Nearly 8,000 miles, an ocean and seven time zones separate the small town of Kannapolis, N.C., from the heartland of southern Africa. Food scientist Mary Ann Lila knows the distance all too well. She’s visited 17 African countries in the past eight years. But she doesn’t measure the distance solely in miles. The sub-Saharan region is, in many respects, a world away from her high-tech laboratory on the expansive North Carolina Research Campus in Kannapolis, just north of Charlotte.

The differences in culture, language and traditions are striking. So too are the economic and health disparities.

In the Republic of Zambia, where half the country’s 14 million citizens live on less than a dollar a day, malnutrition is a persistent problem. UNICEF estimates that 54 percent of children under age 5 in Zambia suffer from stunting, making them susceptible to a variety of preventable diseases and threatening their functional and intellectual capacity well into adulthood.

Lila, who directs NC State’s Plants for Human Health Institute located at the research campus, is combining expertise in plant biology and knowledge of southern Africa to tailor a homegrown solution. The problem, she explains, is Zambia’s climate. During the rainy season, from November to April, villagers grow enough to eat. But during the rest of the year — the dry season — food is scarce.

“They don’t have refrigeration, they don’t have freezers, they don’t have electricity in the rural villages,” she says. “So in the dry season they’re forced to subsist on nshima, a porridge made of corn meal, like grits.”

Though nshima is easy to make and readily available in most homes, the staple lacks the protein and nutrients vital to the healthy development of infants and children. Shipping in meats and produce from Western countries isn’t the answer, Lila says, because villagers in many countries are wary of unfamiliar foods.
“During the famine in Ethiopia, the U.S. Agency for International Development brought in corn, but many people simply would not eat it because it was foreign,” she says. “They just aren't receptive to food that is not their own food — even if they’re starving.”

In addition, the logistical and economic challenges of delivering food to millions of people across the region are well-nigh insurmountable. But thanks to a grant from the Bill and Melinda Gates Foundation, Lila has teamed up with a local nongovernmental organization to launch a pilot program in three Zambian villages. If the program’s early success is replicated on a larger scale, it could significantly reduce the incidence of chronic malnutrition in many African countries.

Her idea is simple: teach villagers how to use some of the crops they harvest during the rainy season to create a shelf-stable protein powder. Then, in the dry season, the powder can be easily added to nshima to boost its nutritional value. The only equipment villagers would need is a low-cost, solar-powered dehydrator.

“It doesn’t take much,” Lila says. “It’s a simple process, so they can make it right in the village. That’s the key to the whole thing.”

Once that key is turned, it unlocks a myriad of nutrients — protein from soy and peanuts, phytochemicals from fruits and vegetables — that are abundant in the crops Zambians grow during the rainy season.

What’s more, harnessing these naturally occurring plant compounds isn’t just an innovative way to combat malnutrition in Africa; it’s the basis for a wide range of human health advances.

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THE WONDERS OF PHYTOCHEMICALS

Since it was founded five years ago under Lila’s leadership, the Plants for Human Health Institute has worked to unlock the mysteries of phytochemicals, the bioactive agents that give plants their color, flavor, taste and smell. Anthocyanins, for example, are the pigments responsible for the dark skin of the blueberry and the rosy blush of the red apple. Phenolic acids give vanilla and licorice their complex aromas and put the zing in chili peppers.

In fact, Lila explains, plants are composed of “a complex cornucopia of chemicals” numbering in the thousands. Their beauty, it turns out, is more than skin deep. There’s mounting evidence that some phytochemicals have beneficial properties, including the ability to reduce inflammation, prevent obesity, relieve pain and lower the risk for diseases like cancer and stroke.

The field is wide open for research, and the Plants for Human Health Institute has quickly emerged as a global leader — literally. Lila travels around the world, leading teams of graduate students and researchers on bioexplorations to discover and test the healing power of plants. In addition to her work in sub-Saharan Africa, she has ongoing research projects in central Asia, Egypt, Mexico, Australia and New Zealand.

“We’re not taking their plants and going off to our lab to make discoveries and keep all the credit,” she says. “We’re right out in the field with them. They get credit and the potential to license the discoveries if it goes that way. But they also get their traditional ecological knowledge validated.”

