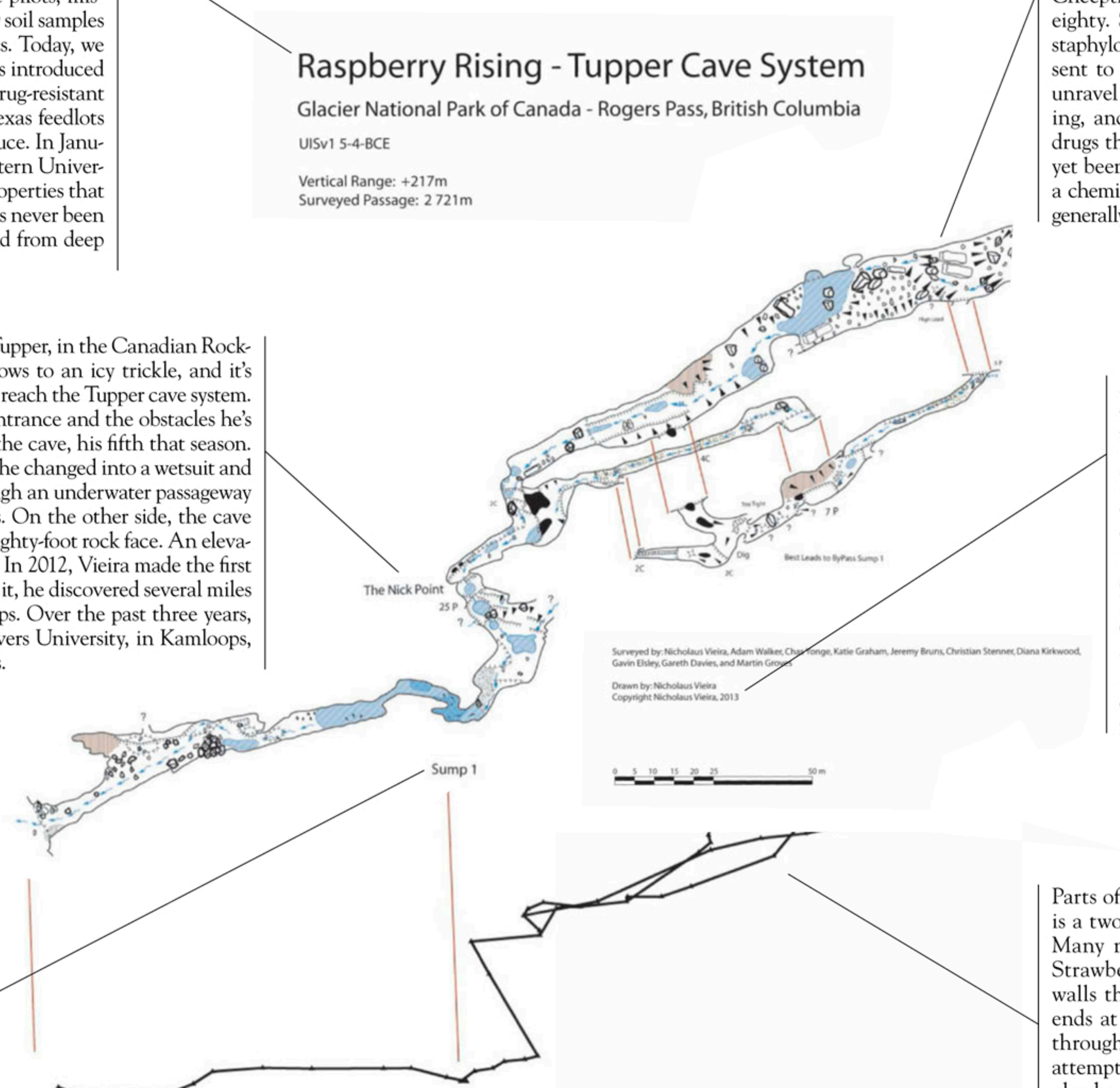
MOTES FROM UNDERGROUND

Will cave soil save us from drug-resistant superbugs?

By Peter Andrey Smith

During the golden era of antibiotics, from the late 1930s to the 1960s, when chemists extracted penicillin, streptomycin, and tetracycline from bacterial and fungal microorganisms, the top layer of the earth's soil appeared to be an endless wellspring of wonder drugs. In 1952, a promotional film by Pfizer claimed that "airline pilots, missionaries, expeditions, and ordinary travelers" had sent more than 100,000 soil samples to the company's Brooklyn laboratory to help in the search for antibiotics. Today, we are living in the so-called Discovery Void. The most recent antibiotic class introduced into clinical practice, known as daptomycin, was discovered in 1987. Drug-resistant pathogens now lurk in hospitals and in nursing homes, in dusty West Texas feedlots and in the Hudson River, in raw meats, poultry, and farmers'-market produce. In January, there was one bit of good news: a team led by Kim Lewis at Northeastern University announced the discovery of teixobactin, a molecule with antibiotic properties that they found in a soil sample from Maine. Others are looking for soil that has never been sampled before—from the bottom of the ocean, from volcanic vents, and from deep within previously unexplored caves.



