How broccoli sprouts became an emerging tool against a range of diseases

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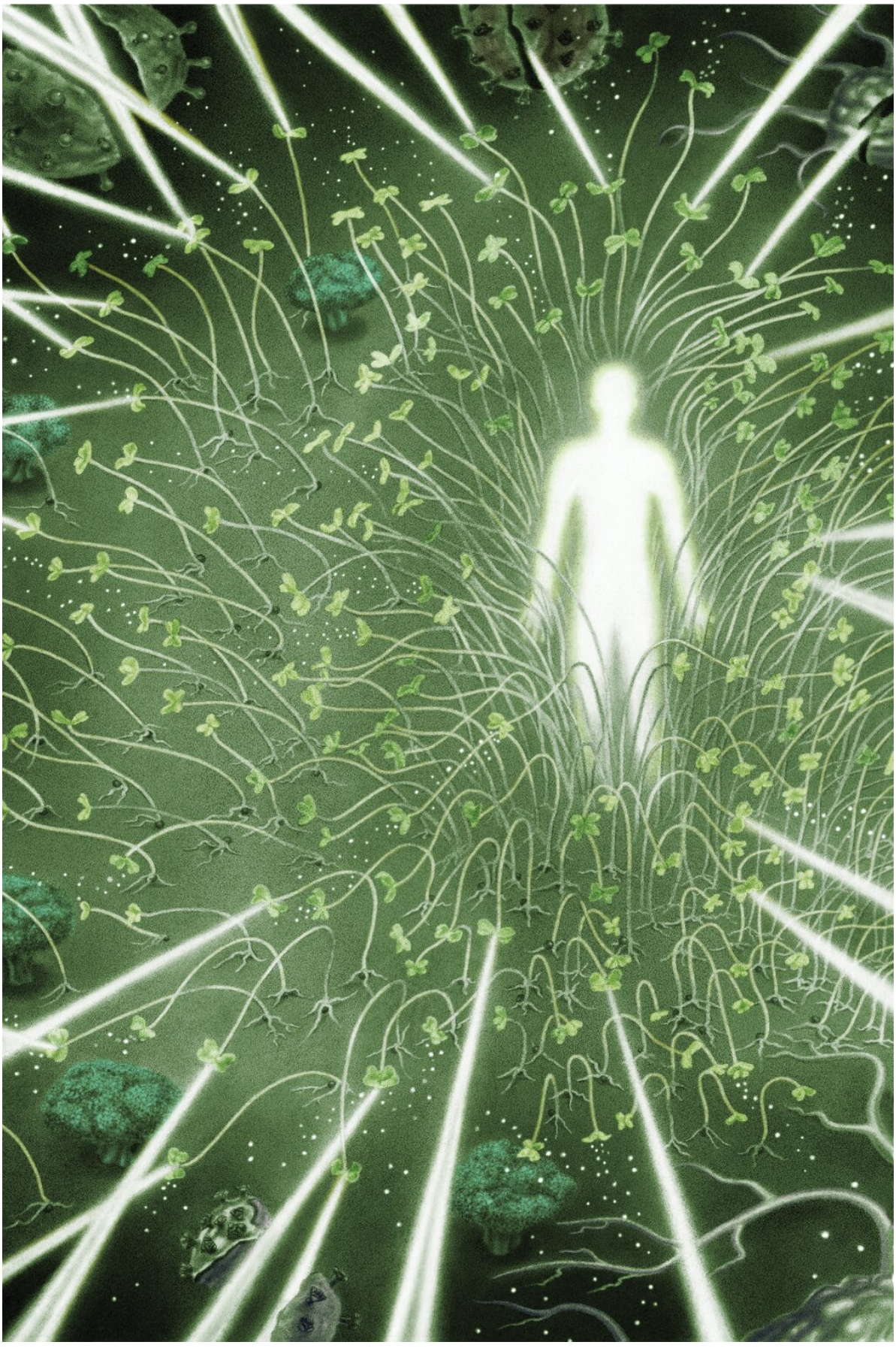

Credit: Chloe Niclas

Strolling through the produce section of your local grocery story, you might notice—tucked between the pre-sliced radishes and the plastic-wrapped mushrooms—a container of broccoli sprouts, a mat of wispy white shoots with spring-green leaves the shape of a handmade valentine. Perhaps you took that container home and discovered the sprouts to be earthy on the tongue, less nutty than their more popular cousin alfalfa. Not pepper-spicy but horseradish-spicy, a heat that tickles the back of the nose. Perhaps you found that just a handful added complexity, a satisfying crunch, to sandwiches and salads.