That last point is an important one. In many native communities, elders worry that young people don’t value their traditional foods and medicines anymore, Lila explains. “Young people want fast food. They don’t really care about wild berries or buffalo or things that are part of their traditional diet.”

Involving school-age children in local research projects may help change that. Participation in research also sparks an interest in science in many young minds.

“It’s a turn-on experience for the kids to get to do hands-on scientific research with their own local plant material,” Lila says. “And it shows them the value of their own resources.”

THE FRINGE OF SURVIVAL

There’s a reason Lila travels to the far reaches of the globe to conduct her research. Whatever their similarities in taste, a berry grown in North Carolina is much different from a berry grown in Alaska.
"The plants up there are on the fringe of survival," Lila says. "They accumulate all kinds of natural chemicals to ward off the ravages of the environment."

For example, in the far north of Alaska, plants must adapt to days with 23 hours of sunlight during the growing season. "If you had that much ultraviolet light hitting a berry in the lower 48, the berry would be fried," she says.

However, berries in Alaska have evolved an extraordinary complement of phytochemicals to help them avoid sun damage and survive in extreme conditions.

"When a human eats the berry, those same phytochemicals that protect the berry interact with targets inside the human body, like membrane receptors, to ward off chronic human disease," Lila explains.

In fact, the institute's tests have shown that a variety of indigenous Alaskan berries — bog blueberries, blue huckleberries, salmonberries and mossberries — constitute "superfruits" with powerful antioxidants capable of offsetting multiple human health concerns, including cardiovascular disease, DNA oxidative damage, neurodegeneration, cancer cell growth, bacterial infections and metabolic syndromes. The implications are exciting, Lila explains, pointing to the potential for sweeping advances in the treatment and prevention of some of the world's most widespread and costly human diseases.

One such disease is diabetes, a chronic condition affecting 285 million people worldwide that is caused by the body's inability to properly regulate blood sugar. The prescription drug most commonly used to treat the disease, Metformin, works by suppressing glucose production in the liver.

If clinical trials of phytochemicals continue to show promising results, Lila says, people may someday opt for a plant-based method to manage the disease.

"What we've shown in animals is that within six hours of consuming blueberries, blood glucose dropped to a comparable or lower level than if they had been given Metformin," she says. "That's pretty strong, because Metformin is expensive and blueberries are not."

The team's research in Alaska also has the potential to advance the economic prosperity of native tribes. In an article published in the Journal of Entrepreneurship, Lila and co-authors Joshua Kellogg, a graduate research assistant, and Clyde Higgs, vice president for business development at the North Carolina Research Campus, say a start-up company operated in partnership with Alaska natives could find a market for the wild berries through health-conscious retailers such as Trader Joe's and Whole Foods Market.

The market for superfoods — defined as foods that are rich in specific nutrients and antioxidants — has doubled in the past decade in Europe and the United States, the researchers note, and industry publications report that more than 50 percent of consumers respond favorably to products branded as antioxidants.

It's not hard to see why antioxidant products are popular. Oxidative stress, caused by particles called free radicals, damages cells and plays a significant role in many human diseases as well as the aging process. Antioxidants act as free-radical scavengers, inhibiting oxidative stress.

PATHWAYS TO HEALTH

In addition to Alaskan wild berries, Lila and her team have tested dozens of plants with the potential to improve human health, from the Chilean wineberry found in South America's temperate rain forests to the muscadine grape, native to the American South.

After returning home from bioexplorations in the shadow of the Andes or on the Arctic tundra of Alaska's North Slope, the researchers hardly have time to unpack before diving back into work. And they have plenty to explore right inside their well-equipped laboratory in Kannapolis, where they analyze the effects of phytochemicals using nuclear magnetic resonance, mass spectrometry and high-performance liquid chromatography.

To fully harness the power of phytochemicals for human health, researchers need to map the chemical reactions that happen inside plants as they adapt to environmental stressors, such as UV light or cold climates. Once these complex pathways are understood, they can be used to engineer plants with specific properties that promote health or prevent disease.

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Here, too, the Plants for Human Health Institute has taken the lead.

“We’re working with sophisticated computer software and systems to elucidate these chemical pathways that have never been looked at before,” Lila says. “It requires huge interactive teams to get to these answers, and nobody’s been able to put them together.”

