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Scientists Unravel Evolution of Highly Toxic Box Jellyfish

Research could help lead to antivenoms and treatments

With thousands of stinging cells that can emit deadly venom from tentacles that can reach ten feet in length, the 50 or so species of box jellyfish have long been of interest to scientists and to the public. Yet little has been known about the evolution of this early branch in the animal tree of life.

In a paper published November 18 in the *Proceedings of the Royal Society*, NOAA scientists Allen Collins, Bastian Benthage and Cheryl Lewis Ames of the Northeast Fisheries Science Center's National Systematics Laboratory and colleagues from the University of Kansas, Pacific Biosciences Research Center in Hawaii and the University of Queensland in Australia have unraveled the evolutionary relationships among the various species of box jellyfish, thereby providing insight into the evolution of their toxicity.

"By determining the relationships among the different box jellyfish, some of which are capable of killing a healthy human, this study can help in the future development of antivenoms and treatments for their stings," said Collins, a specialist in Cnidaria (pronounced nidaria), the phylum of animals that includes box jellyfish. "Researchers will now be able to make more informed choices about organisms for future venom studies, and make predictions on which species are likely to be of public health concern in addition to the known culprits."

Beyond their toxicity, box jellyfish have other interesting characteristics. Some species have as many as 24 eyes, capable of sensing light and forming an image of their surroundings. Why they have complex eyes, how well they see, and what role vision plays in their mating and feeding behavior remain unknown. Their vision may have something to do with the evolution of some extremely unusual mating behaviors. Jellyfish usually mass spawn, with males and females releasing sperm and eggs into the water without any physical contact. Study co-author Cheryl Lewis Ames has documented at least one box jellyfish species, *Copula sivickisi*, that exhibits a courtship of sorts where a male and female interact one on one to mate.

Box jellies, also called sea wasps, stingers or fire jellies, live primarily in warm coastal waters around the world. They are particularly well known in Australia, the Philippines and the rest of southeast Asia, but they also occur in Hawaii and in waters off the United States Gulf and East Coasts. Their toxicity varies among species and ranges from being completely harmless to humans to causing death within minutes after a sting.

Named for their box or cube-shaped body, these animals are members of Cubozoa, the smallest class of Cnidaria, animals ranging from sea anemones and corals to Portuguese man of war and true jellyfish, all of which possess stinging capsules known as nematocysts.

Using DNA extracted from tissue samples, the researchers used a number of genetic tests and analytical techniques to trace the evolution of the various species and their toxicity and to sort out misidentified species. The three-year study looked at dozens of specimens in collections around the world.

The Australian box jellyfish (*Chironex fleckeri*), the largest box jellyfish species, is considered the most venomous marine animal and its sting can be fatal. Its close relative, *Chironex yamaguchii*, has caused deaths in Japan and the Philippines. A much smaller species, *Carukia barnesi*, is the first species known to cause Irukandji Syndrome. Symptoms include severe low back pain, nausea, headache and vomiting, and sometimes “an impending feeling of doom”, but the syndrome is usually not life-threatening. Other box jellyfish species are now known to cause the same symptoms.

“Knowing who is related to whom among the box jellyfish will be very helpful in making predictions about species that are not well known,” said Collins, who began studying the evolutionary links of box jellyfish more than a decade ago. “For example, we may not know how serious the sting is from a particular jellyfish species, but if we know its close relatives cause Irukandji Syndrome, then it is highly likely that this species also causes the syndrome. Similarly, there is an antivenom for *Chironex fleckeri*, whose closest relative is *Chironex yamaguchii*. It may be that the antivenom will work against stings from this species as well.”

The study results indicate that the venoms of box jellies may contain a novel and unique family of proteins. However, further toxicological tests and many more specimens are needed to resolve questions about venom and to develop antivenoms and treatments for box jellyfish stings.

Cnidarians are difficult to study because their relatively simple structure makes it hard to compare to other groups of organisms. Few specimens are available in natural history museums or laboratories preserved for biological and molecular study, and fossil records are rare.

Despite few specimens to study, the scientists found several patterns in the global distribution of box jellyfish species. Some live exclusively in the Atlantic, others in the Pacific, and still others are found in the Indian Ocean. A few are found in all three oceans and may live in tropical regions around the globe. Geography seems to isolate species and most don't seem to cross open ocean habitats. Ancient plate movements and the resulting sea-level changes appear to have forced some of the initial diversity among these species.

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NOAA's National Systematics Laboratory, located in the Museum of Natural History at the Smithsonian Institution, is part of the Northeast Fisheries Science Center but serves as the taxonomic research arm of NOAA's Fisheries Service as a whole. The laboratory describes and names new species, and revises existing descriptions and names based on new information, of fishes, squids, crustaceans, and corals of economic or ecological importance to the United States. Because some important species are highly migratory and many exotic species are

introduced into U.S. waters or markets, the laboratory's research is worldwide. Major products of this research are worldwide and regional taxonomic publications and identification guides.

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