OU researchers in the Natural Products Discovery Group comb the streets and backyards of America for new strains of microscopic organisms that could lead to life-changing medical breakthroughs.

By Chip Minty

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As head of OU's Natural Products Discovery Group, Robert Cichewicz leads a massive "microbial hunting expedition" that rounds up tens of thousands of undiscovered fungal species grown from soil samples contributed by citizen scientists.

The Magnificent

World of Fungi

Fungi often get a bad rap.

After all, they are responsible for mold, rotting food, funny smells and a long list of damage and disarray perpetrated against our homes and bodies. Their population is so enormous that no one knows for sure how many varieties there are. Estimates range somewhere between 1.5 and 5 million species.

Chemist Robert Cichewicz is the leader of a unique group of University of Oklahoma researchers who study fungi in the hope of discovering new chemical compounds that could develop into medical cures of the future.

Fungi have long been recognized for their healing qualities. Penicillin – once proclaimed a miracle drug for its effectiveness against infection – was developed in 1928 from a chemical produced by a fungus. Other modern drugs derived from fungi include cholesterol-reducing statin drugs and cyclosporins, used to prevent rejection in organ and tissue transplant patients.

However, the mainstream of corporate medical research no longer studies fungi and is no longer active in the research area known as "natural products."

For them, the process of studying fungi and the compounds they produce is too time consuming and discoveries are too difficult to patent. That has left small biotech companies and academic laboratories to continue the search, says Cichewicz, a Regent's Professor in OU's Department of Chemistry and Biochemistry.

Photo provided

Karen Wendt, a research assistant in OU's Natural Products Discovery Group, shows off petri dishes hosting various fungi. The discovery group has filtered hundreds of thousands of compounds derived from fungi. One such compound shows signs of treating an incurable form of pediatric cancer.

Cichewicz has been fascinated by nature since he was a boy growing up in western Michigan. To him, fungi are beautiful, intriguing and innovative, but most important, they represent a lockbox of new and unknown chemical resources that could have substantial benefits to humans long into the future. However, that lockbox is enormous, and the secrets are hidden deep inside, requiring considerable time, money, technology, manpower and perseverance to explore.

As director of the Natural Products Discovery Group on the OU Research Campus, Cichewicz and his team have been exploring that lockbox for more than a decade.

Through their work, they focus on the chemicals known as natural products or "secondary metabolites." They are chemical compounds that fungi produce through their normal course of living. Each fungus can produce two dozen or more of them.

While humans use arms, hands and fingers to help them manipulate their environment, fungi produce chemical compounds to serve purposes important for their survival, such as attacking prey, self-defense, communication and reproduction.

Meanwhile, science has found that some of these compounds can serve useful purposes for humans through development into medicine. The penicillin breakthrough is an example.

The first step in the discovery process is collection, which is no small task.

For several years, Cichewicz and his staff have been building a posse of citizen scientists from across the United States as part of a massive, microbial hunting expedition intended to round up tens of thousands of yet-to-be discovered fungal species.

So far, Cichewicz's Citizen Science Soil Collection Program has attracted 17,800 people, and the collection of fungi they have gathered for his lab has swelled to 30,000 species.

"There's a lot of fungi out there, and there was no way we could have gone out and found it all," he says.

The lab sends out thousands of soil collection packets free of charge to anyone who requests them. In turn, school groups, community groups, scout troops and individuals mail in their small plastic pouches of fungi-laden dirt from their own back-

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Robert Cichewicz (left), director of OU's Natural Products Discovery Group, works with researcher Andrew Blattler in "The Chemical Zoo." The team hopes to discover new chemical compounds from nature that can be developed into future medical cures.

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Candace Coker, project manager for the OU Institute for Natural Products Application and Research Technologies, holds up citizen science kits that have been distributed to nearly 18,000 people nationwide. This "posse of citizen scientists" has gathered 30,000 fungal species to date.

yards. Workers at the Natural Products Discovery Group filter through each sample, searching for undiscovered species.

Cichewicz is now getting thousands of dirt samples a year, so it is fair to say that new species discoveries are common, but discovering a new species is just the first step.

Newly discovered fungi are placed into small containers of Cheerios© cereal, where they grow, multiply and release the secondary metabolites that Cichewicz and his team are so very interested in studying. This discovery stage of research is an arduous process, Cichewicz says.