Until now, that is. Last summer, with nearly $1 million in funding from the University of North Carolina General Administration and significant support from the Duke Energy Foundation and other donors, the institute launched an ambitious project to explore the inner workings of plants in relation to human health. The Plant Pathways Elucidation Project gives dozens of college students from across the state the opportunity to conduct hands-on research every summer under the guidance of Ph.D. students, university faculty and industry research leaders. Working in six labs, the students are tasked with mapping plant genomes and then charting specific chemical pathways that may lead to products with health-improving properties.

“We want to know what the plant makes, how the plant makes it, and what good that product is for human health,” Lila says. “That’s really what we’re getting at.”

For example, it may not be enough to measure a plant’s antioxidant capacity, she says. Researchers really need to know whether plant phytochemicals act directly on antioxidant mechanisms, or whether they work indirectly by influencing cellular signaling.

The project is an innovative collaboration that leverages the strengths of the research campus, home to some of North Carolina’s top universities as well as industry giants such as General Mills, Monsanto and Dole Nutrition Research. The 350-acre campus was founded in 2008 by Dole Foods owner David H. Murdock.

“One of our industry partners asked us to figure out the pathway that leads to high fiber in the oats used in breakfast cereal, and that’s exactly what we did,” Lila says. “They formulate questions, we formulate research plans to study and answer them.”

The project also draws on expertise from university partners including bioinformatics researchers at UNC–Charlotte and plant scientists at NC State, among others.

Eric Jackson, principal scientist with General Mills and a member of the project’s leadership team, coordinates the genetic mapping, sequencing and annotation portion of the project. He believes the students’ work will swiftly translate to better products in the marketplace.

“This project will give us the tools to create better varieties of blueberries, strawberries, oats, broccoli and other crops we focus on down the road,” he says. “Once we map the pathways, we can start developing practical, applied technologies to get the science to the table and benefit human health.”

REAL-WORLD SOLUTIONS

It’s not just big food companies that are excited about the research coming out of the Plants for Human Health Institute. Lila has been working with the United States Army to develop better ration packs for soldiers in the field.

“The army is interested in working with us because they need to find some easy way to deliver the immune protection that you get from fruits and vegetables to their people in the field,” she says. “And they need it in a palatable form, in a form that tastes good to the soldiers.”

Soldiers are picky eaters, she says, liable to toss out anything in their ration packs that doesn’t look interesting.

At the Plants for Human Health Institute, researchers have perfected a simple and effective technology that allows them to concentrate phytochemical compounds into a protein-rich soy flour while excluding water, sugars and fats. The result is a tasty protein bar with immune-boosting properties.

“It’s just what the army ordered, Lila says, and could eventually replace the unpopular items in ration packs.

Lila’s work has also drawn the attention of Rafael Correa, president of the Republic of Ecuador, who toured the North Carolina Research Campus with 60 government officials in the fall of 2012. Correa plans to launch a similar research venture in Yachay, a planned city of science and technology under construction in Ecuador’s northern province of Imbabura.

“He wants to support bioexploration and has asked us to help train his faculty,” says Lila, who has conducted extensive
research in Ecuador’s Galápagos Islands. Rain forests cover a third of the South American country, making Ecuador one of the most biodiverse environments in the world.

Closer to home, Lila recently began working with the North Carolina company Metabolon to collect data in the pioneering field of metabolomics, the study of how metabolites — such as vitamins, nucleotides, antioxidants and amino acids — move through and act upon the body.

“When you eat a berry, the phytochemicals don’t just stay in your bloodstream; they’re broken down into a lot of pieces that are dispersed to many targets, different body fluids and tissues,” Lila explains. “Now we can measure that. It’s beautiful.”

It’s also high-powered teamwork. Researchers at Metabolon recently collaborated with scientists at the Plants for Human Health Institute and Appalachian State University’s Human Performance Laboratory, which is also housed at the North Carolina Research Campus in Kannapolis. The researchers used metabolomics to measure oxidative stress and inflammation in long-distance runners who ate a protein bar infused with phytochemicals. The results of that study, published in the *Journal of Proteome Research*, will likely lead to more interdisciplinary efforts.

But the real beauty of metabolomics is its potential to help health providers tailor dietary recommendations to an individual’s metabolic profile.

