Exploring the toxin genes of monocled cobra through venom gland transcriptomics

June 30 2017

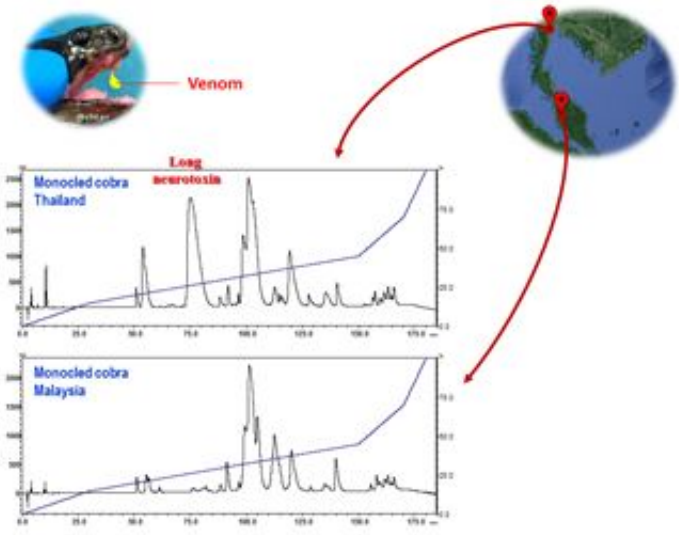
The comparative venom-gland transcriptomic study, led by researchers from the Venom & Toxin Research Laboratory (University of Malaya), provides insights into the toxin genes of monocled cobra (Naja kaouthia). Credit: Dr. Tan Choo Hock

Researchers at University of Malaya investigated the venom-gland transcriptomes of monocled cobra (Naja kaouthia) from Malaysia and Thailand. Their findings unveil a pool of novel bioactive molecules, and provide a solution to the long-standing puzzle of the geographical variability of venom from this important Asian cobra.

Venom researchers from the University of Malaya have been observing

geographical variability of the venom from monocled cobra, a medically important venomous snake in Southeast Asia. The venoms from different geographical populations of the cobra vary in their composition, toxic effect, clinical syndrome induced and even therapeutic response to antivenom. Wondering if this phenomenon is caused by the differences in the gene make-up for venom production in the same species of monocled cobras, the researchers took the challenge to investigate the toxin genes through the venom glands of the cobra.

In their quest to unravel the complex and variable nature of the venom, the latest Next-Generation Sequencing (NGS) technique was used. They found unique expression patterns of toxin-encoding genes in extremely high redundancy across the specimens. This reflects the role of gene duplication and neofunctionalization as one of the evolutionary mechanism in equipping the venom gland to be a "bioweapon warehouse", adapted for foraging, digestion and defence for the advanced venomous snakes. More than 20 toxin gene families were unveiled in both geographical specimens, among which at least 15 belong to classes of novel biomolecules not previously reported in this species.



The venom of monocled cobra from Thailand apparently has a much higher content of long neurotoxin component compared with that of the Malaysian specimens. Here the venom proteins were profiled using reverse-phase high performance liquid chromatography. Credit: Dr. Tan Choo Hock

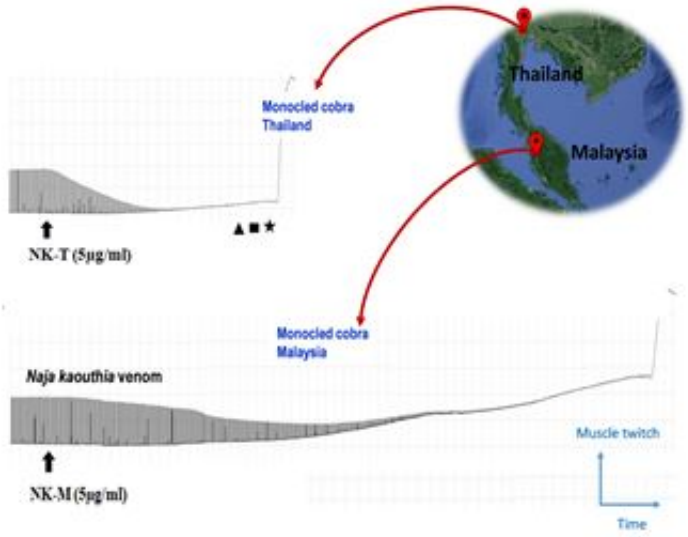
"This means, the venom gland of this unique Asian cobra holds a battery of special molecules for drug discovery – enzymes, channel blockers, receptor activators, cell apoptosis inducers and many more, thus paving our path to the development of novel analgesic, anti-cancer, nerve growth modulator, antibiotic, antiviral and so on. It's like, an unexplored "treasure chest" for health and medical advancement." The authors projected, adding: "What we now look forward to is sustainable funding and positive collaboration with local and foreign experts to take this research to a higher ground."

Comparative molecular analyses and selection study revealed that the venom toxins are genetically well conserved between the geographical specimens, whilst demonstrating distinct patterns of differential expression.

"For example, the Thai cobra transcriptome is packed with long neurotoxins, but the Malaysian specimen has a much lower content." The authors summarized, "By and large, it is the variable content of the long and short neurotoxins that accounts for the high variability of this cobra venom."

The authors suggested that the variable expression of the principal toxins is associated with gene up-regulation for selected principal toxins, enhanced transcript degradation, or lack of transcription of certain traits as in the case of pseudogenization. More importantly, the findings shed

light on the geographical variation of monocled cobra venom, and support the call for the optimization of antivenom production and snakebite management in the region.



The Thai monocled cobra venom caused a much faster neuromuscular paralysis tested on an in vitro chick nerve-muscle preparation than the Malaysian cobra venom did. Credit: Dr. Tan Choo Hock

More information: Kae Yi Tan et al. Comparative venom gland transcriptomics ofNaja kaouthia(monocled cobra) from Malaysia and Thailand: elucidating geographical venom variation and insights into sequence novelty, *PeerJ* (2017). DOI: 10.7717/peerj.3142

Provided by University of Malaya