Secrets to 'extreme adaptation' found in Burmese python genome

December 2 2013

Burmese python, or Python molurus bivittatus. Credit: Dr. Stephen Secor, University of Alabama

The Burmese python's ability to ramp up its metabolism and enlarge its organs to swallow and digest prey whole can be traced to unusually rapid evolution and specialized adaptations of its genes and the way they work, an international team of biologists says in a new paper.

Lead author Todd Castoe, an assistant professor of biology at The University of Texas at Arlington College of Science, and 38 co-authors from four countries sequenced and analyzed the genome of the Burmese python, or *Python molurus bivittatus*. Their work is scheduled for publication this week (Dec. 2) by the *Proceedings of the National Academy of Sciences* along with a companion paper on the sequencing and analysis of the king cobra (*Ophiophagus hannah*). The papers represent the first complete and annotated snake genomes.

Because snakes contain many of the same genes as other vertebrates, studying how these genes have evolved to produce such extreme and unique characteristics in snakes can eventually help explain how these genes function, including how they enable extreme feats of organ remodeling. Such knowledge may eventually be used to treat human diseases.

"One of the fundamental questions of evolutionary biology is how vertebrates with all the same genes display such vastly different characteristics. The Burmese python is a great way to study that because it is so extreme," Castoe, who began working on the python project as a postdoctoral fellow at the University of Colorado School of Medicine in the laboratory of associate professor and paper corresponding author David D. Pollock.

Castoe said: "We'd like to know how the snake uses genes we all have to do things that no other vertebrates can do."

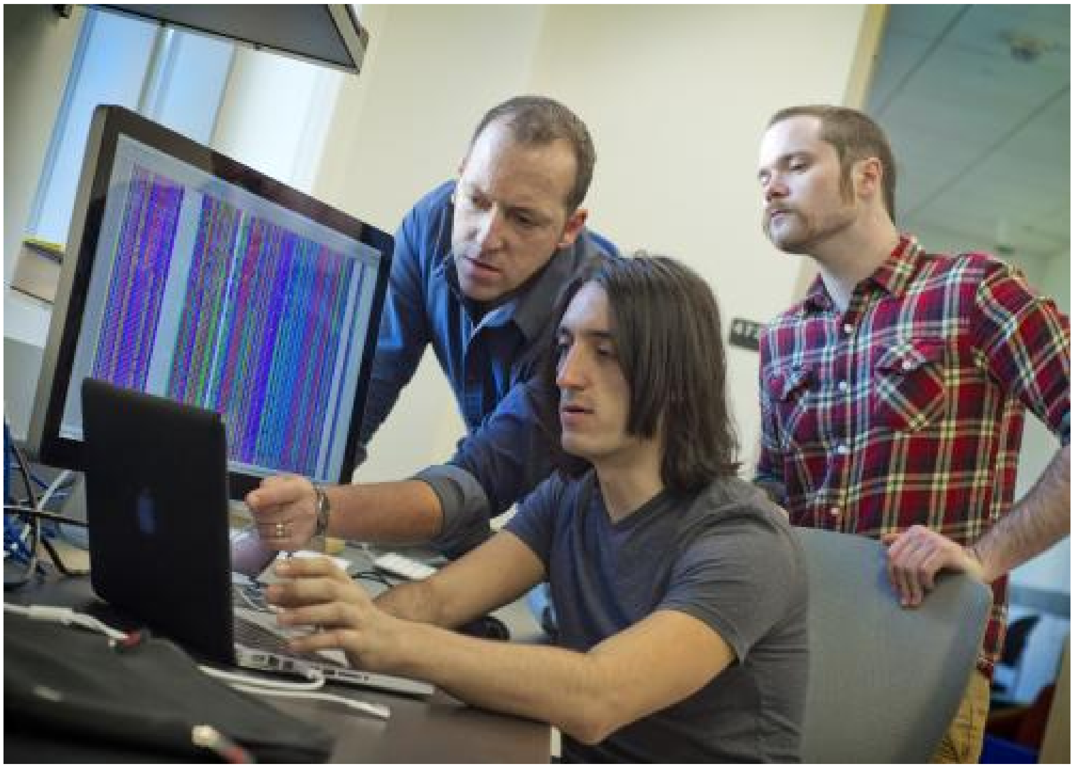
The new python study calls into question previous theories that major obvious physical differences among species are caused primarily by changes in gene expression. Instead, it contends that protein adaptation, gene expression and changes in the structure of the organization of the genome itself are all at work together in determining the unusual characteristics that define snakes, and possibly other vertebrates.