But you probably didn't know that this humble veggie is also a treasure trove of vitamins, a powerhouse of fiber, and—thanks to a cadre of Hopkins scientists working across decades and disciplines—an emerging tool in the fight against an incredibly diverse range of diseases.

It is the sprouts' high concentration of a potent substance called sulforaphane that makes them a so-called superfood, a favorite of dietitians, health bloggers, and homeopaths everywhere. Paul Talalay, a researcher at Johns Hopkins, was the one to find that the sulforaphane in broccoli—the full-grown version of a sprout—significantly increases the body's ability to fend off cancer. The discovery, published in 1992, landed the pharmacologist on the front page of *The New York Times* as well as on *Popular Mechanics*' list of the greatest scientific discoveries of the 20th century.

Thirty years later, the assertion that broccoli is really, really good for you may not sound radical, but Talalay's research emerged at a time when

cancer was considered as preventable as a thunderstorm and President George H.W. Bush had just banned the vegetable from being served aboard Air Force One.

Talalay's front-page debut triggered an avalanche of scholarship on the disease-preventing potential of food in general and of sulforaphane specifically. In 1994, it was Talalay's mentee, Jed Fahey, who thought to analyze the broccoli sprout, finding it harbored 20 to 50 times more sulforaphane than the mature plant.

In the ensuing decades, Talalay's colleagues and acolytes have carried on his life's work, pitting the sprout against ulcers, autism, schizophrenia, cardiovascular disease, COVID, colds, cancer, and more. Their results have built a compelling case for including the spicy little sprout in your diet and elevating Brassica oleracea way beyond side-dish status.

'A pure scientist'

Paul Talalay was 10 years old when his Jewish family fled Germany for England in 1933, not long after Adolf Hitler came to power. Seven years later, the family picked up roots again, this time crossing an Atlantic Ocean teeming with U-boats to get to America, where Talalay had been accepted to study biology at MIT.

After earning his MD at Yale, Talalay arrived at Johns Hopkins in 1963 to head up the Department of Pharmacology and Experimental Therapeutics. During his tenure as chair, Talalay started a Ph.D. program in pharmacology and lured top talent to Baltimore, including renowned urologist Donald Coffey, who would go on to lead research at the Brady Urological Institute, and neuroscientist Solomon Snyder, who discovered opiate receptors in the brain.

After a decade, Talalay made a surprising pivot, resigning as head of the

department and redirecting his attention from treatment and toward prevention, a move that many in the field considered ill-advised. In 1973, the prevailing attitude was that people either got cancer or they didn't, and funding for cancer prevention was virtually nonexistent. (As recently as 2021, only 5.6% of the National Cancer Institute's budget was devoted to prevention.) But as cancer rates continued to rise, Talalay was convinced that stopping cancer was as important as treating it.

"That was his midlife crisis," says Talalay's son Tony. "He didn't get a red sports car; he decided to go back in the lab and do basic science." The younger Talalay says his father was "a pure scientist" with a "restless intellectual mind" and a preternatural drive to help people.

During the 1980s, Talalay began investigating the chemical properties of fruits and vegetables, reasoning that plants, over millennia of evolution, had developed thousands of chemical compounds to protect themselves against oxidation, inflammation, and DNA-damaging agents that cause diseases like cancer. His lab performed experiments to isolate those compounds to see which ones could perform the same disease-prevention functions in humans.

"I cannot say we had a clear vision of where we were going, but we had started with the notion that we could block carcinogenesis if we could isolate these substances," Talalay told Johns Hopkins Magazine in 2008.

In 1991, Talalay sent postdoc Yuesheng Zhang to Baltimore's Northeast Market with a $20 bill and instructions to bring back a variety of vegetables. Together, Zhang and Talalay analyzed the vegetables and found that broccoli was notably high in a compound called sulforaphane, which seemed to trigger the increased production of enzymes that help cells resist toxic substances, including carcinogens. The discovery earned Talalay a slew of media attention as well as funding for a new lab dedicated to investigating the role of plants in cancer prevention.

There was just one problem. "My dad wasn't a plant guy," Tony Talalay says. "That's where Jed Fahey came in."

A better broccoli

There are dozens of varieties of broccoli. White broccoli, purple broccoli, orange. Some types of broccoli, like romanesco, look like short, pointy shrubs; others, like broccolini, resemble tall, skinny conifers. Broccoli rabe could be mistaken for a bouquet of weeds. After the discovery of sulforaphane in 1991, determining what kind of broccoli contained the most potent substance became the next order of business.

But as it turned out, sulforaphane showed up in inconsistent levels across samples of the same variety of the cruciferous vegetable. "There was no physical clue as to which one would have the highest levels of the compound," says Fahey, who became head of the Chemoprotection Lab in 1993. "The consumer would have no way of knowing which one was best."

