Scorpion toxin insights may lead to a new class of insecticides

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In an evolutionary game of cat and mouse, predators have adapted a clever arsenal of new tricks to capture their ever-elusive prey.

Now, new research from Shunyi Zhu et al. appearing recently in the early online edition of *Molecular Biology and Evolution*, has identified the molecular clues driving the effectiveness of scorpion toxins.

Scorpions feast on insects through a neurotoxin, called alpha-like toxins, which are funneled through their stingers to carry out their lethal action. In the new study, the research team performed a molecular dissection of one alpha-like toxin, called MeuNaTxalpha-5 (or MT-5).

MT-5 affects both insects and mammals, and classified by their preference of one over the other. Zhu's team was interested in uncovering the molecular mechanisms behind this tuning, and in particular, the effectiveness of the toxin for insects.

A comparison of activities in insects and mammals was carried out in the study. The team generated different mutants involving single protein amino acid residues indicated as essential for the interaction with their partner receptors, called Nav channels. In their insect toxicity bioassays, a deletion mutation (19AF20) was found to impair its anti-mammalian activity, but substantially enhance its insecticidal activity. This finding could lead to the promising new candidates for insecticides, and fine-tuning these mutants to target a specific pest.

The team identified eight protein hot spots, called positively selected sites (PSSs), which are indicative of adaptive molecular evolution. The authors find evidence that an essential agent of selection for the alpha-toxins comes from the evolutionarily variability of receptor site of sodium, (or Nav) channels from the predators and prey of scorpions. The study's hypothesis is on a key external mechanism driving positive selection of the scorpion toxins and new experimental evidence supporting the opinion.

"It is noteworthy that the location of PSSs at the interface of different complex models and the evolutionary variability of their targets, in particular our perfect mapping of two hot-spot PSSs interacting with two highly variable channel sites, all support the opinion that the evolution of scorpion toxin is driven by their targets," said Zhu, the corresponding author of the study.

Next, they plan to extend their studies to two main scorpion predators, birds and lizards, as well as mammals to better understand the dynamics of toxin-channel interactions and evolution.

More information: Limei Zhu et al. Target-Driven Positive Selection at Hot Spots of Scorpion Toxins Uncovers Their Potential in Design of Insecticides, *Molecular Biology and Evolution* (2016). DOI: 10.1093/molbev/msw065

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