Pollock said the python and king cobra studies represent a significant addition to the field of "comparative systems genomics – the evolutionary analysis of multiple vertebrate genomes to understand how entire systems of interacting genes can evolve from the molecules on up."

He said: "I believe that such studies are going to be fundamental to our ability to understand what the genes in the human genome do, their functional mechanisms, and how and why they came to be structured the way they are."

The Burmese python's phenotype, or physical characteristics, represents one of the most extreme examples of evolutionary adaptation, the authors said. Like all snakes, its evolutionary origin included reduction in function of one lung and the elongation of its mid-section, skeleton and organs. It also has an extraordinary ability for what researchers call "physiological remodeling."

Physiological remodeling refers to the process by which pythons are able to digest meals much larger than their size, such as chickens or piglets, by ramping up their metabolism and increasing the mass of their heart, liver, small intestine and kidneys 35 percent to 150 percent in only 24 to 48 hours. As the digestion is completed, the organs return to their original size within a matter of days. The authors suggest that understanding how snakes accomplish these tremendous feats could hold vital clues for the development of treatments for many different types of human diseases.



Dr. Todd Castoe, of the University of Texas at Arlington, and graduate students Jacobo Reyes-Velasco and Drew Schield are co-authors on a new paper detailing the genome of the Burmese python. Credit: UT Arlington

"The Burmese python has an amazing physiology. With its genome in hand, we can now explore the many untapped molecular mechanisms it uses to dramatically increase metabolic rate, to shut down acid production, to improve intestinal function, and to rapidly increase the size of its heart, intestine, pancreas, liver, and kidneys," said Stephen Secor, associate professor of biological sciences at the University of Alabama and a co-author on the paper. 'The benefits of these discoveries transcends to the treatment of metabolic diseases, ulcers, intestinal malabsorption, Crohn's disease, cardiac hypertrophy and the loss of organ performance."

To complete their work, the research team aligned 7,442 genes from the python and cobra with genes sequences available in the Ensembl Genome Browser from other amphibians, reptile, bird and mammals. They used a statistical method called "branch site codon modeling" to look for genes that had been positively selected (or evolutionarily changed due to natural selection) in the python, the cobra, and early in snake evolution in the common ancestor of these two snakes. They found changes in hundreds of genes. They believe the results demonstrate that natural selection-driven changes in many genes that encode proteins contributed substantially to the unique characteristics of snakes.

Analyses showed a remarkable correspondence between the function of the selected genes, and the many functionally unique aspects of snake biology – such as their unique metabolism, spine and skull shape and cell cycle regulation, Castoe said. Many of the altered genes the team observed also have prominent medical significance. For example, the python genome showed some changes to the gene GAB1, which other research suggests plays a role in breast cancer, melanomas and childhood leukemia.

In addition to changes to individual genes and their expression, researchers also found that the extreme characteristics in snakes could also be linked to duplications or losses in multigene families. Some of those include ancient loss and more recent re-evolution of high resolution vision, and their ability to detect chemical cues from the environment. Researchers also observed that, while most assume that reptile genes and genomes change at a very slow rate, snake genomes evolve at one of the fastest rates of any vertebrate.

More information: "The Burmese python genome reveals the molecular basis for extreme adaptation in snakes," by Todd A. Castoe et al. www.pnas.org/cgi/doi/10.1073/pnas.1314475110

"The king cobra genome reveals dynamic gene evolution and adaptation in the snake venom system," by Freek J. Vonk et al. www.pnas.org/cgi/doi/10.1073/pnas.1314702110

Provided by University of Texas at Arlington