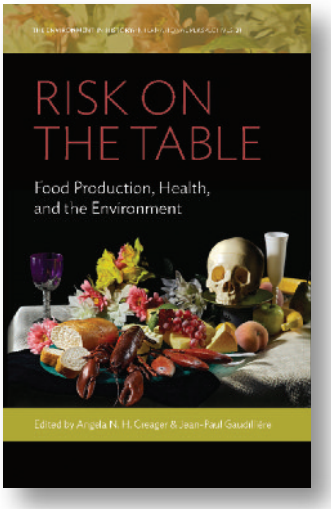
Tolstoy Together: 85 Days of War and Peace with Yiyun Li

A Public Space, 2021

Yiyun Li, professor of creative writing in the Lewis Center for the Arts

From the acclaimed author of *Dear Friend, from My Life I Write to You in Your Life*, comes a book about the art of reading. In *Tolstoy Together: 85 Days of War and Peace*, Yiyun Li invites you to travel with her through Tolstoy's novel — and with fellow readers around the world who joined her for an online book club and an epic journey during a pandemic year. *Tolstoy Together* expands the epic novel into a rich conversation about literature and ways of reading.





Risk on the Table: Food Production, Health, and the Environment

Berghahn Books, 2021

Edited by: **Angela Creager**, the Thomas M. Siebel Professor in the History of Science, and professor of history, and **Jean-Paul Gaudillière**, senior researcher at the Institut National de la Santé et de la Recherche Médicale, and professor at the École des Hautes Études en Sciences Sociales, Paris

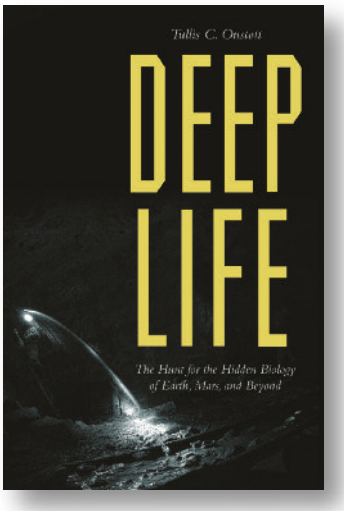
Over the past century, the industrialization of agriculture and processing technologies have made food abundant and relatively inexpensive for much of the world's population. Simultaneously, pesticides, nitrates and other technological innovations intended to improve productivity and safety have generated new, often poorly understood risks for consumers and the environment. *Risk on the Table* highlights historical cases that illuminate the history of food safety, exposing the powerful tensions among scientific understandings of risk, policymakers' decisions and cultural notions of "pure" food.

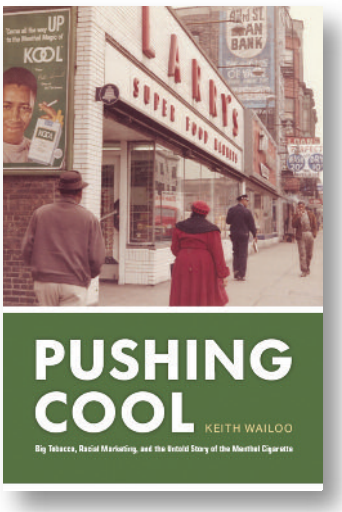
Deep Life:
The Hunt for the Hidden Biology of Earth, Mars, and Beyond

Princeton University Press, 2020

Tullis Onstott, professor of geosciences

Deep Life takes readers to uncharted regions deep beneath Earth's crust in search of life in extreme environments and reveals how astonishing new discoveries are aiding the quest to find life in the solar system. Tullis Onstott (1955–2021) provides an insider's look at the pioneering fieldwork that is shining new light on Earth's hidden biology, a subterranean biosphere thriving with rare and exotic life-forms. An unforgettable scientific adventure, *Deep Life* takes you to the biotic fringe, where today's scientists hope to discover the very origins of life itself.





Pushing Cool:
Big Tobacco, Racial Marketing, and the Untold Story of the Menthol Cigarette

University of Chicago Press, 2020

Keith Wailoo, the Henry Putnam University Professor of History and Public Affairs

Spanning a century, *Pushing Cool* reveals how the twin deceptions of health and Black affinity for menthol were crafted — and how the industry's disturbingly powerful narrative has endured to this day. Keith Wailoo tells the intricate and poignant story of menthol cigarettes for the first time. He pulls back the curtain to reveal the hidden persuaders who shaped menthol buying habits and racial markets across America: the world of tobacco marketers, consultants, psychologists and social scientists, as well as Black lawmakers and civic groups.

