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CONSIDER THE MONSTER

The Greatest Hope for Diabetes Is the Gila Monster—and It's About to Go Extinct

Its spit contains enzymes that treat diabetes—but the lizard could be on its way to extinction.

CARRIE ARNOLD 04.07.16 10:00 PM ET

Medical advances can come from the strangest places. The Sonoran Desert of Arizona and New Mexico is a hostile place to call home, but the Gila monster (*Heloderma suspectumare*) doesn't seem to mind the lack of rain and scorching heat.

North America's only venomous lizard, the Gila monster spends more than 95 percent of its time in underground burrows, emerging only to find something to eat. Its venom creates a sensation like burning lava on the bite, according to the unlucky individuals who have been bitten, although no deaths have been verified. Scientists studying Gila monster venom initially wanted to understand how the proteins in the saliva create such excruciating pain, but a chance discovery that one of these enzymes could potentially help treat diabetes changed everything.

The initial discovery was made nearly 30 years ago, but not much more has been learned about the Gila monster or its genome since that time. On March 31, Arizona State University computational biologist Melissa Wilson Sayres began a crowdfunding campaign on Experiment.com to sequence the Gila monster genome.

“We’re using a protein as a medication, but we know nothing about its genetics. People are typically afraid of this lizard, but it’s saving a huge number of people,” she said.

Sayres studies the evolution of sex chromosomes in mammals, and she expected to keep her focus on the soft and furry when she first came to Arizona. But seeing Gila monsters in and around her house sparked her interest in one of the world’s two only species of venomous lizards. She discovered that Gila monsters don’t actually use venom to kill their prey, which is largely small rodents and eggs.

“You don’t really need to immobilize an egg before you eat it,” Sayres said.

Her casual investigation into Gila monsters led Sayres to their medical significance. That story began with another curious scientist, endocrinologist John Eng of the Bronx VA Hospital. Eng was working to find new hormones in different animal species. As an endocrinologist, Eng was especially interested in hormones that might potentially be useful to treat diabetes. After reading an article that some venom from snakes and lizards, including the Gila monster, could trigger inflammation in the pancreas, Eng decided to investigate Gila monster venom more closely.

In 1992, Eng identified the two proteins he had isolated from the venom. One of them, named exendin-4, was strikingly similar to a human protein called glucagon like peptide-1 (GLP-1). Whereas insulin tells cells to take in and use glucose in the blood, thus lowering blood sugar, glucagon has the opposite effect, telling the body to release glucose into the blood to raise sugar levels. Although insulin is most notably affected in diabetes, glucagon is also misregulated, says biochemist Daniel Drucker, a researcher at Lunenfeld-Tanenbaum Research Institute in Toronto.

“This made it an attractive target for diabetes therapy,” Drucker said.

Drucker had been following Eng’s research, and he began working on the protein, too. Scientists discovered that exendin-4 was 52 percent identical to human GLP-1. This finding was important because the body rapidly degraded human GLP-1. To be effective, a diabetic would have to inject it hourly. Exendin-4, however, was much more stable, and only needed to be injected daily. Eng filed a patent on his work and, after several years of research, found a small biotech startup called Amylin Pharmaceuticals to begin the work of turning this into a drug for diabetes.

In April 2005, the FDA approved exenatide (brand name Byetta), the synthetic form exendin-4, for use in treating diabetes. Exenatide improves the secretion of insulin by the pancreas, reduces glucagon levels that increase blood sugar levels, and slows the emptying of the stomach. In the past few years, Drucker has been at

work on creating other drugs related to glucagon. One of the biggest hurdles in pharmaceutical research is finding molecules that are bioactive. In animals like the Gila monster, Drucker says, the process of natural selection has already taken care of this aspect of R&D.

“We always think that we’re so bright. But of all the people working on this problem, the lizard won the race. It’s a humbling lesson,” Drucker said.

Gila monster proteins are only one of many animal-derived medications that many patients rely on, says internist Matthew Butteri at the University of California, Irvine. Whether it’s leech spit to help break up blood clots or osteoarthritis drugs isolated from rooster combs, these medications are integral to medicine. “Knowing about these proteins and genomes is a crucial step to finding new medications that work better and have fewer side effects,” Butteri said.

It’s entirely likely that the Gila monster contains other secrets, too. However, as the population in the American Southwest has increased, humans have been increasingly moving into the areas that Gila monsters call home. Once they create a burrow for themselves, they stay where they are for the rest of their lives. Forcibly relocating them to a less populated area is nearly always deadly. This has caused Gila monster numbers to tumble in recent years. If action is not taken soon, Sayres says, the Gila monster could be on its way to extinction.

Because Gila monsters are so secretive and spend so much of their time in their burrows, ecologists have had difficulty estimating precisely how many Gila monsters there are and how genetically diverse they are. This diversity is a way of measuring the health of the population; more diversity means more of a chance that Gila monsters will survive threats from humans. Sequencing the Gila monster genome is a way to estimate this diversity.

Sayres’s crowdfunding project seeks to raise $8,665 to sequence the Gila monster genome to discover more of its secrets, as well as the more practical purpose of promoting conservation and potential medical discovery. Since government funding agencies have moved away from funding projects like this, Sayres had no other choice than to try to find alternate funding. To promote her idea and to increase engagement, Sayres created a Gila monster Twitter account (@gilamonsterasu) filled with “science and snark.”

Although Sayres may have started her career with the relatively cute and cuddly mammals, her time in Arizona has turned her into a Gila monster aficionado.

“I never anticipated falling in love with a monster,” she said.