A Conversation with Claire Komives

The chemical engineer wants to develop a low-cost snake antivenom based on an opossum peptide.

When Claire Komives, a chemical engineer at San Jose State University, began planning for a sabbatical in 2014, she had no clue what research project to pursue. But she knew she wanted to do it in India, a country that she fell in love with while completing a fellowship after earning her Ph.D. During her search for ideas, Komives stumbled on a news story about a protein in opossums that makes the animals immune to snakebites. A Texas-based researcher, Binie V. Lipps, had traced this immunity specifically to peptides containing the protein's first 10 or so amino acids, patenting her discovery in 1996.

During her sabbatical at the Indian Institute of Technology (IIT) Delhi, Komives picked up where Lipps left off. She developed a low-cost method for synthesizing the peptides. She engineered Escherichia coli to produce peptide repeats consisting of the first 11 amino acids of the opossum protein and used a protease to snip the product into individual peptides. In tests, the peptide helped protect mice from rattlesnake venom. More recent, unpublished research has shown that it also completely protects mice from the venom of two deadly species of snakes in Africa. Komives and her colleagues estimate that it would cost only about 10 cents per dose to make this antivenom.

Melissa Pandika spoke to Komives about her technology, as well as what it could mean for parts of the world where snakebite deaths are especially common.

What is snake venom made of?
Venom is a cocktail of proteins with different functions. Most of them are enzymes, like metalloproteases, which basically chop proteins indiscriminately in the body, causing hemorrhage. There are also inhibitors of other proteins. These are found primarily in neurotoxic venoms, which paralyze the victim. Hemotoxic venoms cause blood thinning at the site of the wound and coagulation in the veins, while cytotoxic venoms cause swelling, tissue necrosis, and a lot of pain, as well as organ damage in some victims.

What spurred your project to develop a snake antivenom?
Before I left for India, I had bought the peptide Lipps had patented and sent it to collaborators at the National Centre for Biological Sciences in Bangalore. I was able to produce the peptide there, and it helped me to realize the potential of this approach.

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Natural Toxins Research Center at Texas A&M University, Kingsville. There, eight mice that were given a lethal dose of rattlesnake venom died overnight, but another eight mice that got venom along with the peptide all survived for weeks. In fact, we’ve done the same experiment with other snakes’ venom, and the treated mice live healthy, normal lives.

The next step was to express the peptide strain in E. coli. At San Jose State and IIT Delhi, we first expressed the peptide chain with 23 repeats of the peptide. It kept degrading. After my sabbatical, I made a much shorter strain of the peptide chain with only eight peptide repeats, which didn’t give us that problem. It expressed at high levels in E. coli. Our process for purifying it from E. coli achieved over 99% purity.

What are the limitations of the current method for making antivenom, and how might your technology address them?

Antivenoms are mostly produced in horses by injecting them with snake venom, which makes the horses generate antibodies against that venom. These antibodies can be given to snakebite victims. The problem is, if a pharmaceutical company injected the horse with venom from a different type of snake, you won’t get the right antibodies.

So far, our peptide works on venom from different families of snakes. This could never happen with a horse-serum-based antivenom. We’re just beginning studies looking at how the peptide inhibits purified venom proteins to better understand how the antivenom works.

Also, horse serum can only be administered at the hospital. We need something people can take right when they get bitten, which would give them time to go to the hospital before the severe damage starts. That would save a lot of lives. I think our peptide can fill that need. It’s cheap and readily soluble in saline. You could administer it with an EpiPen-type injector or maybe even an inhaler.

What species of snake does your peptide protect against?

So far, we’ve shown it neutralizes up to about 1.3 times the median lethal dose (LD50, the dose needed to kill 50% of test animals) of western diamondback rattlesnake venom, and completely neutralizes up to 5 times the LD50 of Indian saw-scaled viper venom. It neutralizes up to 5 times the LD50 of venoms from the Western African carpet viper and puff adder, two major killers in sub-Saharan Africa. The standard dose for testing the efficacy of snake antivenoms is 3–6 times the LD50. The peptide also neutralizes hemorrhagic toxins in the Indian Russell’s viper venom but not the neurotoxins. We have not tested it against other snake venoms yet.

What are the next steps toward commercializing the peptide?

The first thing is to show you can neutralize not only the target venom proteins’ activity but also their lethality. You might be able to show in a dish that the peptide inhibits phospholipases, which cause cell membranes to break down, for instance, but when you put it in the body, it doesn’t inhibit myotoxic activity, which causes muscle necrosis and death.

We’ll probably test it in pets first. Each year, 100 000 cats and dogs in the U.S. get bitten by the family of snakes that includes rattlesnakes and copperheads. Even if the peptide itself is not the magic bullet, we could chemically modify it, and that could be the basis of a universal snakebite treatment.

Melissa Pandika is a freelance contributor to Chemical & Engineering News, the weekly newsmagazine of the American Chemical Society. Center Stage interviews are edited for length and clarity.