

# Exploration of toxic Tiger Rattlesnake venom advances use of genetic science techniques

January 20 2021

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Mark Margres photographs an Eastern Diamondback Rattlesnake at Caladesi Island, Florida. Credit: University of South Florida

The Tiger Rattlesnake possesses the simplest, yet most toxic venom of any rattlesnake species, and now new research from a team lead by a University of South Florida biologist can explain the genetics behind the

predator's fearsome bite.

Published in the new edition of *Proceedings of the National Academy of Sciences*, USF Department of Integrative Biology Assistant Professor Mark Margres and colleagues across the southeastern United States have sequenced the genome of the Tiger Rattlesnake to understand the genotype of the venom trait. Despite the simplicity of the Tiger Rattlesnake's venom, Margres says it is roughly 40 times more toxic than the venom of the Eastern Diamondback Rattlesnakes here in Florida.

Their work is the most complete characterization of the venom gene-regulatory network to date and its identification of key mechanisms in producing the particularly toxic venom will help scientists explain a wide array of genetic questions.

"Simple genotypes can produce complex traits," Margres said. "Here, we have shown the opposite is also true—a complex genotype can produce simple traits."

Margres collaborated with colleagues at Clemson University, Florida State University and the University of South Alabama, in the project, which sought to explain whether trait differences are derived from differences in the number of [genes](#), their sequence or how they are regulated. Their work is only the second time a [rattlesnake](#) genome has been decoded.

An organism's genotype is the set of genes it carries, and its phenotype is all of its observable characteristics, which can be influenced by its genes, the environment in which it lives, and other factors. Evolutionary biologists work to understand how genes influence the variation in phenotype among otherwise similar organisms. In this case, they looked at why different species of rattlesnakes differ in venom composition and toxicity.

Tiger Rattlesnakes are native to the Sonoran Desert of southern Arizona and northern Mexico where the relatively small pit viper preys on lizards and rodents. While some species of rattlesnakes have complex venoms that are the result of scores of genes, Margres said the Tiger Rattlesnake's venom is quite simple—as few as 15 of its 51 toxic-producing genes actively drive the production of proteins and peptides that attacks its prey's nervous system, forces blood pressure to drop and causes blood clotting to cease.

The team found that the number of venom genes greatly exceeds the number of proteins produced in the simple phenotype, indicating a complex process was at the heart of the toxic venom and the Tiger Rattlesnakes even has toxic genes to spare.

"Only about half of the venom genes in the genotype were expressed," Margres said. "To me, the interesting part is why are the non-expressed genes still present? These genes can make functional toxins, they just don't. That needs to be explored further."



Tiger Rattlesnake used in the study was found in the Santa Rita Mountains in Arizona. Credit: University of South Florida

Beyond understanding this one species of venomous snake, Margres said the research will help advance genetic science by showing the techniques more commonly used on [genetic research](#) on mice and fruit flies, organisms that are often used in genetic studies, can also work when applied to less-studied organisms like snakes. The team used genetic sequencing techniques that are common in human genetics research and in doing so, opened the door for scientists to understand the genotype-phenotype relationship in many other organisms.

Another potential side benefit of the research, Margres said, is that

snake venom is used in medicine for humans to combat stroke and high blood pressure. The more scientists understand about [venom](#), the better medical engineering can apply that knowledge in drug discovery and development.

**More information:** Mark J. Margres et al, The Tiger Rattlesnake genome reveals a complex genotype underlying a simple venom phenotype, *Proceedings of the National Academy of Sciences* (2021). [DOI: 10.1073/pnas.2014634118](https://doi.org/10.1073/pnas.2014634118)

Provided by University of South Florida

Citation: Exploration of toxic Tiger Rattlesnake venom advances use of genetic science techniques (2021, January 20) retrieved 5 May 2024 from <https://phys.org/news/2021-01-exploration-toxic-tiger-rattlesnake-venom.html>

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