The Heart of a Snake

AN UNUSUAL MODEL ORGANISM IS OFFERING INSIGHT INTO CARDIAC PHYSIOLOGY—AND ATTRACTING STUDENTS TO RESEARCH.

YOU WANT TO STUDY EXTREME BIOLOGY? CHECK OUT THE PYTHON. These snakes can go a full year without food, and, once they do score a meal, their heart and liver nearly double in size. HHMI professor Leslie Leinwand's animal model of choice has turned out to be a great way to lure upper class students into hands-on biology.

Because python organs undergo such a dramatic response to feeding, they make an ideal study organism for Leinwand, who is interested in understanding how the genetic landscape of the mammalian heart shifts during feeding, exercise, pregnancy, and disease.

Leinwand, at the University of Colorado, Boulder, had been studying heart biology in mammals, including humans, for 15 years when her research took an unexpected turn. In 2006, she came across an article by reptile physiologist Jared Diamond exhorting researchers to think beyond typical model organisms and study animals with more "extreme" physiology.

Diamond was studying Burmese pythons, which can survive in the wild through these year-long fasts. Their heart and liver balloon after a long-awaited meal; then, within a few days, the organs revert to fasting size. Leinwand was intrigued that pythons thrive under physiological conditions that would be toxic to humans.

"Not only are they not sick [during fasting], they don't even lose muscle by virtue of not taking in nutrition," Leinwand says. "I read this article and said to myself, 'this is the coolest thing. I'm going to work on this.'"

So four years ago, Leinwand placed an order for Burmese pythons. Soon, a gaggle of baby pythons arrived, writhing and tangled inside a pillowcase and packed in a Styrofoam box. "People in my lab thought I had lost my mind," Leinwand remembers.

But she had a hunch her undergrads would think it was as cool as she did. With an HHMI grant, Leinwand developed a course that included a lecture program—"From Bench to Bedside: The Role of Science in Medicine"—and a lab-based class called the "Python Project." The course gives students a chance to learn fundamental molecular biology techniques and make discoveries about python biology.

Brett Ryder

Because of the novelty of working with snakes, and the fact that almost nothing is known about the genetics and molecular biology of pythons, she thought it would create an ideal learning opportunity.

The snakes are housed in a balmy room in the basement of the psychology department. Leinwand's laboratory assistant, Chris Wall, reaches into one of the bins with a gloved hand and deftly retrieves a dappled chocolate brown and tan Burmese python and drops it onto a scale. This 210-gram snake is nowhere near as intimidating as the 20-foot-long, 200-pound specimens that grow in the wild. Burmese pythons are really quite docile, Wall explains, though they can be testy when hungry.

Back in the classroom laboratory, 16 students look on as Wall makes a smooth incision along the length of the euthanized snake's glossy, muscular underbelly, explaining that snake organs are quite similar to humans', only greatly elongated. The young snake hasn't eaten in a month, so the tissues the class collects today will yield genetic information about its fasting condition. "So, pythons have no venom sac?" one student asks. "Nope, they just kill by constriction," says Wall. "They're actually really strong, and you'll see that the entire body, outside of the internal cavity here, is solid muscle."

Wall took Leinwand's course in the spring of 2008 and joined her research group immediately afterward. He has been accepted into a Ph.D. program in biomedical sciences at the University of California, San Diego, and says that Leinwand's course cemented his interest in becoming a researcher.

This semester, the students in Leinwand's lab are analyzing gene expression in a set of python genes that control liver proliferation. They huddle in small groups around their lab benches, painstakingly inspecting agarose gels containing amplified DNA samples from polymerase chain reactions they performed earlier that week. The gels separate DNA fragments by size, allowing the students to compare their amplified product against a standard of known size and identity. Next they will work with RNA derived directly from the python's liver tissue.

Several groups exclaim that they have successfully obtained the DNA product they were after. Kaisa Wallace-Moyer, a junior majoring in chemical and biological engineering, says she enjoys the ownership that comes with running experiments that don't have a predictable outcome. "It's just really cool knowing I get to come in here and do my own experiment," she says.

Senior Ashley Crary agrees that the hands-on experience is critical to learning the techniques. "It's scary but also exciting that we're actually practicing what we say we want to grow up and do."

Leinwand compares the python's dramatic heart enlargement after a meal to the beneficial heart enlargement that occurs in highly trained athletes. "If we can understand how the python does this over and over again throughout its life, it could lead to therapeutics that could promote improved cardiovascular health," she says.

She hopes the students' work will help paint a complete picture of the expression patterns of these python genes during the extreme metabolic shifts before and after feeding. But it's not just the experimental results that Leinwand is after. "My main goal is not the outcomes from the students' experiments," she says. "If they learn to be excited about research and to think scientifically, that would be a success. If great results are a by-product, all the better." ■

–AMANDA MASCARELLI

-Ramos: Mark Harmel