Medical Xpress

Study of pythons could lead to new therapies for heart disease

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A ball python. Credit: Yuxiao Tan/CU Boulder

In the first 24 hours after a python devours its massive prey, its heart grows 25%, its cardiac tissue softens dramatically, and the organ squeezes harder and harder to more than double its pulse. Meanwhile, a vast collection of specialized genes kicks into action to help boost the snake's metabolism fortyfold. Two weeks later, after its feast has been digested, all systems return to normal—its heart remaining just slightly larger, and even stronger, than before.

This extraordinary process, described by CU Boulder researchers this week in the journal *PNAS*, could ultimately inspire novel treatments for a common human heart condition called cardiac fibrosis, in which heart tissue stiffens, as well as a host of other modern-day ailments that the monstrous snakes seem to miraculously resist.

"Pythons can go months or even a year in the wild without eating and then consume something greater than their own body mass, yet nothing bad happens to them," said senior author Leslie Leinwand, professor of molecular, cellular and developmental biology at CU Boulder and chief scientific officer of the BioFrontiers Institute. "We believe they possess mechanisms that protect their hearts from things that would be harmful to humans. This study goes a long way toward mapping out what those are."

Leinwand first started studying pythons nearly two decades ago, and her lab remains one of the few in the world looking to the constricting, non-venomous reptiles for clues to improve human health.

As much as 20 feet long, depending on the species, pythons are typically found in resource-scarce regions of Africa, South Asia and Australia. They fast for extended periods, but when they do have the opportunity to eat, they can swallow a deer whole.

"Most people who use animal models to study disease and health typically focus on rats and mice, but there is a lot to learn from animals like pythons that have evolved ways to survive in extreme environments," said Leinwand.

There are two kinds of heart growth in humans, explains Leinwand: Healthy, such as the kind that comes with chronic endurance exercise, and unhealthy, the kind that comes with disease.

Pythons, much like elite athletes, excel at healthy heart growth.

Her previous work has shown that over the course of about a week to 10 days after a meal, python hearts get much bigger, their heart rate doubles, and their bloodstream turns milky white with circulating fats, which surprisingly nourish rather than harm their heart tissue.

The new study set out to explore how this all happens.

Researchers fed pythons who had fasted for 28 days a meal of 25% of their body weight and compared them to snakes who had not been fed.

They discovered that as the well-fed snakes' hearts grew, specialized bundles of cardiac muscle called myofibrils— that help the heart expand and contract—radically softened, and contracted with roughly 50% greater force. Meanwhile, those same snakes had "profound epigenetic differences," differences in which genes were turned on or off, than the fasting snakes.

More research is necessary to identify precisely which genes and metabolites are at play and what they do, but the study suggests that some may nudge the python heart to burn fat instead of sugar for fuel. Notably, diseased hearts struggle to do this.

Stiff or fibrotic tissue drives disease in other organs beside the heart, including lungs and livers, so there could be applications there, too.

"We found that the python heart is basically able to radically remodel itself, becoming much less stiff and much more energy-efficient in just 24 hours," said Leinwand. "If we can map out how the python does this and harness it to use therapeutically in people, it would be extraordinary."

More information: Leinwand, Leslie A., Postprandial cardiac hypertrophy is sustained by mechanics, epigenetic, and metabolic reprogramming in pythons, *Proceedings of the National Academy of Sciences* (2024). DOI: 10.1073/pnas.2322726121. doi.org/10.1073/pnas.2322726121

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