“If you tell somebody that a plant is anticancer or cardio-protective or anti-diabetic or reduces attention deficit disorder, the next question is, how much do I have to eat? That’s the hard question because there is no universal recommendation,” Lila says. “It falls under the umbrella of individualized nutrition. It depends on the body’s genome and how well a plant acts biomedically in the body.”

That’s one of the reasons medical doctors often resist giving nutritional advice and rely almost entirely on pharmaceutical products to treat diseases. Those days may be coming to a close.

“With metabolomics and genomics and the sophisticated instrumentation we have on this campus, we can get to those answers that were just pie in the sky before,” Lila says.

**STRAWBERRY FIELDS FOREVER**

Even as the Plants for Human Health Institute stretches to meet health needs on a global scale, it remains intimately tied to North Carolina’s agricultural industry — particularly the state’s small farmers. That connection is reinforced by NC State’s mission as a leading land-grant institution.

A case in point is ongoing work by a team of scientists, extension agents and marketing experts to help North Carolina farmers capture a larger share of the increasing consumer demand for strawberries. Horticultural scientist Jeremy Pattison, an expert in strawberry breeding and genetics, believes the state is well positioned to meet the demand.

To do that, he says, researchers must find ways to extend the growing season, maximize fruit quality and improve the stability of the crop after it’s harvested.

Jonathan Baros, an agricultural economist who works with Pattison at the institute in Kannapolis, says the key is developing a strawberry that’s tailored to the North Carolina climate.

“We’re looking at creating a North Carolina-specific variety of strawberry that can provide the yield and the quality and characteristics that our consumers want and that can compete with products from Florida and California,” he says. “You can get that Florida strawberry here, but it may have no flavor because it’s been bred to have a longer shelf life. We could produce a North Carolina variety and get it in our grocery stores faster, and that would result in a better product, a tastier product.”

Researchers and staff from NC State and the Plants for Human Health Institute are also working to help growers better manage their financial resources, diagnose diseases in their plants via a smartphone app, reduce product loss across the supply chain, improve the quality of their soil and acquire energy-efficient cooling systems, among other things.

“We want to help farmers,” says Justin Moore, the institute’s communications chief. “We want to promote growth in the industry.”

Sometimes that help is financial. For the past five years, the institute has been awarded USDA Rural Cooperative

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*ABOVE: Doctoral student Christine Bradish works with horticultural scientist Penelope Perkins-Veazie to investigate the potential for watermelon to reduce skin damage from ultraviolet radiation."

“This project will give us the tools to create better varieties of blueberries, strawberries, oats, broccoli and other crops.”

— ERIC JACKSON, GENERAL MILLS

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REDS: Two key plant compounds responsible for reddish pigments are anthocyanins and lycopene. Research shows they are effective against cancer, heart disease, age-related illnesses, chronic inflammation, osteoporosis and diabetes.

YELLows/ORANGES: Sources of carotenoids, flavonoids, lutein, lycopene, potassium and vitamin C. These nutrients help prevent heart disease, boost immunity, lower blood pressure and cholesterol, promote healthy joints and reduce the risk of cancer.

GREENs: Contain beta carotene, calcium, fiber, folate, lutein, magnesium and vitamin C, which work in synergy to lower the risk of certain cancers and heart disease, protect against inflammatory diseases and osteoporosis, and aid in bowel health and weight management.

BLUES/PURPLEs: Contain powerful phytochemicals like anthocyanins and phenols, which protect against cancer, are healthy for the heart and memory, and can combat the aging process and degenerative diseases like Alzheimer’s.

WHITES/TANS: White fruits and vegetables, though colorless, actually contain many vitamins and phytochemicals, like allacin, beta glucans and flavonoids. White, tan and brown produce help lower blood pressure, maintain cholesterol, promote heart health and lower the risk of some types of cancers.

IN THE HOME: All fruits and vegetables are beneficial to human health in some way. They work together in synergy, which means that as food digests, two or more nutrients combine to do what neither could do as well by itself. Understanding all of the healthy compounds in fresh produce can be overwhelming, but that’s exactly what researchers at the Plants for Human Health Institute are doing. As a result, we know that the colors of fruits and vegetables say a lot about their health benefits. Discover what the colors in your favorite fruits or vegetables mean, and make as colorful a plate as possible!