# Cancer-busting Broccoli Sprout Pills? It’s a Thing.

Cruciferous vegetables (cauliflower, kale, cabbage, Brussels sprouts, broccoli sprouts) trigger a powerful cancer-inhibiting process.

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Worried about health effects from the U.S.’s increasingly smoky summers? One day, not far in the future, you may be able to pop a few pills that will help your cells pinpoint and extract the worst of the airborne carcinogens before they can do any harm.

Sound completely science-fictional? It gets better. Future space travelers bound for Mars may take these chemopreventive — or cancer-fighting — agents as well, to combat the adverse effects of galactic cosmic rays and other harmful space radiation.

For decades, Dr. Thomas Kensler has been on a quest to find a way to exploit a powerful cancer-inhibiting process that’s triggered when you eat cruciferous vegetables like cauliflower, kale, cabbage, Brussels sprouts, broccoli and most especially, broccoli sprouts. The toxicologist and translational researcher at Fred Hutchinson Cancer Research Center and his colleagues are basically trying to one-up Hippocrates, the father of modern medicine, who advised humans to “Let food be thy medicine and medicine be thy food.”

“I’ve been trying to address this question for about 25 years,” said the researcher, recently selected as one of a handful of "champions and changemakers" by the National Cancer Institute’s Division of Cancer Prevention. “Can people be protected from unavoidable exposures to environmental carcinogens by increasing their rates of detoxications and facilitating the elimination of these carcinogens from our body?”

The answer is yes. Meet your favorite new cancer prevention tool: broccoli pills.

## ‘We could reduce carcinogens in the body’

It all started in a remote part of China north of the Yangtze River and the city of Shanghai. Kensler went there in 1993 with his colleagues from the Johns Hopkins Bloomberg School of Public Health in Baltimore, part of an international effort to reduce the high rates of liver cancer that had emerged in the second half of the 20th century in the rural Qidong region.

“It was a ferocious hotspot,” Kensler said. “Upwards of one in 10 adults were developing and dying

of a type of liver cancer, many in their 40s and 50s."

The problem was the corn the subsistence farmers were mandated to grow, and live on, which was "consistently contaminated" with a fungus that produces a potent carcinogen known as aflatoxin.

"They were essentially poisoning themselves through the diet they were eating," he said.

Kensler and colleagues set out to intercept aflatoxin's carcinogenic process through chemoprevention, targeting the toxins driving the liver cancer process by enhancing the body's defense mechanisms to resist carcinogens.

How did they do this? After considerable experimentation, they landed on the idea of packaging up the powerful disease-fighting phytochemicals, or natural plant chemicals, of cruciferous vegetables, all of which derive from the wild mustard plant. Yep, good old broccoli. A year earlier, in 1992, Kensler's colleagues at Johns Hopkins published research identifying a compound known as sulforaphane, produced as a byproduct of processing or chewing these veggies, as a very potent cancer preventative. So the researchers set out to build tiny cancer-busting broccoli bombs that they could deliver via a beverage or supplement.

And the research went well.

"We came up with proof of principle that chemopreventive agents could change the fate of aflatoxin," Kensler said. "We could reduce carcinogens in the body."

As it turned out, it was China's economic and social revolution that finally brought down the rising liver cancer rates. By early 2000, "their diet was just as diverse as the American diet," Kensler said. People didn't have to eat contaminated corn anymore, so their aflatoxin levels dropped rapidly, as did, in time, the liver cancer rates. But industrialization, the rise of smoking and increasing air pollution had by then bumped up lung cancer rates in the entire country.

Kensler and the team realized the "principles we'd employed for other toxins could also work for air pollution," he said. So they pivoted. Instead of looking for biological indicators that their broccoli bombs were disarming and excreting aflatoxin via their trial participants' urine, they learned how to track and measure the agent's impact on carcinogens found in air pollution.

"Those became our new tools for moving forward," Kensler said.

As he and longtime Johns Hopkins collaborator Dr. Jed W. Fahey wrote in a paper published this spring in the journal Frontiers in Nutrition, the team was able to "successfully show favorable changes in biomarkers of both internal exposures to aflatoxin and air pollutants over multiple clinical trials, with multiple dose modalities, over many years."

## Green chemoprevention

Kensler has pursued this work, funded primarily through the National Cancer Institute at John Hopkins, then at the University of Pittsburgh and now, for the three years he's been at the Hutch,

in part through Washington state's Andy Hill CARE Fund for distinguished researchers.

His goal is to create a nimble, low-cost approach he calls "green chemoprevention" which can be used to "enhance the detoxication mechanism for those of us living in dirty air and dirty water environments," he said..

Kensler hopes the agent can eventually be used in cities like Seattle where wildfires, brought on by climate change-driven drought, have created a health hazard every summer, a hazard scientists predict will continue to grow worse.

"With forest fire smoke episodes, Seattle can have double the pollution that Beijing faces on a typical day," Kensler said. "We're seeking to power the individual to be able to facilitate some degree of risk reduction on their own."

So how does it work? You first have to understand what happens when toxins — like aflatoxin or, say, the airborne carcinogen benzene — enter the body.

"Toxins are fat-soluble, so they go into the body and become trapped," Kensler said. "A toxin needs to become water-soluble so you can pee it out."

To detoxify harmful agents, the body attaches what Kensler calls a "hitch," a molecular chain, that can also make the chemical more reactive. But this process can go awry.