From May to October, Raspberry Rising, a spring on the slopes of Mount Tupper, in the Canadian Rockies, gushes with glacial meltwater. Once the snows arrive, the stream slows to an icy trickle, and it's possible to dive into the spring—a resurgence, in speleological terms—and reach the Tupper cave system. These details from a map drawn by Nicholaus Vieira, a caver, show the entrance and the obstacles he's encountered inside. In late November 2014, Vieira made a return trip to the cave, his fifth that season. After snowshoeing up from Rogers Pass with a backpack full of scuba gear, he changed into a wetsuit and dove into the water. Nearly two hundred feet upstream, he squeezed through an underwater passageway that was barely a foot high, with his diving tanks held under his armpits. On the other side, the cave ceiling opened up and he stood in an air-filled chamber at the base of an eighty-foot rock face. An elevation chart at the bottom of the map shows the pitch as a giant inverted Z. In 2012, Vieira made the first known ascent of this section, labeled The Nick Point on the map. Beyond it, he discovered several miles of marble-banded caverns connected by water-filled segments called sumps. Over the past three years, Vieira has provided Ann Cheeptham, a microbiologist at Thompson Rivers University, in Kamloops, British Columbia, with more than twenty soil samples from these caverns.

The attraction of caves for antibiotics research is twofold. First, these isolated ecosystems, being far removed from one another, create opportunities for speciation. Second, the absence of light may cause subterranean organisms to adopt a completely different metabolism from their terrestrial counterparts. At first, Vieira saw few obvious signs of life inside Raspberry Rising: there were mouse skeletons and beetles—probably "accidentals" that had flowed into the cave. But later, above the active streamway, he discovered an older fossil passage that had not contained water in several thousand years. On the walls he saw faint pink and yellow discolorations that hinted at a biofilm mat—microbial communities that can adhere to surfaces as smooth as a marble countertop. These ultracompetitive, light- and nutrient-starved organisms use antibiotic compounds to defend against one another and to communicate. Microbes are said to be the most accomplished chemists on earth; a single organism can produce hundreds of bioactive molecules.

Selecting twenty sampling sites from more than three miles of squeezes and sumps and piles of boulder rubble can seem a bit, as Vieira put it, like throwing a dart. From the first round of samples he sent to the lab in Kamloops, Cheeptham and her students isolated 266 bacteria, of which they've screened eighty. So far, eight of those have shown activity against MRSA, a type of staphylococcus that's resistant to multiple antibiotics. These samples will be sent to Cheeptham's collaborators, who will sequence the organisms' genes, unravel their chemical structure, and begin the process of extracting, purifying, and testing new drugs. (By some estimates, only one in ten candidate drugs that are tested on humans is approved.) No marketable antibiotics have yet been derived from cave-dwelling microorganisms, but Brian O. Bachmann, a chemist at Vanderbilt University, said that "in the field of antibiotic discovery, generally, when people go into new ecosystems, they find new chemistry."

According to William Fenical, a professor of oceanic pharmacology at the University of California, San Diego, who has identified new cancer drugs in marine sediment, "We have our heads in the sand about drug resistance and our antibiotic arsenal." Few pharmaceutical companies fund research and development on antibiotics; there's more money to be made in drugs that treat chronic conditions such as erectile dysfunction or high cholesterol. Vieira covers most of his own expenses, including his scuba and climbing gear, and gets by on a modest grant from the Royal Canadian Geographical Society. He gives his samples to Cheeptham's lab for free. In the United States, the federal government spent $450 million on antimicrobial-resistance research in 2014—less than $1.50 per person. In his 2016 budget, President Obama called for nearly tripling that amount, but the final figure will be set by Congress.

Parts of Raspberry Rising are named for frustrations: the Bridge to Nowhere is a two-foot-wide span that crosses a pit and dead-ends at a boulder choke. Many names have a fruit theme. Near Sump 2, in an area Vieira calls Strawberry Shake, is a narrow, undulating marble passageway with rock walls that look like they were carved out by an ice-cream scoop. The map ends at what's known as Sump 4. On a dive in 2014, Vieira swam 180 feet through the submerged tunnel before his breathing gear failed. He hopes to attempt the passage again in the future and return with whatever soil samples he can gather from the other side. "Unlike Everest," Vieira said, "you can't look around and say, 'Let's climb that way.' We have to go into every hole possible." ■

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