Fahey was a Johns Hopkins freshman in 1971 when he met Paul Talalay, who was teaching an Intersession course on the pharmacology of recreational drugs.

"I was bopping around Baltimore with nothing else to do, and I was intrigued because I was learning how to party in various ways and this class promised to tell me about the coolest drugs," Fahey recalls with a laugh. Jokes aside, the course left "an indelible imprint" on a young Fahey. "I enjoyed it, and I remembered it—and I remembered him."

Twenty years later, Fahey had a master's in botany and a decade of unfulfilling work in the biotech industry under his belt when he saw a job listing to head Talalay's new Brassica Chemoprotection Lab. "He

was looking for someone with a green thumb to help him find a better broccoli."

At his interview, Fahey razzed his former teacher for teaching him how to smoke pot. "Of course he feigned shock," Fahey says. "It may have been that conversation that got me the job."

In the lab, Fahey analyzed different varieties of the plant as well as its different parts, while also comparing broccoli that had been grown organically versus conventionally, broccoli grown in full sun versus partial shade, or broccoli that had been sitting on grocers' shelves for two days versus three. The work was slow-going, made more complicated by Fahey's inconvenient workspace—an old lab on the 13th floor of the Blalock Building, back then the main hospital tower.

"I had a network of about nine farms around Maryland that were growing broccoli for me," he says. "My technicians and I would come back from the Eastern Shore with muddy boots and coolers full of stinky broccoli and go up in the patient elevator, with surgeons in their scrubs … looking at us like, What the hell are you doing?"

Another challenge was the weather. In the winter of 1994, while waiting out the cold temperatures, the botanist-by-training decided to grow broccoli from seed, right there on the 13th floor of Blalock. "The idea was to grow them out to full-size broccoli, but we only had a limited number of growth chambers." To save room, he snipped his plants when they were days-old sprouts. It was a fortuitous decision.

"I discovered that broccoli sprouts were a very potent source of this human protective agent and had way more sulforaphane than market-stage broccoli," he says. The compound actually became diluted as the plant grew.

Since Talalay's 1991 discovery, researchers had been trying to concoct a synthetic version of sulforaphane—an easy way to deliver it to the public—with limited success. Fahey's findings provided the scientists with a sulforaphane delivery vehicle that wouldn't have to endure years of clinical trials and government approval: a clamshell of broccoli sprouts. "I didn't want to be in the drug-creation business. I wanted to get people to eat more healthy diets," Fahey says. "My view of my mission—and Paul's also—was getting this into people's hands."

In the late '90s, customers looking for sprouts at the grocery store were likely to find alfalfa sprouts, which were relatively shelf-stable and unoffensive tasting. Broccoli sprouts, which spoil quickly and boast a sulfurous taste, weren't considered a viable product. In 1997, Fahey and Talalay launched Brassica Protection Products. Tony Talalay wrote the business development plan. To his knowledge, "it was the first time a vegetable was commercially grown solely to deliver a health benefit."

Although the team worked with a nationwide network of local growers and packers, the challenges of broccoli sprouts—their exceptionally short shelf life especially—proved too much to overcome, and by the early 2000s, the company switched to selling extract. By that time, the elder Talalay and Fahey had relinquished their share of the business and handed the reins over to Tony Talalay. "There was a clear conflict of interest," Fahey explains, "as we were getting more involved in clinical studies."

The scientists wanted to get back in the lab to see what this little sprout could do.

Pushing the limits

Around the time Talalay was staffing his chemoprotection lab, translational scientist Thomas Kensler, then a faculty member at the

Bloomberg School of Public Health and a friend of Talalay's, was hard at work trying to address the astronomical rates of liver cancer in Qidong, China. In the early '90s, one in 10 adults in the rural area was diagnosed with the disease. Farmers in the region were mandated to grow corn, which, owing to the area's hot and damp climate, often became contaminated with a fungus that produced the carcinogen aflatoxin.

He and his collaborators had some success during the 1990s with a drug called oltipraz, but Kensler, who says the era's "drug of the week type of approach" had grown dissatisfying to him, was watching as Talalay made waves with broccoli. "He was really flipping the script from drugs to food for preventive interventions."

In 2002, Kensler got Talalay's blessing to try broccoli sprouts in Eastern China—and recruited Jed Fahey to help him grow them there. Together, the two men imported 200 pounds of broccoli sprout seeds and turned an old lab into an improvised greenhouse with heavy plastic sheets and portable heaters. For drainage, they hammered a hole in the wall and used brooms to push out excess water from near constant irrigation. "At the same time, we were trying not to electrocute ourselves because we were using plug-in space heaters," Kensler remembers. "It was like the Wild, Wild West."

