Gator blood contains naturally strong germ fighters, new research finds

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George Mason University professor Barney Bishop poses with Fluffy, an American alligator. Credit: St. Augustine Alligator Farm Zoological Park

Sophisticated germ fighters found in alligator blood may help future soldiers in the field fend off infection, according to new research by George Mason University.

The study, published Feb. 11 in the scientific journal *PLOS One*, is the result of a fundamental research project supported by the Defense Threat Reduction Agency (DTRA) to find bacterial infection-defeating compounds in the blood of the crocodilian family of reptiles, which includes American alligators.

The project is about to start its fourth year and has received $6 million in funding to date from DTRA. If fully funded over five years, the project will be worth $7.57 million.

Alligators live in bacteria-filled environments and dine on carrion. Yet this ancient reptile rarely falls ill.

"If you look at nature, sometimes we can find pre-selected molecules to study," says study co-author Monique van Hoek. "I was surprised to find peptides that were as effective as they are in fighting bacteria. I was really impressed."

Discoveries made by George Mason's 17-member, multidisciplinary research team could eventually find their way to the battlefield to protect warfighters from wound infections and potential exposure to biothreat agents. Researchers believe this work could benefit civilians too.

"We hope that these could be the basis to develop new treatments," says van Hoek, a professor in the School of Systems Biology and the National Center for Biodefense and Infectious Diseases at Mason.

Exploiting innate immunity

Van Hoek and lead co-authors Barney Bishop and Joel Schnur from the College of Science suspected the germ-fighting ability could be in the form of antimicrobial peptides. These very small proteins are part of the innate immunity of alligators and even humans; all higher organisms

make antimicrobial peptides.

"It's that part of your immune system that keeps you alive in the two or three weeks before you can make antibodies to a bacterial infection," van Hoek says. "It's part of your generalized immune response to the world."

Peptides are more general in their activity than antibodies, which are made to fight infections by specific bacteria or viruses.

"Innate immunity may work less well than antibodies, but it works well enough," van Hoek adds. "The reason why we're so interested in them: they are part of nature's way of dealing with the onslaught of bacteria and viruses that we face every day. Every breath that you take, every thing that you eat, you're constantly exposed to bacteria and your body needs to fend them off in some way."

Alligator blood samples were provided by Kent Vliet of the University of Florida and the St. Augustine Alligator Farm Zoological Park in St. Augustine, Fla., which has a wide variety of reptiles, including all 23 species of crocodilians.

Bishop says he was surprised at the sophistication and diversity of the alligator's germ-fighting peptides. These reptiles have evolved with a formidable defense against bacterial infections. The Mason team took an innovative approach in its study of the alligator blood samples. Bishop developed custom-made nanoparticles to preferentially capture the peptides out of the very complex mixture of proteins and peptides in alligator plasma.

This process revealed an unexpected result—the identified potent germ-fighting peptides were only fragments of larger "parent" proteins, says Bishop, who's also a professor in the Department of Chemistry and

Biochemistry.

The custom-made particles used in this project significantly shortened the number of steps required to capture and identify peptides that were present in alligator blood plasma.

Mentoring the next generation of researchers

Mason students also have played a key role in the project. Graduate student Stephanie Barksdale says she stayed at Mason after earning her bachelor's degree so she could work on this research with van Hoek.

Melanie Juba worked on the alligator study for her doctorate and postdoctorate work. The recent doctoral graduate now works for mass spectrometry firm AB Sciex in Northern California. Collaborating with other researchers and learning advanced lab techniques honed her skills, she says.

"Working on the bioprospecting project on the American alligator in the Bishop lab at George Mason gave me all the tools I needed to land a great job," says Juba, who's from Manassas, Va.

Doctoral student Megan Devine says she wants to continue with biomedical research after earning her degree next year. Mason's collaborative, multidisciplinary approach helped set her on a career path, the Springfield, Ill., native says.

"Through this collaboration, I have been given the chance to largely direct my own research on a daily basis, which is a skill that will allow me to continue to take leadership roles in future research projects," Devine says.

The Mason team has other reptiles to tackle. As part of the DTRA grant

called "Translational Peptide for Personal Protection," Mason researchers also will study Siamese crocodiles, Nile crocodiles and gharials.

And they've learned a thing or two along the way about these ancient reptiles.

"You stay away from the business end," Bishop jokes.

More information: The paper, Bioprospecting the American Alligator Host Defense Peptidome, is on the *PLOS One* website.

Provided by George Mason University