

under which scientists from those countries will compete for funding on topics of mutual interest. Talks have also been launched with Germany, Japan, France, and the United Kingdom. "Our vision for the next 5 years will be focused on top-down strategic initiatives," Godbout says. "But we had to first build up the base."

An analysis for the government of published papers showed Canada clinging to the third tier, along with Italy, Australia, and Switzerland, while the United States led the way and the United Kingdom, Japan, Germany, and France were bunched in second place. The investments by Genome Canada should help it move up the ladder, says Francis Collins, director of the U.S. National Human Genome Research Institute, which has recently announced a \$32 million competition to work on the haplotype map. "Until Genome Canada, Canada did not have available the kind of funding capabilities that make it possible to be a player on the big stage," Collins says. The money has been especially useful in providing world-class facilities and equipment, adds Thomas Caskey, president of Houston's Cogene Biotech Ventures Ltd. and head of the 32-member international peer-review panel that waded through the \$1.1 billion worth of applications in the second round.

—WAYNE KONDRÓ

Wayne Kondro writes from Ottawa.

TOXICOLOGY

Fruit Bats Linked to Mystery Disease

Like many scientists who have spent time on Guam, Paul Alan Cox was intrigued by a mysterious malady that stalks the South Pacific island. Victims of the disease that the indigenous Chamorros call "lytico-bodig" may become paralyzed, develop tremors and move sluggishly, or slide into dementia. Unmasking the cause of this invariably fatal neurodegenerative disorder could offer insights into major killers such as Parkinson's and Alzheimer's. But lytico-bodig is dying out—and threatening to take its secrets to the grave. "I felt we were missing a chance to solve an enigma," says Cox, an ethnobotanist who runs the National Tropical Botanical Garden in Kalaheo, Hawaii. Now, he has fashioned a provocative hypothesis around a pair of remarkable coincidences.

In the 26 March issue of *Neurology*, Cox and neurologist Oliver Sacks correlate a sharp rise in flying fox consumption among the Chamorros after World War II with a presumed crest in the disease. They also found that much of the decline in lytico-bodig happened as flying foxes were hunted nearly to

oblivion. Cox and Sacks, of the Albert Einstein College of Medicine in New York City, speculate that Guam's flying foxes may be biological weapons with wings, chock-full of neurotoxins accumulated in their tissues from a favorite food: cycad seeds.

The perplexing Guam disorder first intrigued scientists in the early 1950s, when U.S. investigators reported that the Chamorro population was afflicted with a form of amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease, at a rate roughly 100 times the global average. Some patients displayed the tremors and rigidity of parkinsonism often coupled with an Alzheimer-like dementia—a unique malady called parkinsonism-dementia complex (PDC). Eventually, researchers concluded that the disparate symptoms were all part of the



Recipe for disaster? Guam's flying foxes, like this one prepared in coconut cream for a traditional Chamorro feast, may be laced with cycad neurotoxins.

same disease, lytico-bodig. The U.S. National Institutes of Health set up a center on Guam in 1956 to search for a cause.

Nearly a half-century later, the culprit remains elusive, with suspects ranging from faulty genes to mineral deficiencies and parasites to neurotoxins. Only a handful of Guamanians born after 1960 are known to have developed the disease, and according to neurologist John Steele of the University of Guam, the principal manifestation now is of dementia in women late in life.

Cycad seeds have long been among the suspects. In the traditional Chamorro diet, the seeds of *Cycas rumphii* Miquel, a tree native to Guam, are ground into flour for a kind of tortilla. The Chamorros know that the seeds are toxic and rinse the flour several times to remove the poison. In the lean years after World War II, however, cycad tortillas were a staple of the Chamorro diet, and researchers have speculated that the large quantities ingested, coupled with incomplete detoxification of the flour, might have delivered enough cycad neurotoxin to trigger ALS-PDC. But lab animals fed the most

likely cycad neurotoxin, cycasin, fail to develop an illness resembling ALS-PDC.

"I was puzzled like everybody else," says Cox, "but thought there might be something that ethnobotany could bring to the table." He learned that the Chamorros relish the meat of the flying fox, a kind of fruit bat that on Guam subsists largely on cycad seeds. Cox noted that after World War II, hunting with firearms largely replaced the traditional technique of snaring the animals in thorny vines. The shooting coincided with an apparent sharp increase in ALS-PDC. The hunting took a heavy toll: One of Guam's two species of flying foxes had vanished by the mid-1970s, and the other had dwindled to fewer than 100 individuals. As the bats grew scarce, so did cases of the disease. Last year Cox met Sacks in New

York and sketched out his scenario. "My first thought was that it was charming, ingenious—and unlikely," says Sacks. But Sacks eventually agreed that at least part of the fatal disease's decline could be tied to the demise of a furry flying alembic for neurotoxins.

Some veteran ALS-PDC researchers, however, view the hypothesis as speculation built on a shaky foundation. "If we *knew* that cycad was the cause of the disease, the paper would be enticing," says Ralph Garruto, a biomedical anthropologist at the State University of New

York, Binghamton. Peter Spencer, a neurotoxicologist at the Oregon Health and Science University in Portland, argues that if cycasin was indeed the culprit, the bat theory won't fly: The toxin is soluble in water and thus would not have built up in flying fox tissue. And preliminary inquiries by researchers on Guam suggest that some ALS-PDC patients may never have consumed flying fox.

Sacks says that the flying fox hypothesis was not conceived as an "exclusive cause" for ALS-PDC. He points to unpublished data on a fat-soluble neurotoxin in cycad that may be a candidate for biomagnification. If that were to pan out, "a 1-pound bat is as good as half a ton of seeds," he says.

Cox's group has launched a feeding trial with a common species of flying fox in American Samoa. "We'll see what does bioaccumulate," he says, and compare the toxicological profile to decades-old archival tissue from flying foxes taken on Guam. Whatever they find, notes Spencer, "it's essential that work continue on this tremendously important disease." Time is clearly running out.

—RICHARD STONE