Eventually, the researchers had grown enough sprouts to make a tea for 100 participants for 14 nights (100 others drank a placebo tea). By analyzing participants' urine, Kensler and his team were able to demonstrate that sulforaphane had a dramatic effect on helping the body shed the harmful aflatoxin. "We showed that we could accelerate the detoxification and clearance of aflatoxin from the bodies of these people," Kensler says.

Ultimately, liver cancer rates in Qidong fell dramatically as China underwent major economic reforms at the end of the 20th century.

Farmers were no longer required to grow corn, and by 2010, aflatoxin was "barely detectable in the population," Kensler says. So his team pivoted to the country's next looming public health crisis: air pollution. In 2014, Kensler and a research team—opting this time for a freeze-dried broccoli sprout powder rather than makeshift greenhouses—demonstrated that sulforaphane helped the body excrete 61% more benzene, a carcinogen, and 23% more acrolein, a lung irritant, two toxins prevalent in polluted air.

While Kensler was making sulforaphane tea in China, back in Baltimore, Talalay's chemoprotection lab had pitted the broccoli sprout against the bacterium Helicobacter pylori, the culprit behind gastritis, ulcers, and stomach cancer. In 2009, the team published the results of a study of 50 people in Japan (where treatment-resistant infections are more common than in the U.S.), that suggested eating 2 ounces of broccoli sprouts a day for two months conferred some protection against the nasty bug, reducing by more than 40% the amount of H. pylori shed by infected people.

"To this day I get requests from people who have an infection they can't get rid of," Fahey says.

In 2014, the researchers turned their attention to autism spectrum disorder. While the cause of autism remains elusive, studies had shown that the cells of those with ASD often demonstrated high levels of oxidative stress, something sulforaphane does a good job of protecting against. Indeed, during a small study of 40 males between the ages of 13 and 27, the chemoprotective compound seemed to ameliorate the behavioral symptoms of the disorder in the 26 participants who received it, including repetitive, ritualistic behaviors, and substantially improved their social interaction and verbal communication.

These results intrigued Akira Sawa, a professor of psychiatry and

behavioral sciences and the director of the Johns Hopkins Schizophrenia Center. A mentee of Solomon Snyder, Sawa considers himself "the research grandchild of Paul Talalay." He wanted to see if sulforaphane might be able to address the chemical imbalances that lead to treatment-resistant schizophrenia, and he designed a series of studies to figure it out.

First, Sawa and his colleagues compared the brains of 81 schizophrenic patients who had experienced psychosis with the brains of 90 healthy patients. They found that patients with psychosis had less of the antioxidant glutathione in their brains. In subsequent studies, Sawa and his colleagues demonstrated that sulforaphane could be used to tweak glutathione levels in healthy humans, hinting that the broccoli sprouts could reduce the symptoms of people with schizophrenia.

Sawa warns that more studies are needed to prove sulforaphane could be a future treatment for schizophrenia—a clinical trial is imminent—but he's excited about its potential. "We're on the right track," Sawa says. "We are very hopeful."

The future is green

Lori Jones-Brando, a microbiologist in the School of Medicine, had been working on treating the parasite Toxoplasma with plant compounds when she got an email from Jed Fahey in 2015 suggesting she try sulforaphane. She took his advice, and when the pandemic hit in 2020, Jones-Brando still had some sulforaphane in her freezer. With all research on hold except COVID-related pursuits, she decided to see how the compound would interact with a coronavirus.

"Lo and behold, it had activity against the virus," she says. Jones-Brando's quick experiment spurred two years of "furious" research to see what impact sulforaphane had on SARS-CoV-2, as well as the common

cold, in both human cells grown in the lab and in mice.

In one experiment, the research team first exposed the cells to sulforaphane for one to two hours before adding SARS-CoV-2 and a common cold coronavirus into the culture where the cells were growing. They found that low concentrations of sulforaphane reduced the virus's replication by approximately one-half. Jones-Brando and her colleagues also demonstrated that sulforaphane and remdesivir, an antiviral commonly given to adults hospitalized with COVID, are more effective when used in tandem than when applied on their own.

Jones-Brando says she's working with Fahey, now retired from Hopkins and consulting for Brassica Protection Products, as well as Tony Talalay, who still heads the company, to develop a clinical trial in humans based on this work.

After seven decades of cancer research, Paul Talalay died in 2019 at the age of 95. His legacy lives on in the labs of scholars like Kensler, Sawa, and Jones-Brando—as well as in produce sections across America, where the sprout is now common.

For Fahey, broccoli sprouts remain both professional obsession and personal preference. "On the counter in the kitchen, I'm always growing sprouts," he says. "I sprout all the time."

Provided by Johns Hopkins University