"Depending on the chemistry, it can be a bad actor and cause mutations," he said. "The idea is to make the hitch, then couple it up quickly with sugars or amino acids using additional enzymes — think of it as a trailer on the hitch — that make it no longer reactive. They detoxify it and make it water-soluble."

The liver struggles to do all of this on its own but Kensler's research shows it's possible to give the body an assist by using the phytochemicals found within cruciferous vegetables to boost our natural detoxication mechanisms.

"We're using foods to enhance the activity of the enzyme that puts the 'trailer onto the hitch,'" Kensler said.

## Mustard bombing carcinogens

Cruciferous veggies contain sulfurous phytochemicals called glucosinolates. Eating broccoli sets off a chain reaction between one of these glucosinolates — glucoraphanin — and the enzyme myrosinase. These two compounds are found in separate cellular chambers of the plant; when it's chewed or chopped or otherwise damaged, active myrosinase is released and the two compounds mix.

The upshot? They form the chemoprotective agent sulforaphane, the plant's natural "mustard oil bomb" defense mechanism (no relation to mustard gas, which is not a natural substance).

That's what gives these plants their bitterness and smell and how they fend off predators like fungi or insects. Our gut microbiota, which also produces myrosinase, has a similar effect.

In essence, "we humans have co-opted the plants' system for our defense," Kensler said.

Kensler's broccoli bombs — packed with soon-to-be-sulforaphane — target our body's multifaceted cellular defense mechanism, the Keap1-Nrf2 pathway and the enzymes it regulates. These enzymes can transform fat- or lipid-soluble toxins to a stable molecule that's water soluble. So all those nasty carcinogens can just be flushed away. Literally.

These phytochemicals also provide a broad-based mechanism, Kensler said, one that can "work for airborne, food-borne and waterborne pollutants."

And nothing delivers quite like broccoli. Or rather, its three-day old sprouts grown from glucoraphanin-rich seeds. Over the years, Kensler and colleagues painstakingly researched plant varieties, seed germination, peak harvesting times and much more to achieve the maximum amount of sulforaphane precursor to boost detoxication. They investigated delivery systems and dosing in numerous clinical trials.

Turns out the correct dosing really matters; so does taste.

"Broccoli tea doesn't taste all that good," Kensler said of the beverage they brewed for some of their trials. "Most people find it obnoxiously bitter so we worked with a sensory company to mask the taste and it worked. Compliance was phenomenal."

According to their analysis, Kensler and colleagues were able to increase the elimination of carcinogens from test subjects' bodies by 67%, which he said, "should make a difference."

For their last clinical trial, which ended in December 2019, they worked with a vendor to manufacture tablets from milled and powdered broccoli seeds mixed with freeze-dried broccoli sprouts.

"They're coated so they'll get into your GI tract," he said. "We're finding that this works really well. Much better than our teas."

## No rigor, no regulations

Not surprisingly, the supplement industry — which is unregulated and does not conduct studies with rigor, if at all — has already jumped on the broccoli bandwagon. Go online and you'll find an assortment of products with glucoraphanin, myrosinase and sulforaphane. Kensler said an entrepreneur in China is already marketing a drink called SFN, which is supposed to contain sulforaphane, but doesn't.

"We're going to have to deal with the noise of bad products following good science," the researcher warned.

Kensler's most recent trial, the first evaluation of the supplement approach, ended just as the

coronavirus pandemic closed borders. He came back to Seattle but had to leave most of his biospecimens behind. He said the vendor who created the broccoli sprout tablet for the trial used rigorous quality control through sourcing and manufacturing and distribution.

“That’s not what supplement companies do, but this group did,” Kensler said. “I’m encouraged about the supplement as the delivery tool to provide a quality and defined dose.”

But the data still needs to be analyzed. Kensler had planned to go back to China to retrieve blood samples in early 2020 in order to evaluate the biomarkers. The pandemic had other plans.

“We wanted to clearly define the pharmacological activity,” he said. “We want to do metabolomics and proteomics and analytic measures that will give us insights into the mechanism of action and efficacy of action. But they’re sitting in a minus 80-degree freezer in Qidong.”

Kensler has asked for permission from China and the U.S. to return and retrieve the samples, but so far has not received all necessary clearances, mostly due to the pandemic.

“We don’t really know about the future of the studies,” he said. “It’s complicated scientifically, politically and public health-wise. But we have samples and we continue to think about it and what we want to accomplish.”

## The final frontier

And while his application to return to China and retrieve the samples may be languishing, his research is not.

Kensler is currently working with a team of Japanese scientists investigating whether the green chemoprevention pathway can protect astronauts — or even everyday billionaires — from the harmful effects of cosmic radiation. In 2018, the scientists sent 12 laboratory mice — six normal lab mice and six with Nrf2 knocked out — to the International Space Station to study the effects of space on the pathway. The mice lived in space for a month and then returned safely to earth. The results of the experiment were published in September 2020.

“Our goal is not just watching mice float,” Kensler said. “We’re trying to get a better understanding of the physiology — and how Nrf2 may or may not affect it. Space travel in general is associated with loss of bone density and muscle-wasting. There are many stressors.”

Kensler said the molecular target he’s studying on earth may actually become a useful concept for enhancing health in space.

“Space travelers in the future may be taking broccoli pills to activate their host defense mechanisms to help them deal with the stressors associated with long term space travel,” he said.

“We’re nowhere there conceptually, but Mars travel isn’t that far away.”