BIOTECHNOLOGY

Yellowstone Managers Eye Profits From Hot Microbes

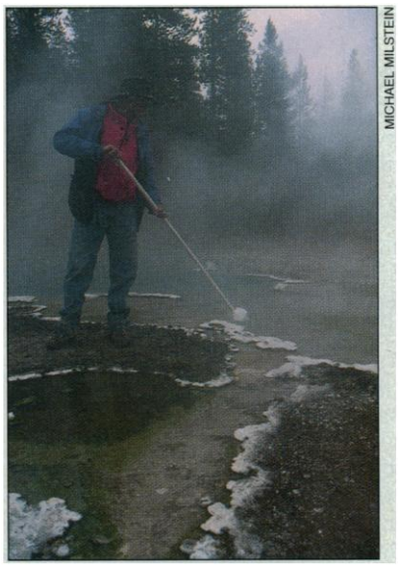
CODY, WYOMING—Each year, some 3 million people visit Yellowstone National Park to see wildlife—bison, elk, moose, and bears—as well as the park's famous geysers and bubbling hot springs. Among them are a few scientists who head to Yellowstone in search of a different breed of wildlife: Their quarry are thermophiles, hot-spring–dwelling microbes so small they are invisible without a microscope, but with such valuable natural powers they may be worth far more than their weight in gold.

This microbiological gold rush was set off by the enormous success of the polymerase chain reaction (PCR), the revolutionary gene-copying technique that since 1991 has earned hundreds of millions for patent-holder Hoffmann-LaRoche. A heat-stable enzyme derived from a Yellowstone microbe drives PCR, and now biotechnology companies and research institutes from around the world are prospecting in the park's steaming springs for new heat-loving microbes and viruses. These microbe miners hope to find profitable thermophiles with enzymes handy as tools in molecular biology or others that can themselves be put to work in high-heat industrial processes such as fermentation and conversion of trash to energy.

But the rising commercial interest in Yellowstone microbes has presented park managers with an unforeseen dilemma: Should they seek a share of profits that might arise from Yellowstone's tiniest attractions, through either up-front fees or royalties? The nation gets a return from oil drawn off federal lands. But never before PCR had private industry profited directly from creatures in a national park. "This is a whole new realm for us, and it's a real sticky one," says Robert Baker, head of the National Park Service's Rocky Mountain Region.

One reason it's so sticky is that demanding payment for moneymaking microbes may run against the grain of the Park Service's mandate to protect all park resources. "Nobody would want us to sell an elk standing in front of Old Faithful, but how do we draw the line between that and a tiny organism most people can't even see?" Baker asks. At the same time, park managers suspect federal laws might actually require them to pursue a cash return for the American people, who ultimately pay for Yellowstone's upkeep. The law stipulates that specimens gathered in a national park—rocks, plants, wildlife, anything—remain the property of the government. If hugely profitable microbes discovered in Yellowstone are forever federal property, does the government deserve a piece of the action? Yellowstone managers are asking federal lawyers to look into the question.

"The microbe issue will overshadow all others" at a conference on national park legal issues set for this fall in Denver, predicts Yellowstone Research Chief John Varley. "Where do these organisms fall into the whole scheme of things?" Varley asks. "You can't come in and take a publicly owned moose, but can you take a test tube full of bacteria that you'll grow in a laboratory to find a gene for a particular enzyme you're interested in? It's hard to know if our laws and policies apply to this kind of science."



MICHAEL MILSTEIN

Hot property. Prospecting for thermophiles in Yellowstone National Park.

If they do, the stakes could be high. Take the case of the bacterium *Thermus aquaticus*, discovered in 1965 by microbiologist Thomas Brock of the University of Wisconsin in an out-of-the-way Yellowstone hot spring called Mushroom Pool. Brock placed a sample in a national bacteria storehouse, and more than a decade later *Thermus aquaticus* yielded Taq polymerase, the thermostable DNA-copying enzyme that now fuels PCR. Brock earned nothing from his discovery of the microbe, but the enzyme is now making millions of dollars annually for Hoffmann-LaRoche, the Swiss pharmaceutical company that in 1991 paid Cetus Corp. $300 million for the still-contested patents on PCR and Taq.

Park managers have no current plans to cash in on Taq's riches. But they are wondering how to handle the future discoveries that are sure to come, since fewer than 1% of Yellowstone's thermophiles have yet been identified.

At present, researchers must satisfy officials only that they are working on a valid scientific project to get permits to collect microbial samples in Yellowstone. Many biotech giants have, or have had, these free permits: They include Genencor International of Rochester, New York, Stratagene Corp. of La Jolla, California, and New England Biolabs of Beverly, Massachusetts. Small companies are also joining the rush. One, J-K Research Inc. in Bozeman, Montana, survives almost entirely by searching for novel microbes in Yellowstone and delivering samples to big biotech concerns. And some academic researchers have ties to private firms.

For their part, scientists who work in Yellowstone agree that the park's microbes are a national treasure—perhaps even a strategic resource as international biotech competition increases. Although the park has no monopoly on thermophiles, it does hold one of the best arrays of accessible hot springs teeming with the tiny wildlife. "There aren't many other places like it in the world," says Eric Mathur, a Stratagene biotechnologist who made a prospecting trip to Yellowstone last fall. "Having that kind of environment and having it protected is very important to science." Unlike a limited commodity such as oil, Yellowstone's microbial riches are renewable and are "great PR for the Park Service," adds microbiologist Norman Pace of Indiana University. "They shouldn't just jump on this as a way of making money."

And if such a step should be taken, researchers are divided over how the National Park Service should proceed. An up-front charge like the entrance fee all park visitors pay might be reasonable, says Robert Ramaley of the University of Nebraska. Long-term royalties would be a less popular choice, since a royalty agreement attached to unknown organisms might be difficult to enforce and could cause bureaucratic tangles that may drive researchers away. "People would avoid going to Yellowstone if they had to agree to give the government a royalty off something not even discovered yet," argues Ira Schildkraut, director of research at New England Biolabs. "The park should encourage scientific work, not discourage it with new regulations."

A simple solution to the Park Service's quandary may be as elusive as a thermophile in a roiling spring. Yellowstone managers have searched law books for an answer, to no avail. They are now compiling a thick report for Interior Department lawyers and policymakers, who must figure out whether the government could or should reap a reward from the park's most profitable residents.

–Michael Milstein

Michael Milstein is a science writer in Wyoming.