Brazilian researchers discover two novel peptides with biotechnological potential in snake venom

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The venom of the South American bushmaster (Lachesis muta) is not especially powerful, but the snake is dangerous because of the large amount of venom it injects into its victims. Credit: Sávio Stefanini Sant' Anna/Instituto Butantan

Brazilian snake and spider venoms continue to be a source of new discoveries with biotechnological potential. Two recently published studies show how this is possible even in relatively well-studied species such as the lancehead pit viper Cotiara (Bothrops cotiara) and the South American bushmaster (Lachesis muta).

"Venoms never cease to surprise us. Even with so much accumulated knowledge, fresh discoveries are possible, such as unpredictable fragments that are parts of known proteins. Despite all the available technology, a great deal remains to be studied in these toxins," said Alexandre Tashima, principal investigator for both studies.

He was referring to a novel peptide (protein fragment) identified in B. cotiara's venom and named Bc-7a. Although it is part of a protein that causes bleeding in the snake's prey, in functional terms it is closer to peptides such as those at the origin of captopril, a drug that lowers blood pressure by inhibiting the activity of angiotensin-converting enzyme (ACE).

The latest study is reported in an article published in the journal *Biochimie*.

Many ACE-inhibiting molecules already exist, but the search continues because of adverse side effects such as a dry cough, dizziness, and high blood potassium levels.

The peptide is one of 197 revealed by the study, 189 of them reported for the first time. In 2012, the group found 73 peptides in the same snake's venom. According to the authors, the difference is due to the use in the more recent study of faster and more sensitive equipment than was available a decade ago, and to the larger number of peptide sequences to be gleaned from databases now.

In previous studies, Tashima and his group had found molecules with biotechnological potential in the venom of another snake, as well as two tarantula spiders.

Bushmaster venom

A study involving bushmaster venom from L. muta, reported in an article published in *Biochemical and Biophysical Research Communications*, identified 151 peptides, of which 126 were previously unknown.

The researchers were particularly interested in a novel metalloproteinase-derived peptide called Lm-10a, a fragment of a hemorrhagic toxin that inhibits ACE and could potentially be used in a drug to treat blood pressure. Their analysis suggested that both Lm-10a from L. muta and Bc-7a from B. cotiara resulted from fragmentation processes during venom maturation in the snake's venom gland and that many more novel peptides could be obtained from the toxins.

"In this kind of analysis, the protein sequence obtained is just a snapshot. Cleavage, enzymatic degradation, and other processes generating novel peptides that aren't necessarily detected occur all the time," Tashima explained.

More research is needed to verify the real potential of the peptides they discovered. Moreover, the dynamic nature of toxin maturation points to the use by venomous snakes of various biological mechanisms to refine venom during their evolution.

"Despite advances in sequencing technology and the production of large amounts of data in recent years, much remains to be discovered about the vast universe of peptides and their biological roles. We must take advantage of our good fortune in being able to study these species, many

of which will be extinct before they've even been discovered," Tashima said.

More information: Jackson Gabriel Miyamoto et al, A novel metalloproteinase-derived cryptide from Bothrops cotiara venom inhibits angiotensin-converting enzyme activity, *Biochimie* (2023). DOI: 10.1016/j.biochi.2023.10.010

Lucas T. Ito et al, Unveiling the peptidome diversity of Lachesis muta snake venom: Discovery of novel fragments of metalloproteinase, l-amino acid oxidase, and bradykinin potentiating peptides, *Biochemical and Biophysical Research Communications* (2023). DOI: 10.1016/j.bbrc.2023.10.022

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