Magical Habits

Duke University Press, 2021

Monica Huerta, assistant professor of English and American studies

Monica Huerta draws on her experiences growing up in her family's Mexican restaurants and her life as a scholar of literature and culture to meditate on how relationships among self, place, race and storytelling contend with both the afterlives of history and racial capitalism. Ultimately, Huerta sketches out habits of living-while-thinking that allow us to consider what it means to live with and try to peer beyond history even as we are caught up in the middle of it.

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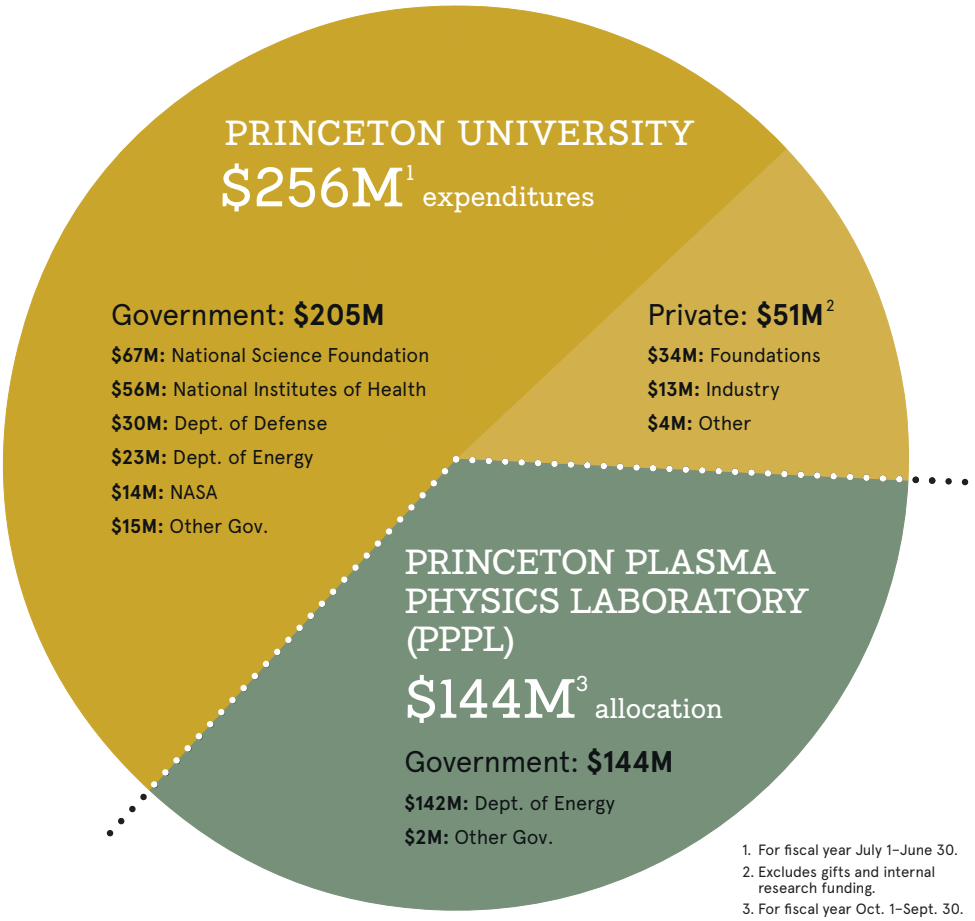
Research drives innovation, which in turn creates benefits for society. Princeton University is home to a thriving research and innovation ecosystem fueled by funding from federal agencies as well as corporate, philanthropic and other sources. This report indicates the primary funding sources and amounts spent on research for fiscal year 2021.

