Molding the business end of neurotoxins

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For snakes, spiders, and other venomous creatures, the "business end," or active part, of a toxin is the area on the surface of a protein that is most likely to undergo rapid evolution in response to environmental constraints, say researchers from Ben Gurion University in Israel. Understanding these evolutionary forces can help researchers predict which part of unstudied toxins will do damage, and may also aid in the design of novel synthetic proteins with tailored pharmaceutical properties. The team will present its results at the 56th Annual Meeting of the Biophysical Society, held Feb. 25-29 in San Diego, Calif.

Scientists have long suspected that evolutionary pressures encouraging diversity could play a role in shaping how a toxin works; if such forces were in play, toxins could rapidly evolve within a single species or change quickly from species to species, supporting predators and prey in the "arms race" that keeps them in competition. Still, it was not clear whether the same rules dictate neurotoxin evolution between animals from different phyla (that is, that have very little genetically in common with each other), or whether there were different rules in play for different organisms.

Using the published gene sequences for dozens of different toxins from various species of poisonous scorpions, spiders, and snakes, the Ben Gurion researchers studied toxins that target a variety of ion channels and receptors. They performed their analysis on individual codons, areas of the genetic sequence that code for a single amino acid, which allowed the team to hypothesize about the evolutionary pathways of individual building blocks of the proteins.

In the venoms of all the species they studied, as well as among all the different toxin families, the researchers found a clear correlation between the active parts of the toxins and the parts that evolve most rapidly. In addition, they determined that the non-active surfaces of the molecules – which tend to contribute to a toxin's structural stability – experience the opposite type of evolutionary force, preventing these surfaces from changing greatly from generation to generation. This makes sense from a fitness perspective, since mutations that significantly change the structure of a toxin run a greater risk of damaging the toxin's efficacy.

"We were pleased to learn how nicely the data fit our initial hypothesis, and how broad this phenomenon is," says Noam Zilberberg, Ben Gurion University microbiologist and lead author of the study. "Our approach should help in locating novel interaction sites between as-yet unstudied toxins and their targets."

The work supports the so-called "Red Queen's hypothesis," which states that constant change is needed for organisms to maintain fitness in a competitive environment. As a next step, the team would like to refine their results by expanding the dataset to include more toxins.

More information: The presentation, "Molding the business end of neurotoxins by diversifying evolution," is at 1:45 p.m. on Sunday, Feb. 26, 2012, in the San Diego Convention Center, Hall FGH. ABSTRACT: http://tinyurl.com/7a6zrk4

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