His lab has filtered through hundreds of thousands of compounds derived from fungi. Only a handful of them will serve a useful application, but Cichewicz says the slow pace is an inherent part of scientific discovery. Meanwhile, there is plenty of opportunity for new discovery, and that is a powerful motivator, he says.

Cichewicz's lab is testing for compounds that could eventually develop into new drugs for fighting cancer, neurodegenerative diseases and parasites, as well as new antibiotic medicines.

While the lab has found many compounds that have shown promise in early testing, most are eliminated in animal testing and other advanced stages of investigation. Currently, the lab has three compounds that appear to be promising as they move through preclinical studies with partnering laboratories.

One compound that shows signs of hope could be used to treat an incurable form of pediatric cancer, Cichewicz says. The compound is undergoing animal testing at the University of Texas Health Sciences Center in San Antonio. If positive results continue, the compound may someday be developed into a drug to treat Ewing's Sarcoma, a rare form of bone cancer that strikes children.

One exciting aspect is the compound originated from a fungus that came to the lab several years ago through the citizen science program, says program manager Candace Coker.

When established in 2010, the program started slowly with only 500 participants, but the numbers have exploded in recent years, she says. Some people have strong personal feelings about the program.

"They lost someone to a disease, and they want to help find a cure," Coker says. "People are engaged. They have stories, they're curious and they have follow-up questions."

For others, it's educational, and that's an important facet of Cichewicz's lab. Through public education, the lab can recruit more citizen scientists and encourage people to participate in science, she says.

That educational component has led the Natural Products Discovery Group to partner with Science Museum Oklahoma in Oklahoma City to create a new science exhibit with live displays, demonstrations and even fungal art. The exhibition, "Decomposition: Discovering the Beauty and Magnificence of Fungi," is on display through mid-August 2018.

"If you know nothing about fungi other than seeing it grow on food in your refrigerator, you're going to come out knowing

all the benefits fungi serve to this world and to human beings, and hopefully see a different side of fungi," Coker says.

People can learn about specific fungi, where they came from and what they do, and there will be more than 100 fungal isolates on display, along with a live demonstration of rot taking place in real time. Using food commonly associated with a person's lunch, the live demonstration will illustrate the rotting process through four stages of advancement, ranging from early stages to two months.

Science Museum Oklahoma

A child peers into a "rot box" showing the progression of fungus on a lunch tray from zero to 10 weeks at Science Museum Oklahoma.

"You will either think it's beautiful or gross, but either way you'll learn something," she says.

Finally, the exhibit will include a fungal art feature.

"It's way cooler than it sounds," she says. "Fungi are just beautiful. How they grow and do their own thing in different colors and textures. Visually, it's just stunning."

Galleries Director Scott Henderson says the exhibit is important to the museum.

"It explores a part of our world – fungi – that we don't think about too often," he says. "When we do think about fungi, they are usually regarded as gross and disgusting, but fungi can be quite fascinating and even beautiful."

They are also essential to the creation of new life, and they play an important role in medical research. It has been a pleasure to work with the lab, which is widely recognized for its contributions to medical discovery, Henderson says.

Coker says the exhibit was designed and built by the OU lab, using the immense fungal collection assembled through the Citizen Science Program.

In addition to the discovery group's educational activities, the lab has become a significant resource for researchers outside of OU, including pharmacologists.

"We have a really unique library of chemistry, derived from fungi," he says. "So, if a pharmacologist wants a new molecule that inhibits their protein, they can team up with us, and through collaborative research, we can start going through the collection."

Cichewicz says the National Cancer Institute also is working to transfer about two-thirds of the lab's collection so researchers at those facilities can work with the fungi.

"Our lab, as big as it is, can't look at all of the diseases and explore all of the potential benefits," Cichewicz says. "These fungi should be made available as widely as possible."

The ultimate goal is for pharmacologists and biologists from anywhere in the United States to have an opportunity to work with the fungi, so the collection can continue living long after the OU lab is gone, Cichewicz says.

"Imagine," he says, "A fungus that you contribute through the Citizen Science Program can make its way to the National Cancer Institute."

From there, someone may get their hands on that fungus and the compounds it makes, and they could develop a new drug to help treat cancer, multiple sclerosis or some other disease, he says.

"That fungus may have come out of your back yard."

Chip Minty is a Norman-based writer and the principal of Minty Communications, LLC.