MAJOR FUNDING SOURCES

TOTAL FUNDING: $400M



1. For fiscal year July 1–June 30.
2. Excludes gifts and internal research funding.
3. For fiscal year Oct. 1–Sept. 30.

PATENTS AND TECHNOLOGY LICENSING ACTIVITY

9	STARTUPS FORMED FROM PRINCETON DISCOVERIES
106	INVENTION DISCLOSURES FILED
171	PATENT APPLICATIONS FILED
54	PATENTS ISSUED
21	LICENSE AND OPTIONS AGREEMENTS

SPONSORED RESEARCH PROJECTS

1,121	GOVERNMENT-SUPPORTED (INCLUDES PPPL)
270	FOUNDATION-SUPPORTED
121	INDUSTRY-SUPPORTED
77	PRIVATE/OTHER SUPPORTED
1,589	TOTAL PROJECTS

SELECTED RESEARCH AREAS

- ENERGY & THE ENVIRONMENT
- DATA SCIENCE
- BIOENGINEERING
- QUANTUM COMPUTING
- LIFE SCIENCES
- HEALTH
- BEHAVIOR
- PUBLIC POLICY
- ECONOMICS
- LITERATURE
- FUSION POWER
- PHYSICS & COSMOLOGY
- MATHEMATICS

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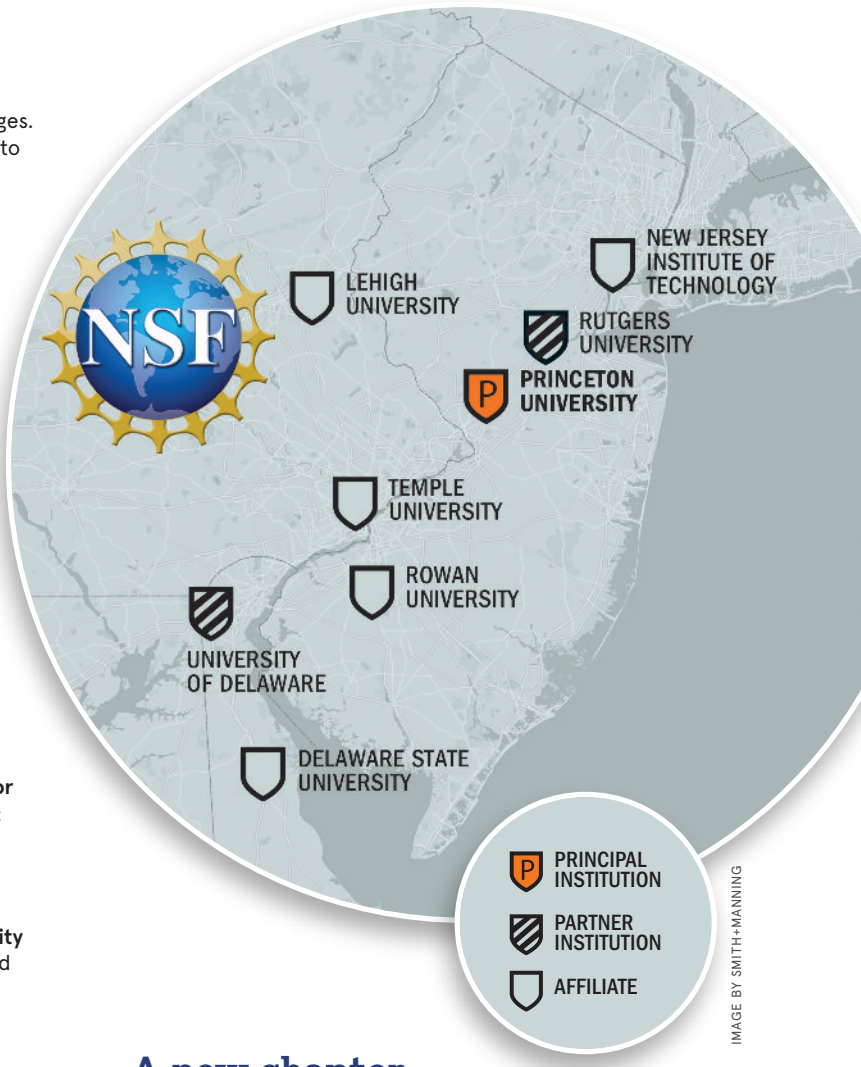

IMAGE BY SMITH+MANNING

A new chapter in innovation at Princeton

Princeton will lead the NSF-funded Innovation Corps (I-Corps) Northeast Hub, formed with partner institutions Rutgers and the University of Delaware plus affiliate universities throughout the region. The five-year $15 million grant will fund training, mentoring and resources, broaden diversity in entrepreneurship, and cultivate startups in health care, energy, the environment, computing, artificial intelligence, robotics, advanced materials and more.
icorpsnortheasthub.org

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Was the medieval period an age of intolerance? Or are scholars ascribing modern conceptions of race to the peoples of the past? Page 26.

SOURCE: CREATIVE COMMONS LICENSE, YELKROKOYADE